NEUROSCIENCE
NEWSLETTER
Georg-August-Universität Göttingen · International Max Planck Research School
DEC 2011

Neuroscience in Göttingen…

… Science without Boundaries !

Welcome to the 2nd Neuro-Newsletter published by the Göttingen International Master/PhD/MD-PhD Program and International Max Planck Research School (IMPRS) Neurosciences.

While 2010 was the year to look back and celebrate the 10th anniversary of the Neuroscience Program, 2011 marks the starting point for the renewal of substantial external funding important for the entire university. In the field of the neurosciences the continuation of our funding through the federal Excellence Initiative will be crucial for the DFG Research Center of Molecular Physiology of the Brain (CMBP) which has been upgraded to the Excellence Cluster Microscopy at the Nanometer Range in 2006. Also the decision on the continuation of Excellence Funding of the Göttingen Graduate School for Neurosciences, Biophysics and Molecular Biosciences (GGNB) will be reached in 2012. For the MSc/PhD/MD-PhD Program and International Max Planck Research School (IMPRS) Neurosciences in Göttingen the successful prolongation of funding by the Max Planck Society will be of utmost importance.

In Göttingen Neurosciences have a long tradition and the Göttingen Research Campus integrating the university and non-university institutions comprises one of the largest neuroscience faculties in Germany. The Göttingen Neuroscience Program/IMPRS, founded as one of the first international schools in the field in Germany, is proud to contribute to the success and growth of the neurosciences over the past years. The fact that almost half of our MSc/PhD alumni came 'back home' to celebrate the 10th anniversary of the program was impressive and reflects lasting connections between our graduates and the Göttingen scientific community. Also the European Neuroscience Institute (ENI-G), which is the home of the Study Program since 2005, celebrated its 10th birthday with many alumni joining the scientific symposium that took place on this occasion. We will further cultivate networking with our alumni and integrate them -as well as our new partners in the EU (new EU-funded MSc and PhD training, see this issue)- into our continuous search for the best scholars in the neurosciences.

NEURIZONS Symposium 2011 at the Max Planck Institute for Biophysical Chemistry

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Neuroscience in Göttingen...

Activities such as the biennial NEURIZONS Symposium organized by the PhD students of the Neuroscience Program also regularly attract national and international scientists (and our alumni) to visit Göttingen (see this issue). Likewise the ELECTRAIN courses in electrophysiology held in the ENI Teaching Labs, originally meant to train local PhD students and postdocs, are now announced also to our international partners such as the Feinberg Graduate School at the Weizmann Institute of Science or the Max Planck Florida Institute affiliated with the Florida Atlantic University. Participants from Florida joined our courses this year for the first time. We are planning to further strengthen these existing networks by developing new ideas for summer schools to increase scientific exchange at all levels.

The rapid growth and establishment of the Graduate School GGNB, now comprising more than 380 PhD students and 180 faculty members, was based on the proven concepts of the Neuroscience Program and would not have been possible without its substantial and continuous support. In fact, the Neuroscience Program together with its partner program in Molecular Biology remain unique within the Graduate School GGNB in offering integrated MSc/PhD curricula with a fast track option which allow excellent BSc graduates to directly enter the PhD phase after successfully absolving the initial 1st year training phase. These international programs have been particularly successful in attracting high numbers of worldwide applicants of good academic quality over the years providing the basis for a selection of the very best candidates.

While preserving its successful structure, the content and focus of the training curriculum of the Neuroscience Program has continuously been adapted to the changing research topics. Noteworthy in this respect is the area of biophysics, which is becoming more important for quantitative approaches and novel imaging techniques or research on mechanisms of neurodegeneration relevant for clinical use. Therefore, the Neuroscience Program has extended its focus by integrating new faculty members to keep pace with the rapid and fascinating developments in the neurosciences and to be prepared for the future.

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Precise timing in the olfactory system

by Stephan Junek

Compared to other sensory systems, the functioning of the sense of smell is still relatively poorly understood. Even simple odors are encoded in the brain by spatio-temporal activity patterns of a large number of neurons, making the investigation of these patterns experimentally very challenging. Using sophisticated microscopic and computational techniques, recent studies indicate that precise timing of neuronal responses might be crucial for coding in the olfactory system.

Humans and animals depend on an interaction with their environment. They must find food and distinguish it from toxic substances, timely discover predators, find mates and recognize and protect their offspring. To meet these tasks, animals need a reliable and immediate knowledge of the world around them. To this end, evolution has developed a variety of sophisticated sensory systems. Each of these systems captures a particular physico-chemical aspect of the environment and translates it into a neural representation. These representations are the basis of a sensation, of an adequate behavioral response or serve a learning process.

The sense of smell has to be able to distinguish a very large and heterogeneous variety of stimuli. For a sufficient sampling of this "stimulus space" a large number of receptors are needed, similar to the receptors in the inner ear for the subtle distinction between different frequencies. Since odors cannot be assigned an order, such as the notes of a scale or the colors of the rainbow, it is not possible to represent them by a functional and efficient "odor map" (similar to the receptor arrangement according to pitch in the ear). Furthermore, there are no "basic odors," according to the five basic tastes. In contrast to other sensory systems, we therefore retain only a vague idea of how the sense of smell represents, identifies and categorizes scents.

Since the pioneering and Nobel Prize-awarded work of Linda Buck and Richard Axel it is known that each olfactory sensory neuron in the nose possesses only one of hundreds of different receptor types. Each of these receptors shows a characteristic binding behavior of fragrances. Even odors that consist only of one kind of molecule activate a variety of receptor types. Natural odors, which often consist of hundreds of components, excite correspondingly large and strongly overlapping populations of receptors.

The receptor neurons send their signals to the olfactory bulb (OB), the only central processing station of the olfactory system. Here, the excitation patterns of the receptor cells are turned into a "code" comprehensible for higher brain areas. It was shown that a temporally constant stimulus causes temporally modulated patterns of activity over the course of seconds (*1, 2*). Since it is also assumed that the olfactory sense is a comparably "slow" sense, it is now generally accepted that time takes on the role of an encoding parameter. However, it is unclear as to which aspects of these spatio-temporal patterns contain odor-specific information to be read by higher brain centers. Studying these patterns is particularly challenging because it requires the simultaneous observation of many neurons, since each stimulus is represent-

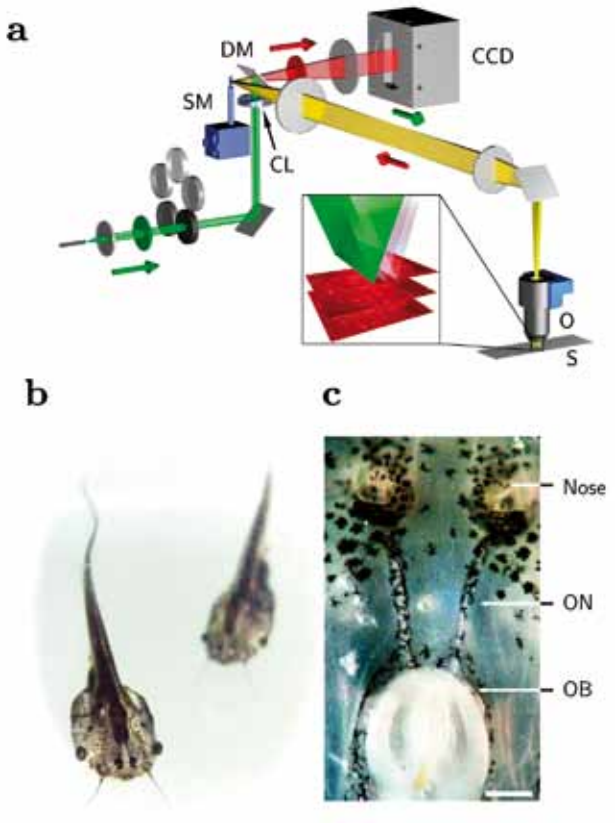

Fig. 1a: Line-illumination microscope. By scanning a line instead of a point across the sample and using a fast CCD camera, very high frame rates can be achieved. (SM: scan mirror, CL: cylindrical lens, DM: dichroic mirror, O: objective, S: sample)

Fig. 1b: Larvae of the experimental animal *Xenopus laevis*.

Fig. 1c: Nose-brain preparation. The preparation includes the intact nose and olfactory nerve (ON) combined with a slice preparation of the olfactory bulb (OB). While presenting natural odors to the nose, imaging or electrophysiological measurements in the OB can be performed.

ed by the activity of many cells. On the other hand, the temporal changes of activity have to be measured with sufficient temporal resolution. Traditionally, electrical recordings of single neurons are used when a high temporal resolution is required. Pooling recordings from different trials and animals is not an adequate solution, since it cannot replace simultaneous measurements (*3*, but see below). Imaging techniques, on the other hand, are used for the simultaneous observation of cell populations, but - due to technical reasons – with low temporal resolution (one to two frames per second). A proper study of the spatial-temporal activity patterns of the olfactory system requires measurements with high-resolution in both space and time.

I thus spend the first part of my PhD in Göttingen designing and building a microscope that would allow me to record the activity of large numbers of neurons with a good temporal resolution. The trick was to combine elements from different microscopic techniques, thereby avoiding the temporal bottlenecks of each of them. By scanning a line – instead of a point – the time consuming two-dimensional scanning of a laser scanning microscope is reduced to one dimension, and by using a linear CCD sensor – which can be read out faster than a 2D array – the time limiting step of a widefield microscope was overcome (Fig. 1a, *4*). Using Ca^{2+}-sensitive fluorescent dyes, I was thus able to record the neuronal activity of dozens of individual nerve cells at a rate of 100 Hz (*3*).

In a preparation of larval *Xenopus laevis* consisting of the intact nose and olfactory nerves, together with a slice preparation of the OB (Fig. 2b,c), I could now measure the neuronal activity patterns in the OB during stimulation with natural odors. One of the long-standing questions of olfactory research is, how "fast" the sense of smell can be. Senses like the auditory, visual or somatosensory sense are known to act on the millisecond time scale. The sense of smell was long-thought to be a slow sense, acting on the second, rather than on the millisecond scale. Many proposed models thus analyzed the evolution of activity patterns over the course of one or two seconds (*5*). Recent behavioral experiments challenged this view, demonstrating, that odors can be recognized and discriminated about ten times faster. The detection time in mammals, for example, appears to be dictated by the duration of a single sniff (*6, 7*). I thus decided to investigate coding schemes that have been implied for fast sensory coding in other senses, in particular coding using first spike latencies (see, e.g. *8 – 10*). By extracting and combining the first spike latencies from the Ca^{2+}-traces of each of the simultaneously recorded neurons, I constructed a "latency pattern" (*3*). These latency patterns turned out to be highly reproducible across repeated presentations of the same odor, but depended strongly on the odor identity (Fig. 2a). I further observed that simultaneous recordings of responses is crucial, since shuffling of responses across trials removed a significant part of the information contained in these patterns. The latency patterns depended on the other hand only weakly on the odor concentration, and only when the concentration varied by a factor larger than 20. The biggest surprise came, however, when I compared the ability to predict odor identity from either the latency patterns or from patterns consisting of initial firing rates. Using the latency patterns, the odor prediction was perfect as long as the latencies of more than ten neurons were recorded. Using the patterns of firing rates, the prediction accuracy rarely exceeded 80 %, even for patterns consisting of up to 15 neurons (Fig. 2b). While this accuracy might

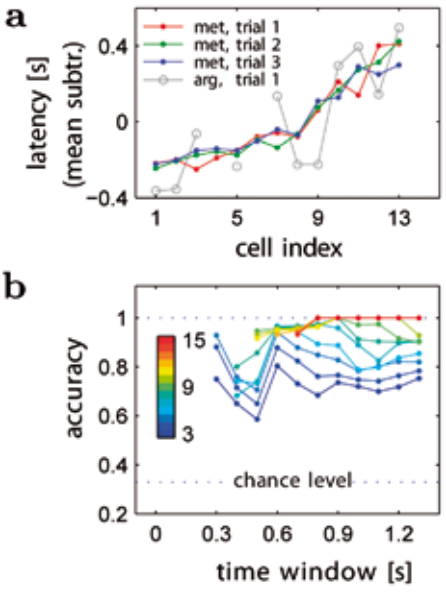

Fig. 2a: Examples of latency patterns (mean subtracted). Each curve depicts the latencies of simultaneously recorded neurons. When the same stimulus is presented repeatedly (e.g. the amino acid methionine: red, green and blue curve), the neurons respond roughly in the same order each time. When another stimulus is presented (arginine; gray curve), the order is markedly different.

Fig. 2b: Odor prediction accuracy. The odor identity is predicted based on the latency patterns from single trials using a classification algorithm. Each curve corresponds to the prediction accuracy as a function of time window upon odor presentation, different colors indicate different lengths of latency patterns (i.e. different numbers of recorded responding neurons).

still sound high, one has to consider that I could only use a limited number of odors in my experiments. In a real world situation with hundreds of potential odors, the difference between these coding schemes would likely be even more pronounced. Latencies thus appear to be more informative about the odor identity than firing rates. To finally answer the question concerning coding on short time scales, I could show that even on short time scales suggested by the behavioral experiments cited above, the prediction accuracy based on latencies exceeds 80 % (Fig. 2b).

Recently, the group of Dimitry Rinberg (Janelia Farm) has used another strategy to examine the role of precise timing in the olfactory system (*11*). They electrically recorded the activity of M/T cells during odor stimulation in mice *in vivo*. While they could only record a small number of neurons at a time, they used the timing of the sniff to align and "time-warp" the responses from successive trials. To their surprise, the responses, which appeared to be highly variable across trials in the raw data, lined up almost perfect after they were warped to the time course of a "standard sniff". As in my experiments, these precise timing patterns cover several hundred milliseconds (the whole sniff duration) and are strongly odor-dependent. Using a different model system and a very different approach, this group arrived thus at a very similar conclusion as us.

In addition another group recently confirmed the high temporal precision of the timing of first spikes using artificially controlled respiration in rats (*12*).

It appears thus, that the sense of smell might not be so slow after all, and that precise timing of neuronal activity at the millisecond time scale might be as pronounced as in other sensory systems. So what's missing? Actually, a lot. While latencies of the OB output neurons appear to be more informative than their firing rates, they might not carry all of the information. Eventually one has to ask what the receivers of these neurons, e.g. the pyramidal neurons in the olfactory cortex, "care about". The detailed investigation of the olfactory cortex has started only very recently. Consequently, our understanding of its properties, structure and function is but in its infancy. During the last years, it has been suggested that no chemotopic map exists, and that the probability that a given odor activates a pyramidal cell is independent of its location in the cortex (for a recent review, see *13*). The olfactory cortex thus seems to function in a different way than other cortical sensory areas, possibly due to the unique properties of the olfactory stimulus space. In my current work at the Max Planck Institute for Brain Research I am trying to contribute to the understanding of olfactory cortical processing. Our group investigates the olfactory and visual cortical areas of turtle, hoping that the parallel investigation of morphologically similar, yet functionally distinct structures might lead us towards a general understanding of cortical processing.

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Confessions of a dangerous peptide

Pyroglutamate Abeta in Alzheimer disease *by Sadim Jawhar*

Pyroglutamate-modified Abeta ($A\beta_{pE3}$) peptides are gaining considerable attention as potential key players in the pathology of Alzheimer disease (AD) due to their abundance in AD brain, high aggregation propensity, stability and cellular toxicity. Recent in vitro and in vivo experiments have proven that the enzyme glutaminyl cyclase (QC) catalyzes the formation of $A\beta_{pE3}$. In the following pages the current knowledge on $A\beta_{pE3}$ is summarized.

When Alois Alzheimer presented the case of his patient Auguste Deter at the Tübingen meeting of the Southwest German Psychiatrists in 1906, he did not attract much attention or stimulated any discussion in the audience. The young doctor likely would not have believed that, 100 years later, the disease that now holds his name would be the most common cause of dementia and a source of a critical medical and economical problem. At this meeting, Alzheimer presented Auguste Deter's symptoms and reported the histopathological features that are now associated with Alzheimer disease (AD): neuron loss, extracellular amyloid plaques and intracellular neurofibrillary tangles. For more than two decades, the amyloid hypothesis has been the cardinal hypothesis in describing the sequence of AD etiology. The amyloid hypothesis considers amyloid beta (Aβ) peptides deposition as the causative event of AD pathology and that neurofibrillary tangles, cell loss, vascular damage and dementia occur as a consequence of it (1).

In vitro and *in vivo* analysis of amyloid deposits in AD revealed various N- and C-terminal variants. Increased C-terminal length of Aβ (from $A\beta_{x-40}$ to $A\beta_{x-42}$) in AD enhanced aggregation, early deposition and promoted the toxicity of Aβ. Beside Aβ peptides, starting with aspartate as the first amino acid ($A\beta_{1-x}$), several N-truncated and modified Aβ species have been described.

In order to unravel the pathogenic properties of Aβ, it was important to develop approaches to extract and study the biochemical nature of Aβ. Limited extraction and sequencing methods rendered it impossible for a long time. Many teams did not succeed in obtaining interpretable N-terminal sequences from plaque cores isolated by different methods. This discrepancy was solved by Mori and colleagues describing the presence of Aβ peptides (15-20% of the total Aβ) bearing a pyroglutamate residue at the N-terminus. By using pyroglutamate amino peptidase, they were able to unravel the N-terminus, which is blocked by the lactam ring and thus resistant to any other peptidase for Edman sequencing used in previous reports (2).

Since then, the interest in dissecting the temporal and spatial deposition of pyroglutamate Aβ increased. Equipped with a set of novel antibodies, Saido et al. showed by immunohistochemical and biochemical means that $A\beta_{pE3}$ is present in equivalent or larger amounts than full-length Aβ in senile plaques. Based on analysis of brain tissue from Down syndrome (DS) cases, the authors also suggested that $A\beta_{pE3-x}$ precedes the deposition of unmodified Aβ ($A\beta_{1-x}$) (3). This was further confirmed by the finding that $A\beta_{pE3-42}$ constituted 25% of the total $A\beta_{x-42}$ in plaques of AD brains (4).

Formation and biochemical properties of pyroglutamate Aβ

Formation of pyroglutamate-modified Aβ is a multistep process requiring the removal of the first two amino acids aspartate and alanine in order to expose the N-terminal glutamate at the third position of Aβ. After cleavage of the transmembrane amyloid precursor protein (APP) by the major beta-site APP cleaving enzyme (BACE1) and gamma-secretase, $A\beta_{1-40/42}$ is liberated. Then, $A\beta_{1-x}$ is cleaved by unknown peptidases to release the truncated Aβ peptides starting with glutamate at the 3rd position. After exposure of the glutamate, the enzyme glutaminyl cyclase

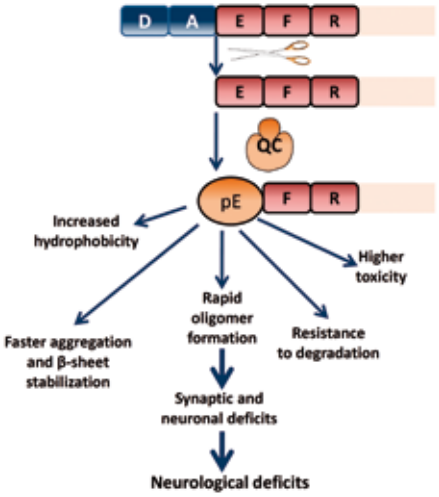

Fig. 1: Generation of pyroglutamate Aβ. The first N-terminal two amino acids aspartate and alanine are cleaved off by an unknown mechanism exposing glutamate at position three of the N-terminus of Aβ. Subsequently, glutamate is post-translationally modified into N-terminal pyroglutamate (pE) by dehydration catalysed by glutaminyl cyclase (QC) activity. The novel peptide has altered biochemical properties with severe pathological consequences. The enhanced toxicity is likely due to the higher aggregation propensity and the longer bioavailability of the $A\beta_{pE3-x}$ oligomers.

(QC) catalyses pyroglutamate formation by dehydration of glutamate (5) (Fig. 1).

The conversion of Aβ into $Aβ_{pE3}$ leads to altered biophysical and biochemical characteristics pointing to changes in aggregation and stability. The formation of the lactam ring and the loss of two negative charges and one positive charge results in higher hydrophobicity of the $Aβ_{pE3-x}$ peptides. In addition, the formation of the N-terminal pyroglutamate, which is resistant to degradation by peptidases, increases the stability of the peptide. He and Barrow reported that $Aβ_{pE3-x}$ peptides show enhanced β-sheet formation and aggregation propensity in aqueous and hydrophobic media compared to full-length Aβ (6). Interestingly, $Aβ_{pE3-x}$ displayed up to 250-fold accelerated formation of aggregates compared to $Aβ_{1-x}$ irrespective of the C- terminus of Aβ (7).

Moreover it has been claimed that $Aβ_{pE3-40}$ is more toxic for neurons and astrocytes as compared to full-length $Aβ_{1-40}$ (8). Similarly, Aβ mixture with high $Aβ_{pE3-x}$ content similar to the ones found in the brain of AD patients resulted in increased cell membrane permeability leading to reduced cell survival in neuroblastoma cells (9). It is worth mentioning that in contrast to what has been described above, some studies have indicated that the secondary structure and toxicity of $Aβ_{pE3-40/42}$ peptides are similar to that of $Aβ_{1-40/42}$ peptides (10,11) (Fig. 1).

Soluble oligomeric pyroglutamate Aβ – the missing link in Aβ toxicity?

For more than two decades, the amyloid hypothesis has been the central hypothesis in coining the molecular pathology of AD (12). This hypothesis argued that amyloid fibrils, which are large insoluble polymers of Aβ found in senile plaques, are the trigger of neuron loss and dementia typical for AD. Albeit the convincing genetic, biochemical and cell biological data for a major role of Aβ in AD, growing evidence points towards soluble Aβ oligomers.

One of the major flaws in the amyloid hypothesis is the weak correlation between the severity of dementia and the density and localization of amyloid plaques in the brain of AD patients. Memory impairment and pathological changes in many AD mouse models occur before the first signs of plaque deposition. Soluble oligomers are low molecular weight non-fibrillar structures, which are stable in aqueous solution and remain soluble even after high speed centrifugation. Results from several labs propose these oligomers to be the missing link in the amyloid hypothesis. While Aβ plaques are poor correlates for the clinical symptomatology in AD and DS patients, soluble oligomers are suggested to be good predictors for synaptic loss, neurofibrillary tangles and clinical phenotype. With regard to short-term effects, oligomers have been shown to impair synaptic plasticity by blocking long term potentiation and reinforcing long term depression. Neuron loss is a consequence of oligomer exposure at low doses that occurs within several days (13).

Analysis of water-soluble Aβ in AD, DS as well as non-demented elderly brain specimens indicated the presence of $Aβ_{1-42}$, $Aβ_{pE3-42}$ and $Aβ_{pE11-42}$. In DS, water soluble Aβ appeared early (around 20 years before the appearance of the plaques) and increased with age and the progression of the amyloid pathology. Interestingly, water-soluble Aβ increased by 100-fold in young cases accompanied with an increase in $Aβ_{pE3-42}$. In line with this observation, water-soluble Aβ from brains of normal elderly individuals with abundant amyloid and neurofibrillary pathology demonstrated a decreased $Aβ_{pE3-42}$ to $Aβ_{1-42}$ ratio when compared to AD cases (14). Overall, the ratio of water-soluble $Aβ_{pE3-42}$ to $Aβ_{1-42}$ seems to be proportional to the clinical phenotype and the severity of the disease.

Passive immunization against low molecular weight pyroglutamate Aβ oligomers

In light of that, antibodies that are exclusively selective for oligomeric Aβ are promising tools for therapeutic intervention in AD for many reasons. Aβ oligomers represent less than 2% of the total Aβ pool in the brain which makes them an achievable therapeutic target especially assuming that only a minor amount of the antibodies can cross the blood brain barrier (0.11% of the circulating antibodies enter the brain (15)). Thus, targeting oligomeric Aβ can tremendously reduce the amount of antibodies needed to achieve the desired effect in comparison to fibrillar (plaques) Aβ representing the predominant species in AD brain. Also, antibodies against Aβ oligomers bind the pernicious toxic species and decrease the building units for fibrils; thereby hindering plaque formation. On the other hand, immunization against fibrillar forms may dissolve the plaques into soluble Aβ forms and thus increase the potentially toxic species in the brain. Furthermore, immuniza-

tion against the oligomeric Aβ minute species might spare patients from the drawbacks of some clinical trials such as microbleeds and hemorrhages that might result from an excessive immune reaction against Aβ plaques (16).

Our group has recently generated novel monoclonal antibody (9D5) that detects low molecular weight pyroglutamate modified Aβ oligomers (11). When the 9D5 antibody was added to $Aβ_{pE3-42}$ monomers, it efficiently decreased the formation of higher aggregates of the $Aβ_{pE3-42}$ peptide, but did not interfere with the rapid formation of $Aβ_{1-42}$ aggregates. Furthermore, adding the 9D5 antibody to SY5Y neuroblastoma cells completely abolished the toxic effects of $Aβ_{pE3-42}$ peptides, whereas the toxicity of $Aβ_{1-42}$ was unaltered. Interestingly, 9D5 showed a specific staining pattern in AD cases differentiating between non-demented control cases and AD. The therapeutic value of the 9D5 was tested in an AD mouse model, the 5XFAD model, with a relatively early and abundant $Aβ_{pE}$ levels compared to most of the currently used AD models (17). Passive immunization with 9D5 antibody in 4.5-month-old 5XFAD mice for six weeks was capable of reducing overall Aβ plaque load and $Aβ_{pE3-x}$ levels, leading to a normalization of the behavioral phenotype. Based on that, 9D5 represents a therapeutically and diagnostically effective monoclonal antibody targeting low molecular weight $Aβ_{pE3}$ oligomers (11).

Pyroglutamate Aβ as a potential diagnostic marker

The diagnosis of AD relies on neuropsychological tests, neuroimaging and CSF biomarkers. Nonetheless, the exact diagnosis is not definite unless the autopsied brain is examined and neuropathologically evaluated. Pittsburgh compound-B (PIB) is a modified form of thioflavin-T that crosses the blood brain barrier and binds to amyloid in nanomolar concentrations. Maeda et al. (18) demonstrated that the [11C]PIB signal correlated with the localization and abundance of $Aβ_{pE3-x}$ positive plaques. An *in vitro* binding assay revealed that specific binding of [11C]PIB to $Aβ_{pE3-x}$ fibrils was 4- to 5-fold higher than that to $Aβ_{1-x}$.

It has been observed that many AD and healthy control plasma samples showed the existence of IgG autoantibodies against $Aβ_{pE3-42}$ and $Aβ_{pE11-42}$ (19). Two studies from our group have shown that $Aβ_{pE3}$ might be of potential benefit as an AD biomarker. In the first study, the titer of IgM autoantibodies against $Aβ_{pE3}$ correlated with the cognitive status of individuals at risk to develop AD (20). In good agreement, the level of $Aβ_{pE3}$ oligomers was significantly decreased in plasma of AD patients (11). However, it is noteworthy to mention that these studies are pilot studies with small group sizes and need to be further replicated and confirmed using larger cohorts of patients and controls.

Pyroglutamate Aβ cyclization is catalyzed by glutaminyl cyclase

Glutaminyl cyclase (QC) belongs to the metal-dependent acyl transferase family converting glutamine (or alternatively glutamate) into pyroglutamate with the liberation of ammonia (or water) (21). Compelling evidence demonstrates the role of QC in the generation of $Aβ_{pE}$. Incubation of synthetic $Aβ_{3-x}$ with recombinant QC resulted in the conversion into $Aβ_{pE3-x}$; a reaction that is favored under acidic pH conditions and blocked by the presence of a QC inhibitor (5). Furthermore, in two different cell lines QC stimulated $Aβ_{pE3}$ generation (22,23). Application of a QC inhibitor suppressed the cyclization reaction to $Aβ_{pE3}$.

In agreement with *in vitro* studies, several *in vivo* reports have supported the role of QC in the production of $Aβ_{pE3}$. Oral administration of a QC inhibitor to two different transgenic mice reduced $Aβ_{pE3}$, $Aβ_{40}$ and $Aβ_{42}$ levels. This was accompanied by a reduction in plaque load and gliosis in addition to improvements in contextual fear memory and spatial memory. Similarly, treatment of transgenic Drosophila expressing $Aβ_{Q3-42}$ with a QC inhibitor led to reduced $Aβ_{pE3-42}$ (24).

In my doctoral project, the contribution of QC to the pathology of AD was investigated. In order to study the effect of ectopic human QC overexpression, 5XFAD mice were crossed with transgenic mice expressing human QC (hQC) under the control of the neuron-specific Thy-1 promoter. 5XFAD/hQC bigenic mice showed significantly increased levels of TBS-, SDS-, and formic acid-soluble $Aβ_{pE3-42}$ peptides and aggregation in plaques. 6-month-old 5XFAD/hQC mice developed accelerated motor and working memory impairments compared to 5XFAD mice. The effect of endogenous QC was studied by generating 5XFAD/QC-KO mice (mouse homozygous for murine QC knock-out). 5XFAD/QC-KO mice showed a significant reduction in $Aβ_{pE3-42}$ levels, decreased plaque pathology, and a rescue of the behavioral phenotype (25). These data clearly

demonstrate that QC is a key player in modulating $A\beta_{pE3-x}$ levels *in vivo* and support the concept that QC is a therapeutic target for AD. Interestingly, $A\beta_{pE3-42}$ levels were not completely reduced in homozygous 5XFAD/QC-KO; thereby shedding light on QC isoenzymes that might also play a role in $A\beta_{pE3-x}$ formation.

In summary, compelling evidence of a significant contribution $A\beta_{pE3}$ has been accumulated since its discovery in 1992. Its specific biochemical properties and the molecular events controlling the formation of $A\beta_{pE3}$ provide a better understanding of the pathology leading to AD and have the potential as a target for therapy as well as a marker for diagnosis (Fig. 2). Although $A\beta_{1-42}$ is a toxic peptide, a normal physiological function cannot be excluded. Current knowledge indicates that $A\beta_{pE3}$ is a solely pathological cousin of full-length Aβ acting as a dangerous "hatchet man" in AD.

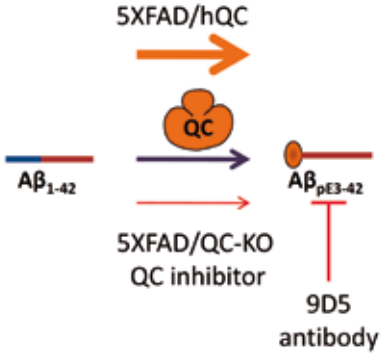

Fig. 2: Strategies for modulating $A\beta_{pE3-x}$ peptides by genetic modulation of QC, treatment with QC-inhibitor or by antibodies against $A\beta_{pE3.-x.}$

Sadim JAWHAR did her doctoral thesis in Thomas Bayer's dgroup, University Medicine Göttingen, Division Molecular Psychiatry. She was awarded a GGNB Excellence stipend in 2010. She will defend her PhD thesis in January 2012.

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Two pools or not two pools?

Synaptic vesicles for active and spontaneous transmitter release *by Benjamin Wilhelm*

During transmission at chemical synapses the synaptic vesicles fuse with the plasma membrane of the neuron, thereby releasing their neurotransmitter content into the synaptic cleft. As a result of this, the neurotransmitter is released from presynaptic terminals in equally sized amounts (referred to as quanta). Two distinct modes of vesicular release have been described in neurons: (i) spontaneous release of vesicles at rest and (ii) active (evoked) release triggered by an incoming action potential. For almost six decades it has been assumed that the very same vesicles are exocytosed during both types of activity. However, recently several studies have reported evidence for a separate pool of vesicles specifically maintaining spontaneous release. The existence of such a separate pool would substantially influence our current understanding of the synaptic vesicle cycle, and therefore we used several assays, in different preparations, to test the vesicles identity.

The quantal nature of synaptic release has been first described by Fatt and Katz in 1952[1]. Their recordings from the frog neuromuscular junction showed postsynaptic potentials (response of the postsynaptic cell to the release of neurotransmitter) which occurred spontaneously but with constant amplitude (approximately 0.5 mV). These have later been termed miniature electrotonic postsynaptic potentials (mEPPs) or simply "minis". Although Katz and colleagues were able to artificially evoke smaller postsynaptic responses (by directly applying small amounts of transmitter molecules to the muscle) the smallest response under physiological conditions at rest were the before mentioned minis[1, 2]. These findings led them to the conclusion that neurotransmitter molecules are released in increments of a constant size termed quanta. The findings on the nature of spontaneous release raised questions concerning the origin of evoked release. By lowering the external calcium concentration during active muscle stimulation it was discovered that the postsynaptic response could be reduced to a level where shape and size were identical to a mini[3]. An analysis of the fluctuations of evoked postsynaptic potentials revealed that they are composed of the same units (i.e. quanta)[4]. While during spontaneous release generally only a single quantum is released, during evoked release multiple of such quanta are released. It was shown later that a quantum corresponds to the fusion of a single vesicle giving rise to the quantal hypothesis that states that fixed neurotransmitters amounts are contained within synaptic vesicles[5], and for which Bernard Katz received the 1970 Nobel Prize in Physiology and Medicine.

As indicated above, their hypothesis is based on the assumption that spontaneous and active release are made of the same units. However, this concept

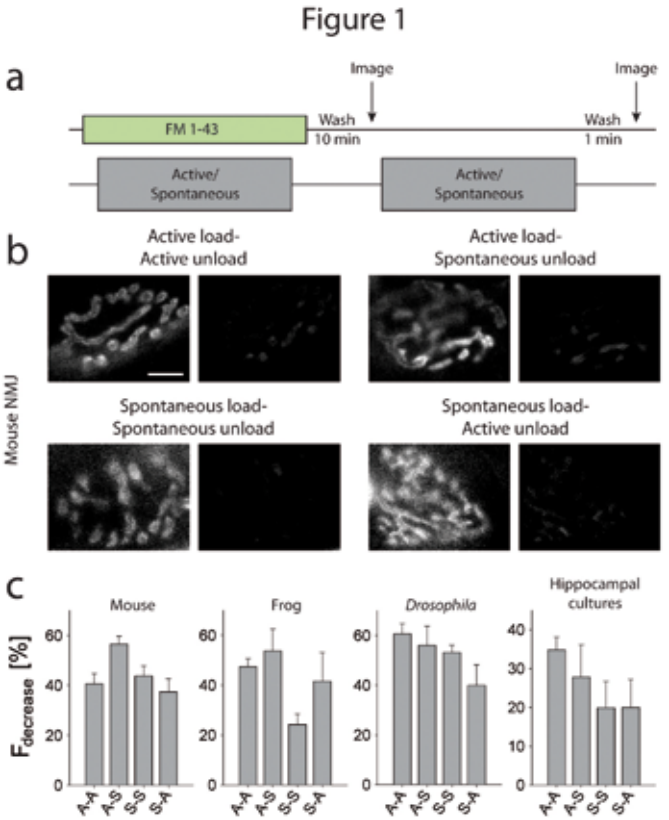

Fig. 1:Visualizing repeated synaptic vesicle recycling using the styryl dye FM 1-43. (A) Schematic of the experimental procedure: preparations are incubated in FM 1-43 while stimulated either actively or spontaneously. The preparations are then briefly washed and imaged followed by a second release period (again either actively or spontaneously). This unloading is then followed by a brief wash (1 min) prior to the second round of imaging. (B) Representative images of mouse neuromuscular junctions of all four loading-unloading combinations. Scale bar represents 10 µm. (C) Fraction of fluorescence decrease for all loading and unloading combination for the four model systems investigated (A – active, S – spontaneous). Bars show average ± SEM of 4-10 independent experiments. No statistically significant differences could be found ($P > 0.05$, one-way ANOVA tests). Figure reproduced from Wilhelm et al 2010[12].

has never been demonstrated. Recently, direct evidence for the existence of a separate SV pool maintaining spontaneous release has challenged this view. In hippocampal cultures, vesicles that were spontaneously labeled with a fluorescent dye (FM 2-10) showed only reluctant release of the dye upon stimulation (active release)[6].These findings have later been confirmed with different dyes (for example FM 1-43[7]) and also by using hippocampal brain slices in similar experiments[8]. Further evidence for a spontaneous pool of vesicles came from a study introducing a novel labeling technique where a protein of interest was biotinylated *in vitro* and detected by fluorescent streptavidin (which binds to the biotin). In this study the synaptic vesicle protein synaptobrevin was fluorescently labeled and changes in fluorescence upon active and spontaneous release were monitored. As their labeling protocols did not show any cross depletion of actively and spontaneously recycling vesicles (i.e. after depletion of the actively releasing pool of vesicles, spontaneous release could still take place) they also reached the conclusion of two separate vesicle pools maintaining the two modes of release[9].

All of the above outlined studies came to similar conclusions – i.e. that the synapse hosts completely independent actively and spontaneously recycling vesicles. However, these studies received substantial criticism. A number of issues have been raised: most of the studies used cultured hippocampal neurons which are highly sensitive to culturing and stimulation conditions. Minor differences in cell health for example might induce conflicting results. Also, different densities, ages and activity rates of the cultures might bias the experimental readout. Furthermore, some of the FM studies used them at extremely high concentrations, which may have affected vesicle release[10]. Finally, studies which based their findings on distinct kinetics of evoked and spontaneous release suffered from difficulties with the data analysis that may have altered the interpretation substantially (as suggested by Grömer and Klingauf 2007[11]).

The ongoing controversy about the existence of two separate vesicle populations that maintain active and spontaneous transmission (see models in Figure 1) renders the question important for the scientific community. Proof for either of the two models would cement what has been assumed for the past 60 years (in the case of one vesicle pool for both activities) or would to some extend break the foundation of the quantal theory (in the case of two separate pools).

In our study we tried to address this question with a simple approach: if the same vesicles maintain both types of activities one would be able to release them during active release as well as during spontaneous release[12]. If two separate pools exist, any individual vesicle would only recycle during one or the other paradigm. To test this we labeled synaptic vesicles of four different preparations (neuromuscular junctions of mouse, frog and Drosophila larvae as well as hippocampal cultures) with FM 1-43 during a first round of release either actively (electrical stimulation) or spontaneously (at rest), and then tried to unload the dye from them during a second round of release (again either actively or spontaneously) (see Figure 2a). The combination of the same loading and unloading paradigm (i.e. active-active and spontaneous-spontaneous) serves as a positive control, as it would be in agreement with both models. Interestingly, we were able to show that the active-spontaneous and the spontaneous-active combination unloaded to approximately the same extent (see Figure 2b and c), demonstrating that the same vesicles could indeed respond to both types of release. We further confirmed our findings in two different antibody based assays, labeling the synaptic vesicles calcium sensor synaptotagmin (data not shown). For imaging we turned to a variant of super-resolution STED microscopy – isoSTED[13] which provides a virtually isotropic resolution of <50 nm. Here we found that vesicles la-

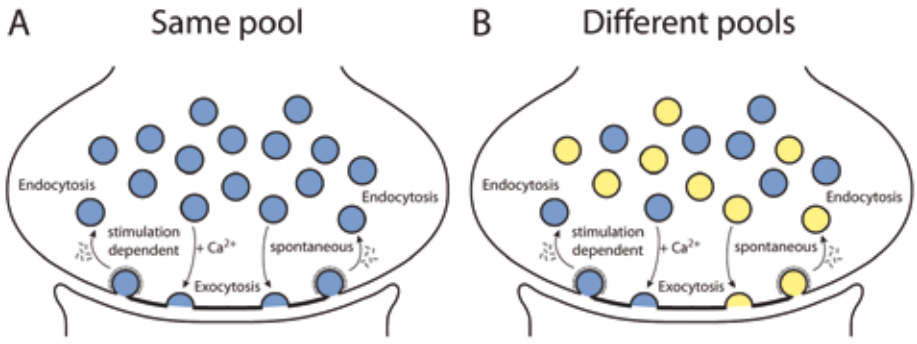

Fig. 2: Models for presynaptic vesicle pools (A) The same synaptic vesicles maintain active as well as spontaneous release. (B) Separate pools of synaptic vesicles maintain active (blue) and spontaneous (yellow) release.

beled during active release could be colabeled during spontaneous release even on the single vesicle level.

As one of the studies which suggested a separate pool of vesicles had used an over-expression system to address the topic, we decided to do the same in order to rule out any bias introduced by over-expression. Using the genetically encoded synaptopHluorin molecule (a pH dependent GFP variant[14] fused to the luminal side of the vesicle protein synaptobrevin) we probed again whether the very same vesicles would be recycled during a round of active and a consecutive round of spontaneous activity (data not shown). The exact same vesicles are released during both periods – hence the over-expression does not bias the experimental outcome towards separate pools of vesicles.

Thus, using four different experimental approaches and four different model organisms we could show that the same lipid membranes (styryl dye experiments), the same synaptotagmin molecules (antibody assays) and the same over-expressed synaptobrevin molecules were used during active as well as during spontaneous release. These findings strongly suggest that both types of release share a common pool of synaptic vesicles and confirm the 60 years old findings and interpretations by Bernard Katz and his colleagues (see also Hua et al. 2010[15]).

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

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Master's class 2010/11

Bekir Altaş (Turkey) BSc from Middle East Technical University (METU), Turkey

Mateusz Ambrożkiewicz (Poland) BSc from Warsaw University of Life Sciences, Poland

Vinita Bharat (India) BSc from Sri Venkateshwara College, Delhi University, India

David Brockelt (Germany) BSc from Georg August University Göttingen, Germany

Han-Yun Chen (Taiwan) BSc from National Yang-Ming University, Taiwan

Yen-Ying Chen (Taiwan) MSc from National Taiwan University, Taiwan

Ananya Chowdhury (India) MSc from Jawaharlal Nehru University, India

Wan Ilma Dewiputri (Malaysia) BSc from The University of Adelaide, Australia

Zohreh Farsi (Iran) BSc from Shahed University, Iran

Lauren Haag (USA) BSc from Emory University, USA

Ulrike Leipscher (Germany) BSc from University of Lübeck, Germany

Lawrence McKechnie (Scotland) MSc from University of Glasgow, Scotland

Kareem Soliman (Egypt) BSc from German University in Cairo, Egypt

Markus Stahlberg (Germany) BSc from University of Heidelberg, Germany

Ananya Tiwari (India) BSc from St. Stephen's College, Delhi, India

Oana Toader (Romania) BSc from University of Bucharest, Romania

Siv Vingill (Norway) BSc from University of Oslo, Norway

Welcome to Göttingen in the MSc class 2011/2012!

Mohammed Adel Gomaa, Egypt
Olga Babaev, Israel
Tanvi Butola, India
Hugo Cruces Solís, Mexico
Kirsten Emmert, Germany
Myroslav Gebura, Ukraine
Annika Graß, Germany
Leandra Hahn, Germany
Ja Bin Hong, South Korea
Mohammad Hossein Khani, Iran
Ricardo Martins Merino, Brazil
Ramanathan Narayanan, India
Dennis Nestvogel, Germany
Achintya Prahlad, India
Samyutha Rajendran, India
Julio Santos Viotti, Brazil
Nidhi Subhashini, India
Adam Tomczak, Poland
Simon Weiler, Germany/Switzerland
Man Ho Wong, Hong Kong SAR

Applications 2011

In the year 2011, the Neuroscience program received 247 applications from 51 countries.

Germany 24
other Western Europe 9
Eastern Europe 33
North America 5
Central/South America 16
North Africa 10
Central/South Africa 14
Asia / Near East 42
Central Asia / Far East 93
Australia 1

New Students

PhD projects started in 2010 and 2011

2010

Dorota Badowska
Studying gene - environment interactions in TCF4 transgenic mice
Hannelore Ehrenreich, André Fischer, Moritz Rossner

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

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

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

Pooja Rao
Epigenomic imaging of Alzheimer's Disease: novel strategies to treat dementia
André Fischer, Judith Stegmüller, Wolfgang Fischle

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

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

Diana Urrego Blanco
Control of KCNH1 functional expression by the P53/miR34/E2F1 axis in neurons and tumor cells
Luis Pardo, Tobias Moser, Detlev Schild

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

2011

Mateusz Ambrożkiewicz
The Function of the NEDD4 Family Helt Type E3 Ubiquitin Ligases in the Nerve Cell Development
Nils Brose, Judith Stegmüller, Ahmed Mansouri

David Brockelt
Role of the E3 ligase FBX07-SCF in early onset Parkinsonism
Judith Stegmüller, Tiago Outeiro, Klaus-Armin Nave

Wan Ilma Dewiputri
Neurofeedback fMRI-mediated training in cognitive processes
Jens Frahm, Stefan Treue, Michael Waldmann

Hung-En Hsia
Roles of HECT Type Ubiquitin E3 Ligases in the Development of the Brain
Nils Brose, Judith Stegmüller, Andreas Wodarz

Chaitali Mukherjee
The role of the F-box protein FBX041 in neuronal morphology and its implications in Schizophrenia
Judith Stegmüller, Mikael Simons, Michael Hörner

Natalia Revelo Nuncira
Localized signaling reactions in the developing growth come during navigation / Membrane trafficking in sensory synpase
Silvio Rizzoli, Mikael Simons, Tobias Moser

The Doctors of 2010 and 2011

2010

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

Thomas Frank
Investigating the Calcium Signaling at Ribbon Synapses
Tobias Moser, Detlev Schild, Erwin Neher

Sebastian Gliem
Characterization of olfactory receptor gene expression in the olfactory epithelium of larval Xenopus laevis
Detlev Schild, Ralf Heinrich, Jürgen Wienands

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

Wen Hu
Effects of stress on the GABAergic system in the hippocampal formation and medial prefrontal cortex of the adult male rat
Gabriele Flügge, Ralf Heinrich, Hubertus Jarry

Chao-Hua Huang
The mechanisms underlying synaptic transmission at the layer 4 of sensory cortical areas
Erwin Neher, Oliver Schlüter, Tobias Moser

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

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

Shahaf Peleg
Altered Histone 4 K12 Acetylation is Associated with Age Dependent Memory Impairment in Mice
André Fischer, Mathias Bähr, Wolfgang Fischle

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

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

2011

Ramya Nair
Synaptic Targeting of Neurotransmitter Receptors is Regulated by Neurobeachin
Nils Brose, Tobias Moser, Erwin Neher

Pinar Öz
Theoretical analysis of membrane properties underlying action potential phase-locking in noise-driven cells
Tobias Moser, Fred Wolf, Walter Stühmer

Kirsten Reuter
Biochemistry and physiological role of otoferlin
Tobias Moser, Reinhard Jahn, Nils Brose

Nikhil Sasidharan
Analysis of the RAB family of GTPases in C. elegans and their role in regulating neuronal membrane trafficking
Stefan Eimer, Nils Brose, Walter Stühmer

Raunak Sinha
Optical analysis of synaptic vesicle protein molecules during exo- and endocytosis using pH-switchable fluorescent probes
Jürgen Klingauf, Erwin Neher, Walter Stühmer

Postdoc in Seattle?

by Mrinalini Hoon

Moving continents wasn't new to me. I had done it before when I moved from India to join the MSc/PhD Neuroscience program, and now I was going to move from Göttingen to Seattle to start my Postdoc at the University of Washington. I guess the first question that most people wondered about was: Why Seattle? When you say you are going to the US for a Postdoc everyone assumes that it will be in the east coast or California. But to my surprise Seattle is a beautiful city with an enriching scientific environment. It is more 'European' than most US cities and apart from tall skyscrapers, which are the hallmark of every large US city, Seattle is enveloped by natural beauty with snow-capped mountains on all sides, lakes within the city and forests surrounding the city. Apart from that there is a scientifically inspiring atmosphere with several leading research institutes, which facilitates a friendly exchange of ideas and resources that is very reminiscent of the vibrant scientific environment in Göttingen.

Every country has its own rhythm and pace and the transition to a big US city from our small town Göttingen took me some time. I took the longest to get back my sense of security. I remember walking down the streets of Göttingen late at night and feeling completely safe. Of course, I was advised not to try this in the US. But Seattle is safer than most US cities and as the University is a big part of the city, one can find loads of ambitious students and curious researchers roaming around, very similar to Göttingen. The main campus of the University of Washington is, indeed, impressive, with architecturally inspiring buildings housing different faculties and exhaustive libraries like the Suzzallo Library, the interior of which seems to fit right into a 'Harry Potter' movie. The cherry blossom quad, the rose gardens and the Drumheller fountain surrounding these buildings provide the right balance between work and relaxation. Moreover, there is an array of restaurants and shops lining the University Avenue beside the main campus to ensure that students never go hungry. The Health Sciences' building, where I work, is situated beside the lake, and one can always find some peaceful thinking time in the cafeteria overlooking the lake. Moreover, for all the over-worked staff, there is always an option to rent a kayak just a few steps from the lab!

The administrative part of my move to US was tougher than what I faced when I moved to Göttingen from India. We were pampered when we joined the Neuroscience program with the Coordination Office taking care of all the administrative formalities. Here in the US, I had to deal with all these formalities (insurance, social security, finding an apartment with no US financial history etc.) completely on my own, which was often quite overwhelming. Shifting from the Max Planck Institute, where I did my PhD, was also a transformation. I remember the mouse facility and the well-organized staff of the Max Planck Institute with much nostalgia!

I must say that dealing with my new Postdoc life would have been far more difficult had I not had the support of all my lab members. In my new lab we deal with problems (personal and professional) with cupcakes and chocolates (!), and although I miss the German pastries and chocolates, Seattle has a very good array of cuisines from all over the world. One can spoil oneself with a choice of gelatos, hand-made chocolates, sushi, mouth-watering Pad Thai, and of course lots of Starbucks coffee. The 'Seattleites' love sports and you can find people jogging at all times of the day, and this also inspired me to make exercise a part of my life.

Moving from tropical India to Göttingen took a lot of adjusting weather-wise. The cloudy days in Göttingen and the long winter pushed all scientists to stay in the lab and focus on the experiments! Well this part is very similar to Seattle, which is the 'rainy city'. But Seattle can also be breathtakingly beautiful on a clear sunny day, when one can catch a glimpse of Mount Rainier from the main campus.
All in all moving from Göttingen was like a mini-adventure for me. I enjoyed getting to know Seattle and meeting new friends and work colleagues. Of course a Postdoc teaches you to think independently as a researcher, but the move to the US also taught me one more time how to adapt to a new environment. I guess it is true when people say : *Change is the only constant in life.*

Mrinalini HOON did her doctoral thesis in Nils Brose's department, Max Planck Institute for Experimental Medicine, Molecular Neurobiology. She defended her PhD thesis in April 2010.

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School excursion

... and back to science *by Andrea Wirmer*

After nine years at university, I was exhausted and a bit fed up with science. Bitterly, I had the impression that being a scientist had almost nothing to do with the honorable search for truth but with competition, pressure to publish and never ending work. I didn't want to muse about experiments every minute of my life anymore, I wanted to know when the work was done, go home after eight hours without remorse and simply enjoy my leisure-time. So, I thought: "Hey, school!"
I had always liked teaching students in the seminars and was under the impression, they had liked it, too. I liked explaining things to others including tinkering of models or drawing pictures at a board. Teaching biology wouldn't be too hard and work was over when the lessons or the tests were prepared. As a nice side effect, I considered me teaching at a school much more useful than me sitting in front of a cage full of grasshoppers, what I had done most of the time during my PhD.
Luckily, I got the opportunity to work at a vocational school immediately after finishing my PhD and teach biology, math, microbiology and science (a mixture of biology, chemistry and physics). My youngest student was 15 and the oldest about 35, so no problems with little children and teens in puberty, I thought.
But teaching a school class is very different from teaching a small group of university students in a seminar, and the school subject biology is very much different from the study of biology. While in your research studies you want to "boldly go where no man has gone before", at school you focus on the things that are known for the last say fifty years, you pretend that everything in the world of biology is explored and explicable.
Sometimes I wished, I could simply stand in front of the class and give them the information about photosynthesis I had found in a book but that is far away from the up-to-date-education-style. Today, the teacher has the function of a moderator. One starts a lesson with a few words, then gives a task, leads discussions and summarizes the answers at the board. To somehow get the students' attention and their interest I spent hours and hours with developing funny games, experiments and group exercises, and the work was never done. While, presumably, the students had only one question in their

mind: "Which part of this (nonsense ..) do I have to know for the test?" And with this attitude the simplest logical relation becomes very difficult to grab. And when I waited for the students to finish some task, I thought: "What have I already done to cells? I stained them with different antibodies, recorded their action potentials, let them grow in a cell culture, monitored exocytosis, and here I'm standing and those people are not able to memorize ten cell organelles."

Twice the term I had to make the students write a test. There were strict regulations how a test had to look. Questions may not start with: how, what, where... but only with verbs. As a consequence, I had to explain to half of the class: "Describe means: How does it look? No, if you read explain you have to give an explanation like: How does it work?" And I always wished I wouldn't catch somebody cheating but it happened a few times. After the test correction, which sometimes lasted several afternoons because it was not enough to just mark the mistakes I always had to write a short explanation at the margin and punish every spelling mistake, came the returning of the test. And that sometimes was the hardest time for me: As a tutor in a university seminar I myself was never fully responsible, since some professor had designed and graded the test; I had just done what I was paid for. As a school teacher I was in full responsibility and after having put so much work into a test, I had to listen to fierce accusations after correcting and returning it. ..the questions were too difficult, too unfair, too unclear, my teaching style was completely misleading etc. …

After half a year, I could see all the advantages of science crystal clear. At school and for school I had to do loads of tedious work. A science project also means a lot of work but you can decide what you want to do, what you think is the most interesting question, and you can develop your own methods to answer it. You can do presentations in front of an interested audience, you can think about the content of your talk and not about ways to wrap it in tiny packages and how to make a game out of it. You can travel, meet interesting people, design posters and have fruitful discussions about them.

In retrospect, it wasn't a bad idea to go 'back' to school to teach. At the beginning I was afraid that students would be mean or impolite but most of the times, I was surprised how calm, friendly and likable teens can be (except when getting back a test). But I didn't expect my difficulties with playing the role of a school teacher. It felt a bit strange to fulfill the assignment to educate the students not only academically but also socially when some of them were not so much younger or even older than me. At least this experience opened my eyes again for the bright sides of science.

Since September I'm working as a Post-Doc in the department of Neurobiology at the University of Ulm and am very, very happy to be back in science!

Andrea WIRMER did her doctoral thesis in Ralf Heinrich's group, University of Göttingen, Johann Friedrich Blumenbach Institute for Zoology and Anthropology. She defended her PhD thesis in July 2010.

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Science Management in Heidelberg

by Esther Breunig

For me science and applied research are amazing and fascinating. During my PhD thesis and the time as a Postdoc I learned how to solve scientific problems and how satisfying it is to generate knowledge together with other scientists.

Besides working in a university department I was also interested in changing the perspective and looking at a whole research institution. I wanted to know how goals of research institutions are defined, how strategies to reach these goals are developed and how single departments contribute to the implementation.

In order to combine these two interests I joined the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ; *http://www.dkfz.de*) in Heidelberg. At the DKFZ I work as the Scientific Assistant to the Chairman and Scientific Director of the Management Board. In this position I am surrounded by science every day and at the same time I directly contribute to the management of such a huge institution.

dkfz. DEUTSCHES KREBSFORSCHUNGSZENTRUM IN DER HELMHOLTZ-GEMEINSCHAFT

The DKFZ is the largest biomedical research institute in Germany and is a member of the Helmholtz Association of National Research Centers. More than 2,200 staff members, including 1,000 scientists, are investigating the mechanisms of cancer and are working to identify cancer risk factors. They provide the foundations for developing novel approaches in the prevention, diagnosis, and treatment of cancer. In addition, the staff of the Cancer Information Service (KID) offers information about the widespread disease of cancer for patients, their families, and the general public. The Center is funded by the German Federal Ministry of Education and Research (90%) and the State of Baden-Württemberg (10%).

In my current position I am directly involved in the operative business of the Scientific Director of the DKFZ. For example, I attend meetings together with the Scientific Director and thereafter it is also my responsibility to follow up the decisions of these meetings. Another important aspect of my work is to prepare decisions made by DKFZ committees, e. g. the Scientific Advisory Board. Moreover, I have to accompany new initiatives and projects at the DKFZ.

Since these responsibilities may sound very abstract, I want to give you an example: After recruitment of a junior group leader I have to take care about the integration of this group into the DKFZ. This means that I arrange the establishment of the group, clarify the affiliation to a specific research program at the DKFZ and the access to required equipment. Whenever they have questions they contact me. I regularly organize meetings with all junior group leaders to discuss their current concerns and during their tenure evaluation I will coordinate the evaluation

Outside Academia

procedure and thereafter I am responsible for the implementation of the evaluation result.

These tasks are only a few of the things I deal with. There are many more issues that I cover and make my working days diverse.

Besides these new tasks, I have to deal with the "way of working" which is completely different from the way of working in a lab. In an institution with about 2,200 staff members one can imagine that it takes a while to get to know all departments, the head of the departments as well as the administration and the activities going on there. Every day I interact with people from scientific departments, from the human resources, from the finance department, the technical department and even with people from other institutions. There are almost no topics that I work on alone. Also, the rhythm of work changed completely. It is necessary that all meetings and activities are fast and well-structured.

Esther BREUNIG did her doctoral thesis in Detlev Schild's department, Neurophysiology and Cellular Biophysics, Center of Physiology and Pathophysiology, University of Göttingen. She defended her PhD thesis in October 2009.

German Cancer Research Center Heidelberg
Im Neuenheimer Feld 280
69120 Heidelberg / Germany

In my opinion, the position as a scientific assistant to a key person is perfect to learn and qualify for science management. It is a very diverse and interesting function that allows me to look at scientific activities from a completely different perspective.

A bridge linking science to investment

by Ling Luo

2011 has been the most important year in my career life, since I switched my direction twice, from science to biotechnology, and then to finance. This, indeed, sounds a little bit too fast, but I am happy that I found what I really want and enjoy what I am doing right now.

I have to say that I chose an unusual way after my PhD. Every time I told my friends, especially Chinese friends, that I was going back to China directly after PhD, I got questions like "What? Why not continue with a Post-doc in Germany or the US?". And in fact, not so many Chinese went back to China after receiving a PhD in Europe or the US. The reasons for me to make this decision were complex, but one of them is that I believe the world is changing. China today is so different from what it was like when I came to Germany six years ago. Although challenging, it is also exciting to be part of the 'booming times'.

Although I attended university in Beijing, I like Shanghai much better, because this city is more international in every aspect. I was so lucky that in the train to Shanghai I received a call inviting me for an interview. After two rounds of interviews I got a job as a senior research scientist in Shanghai Chempartner, which is a NYSE listed CRO (Contract Research Organization) company. Nowadays, more and more pharmaceutical companies outsource their R&D sectors to CRO companies, in order to cut cost and raise efficiency. I did learn a lot from this job. We collaborated with clients like Kimberly-Clark, Sanofi, GlaxoSmithKline and Roche, as well as some small biotechnology companies. I took projects like "screening natural compounds that inhibit PGE2 mediated inflammation" and "identifying biomarkers in hepatocellular carcinoma tissues". Daily life in the CRO company was not different from what I was used to in the lab: Western blot, PCR, cell-based assay... The work load was also OK, from 9:00 to 5:00, no extra time. However, I realized that preclinical research is only

a part of the whole pharmaceutical industry. What I want to know is how the whole system is running, which is hard to achieve if I would have sticked to benchwork.

Another reason why I like Shanghai is that there are always plenty of opportunities for you. After working in the CRO company for half a year, I got my present job as an equity researcher in a PE (private equity) fund. We invest into companies before IPO ('initial public offering') and also in the secondary market. This really opens a new door for me, but it is also a big challenge. Although still focusing on the biomedical area, I have to learn a lot about other aspects of the pharmaceutical industry. In order to judge whether a company is worth investing into, I must cover all important details about the company and its drugs: What is the molecular mechanism? How good is the data from *in vitro* and from animal models? How is the clinical trial going on? Are there patent issues? What is the status of the regulatory affairs? Are there other drugs targeting the same disease and at what stage are the clinical trials? Will the drug show a good market performance, if it is approved? How is the managing team? Not all the questions can be addressed by reading literature and reports, so I also have to talk to the key persons of those companies and experts in different disease areas, which is somehow like what a journalist does. At the same time, financial analysis is also important. I have to set

Outside Academia

up quantitative models to estimate the value of the company. To make the final investment decision is not easy. I have to write a detailed report at least 40-50 pages and do several presentations to persuade my colleagues. This is like writing a small thesis and quite similarly the key is the data and your logic behind it.

Our research team consists of a chemist, an electric engineer, a software engineer, a financial expert and me, a biologist. Although our team is small, we collaborate quite efficiently, and also learn a lot from each other. Now I know quite much about nanotechnology, new energy technologies, softwares … I am often amazed by how science and technology dramatically changed our life. Finance is the catalyzer that makes this process faster. Biotechnology in China is still in the starting stage; I hope I can contribute to this emerging industry by bridging the gaps between scientists and investors.

On the other hand, doing investment to me seems much more stressful than doing experiments. For good investment candidates, we do not have too much time for making decisions. I often work after dinner till 11-12pm, and sometimes over the weekend. But it really pays back when you successfully persuade others to invest and the candidate company then performs well, or even better than you expected.

Having stayed in Shanghai for nearly a year, I really miss Göttingen's relaxing atmosphere. I now spend 50 minutes single way to commute from home to office, whereas I biked for just 10 minutes to the ENI lab in Göttingen. Anyway, there are good and bad things in both worlds. But the most important thing is to find what you really want to do. My advice when the question eventually comes whether to stay in science or not, just try different possibilities if you can, and you will find the answer.

Ling LUO did his doctoral thesis in Stefan Eimer's department, Molecular Neurogenetics, European Neuroscience Institute Göttingen (ENI-G), University of Göttingen. He defended his PhD thesis in July 2010.

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China

Creutzfeldt Award

Stipends/Honors/Prizes

Alonso Barrantes Freer selected participant of the Lindau Nobel Laurate Meeting in Konstanz

Ioanna Bethani Winner of the Creutzfeldt PhD Price 2011

Ilma Dewiputri PhD stipend from the Ministry of Higher Education Malaysia (MOHE)

Stephan Junek Winner of the Creutzfeldt PhD Price 2011

Shahaf Peleg Schilling Research Award by the German Neuroscience Society 2011 for young researchers

Chor Hoon Poh PhD stipend from the University Clinics Göttingen (UMG)

Pooja Rao PhD Fellowship by the European Neuroscience Campus Network (ENC Network)

Swathi Srivatsa PhD Fellowship awarded by Boehringer Ingelheim Fonds

Juan Daniel Flórez Weidinger PhD stipend 'Neurosenses' from the State of Lower Saxony ('Lichtenberg Stipend')

Nora Wender Stipendiary of the Studienstiftung des deutschen Volkes, PhD stipend by the Dorothea Schlözer program

Benjamin Wilhelm PhD Fellowship awarded by Boehringer Ingelheim Fonds; selected participant of the Lindau Nobel Laurate Meeting in Konstanz; Best Poster Award for the contribution "New Optical Methods in Cell Physiology" at the yearly symposium of the "Society of General Physiologists" in Woods Hole, MA/USA

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 price is awarded since 2007 to PhD graduates of the Neuroscience program based on excellent achievements during the PhD and the grading of the written dissertation and the oral defense. In 2011 for the first time 2 winners have been selected for the Creutzfeldt Prize.

The award ceremony took place on 25. May (2011) during the opening of the NEURIZONS Symposium 2011 in the presence of Erwin Neher, Dieter Melzner (Sartorius stedim AG) and Mary Creutzfeldt, who presented 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 generously supports 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 and Dr. Stephan JUNEK (2011)

Dr. Ioanna Bethani
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
Max Planck Institute for Brain Research
Neural Systems and Coding Group
Deutschordenstraße 46
60528 Frankfurt am Main

Creutzfeldt Award Ceremony during the opening of the NEURIZONS Symposium 2011 (from left to right): Erwin Neher, Dieter Melzner, Ioanna Bethani, Stephan Junek, Mary Creutzfeldt, Michael Hörner

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

New Faculty

Joining the program since 2010

Camin Dean
has been a group leader in the European Neuroscience Institute Göttingen since 2010. Working on trans-synaptic signaling, her lab is interested in the mechanisms by which individual synapses, neurons and circuits dynamically adjust their transmission properties in response to changes in neuronal network activity. During her first year in the institute, Dr. Dean was awarded the prestigious Sofja Kovalevskaja prize by the Alexander von Humboldt Foundation. In addition, she received an ERC (European Research Council) Starting Grant funded be the EU in 2010. Dr. Dean hosted several lab rotation students and will now also supervise students from the Neuroscience program during their MSc/PhD projects.
Further information: http://www.uni-goettingen.de/en/215192.html

Alexander Flügel
works in the field of neuroimmunology, T cell biology, and intravital imaging. Prof. Flügel came to Göttingen in December 2008 and was appointed as full professor and director of the Department of Neuroimmunology / Institute for Multiple Sclerosis Research , which is supported by the Hertie Foundation. After his arrival in Göttingen, Prof. Flügel joined the Göttingen Graduate School for Neurosciences and Molecular Biosciences and became a member of the Neuroscience program.
Further information: http://www.uni-goettingen.de/en/215604.html

Tim Friede
worked as lecturer and professor at universities in the UK and as expert statistical methodologist in the pharmaceutical industry before he became the Director at the Department of Medical Statistics at the University Medical Clinics Göttingen in 2010. His major research interests comprise the design and analysis of clinical trials, particularly the so-called adaptive designs. Giving lectures in the Neuroscience program since 2010, Prof. Friede became faculty member in 2011.
Further information: http://www.uni-goettingen.de/en/215207.html

Stefan Hell

moved to Göttingen in 1997 as head of the Max-Planck Junior Group High Resolution Optical Microscopy and became Director at the Max Planck Institute for Biophysical Chemistry, Head of Department of NanoBiophotonics in October 2002. Prof. Hell works on optical microscopy beyond the diffraction barrier with far-field optics and the invention of STED and 4Pi microscopy and related techniques. He and his group have received several prestigious awards and hold many patents. Prof. Hell is a member in three programs of GGNB: Neurosciences (IMPRS), Molecular Physiology of the Brain (CMPB), and Physics of Biological and Complex Systems.
Further information: http://www.uni-goettingen.de/en/57981.html

Siegrid Löwel
came to Göttingen in 2010 where she is affiliated with four GGNB programs: Sensory and Motor Neuroscience, Theoretical and Computational Neuroscience, Systems Neuroscience, and the IMPRS Neurosciences. The Löwel lab has made major contributions to experience-dependent changes in nerve cell networks and only recently helped to establish optical imaging of intrinsic signals as a screening tool for cortical plasticity in mice and started characterizing various mutant mice.
Further information: http://www.uni-goettingen.de/en/201987.html

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 is a member of the Neuroscience (IMPRS) and the CMPB program (Molecular Physiology of the Brain).
Further information: http://www.uni-goettingen.de/en/215200.html

Jochen Staiger
has been appointed as professor and director of the Department of Neuroanatomy at the Georg August University Göttingen since 2010. His research focusses on developmental plasticity, sensory information processing and analysis of synaptic connectivity in the neocortex or genomic regulation of experience-dependent plasticity in the trigeminal somatosensory system. Prof. Staiger is member of the Neuroscience and the GGNB PhD Program Sensory and Motor Neuroscience.
Further information: http://www.uni-goettingen.de/en/189453.html

Left the program since 2010

Edgar Brunner
was the Head of the Department of Medical Statistics at the University Medicine Göttingen and a member of the Neuroscience program since the beginning in the year 2000. From 2004 until 2009 he edited the Biometrical Journey and was an associated editor of the Journal of Statistical Planning and Inference since the year 2000. In the Neuroscience Program, Prof. Brunner taught the Neuroscience students with great enthusiasm and helped them understanding the relevant concept and principles of statistics needed for the quantification of experimental data in diverse fields. All Board Members of the Neuroscience Program thank Prof. Brunner very much for his engagement and valuable contributions, which firmly integrated the topics of statistics and applied mathematics in the MSc curriculum.

Victor Tarabykin
obtained his medical degree from the Russian State Medical University Moscow in 1993 and graduated with a Ph.D. from the Russian Academy of Sciences in Moscow in 1996. He joined Prof. Peter Gruss' lab at the Max Planck Institute for Biophysical Chemistry and became a research group leader at the Max Planck Institute for Experimental Medicine in 2002. Prof. Tarabykin joined the Neuroscience Program in 2006. Prof. Tarabykin's group focuses on mechanisms controlling cortical development and the generation of cortical layers, and cellular and molecular mechanisms underlying cell specification. Prof. Tarabykin took over a position at the Charité Berlin and is now project leader in the Institute of Cell Biology and Neurobiology.
Further information: http://cbn.charite.de/en/institute/team/profile_tarabykin/

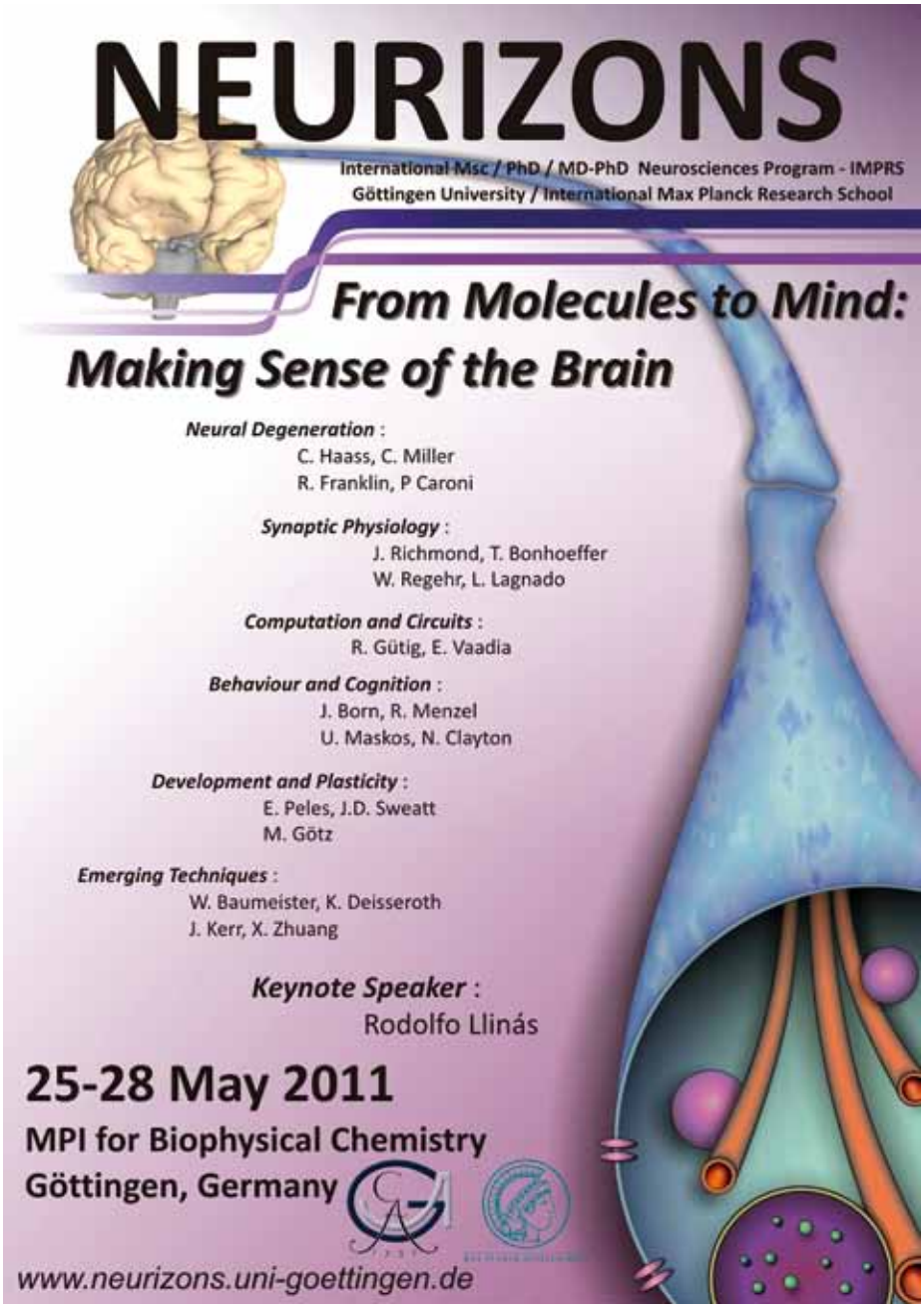
Current Faculty Members

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

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

NEURIZONS 2011

A meeting of the minds *by Pooja Rao and Sanaz Bahari Javan*



The Neurizons conference 2011, organized by students of the IMPRS Neuroscience program, took place at the Max Planck Institute for Biophysical Chemistry, Göttingen from 25th to 28th May, bringing together neuroscientists from a wide range of disciplines such as synaptic physiology, computational neuroscience, cognition, and neural dysfunction. This was the fourth in a series of biennial conferences organized solely by the students of the program, supported by the Max Planck Institutes for Biophysical Chemistry and Experimental Medicine, the European Neuroscience Institute, the Center for Molecular Physiology of the Brain, and the University of Göttingen. Generous donations from various private and industry donors also helped to cover the costs of the Neurizons meetings.

With a new record number of more than 250 registered participants from all over the globe and 22 invited speakers, Neurizons 2011 provided exciting opportunities for direct communication of young and more advanced scientists from many different institutions and nationalities in the interdisciplinary field of neuroscience.

The theme of this year's conference was "From Molecules to Mind – Making sense of the Brain", and the 4-day meeting was organized subject-wise into 5 sessions. For the first time, Neurizons 2011 offered "NeuroNetwork" meetings, in which scientists provided insights into their personal biography, career planning and daily work to small groups of PhD students. This format was generously supported by the Boehringer Ingelheim Fonds.

The conference kicked off with a talk by Jan Born about the role of sleep in memory formation as a part of the Behavior and Cognition session, which also featured Uwe Maskos, Rex Jung, and Randolf Menzel. The speakers in the Synaptic Physiology session the following day included Tobias Bonhoeffer who is credited with pinwheels in the mammalian visual system and the role of neurotrophins and BDNF in synaptic plasticity, Janet Richmond, who was among the first to work on electrophysiology in *C.elegans*, Leon Lagnado and Wade Regehr. Robert Gütig, who was involved in developing the tempotron, a novel neuronal network model of supervised spike-timing based synaptic

plasticity, and Eilon Vaadia director of the Motor Cortex Research Laboratory at the Hebrew University of Jerusalem, from whom the audience learned about a new brain machine interface, constituted the Circuits and Computation session.

The morning session on the third day of the conference was titled Neural Dysfunction. The speakers in this session were Christian Haas, known for his work on amyloid beta pathology in Alzheimer's disease, who spoke about his research in the Zebrafish model, Pico Caroni, Robin Franklin and Chris Miller. The afternoon session, Development and Plasticity, involved aspects of synaptic plasticity, myelination and neurogenesis, from David Sweatt, Elior Peles and Magdalena Goetz, respectively. The concluding session, Emerging Techniques, which focused on recently developed methods that have generated interest in the neuroscience community, included talks by Karl Deisseroth, who coined the word 'optogenetics', and Wolfgang Baumeister, who pioneered the cryo electron tomography technique. All talks were well attended and varied in nature, with several speakers choosing to share new and soon-to be-published findings.

The keynote speaker was Rodolfo Llinás, Thomas and Suzanne Murphy Professor of Neuroscience and Chairman of the department of Physiology & Neuroscience at the NYU School of Medicine and author of the book ' "I" of the Vortex '. While Prof. Llinás' research interests focus on the intrinsic properties of neurons, he is well known for his theories on the evolution and development of consciousness. In a thought-provoking keynote lecture on the astounding abilities of the brain he stressed that "The most important task of the brain is active movement."

A new feature of the 4th Neurizons meeting was a networking event sponsored by the Boehringer Ingelheim Fonds. The NeuroNetwork session, focusing on direct dialogue between students and certain invited speakers, gave students and young scientists the opportunity to have a 'heart-to-heart' in small groups of up to 8 participants. "We wanted to provide the students a source of wisdom concerning their questions, fears and uncertainties for a career in science", said Benjamin Wilhelm, one of the PhD students who organized the meeting. Scientists who shared the ups and downs in their own career and answered questions about what happens behind the scenes in science included Janet Richmond, Leon Lagnado, David Sweatt, Chris Miller and Rex Jung, as well as the local Nobel laureate Erwin Neher.

NeuroNetworks (David Sweatt meeting with students)

The poster sessions, with more than 70 posters displayed over 2 days, were held in the evenings. The posters spanned a wide range of topics, and a significant international contribution was evident.

In keeping with the tradition that no conference is complete without its social events, the Neurizons 2011 included a guided "pub crawl" or a tour of the pubs in Göttingen, a conference party, as well as wine and cheese evenings accompanying the poster sessions.

NeuroNetworks (Leon Lagnado meeting with students)

The largest contributors to the success of the event were the student organizers. When asked about his motivation to speak at the Neurizons, Prof. Llinás said "An invitation from students is like an invitation from the future", echoing a theme that many other invited speakers emphasized. This year's organizing team included Derya Akad, Alonso Barrantes Freer, Jonas Barth, Ahmed El Hady, Cordelia Imig, Juan Daniel Flórez Weidinger, Natalia Manrique Hoyos, Alejandro Mendoza Schulz, Sünke Mortensen, Jatin Nagpal, Christina Reetz, Natalia Revelo Nuncira, Meike Schweisfurth, Nicolas Snaidero, Roman Stilling, Nora Wender, Benjamin Wilhelm, and Aaron Wong of the IMPRS Neuroscience program.

Neurizons 2011 was supported by the Boehringer Ingelheim Stiftung, Synaptic Systems, Mobitec, Leica, Zeiss, the European Neuroscience Institute Göttingen, NPI, iBA bioTAGnology, Sartorius Stedim biotech, and refreshments at the social events were sponsored by Einbecker and Göttinger breweries.

What most people look forward to at such a meeting is to exchange ideas and foster collaborations. As in previous years, scientists from the Weizmann Institute of Science in Israel cooperating with the IMPRS Neuroscience Göttingen since 2005 were invited for the Neurizons symposium, and a group of 6 PhD students joined the meeting and presented posters. Similar to Neurizons, students of the Weizmann Institute of Science have initiated the NeuroWISE meeting and some students of the Göttingen PhD programs will have the opportunity to attend the next meeting scheduled for January 2012 in Rehovot, Israel and to continue and further develop this German Israel science connection.

All in all, the event not only helped create connections between young neuroscientists and established researchers in the field, but also served up a dose of inspiration to the neuroscience community in Göttingen. We look forward to an equally successful Neurizons 2013.

The Neurizons 2011 Organizing Team

Simplicity beyond complexity

Thoughts on communicating science *by Nora Wender and David Hofmann*

Rodolfo Llinás, Professor of Neuroscience and Director of the Neuroscience graduate program at the New York University School of Medicine, was the Neurizons 2011 key note speaker. Llinás has spent more than 50 years studying the brain and as a leader in the field has received many prestigious awards for his work. His research covers a broad spectrum of neuroscientific topics ranging from electrophysiological properties of single neurons to thalamocortical interaction using magnetoencephalography. Among his many contributions, he was the first to describe calcium microdomains. Professor Llinás kindly agreed to give an interview regarding his decision to become a neuroscientist and his view on communicating science to the public. The interview with Rodolfo Llinás (***RL***) was done by Nora Wender (***NW***) and David Hofmann (***DH***).

Rodolfo Llinás

Nora Wender: When did you actually take the decision of becoming a scientist?

Rodolfo Llinás: I never had any questions about what to do, the issue was how to be able to do science. I remember thinking that I might have to make money by other means to pay for my science. And then I was told: "If you become part of a University and you teach you may be able to do research, the pay is not great but you can survive." My view was: "I don't need to be rich, I would prefer to understand what being alive is about. Even as a child I couldn't understand religion as an explanation for anything and what is more I was really afraid of dropping dead before I could make some personal sense about it all.

David Hofmann: What was your motivation to go into the field of neuroscience? Is it because neuroscience is so close to us?

RL: Well, we are brain, not more nor less; the rest of the body is support machinery. Damage your brain and even if we can keep the body alive "you" have ceased to exist.
I remember when I was very young staying with my grandfather for a period. He was a Professor of Psychiatry and a very important person in my life. He had his office annexed to his home and the waiting room, covered with a glass roof allowed me to see the patients from the second floor of his home. Once I saw a patient sitting in the waiting room who suddenly threw himself on the ground and started shaking, salivating and making strange sounds. I was very surprised and when grandfather came for lunch I ran to ask: "What happened to that person?" and he said: "Well, he has epilepsy." – "But why would he want to behave like that?" – "He didn't want to do it." – "If he didn't want to do it, why did he do it?" He said: "Well, not everything that happens inside your head, in your brain, is under your control." – "So, what's this about "the brain" and what is it the brain made of?" And so began the problem.

DH: Neurosciences is close to us, close to everybody, close to the public. Therefore, it is an issue communicating the scientific results to the public and I am sure you have plenty of experience in doing that.

RL: Well, very much like many of my colleagues we get invited by people who know little about neuroscience to discuss what we do. I feel it is important as it may be helpful, but more fundamentally, they support us and so we have a dept to them. The challenge of course is whether you can honestly explain it to lay people what you do. My own take is that if you understand it you can explain it to anybody. I remember discussing this issue, once, with Richard Feynman, the great physicist, who would say something like "It's only difficult if you yourself don't understand it in general terms". And it's the same thing with students. The issue is that science can be explained in principle in very different ways and levels. And so the issue is what level of explanation is optimal.

DH: Do you have any preferred way to communicate your science?

RL: No, not really. The central issue of communicating is the use of concepts. Content is only good if you give context to it. Otherwise it's just data and you can completely drown people with detail, and what is more, the possible detail of knowledge attainable is an infinite series and we all know only some issues are relevant. The way I put it to my students is: simplicity before complexity is mostly triviality, simplicity after complexity is the ultimate goal.

DH: Did you ever experience a situation where you were cited or something was picked that you said but totally misunderstood.

RL: Yes sure, and there are at least two reasons: One is that sometimes people really misunderstand. But the other, which is harsher, is when people think that modifying what you said may make it more appealing to the reader.

NW: Do you think the scientists themselves are responsible for communicating their research to the public?

DH: Or is it that the public has to be educated more to better understand or is it the journalists who have to stick to the truth?

RL: Everybody is involved. The scientists should be able to communicate as clearly as possible and that is part of their job. That is, we owe it to the society. The journalists have the responsibility of writing what is said clearly and honestly. Finally, the public must want to understand. I find most people being actually quite ready and excited about understanding and believe the problem is, partly with us as scientists not wanting to make the effort to put it simply. In our defence, however, the real issue is that science is difficult and making it simple is sometimes almost as difficult as doing the science itself.

Rodolfo Llinás and Natalia Manrique Hoyos

Neuroscience Program joins NEURASMUS

A new European joint MSc program

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

In conjunction with the establishment of the European Neuroscience Campus training network (ENC: *http://www.enc-network.eu*) for doctoral candidates the new European Master Neuroscience program 'NEURASMUS' was founded in 2010. with the aim to extend exchange and training opportunities also for MSc students.

NEURASMUS is a 2 year full-time study programme taught in English, with a strong emphasis on training in cutting-edge techniques in all major topics of brain research, from molecules to cognition. Its main objec-

tive is to foster Neuroscience education and to train new brain scientists, by offering a unique interdisciplinary and integrated approach of normal brain function and of brain diseases. NEURASMUS is offered by 5 European Institutions (Bordeaux/coordination, Amsterdam, Berlin, Coimbra, Göttingen) and 1 external partner (Laval University in Quebec, Canada).

In 2011 three NEURASMUS MSc students (Myroslav Gebura/Ukraine, Samyutha Rajendran/India, Julio Santos Viotti/Brazil) joined the Göttingen Neuroscience Program. They will be 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 five neuroscience programs of the participating home institutes after successfully graduating from the MSc program.

Lindau Nobel Laureate Meeting 2011

by Alonso Barrantes Freer

Every year, since 1951, the Council for the Lindau Nobel Laureate Meetings and the Foundation Lindau Nobelprizewinners Meetings at Lake Constance organizes the Lindau Nobel Laureate Meeting, in which young researchers have the unique opportunity to interact with Nobel Laureates in their own field of research.

Nobel Laureate Meeting 2011 in Konstanz (Nobel Laureate Erwin Neher and IMPRS PhD student Benjamin Wilhelm)

The 61st meeting took place from June 26th to July 1st, 2011 and was dedicated to Physiology or Medicine and Chemistry. It gathered 25 Nobel Laureates and 570 young researchers from 80 countries.

The meeting had a very dynamic arrangement in which plenary lectures held by the laureates were followed by discussions where a small group of students discussed in depth scientific topics, but also reflect about the current status and future direction of science as a whole. Other sessions were meant to put the young researchers on the spotlight, for example "Turning the Tables", in which the students were part of the panel and answered questions from the laureates, and also the "Master Class" that was an opportunity for a young researcher to present his/her work to a laureate and a small group of students.

A strong focus was given to the social and ethical aspects of science, the meeting's central topic being "World Health". Several panel discussions dealt with the current great challenges of humanity like: Overpopulation, health and disease in developing countries, energy and climate change and the responsibility that we, scientists, have to address these issues and propose new strategies to deal with them.

Göttingen was represented by Prof. E. Neher and a small group of students from different scientific institutions among them the Max Planck Society and the European Neuroscience Institute (ENI).