NEUROSCIENCE
NEWSLETTER
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Ten years after …

… and beyond !

Welcome to the 1st Neuro-Newsletter published on the occasion of the 10th Anniversary of the Göttingen International Master/PhD/MD-PhD Program and International Max Planck Research School (IMPRS) Neurosciences.

Since its foundation in the year 2000 the Göttingen program truly has undergone significant changes and still strives to improve even further. However, the founding idea, namely to create an internationally attractive program with a research-oriented curriculum offering a 'fast track' option for qualified students to directly start a PhD project without a Master degree, is a valid and successful concept. The Neuroscience Program now provides a solid teaching platform for neuroscientists in Göttingen irrespective of their institutional affiliation. The program, thus, contributes to the (sometimes challenging yet effective and desirable) integration of university and non-university faculty in terms of PhD training. In conjunction with the services provided, especially for international scholars, the Göttingen Program has become a ‚role model' for other programs in the natural sciences in Germany. In 2005 the coordination office moved into the new building of the European Neuroscience Institute (ENI-G) which now has become its 'home base'.

The program has won several awards and has contributed to the success of research centers like the CMPB, PhD and graduate programs and various EU initiatives. Moreover, the Neuroscience Program together with its partner program in Molecular Biology provided the 'proven concept' for the foundation of the Göttingen Graduate School for Neurosciences and Molecular Biosciences funded by the Excellence Initiative since 2007. The commitment of the neuroscience faculty in conjunction with the Excellence funding allowed establishing the 'Neuroscience Teaching Labs' in the ENI, substantially extending the training opportunities available in Göttingen.

The program attracted more than 2000 applicants from over 40 countries, so far. And, despite the fact that the number of study opportunities especially in the neurosciences increased in Germany and worldwide over the last 10 years, the Göttingen program manages to attract high numbers of qualified applicants. Of those who graduated from the MSc/PhD Program Neurosciences more than 80% are holding postdoc positions at prestigious institutes including ETH, Yale, Harvard, or Stanford. The 'drop-out' rate is negligible (< 3 %), and the majority of PhD candidates publishes more than one scientific article from their PhD projects.

Erwin Neher Speaker of the Max Planck Research School, Detlev Schild Speaker of the MSc/PhD program, Sandra Drube Program Assistant, Michael Hörner Scientific Coordinator

Surely, given the worldwide increasing demand for well-trained young scholars, recruiting excellent PhD students to Göttingen will remain a challenging task. To be successful also in the future the Göttingen program has recently joined efforts with European partners in order to extend the training opportunities for MSc and PhD students (see article in this issue, page 27). We are optimistic that the Neuroscience Program will further facilitate local and EU-wide scientific cooperation and trigger the formation of interdisciplinary teaching alliances in the neurosciences for the benefit of the Göttingen Research Campus and beyond.

CONTENT

Imaging in Neuroscience

– connecting the brain with its neurons *by Henry Lütcke*

A significant challenge in neuroscience remains the integration of knowledge from diverse spatial scales, incorporating knowledge at the level of single cells, networks of neurons or even whole brain areas. It is likely that imaging techniques will contribute greatly to this goal, as they allow for visualization of neural structure and function at all levels of description.

On the largest spatial scale, functional magnetic resonance imaging (fMRI) allows for measurements of neural activity in a completely non-invasive fashion both in human volunteers as well as in animals *(1)*. Blood oxygen level dependent (BOLD) fMRI, which was pioneered in the early 1990s by several groups *(2, 3)*, benefits from good spatial resolution (see below) while at the same time allowing imaging of the whole brain near-simultaneously. Since fMRI is readily applicable to healthy human volunteers, it has been used extensively in cognitive neuroscience to infer the neural correlates of complex cognitive, emotional or even social phenomena.

My initial research, carried out at the Biomedizinische Forschungs GmbH at the Max-Planck-Institute for Biophysical Chemistry under the supervision of Prof. Jens Frahm, involved the development and use of advanced fMRI techniques for studying neural processing in the intact human brain. In this work, we focused on the human medial frontal cortex (MFC), and especially its anterior cingulate part (ACC), which plays an important role in adaptive behavioral modifications in response to changing environmental demands *(4)*. Based on EEG experiments, ACC had initially been associated with the detection of errors *(5)*, while subsequent fMRI studies argued for a more global role in monitoring of conflicting action sequences *(6)*. Importantly, however, the spatial resolution of previous experiments has been limited, so that differences at finer scales may have been missed. In fact, most standard fMRI studies at the time employed voxel sizes on the order of $3 \times 3 \times 3$ mm^3, while the technique itself allowed for acquisitions with at least an eight times smaller voxel size of $1.5 \times 1.5 \times 1.5$ mm^3. The goal of our work therefore was to use high-resolution fMRI in combination with a conflict eliciting GoNogo task *(7)* to investigate the functional anatomy of the ACC at a previously unaccomplished spatial scale. The task, which was designed to generate high proportions of errors on Nogo trials, allowed us to dissociate putative neural correlates of conflict as well as of error monitoring processes.
Functional MRI at high spatial resolution had previously been used to study early sensory processes *(8)*, benefiting

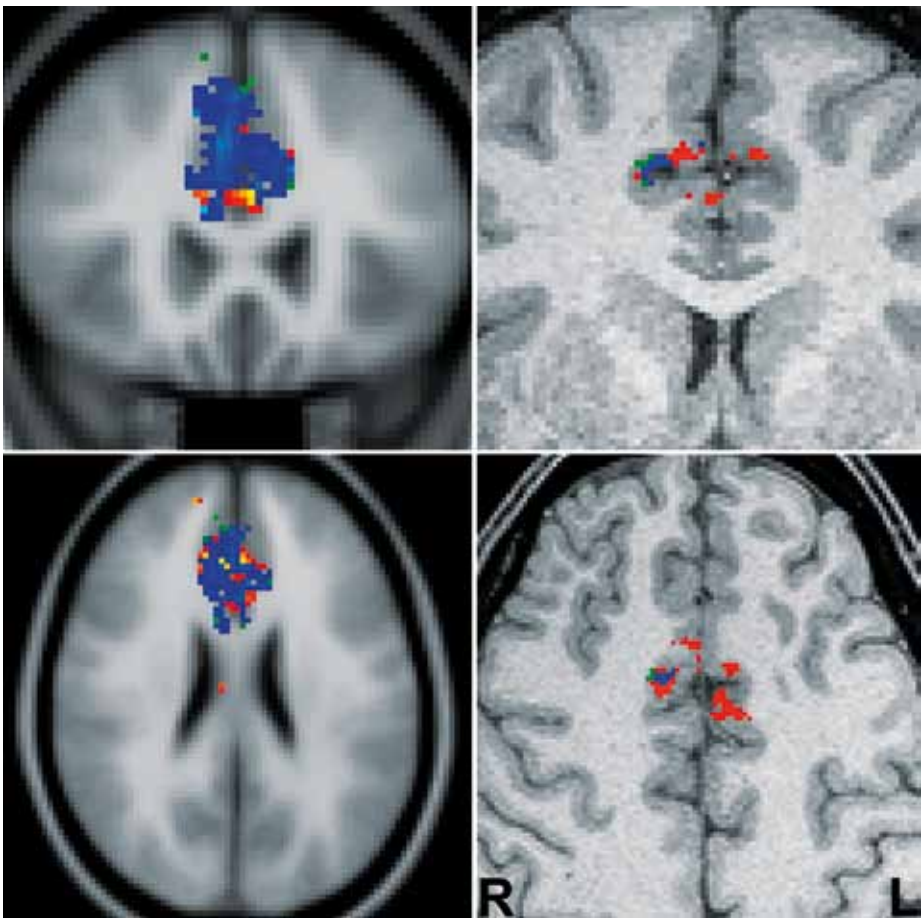

Fig. 1: While conventional fMRI (left) fails to reveal a difference in activation of ACC in response to erroneous (red) and successful (green) response inhibitions, a clear lateralization is evident at higher spatial resolution (right). Correct responses as well as errors, frequently overlapping (blue) are represented in right ACC. Left ACC, on the other hand, activates solely for erroneous responses. (R: right, L: left)

from the good functional contrast-to-noise ratio (CNR) in these areas. Cognitive neuroimaging, on the other hand, suffers from low CNR making it apparently unsuitable for high-resolution fMRI. Thus, a more general aim of our work was to investigate the feasibility of a new strategy for cognitive neuroimaging combining low and high spatial resolution.

In the experiments, participants performed multiple repetitions of the GoNo-go task while being imaged initially at standard and subsequently at high spatial resolution *(9)*. This approach allowed us to functionally define the location of ACC at standard resolution and subsequently 'zoom into' the structure to investigate its functional microanatomy. At standard resolution, both conflict and error processes elicited strong and largely overlapping responses in both hemispheres of ACC (Figure 1, left panel). High-resolution measurements, on the other hand, revealed a striking dissociation between the two cognitive components, with a bilateral distribution of error-related activations whereas neural responses to conflict processing were consistently right lateralized (Figure 1, right panel).

In our experiments, improving the spatial resolution of cognitive neuroimaging by a factor of 8 enabled us to explore the functional organization of ACC at a previously unaccomplished spatial scale *(9)*. Importantly, high-resolution fMRI should be considered as a complementary technique to standard neuroimaging rather than as a replacement. The approach may be envisaged as ''zooming into'' a region that was previously identified as active by established imaging strategies and may therefore contribute to bridging different spatial scales in the neurosciences.

While it is promising to see that subsequent fMRI studies have employed similar high-resolution approaches, it is unlikely that the spatial resolution of human cognitive neuroimaging techniques will increase even further in the coming years. Furthermore, fMRI suffers from the fundamental limitation that it measures metabolic processes in order to infer neural activity. While the link between the fMRI signal and neural activity is becoming clearer *(10, 11)*, more direct measurements of neural activity would be highly desirable.

To address these limitations, I recently started to employ two-photon calcium imaging *(12)*, which allows the functional interrogation of networks of tens to hundreds of neurons in the neocortex of living animals. Most importantly, since calcium provides a much more direct read-out of neuronal activity than the BOLD signal, calcium indicators frequently even permit the detection of single action potentials. Finally, the growing arsenal of fluorescent proteins allows the combination of optical imaging techniques with the powerful tools of genetics. As an example, we recently showed that the genetically-encoded calcium indicator Yellow Cameleon 3.60 (YC3.60) can be specifically expressed in neurons of the mouse neocortex and reports neuronal activity with exquisite sensitivity, down to single action potentials (Figure 2, *(13)*). In subsequent experiments, we then employed YC3.60 to monitor neuronal activity at diverse spatial scales, from single dendrites over local populations of neurons to large-scale brain areas, even in the awake, behaving mouse (Figure 3). In summary, cell-type specific expression of YC3.60, in combination with various optical techniques, allows the functional correlation of neuronal activity with animal behavior at diverse spatial scales, from dendrites to the levels of local and large-scale neuronal populations.

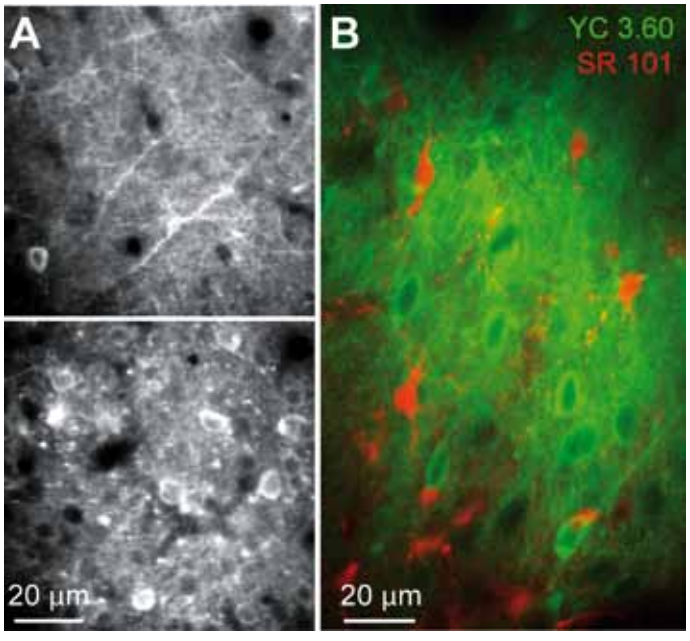

Fig. 2: *In vivo* two-photon images of neurons expressing a genetically-encoded calcium indicator (YC3.60). Images were taken in superficial layer 1 (86 µm depth from pia, top) and upper layer 2/3 (234 µm depth, bottom) in the mouse barrel cortex. (B) *In vivo* two-photon image of neuronal YC3.60 expression (green) together with counterstaining of astrocytes with SR101 (red).

Science Spotlight

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A central theme in my research thus far has been the bridging of different levels of investigation in the nervous system. In that respect, I have benefited greatly from the broad and comprehensive training in all aspects of neuroscience during my time in Göttingen. A particular strength, in my opinion, lies in the program's emphasis on practical lab experience, even during the first year. The 'lab rotation' projects offered to Masters Students already provide the possibility to experience the whole breadth of neuroscience, from the molecular to the systems level. This has been a truly formative experience that I can only recommend to anyone wishing to build a research career in the Neurosciences.

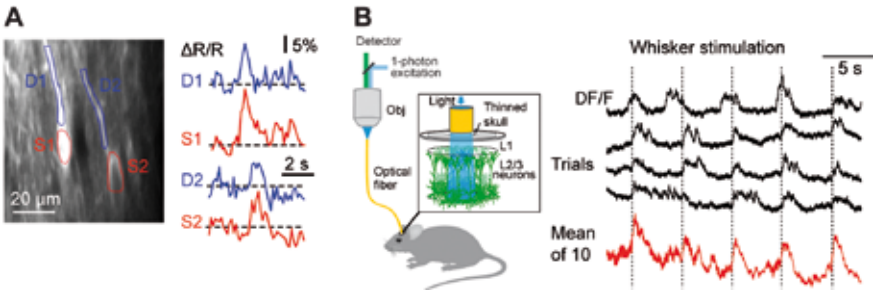

Fig. 2: (A) Simultaneous two-photon Ca^{2+} imaging in soma and dendrites of L2/3 neurons using vertical (xz-)imaging. Examples of spontaneous somatic (S, red) and apical dendritic (D, blue) YC3.60 Ca^{2+} transients for the cells depicted in the left image. (B) Fiber-optic bulk recording of YC3.60 signals in mouse barrel cortex. Fluorescence excitation and detection were both accomplished through the optical fiber, the tip of which was placed on the cortical surface. Right: Examples of single-trial YC3.60 fluorescence traces and mean of 10 traces upon air-puff whisker stimulation (dashed vertical lines).

Henry Lütcke did his doctoral thesis in Jens Frahm's department, Max Planck Institute for Biophysical Chemistry Göttingen. He defended his PhD thesis in October 2007.

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Spatial Organization

of Transmembrane receptor signaling *by Ioanna Bethani and Amparo Acker-Palmer*

The spatial organization of transmembrane receptors is a critical step in signal transduction and receptor trafficking in cells. Transmembrane receptors engage in lateral homotypic and heterotypic cis-interactions as well as intercellular trans-interactions that result in the formation of signaling foci for the initiation of different signaling networks. Several aspects of ligand-induced receptor clustering and association with signaling proteins are also influenced by the lipid composition of membranes. Here, we discuss the current knowledge about the roles of clustering of transmembrane receptors via protein-protein interactions important for the spatial organization of signaling at the membrane.

Introduction

Receptor-mediated signaling is a highly conserved mechanism that allows communication between cells and their environment. Efficiency and specificity are required to transmit only relevant signals to the appropriate target cells and the organization of receptors in higher order clusters contributes to this end. The importance of the receptor-receptor associations in regulating signaling specificity and sensitivity is discussed here, emphasing that receptor cooperativity is absolutely necessary for the integration of multiple signals and for the achievement of a coordinated cellular response.

Homotypic receptor clustering in *cis*

Many basic principles governing the organization and functional importance of receptor-receptor complexes come from the study of the receptor tyrosine kinases subfamily, the Eph receptors (Ephs) and their ligands, the ephrins. Once receptors and ligands from opposing cells come into contact, bidirectional downstream signaling in each cell occurs only after tetramerization of the *trans*-complex [1]. In a unique way, the tetramers can be further clustered in higher-order assemblies regulating the mode and strength of signaling.

Importantly, size and spatial patterning of signaling assemblies contribute significantly to the specificity of the signaling outcome, with small variations often resulting in opposite cellular responses. Dimeric-ephrinB1 can activate EphB1, but only higher multimeric states of receptor complexes are able to recruit downstream effectors and promote cell attachment [2]. In accordance, Salaita and colleagues [3] geometrically interfered with the size and pattern of EphA2 clusters and observed a strong impact on the intracellular distribution of f-actin, as well as the amount of recruited ADAM2 (Fig 1A).

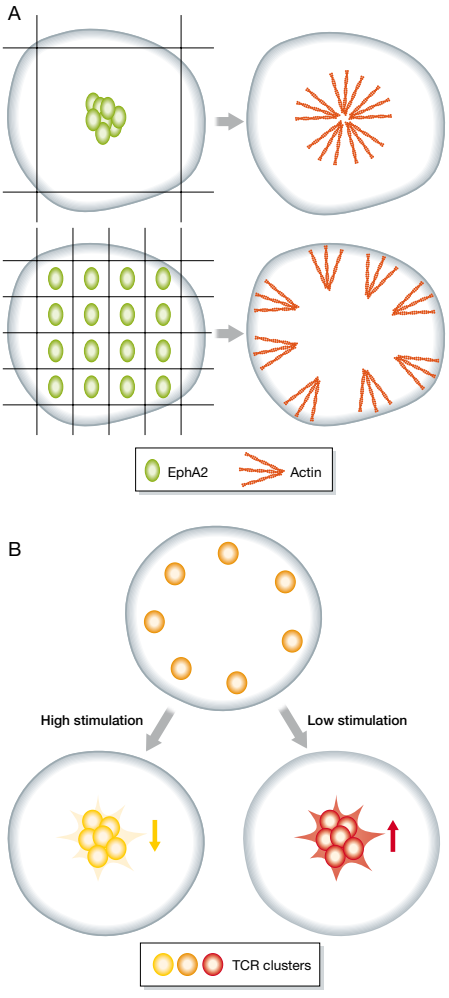

Fig. 1: Spatial distribution of membrane receptors. A) The size and organization of EphA2 membrane clusters determines the distribution of downstream effectors. Under conditions of unrestricted membrane transport of EphA2 (green), f-actin (red) accumulates in the periphery of activated ephrinA1-EphA2 clusters. Upon introduction of a spatial mutation that restricts EphA2 organization at the membrane, the distribution of f-actin shifted to the cell periphery. B) Redistribution of T cell receptors (TCRs) to the center of the immunological synapse results in different signaling states depending on the stimulus strength. Upon high stimulation, transport of TCRs (yellow) to the center of the synapse results in receptor deactivation and attenuation of signaling (pale yellow receptors). In contrast, under low stimulation conditions, activated TCRs accumulate at the center of the synapse and promote downstream signaling.

Interestingly, these results are highly reminiscent of how the differential spatial patterning of T-cell receptors (TCRs) elicits different signaling outcomes at the immunological synapse. Under high stimulation conditions, the transport of TCRs to the center of the synapse leads to an attenuation of the signaling by receptor inactivation and endocytosis (Fig. 1B). Blocking this translocation step by artificial barriers prolongs the presence of the receptors at the periphery of the synapse and results in a stronger T-cell response. On the contrary, when the receptors are experimentally forced to occupy the center of the synapse under conditions of low stimulation, the T-cell response is strongly enhanced (Fig. 1B) [4].

Receptor clustering also contributes to the increase in cellular sensitivity to external stimuli or even plays a purely mechanistic role, by enhancing the strength of cellular contacts to the extracellular matrix. For example, signaling sensitivity highly depends on the organization of receptor complexes on bacterial membranes upon chemotaxis. The key feature of these associations is that receptors of different types co-cluster and functionally interact in a highly orchestrated manner. Conformational changes of stimulated receptors increase allosterically the sensitivity of other receptors for their ligands and therefore efficient signal transduction and amplification of weak signals are ensured [5]. Another example of

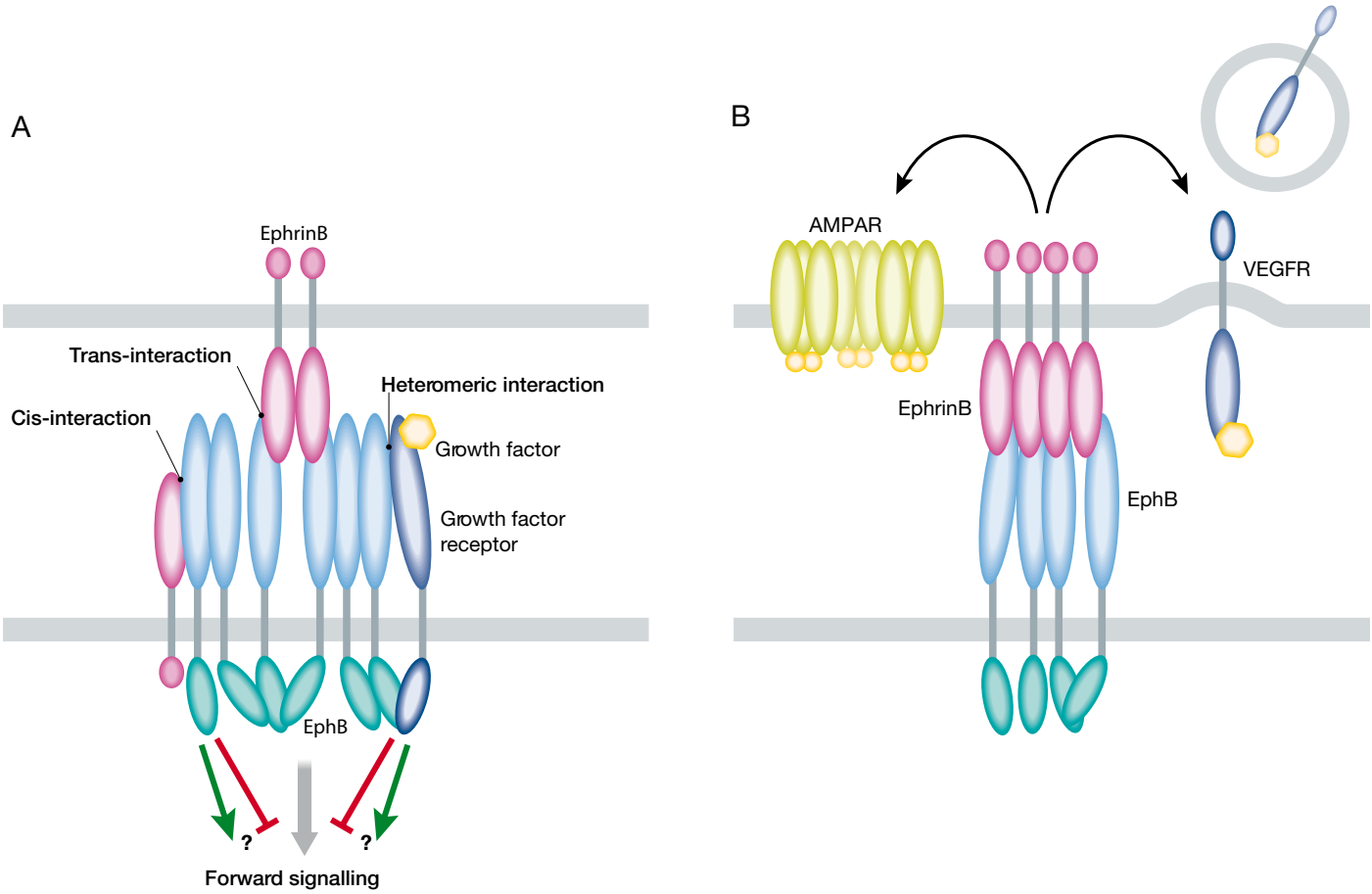

Fig. 2: Receptor-receptor complexes regulate signaling specificity and receptor trafficking. A) Eph receptors (Ephs) are clustered on the membrane via trans-interactions with pre-clustered ephrin ligands or via homomeric interactions of their extracellular or intracellular domains. Clustering is necessary for the receptor activation and signaling. The downstream signaling of activated Eph receptors can be further modulated by interactions with ephrin ligands in cis or by heteromeric associations with other receptor types. B) EphrinB2 differentially regulates the trafficking of AMPA and VEGF receptors. Serine phosphorylation of ephrinB2 promotes AMPAR stabilization at the cellular membrane of neurons whereas ephrinB2 positively regulates VEGFR endocytosis via its PDZ-binding domain.

signaling enhancement by receptor clustering can be found on the integrin signaling system. Extensive receptor clustering enhances cell adhesion by increasing the contact area between the cell and the matrix and can resist more efficiently to detachment forces. In contrast, under a random distribution of individual receptors, the same forces would be unevenly exerted in fewer and weaker connections, increasing the risk of breaking [6].

Heterotypic receptor clustering

Efficiency and specificity in signaling are additionally enhanced by the co-operative spatial accumulation of different receptor types. The co-existence of different receptors in the same signaling complex determines the molecular and cellular context that each receptor is facing and modulates accordingly its signaling outcome, serving as a mechanism to efficiently integrate multiple environmental signals to one common signaling pathway.

Known for their role during development, semaphorins are a group of receptors that often require multiple co-receptors for their function. They associate mainly with plexins but their signaling might also require neuropilins (Npns) or the Ig superfamily cell adhesion molecules (IgCAMs). For instance, Sema3s has to first bind to Npn-1 or -2 in order to get incorporated in Npn–plexinA complexes and induce signal transduction via the plexins. The final recruitment of either IgCAM L1 or NrCAM determines whether the signaling will lead to repulsive or attractive axonal guidance [7, 8]. Following similar principles, Ephs and ephrins also crosstalk physically with other receptors to mediate many of its biological functions (Fig. 2). For example, EphAs can function as tumor suppressors when they are solely activated by their ephrin ligands, but can turn into potent tumor enhancers, via their associations with oncogenic receptors, such as the members of the EGF or FGF receptor families [9].

Functional interactions between receptors that have antagonistic functions can provide an elegant fine-tuning mechanism of signaling regulation. EphrinB1 promotes the progenitor cell movement into the eye via its association with the scaffold protein Dishevelled (Dsh). The ability of FGFR to interact with ephrinB1 disrupts the ephrinB1-Dsh interaction and results in suppression of the retinal fate [10]. Modulation of synaptic morphogenesis and activity by the cross-talk of the Eph/ephrin bidirectional signaling with the NMDA and AMPA receptors constitutes an additional example on how receptor coordinated function efficiently intermingles different signaling pathways in one developmental process. The interaction of EphB2 with the NMDA receptor increases the clustering of NMDA receptors and the number of newly-formed synapses, EphB2 co-clusters with AMPA receptors at synapses and regulates their activity [1], while ephrinB2 modulates the trafficking and activity of AMPA receptors [11] (Fig. 2B). Interestingly, recent work has revealed a novel crosstalk of ephrinB2 with the VEGF receptors. EphrinB2 associates with VEGFR2 [12] and VEGFR3 [13] at the membrane regulating the trafficking of these vascular receptors during developmental and tumor angiogenesis as well as lymphangiogenesis (Fig. 2B).

Receptor associations in *trans*

Receptor-receptor associations are not restricted in one membrane plane but can be located on the membranes of different cells and associate in a *trans*-configuration, driving signaling cascades in both cells (bidirectional signaling). However, receptor associations in *cis* are still possible and can interfere with the functions of the *trans*-complexes, so additional regulation on the spatial domain is required to ensure appropriate distributions between *cis* and *trans* assemblies.
Bidirectional signaling of Eph receptors and their ephrin ligands mediates cell proliferation, survival and differentiation but also cell adhesion, shape and motility, via a variety of common downstream effectors. Nevertheless, a recent study revealed that the downstream signaling networks activated in the two participating cells upon Eph/ephrin binding involve either different molecules or the same molecules but regulated in opposite manners [14]. Additionally, stimulation of cells with recombinant ephrins results in different downstream signaling compared to the one induced by cell-presented ephrins. Therefore, bidirectional signaling is not a cell-autonomous process - the functional bridge built by the interaction of receptors in *trans* regulates cellular responses depending on the molecular status of the co-signaling cell.

An interesting aspect concerning the spatial organization of receptor complexes involved in bidirectional signaling is the discrimination between *trans*- and *cis*-receptor associations and signaling. In neuronal axon targeting, EphA forward signaling results in growth cone collapse and cell repulsi-

on, while ephrinA signaling promotes axonal growth and attraction [15]. Nevertheless, both molecules manage to keep their signaling activities separate by segregating in distinct membrane micro-domains thereby preventing their *cis*-association [16]. Similarly, Sema3A signaling can lead to cell attraction or repulsion depending on whether its interaction with the neuronal adhesion molecule L1-CAM and Neuropilin 1 occurs in *cis* or *trans* configuration [17]. In conclusion, the absolute spatial distribution of receptor complexes but also its relative positioning to other signaling clusters seems to be a necessary mechanism ensuring specificity in bidirectional signaling.

Conclusions and future perspectives

Studying the assembly and function of receptor complexes will advance significantly our understanding on receptor-mediated signaling and it is the next challenge to elucidate this extra level of complexity in receptor-mediated signal transduction. Which are the mechanisms that cluster or segregate receptors? What modes of receptor-receptor associations are conserved and important? How can the activation of a single receptor be translated in different cellular responses depending on a differential organization and activation in space and time? Or vice versa, how can the cell coordinate the cross-talk among different receptors to achieve one single cellular response? In addition, dysfunction in signal transduction pathways is often main cause of diseases and cancer. The signaling network built by clustering of multiple receptors complicates the manipulation of individual signaling pathways, since disrupting the signaling of one receptor type might trigger unpredictable reactions from other co-functioning signaling pathways. Interfering with receptor clustering, either by preventing receptor-receptor associations or disrupting membrane lipid organization, might be an intelligent novel direction in receptor targeting.

Ioanna Bethani did her doctoral thesis in Reinhard Jahn's department, Max Planck Institute for Biophysical Chemistry Göttingen. She defended her PhD thesis in April 2009.

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Myelination-Origin and molecular players

What is myelination and why investigate it? *by Amit Agarwal*

Myelination is the process by which glial cells enwrap axons with several layers of membrane sheaths. Myelin sheaths are enormous membranous extensions made by glial cells, which include oligodendrocytes (OL) in the central nervous system (CNS) and Schwann cells (SC) in the peripheral nervous system (PNS). The sheaths insulate axons and thereby ensure the rapid propagation of electrical impulses with millisecond precision (reviewed in 1). The process of myelination is one of the most impressive and least understood examples of cellular interaction invented by nature.

The speed of an electrical impulse propagated by a myelinated axon is directly proportional to the diameter of the fiber. In contrast, impulse propagation speed by an unmyelinated axon is proportional to the square root of axonal diameter *(2, 3)*. This startling effect of myelination can be illustrated by the fact that an unmyelinated squid giant axon (diameter of ~500 µm) and a mammalian myelinated axon (outer diameter of ~4 µm) both propagate electrical impulses at a speed of about 20 m/sec *(4, 5)*. For a given length the squid axon occupies up to 15,000 times more volume compared to myelinated mammalian axons. Moreover, the squid giant axon consumes 5,000 times more energy than a myelinated frog axon with a diameter of 12 µm, although the latter conducts more rapidly *(5, 6)*. Thus, in addition to high conduction velocity, the evolution of the mammalian myelinated axon has resulted in a remarkable saving of space and energy. These observations suggest that for the CNS to evolve, with its colossal computation power and space constraints, myelination was a necessary and critical process. However, myelination involves a high level of developmental, structural, metabolic and electrophysiological complexity. This makes the whole process highly vulnerable to cellular and molecular disturbances that may result in severe neurological disorders. Currently, most of the patients affected by a myelin-related disorder cannot be effectively treated. Therefore, deciphering the mechanisms and key players involved in the formation and maintenance of the myelin sheath is critical to an improved understanding of the pathophysiology of myelin-related disorders such as multiple sclerosis.

A brief history of myelin

The first description of myelinated nerve fibers came as early as 1717, from the microscopic analyses of animal tissues and nerves, by Leeuwenhoek. Later in 1791, Galvani hypothesized that the inner ‚tenuous lymph' of the nerve conducts electricity and the outer oily layer prevents dispersion of this electricity *(reviewed in 7)*. For a long time this oily substance surrounding nerves was believed to be secreted within the nerve fiber and was thought to be analogous to the bone marrow (‚Markstoff'). In 1858, based on this erroneous belief, Virchow hellenized ‚Markstoff' to ‚myeline' from the Greek myelos, meaning marrow. This dogma held sway for almost a century until in 1932, Penfield *(8)* put forth his hypothesis that myelin is chiefly maintained by oligodendroglia.

Two decades later in 1954, to solve the long-standing mystery of myelin genesis, Betty Ben Geren *(9)* used electron microscopy to evaluate various stages of myelin formation in the chick nerve. Her studies were the first to reveal that myelin forms by the elongation and spiral wrapping of SC membrane around the axon. This landmark discovery provided the key to the understanding of myelin structure and development. The whole new concept put forth by Betty Geren completely changed the way myelin was looked at. Now, myelin was not merely an oily sheath secreted by an axon but was produced as a result of complex interactions between neurons and glia *(10, 11)*. Shortly after this revolutionizing finding, concerning the genesis and structure of peripheral myelin, Maturana *(12)* and Peters *(13)* reported that myelin in the CNS also consists of membrane spirals. In contrast to the situation in the PNS, where SCs can form only single myelin segments, each segment of CNS myelin could be traced back to a single process of an OL. Surprisingly each OL can give rise to multiple myelin segments belonging to different axons *(14, 15)*.

Does size matter for getting wrapped?

Enigmatically, the myelin thickness is proportional to the diameter of the axon with only minor differences in this ratio (termed as g-ratio) across the species *(16)*. The axon calibre appears to be a critical determinant of myelination and its thickness *(17)*. In the mammalian PNS, all axons with a diameter of about 1 µm or more are myelinated. This observation laid the foundation for the „critical axon diameter" concept *(18)*. This idea was further supported by the observation that unmyelinated PNS axons become myelinated if their diameter is experimentally increased

(17). Originally, it was assumed that also in the CNS a „critical axon diameter" exists for axons to become myelinated *(19)*. However, in the CNS unmyelinated axons with diameters of up to 0.8 µm exist, while myelinated axons below 0.2 µm in diameter can also be found. Thus, in contrast to the PNS, the size spectrum of myelinated and unmyelinated axons overlap considerably in the CNS *(20)*. While the basic ultrastructure of myelin is comparable in the CNS and PNS, there seemed to be a fundamental difference with respect to the determinants of whether an axon will become ensheathed and myelinated.

These two principal observations of the constant g-ratio and the "critical axon diameter" rose the fundamental question ***"what is the biochemical measure of axonal size by glial cells, in particular Schwann Cells?"*** Five years back, two landmark studies, one of them carried out in the laboratory of Prof. Klaus-Armin Nave at Max-Planck Institute in Goettingen, elegantly deciphered that Neuregulin1 (NRG1) is the key axonal signal that regulates both these features *(21, 22)*. NRG1s are a family of membrane-associated growth factors with an epidermal growth factor (EGF)-like signaling domain. This EGF-like domain is necessary and sufficient for signaling mediated by NRG1. Binding of the EGF-like domain leads to the activation of ErbB receptor tyrosine kinases *(23)*. Additional detailed analysis have potentiated that NRG1 is the ‚master regulator' of myelination in the PNS *(reviwed by 24)*.

Now, with these findings there was a common enthusiasm among myelin biologists to answer whether NRG1 can be the universal "regulator" of myelination i.e. whether NRG1 can also regulate myelination in the CNS. I was among the fortunate ones who took this question as a part of my doctoral project, in the laboratory of Prof. Nave. Basically, this was my first confrontation with glial cell biology and the world of "fatty" myelin. To begin with, there were already several indirect evidences that suggested an important role of NRG1 during OL development *(25-27)*. But to everyone's surprise! In my studies we could show that this was not the case; 'physiologically NRG1 did not seem to regulate myelination in the CNS as it does in PNS' *(28)*. This was an astonishing finding with a great impact; we had to use up to 12 different transgenic mouse lines to prove the validity of our results. However, this finding raised several important issues, one of them being, why the mammalian CNS had to evolve a distinct myelination signal when the one mediated by NRG1 was successfully being used in PNS.

This brings me to another quest, a small part of this mystery I will try to solve over my postdoctoral training in the laboratory of Prof. Dwight Bergles, at John Hopkins University, USA. Since the last 20 years, it has been believed that electrical activity regulates the proliferation and survival of oligodendrocyte precursor cells (OPCs) and their terminal differentiation into myelin forming cells *(29-31)*. But how is this activity sensed by OPCs? Recently, the laboratories of Prof. Bergles and others have shown that OPCs are electrically active and respond to the electrical impulses propagating through an axon *(32, 33)*. OPCs express similar neurotransmitter receptors for communication, as used by neurons. These evidences indicate that OPCs are armored with all the

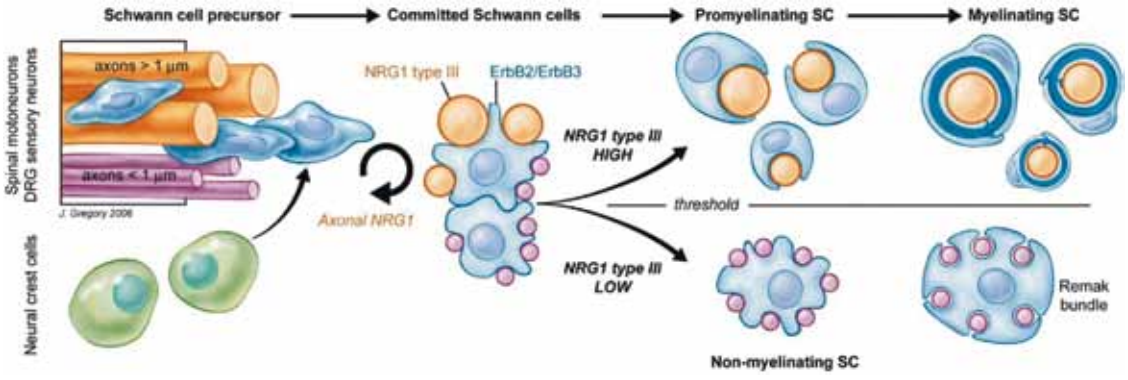

Fig. 1: Schwann cells (SC, in blue) arise from neural crest cells (in green) and interact with axons. The amount of NRG1 on the axon sensed by SC commits them into either myelinating (top) or non-myelinating i.e. Remak bundle forming phenotype (bottom). NRG1 signals axon size to SC to adjust myelin sheath thickness [adapted from (24)]

tools necessary to understand the language of neurons *(34)*. Unlike the PNS, where size (caliber) of axons matters, there seemed to be a complex cross talk between axons and OPCs to make a final decision of whether particular axon will be myelinated or not. Understanding the molecular players that might be involved in this intricate discussion making will shed more light on the complexities of CNS myelination. This crucial step determining the fate of the axons (in the CNS) to be myelinated or not will add yet another level of plasticity in the brain *(35)*. Can this be a brain's way to fine-tune the neural networks? Can the impairment in this precise communication between neurons and glia help us understand some of dubious psychiatric disorders?

Amit Agarwal did his doctoral thesis in Klaus-Armin Nave's department, Max Planck Institute for Experimental Medicine Göttingen. He defended his PhD thesis in April 2008.

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New Students

Master's class 2009/10

Dorota Badowksa Poland, BSc from University of Warsaw, Poland

Sarah-Anna Hescham Germany, BSc from Albertus-Magnus University Köln, Germany

Hung-En Hsia Taiwan, BSc from National Taiwan University, Taiwan

Ziqiang Huang P.R. China, BSc from Nankai University, China

Oleksandr Korolov Ukraine, BSc from National Taras Shevchenko University of Kiev, Ukraine

Este Leidmaa Estonia, BSc from University of Tartu, Estonia

Chaitali Mukherjee India, BSc from Mount Carmel College (Bangalore University), India

Pooja Rao India, MBBS from Maharashtra University of Health Sciences, India

Christina Reetz Germany, BSc from University of Göttingen, Germany

Anthony Tsang Hong Kong, MPhil from The Hong Kong University of Science and Technology, Hong Kong

Diana Elizabeth Urrego-Blanco BSc from Universidad Nacional de Colombia, Bogotá, Colombia

Welcome to Göttingen in the MSc class 2010/2011!

Bekir Altas, Turkey
Mateusz Ambrozkiewicz, Poland
Vinita Bharat, India
David Brockelt, Germany
Han-Yun Chen, Taiwan
Yen-Ying Chen, Taiwan
Ananya Chowdhury, India
Wan Ilma Dewiputri, Malaysia
Zohreh Farsi, Iran
Lauren Haag, USA
Ulrike Leipscher, Germany
Lawrence McKechnie, Scotland
Kareem Soliman, Egypt
Markus Stahlberg, Germany
Ananya Tiwari, India
Oana Toader, Romania
Siv Vingill, Norway

Applications 2010

In the year 2010, the Neuroscience program received 207 applications from 48 countries.
Germany 27
other Western Europe 7
Eastern Europe 11
North America 7
Central/South America 15
North Africa 10
Central/South Africa 15
Asia / Near East 26
Central Asia / Far East 88
Australia 1

PhD projects started in 2009/2010

2009

Hope Agbemenyah
The role of DNA methylation during aging and Alzheimer's disease
André Fischer, Klaus-Armin Nave, Judith Stegmüller

Derya Akad
The Role of PSD-95 and Kinase Interactions in Synaptic Function
Oliver Schlüter, Nils Brose, Till Marquardt

Jonas Barth
Olfactory perception and physiology in Drosophila
André Fiala, Andreas Wodarz, André Fischer

Juan Daniel Flórez Weidinger
Modelling the origins of spatial and temporal variability in visual cortical representations
Fred Wolf, Detlev Schild, Stefan Treue

Sadim Jawhar
Different therapeutic approaches in Alzheimer's disease mouse models
Thomas Bayer, André Fischer, Fred Wouters

Natalia Manrique Hoyos
Mechanism of neuroprotective function of myelin
Mikael Simons, Wolfgang Brück, Till Marquardt

Alejandro Mendoza Schulz
Imaging Synaptic Transmission at Auditory Brainstem Synapses
Tobias Moser, Erwin Neher, Reinhard Jahn

Chor Hoon Poh
Neuromuscular specification and plasticity: coordinating motor neuron and muscle fiber properties
Klaus-Armin Nave, Till Marquardt, Tomas Pieler

Natalia Revelo Nuncira
Localized signaling reactions in the developing growth come during navigation
Fred Wouters, Silvio Rizzoli, Mikael Simons

Meike Schweisfurth
Mapping of the Primary Somatosensory Cortex: Identifying borders and attentional influences
Jens Frahm, Stefan Treue, Christiane Thiel (extern), Renate Schweizer

Roman Stilling
Altered chromatin plasticity as a risk factor for brain diseases
André Fischer, André Fiala, Judith Stegmüller

Aaron Wong
Confocal imaging of Ca signal and exocytosis at single synapses of cochlear inner hair cells
Tobias Moser, Nils Brose, Erwin Neher

2010

Cordelia Imig
Comparative EM tomography studies in different neuronal cell types
Nils Brose, Reinhard Jahn, Stefan Eimer

Zhizi Jing
Sound encoding in the mouse cochlea
Tobias Moser, Martin Göpfert, Fred Wolf

Srinivas Parthasarathy
Investigating the role of CbIn4 in cortical feedback signaling during neocorticogenesis
Victor Tarabykin, Judith Stegmüller, Till Marquardt

Nicolas Snaidero
Mechanisms underlying myelination
Mikael Simons, Uwe-Karsten Hanisch, Holger Stark

Swathi Srivatsa
Functional characterization of Satb1 gene in neocortical development
Victor Tarabykin, Judith Stegmüller, André Fischer

Benjamin Wilhelm
Stoichiometric biology of the synapse
Silvio Rizzoli, Erwin Neher, Michael Hörner, Stefan Hell

The Doctors of 2009/2010

2009

Ioanna Bethani
Investigation of SNARE function in the early endosomal compartment
Reinhard Jahn, Nils Brose, Evgeni Ponimaskin

Esther Breunig
Transduction in Olfactory Receptor Neurons of Xenopus laevis Larvae: Pharmacological Blockage with FM1-43 and Endocannabinoid Modulation
Detlev Schild, Tobias Moser, Walter Stühmer

Annette Heinrich
Molecular mechanisms of the effect of the mood stabilizer lithium on cAMP-induced CREB transcriptional activity
Gabriele Flügge, Ralf Heinrich, Klaus-Armin Nave

Min Huang
Spatio-Temporal Dynamics of Pattern Formation in the Cerebral Cortex: Visual Maps, Population Response and Action Potential Generation
Fred Wolf, Stefan Treue, Tobias Moser

Stephan Junek
Investigation of spatio-temporal coding in the olfactory bulb of larval Xenopus laevis using fast confocal imaging
Detlev Schild, Erwin Neher, Fred Wolf

Schanila Nawaz
The Role of Phosphoinositides in the Interaction of Myelin Basic Protein with the Oligodendroglial Cell Membrane
Klaus-Armin Nave, Reinhard Jahn, Evgeni Ponimaskin

Anjana Nityanandam
Investigation of SIP1 gene interactions in the development of the mammalian tetencephalon
Walter Stühmer, Klaus-Armin Nave, Kerstin Krieglstein

Marija Sumakovic
The role of UNC-108/RAB-2 in neuronal dense core vesicle maturation in C. elegans
Stefan Eimer, Reinhard Jahn, Herbert Jäckle

Alexander Walter
The timing of the final assembly of the SNARE complex in exocytosis
Jakob Sørensen, Reinhard Jahn, Tobias Moser

Arwed Weigel
Quantitation Strategies in Optically Sectioning Fluorescence Microscopy
Detlev Schild, Walter Stühmer, André Zeug

2010

Ye Chen
Subcellular localization of Kv10.1 (Eag1): functional ion channels on the inner nuclear membrane
Walter Stühmer, Dirk Fasshauer, Jakob Sørensen

Thomas Frank
Investigating Ca-Signaling at Ribbon Synapses
Tobias Moser, Detlev Schild, Erwin Neher

Mrinalini Hoon
Role of Neuroligins at the Inhibitory Postsynaptic Compartment of the Retina
Nils Brose, Tobias Moser, Frederique Varoqueaux

Ling Luo
Regulation of intracellular trafficking by UNC-50 and the GARP complex in C. elegans
Stefan Eimer, Erwin Neher, Fred Wouters

David Owald
Early Active Zone Assembly in Drosophila
Erwin Neher, Stephan Sigrist, Evgeni Ponimaskin

Andrea Wirmer
Modulatory effects of NO and JH on the control of reprod. behavior in female Chorthippus biguttulus
Ralf Heinrich, Gabriele Flügge, Andreas Stumpner

Andrew Woehler
Quant. analysis of FRET from spectrally resolved fluorescence measurements
Erwin Neher, Evgeni Ponimaskin, Detlev Schild

Göttingen@Yale

Ira Milosevic

The idea that I need to relocate to New Haven, CT, USA, has sunk in few days after I accepted my postdoctoral job offer at Yale University. I never left Europe before and the new world seemed so far away. I went through emotional goodbyes and was making a careful choice of items that are worth bringing along for days, so imagine my surprise when hearing a noise of a hair-dryer at 120V, just after struggling to grasp how water faucet operates. My cultural adjustment went through all six classical stages: I felt sad to leave Europe, but was excited about new job; the new culture was a challenge, but I felt adjusted after receiving a social security number; I realized that not everything new is better, but finally managed to establish comfortable routine and new habits. The first "honeymoon" days at Yale will stay with me forever: I got accepted by new colleagues quickly and felt that they are there for me, both professionally and privately. My colleagues soon became my friends and one can really use friendly advice when the new world differs from the place you came from. Days after giving away everything I owned, I needed to buy it all again, and even shopping was not without challenges, many items ended up unused before I found my favourite yogurt or oil brand. Simple things as different units can shake the everyday life: I needed to walk 0.7 miles to buy 8 ounces of cheese and half a gallon of milk. My weight was now in pounds and height in inches, I had a new dress and shoe size. It is a challenge to buy a manual gear car as most of them are automatic, to rent a brick home as most of the houses are made of wood. The openness of people was both surprising and fascinating. Despite it all, I did not feel so much as a foreigner (or non-resident alien as my immigration card said), since everyone here came from somewhere else.

Over the last three years I got used to the life at Yale and in New Haven, and accepted that many things are just different, rather then better or worse. New England winters can be really cold and summers can be quite humid, but the autumn foliage is something you have to see. The university campus is so big that you need to take a shuttle bus to attend a scientific talk, but on the way you may see a racoon or a squirrel. The Yale scientific community is large and helpful, and there is a good chance that you can find a next-door expert for any interesting scientific question. There are enough good lectures and talks that one needs to make a choice which one to attend. I find an opportunity to work at Yale rewarding on many levels, enjoy that my research work receives attention and that my scientific presentations are followed up by active discussions. It always feels good to be a part of such productive community, even if it is sometimes hard to balance such demanding job with other aspects of life. The recent birth of my son Adrian posed new challenges to my husband Nuno (also a postdoctoral fellow at Yale Medical School) and me to find enough time for both our scientific work and our newborn. Raising a baby at Yale is not always simple: there are few daycares in New Haven and their waiting lists are long (up to two years for infants), the tuition fees are substantial (about half of the postdoctoral salary) and the shops that sell baby supplies are sparse. However, the fact that each infant in Adrian´s group have parents with different citizenships is remarkable and it is nice that our baby is exposed to such multicultural surrounding. I hope that our stay at Yale will enrich his life as much as it does ours.

There are still moments when I miss Goettingen´s strong scientific community and its support, the great discussions on the balconies of the MPIbpc and the view of the horses on the slopes of Nikolausberg. The efficient administration and in-house animal facility are irreplaceable. I miss my friends and our study times, cakes from Cron & Lanz Konditorei and Saturday morning strolls on Weeender Strasse to see the new flowers on Gänseliesel fountain which I consider a mark of flourishing science in Goettingen.

Ira Milosevic did her doctoral thesis in Erwin Neher's department, Max Planck Institute for Biophysical Chemistry Göttingen. She defended her PhD thesis in January 2006.

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Laura Swan

It really is true that in America everything is larger- engines noisier, streets broader, police sirens louder, milk by the gallon, and universities which stretch over miles.

Living and working at Yale has been a fascinating experience, and certainly one in which I am in good company: Yale boasts more than 4000 international students and scholars and their families- so there are plenty of people who share similar dreams and dedication for doing science coming from all kinds of places and traditions. The City of New Haven is arranged around Yale, which is almost a city unto its self: it organises its own bus routes, rental accommodation, private lake, boats, stables, shooting range, sports fields, six-storey gymnasium, radio station and police force.

Everything about Yale suggests the casual accumulation of a great deal of wealth- two museums composed only of art donated by their alumni include "spare" Picassos, Turners and Breugels and a whole section of an Assyrian gate. The campus itself is beautiful-most of it was built during the Great Depression to out-Cambridge Cambridge (Harry Potter fans take note!), including an entire cathedral shaped library, where all the iconography is secular: a creative solution to a bequest to build a place of worship, when Yale needed somewhere to store its books. In fact, this cathedral-library became the inspiration for Umberto Eco to write 'Il nome della rosa', though rather than monks who meditate on the evils of laughter, the cathedral guards thousands of stressed-out students under the watchful eyes of Issac Newton and Babylonian scribes.

Laura Swan and Ira Milosevic

Right now it's graduation season, so the city turns its prettiest face to families coming to see where their children have spent their years and where the parents have spent their tuition fees, banking, as we postdocs do, that the excellent resources, mentorship and connections that we have here will make a positive difference on our paths to achieving our dreams. And as for the students, for us too, only time will tell.

I can't say that I don't have moments of nostalgia for Goettingen, and for the German way of doing science, its high priority on pure academia, the intimacy of a small city which bends its energy to one or two fields done to their utmost. Certainly on an icy winter's evening, the idea of a gluehwein in the cracking cold of the Weihnachtsmarkt is enough to have me scanning ticket prices back to the place where, scientifically, I grew up. I hope that the lessons and approaches that I learnt, both in Goettingen and in New Haven, will prove as important to me in informing the science I will do, as the friendships and memories of these places have been in my heart.

Laura Swan did her doctoral thesis in Stephan Sigrist's department, European Neuroscience Institute Göttingen (ENI-G). She defended her PhD thesis in April 2005.

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My next post doc is in China

…yes I am serious!

At the time when most of my colleagues in Goettingen were packing to "hit the road" towards West, I was probably the only one who was hitting towards Far-East. I still remember some smiling faces turned into shocked ones whenever I mentioned that my next postdoctoral station after Germany is China. They probably did not know that I have visited China several times before and I was aware of a silent and enormous work aims at building a juvenile and modern body of scientific research.

In this body of research, after recruiting established scientists, special attention was given to competent postdoctoral researchers. Several regulations were established to attract young investigators to come to China from abroad. The most attractive thing is the research funding programs and regulations for young investigator. Research funding in China might win against Europe and North America in terms of number of grants and opportunities given for young investigators, if we ignore the exchange rate (i.e. consider 1 RMB in China as 1 Euro in Europe). Thus, as a young foreign investigator, one can become a multi-grantee scientist within short period, which should enhance independence and career establishment. Young investigators are also given decent space of freedom to carry on their own project of interest. For example, within the scope of interest of my lab, I have been working on topics related to enhancement of learning and memory. Then, I wanted to study if our approach that enhances memory might also enhance the formation of aversive memories, which can cause many psychiatric disorders. My second project could have a major negative impact on my mentor's entire work. However, when I explained to him my next project and my arguments, he simply said "Yes, do it".

Becoming a post doc in Tsinghua means you will have a two years contract, salary, insurance-packages, and an apartment, all within the range of local life-standards. As in other Universities and institutes people spend most of their time in the lab. So the lab becomes like home and colleagues are new family members. Besides working hard, I and my colleagues also enjoy our life; we play sports, go for shopping, celebrate our birthdays, go for watching movies…etc. The family-like feelings are very strong here; it happened that a colleague went to register his marriage, and then, instead of going home he came to the lab with his bride! We also exchange gifts frequently, which is a very interesting feature of the society here that strengthens and personalize the relationships. In China, one should accept the gift (do not say NO). One should also remember to pay back in a different way. Beware you have to insist on giving the gift even if the person said NO. I found integrating me within my lab family was a major shield from the complicated administration and relationship hurdles that still exist in China.

What about the integration within the society outside the University? Once you are in, get yourself a bike, learn how to eat with chop-sticks, enjoy Chinese food, and learn how to bargain (I usually divide the given price by five when I bargain). Chinese know that they do not follow the rules, e.g. traffic rules and/or standing in cues, but they like foreigners who follow the rules. By now I learned NOT to follow the rules, which I consider an evidence for my successful integration within the society! The major hurdle for integration is the language; it is difficult. Try to learn

the language, I say try because I personally failed to do so. I blame this on me; since I am lazy, and on my kind

colleagues; since they are kind! Now my Chinese is becoming better; I have my three years old son as professional teacher. Unlike other places, a foreigner will always be reminded that he/she is "a foreigner". Almost on daily basis I hear somebody whispering somewhere "Wai Guo Ren" means "foreigner". I still do not know how they can recognize me! This does not mean that you will be discriminated. On the contrary Chinese people, in general, are very kind and respectful with foreigners.

One thing I did not expect is that competition for faculty position or for surviving in science is more difficult than Germany or even the US. I learned the importance of two concepts here the "I.F." and the "CNS". The first means "impact factor"; a journal with impact factor below five does not count! The second is really interesting; in China CNS does not mean "Central Nervous System" only, but also means "Cell Nature Science". Therefore, unless you have a smart CNS to get a CNS paper it is difficult to get a position in the CNS-oriented prestigious Universities.

In conclusion, despite some difficulties, I have to say that over the past three years I enjoyed the ecstasy of living and doing science in China. I also developed a sort of independence at the career level. My view on handling scientific problems became different; it is influenced by the philosophy of Chinese culture, i.e. each Yan has a Yin. Finally, I have one word for those who might consider doing science in China: "if you believe in the potential of China, then yes do it, but carefully decide where to go and whom to work with". Here in China, circumstances are improving so fast, however they differ a lot among cities, Universities, and laboratories.

Nashat Abumaria did his doctoral thesis in Gabriele Flügge's department, German Primate Center Göttingen. He defended his PhD thesis in March 2006.

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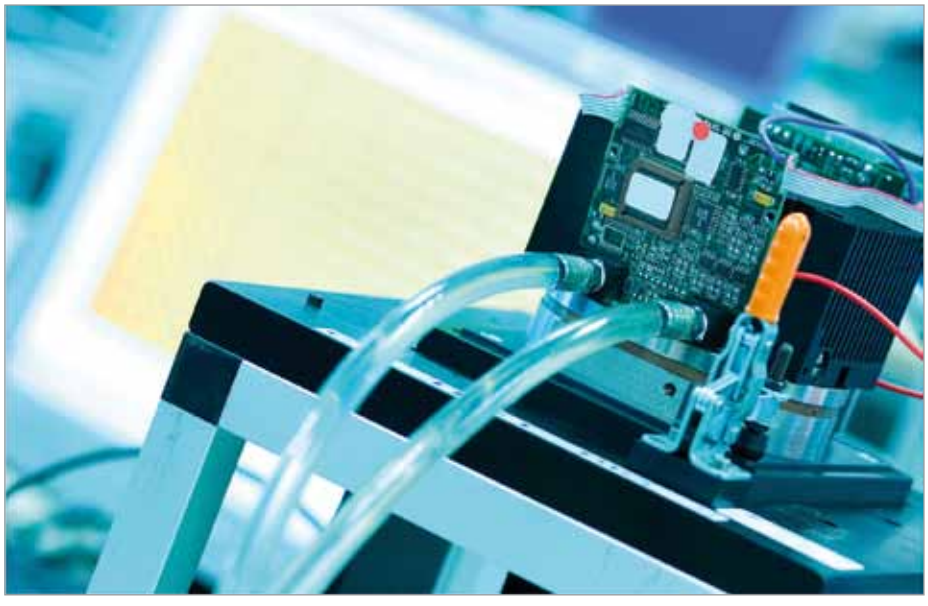
Discovering new ways of seeing

The main reason for me to leave research was rather poor correlation of actual workload / research efforts and measurable, rewarding outcome, i.e. a paper. Another closely related issue was the time that was required to produce these meaningful results. I felt that spending 13 hrs / day did not allow me to enjoy my life outside research hours. During 3+ years of my PhD my life was subject to schedules of splitting flasks of cells and finding the time to book a microscope slot from late in the evening. Last but not least, academia is not known to offer the best remuneration packages…

I didn't know what to expect being fresh out of grad school and being thrown in the deep end. I was, rightly or wrongly, expecting a very similar working environment to what I have experienced back in the lab but this did not prove to be the case. I was positively surprised by the degree of mutual respect at work and that my opinions count and bear weight. People are more focused and pay a lot of respect to their colleagues time – very little slacking especially when communal / corporate goods are concerned (.. no equivalents of dirty FPLC columns/messed up stirrer left overnight for the next person to sort out ..). I experienced much shorter fruition time for projects – probably my personal preference as I like to see the immediate effects of my work without delaying them for 2 years. There is a lot of global business travels to scientific conferences and symposia – several fold more than during my time at academia. And, of course, fixed work hours: 9-16:30 are great and you can go back home and watch a movie or read a book without collapsing after 14 hrs at the scope and cell culture, Finally, all this pays much better !

In essence, my experience from the first 100 days was: Faster pace of everything! You need to be a lot more focused and able to process multiple inputs at the same time. Lots of cycles of analysis and synthesis going on in parallel – working with R&D on new CCD readout patterns while doing a summary of recent interesting imaging technology and maybe working with an existing user on optimization of their optical setup for microtubule imaging.

My current projects focus on novel and up-and-coming applications – being on top of what's going on in the field of imaging: anywhere from AFM to X-ray. I am organizing tutorials for Andor's global sales force, distributors, part-



Outside Academia

ners and collaborators with updates on products, technologies, trends, gimmicks etc. I also compile case studies and tech notes based on recent publications done with Andor products and thousands of other things in parallel.
My responsibilities also include interactions with our key research partners, updating our R&D on new trends in the field of imaging, translating Andor's new developments to users and making them understand the benefits of these technologies in the context of their research. Furthermore, I am working on EU R&D proposals and FP6/7 projects that involve Andor as industry partner. There is career development path and various coaching programs do exist so it is possible to progress towards more senior positions.

The general differences between my experiences during the PhD time and my current occupation are difficult to summarize briefly – the first and foremost is the fact that academia is essentially non-profit establishment even though spin-outs and technology transfers do indeed occur providing some return from investment. Stock exchange listed enterprises must primarily bring profit and then keep increasing profitability. Focus therefore is very different – here one cannot embark on "a discovery journey" without a sound business case. I'm under the impression that research offers much wider margins to explore and tolerate potential pitfalls.

To be successful in a company one has to be capable of heavy duty multitasking. It takes some time to get used to much tighter deadlines, schedules and overall pace of things. Other than that most people with PhD have good analytical and communication skills anyway and these come in very handy. One should like travelling all over the planet because one week I can be in Johannesburg and the next one in Mumbai, Beijing or Amsterdam. This is great fun and when you combine it with attending several meetings like Gordon Research Conference, Biophysics Meeting etc. it is then when I start enjoying pure science again without worrying about results, the supervisor's comments, the next grant revision or even a messy TIRF someone set up without making it work properly.

Finally, in technical companies you ought to be at least a bit geeky to understand engineering lingo to be able to translate it to a "regular user", who after all wants to look at his cell sample and doesn't necessarily want to listen about driving voltage's jitter…

What I miss a bit is Göttingen's little town's atmosphere, a bit slower pace of life, several of my former Neuroscience teachers, whose lectures I still remember, friendships that didn't (couldn't?) last after I left it, proper bread and food in general, cleaner and safer surroundings, and the proverbial German punctuality.

Marcin Barszczewski did his doctoral thesis in Reinhard Jahn's department, Max Planck Institute for Biophysical Chemistry Göttingen. He defended his PhD thesis in June 2005.

Andor Technology,
Springvale Business Park,
7 Millennium Way,
Belfast,
Northern Ireland

Technology (and career) transfer

I am not going to say that changes, big changes, are easy. Actually, they never are. Those of you who are currently studying at the Neuroscience Programme know this as much as we Alumni do. Leaving home, starting again somewhere else with no friends, and a completely different language is no piece of cake. Some adapt earlier, some later, but at one point in our new endeavour everything fits in place again. Change takes time, but is beautiful and exciting because it comes full of surprises, constant learning and stimulating adventures. In the next few paragraphs, I would like to share my short experience with change, more specifically a change that involved leaving science to join the 'dark side' of business (scientists know what I mean).

After finishing my studies in Göttingen, I decided to move away from the lab (not science) and continue studying. What? After no getting results for two years, writing a extremely long thesis and coping with the stress of defending it (the usual situation), you still want to keep studying? Well, in my case I was lucky. I've got results pretty fast with my experiments and wrote a rather short thesis (at least for what I expected), but yes… it was definitely stressful at the end. Anyways, I've joined an MBA because it was part of a major career plan. I always wanted to link science and business, and to understand what scientists can do in order to transfer their innovations into marketable products.

I've chose IE Business School in Madrid (currently Top 6 in Financial Times Global MBA ranking) to jump into the 'market' because they specialise in entrepreneurship, which is my final career goal, i.e. to build my own technology-based company. Although quite expensive (I've spent around 80,000€ between course fees and living expenses, but scholarships are available), it was absolutely worth it to share different point of views with so many diverse backgrounds for 14 months.

It also gave me the opportunity to work in completely different sectors. For example, my final thesis project was to start-up a new (virtual) energetically self-sustained hotel in Patagonia, lost in the wilderness. Our team, all nature lovers, was composed of a lawyer, a financial expert, an architect, one electrical engineer and myself, a neuroscientist. Imagine the brainstorming sessions!

Emilio with his wife Teresa in the Asturian mountains / Picos de Europa

Moreover, during the MBA it felt as I was in first grade of preliminary school again. I had to learn every single topic from scratch, and I have to admit that at the beginning it was like hearing Chinese for the first time (now it would be right to say that I am a Spanish speaker, no?). I knew zero, but that was the most interesting part! I couldn't get bored because I was discovering a completely new world. And besides, I've met my lovely wife at school (the final project lawyer). So you see, you can even get things that you are not looking for! That's what I meant when saying that change is full of beautiful surprises.

Just before finishing the MBA, I was lucky enough (again) to find a job in a consulting firm specialised in the Bio-technology, Pharma and Life Sciences Industry. I am still there, and what we do is basically helping scientists to make the connection with, and transferring new technologies to companies from different sectors. For example, we are working with a pharmaceutical company, which wants to diversify their core business (drugs) into innovative and future technological applications that will enter the market in the next 10 years. We make research on what is the hottest-cutting-edge sci-

ence today that has a strong potential to jump into the market tomorrow.

Working for external clients gives you the chance to interact with different types of people, from CEOs of start-up biotech companies to the innovation manager of a big pharmaceutical enterprise, and also directors and managers of public institutions including Bioclusters and Technological Centres. You get the opportunity to learn from first-line professionals on how science is being transferred to a wide range of market applications. Our daily work includes selling new projects to clients (based on their needs), researching new transferrable technologies and their potential markets, and designing solid strategies to implement them in new products and services. From here, our best success measure is to finally see that the project is implemented.
The main difference between working in the lab and doing so in an office, besides the uncomfortable suit, is the pace of things. In the lab we have plenty of time. We could read the news, start an experiment, go back and check the weather for an hour, continue with the experiment, and so on… In consulting at least, everything is for 'yesterday'. And sometimes clients want reports on Monday so you have to open your laptop during the weekend (and I mean the whole weekend). Don't get me wrong, everything is faster and more stressful, but it also pays back. I am learning tons of new technologies from neuroscience to clean energy. It is amazing how science gives you the tools to think creatively and find new market applications for many scientific discoveries.

In summary, I would like to encourage all of you who are thinking of leaving science… to stay! No, I am kidding. I believe science is an amazing world to discover, but I also think not all of us are made to take part in it our whole life. There is another very different point of view of how progress, economies or people revolve around us, which is absolutely worth trying. And the best part of all is that we can learn from and participate in both, acting as 'translators' between jobs that are quite far away from each other (as a scientist vs. a businessman).

It is not easy, as I said in my first sentence. Change is tough especially through an MBA, but it will definitely help you to clarify what you want to do next. It will give you the tools to make a smoother career change. Think about it. For now, my advice to you all would be to enjoy Göttingen as much as you can, and make friends that will last forever. That, I am completely sure of.

Emilio Erazo-Fischer did his doctoral thesis in Erwin Neher's department, Max Planck Institute for Biophysical Chemistry Göttingen. He defended his PhD thesis in October 2006.

Emilio Erazo-Fischer, PhD, MBA
Senior Consultant,
BioSerentia
Calle de Alcántara 11, 3C,
28005 Madrid, Spain

Creutzfeldt & teaching award

Stipends

Malte Alf DAAD „Stipendium zur Durchführung einer Abschlussarbeit“ and Bayer Science & Education Foundation

Ahmed El Hady Neurosenses Georg Christoph Lichtenberg Fellowship

Thomas Frank Graduates‘ stipend of the „gemeinnützige Novartis-Stiftung für therapeutische Forschung“

Srinivas Parthasarathy Boeringer Ingelheim Fonds PhD Fellowship

Shahaf Peleg PhD stipend Minerva Foundation, Spetses Summer School stipend and Spetses Summer School best poster Award

Meike Schweisfurth Studienstiftung des Deutschen Volkes, Neurosenses fellowship

Nora Wender Dorothea Schlözer Stipend

Aaron Wong Neurosenses Georg Christoph Lichtenberg Fellowship and Croucher Foundation Scholarship (Honorary)

The following students have been awarded a GGNB Excellence Stipend:
Alonso Barrantes Freer, Pitchaiah Cherukuri, Sadim Jawhar, Natalia Manrique Hoyos, Alejandro Mendoza Schulz, Nikhil Sasidharan

Creutzfeldt PhD Prize

The Creutzfeldt PhD Prize is awarded for the best PhD thesis in memoriam of Otto Detlev Creutzfeldt, founding director of the department of Neurobiology at the Max Planck Institute for Biophysical Chemistry in Göttingen. The prize is awarded since 2007 to PhD graduates of the Neuroscience program based on excellent achievements during the PhD and the grading of the written dissertation and the oral defense. The award includes a gift of 500,-€ which is sponsored by the Göttingen biotech company Sartorius AG, which generously supports the Neuroscience program since its foundation.

2007 Prize winner Dr. Irina DUDANOVA
awarded by Christian Wulff, then Prime Minister of the State of Lower Saxony

Max Planck Institute of Neurobiology
Department of Molecular Neurobiology
Am Klopferspitz 18
D-82152 Martinsried

2009 Prize winner Dr. Henry LÜTCKE
awarded by Dr. Annette Reiche, Sartorius AG

Brain Research Institute
University of Zurich
Winterthurerstrasse 190
8057 Zurich, Switzerland

Teaching Award of the Neuroscience Program

The teaching prize of the Neuroscience Program is meant to acknowledge outstanding efforts and achievements in academic teaching. It has been awarded for the 1st time in 2008 as part of a ceremonial act, which included an invited guest seminar by Dr. Shu-Chen Li from the Max Planck Institute for Human Development in Berlin. The award is based on the regular teaching evaluation by the MSc students carried out throughout the 1st year MSc curriculum. The student jury judged the performance and the prize was awarded in the 3 categories, namely student tutor, course instructor, and faculty.

The awardees of the teaching prize 2008 are **Prof. Gabriele Flügge**, Clinical Neurobiology Laboratory, German Primate Center Göttingen (Faculty) **Dr. Ivo Chao**, University Medicine Göttingen, Dept. Neuroanatomy (Course instructor) **Dr. Alexander Walter** and **Dr. Kristian Wadel**, formerly Max Planck Institute for Biophysical Chemistry

New Faculty

Joining the program since 2008

Thomas Bayer
moved to Göttingen in 2007 as a Professor in Molecular Psychiatry at the University Medicine Göttingen, Department of Psychiatry. Since 2006, Prof. Bayer is the Coordinator of the European Commission funded International Alzheimer PhD School «Neurodegeneration in Alzheimer's disease – mechanism, consequence and therapy» (NEURAD).

Hannelore Ehrenreich
has been in Göttingen since 1992 and did her habilitation here in Neurology and Psychiatry in 1994. Prof. Ehrenreich is the head of the Division of Clinical Neuroscience at the Max Planck Institute for Experimental Medicine and Professor of Neurology & Psychiatry at the University of Göttingen. Her research is focused on the molecular/cellular basis of neuropsychiatric disease, mechanisms of neuroprotection in acute (ischemia/hypoxia, trauma) and chronic brain disease (schizophrenia, autism, ALS, MS).

André Fiala
came to the University of Göttingen as a Professor of Molecular Neurobiology of Behavior in 2008 after his habilitation in Neurobiology and Genetics in Würzburg. Prof. Fiala's studies include neuronal mechanisms underlying olfaction, learning and memory, and goal-directed behavior using the model organism *Drosophila melanogaster*.

Martin Göpfert
is professor for Cellular Neurobiology at the University of Göttingen since 2008. Prof. Göpfert's group studies fundamental processes in hearing. The preferred model system is the hearing organ of the fruit fly *Drosophila melanogaster*, the auditory sensory cells of which share conserved molecular modules with the hair cells in human ears.

Uwe-Karsten Hanisch
joined the Experimental Neurobiology Institute for Neuropathology at the University Medicine Göttingen in 2004 and is a guest professor of Medical Physiology at the University of Groningen. Prof. Hanisch's major research interests lie in the expression and functions of cytokines in the CNS, the mechanisms and consequences of microglial and in the role of plasma factors as endogenous signals for microglial cells.

Luis Pardo
obtained his MD and PhD degrees from the University of Oviedo, Spain, and has been a group leader in the department of Molecular Biology of Neuronal Signals at the Max Planck Institute for Experimental Medicine since 2004. Dr. Pardo's research focuses on the role of ion channels in the initiation and progression of tumors.

Silvio Rizzoli
was a post doctoral fellow with Reinhard Jahn at the Neurobiology Department of the Max Planck Institute for Biophysical Chemistry from 2004 until 2007. In 2007, Dr. Rizzoli became a group leader (STED Microscopy) at the European Neuroscience Institute Göttingen (ENI-G). The group takes advantage of the increased imaging resolution provided by STED to investigate synaptic vesicle function, with an emphasis on synaptic vesicle recycling.

Mikael Simons
is a medical doctor with specialty qualification in Neurology. He came to Göttingen as a junior group leader at the Centre for Biochemistry and Molecular Cell Biology in 2004, affiliated to University Medicine and MPI exp. med. Prof. Simon's research focuses on mechanisms of myelin biogenesis, neuron and glia interactions, membrane trafficking in oligodendrocytes, mechanisms of remyelination in multiple sclerosis, and amyloid precursor protein processing in Alzheimer's disease.

Judith Stegmüller
graduated from the University of Heidelberg and did a postdoc at Harvard Medical School, Boston, USA. Since 2008, Dr. Stegmüller is an independent group leader at the Max Planck Institute for Experimental Medicine in Göttingen. Her research deals with the role of the ubiquitin proteasome systems (UPS) in axon growth and regeneration.

Left from Göttingen in 2009

Jürgen Klingauf
graduated from the University of Göttingen and became a junior group leader at the Max Planck Institute for Biophysical Chemistry. Prof. Klingauf joined the Neuroscience Program in 2001. The focus of his research is the study of synaptic transmission, with emphasis on presynaptic mechanisms. Prof. Klingauf is now the head of the department of Cellular Biophysics at the Institute of Medical Physics and Biophysics at the University of Münster. His group currently adapts and develops high-resolution imaging techniques for studying cellular signaling and trafficking during synaptic transmission between neurons.
Further information: http://www.campus.uni-muenster.de/index.php?id=744&L=1

Jörg B. Schulz
joined the Neuroscience Program in 2006 as the head of the department of Neurodegeneration and Restorative Research. His department studied the mechanisms of degeneration in neurodegenerative disorders like Parkinson's and Alzheimer's disease and cerebral ataxias. Since January 2009, Prof. Schulz is professor of Neurology at the Medical Faculty of the RWTH and director of the Neurology department of the University Clinics Aachen.
Further information: http://www.rwth-aachen.de/aw/main/deutsch/Themen/aktuelles/Neuberufene_Professoren/_/~xvq/univ_-prof_dr_med_joerg_b_schulzhilfe/

Stephan Sigrist
was a member of the Neuroscience faculty from 2001 until 2009. He was an independent group leader at the European Neuroscience Institute Göttingen (ENI-G) in the field of neuroplasticity. In 2006, Prof. Sigrist moved to the Rudolf-Virchow-Center in Würzburg; since October 2008 he is a professor of Genetics at the Institute for Biology, Freie Universität Berlin. His current research focuses on the presynaptic compartment organizing release of neurotransmitter filled vesicles.
Further information: http://genetik.bcp.fu-berlin.de/

Former Faculty Members (since 2000)

Edgar Brunner
Nicole Dünker
Norbert Elsner
Peter Gruss
Folker Hanefeld
Herbert Jäckle
Uwe Jürgens
Bernhard Keller
Jürgen Klingauf
Reiner Kree
Kerstin Krieglstein
Reinhard Lakes-Harlan
Gerd Lüer
Markus Missler
Harald Neumann
Evgeni Ponimaskin
Thomas Rammsayer
Eleni Roussa
Christian Rosenmund
Marjan Rupnik
Ralf Schneggenburger
Jörg B. Schulz
Friedrich-Wilhelm Schürmann
Stephan Sigrist
Jakob Sørensen
Heinrich Terlau
Michael Waldmann
Wolfgang Wuttke
Weiqi Zhang
Annette Zippelius

Faculty
Leaving

Jakob Sørensen
did his MSc and PhD in Biology at the University of Copenhagen, Denmark before he came to the Max Planck Institute for Biophysical Chemistry Göttingen as a postdoc in the year 2000. Since 2005 he was a research group leader at the MPI-bpc and joined the Neuroscience program in 2006. Dr. Sørensen is now group leader of the neurosecretion group in the Department of Neuroscience and Pharmacology at the University of Copenhagen. The focus of his research interest is the molecular mechanism of neurotransmitter release in central neurons and neurosecretory cells.
Further information: http://inf.ku.dk/Forskning/forskningsgrupper/neurosecretion

Weiqi Zhang
came to Göttingen as a research group leader at the Center of Physiology in 1997 and became a Neuroscience faculty member in 2002. Prof. Zhang did his habilitation at the University of Göttingen in 2003. His research interests lie in the analysis of disease-related changes of the expression of receptor subunits, the properties of ion-channels and dysfunction synaptic transmission within neuronal networks. Prof. Zhang is now the head of the Laboratory for Molecular Psychiatry at the University of Münster.
Further information: http://www.campus.uni-muenster.de/mpsy_home.html?&L=1

Current Faculty Members

Mathias Bähr
Thomas Bayer
Nils Brose
Wolfgang Brück
Hannelore Ehrenreich
Stefan Eimer
Wolfgang Engel
André Fiala
André Fischer
Gabriele Flügge
Jens Frahm
Eberhard Fuchs
Theo Geisel
Martin Göpfert
Uwe-Karsten Hanisch
Ralf Heinrich
Michael Hörner
Swen Hülsmann
Reinhard Jahn
Hubertus Jarry
Till Marquardt
Tobias Moser
Klaus-Armin Nave
Erwin Neher
Luis Pardo
Walter Paulus
Diethelm W. Richter
Michael Rickmann
Silvio Rizzoli
Detlev Schild
Oliver Schlüter
Mikael Simons
Judith Stegmüller
Nicole von Steinbüchel-Rheinwall
Anastassia Stoykova
Walter Stühmer
Andreas Stumpner
Victor Tarabykin
Stefan Treue
Andreas Wodarz
Fred Wolf
Fred Wouters

For details regarding the research of all faculty members, please see www.gpneuro uni-goettingen.de/content/c_faculty.php

Campus events

NL \ YPaVUZ 2011

The Neurizons conference is a biennial meeting organized by graduate students of the MSc/PhD Program / International Max Planck Research School Neuroscience in Göttingen.The conference aims to provide a platform for scientific exchange between internationally acclaimed senior scientists and young researchers working in different areas of neuroscience. The meeting is supported by the Max Planck Institutes for Biophysical Chemistry and Experimental Medicine, the European Neuroscience Institute, the Center for Molecular Physiology of the Brain, and the University of Göttingen. Generous donations from various private and industry donors also help to cover the costs of the Neurizons meetings.
The 2011 meeting "Neurizons 2011: From molecules to mind – making sense of the brain" will be held from May 25th to May 29th 2011 in Göttingen and will cover topics ranging from emerging techniques to molecular/cellular neuroscience, neural dysfunction and cognitive processes. Confirmed speakers include Karl Deisseroth, Tobias Bonhoeffer, David Sweatt, and Magdalena Götz. In addition, a special keynote lecture will be given by Rodolfo Llinás.

For the first time, Neurizons 2011 will offer "career talks", in which professionals will provide an insight into work outside academia to inform about alternative career options.

Previous meetings have been very successful both in gathering scientists from many different institutions and nationalities as well as offering a stimulating scientific exchange. Again, Neurizons 2011 promises to be an exciting space of direct communication between present and the future scientists in the interdisciplinary field of neuroscience.

The Göttingen Neuroscience Program goes Europe

In 2008 four home institutes of European Neuroscience Institute Net (http://www.eni-net.org, consisting of 22 institutes in Europe) have decided to take a concerted action towards a new initiative aimed at organizing PhD training - and funding at an European level. Funded by the European Commission since 2009 under the Erasmus Mundus scheme the universities Amsterdam, Bordeaux, Coimbra, Göttingen and Zurich are now joining efforts to create a professional training network for doctoral students in the field of the neurosciences.

The doctoral programs within the newly established European Neuroscience Campus Network (www.enc-network.eu) are focused on brain disease mechanisms and the development of novel tools and approaches in experimental and clinical fields of the neurosciences. Each partner institute will host doctoral students and contribute to the education and training by providing methods (and academic skills) courses based on the specific research strength and expertise of each partner institute.

The ENC doctoral students will be trained in at least two home institutes in the ENC Network and have the option to enroll in existing PhD courses in each of the five neuroscience programs of the ENC institutes. The Neuroscience Campus Amsterdam coordinates all activities including selection and admission, organizing yearly conferences, introductory courses and core curriculum.

European Neuroscience Campus Network

In conjunction with the establishment of above mentioned ENC training network for doctoral candidates, the new European Master of Neuroscience program 'NEURASMUS' has been founded with the aim to extend exchange opportunities also for MSc students.

Neurasmus is a 2 year full-time study programme taught in English, with a strong emphasis on training in cutting-edge techniques in all major topics of brain research, from molecules to cognition. Its main objective is to foster Neuroscience education and to train new brain scientists, by offering a unique interdisciplinary and integrated approach of normal brain function and of brain diseases.

Neurasmus is offered by 5 European Institutions (Bordeaux/coordination, Amsterdam, Berlin, Coimbra, Göttingen) and 1 external partner Laval University in Quebec, Canada.

IMPRESSUM

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