NEUROSCIENCE
NEWSLETTER
Georg-August-Universität Göttingen · International Max Planck Research School
MAY 2015

The Nobel Prize, ...

… the 15th Anniversary, and the three new institutes

Welcome to the 4th Neuro-Newsletter published by the Göttingen International Master/PhD/MD-PhD Program and International Max Planck Research School (IMPRS) for Neurosciences.

First of all, congratulations to Stefan Hell who was awarded the Nobel Prize for Chemistry in 2014 (together with Eric Betzig, William E. Moerner). The Neuroscience program is delighted to again have a Nobel laureate among its members, after Erwin Neher, Nobel laureate in Physiology or Medicine in 1991 and founding member of the IMPRS for Neurosciences, retired.

Gregor Eichele, Stefan Hell, Martin Stratmann, Manfred Eigen, Erwin Neher (from right to left)

In addition to the glamour of the Nobel Prize it is noteworthy that other program members have been conferred prestigious research prizes as well (see section 'Honors & Awards'). The fact that neuroscientists at all levels, from senior scientists to junior group leaders and PhD students, competed successfully for national and international awards, reflects the competitive research efforts of one of the largest research communities in the field in Germany. The Neuroscience Program is pleased to contribute to the success and growth of the neurosciences on the Göttingen Campus for more than a decade now.

Founded in the year 2000 as one of the first international schools in the field in Germany, the Neuroscience Program celebrates its 15th Anniversary in May 2015. The alumni day activities, which are organized together with the Molecular Biology Program / IMPRS, take place during the weekend directly after the NEURIZONS symposium. This arrangement will hopefully again allow many MSc/PhD alumni to come to Göttingen for a scientific meeting and subsequent alumni get-together to renew the connections between the graduates and the local scientific community.

While the program keeps its tradition to offer a full year intensive MSc curriculum providing a comprehensive overview on relevant disciplines in the neurosciences, the content and focus have continuously been adjusted to the most actual research topics. Namely the area of biophysics relevant for quantitative approaches in the life sciences and the introduction to novel imaging techniques important for clinically-related research on neurodegeneration have been integrated into the teaching canon.

These adjustments in teaching reflect the dynamic changes in research and go along with the construction of two new research buildings accommodating three new institutes directly re-

CONTENT

Neuroscience in Göttingen...

lated to the neurosciences on the Göttingen Campus.

The new Imaging Center of the German Primate Centre (DPZ) and an additional 'multifunctional' building with a lecture hall and space for offices and laboratories have been opened in April 2015. Financed by the Leibniz Society and the State of Lower Saxony the DPZ imaging center will operate two magnetic resonance tomography scanners for use in primates and small laboratory animals in direct vicinity of a modern animal care facility.

The University Medical Center Göttingen (UMG) plans to open two new institutes focusing on high-resolution imaging on the molecular and cellular level in 2016. The 'twin' facility currently still under construction will house two research institutes located close to the university clinics. The Biostructural Imaging of Neurodegeneration (BIN) institute will be operated by the UMG; the Göttingen section of the German Center for Neurodegeneration (DZNE) will be supported by the Helmholtz Society. Concentrating on high resolution imaging and the investigation of mechanisms of neurodegenerative diseases, the two new institutes will enable a close cooperation between basic researchers and clinical scientists towards the development of novel early diagnostic tools. The U-shaped building architecture with over 200 rooms on 5 floors allows for efficient joint use of common facilities and research equipment.

These new institutes extend the basis for competitive research and the formation of networks and new forms of co-operation between scientists in the future allowing the development of novel fields and further growth of the neurosciences in Göttingen. Nonetheless, given the worldwide increasing number and quality of research and teaching facilities in the neurosciences, it will remain a challenge to attract sufficient numbers of young talented scholars and scientists to the Göttingen Campus.

Gregor Eichele
Speaker of the Max Planck Research School

Detlev Schild
Speaker of the MSc/PhD/MD-PhD Program

Sandra Drube
Administrative Coordinator of the Program

Michael Hörner
Scientific Coordinator

DISCLAIMER / IMPRINT

Publisher: Coordination Office of the international MSc/PhD/MD-PhD Neuroscience Program
Design and page layout: LifeTechMedia (Martin Nolte, Eva-Maria Twehues) and
Neuroscience Coordination Office (Sandra Drube, Michael Hörner)

One step closer...

towards the understanding of the CNS myelination process *by Nicolas Snaidero*

Central nervous system myelin is a multilayered membrane sheath generated by oligodendrocytes for rapid impulse propagation. However, the underlying mechanisms of myelin wrapping have remained unclear. Using an integrative approach of live imaging, electron microscopy, and genetics, we show that new myelin membranes are incorporated adjacent to the axon at the innermost tongue. Simultaneously, newly formed layers extend laterally, ultimately leading to the formation of a set of closely apposed paranodal loops. An elaborated system of cytoplasmic channels within the growing myelin sheath enables membrane trafficking to the leading edge. Most of these channels close during development but can be reopened in adults by experimentally raising phosphatidylinositol-(3,4,5)-triphosphate levels, which reinitiates myelin growth. In addition, we could better our understanding of the mechanisms responsible for the intra and extracellular compaction of this highly ordered structure. Our model can explain assembly of the myelin as a multilayered structure, abnormal myelin outfoldings in neurological disease, and plasticity of myelin biogenesis observed throughout adult life.

In the nervous system of vertebrates axons are ensheathed with myelin, which is one of the most remarkable and complex transformations of a plasma membrane achieved by a single cell. In the CNS, one single oligodendrocyte can produce up to 50 myelin sheaths of around 200 µm length. Each sheath is composed by a tightly compacted spiral of a membrane that is wrapped several times around the axon. More than 60 years after the seminal discovery demonstrating that myelin is made by axon-associated glial cells, and not by the axon itself, the molecular mechanisms by which the myelin sheath is wrapped around the axon are still largely unknown. Several key questions remain unanswered, such as what is the morphology of a growing myelin sheath? Where is the synthesized material added during myelination? How does the myelin sheath reach such an organized state of compaction? Is there a way for the material to go through the compacted myelin to ensure the growth and the axo-glia communication?

The investigation of the myelination process is directly correlated with the capacity to visualise the morphology of such a complex structure. Several technical challenges are on the way to investigate the myelin biogenesis due to the physical limitations of visualizing membrane dynamics at the nanometre scale and the duration of the wrapping process (few days *in vivo*). As a consequence of these imaging limitations there is no unified theory of myelination and several myelin models presenting different modality of membrane wrapping were proposed.

According to the "carpet crawler" model, the oligodendrocyte forms a process that broadens and extends along the entire axonal segment (the future internode) before it makes one turn and moves underneath the growing sheet (Bunge et al., 1961). However, at least in the CNS, several morphological features of myelin are incompatible with this model, such as an uneven myelin thickness along the myelin sheath during its formation. Some of these shortcomings were reconciled in the "yo-yo" model (Knobler et al., 1974, Pedraza et al., 2009). In the latter case, myelin growth begins with a single glial process that, after making axonal contact, spirally encircles the future internode, followed by the lateral growth of the individual membrane layers. More recent models, like the "liquid croissant" and the "Ofiomosaic model", based on light microscopy imaging implied a growth from the outer surface of the myelin sheath and the involvement of the axon membrane rotation as an active force driving the myelination (Sobottka et al., 2011, Ioannidou et al., 2012). However, due to the physical limitations of imaging such processes, it has not been possible to experimentally support any of these models of myelin wrapping.

In order to investigate the myelin biogenesis, a critical step was to understand the exact morphology of the myelin sheath at various time points during its development. To achieve this, we prepared mouse CNS tissue using the high pressure freezing technique for electron microscopy described to give preservation close to native state (Mobius et al., 2010). To cover a large volume of tissue and, at the same time, being able to reach a very high resolution we used serial block face imaging of high pressure frozen optic nerve by scanning electron microscopy. By combining volume microscopy with conventional TEM of high pressure frozen optic nerve and live imaging of myelin biogenesis in zebrafish, we could reconstruct the 3D organization and follow the changes of the myelin sheath during its growth, allowing us

to propose a new model of CNS myelination. We suggest that myelin grows by two coordinated motions: (1) wrapping of the leading edge at the inner tongue around the axon in a triangle-like shape, underneath the previously deposited membrane; together with (2) the lateral extension of myelin membrane layers toward the nodal regions. In this model, the lateral cytoplasmic domains of each myelin layer are always in contact with the axonal surface and move in a continuous helical manner toward the future node, where they align and form paranodal loops. In addition to the detailed morphology of the growing sheath, using viral reporter approach combined with immune electron microscopy we could identify that the newly synthesised material was inserted into the growing myelin sheath at the inner tongue (Snaidero et al., 2014a, Fig 1).

It has also become apparent that myelin is a dynamically active structure that can provide metabolic support to associated axons. However, it remains completely unclear how molecules reach the innermost myelin layer, i.e., passing through a multilamellar stack of membranes. Based on the preservation of the sample by high pressure freezing we could identify an elaborated system of cytoplasmic channels within compacted myelin that provides shortcuts for the transport of membrane to the growth zone at the inner tongue in the developing myelin sheath. We could show that most channels appear transiently in development at the most intense phase of membrane growth and are regulated by PI(3,4,5)P3 levels. Indeed, even in adult mice the network of cytoplasmic channels could be reopened prior to the myelin thickening in response to an increase of PI(3,4,5)P3 levels specifically in oligodendrocytes (Goebbels et al., 2012). Fig 1.

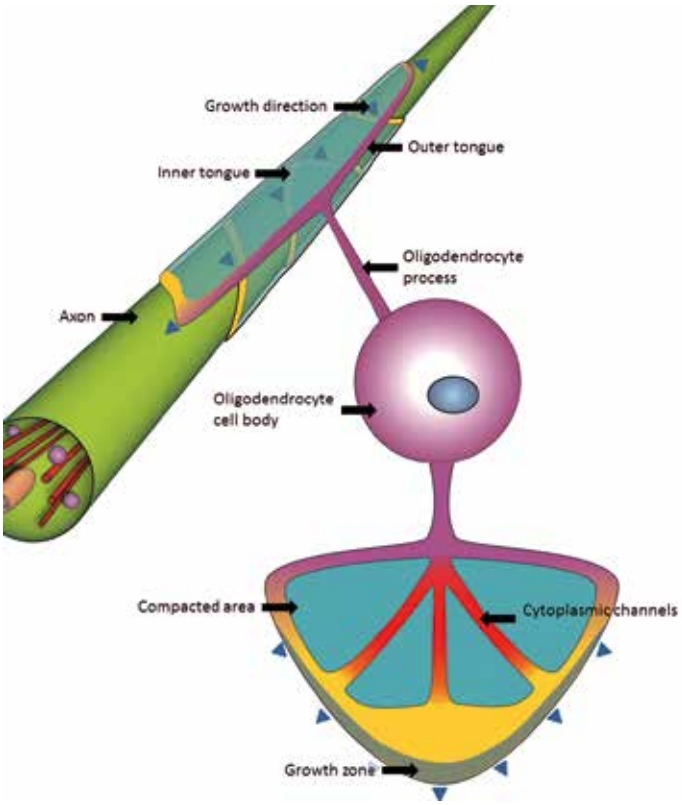


Fig. 1a: Morphology of the growing myelin sheath in the CNS. Wrapped and unrolled views of the growing myelin showing the geometry of the sheath and the direction of growth (blue arrow heads). The cytoplasmic channels are connecting the cell body with the inner tongue where the newly synthesised material is added. The wrapped view illustrates that the lateral cytoplasmic rich areas of the sheath are in constant contact with the axon, forming a coiled structure towards the both ends of the segment.

Conjointly with the morphological analysis of the myelination we could gain a better understanding of the cytoplasmic compaction of the myelin sheath mediated by MBP, as well as the mechanisms that are responsible for the close interactions between myelin membranes at their external surfaces. Indeed, valuable insides were gained on the role of MBP in extruding proteins with large cytoplasmic domains from the compacted areas (Aggarwal et al 2011), as well as on the molecular basis that drive myelin membrane assembly by a phase transition of the MBP into a cohesive protein meshwork. (Aggarwal et al 2013). In addition, we could observe that, while the growth occurs at the inner tongue, the compaction of the intracellular domain of the myelin sheath by MBP progresses from the outer layers towards the inner tongue, spatially separating these two processes (Snaidero et al., 2014a). Furthermore, when considering the compaction of the extracellular leaflets of the myelin sheath, the loss of electrostatic cell surface repulsion mediated by oligosaccharides of the glicocalix together with transmembrane tetra span (PLP) homo-interaction were shown to mediate the extracellular adhesion (Bakhti et al 2013a, Bakhti et al 2013b).

Taken together, we have used an in-depth integrated approach of advanced imaging at the light and electron mi-

croscopic level, as well as molecular tools, to dissect the morphogenesis and stabilization of myelin membrane wrapping. Combined with the discovery of the previously unknown myelin growth zone and identification of transient cytoplasmic channels in myelin that allow membrane trafficking toward the growing tip (at the inner tongue), our observations led to a model where the inner layer of the myelin sheath would advance beneath the already present layers (Snaidero et al., 2014a). In addition, we described the mechanisms of intracellular compaction by MBP and extracellular week adhesions that would allow the membrane gliding during myelin formation and myelin remodelling (Bakhti et al 2013b). This model not only fills a gap in our understanding of myelin biogenesis

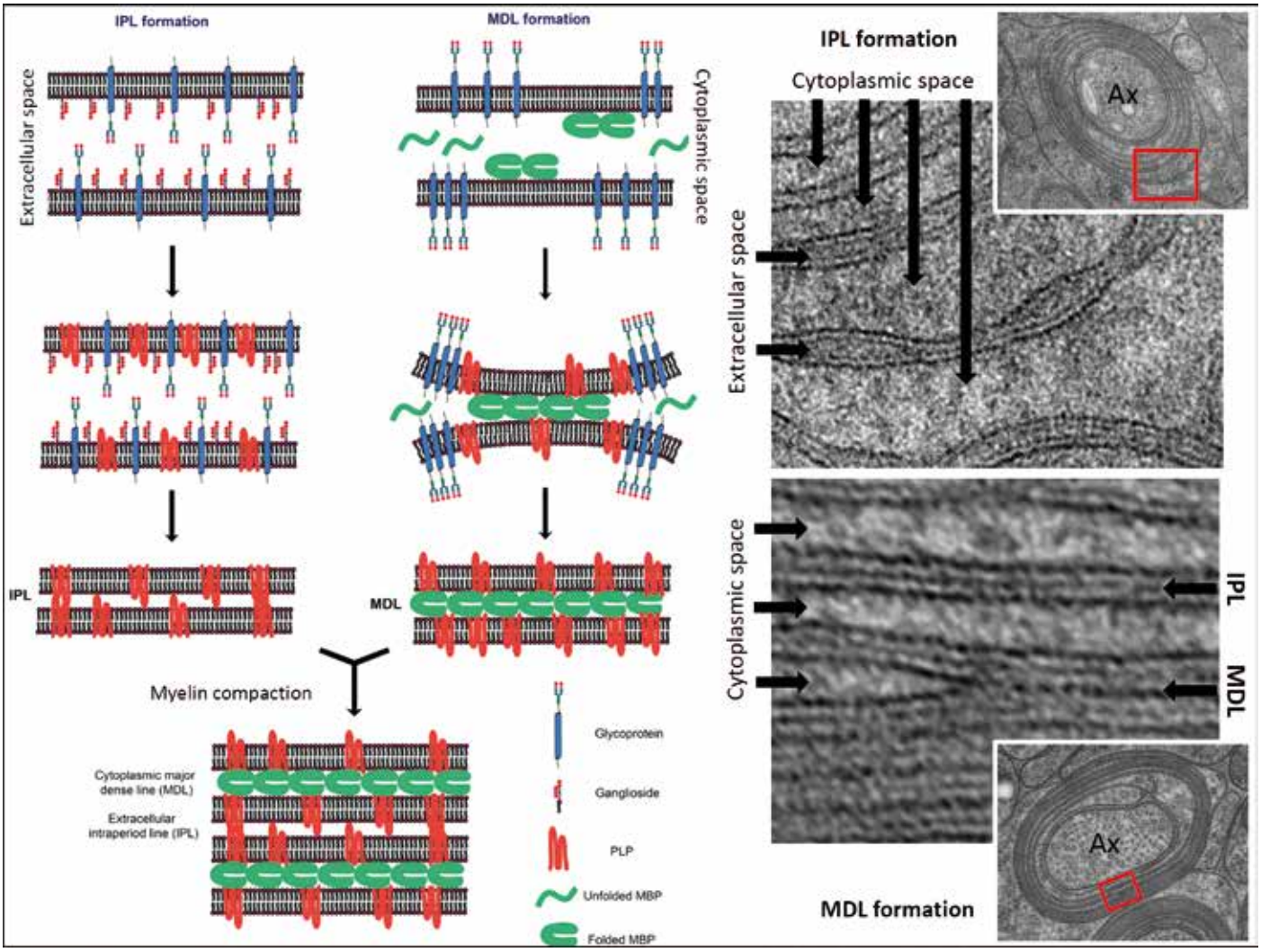


Fig. 2: Compaction of the myelin sheath from the extracellular and intracellular leaflets. The formation of the intraperiod line (IPL) is thought to be mediated by the removal of the glycocalyx components along with the PLP expression of the membrane. On the cytosolic surface, upon interaction with the membrane, the MBP protein is undergoing a conformational change that allows self-assembly. Resulting protein meshwork extrudes bulky cytoplasmic proteins, which results in the formation of the major dense line (MDL). The formation of the IPL is happening prior to the MDL which, in its turn, occurs starting from the more superficial layers of the myelin sheath towards the inner tongue.
Scale bar: 100nm
Picture adapted from Bakhti et al., 2013 (License Number: 3474830244857)

Nicolas SNAIDERO did his doctoral thesis in Mikael Simon's department, Max Planck Institute for Experimental Medicine, Centre for Biochemistry and Molecular Cell Biology. His doctoral thesis and oral defense were rated 'summa cum laude' by a team of internal and external reviewers. He defended his PhD thesis in July 2013. He will be awarded the Otto-Creutzfeldt PhD Award in 2015.

Institute of Neuronal Cell Biology
Technical University München
Biedersteiner Str. 29
80802 München

Institute of Clinical Neuroimmunology
Ludwig-Maximilians University Munich
Marchioninistr. 17
81373 München

in brain development, but also sheds light on myelin pathology in various neurological disorders (Snaidero et al., 2014b).

References

1. Aggarwal, S., Snaidero, N., Pahler, G., Frey, S., Sanchez, P., Zweckstetter, M., Janshoff, A., Schneider, A., Weil, M.T., Schaap, I.A., et al. (2013). Myelin membrane assembly is driven by a phase transition of myelin basic proteins into a cohesive protein meshwork. PLoS Biol 11, e1001577.
2. Aggarwal, S., Yurlova, L., Snaidero, N., Reetz, C., Frey, S., Zimmermann, J., Pahler, G., Janshoff, A., Friedrichs, J., Muller, D.J., et al. (2011). A size barrier limits protein diffusion at the cell surface to generate lipid-rich myelin-membrane sheets. Dev Cell 21, 445-456.
3. Bakhti, M., Aggarwal, S., Simons, M. (2013). Myelin architecture: zippering membranes tightly
4. together. Cell Mol Life Sci. 71(7):1265-77.
5. Bakhti, M., Snaidero, N., Schneider, D., Aggarwal, S., Mobius, W., Janshoff, A., Eckhardt, M., Nave, K.A., and Simons, M. (2013). Loss of electrostatic cell-surface repulsion mediates myelin membrane adhesion and compaction in the central nervous system. Proc Natl Acad Sci U S A 110, 3143-3148.
6. Goebbels, S., Oltrogge, J.H., Wolfer, S., Wieser, G.L., Nientiedt, T., Pieper, A., Ruhwedel, T., Groszer, M., Sereda, M.W., and Nave, K.A. (2012). Genetic disruption of Pten in a novel mouse model of tomaculous neuropathy. EMBO Mol Med 4, 486-499.
7. Knobler, R.L., Stempak, J.G., and Laurencin, M. (1974). Oligodendroglial ensheathment of axons during myelination in the developing rat central nervous system. A serial section electron microscopical study. J Ultrastruct Res 49, 34-49.
8. Ioannidou, K., Anderson, K.I., Strachan, D., Edgar, J.M., and Barnett, S.C. (2012). Time-lapse imaging of the dynamics of CNS glial-axonal interactions in vitro and ex vivo. PLoS One 7, e30775.
9. Pedraza, L., Huang, J.K., and Colman, D. (2009). Disposition of axonal caspr with respect to glial cell membranes: Implications for the process of myelination. J Neurosci Res 87, 3480-3491.
10. Snaidero N, Moebius W, Czopka T, Hekking L., Mathisen C, Verkleij D, Goebbels S, Edgar J, Merkler D,Lyons D, Nave K, Simons M. (2014). Myelin Membrane Wrapping of CNS Axons by PI(3,4,5)P3- Dependent Polarized Growth at the Inner Tongue. Cell. 156, 277-90
11. Snaidero N, Simons M. (2014). Myelin at a Glance. J Cell Sci. 127, 2999-3004.
12. Sobottka, B., Ziegler, U., Kaech, A., Becher, B., and Goebels, N. (2011). CNS live imaging reveals a new mechanism of myelination: the liquid croissant model. Glia 59, 1841-1849.

Molecular espionage:

revealing the identity of endocytosed organelles *by Natalia H. Revelo*

Membrane trafficking is of capital importance in the function of eukaryotic cells. The simultaneous study of the morphology and molecular composition of trafficking organelles was not possible due to the lack of a suitable and efficient technique. To overcome this difficulty, we developed a membrane-binding fluorescent marker compatible with immunostaining. Using this tool we could reveal endocytotic structures and their molecular identity in a multitude of biological preparations.

The main characteristic of eukariotic cells is the compartmentalization and separation of the different cellular processes into membrane-bound structures. This leap forward in evolution meant an easier "administration" of the cellular resources and isolation of specific biochemical processes, contributing to cell complexity and specialization. The outer surface of the cell, the plasma membrane, constitutes not only a barrier between the cell and its environment but also an exchange platform. It internalizes nutrients necessary for the cell function or receptors molecules for their recycling (endocytosis), and secretes synthesis products, like chemical signals (exocytosis). These basic functions are supported by a highly active trafficking network, which constantly exchanges cargo molecules and solutes between the plasma membrane and the different membranous compartments (for review see 1). The fusion and fission events required for such traffic are orchestrated by a plethora of proteins, some of which preferentially residing in or returning back to a specific type of compartment. This molecular behavior and the identification of morphological hallmarks have led to identification of different organelle types.

Membrane trafficking processes were initially studied with electron microscopy (2–4). Later on, with the development of immunostaining procedures based on metallic or fluorescent markers (5–7), it was now possible to identify the molecular players of these processes. Moreover, with the increasing use of fluorescence microscopy, fluorescent lipid-soluble molecules were developed to label membranes in living cells and follow physiological processes like endocytosis and organellar trafficking (8). The combination of two of these approaches led to photo-oxidation, a technique that converts an endocytosed fluorescent marker into an electron-dense precipitate, making endocytosed organelles visible for electron microscopy (EM) (9). Despite these advances, one important question has remained difficult to solve: can one track an endocytosed organelle and simultaneously establish its molecular identity? One possibility would be to combine photo-oxidation and immuno-EM (10). However, this approach has several disadvantages: laborious sample preparation and extensive imaging time resulting in low throughput; difficult data interpretation due to typical low labeling density of immuno-EM; parallel labeling of several proteins limited by the use of different sizes of metallic particles.

To solve this problem one would require an endocytosis marker that, once internalized, could be chemically fixed (e.g. with aldehyde fixatives), in order to allow subsequent immunolabeling of typical organellar markers or proteins of interest (Figure 1A). Moreover, due to the typical small size of trafficking organelles, imaging should be performed under high-resolution microscopy (nanoscopy). During my PhD project we developed such an endocytosis probe and named it mCLING (membrane-binding fluorophore-Cysteine-Lysine-Palmitoyl Group)(Figure 1B). It is composed of a hydrophobic tail that allows binding to membranes; a peptide containing seven lysine molecules that provide amine groups for aldehyde fixation; and finally, a fluorescent molecule (Atto647N) suitable for stimulated emission depletion (STED) nanoscopy (11).

We found that mCLING is not toxic for the cells at the concentration required for its imaging. It is readily taken up by the cells once it reaches the plasma membrane and, in contrast to other endocytosis markers, it is not washed off the cell surface, due to its strong binding to membranes. Co-incubations with mCLING and fluorescently labeled ligands for surface receptors like epidermal growth factor (EGF), transferrin or low-density lipoprotein (LDL), showed colocalization of both signals in endocytosed organelles, indicating that mCLING is successfully endocytosed and that it can label different trafficking pathways.

In biological preparations, aldehyde fixatives mainly crosslink with amine groups found in proteins, thereby stopping cellular processes and preserving the subcellular structure. Several endocytosis markers have been modified with one amine group to render them fixable. We evaluated the fixability of amine-modified versions of molecules from the FM family, a group of styryl dyes widely used to monitor

membrane uptake and recycling (12). We found that after fixation these molecules were lost from the originally labeled membranes, reflected in fluorescence intensity reduction and/or mobilization of the dye molecules into other compartments. After permeabilization, a detergent-based procedure that extracts lipids from membranes to allow antibody penetration during immunostaining, the fixable FM dyes were largely lost, indicating that one amine group is not sufficient to keep these molecules in place. In contrast, mCLING remained attached to the plasma membrane and endocytosed organelles after fixation and permeabilization, confirming its fixability and suitability for immunostaining procedures (Figure 1C).

We then used mCLING to answer long-standing biological questions. Our first study focused on understanding synaptic vesicle recycling in the auditory inner hair cells (IHCs), responsible for sound encoding in mammals. In conventional chemical synapses, like those in the central nervous system or at the neuromuscular junctions, neurotransmitter-filled synaptic vesicles are exocytosed upon the arrival of an electrical stimulus and then internalized back via endocytosis (see (13)). This process of vesicle recycling is isolated into the presynaptic bouton, separated from other membrane trafficking processes required for normal cell function, referred here as constitutive trafficking (e.g. receptor internalization, nutrient uptake, or membrane traffic between the organelles involved in protein synthesis). However, IHCs are polarized cells that do not have synaptic boutons, developing instead vesicle release sites directly at the cell soma, concentrated at the cell base. This implies that synaptic vesicle recycling shares the same cytoplasmic volume as the constitutive pathways, making it difficult to assign trafficking routes to an endocytosed organelle. Additionally, IHCs present specialized active zones, topped with a proteinaceous structure called synaptic ribbon, which tethers and concentrates synaptic vesicles, resulting in high rates of release (14, 15). Two models of synaptic vesicle recycling in IHCs have been proposed: 1) vesicles recycle at the base of the cell, in proximity to the synaptic ribbons (16–18). 2) Vesicles are endocytosed at the cell top, then fused with organelles residing at the cell upper level, like the Golgi apparatus, and from there regenerated and sent towards the cell base (19–21).

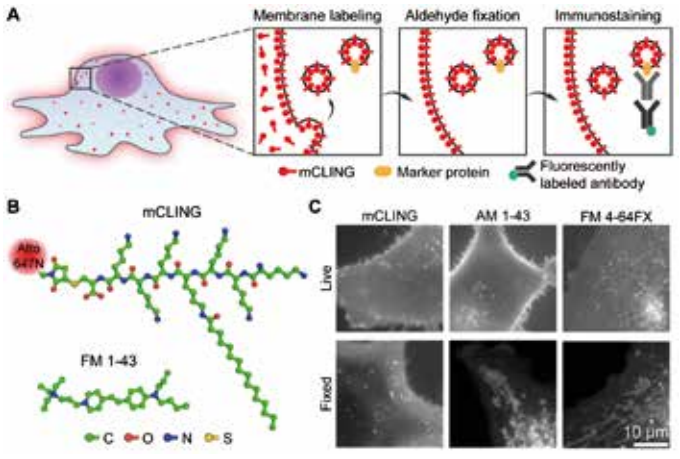


Fig. 1 A: Experimental workflow to reveal the molecular identity of trafficking organelles. Living cells are incubated with the marker for its uptake (red), then fixed and immunostained for organellar marker proteins. Samples can then be imaged in conventional or high-resolution microscopy. B. Molecular structure of mCLING compared with a smaller non-fixable membrane-binding probe. C. mCLING labeling after fixation is comparable to that in living cells. In contrast, conventional fixable membrane-binding dyes (AM 1-43 and FM 4-64FX) are largely lost from membranes after fixation, ending up in mitochondria-like structures.

In order to test these models, we applied mCLING to IHCs at resting conditions (low K^+) expecting to label only constitutive traffic, and at stimulating conditions (high K^+) to label both constitutive and synaptic traffic. STED imaging on mCLING-labeled organelles showed that constitutive traffic is abundant in these cells, it occurs mainly at the cell top and nuclear levels, and it involves tubulocisternal structures as recycling intermediates. Conversely, synaptic vesicle recycling takes place at the cell base. These results are in agreement with a previous morphological study we performed using electron microscopy (22). Combining mCLING and immunostaining against the synaptic ribbon we found that important processes of membrane remodeling take place in the vicinity of this structure. Depending on the stimulation strength (i.e. K^+ concentration) synaptic vesicles will be directly retrieved from the plasma membrane, or rather from membrane invaginations and cisterns formed in response to abundant vesicle release (bulk endocytosis).

To confirm the previous results we combined mCLING labeling with immunostaining against synaptic vesicle markers (VGLUT3, Rab3) or proteins belonging to the constitutive trafficking pathways (GM130,

Syntaxin 6, Syntaxin 16, Vti1a). The vesicular markers colocalized only with the organelles recycled at the cell base (Figure 2A). On the contrary, the constitutive markers colocalized mainly with the structures at the top and nuclear cell levels. Furthermore, the tubulocisternal structures strongly colocalized with Syntaxin 6 and 16, suggesting that these could be recycling endosomes (Figure 2B). From these results we concluded that IHCs functionally and spatially separate synaptic vesicle recycling from constitutive membrane trafficking pathways (Figure 2C).

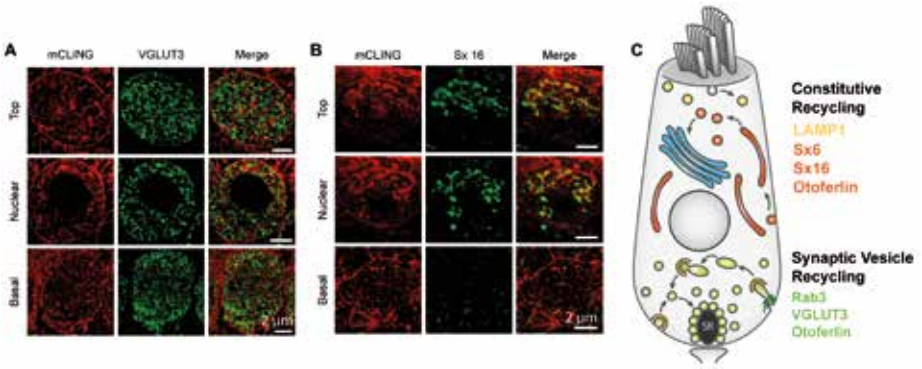


Fig. 2 A-B: Two-color STED imaging of mCLING-labeled endocytosed organelles (red), combined with immunostaining against a synaptic vesicle marker (A. VGLUT3, green) or against a constitutive endosomal marker (B. Syntaxin 16, green) at three different cellular levels. C. Model of membrane trafficking in IHCs. Constitutive membrane trafficking and synaptic vesicle recycling are functionally and spatially separated, the former taking place at the top and nuclear levels of the cell and the latter at the base of the cell. SR, synaptic ribbon.

We then addressed a highly debated question: are there differences in molecular composition between actively and spontaneously released synaptic vesicles? (23–25). For this we incubated cultured hippocampal neurons with mCLING during electrical stimulation (active release) or inhibition with tetrodotoxin (spontaneous release). Subsequently, these were immunostained for synaptic vesicle or endosomal markers. Two-color STED imaging showed that spontaneously released vesicles have higher levels of endosomal proteins and lower levels of synaptic vesicle proteins. This indicates that the two groups of vesicles are different in composition, with the spontaneously released ones more related to constitutive recycling.

Finally, we tested mCLING in other preparations. We could label synaptic vesicle recycling in the *Drosophila* neuromuscular junction. We imaged labeled, endocytosed organelles in live, fixed or immunostained yeast cells (*Saccharomyces cerevisiae*), outperforming FM4-64, the standard dye used in these cells. We could also label the membrane of *Escherichia coli* cells and image them at high-resolution microscopy finding heterogeneous labeling patterns.

Conclusions and Perspectives

Our study shows that mCLING is the first fluorescent probe that allows morphological and molecular characterization of subdiffraction-sized endocytotic organelles. mCLING is not only suitable for studying membrane traffic in cultured cells and microorganisms, but also in complex tissues. Another application of mCLING, not presented here, is its application at low temperature leading to endocytosis inhibition. The result is a surface labeling that can be used to distinguish the immunostained proteins sitting on the plasma membrane, from those located inside the cell.

Natalia REVELO NUNCIRA did her doctoral thesis in Silvio Rizzoli's group, STED microscopy of synaptic function group, European Neuroscience Institute Göttingen (ENI-G). Her doctoral thesis and oral defense were rated 'summa cum laude' by a team of internal and external reviewers. She will be awarded the Otto-Creutzfeldt PhD Award in 2015. She defended her PhD thesis in June 2014.

Dept. Neuro- and Sensory Physiology
University Medical Center
Humboldtallee 23
37073 Göttingen

The versatility of mCLING is further broadened by the possibility of replacing the fluorophore according to the investigator's needs or the requirements of a particular microscopy technique. The success of mCLING will also be complemented by the development of novel protein labeling tools that are smaller and therefore more efficient than antibodies (~150 kDa) at binding to epitope regions. Examples are nanobodies (obtained from camelids, ~13 kDa) and aptamers (DNA or RNA oligonucleotides, ~15 kDa) (see for example 26).

References

1. J. S. Bonifacino, B. S. Glick, The mechanisms of vesicle budding and fusion. Cell. 116, 153–66 (2004).
2. D. W. Fawcett, Surface Specializations of Absorbing Cells. J. Histochem. Cytochem. 13, 75–91 (1965).
3. J. E. Heuser, T. S. Reese, Evidence for recycling of synaptic vesicle membrane during transmitter release at the frog neuromuscular junction. J. Cell Biol. 57, 315–44 (1973).
4. R. G. Anderson, M. S. Brown, J. L. Goldstein, Role of the coated endocytic vesicle in the uptake of receptor-bound low density lipoprotein in human fibroblasts. Cell. 10, 351–64 (1977).
5. J. Marrack, Nature of Antibodies. Nature. 133, 292–93 (1934).
6. A. H. Coons, H. J. Creech, R. N. Jones, Immunological properties of an antibody containing a fluorescent group. Proc. Soc. Exp. Biol. Med. 47, 200–202 (1941).
7. W. Faulk, G. Taylor, An immunocolloidal method for the electron microscope. Immunochemistry. 8, 1081–1083 (1971).
8. M. G. Honig, R. I. Hume, Fluorescent carbocyanine dyes allow living neurons of identified origin to be studied in long-term cultures. J. Cell Biol. 103, 171–87 (1986).
9. J. H. Sandell, R. H. Masland, Photoconversion of some fluorescent markers to a diaminobenzidine product. J. Histochem. Cytochem. 36, 555–559 (1988).
10. M. Malatesta, C. Zancanaro, M. Costanzo, B. Cisterna, C. Pellicciari, Simultaneous ultrastructural analysis of fluorochrome-photoconverted diaminobenzidine and gold immunolabelling in cultured cells. Eur. J. Histochem. 57:e26, 168–171 (2013).
11. N. H. Revelo et al., A new probe for super-resolution imaging of membranes elucidates trafficking pathways. J. Cell Biol. 205, 591–606 (2014).
12. W. J. Betz, F. Mao, G. S. Bewick, Activity-dependent fluorescent staining and destaining of living vertebrate motor nerve terminals. J. Neurosci. 12, 363–75 (1992).
13. T. C. Südhof, The synaptic vesicle cycle. Annu. Rev. Neurosci. 27, 509–47 (2004).
14. G. Zanazzi, G. Matthews, The molecular architecture of ribbon presynaptic terminals. Mol. Neurobiol. 39, 130–48 (2009).
15. G. Matthews, P. Fuchs, The diverse roles of ribbon synapses in sensory neurotransmission. Nat. Rev. Neurosci. 11, 812–22 (2010).
16. J. H. Siegel, W. E. Brownell, Synaptic and Golgi membrane recycling in cochlear hair cells. J. Neurocytol. 15, 311–328 (1986).
17. J. Neef et al., Modes and regulation of endocytic membrane retrieval in mouse auditory hair cells. J. Neurosci. 34, 705–16 (2014).
18. D. Lenzi, J. Crum, M. H. Ellisman, W. M. Roberts, Depolarization Redistributes Synaptic Membrane and Creates a Gradient of Vesicles on the Synaptic Body at a Ribbon Synapse. Neuron. 36, 649–659 (2002).
19. J. Meyer, a F. Mack, a W. Gummer, Pronounced infracuticular endocytosis in mammalian outer hair cells. Hear. Res. 161, 10–22 (2001).
20. C. B. Griesinger, C. D. Richards, J. F. Ashmore, FM1-43 reveals membrane recycling in adult inner hair cells of the mammalian cochlea. J. Neurosci. 22, 3939–52 (2002).
21. C. B. Griesinger, C. D. Richards, J. F. Ashmore, Fast vesicle replenishment allows indefatigable signalling at the first auditory synapse. Nature. 435, 212–5 (2005).
22. D. Kamin, N. H. Revelo, S. O. Rizzoli, FM Dye Photo-Oxidation as a Tool for Monitoring Membrane Recycling in Inner Hair Cells. PLoS One. 9, e88353 (2014).
23. T. W. Groemer, J. Klingauf, Synaptic vesicles recycling spontaneously and during activity belong to the same vesicle pool. Nat. Neurosci. 10, 145–7 (2007).
24. B. G. Wilhelm, T. W. Groemer, S. O. Rizzoli, The same synaptic vesicles drive active and spontaneous release. Nat. Neurosci. 13, 1454–6 (2010).
25. Y. Sara, T. Virmani, F. Deák, X. Liu, E. T. Kavalali, An isolated pool of vesicles recycles at rest and drives spontaneous neurotransmission. Neuron. 45, 563–73 (2005).
26. F. Opazo et al., Aptamers as potential tools for super-resolution microscopy. Nat. Methods. 9, 938–9 (2012).

Understanding progenitor fate switch...

in the developing neocortex *by Srinivas Parthasarathy*

The mammalian neocortex is composed of six layers of neurons, which are responsible for our highest cognitive abilities. This extremely heterogeneous population of neurons is born sequentially from a small pool of relatively homogenous progenitor cells. Cortical neurons are produced in an inside first-outside last manner, whereby deeper layer neurons are generated before upper layer neurons. After their birth in the ventricular zone these neurons migrate and occupy their final position in the developing cortical plate. Understanding how cortical progenitors sequentially undergo fate restriction to produce these diverse classes of pyramidal neurons has always attracted great interest. Here, I summarize our latest findings which highlight how previously generated populations of neurons signal back to the progenitors instructing them to change their cell fate, thereby forming a cortical feedback loop. We then investigated how cortical progenitors respond to these feedback cues, thereby finally leading to a fate switch.

Introduction

Within the neocortex hundreds of different cell subtypes are arranged into specific neuronal networks that are engaged in receiving, processing and responding to complex stimuli. The neocortex consists of two major neuronal subtypes- excitatory projection neurons and inhibitory interneurons. While interneurons are born in the ganglionic eminence, cortical projection neurons arise from progenitors lining the dorsal aspects of the lateral ventricles. These progenitors give rise to the different cortical layers sequentially. During this process, later born neurons must migrate past earlier born neurons to occupy their final position in the cortex, thus giving rise to the 'inside first-outside last' cortex (Angevine and Sidman, 1961; Rakic, 1974). The various layers of the cortex show a high degree of heterogeneity with respect to their functions. This correlates to the fact that these neurons also show great variation with respect to their molecular and morphological characteristics (Fishell and Hanashima, 2008). However, such diverse groups of neurons are born from a relatively homogenous progenitor population. Thus, how progenitors undergo successive fate restriction to generate the entire repertoire of cortical neurons, has invited detailed study and research over the last two decades.

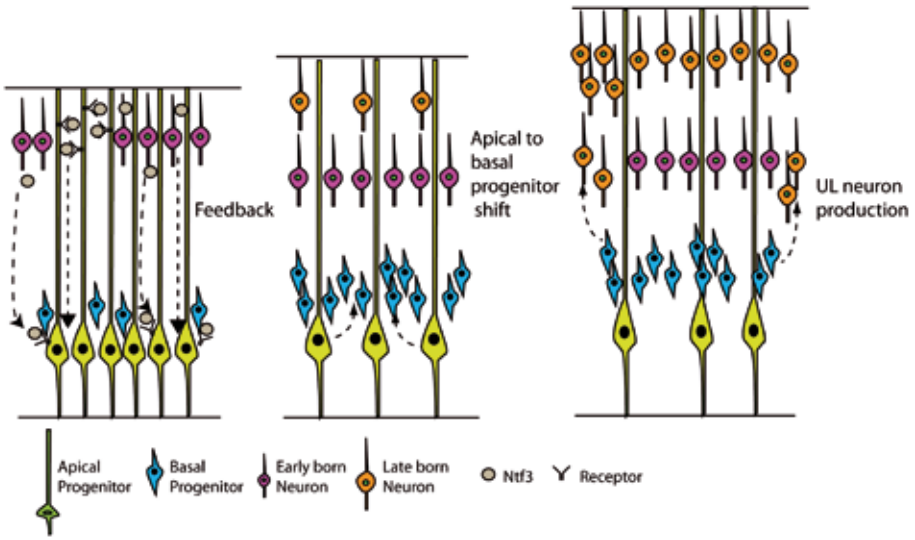


Fig. 1: Model depicting the two possible modes of Ntf3 mediated signaling. Receptors located along the radial glial process or on the cell body could sense Ntf3 released by postmitotic neurons. Such a signaling initiates the generation of basal progenitors, which in turn could lead to the expansion of UL neurons

Similar to all progenitor populations, cortical progenitors too loose their multi-potency over time. As development progresses, cortical progenitors become more restricted with respect to the types of cells they can produce. Individual cortical progenitors cultured *in vitro* can faithfully recapitulate the entire sequence of corticogenesis (Shen et al., 2006). This suggests that successive fate restriction is hardwired into a progenitor cell. Transplantation experiments showed that when younger cortical progenitors are transplanted into an older brain, they adapt to producing neurons appropriate to their new environment (Desai and McConnell, 2000). This would suggest that environmental cues also dictate the ability of a progenitor to produce one neuronal subtype over another. However, consistent with the progressive fate restriction theory, older progenitors when transplanted into an younger environment, do not adapt and continue to produce late born upper layer neuron (Desai and McConnell, 2000). Thus, collectively it is well established that while cortical progenitors undergo self-programmed fate restriction, en-

vironmental cues influence this process to a large extent. Work from our lab suggested that cortical postmitotic neurons signal back to the progenitors thereby forming a negative feedback loop (Seuntjens et al., 2009). We proposed that neurons within each cortical layer signal back to the progenitors, instructing them to change their fate and start producing the next layer of neurons. This would ensure that neurons of a particular kind are not overproduced, thereby laying the foundation for the generation of the different layers at the right time and in the right amount.

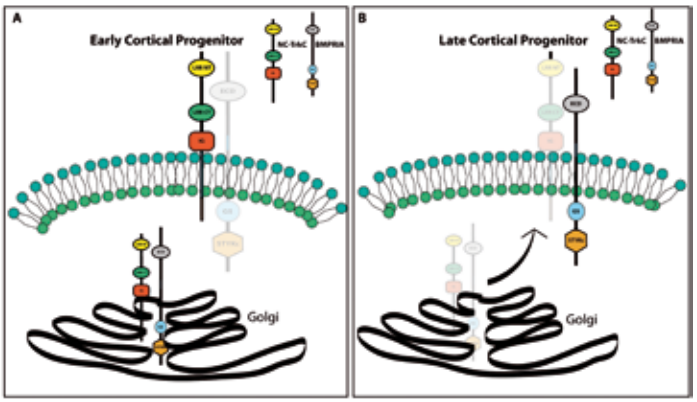


Fig. 2: Effect of miR-34c on its targets under physiological conditions and upon insults with increased expression of miR-34c leading to inhibition of target expression.

First insights into the mechanism underlying cortical feedback signaling came from the analysis of a knockout mouse of the transcription factor Sip1 (Seuntjens et al., 2009). Sip1 is expressed exclusively in postmitotic neurons of the cortex. Deleting Sip1 within cortical neurons had a profound effect on the timing of neurogenesis. In the Sip1 mutant, the entire process of neurogenesis was temporally shifted such that the production of deep layer neurons stopped earlier with a concomitant premature start of upper layer neurogenesis. Subsequently, neurogenesis ended prematurely giving way to gliogenesis (Seuntjens et al., 2009). The deletion of a postmitotic specific transcription factor leading to changes in progenitor fate switch lead us to hypothesize about a possible cortical feedback mechanism.

To identify molecules that were possibly involved in this signaling between postmitotic neurons and progenitors, we performed microarray analysis to compare gene expression profiles between wildtype and Sip1 mutant cortices. We then narrowed our search to genes encoding for secreted proteins, as these would be the most suitable for carrying out a feedback function.

Amongst many candidates, we studied the role of the neurotrophin- Ntf3, and its roles as a Sip1 downstream effector molecule that contributes to feedback signaling (Seuntjens et al., 2009; Parthasarathy et al., 2014). Neurotrophins are a class of small-secreted molecules that have profound influence on a large variety of neuronal functions. Each of the family members binds to a specific Tropomyocin related kinase (Trk) receptor with maximum affinity and with one or more of the other receptors to a lesser account. (Cordon-Cardo et al., 1991; Klein et al., 1991; Lamballe et al., 1991).

Using a variety of gain and loss-of-function experiments we demonstrated that Ntf3 indeed functions as a cortical feedback signal (Figure1, Parthasarathy et al., 2014). Over-expression of Ntf3 specifically in cortical postmitotic neurons, led to a premature shift from deep layer to upper layer neurogenesis, replicating the Sip1 phenotype. We further showed that Sip1 directly controls Ntf3 expression by binding to the *Ntf3* enhancer region (Seuntjens et al., 2009; Parthasarathy et al., 2014).

While from these studies we gained a better understanding of how postmitotic neurons influence the fate of cortical progenitors, we had little idea about how progenitors sense these feedback signals and respond to them. We started by studying the localization of the known Ntf3 receptor- TrkC, using *in situ* hybridization. Much to our surprise, we did not find any expression of the receptor in cortical progenitors. This led us to study the expression of the alternate splice variants of TrkC, which lack the intracellular autocatalytic kinase domain. These Non-catalytic isoforms (NC-TrkC) also have a distinct 3′ UTR, suggesting differential post-transcriptional control. Using riboprobes specifically targeting the truncated isoform, we observed that NC-TrkC was indeed expressed in the ventricular zone of the developing cortex. However, the most interesting feature about the expression pattern of NC-TrkC was that it mirrored the generation of deep layer neurons. NC-TrkC expression was highest within cortical progenitors when they were producing deep layer neurons and decreased sharply as they started producing upper layer neurons.

This drove us to study the role of NC-

TrkC in fate determination of cortical neuron identity. We used gain and loss-of-function experiments *in vivo* to study its role. These experiments showed that NC-TrkC over-expressing progenitors favored the production of deep layer neurons, while those in which NC-TrkC was down regulated were inclined towards producing upper layer neurons.

However, we still did not understand how NC-TrkC signals within cortical progenitors, since it lacks a kinase domain. In a completely serendipitous experiment, we observed that NC-TrkC physically interacts with the BMP class I receptor- BmprIA. We showed that the interaction between these receptors is important and necessary for cortical fate determination. We further went on to show that these receptors interact intracellularly and not on the plasma membrane. We have identified that the interaction of BmprIA with NC-TrkC prevents it from being trafficked to the plasma membrane, thereby retaining it within the secretory pathway, mostly within the Golgi apparatus (Figure 2). While we have still not answered how Ntf3 affects this interaction, we speculate that it disrupts the interaction by changing the ratio of plasma membrane NC-TrkC to that which is present within the secretory pathway. This novel and non-classical interaction between two membrane proteins away from the plasma membrane opens up exciting new insights into signaling within cortical radial glial progenitors that controls neuronal fate determination.

Srinivas PARTHASARATHY did his doctoral thesis in Victor Tarabykin's group, Max Planck Institute for Experimental Medicine Göttingen. During his doctoral thesis he moved to the Institute of Cell Biology and Neurobiology, University Medicine Charité Berlin. His doctoral thesis and oral defense were rated 'summa cum laude' by a team of internal and external reviewers. He defended his PhD thesis in June 2014.

Charité-Universitätsmedizin Berlin
Anatomy, Inst itute of Cell Biology and Neurobiology
Charitéplatz 1 Charité CrossOver
10117 Berlin

References

1. Angevine, J. B., Jr. and Sidman, R. L. (1961) 'Autoradiographic study of cell migration during histogenesis of cerebral cortex in the mouse', Nature 192: 766-8.
2. Cordon-Cardo, C., Tapley, P., Jing, S. Q., Nanduri, V., O'Rourke, E., Lamballe, F., Kovary, K., Klein, R., Jones, K. R., Reichardt, L. F. et al. (1991) 'The trk tyrosine protein kinase mediates the mitogenic properties of nerve growth factor and neurotrophin-3', Cell 66(1): 173-83.
3. Desai, A. R. and McConnell, S. K. (2000) 'Progressive restriction in fate potential by neural progenitors during cerebral cortical development', Development 127(13): 2863-72.
4. Fishell, G. and Hanashima, C. (2008) 'Pyramidal neurons grow up and change their mind', Neuron 57(3): 333-8.
5. Klein, R., Nanduri, V., Jing, S. A., Lamballe, F., Tapley, P., Bryant, S., Cordon-Cardo, C., Jones, K. R., Reichardt, L. F. and Barbacid, M. (1991) 'The trkB tyrosine protein kinase is a receptor for brain-derived neurotrophic factor and neurotrophin-3', Cell 66(2): 395-403.
6. Lamballe, F., Klein, R. and Barbacid, M. (1991) 'trkC, a new member of the trk family of tyrosine protein kinases, is a receptor for neurotrophin-3', Cell 66(5): 967-79.
7. Parthasarathy, S., Srivatsa, S., Nityanandam, A. and Tarabykin, V. (2014) 'Ntf3 acts downstream of Sip1 in cortical postmitotic neurons to control progenitor cell fate through feedback signaling', Development 141(17): 3324-30.
8. Rakic, P. (1974) 'Neurons in rhesus monkey visual cortex: systematic relation between time of origin and eventual disposition', Science 183(4123): 425-7.
9. Seuntjens, E., Nityanandam, A., Miquelajauregui, A., Debruyn, J., Stryjewska, A., Goebbels, S., Nave, K. A., Huylebroeck, D. and Tarabykin, V. (2009) 'Sip1 regulates sequential fate decisions by feedback signaling from postmitotic neurons to progenitors', Nat Neurosci 12(11): 1373-80.
10. Shen, Q., Wang, Y., Dimos, J. T., Fasano, C. A., Phoenix, T. N., Lemischka, I. R., Ivanova, N. B., Stifani, S., Morrisey, E. E. and Temple, S. (2006) 'The timing of cortical neurogenesis is encoded within lineages of individual progenitor cells', Nat Neurosci 9(6): 743-51.

A SIP of Ninein...

for the formation of neocortical projections *by Swathi Srivatsa*

Neuronal connections in the neocortex that relay and integrate information form the basis of our higher cognitive abilities. Transcription factors play an important role in controlling the trajectory of neuronal projections. Sip1 is an important transcription factor that regulates many different aspects of CNS development. In this study, using a series of *in vitro* and *in vivo* experiments performed in mice, we have shown that, Sip1 plays an important role in the development of neocortical projections. First, the alteration in cortical axonal tracts was examined in case of the Sip1 mouse mutant followed by a detailed analysis of the cell autonomous requirement of Sip1 within pyramidal neurons. Next, the effector molecule downstream of Sip1 was identified and its mechanism of action was also uncovered.

Our brain acts as the central processing unit of our entire being, helping in orchestrating, controlling and coordinating a myriad of complex tasks with seeming ease. Where different regions in the brain are specialized to perform different roles, the neocortex, which is the biggest and the most recently evolved structure in the brain, is responsible for all our higher cognitive functions, which include sensing our environment, generating motor output, language, thinking, creativity, problem solving and imagination (Geschwind & Rakic, 2013). This is made possible by the billions of neocortical neurons and their connections to different regions within the neocortex as well as with other parts of the central nervous system. Thus the correct formation of these neuronal circuits is of paramount importance for the regular functioning of the brain (Innocenti & Price, 2005).

It is extremely interesting to note that the axons of necortical neurons follow extremely organized and stereotypical pathways to reach their target. Due to this, axons of neurons projecting towards a similar target fasciculate together to give rise to thick axonal bundles or white matter tracts. Within the mammalian brain there are two types of tracts origina-ting from the neocortex, the commissural projections and the corticofugal connections. The commissural connections connect the two hemispheres of the brain. These include the corpus callosum (CC) that connects the two neocortical hemispheres and the anterior commissure (AC) that connects the two piriform cortices (Aboitiz & Montiel, 2003; Fame, MacDonald, & Macklis, 2011; Robin, 2006; Schüz & Preißl, 1996). The corticofugal projections on the other hand, are formed by axons that leave the neocortex and project to various sub-cortical structures. These include the corticothalamic tract (CT) and the corticospinal tract (CST) (Aronoff et al., 2010; Fame et al., 2011; Kennedy & Dehay, 1993; Molnár et al., 2007). Apart from these projections that arise from within the neocortex, the thalamocortical axons (TC) project from the thalamus into the neocortex and the hippocampal commissure (HC) interconnect the two hippocampi. Since all of these cortical projections act as conduits for the passage of information to and from the cerebral cortex, understanding how these connections are established forms an integral part of understanding brain function (Innocenti & Price, 2005).

In this research report I would like to focus on some of the work that I conducted during my PhD to better understand the molecular programs involved in the formation of these stereotypical neocortical connections. I have focused on a transcription factor called Sip1 (Smad interacting protein 1) and have studied its role in the formation of neocortical axonal pathways within the mouse brain. Sip1 exhibits a very interesting pattern of expression within the brain being expressed selectively in the postmitotic neurons of the neocortex (Miquelajauregui et al., 2007; Seuntjens et al., 2009). Examining the Sip1 mutant mouse brains through histological techniques and tract tracing using dye injections revealed that multiple axonal tracts were disrupted in the absence of Sip1. While commissural connections such as the CC and AC were absent in the Sip1 mutant, cortico fugal connections such as the projections forming the CST were also not formed. Interestingly, similar to the phenotype in mice, haploinsufficiency of the human SIP1 gene has been found to cause a neurological disorder called the Mowat-Wilson syndrome (MWS) which apart from being associated with severe mental retardation, motor deficits, epilepsy and craniofacial abnormalities is frequently accompanied by the agenesis of the CC, thus further linking the function and importance of Sip1 in the correct establishment of neocortical projections (D R Mowat, M J Wilson, 2003; Garavelli & Mainardi, 2007; Moal et al., 2007; Wilson et al., 2003).

As a first step in understanding the cell autonomous contribution of Sip1 in the formation of neocortical projections we used a technique called *in utero* electroporation together with Cre and lox p mediated gene deletion to establish a system where Sip1 could be deleted in a mosaic manner. This meant that we could study the behavior of the axons of these Sip1 negative neurons within a native, unaltered wild type brain. We observed that in the absence of Sip1, rate of axonal extension was severely retarded. While by embryonic day E18.5 (a day before birth of the pups) wild type axons have already crossed the midline forming the CC, Sip1 deficient neurons are unable to extend their axons through the callosal white matter tract (Fig 1A, C). Additionally, Sip1 negative axons also show a delay in the formation of ipsilateral axonal branches. While wild type pyramidal neurons that occupy the upper layers of the neocortex extend axonal branches to connect with deeper layer neurons, commencing four days after birth (P4), the Sip1 deficient upper layer neurons are unable to form such branches even 7 days after birth (P7) (Fig 1B, D).

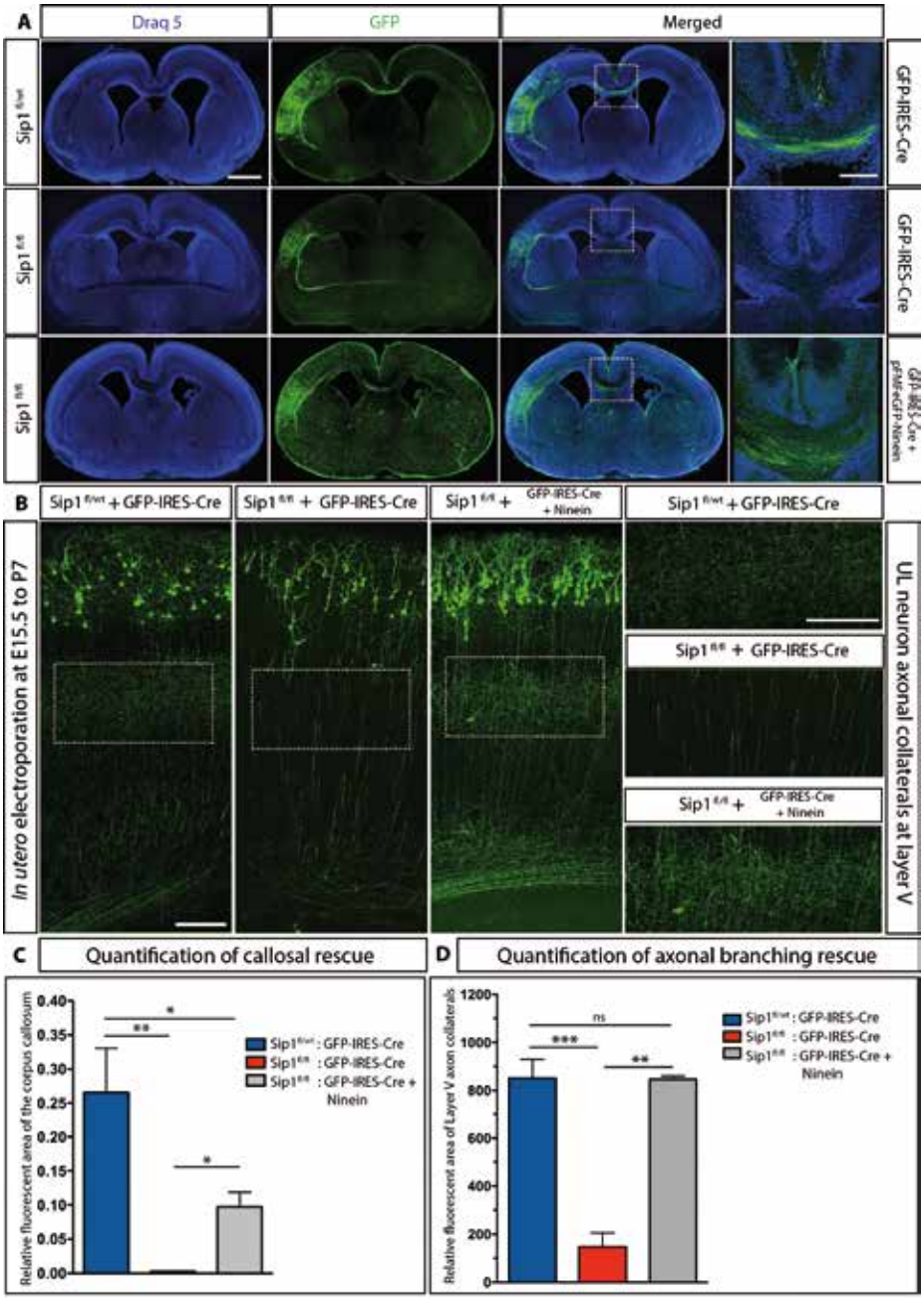


Fig. 1 (A): In the mouse brain, wild type callosal axons are able to cross the midline by E18.5 while Sip1 deficient axons are unable to do so. Reintroduction of ninein expression in these Sip1 deficient neurons restores CC formation. (B) Interstitial branches by upper layer neurons on deeper layer neurons are abolished on deletion of Sip1. The branching is also restored on ninein re-expression. (C, D) Quantification of the CC and interstitial branching indicating the extent of rescue.

In order to characterize the underlying mechanism involved in Sip1 mediated axonal extension and branching we performed microarray screening to identify probable target molecules that might be acting downstream of Sip1 in mediating these above mentioned effects. We zeroed in on a molecule called *ninein* because it was expressed in the developing neo-cortex, it showed a four-fold down regulation in the Sip1 mutant and the protein has been previously shown to be associated with microtubules, which being the building blocks of the cytoskeleton are directly linked to axonal growth and branching. To validate if ninein is indeed acting downstream of Sip1 and is a direct target, we per-

formed chromatin immunoprecipitation assay and luciferase assays which went to show that Sip1 binds directly to the enhancer region of the *ninein* gene and acts as a transcriptional activator.

We then introduce the expression of ninein in the Sip1 negative neocortical neurons and followed the rate of extension and branching of their axons. The rationale behind this experiment was that if ninein is indeed acting downstream of Sip1 to control axonal growth rate or branching, then re-expressing it in theses Sip1 deficient neurons would rescue the effect and restore wild type conditions. In fact, the experiment showed that these Sip1 deficient neurons with ninein expression were capable of crossing the midline by E18.5 forming the CC as well as forming interstitial branches (Fig1).

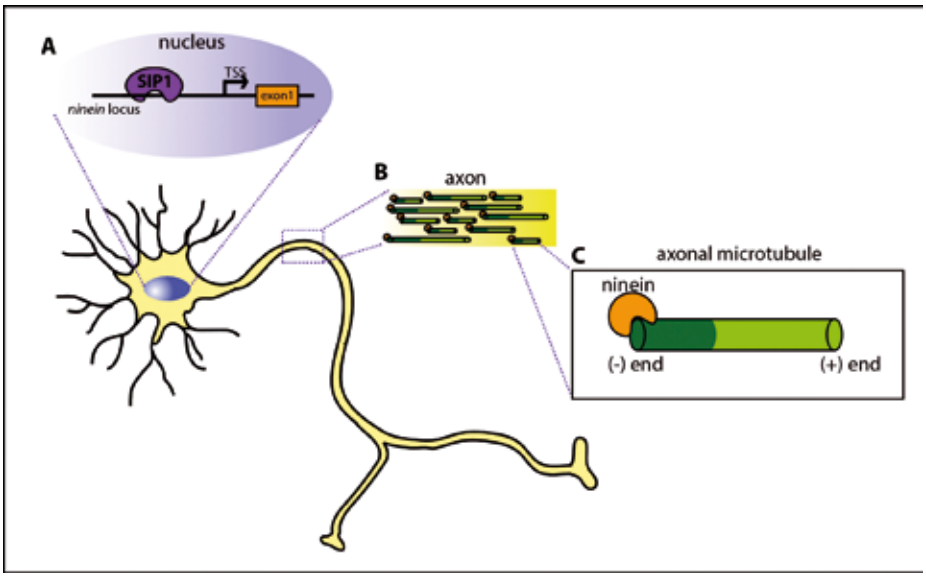


Fig. 2 (A): Transcriptional factor Sip1 is expressed in all postmitotic neocortical neurons and activates the expression of downstream molecule ninein. (B) Ninein binds axonal and dendritic microtubules (C) Within the cytoskeleton ninein confers microtubule stability and controls microtubule dynamics thus influencing axonal growth rate and branching.

We have, there after tried and uncovered the mechanism with which the molecule ninein might be exerting its influence over axon extension. We observed that when neuronal microtubules are challenged with a microtubule depolymerizing agent, in the presence of ninein they are much more resistant to breakdown. Additionally in the absence of Sip1 and hence ninein, the rate of growth of microtubules is diminished, which can be brought back to normal levels on reintroducing ninein. These experiments indicate that ninein is an important protein that helps stabilize microtubules and maintain a set rate of microtubule growth, which aid in axonal extension and branch formation.

In conclusion this work illuminates how molecular programs are intricately fine-tuned in the brain to control specific aspects of circuit formation and hence in the larger picture, CNS function. It helps to directly link transcriptional activity of Sip1 to sub cellular movements and modifications (Fig2). It could further help in understanding the molecular underpinnings of the MWS, the human disorder associated with SIP1. This work has been published in the journal Neuron - 2015.

Swathi SRIVATSA did her doctoral thesis in Victor Tarabykin's group, Max Planck Institute for Experimental Medicine Göttingen. During her doctoral thesis she moved to the Institute of Cell Biology and Neurobiology, University Medicine Charité Berlin. Her doctoral thesis and oral defense were rated 'summa cum laude' by a team of internal and external reviewers. She defended her PhD thesis in June 2014.

Charité-Universitätsmedizin Berlin
Anatomy, Inst itute of Cell Biology and Neurobiology
Charitéplatz 1 Charité CrossOver
10117 Berlin

References

1. Aboitiz, F., & Montiel, J. (2003). One hundred million years of interhemispheric communication: the history of the corpus callosum. Brazilian Journal of Medical and Biological Research = Revista Brasileira de Pesquisas Médicas E Biológicas / Sociedade Brasileira de Biofísica ... [et Al.], 36(4), 409–20.
2. Aronoff, R., Matyas, F., Mateo, C., Ciron, C., Schneider, B., & Petersen, C. C. H. (2010). Long-range connectivity of mouse primary somatosensory barrel cortex. The European Journal of Neuroscience, 31(12), 2221–33. doi:10.1111/j.1460-9568.2010.07264.x
3. D R Mowat, M J Wilson, M. G. (2003). Mowat-Wilson syndrome, (Table 1), 305–311.
4. Fame, R. M., MacDonald, J. L., & Macklis, J. D. (2011). Development, specification, and diversity of callosal projection neurons. Trends in Neurosciences, 34(1), 41–50. doi:10.1016/j.tins.2010.10.002
5. Garavelli, L., & Mainardi, P. C. (2007). Mowat-Wilson syndrome. Orphanet Journal of Rare Diseases, 2, 42. doi:10.1186/1750-1172-2-42
6. Geschwind, D. H., & Rakic, P. (2013). Perspective Cortical Evolution : Judge the Brain by Its Cover. Neuron, 633–647.
7. Innocenti, G. M., & Price, D. J. (2005). Exuberance in the development of cortical networks. Nature Reviews. Neuroscience, 6(12), 955–65. doi:10.1038/nrn1790
8. Kennedy, H., & Dehay, C. (1993). Cortical specification of mice and men. Cerebral Cortex (New York, N.Y. : 1991), 3(3), 171–86.
9. Miquelajauregui, A., Van de Putte, T., Polyakov, A., Nityanandam, A., Boppana, S., Seuntjens, E., … Tarabykin, V. (2007). Smad-interacting protein-1 (Zfhx1b) acts upstream of Wnt signaling in the mouse hippocampus and controls its formation. Proceedings of the …, 104(31), 12919–12924.
10. Moal, F. D., Wilson, M., Mowat, D., Collot, N., Niel, F., & Ã, M. G. (2007). ZFHX1B Mutations in Patients With Mowat- Wilson Syndrome, 28(4), 313–321. doi:10.1002/humu
11. Molnár, Z., Hoerder-Suabedissen, A., Wang, W. Z., DeProto, J., Davies, K., Lee, S., … Cheung, A. F. P. (2007). Genes involved in the formation of the earliest cortical circuits. Novartis Foundation Symposium, 288, 212–24; discussion 224–9, 276–81.
12. Robin, M. (2006). The Corpus Callosum as an Evolutionary Innovation. JOURNAL OF EXPERIMENTAL ZOOLOGY, 17(August 2005), 8–17. doi:10.1002/jez.b
13. Schüz, A., & Prei l, H. (1996). Basic Connectivity of the Cerebral Cortex and some Considerations on the Corpus Callosum. Neuroscience & Biobehavioral Reviews, 20(4), 567–570. doi:10.1016/0149-7634(95)00069-0
14. Seuntjens, E., Nityanandam, A., Miquelajauregui, A., Debruyn, J., Stryjewska, A., Goebbels, S., … Tarabykin, V. (2009). Sip1 regulates sequential fate decisions by feedback signaling from postmitotic neurons to progenitors. Nature Neuroscience, 12(11), 1373–80. doi:10.1038/nn.2409
15. Wilson, M., Mowat, D., Dastot-Le Moal, F., Cacheux, V., Kääriäinen, H., Cass, D., … Goossens, M. (2003). Further delineation of the phenotype associated with heterozygous mutations in ZFHX1B. American Journal of Medical Genetics. Part A, 119A(3), 257–65. doi:10.1002/ajmg.a.20053
16. Srivatsa, S., Parthasarathy, S., Molnár, Z., Tarabykin, V. (2015) Sip1 Downstream Effector ninein Controls Neocortical Axonal Growth, Ipsilateral Branching, and Microtubule Growth and Stability. Neuron. 85(5), 998-1012. doi: 10.1016/j.neuron.2015.01.018.

Master's class 2014/15

Reham Abdelaziz Egypt, BSc from German University in Cairo, Egypt

Martina Arends Germany, BSc from Carl Ossietzky University Oldenburg, Germany

Mar Bosch Queralt Spain, BSc from Autonomous University of Barcelona, Spain

Lucas Caldi Gomes Brazil, BSc from State University of Maringá, Brazil

Leonard Frederik Engels Germany, BSc from University of Cologne, Germany

Madhura Ketkar India, BTech from the National Institute of Technology Warangal, India

Albert Lehr Germany, BSc from Rheinische Friedrich-Wilhelms-Universität Bonn, Germany

Yi An Liao Taiwan, MD from National Yang-Ming University, Taiwan

Noam Nitzan Israel, BSc from Humboldt University Berlin, Germany

Myrto Panopoulou Greece, BSc from National and Kapodistrian University of Athens, Greece

M Sadman Sakib Bangladesh, BSc from University of Dhaka, Bangladesh

Erik Schäffner Germany, BSc from University of Würzburg, Germany

Sinem Meleknur Sertel Turkey, BSc from Bilkent University, Turkey

Jiyun Shin Republic of Korea, BSc from Seoul National University, South Korea

Lenka Vaculčiaková Slovakia, BSc from Charles University in Prague, Czech Republic

Dennis Vollweiter Germany, BSc from Georg August University Göttingen, Germany

Kanishka Waghmare India, BTech from the Indian Institute of Technology Madras, India

Rebecca Wallrafen Germany, BSc from Radboud University Nijmegen, The Netherlands

Lukas Weiss Italy, BSc from University of Cologne, Germany

Rashad Yusifov Azerbaijan, BSc from McGill University Montreal, Canada

Applications 2014/15

In the year 2014, the Neuroscience program received 324 applications from 57 countries.

Germany 41
other Western Europe 36
Eastern Europe 19
North America 10
Central/South America 13
North Africa 19
Central/South Africa 24
Asia / Near East 53
Central Asia / Far East 107
Australia 2

In the year 2015, the Neuroscience program received 363 applications from 59 countries.

Germany 35
other Western Europe 33
Eastern Europe 32
North America 17
Central/South America 19
North Africa 28
Central/South Africa 42
Asia / Near East 55
Central Asia / Far East 100
Australia 2

PhD projects started in 2014

Tamer Abdelaal
The role of glial cell differentiation phenotypes in demyelinating diseases of the PNS and CNS
Michael Sereda, Klaus-Armin Nave, Wolfgang Brück

Diego Giraldo Sánchez
Linking senses: rhodopsin's role in mechanoreception
Martin Göpfert, André Fiala, Manuela Schmidt

Sharlen Moore Corona
Role of oligodendrocytes in supporting axonal metabolic demands during cognitive processes
Klaus-Armin Nave, Mikael Simons, Swen Hülsmann

Erika Avendaño Guzmán
Evaluating the function of cytotoxic leukocytes in CNS autoimmunity
Wolfgang Brück, Klaus-Armin Nave, Alexander Flügel

Sindhuja Gowrisankaran
The significance of rab-connectin3 - endophilinA interaction for synaptic vesicle recycling
Ira Milosevic, Reinhard Jahn, Nils Brose

Pratibha Narayanan
Characterization of protein complexes involved in mechanosensation in vertebrates
Manuela Schmidt, Luis Pardo, Martin Göpfert

Chi Chen
Neural Correlates of Categorization Behavior in Auditory System
Robert Gütig, Tim Gollisch, Alexander Gail

Florentin Masurat
Control of sleep through sleep-active neurons
Henrik Bringmann, Ralf Heinrich, Nils Brose

The Doctors of 2014

Dorota Badowska
Schizophrenia Risk Factor Tcf4 and Gene x Environment Interaction in Mice
Moritz Rossner, Hannelore Ehrenreich, André Fischer

Srinivas Parthasarathy
Molecular Control of Pyramidal Neuron Fate Determination in the Developing Neocortex
Victor Tarabykin, Judith Stegmüller, Till Marquardt

Nicolas Snaidero
Mechanisms underlying the CNS myelination: A molecular and morphological analysis of the wrapping process
Mikael Simons, Uwe-Karsten Hanisch, Holger Stark

Wan Ilma Dewiputri
An Exploration of Real-time Functional Magnetic Resonance Imaging Neurofeedback in Cognition
Jens Frahm, Stefan Treue, Michael Waldmann

Pooja Rao
Coding and Non-Coding RNA in Age-Associated Memory Impairment and Alzheimer's Disease
André Fischer, Wolfgang Fischle, Judith Stegmüller

Swathi Srivatsa
Transcriptional control of the establishment of neocortical projections in the mammalian telencephalon
Victor Tarabykin, Judith Stegmüller, André Fischer

Hung-En Hsia
Roles of HECT-Tpye Ubiquitin E3 Ligases of the Nedd4 and WWP Subfamilies in Neuronal Development
Nils Brose, Judith Stegmüller, Andreas Wodarz

Natalia Revelo Nuncira
A novel membrane-binding probe for the morphological and molecular characterization of synaptic vesicle recycling pathways
Silvio Rizzoli, Mikael Simons, Tobias Moser

Diana Urrego-Blanco
Dynamics of Kv10.1 expression through the cell cycle of cancer and non-cancer cells
Luis Pardo, Tobias Moser, Detlev Schild

Fitting into new shoe in the Netherlands

by Aaron Wong

When I went to Germany seven years ago, I did not have the slightest clue where I would end up next. Two years ago when I defended my thesis, I was still wondering whether I would still continue with science or not. What I did know, after staying several years in the dry Göttingen, is that I was hoping to be closer to water in the next position. That part did come true, as I am now at the largest port in Europe.

Surely, Rotterdam is a much bigger city than the little town of Göttingen. Not that you will bump into a colleague every Saturday at the city center, and who needs to be out on Saturday anyway? I have finally got rid of the "stock-up-for-Sunday-or-you-will-starve" curse. What is more, everybody speaks English! What a relief after failed attempts in trying to get by with German with an accent.

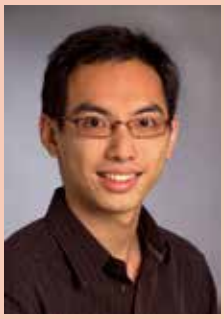
Science goes on, and the tree of wisdom grows on. (Yes, mine has not jumped out of the window yet, which allegedly happened to some others.) After learning about the development of cochlear hair cells, I decided to leave the auditory periphery and venture deeper into the auditory midbrain. Now at the Erasmus MC, I try to decipher how and which behaviorally relevant parameters are extracted by the inferior colliculus. I still remember how one professor in Göttingen questioned "what is the point of studying brainstem nuclei in the auditory system? They are like the retina, just scattered within the brainstem." I couldn't answer at the time, but I think it is precisely the reason it allures me. Decades of research on the much more accessible retina, and people are still studying how it works.

Being in a new environment is not easy, especially as a postdoc. Getting my own funding via fellowship was exciting, while the experience and results from my PhD certainly helped a lot, not to mention the help from successful predecessors from the program. Before starting out, I often heard that becoming a postdoc implies the magical switch of expectation in which you are now supposed to know everything. Interestingly, I found myself trapped into an even stranger dichotomy between that and the label of a "fresh student". As I was pampered and instructed in histology by experienced technician, a PI in the department asked, "You are a postdoc, right? Why are you taking a course?" I guess that captures the mysterious sandwich status of a postdoc.

Switching to a small group means I need to be more proactive in seeking out help. It is not uncommon to find long-forgotten equipment which nobody knows how to use. It also means I have to handle slightly more on the administrative and bureaucratic side. That is something that I am slowly learning. On the upside, I am always excited to learn new things that I do not know, and also amazed at how things I learnt from my PhD helped me in unexpected ways. The ample opportunities for supervising lab rotation and master students in Göttingen definitely helped me build confidence in taking up my own students now. Know-how in things such as image analyses, programming and micro-dissection do come in handy for *in vivo* imaging. I must also thank my oral examiners in the IMPRS master program for brutally slaughtering me, and thus motivated me in lear-

ning all the basic principles behind techniques I am using.

Continuing my scientific journey in the new, hopefully not wooden, schoen has so far been challenging yet exciting. Let us see where it will bring me next.



Aaron WONG did his doctoral thesis on calcium signaling during exocytosis in hair cells in Tobias Moser's group, Dept. of Otorhynolaryngology, University Medical Center Göttingen. He was awarded a doctoral scholarship by the Croucher Foundation in Hong Kong and a Georg-Christoph-Lichtenberg Scholarship in 2010. He defended his PhD thesis in May 2013.
He was awarded a Marie Sklodowska-Curie individual Fellowship in 2015 to pursue his studies as a postdoctoral fellow in Rotterdam.

Department of Neuroscience (Prof. J. Gerard G. Borst)
Synaptic transmission in the auditory brainstem and midbrain
Erasmus MC
Wytemaweg 80, NL-3015 CN Rotterdam
P.O.Box 2040, NL-3000 CA Rotterdam

My pathway to independence:

from being mentored as a student in Göttingen to mentoring students in New York *by Jayeeta Basu*

I have recently started my own laboratory and independent research program at the Neuroscience Institute at New York University School of Medicine. The journey to get here has been truly exhilarating. And it all began when I set foot in a small but grand and historic university town nestled in the heart of Germany, twelve years ago on a rainy mid-September afternoon. Göttingen, the city of Gänseliesel, boasting of the largest number of Nobel laureates amongst all European cities and home to the 281 year old Georg August University, several Max Planck Institutes and last but not the least Cron & Lanz confectionary was also my home for two of my most formative years as a neuroscientist.

I grew up in Calcutta, India and went to Presidency College, one of the country's oldest institutions of western education, to earn my bachelor's degree in Physiology (B.Sc. Hon.'s). A whole year of our BSc curriculum was dedicated to neurophysiology and biophysics and this is where I developed my fascination for neuroscience, specifically synaptic physiology. While I was away on a college field trip in central India, where we were studying the anthropometric and cardiovascular physiology of coal miners and a native tribal hill population, the German DAAD education fair was held in Calcutta. My mother offered to go and sample the offerings of this fair and chanced upon the International Max Planck Research School, Göttingen booth. This is what got me started on the path of becoming a neuroscientist. I applied to the Neuroscience MSc/PhD program in Göttingen and was invited to sit for the admission test in New Delhi. The date of the test fell during my college BSc written final exams and the IMPRS program was surprisingly accommodating to send the test to the Goethe Institute in Calcutta, so I could take the test in their library, without hindering my exam schedule. Things moved fast after that, with the call for an in person interview to Göttingen in May 2002. My first trip abroad fell right in the middle of the university practical final exams. This time, our Physiology head of the department, Dr. Chandan

Mitra came to my rescue. He appealed to the University of Calcutta and shifted our college's entire practical block to two weeks later so I could go to Germany and interview for the program. I do remember distinctly the interviews at the Deutsche Primatum Zentrum (DPZ) in Nord Kampus and the neurophysiology department in Humboldtallee with Profs. Fuchs, Richter, Schild, Missler and Moser, being housed in the Studentenwerk youth hostel, my first meal at a German Mensa – one of many hundreds in the future. And of course the sheer joy of being admitted to the program!

Neurowissenschaft: The neuroscience graduate program in Göttingen was and continues to be excellent. Unlike most European and UK based MSc/PhD programs it is modeled on US graduate program featuring coursework, lab rotations and qualifying exams. My tryst with formal coursework and hands on training in neuroscience began with our theoretical and practical classes spread across the Max Planck Institute for Experimental Medicine, Klinikum, University Medical Center, DPZ, Zoology department and even the Max Planck for Fluid Dynamics. A small class size, with intensive lectures by experts in the field, exposure to workshops, seminars, presentations and tutorials comprised just the right ingredients to form a rock-solid foundation in Neuroscience. This is the underpinning upon which my career as a neuroscience researcher and faculty was built upon.

I came in to the Neuroscience program with a broadminded research focus and tried to get a flavor for diverse techniques and research topics during my rotations. We had the benefit to choose from a wide array of top-notch labs that employed path-breaking approaches in Neuroscience. My first rotation was at the European Neuroscience Institute with Dr. Fred Wouters. We were exploring how phosphorylation of the Alzheimer's protein Tau impacts tangle formation using molecular biology and fluorescence recovery after photobleaching (FRAP) imaging. It was fun working in Fred's group and getting to know the other graduate students, post-docs and group leaders in the ENI community. The second rotation was in Prof. Jens Frahm's lab up the hill at the Max Planck Institute for Biophysical Chemistry. It was a shared rotation with two of my classmates Ben Cooper and Katharina Anton-Erxleben; we had several theoretical lectures on fMRI within the rotation and then served as each other's subjects in the MRI scanner. It was quite fascinating to get these high-resolution functional images of BOLD activity in our visual cortices during stimulus presentations.

With Prof. Erwin Neher and Dr. Ira Milosevic

Mathematicians and physicists heavily populated the department and it was a unique experience catching a glimpse of their world.

Learning patch clamp electrophysiology during my third lab rotation with Dr. Rosenmund at the Max Planck Institute for Biophysical Chemistry was a technological revelation for me. The department of Membrane Biophysics headed by Prof. Erwin Neher was the birth-place of this technique and it is with utmost pride that I can claim that lineage. Christian literally taught me with his own hands how to record intracellular currents by patch clamping the hippocampal neurons. He would initially perform the experiments with me. This left a strong impression on me through the years and I value this as being an important part of training my own graduate students. During this rotation, I characterized the Ca^{2+} dependence of vesicular release probability and how pre-synaptic protein Rab3 regulates short-term plasticity. We published this work as part of a Rab3 knockout mouse study in collaboration with Dr. Thomas Südhof (Schlüter, Basu et al. 2006, Journal of Neuroscience). I spent the next four years in the Rosenmund lab first in Göttingen followed by Baylor College of Medicine, Houston studying the molecular mechanism of neurotransmitter release in mouse hippocampal cultured neurons.

In 2003, soon after I started my PhD thesis project at the Max Planck Institute (MPI) for Biophysical Chemistry, my primary advisor Dr. Rosenmund moved his lab from Germany to Baylor College of Medicine in Houston, Texas. I stayed on in Dr. Erwin Neher's research group at the MPI to finish a

Master's degree from the Max Planck Neuroscience program. My MSc thesis research at MPI-BPC examined biophysical methods to quantify vesicular release kinetics and explore how synaptic vesicles overcome the energy barrier for fusion and release neurotransmitter spontaneously or sucrose induced and Ca^{2+}evoked stimulation. Being in Prof. Neher's department and interacting with him and the other groups was a privilege and great learning experience. The weekly group meetings, the invigorating scientific discussions, journal clubs were some of the highlights of my time there. One thing I remember from Prof. Neher is the amount of attention to detail he dedicated to looking at our electrophysiological traces and the stress he laid on doing the right and meticulous control experiments. These aspects of my training have shaped how I have been conducting my own research since.

With Drs. Ben Cooper, Zaved A. Khan and Fernando Rodriguez at the Gänseliesel, Göttingen

In 2004, I enrolled in the Neuroscience Graduate program at Baylor College of Medicine (BCM), and started my PhD thesis in Dr. Rosenmund's lab. All my curricular coursework from Göttingen were at par with that of the BCM graduate program and my credits got transferred over. As Dr. Rosenmund's first graduate student at BCM, I worked very closely with him and learnt a great deal from him, from building an electrophysiology setup, to developing new assays for quantifying synaptic release, to writing our first scientific paper together. My PhD research on synaptic vesicle priming and short-term plasticity was highly collaborative and interdisciplinary combining electrophysiology, genetics and fluorescent imaging. It culminated in two first- and one co-author research papers. My first study performed in close collaboration with Dr. Jose Rizo Rey's lab at UT Southwestern, Dallas, identified the minimal functional domain of the presynaptic protein Munc13 for its essential role in synaptic vesicle fusion (Basu et al. 2005, Nature Structural and Molecular Biology). Next using a biophysical method we had devised during my MSc to quantify the rate of synaptic vesicle release in Munc13 knock in mutant mice, I uncovered a regulatory role of Munc13 in vesicular release kinetics (Basu et al. 2007, Journal of Neuroscience). Finally, I performed a structure-function based mapping study of the Munc13 N-terminus using several loss and gain of function point and deletion mutations. I identified an inhibitory region in Munc13 that gates vesicular release efficacy through its interaction with the active zone protein Rab Interacting Molecule (RIM). A Cold Spring Harbor Laboratory imaging course during my PhD, in 2006, opened my eyes to all the innovative technologies for quantitative fluorescent microscopy of cells and molecules. Using these insights, I designed a novel FRET based Munc13 biosensor probe to detect activity-dependent presynaptic plasticity. I realized that moving forward, I wanted to rigorously dissect and manipulate activity in neural circuits to study how changes in information flow resulted in the formation of long-term memories and learning behavior. I was convinced to pursue such a research goal, I could not be limited by techniques and had to go where the science took me. I decided to follow these objectives at Columbia University, under the mentorship of Dr. Steven Siegelbaum, whose research I had been closely following since 2006, when I had first hosted him as a seminar speaker at BCM.

Since the 1950s, the hippocampus has been extensively studied as the seat of learning and episodic memory, our knowledge of people places, objects and events. However intact connections with the entorhinal cortex, an adjacent area that acts as a hub for routing information about the outside world, are crucial for these functions and for spatial navigation. During my post-doctoral research with Dr. Siegelbaum at Columbia University, I worked on how precisely timed activity of glutamatergic and GABAergic inputs from the entorhinal cortex to CA1 neurons, the principle output source of the hippocampus can enhance information flow within the circuit through an input timing-dependent plasticity. In the Siegelbaum lab, I have learnt, established and implemented several avant garde approaches in neuroscience, including electrophysiology coupled with high-resolution two-photon Ca^{2+} imaging, optogenetics and pharmacogenetics and behavioral analysis. One of my most exhilarating accomplishments as a patch clamp electrophysiologist is performing long-term

intracellular recordings from extremely thin sub-micron dendritic processes of mouse CA1 pyramidal neurons (Basu et al., Neuron, 2013; Kupferman, Basu et al., Cell, 2014; Basu et al., accepted Science, 2015). Using somatic and dendritic recordings with functional mapping approaches, I identified two kinds of GABAergic circuits that are important for dynamically regulating excitation in the hippocampus. The first is a local microcircuit that is activated by excitatory inputs to provide the major feed-forward inhibition to CA1 pyramidal neurons (Basu et al., 2013, Neuron). Modulation of somatic inhibition from these interneurons is required to increase the magnitude of long-term plasticity in CA1 pyramidal neuron soma. The second is a 'disinhibitory' GABAergic long-range projection circuit from the entorhinal cortex to the hippocampus (Basu et al. 2015 accepted Science). These inputs suppress local hippocampal dendritic feed-forward inhibition at a precise time interval, thereby disinhibiting CA1 pyramidal neuron excitation. This disinhibition triggers dendritic spikes and long-term plasticity. Furthermore, *in vivo* two-photon imaging in awake behaving mice, showed that contextual sensory stimuli trigger Ca^{2+} activity in these long-range GABAergic projection inputs from entorhinal cortex to CA1. Finally pharmacologenetic silencing of the activity of these inputs during contextual fear learning impairs the precision of encoding contextual information.

The past three months have been thrilling in populating and setting up my own laboratory at New York University. We are a growing group, soon to be of six members – a graduate student, two postdocs, two technicians and I. I hope to transfer the good experiences I have had in being mentored as a graduate and post doc to my own mentees. The idea is to be a close-knit, highly collaborative group, where all of us work together towards a common overarching research goal: ***How does the brain encode and recall memories and produce adaptive behaviors based on past experience?***

We have chosen to address this through studying how hippocampal memory information may shape the processing and perception of sensory information in the cortex. Spatial navigation is a critical brain function that requires neural circuits to form a representation of the environment. Both the hippocampus and entorhinal cortex have cells that show increased firing at distinct locations in space during exploratory behavior. The discovery of these "nerve cells in the brain that enable a sense of place and navigation" was recently recognized with the Nobel Prize in Physiology and Medicine (2014). There has been great theoretical interest in the field to understand how the properties (fields, firing rates, patterns) of these cells are shaped. For example, modeling suggests that the distinct firing patterns in entorhinal cortex require inputs from hippocampus. My laboratory is in a position to put some of these ideas to the test experimentally based on the ability to electrically and optically monitor activity in acute brain slices and in brains of head-fixed awake behaving mice.

The hippocampus receives information about space and contexts from the entorhinal cortex. Once processed, the hippocampus feeds back the information to the entorhinal cortex. Is the hippocampal feedback relevant for maintaining the native firing properties of entorhinal cortex neurons? To address this we are first characterizing the much elusive connectivity of inputs that feedback from the hippocampus to the entorhinal cortex. We are using functional mapping approaches where we can genetically target the hippocampus to entorhinal cortex pathway and probe using electrical recordings which neurons in the entorhinal cortex receive the hippocampal inputs. We will further investigate how these hippocampal inputs can influence cellular activity and flow of sensory infor-

With my classmates Dr. Fernando Rodriguez and Dr. Dragana Jancic at rajesh and my wedding in Calcutta.

mation in the entorhinal cortex. Our research will fuel our understanding of how the mammalian brain builds a map of the environment.

Gesellschaft, Gemeinschaft, Freundschaft: A major part of my positive experience in Göttingen comes from the people interactions – the effort the program put in to integrating us international students into the German way of life, learning the language and sharing each other's cultures through organized events. I learnt German in high school back in Calcutta, which did give me a head start conversing with my Mitbewohner in Rosenbachweg. As a member of Sabine Ihlenfeld's German language class at Uni Göttingen, I learnt the correct German etiquette of never using a knife while eating potatoes, of always being dot on time punctual for a dinner invitation but how it is acceptable to be late at a casual party. We also visited her place in the countryside to learn how to make Zwiebelkuchen. I remember organizing the first poetry night with my classmates Dragana and Primoz in the library of MPI-EM. These culture nights introduced by the program were a huge success and I cherish those memories dearly. The interactions at class or lab as well as outside socially with my fellow classmates lead to several life-long friendships, bound by a common thread – being proud alumni of the IMPRS Göttingen. Twelve years since the time we met I still see some at least once a year, we have shared many a special occasions in life – including my grand Indian wedding in Calcutta in 2007 to thanksgiving at our place in New York in 2014.

Jayeeta BASU did her Master's thesis in Christian Rosenmund's group at the Max Planck Institute for Biophysical Chemistry. She started her PhD thesis in April 2004 in the Rosenmund group in Göttingen and moved with the lab to the Baylor College of Medicine where she graduated in 2007.

Jayeeta Basu, PhD, Assistant Professor,
NYU Neuroscience Institute,
Department of Neuroscience and Physiology,
New York University School of Medicine

Beyond Academia - Making the transition

by Pooja Rao

In January 2014, I graduated from the Neuroscience program and moved from Göttingen to The Netherlands. At the same time, I took my first steps away from academia towards a career in the industry. After doing a brief postdoc stint at a biotech company in Leiden, I currently work at Excerpta Medica, a medical communications consultancy in Amsterdam. In my role as medical publications manager, I work with pharmaceutical companies to help communicate their clinical research.

Long before I graduated, I realized that I preferred reading, writing, and thinking about research to working at the bench. I was also keen to work more closely with human clinical research, and to learn about its commercial side. While working on my PhD at the ENI, it often seemed as if the main goal of research was publishing papers, and that the science world was largely dominated by professors, universities and research institutes. I later learned that this is far from true, especially for clinical studies, and that there is plenty of science outside academia. While I was surprised to see that plenty of scientific research takes place outside universities and research institutes, this also meant that there was a world of interesting career opportunities in pharmaceutical companies, biotech, publishing and many other industries. Further, there are several non-research jobs that fit very well with the skills one acquires during a PhD.

While I was looking for positions in the industry, I had the opportunity to learn

which of these skills I could take with me. I found that analyzing data critically, visualizing it and presenting my work, were perhaps the most transferable skills from my time in the Fischer lab at the ENI. By the time I had defended my PhD thesis, I had made so many different kinds of presentations in the form of lab seminars, journal clubs and retreats that it had become second nature to me to use data to build a story and to present it in a concise, engaging manner. Equally handy were the numerous tips on writing, presentation, and communication that I had picked up from GGNB soft skill courses. Finally, the large number of alumni that the IMPRS has accumulated around the world, and who have chosen various career paths was also a helpful source of information. I was able to locate an ex-Neuro in most jobs that I was considering, and pleasantly surprised by how willing they were to help out, share their experience or give advice.

Moving away from Göttingen, I was keen to find another equally multicultural place to live in, and preferably a larger city. I found both of these in The Hague in The Netherlands. Even after the relatively international environment of the IMPRS, I am amazed by how diverse and multilingual my new city is. Since the country is so small, commuting to work is a way of life in Holland. For most of my colleagues, like me, the city they live in is not the same city they work in. It's quite common to take the train to work every day and I commute from The Hague to Amsterdam daily, using the time to read or to catch up on work.

For my first job as a 'postdoc in the industry' I worked at a small biotech company that specializes in next-generation sequencing. In addition to my own bioinformatics research projects, my role was to analyze genome and transcriptome data for clients - mostly scientists doing clinical and preclinical research. Working with university scientists from within a commercial organization gives you a unique perspective on the similarities and differences between the two and on the motivations that drive academic research versus those that drive commercial R&D. Working at a small company also meant that I got to see many sides of the business, doing a bit of project management, setting up new research collaborations and even helping out with sales and marketing.

Soon, I decided to move into a job where I could write about research rather than do it myself. The focus of my current work is performing literature searches, data analysis, writing and editing. I spend a lot of time in meetings with clients and colleagues. My projects tend to be shorter, lasting weeks to months, and have clearly defined goals and tight deadlines. The pace of work can be quite hectic and since clients are based across the globe, there are tele- and web-conferences on a daily basis. I find it satisfying and motivating to have concrete time-bound goals and to achieve them. My work usually spans a broad overview of a therapeutic area or disease rather than a being a dive deep into a molecule, pathway or synapse. This means that I'm always learning new things. One of the most interesting parts of my job is keeping on top of new therapies as they pass through clinical trials and are brought into practice.

All in all, I enjoy my new job tremendously, but it's too soon to say what the future will bring. I learned a lot during my years in Göttingen, and a lot more in the time since I graduated and moved out of academia, but I am sure that there are many more new experiences to come. It's been an interesting journey so far and I look forward to seeing what lies ahead.

Pooja RAO did her doctoral thesis in André Fischer's group at the European Neuroscience Institute in Göttingen. She was awarded a stipend of the European Neuroscience Campus Network and defended her PhD thesis in October 2013.

Excerpta Medica Amsterdam
Apollo Building
Herikerbergweg 17
1101 CN Amsterdam
Netherlands

So – why did you do this…?

by Benjamin Wilhelm

This is by far the question I have heard most in the past year and a half and in the following paragraphs I will try to illustrate why…

But let me start from the beginning: I have done my entire university studies in Göttingen. Starting with my undergrads in Biology and transferring to the Neuroscience program for my Master's and PhD. For the latter I was lucky enough to join the lab of Silvio Rizzoli at the ENI. To be frank, I think I had quite an unusual PhD as I was spoiled with a great supervisor, a very promising and straight forward project and awesome colleagues in the lab. I am very grateful for this because I know that not many of my peers can actually tick all these boxes. When I graduated in April 2013 I decided to take an early sabbatical to travel around the world for almost an entire year together with my wife before deciding what to do next.

We had planned the trip for at least two years and hence were thoroughly excited when we finally got going. We started our trip with three months in Africa where we climbed Mt. Kilimanjaro and did an overlanding tour from Uganda all the way down to South Africa via Kenya, Tanzania, Zanzibar, Malawi, Zambia, Zimbabwe, Botswana and Namibia. If we had to pick our personal highlights it would probably be the Balloon-Safari over the Masai Mara in Kenya (seeing millions of animals migrating) and hiking to the Mountain Gorillas in the forests of Uganda – simply breathtaking! Our next stop was Moscow where we got on the Trans-Mongolian train to take us East. Two stops (Lake Baikal and Ulaanbaatar) and countless hours in the train later we arrived in Beijing. After a few more weeks in China we moved on to South East Asia were we spend the next 4 months exploring Vietnamese food, Laotian jungles, Cambodian ruins, Thai beaches, Indonesian dive sites and the friendliness of the people in Myanmar. During this time we also hopped over to India for two weeks to attend the wedding of our good friends Mrinalini and Raunak (and saw a lot of familiar faces…). Our next flight brought us to New Zealand. Here we hired a camper and cruised both the north and the south island. From beautiful beaches to snow-capped mountains, from an incredible wildlife to warm hearted Kiwi's – NZ really has it all! After such an amazing time it was of course difficult to move on but we still had one gem on our list: Mexico! Mexico spoiled us with pristine beaches, whales, baby turtles, ancient ruins and fabulous food and it was certainly a worthy highlight to end the trip.

Upon returning from the big trip I decided to finally leave science for good and to start as a business consultant. After such a long time "on the road" it was of course quite a change returning to Germany in Mai 2014, but we were also ready to start the next adventure: new city and job. We moved to Hamburg where I started with McKinsey in July. When you start at McKinsey without a business background the firm provides you with a crash course (mini MBA) on economics and business administration. Although the mini MBA provides you with thorough business knowledge I was still quite nervous when I got staffed on my first project – how could I possibly add value? But believe it or not after a few days into the project I was amazed how much one can actually do. Being critical and asking the right questions, dissecting a problem to get to its core and finding creative

solutions to solve it are essential skills and I had learned all of this in the past years in Göttingen. Equipped with this it is secondary how much knowledge you have about economics – this will come with time and actually much faster than one would think. So how do I feel after the first 6 months? I have been challenged more than ever before and the "learning curve" has most likely only been steeper in the first couple of years of my life. Is it stressful? I'd call it intense! Do I like it? Yes, it is exactly what I was looking for!

In a GGNB class on writing for the public I have learned that at the end of an article it is good practice to close the narrative loop and get back to where you started. In this sense: why have I done it? Well for the world trip – I just had the feeling I needed an inspirational and mental break before I would start the next phase of my life and I most certainly got what I was looking for! For the second part – I joined McKinsey because they offer me a unique opportunity to challenge me in ways science could not. Looking back I would lie if I'd say that I did not miss my old friends, my supervisor and the lab, the coordination team and the ENI as well as Göttingen as a whole (I spent 8 years there!). But as I said it was time to move on, to learn and see something new and even in rough times I have not yet regretted it and am still enjoying the new adventure.

Benjamin WILHELM did his doctoral thesis in Silvio Rizzoli's department, STED-Microscopy of Synaptic Functions, European Neuroscience Institute Göttingen (ENI-G). He was awarded a GGNB Excellence stipend in 2010 and a Boehringer Ingelheim Foundation stipend in 2011. He graduated in March 2013.

McKinsey & Company, Inc.
Am Sandtorkai 77
20457 Hamburg
Germany

Honors & Awards

Creutzfeldt Award

Honors and Awards

Students

The following doctoral students have been awarded a GGNB Excellence Stipend:
Tanvi Butola (2013),
Ricardo Merino (2013),
Florentin Masurat (2014),
Julio Santos Viotti (2014)

Junior Group Leaders

Henrik Bringmann:
ERC Starting Grant
Marion Silies:
Emmy Noether independent junior research group funding, Schilling Prize of the German Neuroscience Society (NWG)

Faculty

Stefan Hell:
Nobelprize for Chemistry,
Kavli Prize
Reinhard Jahn:
Heinrich-Wieland-Prize
Tobias Moser:
Leibniz Prize
Silvio Rizzoli:
ERC Consolidator Grant
Mikael Simons:
Alzheimer Research Award

Creutzfeldt PhD Prize

The Creutzfeldt PhD Prize is awarded for the best PhD thesis in memoriam of Prof. Dr. Otto Detlev Creutzfeldt, founding director of the department of Neurobiology at the Max Planck Institute for Biophysical Chemistry in Göttingen. The prize has been 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. In 2011 for the first time 2 winners were selected for the Creutzfeldt Prize. Traditionally, the award ceremony is part of the official opening of the NEURIZONS Symposium and will take place on 26 May 2015 in the presence of Gregor Eichele (Dean of the IMPRS for Neurosciences), Denise van Rossum (Sartorius stedim AG) and Mary Creutzfeldt, who will present the book 'Cortex Cerebri' written by her late husband Otto Creutzfeldt to the awardees. The award also includes a gift of 500,-€ which is sponsored by the Göttingen company Sartorius stedim biotech AG, which has generously supported the Neuroscience program since its foundation.

Dr. Irina DUDANOVA (2007)
Max Planck Institute of Neurobiology
Department of Molecular Neurobiology
Am Klopferspitz 18
D-82152 Martinsried

Dr. Henry LÜTCKE (2009)
Brain Research Institute
University of Zurich
Winterthurerstrasse 190
8057 Zurich, Switzerland

Dr. Ioanna BETHANI (2011)
Goethe-Universität Frankfurt
Institute of Cell Biology and Neuroscience Cluster of Excellence Molecular and Cellular Neuroscience Macromolecular Complexes (CEF)
Max-von-Laue-Str. 9,
60438 Frankfurt am Main

Dr. Stephan JUNEK (2011)
Max Planck Institute for Brain Research
Neural Systems and Coding Group
Deutschordenstraße 46
60528 Frankfurt am Main

Sadim JAWHAR, Ph.D. (2013)
Biomedical Research Institute
Doha, Qatar

Dr. David OWALD (2013)
Center for Neural Circuits and Behavior
Oxford University,
United Kingdom

Dr. Natalia REVELO NUNCIRA (2015)
Dept. Neuro- and Sensory Physiology
University Medical Center
Humboldtallee 23
37073 Göttingen

Nicolas SNAIDERO, Ph.D. (2015)
Institute of Neuronal Cell Biology
Technical University München
Biedersteiner Str. 29
80802 München

Institute of Clinical Neuroimmunology
Ludwig-Maximilians University Munich
Marchioninistr. 17
81373 München

Joining the program from 2013

Tim Gollisch
was appointed Professor for Sensory Processing in the Retina, School of Medicine, University of Göttingen in 2010. He joined the Neuroscience program in 2013 and is engaged in teaching in the MSc curriculum (Sensory and Motor Systems lectures) and hosts MSc and PhD candidates from the program and from GGNB. The focus of his work is the function of the various neuron types in the retina and to better understand neural computation in the retina. On this basis, he also studies dysfunctions of the retinal circuitry.
He uses various techniques of recording the activity of neurons in the retina including multi-electrode array recordings, whole-cell patch-clamp recordings, and fluorescence imaging and combines the experiments with statistical analyses and mathematical mo-deling.
Further information: http://www.uni-goettingen.de/en/201928.html

Marion Silies
holds a group leader (Emmy Noether Group) position at the European Neuroscience Institute, Göttingen since 2014. In the MSc part of the neuroscience program and in GGNB she is engaged in training activities introducing the genetics and quantitative behavioral analysis in fruit flies.
Her group aims to understand how neural networks receive, analyze and extract visual information from the environment to guide adaptive behavior. By studying motion detection in the visual system of fruit flies using cell biological and genetic approaches in combination with physiology and quantitative behavioral analysis, she aims to identify mechanisms by which nervous systems integrate molecular, cellular and circuit characteristics to compute behaviorally relevant outputs.
Further information: http://www.eni.gwdg.de/index.php?id=356&L=1%27a

Henrik Bringmann
has been appointed as a Max Planck research group leader at the Max Planck Institute for Biophysical Chemistry, Dept. of Sleep and Waking in 2009. He joined the Neuroscience program in 2013 and introduces invertebrate models in the MSc curriculum ever since. He also hosts PhD program candidates from GGNB. He investigates the function and regulation of sleep by studying different model organisms, especially in the larva of the nematode Caenorhabditis elegans, and in mice using behavioral assays, genetics and functional imaging. Recently his group identified a single sleep-inducing neuron in *C. elegans* that is homologous to mammalian sleep neurons. This provides a starting point to understand the regulation of sleep and to manipulate sleep towards functional sleep studies.
Further information: http://www.uni-goettingen.de/en/138623.html

Jeong Seop Rhee
is a research group leader at the Max Planck Institute of Experimental Medicine, Göttingen since 2006. He studies synaptic signaling between nerve cells to elucidate the molecular mechanisms that underlie synaptic plasticity at synapses in the central nervous system. Various techniques including mouse genetics, molecular biological and morphological methods, and patch clamp electrophysiological analyses of autaptic cultured neurons, organotyptic brain slice cultures, acute brain slices, or acutely isolated neurons are used to identify the molecular mechanisms underlying individual synaptic vesicle recycling steps.
Further information: http://www.uni-goettingen.de/en/122329.html

Faculty Leaving

Left the program since 2013

Uwe-Karsten Hanisch
Very sadly, the program has to announce that Uwe-Karsten Hanisch unexpectedly passed away on 18. April 2015. The Medical Faculty of the University of Göttingen and the University of Leipzig, where he was recently appointed as Professor for Dynamics of Brain Function at the prestigious Paul-Flechsig-Institute for Brain Research, have expressed deep sorrow. He leaves behind his wife and 2 children with who is the compassion of his colleagues, co-workers and friends.

Uwe Karsten Hanisch, born May 6, 1961 in Lützen, studied biochemistry in Leipzig and did his doctoral thesis in 1990 at the Paul-Flechsig-Institute, the very same institute he returned to as professor and designated director 25 years later. As a postdoctoral fellow he worked at McGill University in Montreal/Canada and at the Max Delbrück Centre for Molecular Medicine in Berlin. He took over a professorship at the University of Applied Sciences in Senftenberg in 2002 and accepted an appointment as Professor for Experimental Neurobiology, Institute for Neuropathology at the University of Göttingen in 2004. Prof. Hanisch's major research interests focussed on the expression and functions of cytokines in the CNS and the role of plasma factors as endogenous signals for microglial cells. He joined the Neuroscience program in 2010.

Moritz Rossner
came to Göttingen as a group leader at the Max Planck Institute for Experimental Medicine in 2003. The group's research interest is directed towards the generation and analysis of transgenic mouse mutants in order to understand individual gene functions in the adult brain. Dr. Rossner has been a member of the Neuroscience (IMPRS) and the CMPB program (Molecular Physiology of the Brain). In 2014 he accepted a position at the Ludwig Maximilians University in Munich Clinics, and became full professor at the Dept. Molecular Neurobiology and Behavioral Biology of Psychiatric Disorders.
Further information: http://www.klinikum.uni-muenchen.de/Klinik-und-Poliklinik-fuer-Psychiatrie-und-Psychotherapie/de/mitarbeiter/rossner.html

Andreas Wodarz
was appointed Head of the Department of Stem Cell Biology at the University of Göttingen in 2004. From 2005 until 2013 he was a member of the Neuroscience program. His research activities focus on different aspects of the asymmetric division of neural stem cells. He was appointed full professorship at the University of Cologne, Faculty of Medicine, Institute of Anatomy, head of the Dept. Microscopic Anatomy and Molecular Cell Biology.
Further information: http://www.anatomie.uni-koeln.de/404.html

Current Faculty Members

Matthias Bähr
Thomas Bayer
Henrik Bringmann
Nils Brose
Wolfgang Brück
Camin Dean
Thomas Dresbach
Hannelore Ehrenreich
Gregor Eichele
André Fiala
André Fischer
Alexander Flügel
Jens Frahm
Tim Friede
Theo Geisel
Tim Gollisch
Martin Göpfert
Robert Gütig
Ralf Heinrich
Stefan Hell
Michael Hörner
Swen Hülsmann
Reinhard Jahn
Hubertus Jarry
Siegrid Löwel
Till Marquardt
Ira Milosevic
Tobias Moser
Klaus-Armin Nave
Luis Pardo
Walter Paulus
Jeong Seop Rhee
Michael Rickmann
Silvio Rizzoli
Detlev Schild
Oliver Schlüter
Manuela Schmidt
Michael Sereda
Marion Silies
Mikael Simons
Jochen Staiger
Judith Stegmüller
Anastassia Stoykova
Walter Stühmer
Stefan Treue
Fred Wolf
Fred Wouters

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

Neurizons 2015 –

notes of an orchestrated brain

This May, the city of science Göttingen comes alive to host its 6th biennial neuroscience conference – Neurizons 2015. Neurizons is the flagship neuroscience conference organized by the students of the International Max Planck Research School (IMPRS) Göttingen. The conference is to be held from the 26th to the 29th of May this year, at the Max Planck Institute for Biophysical Chemistry, Am Fassberg, Göttingen. Keeping with tradition, this year's conference boasts an exciting line-up of speakers, including the Brain prize winner, Dr. György Buzsáki, who will deliver the keynote speech. The speakers will delve on a range of topics including synaptic physiology, sensory and motor systems, developmental neuroscience, translational neuroscience, systems neuroscience and cognition, in five sessions spread over three days.

As a student organized conference, Neurizons recognizes and caters to the needs and interests of the student community. The conference is set to begin with a series of workshops on critical research methods and a career fair which includes talks from the representatives of Sartorius AG, McKinsey and Company Inc., and Georg-August University Göttingen. In addition to the quintessential poster sessions, Neurizons 2015 also provides a platform for students to present their work through "Young Investigator Talks", short talks nestled in between the five sessions. Strong emphasis is laid on personal communication, with "Coach Me", a one-on-one mentoring session with guest speakers.

As neuroscientists, the organizers realize the importance of social behavior. The issue is addressed with pub crawls and guided city tours to ensure interaction in enriched environments. The final day of the conference, 29 May 2015 also marks the 15th Anniversary of the International Max Planck Research Schools for Neurosciences and Molecular Biology. The celebration features the scientific keynote lecture on super-resolved fluorescence microscopy from Göttingen's very own Nobel laureate Prof. Stefan Hell. With renowned experts orchestrating this symphony, a strong platform to interact and forge connections, interspersed with fun and frolic, Neurizons 2015-notes of an orchestrated brain, promises to enthrall.

Joint Retreat with Max-Delbrück-Center...

Helmholtz International Research School Molecular Neurobiology *by Dennis Nestvogel*

Brain: the final frontier. These are the voyages of the IMPRS for Neurosciences. Its mission: to explore strange neural networks, to seek out mechanisms that contribute to brain function and behavior, to boldly go where no man has gone before.*

On that note and in the spirit of the 25 years of the fall of the Berlin wall, students from the MSc/PhD/MD-PhD Program and IMPRS for Neurosciences in Göttingen and the Helmholtz International Research School Molecular Neurobiology Max-Delbrück-Center for Molecular Medicine in Berlin-Buch gathered together in September 2014 for a joint retreat in Lychen, Brandenburg.

Well-equipped with poster boxes, snacks and an omnipresent motivation to discuss science, the IMPRS students together with their office team, engaged into a lengthy bus ride from Göttingen to Lychen on the first day of the retreat. Possible doubts or discontents with regards to the length of the bus ride immediately vanished upon arrival at the beautiful venue that was carefully chosen by the coordinator of the Helmholtz International Research School. The first day ended with a delicious barbecue, a session of "PowerPoint-Karaoke" and stimulating conversations on the lakeshore.

The next day was particularly dedicated to scientific exchange. Eugenia Chiappe (Champlimaud Foundation, Lisbon) opened the first session on "Sensory and Motor Neuroscience" with an inspiring talk on linking motion-vision to walking in flies and was followed by two student talks. After a short coffee break, Yang Dan (University of California at Berkeley) presented some of her latest research in the field of vision and gave some valuable career advice to the graduate students. She was followed by three more student talks, before lunch was served. The final session of the day on "Neural Development" was opened by Till Marquardt (ENI, Göttingen), who shared some of his newest insights on the development of motor neurons with the participants and ended with three student talks. In the evening, all of the participants gathered together for a poster session. The topics presented on the posters ranged from the structural analysis of single ion channels to complex behavior of flies and mice. The prize for the best poster went to Diego Giraldo, whose poster dealt with the role of rhodopsins 1 and 6 in thermoreception and proprioception.

Sven Truckenbrodt from the laboratory of Silvio Rizzoli (UMG, Göttingen) was the first speaker of the session on "Synaptic Research", on the third and last day of the retreat. He gave a very entertaining and thought-provoking talk on the molecular architecture and organization of chemical synapses and was followed by three student talks. The prize for the best student talk of the retreat was awarded to Mohammed Khani, whose talk was on chromatic signal integration in the mouse retina. After some concluding remarks by the student organizers and a refreshing lunch, the participants traveled back to Berlin or Göttingen, respectively.

Overall, the joint-retreat offered a great opportunity for the students of the IMPRS to discuss science with experts, as well as with graduate students that are at a similar stage in their career and to make new friends – within and across the programs.

**Modified after the title sequence of Star Trek and with apologies to James Tiberius Kirk, Captain of the USS Enterprise*

ELECTRAIN courses...

at the European Neuroscience Institute supported by FENS

The ELECTRAIN courses in electrophysiology are held in the ENI teaching labs since 2009. Started as one of the training initiatives of the Graduate School GGNB the course is meant to train local PhD students and postdocs in advanced electrophysiological techniques. Meanwhile, ELECTRAIN also attracts external participants, who take the course together with local doctoral students. In 2015 again 2 participants from Florida Atlantic University in Jupiter join the course in the ENI. This brings again life to the partnership with the Florida campus, which also hosts the Max Planck Florida Institute, the only MPI in the US.

This extended methods course provides both theoretical and practical knowledge and skills of modern electrophysiology, with lectures in the morning and hands-on lab work in the afternoons. The ELECTRAIN course concept was awarded by the Federation of European Neuroscience Societies (FENS) following calls for neuroscience training courses launched by FENS since 2013. The GGNB course was selected for FENS funding in 2014 and 2015. ELECTRAIN will, thus, again host 3 FENS participants, who receive financial support to cover their living and travel costs.

Info Booth at SFN

'Neuroscience in Germany'

The Society for Neuroscience Annual Meeting 2014 was held 15.-19. November 2014 in Washington DC.

Based on the experience of the existing network of international graduate programs in the neurosciences in Germany ‚Neuro Schools Germany' comprising the universities in Berlin, Bochum, Bonn, Göttingen, Magdeburg, Mainz, München and Tübingen (http://www.neuroschools-germany.com) thoughts to join forces with other German institutions in the field of neuroscientific research have finally been realized in fall 2014 in Washington. The idea was to create a common landmark German platform at the Society for Neuroscience meeting including the Excellence Clusters in the neurosciences, the national Bernstein network (http://www.nncn.de/de) and the organization 'Research in Germany' (http://www.research-in-germany.org/en; Alexander von Humboldt Foundation, the German Academic Exchange Service, the German Research Foundation). The common booth 'Neuroscience in Germany' was also supported by the local office of the German Research Foundation in Washington.

This booth provided comprehensive information on the German research landscape, training options, funding opportunities, and open positions in the neurosciences at German research institutions. Compared to similar marketing efforts in previous years with all partners running their own booths separately, the joint booth attracted significantly more meeting participants. The joint financial support by the above mentioned partners allowed to set up one of the largest booth areas in the non-commercial exhibition area directly at the main poster passage. More than 550 visitors discussed in detail with the representatives of the different research organizations research and funding opportunities in Germany. The main advantage turned out to be the fact that visitors with very different specific interests could directly be guided to the suitable partners of teaching programs, research institutions or funding agencies at the very same booth.

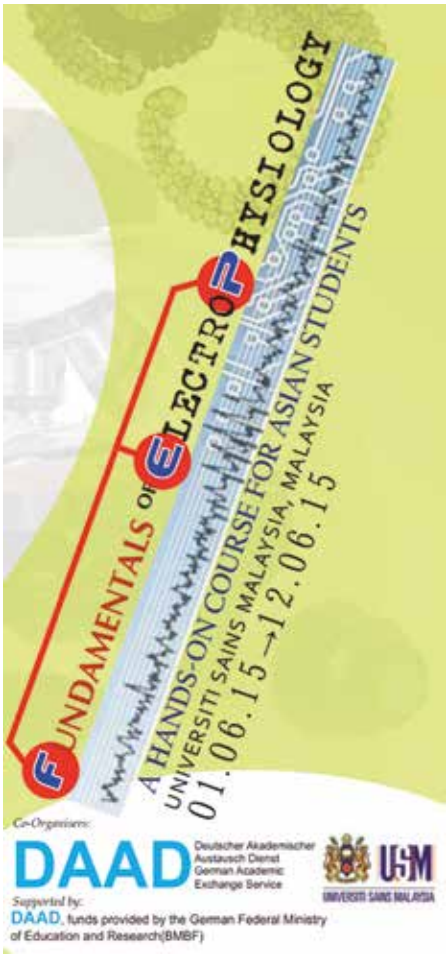
After successfully establishing the 'Neuroscience in Germany' booth the organizing team has already started to plan a similar joint outreach stand at the next Society for Neuroscience Meeting in Chicago in fall 2015.

3rd DAAD Summer School...

at Universiti Sains at Kota Bharu, Malaysia

Neuroscience is one of the most internationally oriented fields of scientific research. Based on existing research cooperation and recognizing the importance of research-orientated training, neuroscientists from Germany in cooperation with colleagues at the Department of Neurosciences of the School of Medical Sciences and the Universiti Sains Malaysia (USM) developed plans for a joint international summer school. Following the experience of international training courses established in the European Neuroscience Institute in Göttingen (ENI-G), the 1st DAAD (German Academic Exchange Service) summer school in the field of the neurosciences was organized at the Kota Bharu campus in 2009. This summer school has been the nucleus for establishing an interdisciplinary training laboratory for excellent MSc and PhD students, integrating scholars from medical school and the natural sciences and related fields. The 2nd DAAD summer school 'Fundamentals of Electrophysiology' ('FEP Course') was conducted in 2012.

Meanwhile a formal cooperation treaty was signed by USM and the Georg August University, Göttingen, which was instrumental for the continued support by the DAAD. Following the success and proven concept of the 1st and 2nd DAAD summer schools, the FEP course 2015 was again selected for DAAD funding. The course is meant to expose the participants to state-of-the-art theoretical and practical coursework introducing relevant techniques with a focus on science-oriented neurophysiology. For the first time, also the USM main campus is part of the DAAD summer school and scientists at Penang actively conduct one module of the FEP course. All DAAD-USM summer school organizers are part of international study/research programs and, thus, believe in international exchange in teaching and science. In this respect, the DAAD-USM summer school series also marks our efforts to recruit excellent scholars worldwide. The organizers of the DAAD Summer School are convinced that the now established DAAD-USM summer school provides the basis for a continuous and sustainable training scheme making use of the neuroscience training laboratory at USM. In fact, based on the training activities numerous scientific co-operations were successfully started and will be useful for further joint activities between neuroscientists in Malaysia and Germany in the future.



European Neuroscience Campus Network

New Proposal submitted

The ENC-Network is the organization that hosts both the Erasmus Mundus Master Course (EMMC) and the Erasmus Mundus Joint Doctorate (EMJD) program, in addition to two ITN (BrainTrain and SymBad). The ENC-Network (ENC: http://www.enc-network.eu) was founded in 2009 with EU funding granted in 2010 (doctoral positions, overhead of 1.3 Mio €/year).

The Consortium Agreement stated that ENC doctoral students in Göttingen will be integrated into GGNB. In addition, ENC partners are asked to implement joint/double degree regulations for ENC doctoral students. GGNB supports the further development of joint EU research/teaching partnerships, including the ENC Network.

In conjunction with the establishment of the European Neuroscience Campus training network for doctoral candidates the European Master Neuroscience program 'NEURASMUS' has been launched in 2010 with the aim to extend exchange and training opportunities also for MSc students. Since 2011 three to five NEURASMUS MSc students join the Göttingen Neuroscience Program per year. They are trained in at least two home institutes of the ENC Network and have the option to enroll in existing and established PhD courses in each of the participating home institutes after successful graduation from the MSc program.

A new proposal to further develop and extend the joint MSc training scheme called 'NEUROMUNDUS' has been submitted to the EU authorities in February 2015 and will be decided upon by fall 2015.

Live the Weizmann Cooperation

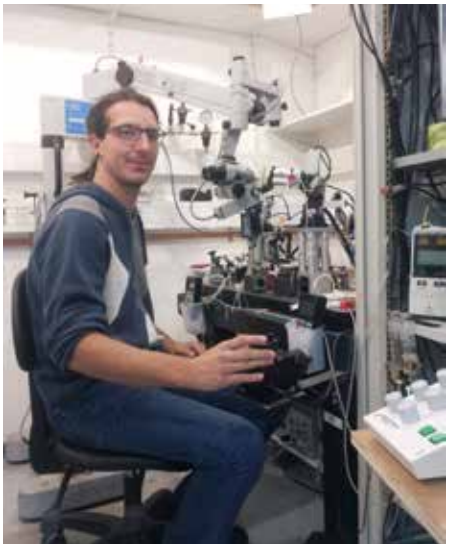
External Master Thesis project at the Weizmann Institute of Science in Israel *by Alexander Dieter*

הזתה תא בותכל יתטלחהו סקלא ימש ,ולהא תובוחר ,עדמל ומציו וכמב ינש רותל ילש ,לארשי. Ahlan, shmi Alex v'hechlat'ti likhtov et hateza sheli l'tor sheni bimkhon Vaitzman l'mada', Rechovot, Yisrael.

Hey, my name is Alex Dieter, I am currently a MSc student of the Neuroscience Program, class of 2013. I decided to write my Master's thesis at the Weizmann Institute of Science (WIS), Rehovot, Israel. More or less half a year after I made this decision I am finally working here. Actually the decision has been made long before. Not for Israel and not for the WIS, but for spending time of my studies abroad. During my bachelor studies I have already stayed in laboratories of different countries and always profited from these times, both in a personal and a professional way. When I started my Master's degree at the IMPRS for Neuroscience in Göttingen I was a bit jealous of many of my mostly international classmates, who combine continuing their graduate education in Göttingen, with the adventure of coming to a new country and experiencing a different culture. When I then heard about the collaboration between the IMPRS in Göttingen and the Feinberg Graduate School at the WIS for the first

time, I immediately started thinking about ways to do my master studies at the Weizmann Institute.

The WIS, as one of the leading research institutions in Israel, has an excellent reputation worldwide and provides on the one hand a solid base for interdisciplinary research by uniting scientists



from a wide variety of fields but on the other hand focuses the research by its specialization on natural and computer sciences. This unique feature finally convinced me to join a lab at the WIS instead of looking for laboratories in other places of the world. Thanks to the support of the IMPRS and established collaborations between laboratories in Göttingen and Rehovot, it was really easy to get in contact with people at the WIS and to find the right lab for the work of my master thesis, which turned out to be the one of Professor Ilan Lampl. In this lab I experience a lot of contact with all postdocs and the PI himself on a daily basis in order to review recent results, solve technical problems and discuss new ideas. Using stereotactic injections, optogenetics and patch-clamp recordings I contribute to a project that deals with the balance between excitation and inhibition in the mouse barrel cortex. By optogenetic inactivation (using either archaerhodopsin or halorhodopsin, two light activated ion pumps that enable hyperpolarization of transfected neurons) of excitatory cortical neurons I dissect thalamic feedforward- from intra-cortical feedback-inhibition. The proportions of feedforward- vs feedback inputs can then be quantified by patching inhibitory neurons in the cortex and compare their firing behavior during the somatosensory response (feedforward and feedback contributions) vs the somatosensory response while shining laser on the cortex (i.e. inhibiting excitatory cortical neurons, leaving just feedforward-inhibition). The establishment of the model system as well as the scientific findings subsequently then get confirmed with extracellular multi-unit recordings and with histology. During the establishment of our model system I found differences in cytotoxicity caused by archae- and halorhodopsin, which lead to extensive cell death in the cortex. Now that these problems are settled and we have a working model system, I recorded the first (quite promising) data to answer the original questions. Overall, I am working with diverse techniques which I will hopefully be able to use during my PhD in Göttingen.

Even though the lab-life is quite busy, there is of course always time to grab some of the delicious Hummus (a local specialty made from chickpeas) in the cafeteria with my colleagues! Apart of the lab-work, there is, of course, also time left to discover the country and experience the Israeli culture and lifestyle. Rehovot itself is famous for the science that is done here and for its flowering orange industry. Apart from this it is a relaxed and quiet city. During the week it is really nice to stay here, there are a lot of pubs and restaurants where one can meet both local and international people, mainly connected via the WIS. The international people I meet here are a more than welcome company for traveling, since a lot of Israelis in my age are already settled and often have family. Compared to Europe, people are married and have children much earlier. On the weekends, however, I try to 'escape' from the life in Rehovot and either go to Tel Aviv, which one can reach in 30 minutes by train from Rehovot, or to explore other parts of Israel. Tel Aviv is a highly diverse city, which offers ancient as well as colorful alternative districts and a modern, business-governed city center, just to mention a few.

Israel as a whole is even more diverse, which I experience as a country with a lot of contrasts on many levels. Most

obvious of course Arab vs. Israeli culture, but also religious vs. secular life, the ubiquitous rich vs. poor, war vs. peace and apart from this, in a more pleasant way, beachside vs. deserts and a huge number of important ancient sites vs. multifarious modern cities. Due to a lot of diversity in a relatively small area, Israel is the perfect location for everyone who wants to experience something different in daily

life. The Dead Sea, the ancient fortress Masada, the diving paradise Eilat, the Golan Heights and of course Jerusalem are just a few highlights that I would like to mention here. In conclusion I have to say that even though Israel was not the first country coming to my mind when it comes to study abroad I have no regrets about the decision of coming here. I enjoy every minute of my stay and I am convinced that the stimulating atmosphere I am experiencing over here will again benefit me in both personal and professional aspects of my life.

15th Anniversary...

and International Alumni Day

From 29 to 31 May 2015 the Neuroscience program and International Max Planck Research School (IMPRS) together with its partner program and IMPRS Molecular Biology will celebrate their 15th Anniversary in Göttingen. Many alumni from both programs have already confirmed that they will join the activities organized for this weekend to celebrate with the local students and faculty.

The celebrations will start in the University Aula with a scientific keynote lecture by Stefan Hell, Nobel Prize laureate in Chemistry 2014. Subsequently, the president of the University of Göttingen, Ulrike Beisiegel, will officially open the 15th Anniversary celebrations to which all current and formers members, colleagues and friends of both graduate programs have been invited.

The celebrations mark the end of the NEURIZONS week (www.neurizons.uni-goettingen.de; 26-29 May 2015), which gives the alumni the opportunity to combine their return to Göttingen with a scientific meeting, organized by the PhD students of the Neuroscience program. Saturday is reserved for the International Alumni Day. In the morning, all alumni are invited to participate in guided tours on the Göttingen campus. These site visits include the university's collections such as the cast collection of antique sculptures or the art collection or an introduction into the work of the Center for Retrospective Digitization Göttingen. On the North Campus, site visits are offered to the new Max Planck Institute for Solar Systems Research, to the Laser-Laboratorium Göttingen, which closely collaborate with industry partners in the area of application-orientated laser research, and to the Microscopy Lab of Stefan Hell at the MPI for Biophysical Chemistry.

The day continues with the Alumni Career Forum, intended to promote the interaction of alumni among each other across the different generations and disciplines. This forum also gives our current students the opportunity to meet the graduates of former years and benefit from their experience. One key element of the International Alumni Day is a series of 'Vision Talks', for which distinguished guest speakers will outline their personal view on current and expected future developments in their field with reference to the professional perspectives for alumni. The three talks will be given by Prof. Jochen Maas (Sanofi, General Manager R&D Germany, Head R&D Germany), Tamara Darsow, PhD (Vice President, Research Programs, American Diabetes Association, Washington DC) and Prof. Jan Philipp Reemtsma (Professor of German literature, founder and director of the Hamburg Institute for Social Research, sponsor and promoter of the Max Planck Foundation). The talks are followed by a podium discussion with additional invited guests.

On Sunday, the 15th Anniversary celebrations and alumni meeting end with a hike to the nearby Plesse Castle for a farewell brunch in the castle's inner courtyard.

Neurofaces

2000 – 2015