# Yearbook 2003/04

# MSc/PhD/MD-PhD Neuroscience Program at the University of Göttingen

# International Max Planck Research School

# Imprint

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### Letter from the President



In 2000, the Georg August University of Göttingen, together with the Max Planck Society for the Advancement of Science established two international MSc/ PhD programs, namely *Neurosciences* and *Molecular Biology*.

Both programs met with immediate success: Some 500 students from more than 70 countries applied for the 40 study places available.

These intensive research-oriented programs are taught by internationally renowned scientists from five Göttingen University faculties, from the Max Planck Institutes for Biophysical Chemistry and for Experimental Medicine as well as from the German Primate Centre. International guest lecturers also participate in the programs. The Max Planck Society contributes through its newly established International Max Planck Research Schools.

Both programs keep close contacts with the relevant industries in order to also meet market requirements, thus enhancing the chances for successful graduates to find attractive professional careers.

I would very much like to thank all scientific bodies and institutions for their keen support in establishing our new international programs and, last but not least, the German Academic Exchange Service (DAAD) as well as the Lower Saxony Ministry of Science and Culture.

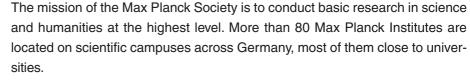
The Georg August University of Göttingen is proud of its long international experience and very much looks forward to offering two attractive and innovative programs within the setting of a lively urban cultural and social background, a prerequisite for creative teaching and research.

for them

Prof. Dr. Horst Kern (President of the Georg August University, Göttingen)

### Letter from the Max Planck Society





Scientific ties between Max Planck Institutes and universities are traditionally strong. In 1998, during the 50th year celebration of the Max Planck Society 1998 in Göttingen, the Max Planck Society - together with the Hochschulrektoren-konferenz - launched the International Max Planck Research Schools as a new joint program to further intensify cooperation.

The goals of the International Max Planck Research Schools are

- to attract excellent students from all around the world to intense Ph.D.
- training programs in Germany, preparing them for careers in science, - to integrate Max Planck scientists in top-level scientific training of junior scientists.
- to intensify the ties to the Universities owing to the participation of i n t e r nationally renowned Max Planck scientists in joint teaching activities, and
- to strengthen international relationships by providing individual support to each student and by exposing foreign students to German culture and German language.

By now, 29 International Max Planck Research Schools have been established involving 34 Max Planck Institutes and 26 German universities. More than 950 (mostly PhD-) students from 70 countries are presently enrolled.

The success of the Göttingen International Max Planck Research Schools in Molecular Biology and Neurosciences is evident from the high quality of the students and from the hundreds of applications the programs receive each year. The Schools also re-shaped the local scientific community, strengthened the ties between the participating institutions, and initiated new scientific collaborations that augment the international reputation of Göttingen as a center for scientific excellence. We hope that in the years to come the students of the International Max Planck Research Schools will be successful in their professional careers. We also hope that they will remember their training period in Göttingen as an exciting and stimulating phase of their lives.

Peter Gruss President Max Planck Society for the Advancement of Science Reinhard Jahn Coordinator, IMPRS Göttingen Director, MPI for Biophysical Chemistry



## Overview

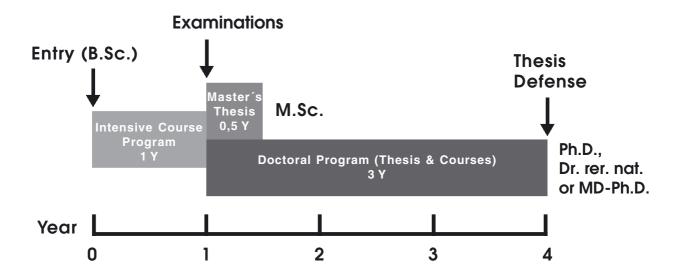
This yearbook is intended to inform about the International MSc/PhD/MD-PhD Neuroscience Program in Göttingen, Germany, that was established in the year 2000. Beyond general information, the yearbook introduces students, faculty, the program committee and the coordination team.

The program is jointly conducted by the University of Göttingen, the Max Planck Institute for Biophysical Chemistry, the Max Planck Institute for Experimental Medicine, the German Primate Center and the European Neuroscience Institute. Beyond their active participation in the Neuroscience Program, the above-mentioned partners closely cooperate in the DFG Research Center for Molecular Physiology of the Brain (CMPB), the Göttingen Center for Molecular Biosciences (GZMB), the Center for Systems Neuroscience (ZNV), in three collaborative research centers (Sonderforschungsbereiche, SFB), and in five interdisciplinary doctoral programs (Graduiertenkollegs, GK).

The International MSc/PhD/MD-PhD Neuroscience Program qualifies students for professional work in the neurosciences. The program is open to students from Germany and from abroad, holding a Bachelor's degree (or equivalent) in the biosciences, medicine, psychology, physics, or related fields. All courses are held in English. Tuition fees are waived, scholarships are available. The academic year starts in mid-October, preceded by four weeks of orientation. Applications are welcome until January 31 of the year of enrollment. To assure individual training on a high standard, the number of participants is limited to 20 students per year.

All students first participate in one year of intensive course work. This first segment of the program comprises lectures, tutorials, seminars, methods courses, and independent, individually supervised research projects (laboratory rotations). The traditional German structure of academic semesters is abandoned. The condensed schedule allows students to accumulate 90 credits (ECTS) within one year, which would normally require 3 semesters. Subsequently, two separate segments are offered:

- PhD Program: Good to excellent results after the first year qualify for direct admission to a three-year doctoral project in one of the participating research groups. The Master's thesis requirement is waived. After successful defense of a doctoral thesis, the degree Doctor of Philosophy (Ph.D.) or the equivalent title Doctor rerum naturalium (Dr. rer. nat.) is conferred. Students that finished medical school can apply for an MD-PhD title.
- **MSc Program:** Alternatively, students may conclude the program with a Master's thesis, based on six months of experimental, scientific research. The degree Master of Science (MSc) is awarded upon successful completion of the Master's thesis.

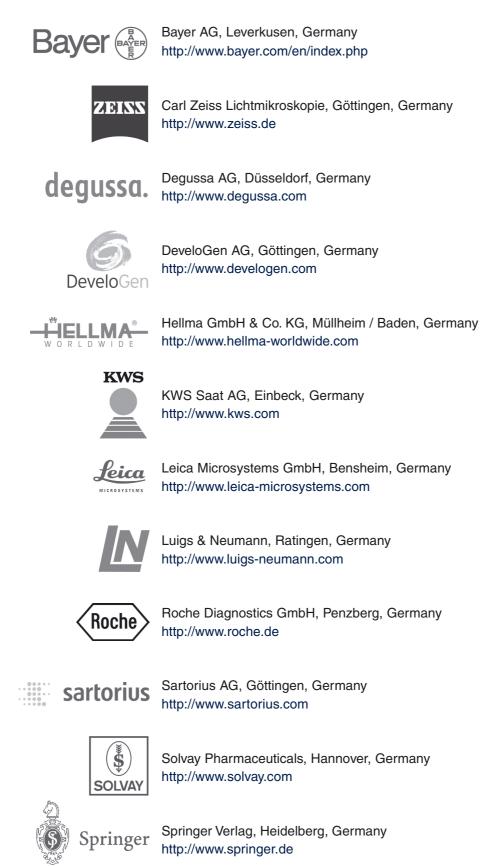


### Funding of the Program



# **S** ponsors

The following companies contributed stipends:



### Intensive Course Program (First Year)

Throughout the first year, current topics in the neurosciences are covered by

- lectures
- tutorials
- methods courses
- laboratory rotations
- seminars

### Lectures and Tutorials

A comprehensive lecture series is organized into a sequence of 4-6 week units. The following topics are taught on an advanced level throughout the first year (36 weeks, 4 hours per week):

- A. Neuroanatomy
- B. Physiology and Basic Statistics
- C. Methods in the Neurosciences
- D. Molecular Biology, Development and Neurogenetics
- E. Sensory and Motor Systems
- F. Clinical Neurosciences and Higher Brain Functions

Each lecture is accompanied by a tutorial session, where students meet with a tutor in small groups. Tutorials involve exercises, review of lecture material, and discussion of related topics.

### Methods Courses

During the first months of the Neuroscience Program, students participate in a series of methods courses to introduce them to principles and practical aspects of basic scientific techniques and the handling of model organisms. The methods courses comprise the following topics:

### I Neuroanatomy

- histology and development of the brain
- cytology of the cortex (EM)
- sensory systems
- neuronal stem cells
- hippocampus
- monamine systems
- human brain
- spinal cord/cerebellum
- anatomy of leech nervous system, behaviour of leeches

### II Membrane Physiology and Neurophysiology

- membrane physiology
- sensory physiology
- ca-imaging
- FCS
- motor reflexes
- FLIM
- communication of weakly electric fish
- ERG of the fly
- neuronal basis of acoustic communication
- pharmacological brain stimulation

### III Methods in Neurosciences

- neuronal Modelling
- tissue slicing and cell culture
- optical Imaging
- patch clamp data analysis
- behavioral analysis

### Laboratory Rotations

Starting in January, every student carries out four independent research projects (laboratory rotations) in participating laboratories. Each project is individually supervised and involves five to six weeks of experimental work, followed by one week for data analysis and presentation. For each project, a report must be completed in the format of a scientific publication. The laboratory rotations must cover at least three different subjects.

### Seminars

Seminars start in February. The class meets weekly for two hours to discuss two student presentations. The presentations are research reports based on work from the laboratory rotations.

### Examinations

After the first year of intensive training, all students take one written and two oral Master's examinations. The Master's examinations explore the students' theoretical background in topics covered by lectures and tutorials. Furthermore, topics covered by the laboratory rotations will be examined.

### PhD Program

Students who have passed the Master's examinations with good or excellent results qualify for direct admission to a three-year doctoral project in one of the participating research groups without being required to complete a Master's thesis first.

The PhD program emphasizes independent research of the students. Doctoral students select three faculty members as their doctoral committee which closely monitors work progress and advises students in their research project. Laboratory work is accompanied by seminars, training of scientific writing and oral presentation skills, elective courses, and participation in international conferences or workshops.

At the end of the PhD training program, a doctoral thesis is submitted either in the traditional format, or as a collection of scientific publications in internationally recognized journals along with a general introduction and a discussion of the results. The degree PhD or, alternatively, Dr. rer. nat. will be awarded after the successful defense of the doctoral thesis. Having received the PhD degree, medical students may apply for the degree of an MD-PhD at the Medical Faculty.

### Master's Program

After the first year of intensive training, students may conclude the program with a six-month thesis project, leading to a Master of Science degree. The thesis project involves experimental work under the supervision of faculty member of the Neuroscience Program.

### Orientation, Language Courses, Social Activities

A four-week orientation prior to the program provides assistance and advice for managing day-to-day life, including arrangements for bank account, health insurance, residence permit, housing, and enrollment. Students have the opportunity to meet faculty members and visit laboratories of the participating institutions. In addition, the orientation program informs students about computing and library facilities, the city and university of Göttingen, sports facilities, and cultural events.

An intensive basic language course in German is offered in cooperation with *Lektorat Deutsch als Fremdsprache* to facilitate the start in Göttingen. Additional language courses and social activities accompany the program.

### **Application, Selection and Admission 2003**

Applicants must hold a Bachelor's degree or equivalent in biology, medicine, psychology, physics, or related fields. They are required to document their proficiency in English and should not be older than 27 years.

In the year 2003, the coordination office received 164 applications from 30 countries.

Continent	Applications	Admissions
Europe (total)	49	13
Germany	16	8
other West Europe	3	1
East Europe	30	4
America (total)	9	2
North America	3	1
Central/South America	6	1
Africa(total)	18	0
North Africa	6	0
Central/South Africa	12	0
Asia (total)	88	4
Near East	4	0
Central Asia/ Far East	84	4

# Students 2003/2004

	Home Country
Agarwal	India
Chen	Taiwan
Dammeyer	Germany
Djannatian	Germany
Huang	China
Junek	Germany
Kunst	Germany
Lütcke	Germany
Medrihan	Romania
Nawaz	Germany
Opazo	Chile
Poulopoulos	Greece
Raja	USA
Sargin	Turkey
Sroka	Poland
v. Saint Paul	Ireland
Weigel	Germany
Wunderlich	Germany
Xiao	China
	Chen Dammeyer Djannatian Huang Junek Kunst Lütcke Medrihan Nawaz Opazo Poulopoulos Raja Sargin Sroka v. Saint Paul Weigel Wunderlich

### Amit Agarwal

## EDUCATION

### College / University:

1999 - 2003: Guru Gobind Singh Indraprastha University, School of Biotechnology, India Highest Degree:

B.Tech in Biotechnology (First class)

Major Subjects:

Biochemistry, fermentation technology, biotechnology, molecular biology Lab Experience:

Stem cell culture, tissue culture, immunological techniques, recombinant-DNA technology, microbiology and histopathology, bioinformatics

### Projects / Research:

2002 (Jun - Aug): Summer Projects at Shriram Institute for Industrial Research, Delhi 1) Identifying and studying microbes and pathological agents in snacks sold on the sidewalk 2) Qualitative and quantitative analysis of various products of pineapple Juice fermentation by Saccharomyces cerevisiae 3) Acute toxicological studies on mice 2003 (Jan - Jul): B.Tech Final Semester Thesis Project: Functional analysis of domains

of Saccharomyces cerevisiae RNA polymerase II subunit 4

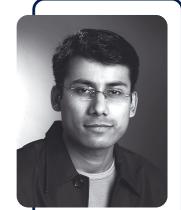
### Scholarships:

1999 - 2003: "University Scholarship of Full Tuition Fee Waiver", G.G.S. Indraprastha University. Delhi

2003 - 2004: Stipend International Max Planck Research School

# SCIENTIFIC INTERESTS AND GOALS:

I want to study and understand how the brain, a simple looking mass of tissue, can control complex body functions and emotional and psychological aspects of life. My career objectives lie in the pursuance of research and academics in neuroscience, especially in deciphering the causes of neurodegenerative diseases, in order to devise novel therapeutic cures and drugs. I'm fascinated by stem cells and want to look for possibilities of using them as a possible cure for neurodegenerative diseases.



First Name: Amit

Last Name: Agarwal

Date of birth: 13 September 1980

> Country: India

## Tsai-Wen Chen

# EDUCATION

### College / University:

1997 - 2001: National Taiwan University. Taipei. Taiwan

### Highest Degree:

B.Sc., College of Electrical Engineering and Computer Science, National Taiwan Universitv

### **Maior Subjects:**

Electrical engineering, digital signal processing

### Lab Experience:

Signal processing algorithm development and simulation, microprocessor programming, electronic interfacing

### Projects / Research:

1999: "From music to score, audio signal processing and recognition" 2000: "Design and implementation of a Left Ventricular Aided Device (LVAD) controller" 2001: "Implementing a Rate-Adaptive wireless OFDM High-Speed Transceiver" Scholarships:

2003 - 2004: Stipend International Max Planck Research School Awards:

1996: Gold medal, "27th International Physics Olympiad (IPHO)", Oslo, Norway 1998: The Wu Chien-Shiung Science Award, for outstanding performance in physics 2001: Asian Championship, "DSP and analog solution challenge" held by Texas Instrument, invited for presentation at TI headquarter, Dallas, USA

2001: First Prize, 10th National Taiwan University Engineering Technology Thesis Contest

# SCIENTIFIC INTERESTS AND GOALS:

I am interested in the signal processing mechanisms used by the nervous system, such as learning, memory and perception. I wish to apply physical, molecular as well as mathematical modeling approaches to improve our understanding of these fundamental functions.



First Name: Tsai-Wen

Last Name: Chen

Date of birth: 4 July 1979

> Country: Taiwan

### **Pascal Dammeyer**



First Name: Pascal

Last Name: Dammeyer

Date of birth: 8 April 1977

Country: Germany

# EDUCATION

### College / University:

1997 - 2003: Technische Universität Berlin (TUB), Germany 2001 - 2002: University of Arizona (UofA), USA 2000 & 2003: Dongseo University (DSU), Republic of Korea **Highest Degree:** Vordiplom (Dipl.-Ing. cand. TUB, M.Sc. cand. DSU) Major Subjects: Medical biotechnology (molecular medicine), immunology Lab Experience: Genetic engineering, molecular biology, immunological techniques, protein purification, patch clamp, cell culture Projects / Research: "Construction and in vitro characterization of a new, heat-inducible amplification vector for local GM-CSF overexpression with antitumor efficacy", Master's thesis, Univ. Arizona, USA "Identification of chloride channels involved in chemotactic migration in microglial cells "; Max Delbrück Center for Mol. Medicine, Germany "Construction and implementation of Exosome Expression Protein Database"; Pusan National University, Republic of Korea Scholarships: 2000: Participation in the "Dual Degree Program" between the TUB and DSU 2001 - 2002: Stipend TU Berlin, tuition waiver Univ. of Arizona 2003: "Summer Institute Program 2003", DAAD and KOSEF 2003 - 2004: Stipend International Max Planck Research School SCIENTIFIC INTERESTS AND GOALS:

I am interested in combining neurosciences, immunology, and molecular biology to develop new therapeutic approaches. Thereby, neurosciences can incorporate different aspects which involve the molecular level on one hand and the whole organism with its central nervous system on the other.

# Jasmin Roya Djannatian



First Name: Jasmin Roya

Last Name: Djannatian

Date of birth: 12 February 1981

Country: Germany

# EDUCATION

College / University: since 2000: Georg August University Göttingen, Faculty of Medicine

Highest Degree:

1. Staatsexamen in medicine

Major Subjects:

Molecular biology, medicine, cancer

### Lab experience:

Molecular biology and biochemistry, RNA work, PCR, cell culture, flow cytometry **Projects / Research:** 

1999 - 2000: "Composition and cytotoxicity of different mistletoe preparations on leukemic cells", German Center for Biotechnological research in Brunswick since 2001: "The role of the voltage-gated  $K^+$  -channel ether-a-gogo in leukemias",

Max Planck Institute for Experimental Medicine, Prof. Stühmer, Göttingen

### Scholarships:

2000 - 2002: Foundation "Stipendien-Fonds des Verbandes der chemischen Industrie" 2003 - 2004: Stipend International Max Planck Research School

### Awards:

1999: Second prize, "Jugend forscht", Lower Saxony

2000: Second prize, "Jugend forscht", Germany

2000: Second prize, "12th European Union Contest for Young Scientists", Amsterdam 2000: Participation at the "Stockholm International Youth Science Seminar", including the participation at the Nobel prize ceremony

# SCIENTIFIC INTERESTS AND GOALS:

My main interest focuses on the development, behaviour and therapeutical treatment of cancerous diseases. In detail I am interested in the role of ionic channels and channelopathies in the development of cancer. I would like to understand the functions of the nervous system on a molecular level and how neuronal disorders develop. I hope to be able to contribute to the development of advanced therapies in the future.

### **Min Huang**

### EDUCATION

### College / University:

1999 - 2003: Peking University, P.R. China **Highest Degree:** B.Sc.

Major Subjects: Biological science

# Lab Experience:

Cell culture, gene cloning, GFP expression, yeast hybrids, etc.

### Projects / Research:

2001 - 2003: National laboratory of protein engineering and plant genetic engineering Oct. 2001 - Nov. 2002: Identification of a DNA activation domain in the MRDV (Maize rough dwarf virus) genome. Protein interaction between MRDV S7 and other segments using a yeast hybrid system

Sep. 2002 - July 2003: Expression of the fusion protein of MRDV S7 and GFP; Research on the nuclear location signal in MRDV S7

### Scholarships:

2003 - 2004: Stipend International Max Planck Research School

### SCIENTIFIC INTERESTS AND GOALS:

I will try to understand the human brain from the perspective of cellar and molecular biology. My special interest lies in neurogenetics and developmental neuroscience.



First Name: Min

Last Name: Huang

Date of birth: 19 September 1981

> Country: P.R. China

### **Stephan Junek**

### EDUCATION

### College / University:

2000 - 2002: Humboldt-Universität zu Berlin 2002 - 2003: University of California, San Diego **Highest Degree:** 

Vordiplom

Major Subjects: Biophysics

### Lab Experience:

1996 - 1997: Civil Service at the GeoForschungsZentrum Potsdam 2001 - 2002: Student assistant at the Fraunhofer Institut 2003: Student assistant at the Salk Institute San Diego

### Projects / Research:

Firing reliably with unreliable synapses (Salk Institute, CNL lab: T. Sejnowski) NanoVirDetect: Detection of viral particles (Fraunhofer Gesellschaft Berlin) **Scholarships:** 

### 2002: Humboldt-Stipendium

2003 - 2004: Stipend International Max Planck Research School

### Publications & Poster:

Fellous JM, Spencer D, Wang HP, Junek S, Eagleman DM, Sejnowski TJ: Firing reliably with unreliable synapses. Society for Neuroscience, New Orleans, 2003

### SCIENTIFIC INTERESTS AND GOALS:

I am interested in finding basic principles that underlie the functions of the nervous system. Examining species with comparable simple nervous systems might help to find and understand those principles. In applying them to more complex systems, one might be able to understand how a brain is able to recognize, memorize, learn and think.



First Name: Stephan

Last Name: Junek

Date of birth: 17 April 1977

> Country: Germany

# **Michael Kunst**



First Name: Michael

Last Name: Kunst

Date of birth: 19 July 1980

Country: Germany

## Henry Lütcke



First Name: Henry Harry

Last Name: Lütcke

Date of birth: 19 October 1979

Country: Germany

# EDUCATION

College / University: 2000 - 2003: Georg August University Göttingen Highest Degree: Vordiplom Major Subjects: Biology Lab Experience: Pharmacological brain stimulation of grasshoppers (of experiments with honeybees, Signal cascades du

Pharmacological brain stimulation of grasshoppers (chorthippus biguttulus), Behavioural experiments with honeybees, Signal cascades during the olfactory conditioning of honeybees, Immunohistochemistry from the CNS of crayfish

### Projects / Research:

Agonistic behaviour of crayfish (Procambarus spec.) Bidirectional communication of bushcrickets **Scholarships:** 

2003 - 2004: Stipend International Max Planck Research School

# SCIENTIFIC INTERESTS AND GOALS:

I want to gain a broad education in the neurosciences in order to understand the molecular basis of behaviour. I am mostly interested in neuropharmacology and neurogenetics. I want to understand in which way genes and their products, the proteins, influence behaviour.

# EDUCATION

College / University: 1999 - 2003: University of Edinburgh, Scotland 2001 - 2002: UPMF Grenoble, France Highest Degree: B.Sc. (first class honours)

Major Subjects: Psychology

### Projects / Research:

Honours Thesis "Alcohol selectively impairs kinaesthetic perception in fine motor tasks - a pilot study" Department of Psychology, University of Edinburgh and AstraZeneca Clinical Research Unit, Edinburgh, Scotland

Scholarships: 2001 - 2002: Erasmus Fellowship 2003 - 2004: Stipend Max Planck International Research School

# SCIENTIFIC INTERESTS AND GOALS:

Human behavior can be described and investigated at different levels of description. This interdisciplinary course provides an understanding of nervous system function from the molecular to the behavioral level. My main goal is to learn a number of different techniques which I can apply to new problems in my later scientific career. I am particularly interested in neuron modeling as well as nervous system development and its relation to developmental disorders.

## Lucian Medrihan

## EDUCATION

### College / University:

1999 - 2003: University of Bucharest, Romania **Highest Degree:** 

B.Sc. Major Subjects: Biochemistry

### Lab Experience:

Basic biochemistry techniques, cell cultures, molecular biology techniques (DNA purification, transformation, amplification, transfection), calcium imaging, patch-clamp techniques

### Projects / Research:

2002 - 2003: BSc Thesis: "Phorbol-esters effects on PKC activation of VR-1 receptor heterologously expressed in HEK293 cells"

2003: Team project concerning molecular mechanisms involved in cold transduction through TRPM8 receptor (Romanian Government Research Grant)

### Scholarships:

2000 - 2002: University of Bucharest Scholarship 2003 - 2004: Stipend International Max Planck Research School

# SCIENTIFIC INTERESTS AND GOALS:

I would like to understand as much as possible about the brain. My main interest is to search for the molecular basis and signaling pathways of neurological diseases.



First Name: Lucian

Last Name: Medrihan

Date of birth: 22 November 1978

**Country:** Romania

# Schanila Nawaz

### EDUCATION

College / University: 1999 - 2003: University of Stuttgart Highest Degree: Vordiplom in Technical Biology Major Subjects: Cell biology, biochemistry, neurology, biophysics Projects / Research: Laboratory work (=Praktika) in cell biology, biochemistry, electrophysiology, bioenergetics, tutorship in physics Scholarships: 2003 - 2004: Stipend International Max Planck Research School

# SCIENTIFIC INTERESTS AND GOALS:

My goal is to understand many of our brain functions on a molecular level, as well as how the brain functions as a whole in our being. By doing so, I would like to try and understand human social behavior in our time.



First Name: Schanila

Last Name: Nawaz

Date of birth: 27 June 1980

Country: Germany

### Felipe Opazo



**First Name:** Luis Felipe

Last Name: Opazo

Date of birth: 22 May 1978

Country: Chile

# EDUCATION

College / University: 1997 - 2003: Universidad de Chile 2000: State University of New York SUNY **Highest Degree:** B.Sc. Molecular Biotechnology Engineering Major Subjects: Bioinformatics, biochemistry, cell viology, molecular biology, biotechnology Lab Experience: Protein modeling, bioinformatics, protocols in molecular biology, cell biology, proteins biochemistry: expression & purification Projects / Research: 1998 - 1999: Microbiology and Biotechnology Laboratory, University of Chile, Chemotaxis in Thiobazilus ferrooxidans 2000: Plattsburg State University of New York, Alternative Oxidase Pathway (AOX) in Chlamidomonas reindhardii 2001: San Diego, California, International Workshop on "Drug Design" and "How to use CHARMm force field" in SGI interface with Insight II tools. 2002 - 2003: Millennium Institute CBB. University of Chile & EMBL Heidelberg: Master's thesis entitled "Theoretical and Experimental Studies of the inhibition mechanism of the cycline dependent kinase. Cdk5 and it implication on Alzheimer disease" Scholarships: 2002 - 2003: Millennium Institute for Advances Studies in Cell Biology (CBB) 2003 - 2004: Stipend International Max Plank Research School

# SCIENTIFIC INTERESTS AND GOALS:

Know a bit more of the complexity of the brain, looking forward to study neuropathologies and hopefully we could give some explanation of neurodegenerative phenomena.

# **Alexandros Poulopoulos**



First Name: Alexandros

Last Name: Poulopoulos

Date of birth: 6 May 1980

Country: Greece

# EDUCATION

College / University: 1998 - 2003: National and Kapodistrian University of Athens Highest Degree: Diploma Major Subjects:

Biology

Lab Experience:

Molecular biology techniques, mammalian cell culture, transfection, immunoassays **Projects / Research:** 

2001 - 2002: "Identification of proteins that differentially interact with wild-type and amyloidogenic mutant forms of the Bri protein" Dr. Spiros Efthimiopoulos, Dept. of Human and Animal Physiology, Faculty of Biology, University of Athens., Athens, Greece 2003: "Transcriptional intensity of three genes commonly implicated in end-stage renal failure, diabetes and Alzheimer's disease in patient lymphocytes" Dr. Cornelia Poulopoulou, Neurology Dept. University of Athens Medical School, Athens, Greece **Scholarships:** 

1998 - 1999: State Scholarship Foundation (of Greece)

2003 - 2004: Stipend International Max Planck Research School

# SCIENTIFIC INTERESTS AND GOALS:

I am interested in cellular processes of neuronal development and mechanisms dictating the scheme of neuronal circuitry.

### Anjali Raja

### EDUCATION

College / University:

1997 - 2001: Northwestern University, Evanston, IL, U.S.A. **Highest Degree:** 

B.A. Major Subjects:

Psychology, pre-medicine Lab Experience:

PCR, Immunohistochemical staining, event-related potentials, fMRI

### Projects / Research

Undergraduate Research Project: Effects of the implicit categorization of dot patterns on the P100 wave: an ERP study, Cognitive Neuroscience Lab, Northwestern University, Evanston, IL, U.S.A.

6/2000-9/2000: "Bone Matrix Proteins (Osteopontin, Bone Sialoprotein, Osteonectin, and Bone Acidic Glycoprotein-75) in Muscle Biopsies from Children with Untreated Juvenile Dermatomyositis (JDM)", Children's Memorial Institute for Education and Research, Chicago, IL, U.S.A.

2002/2003: "Funtional neuroimaging of observation and execution of limb-movements in patients with phantom-limb sensation", Zürich Neuroscience Institute, Switzerland **Scholarships:** 

June 2000 - Sept. 2000: Erwin Macey Research Scholarship Sept. 2002 - July 2003: Fulbright/Seydel Fellowship 2003 - 2004: Stipend International Max Planck Research School

# SCIENTIFIC INTERESTS AND GOALS:

I would like to gain a better understanding of the neural substrates underlying higher cognitive processes such as memory and learning. In addition, I would like to research neurodegenerative disorders.



First Name: Anjali

Last Name: Raja

Date of birth: 5 October 1979

Country: USA/Germany

# Derya Sargin

# EDUCATION

College / University: 1998 - 2003: Bogazici University Highest Degree: B.Sc.

Major Subjects: Molecular biology, genetics

Lab Experience:

Basic techniques in the fields of genetics, molecular biology, biochemistry and histochemistry

### Projects / Research:

"NGF induced neuronal differentiation of PC12 cells", "Mutational analysis in parkin gene", Molecular Biology & Genetics Research Lab Bogazici University, Turkey "Sequencing Sepiapterin, a candidate gene on chr2p13 for PARK3", "Linkage and sibpair analysis on chr2 with European PD families", "Detection of a new parkin interactor", The Molecular Neurogenetics Laboratory, Ludwig Maximilians University, Munich **Scholarships:** 

2003 - 2004: Stipend International Max Planck Research School

# SCIENTIFIC INTERESTS AND GOALS:

My research interest is in the field of Human Molecular Genetics especially related to human diseases, their causes and different approaches to new therapies. I would like to deal with apoptotic and neuroprotective signaling pathways in order to identify the specific molecular triggers of neuronal apoptosis in different neurodegenerative disorders with the aim of developing drugs that interact with and block the cell death cascade. I am also interested in oxidative stress, calcium regulation, aging, synaptic signaling and plasticity.



First Name: Derya

Last Name: Sargin

Date of birth: 16 October 1980

> Country: Turkey

# Kamila Sroka



First Name: Kamila

Last Name: Sroka

Date of birth: 14 October 1981

Country: Poland

# EDUCATION

College / University: Jagiellonian University, Krakow Highest Degree: Equivalent of B.Sc. Major Subjects: Biotechnology Lab Experience: Basic techniques in molecular biology Projects / Research: 2002 / 2003: The effect of fluoxetine and tianeptine on the fluidity of neuronal membranes (Bachelor thesis)" Scholarships: 2003 - 2004: Stipend International Max Plank Research School

# SCIENTIFIC INTERESTS AND GOALS:

I am interested in studying the complexity of human brain and I would be happy if I could contribute to the discovery of some of its mysteries. Apart from that I am interested in neurological diseases and their biochemical basis.

# Francisca v. Saint Paul



First Name: Francisca

Last Name: v. Saint Paul

Date of birth: 17 September 1981

Country: Ireland

# EDUCATION

College / University: 2000 - 2002: Eberhard Karls University Tübingen (Germany) 2002 - 2003: University of Missouri-Columbia (USA) Highest Degree: Vordiplom in Chemistry Maior Subjects: Chemistry, biochemistry, molecular biology, physics Lab Experience: Computational chemistry, molecular biology Projects / Research: Univ. Missouri-Columbia, "Theoretical approach to DNA deamination by analysis of a novel pathway for the cytosine to uracil mutation". MPI for Developmental Biology, "Investigating the cellular location of Staufen's RNA binding" Scholarships: 2000 - 2002: Association of German Chemical Industry Stipend 2002 - 2003: Federal State Scholarship Baden-Württemberg 2002 - 2003: LS UROP Internship, Univ. Missouri-Columbia 2003 - 2004: Stipend International Max Planck Research School Honors & Awards: 1999: "Deutsche Schülerakademie" 1999: German National Maths Competition - Special Merit Award

# SCIENTIFIC INTERESTS AND GOALS:

How does the brain make decisions? How free is our "free will" – is my decision mine or the result of the chemical composition of my brain? Would we understand anything more if we knew everything about the molecular processes in the brain? I would like to work on these questions at a molecular level and with an emphasis on the role of hormones in decision making.

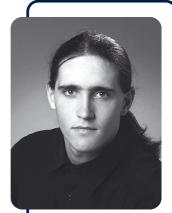
### **Arwed Weigel**

# EDUCATION

College / University: 2000 - 2003: Universität Potsdam Highest Degree: Vordiplom Major Subjects: Physics Lab Experience: Basic and advanced practical training in experiments in physics, microscopic techniques Scholarships: 2003 - 2004: Stipend International Max Planck Research School

# SCIENTIFIC INTERESTS AND GOALS:

- General functioning of the mammalian nervous system
- Learning and behavior on all levels of research: the interdisciplinary integration from synaptic plasticity to self-consciousness
- Neurodegenerative diseases, especially HD



First Name: Arwed

Last Name: Weigel

Date of birth: 16 July 1979

> Country: Germany

# **Klaus Wunderlich**

# EDUCATION

### College / University:

2001 - 2003: University of Göttingen 2000 - 2003: University of Hagen **Major Subjects and Highest Degrees:** Psychology (Vordiplom) Economic science (Vordiplom)

### Projects / Research:

Research assistant at the department of differential psychology, Prof. Rammsayer: Studies on sensomotoric infromation processing and on selective attention (experimental design, EEG recording, data analysis)

Research assistant at the department of psychology, Prof. Waldmann: Tutoring of seminars on statistics, decision-making, and a summer course on game theory within the frame of neuroeconomics; Modeling of causal chains with Bayesian networks; Conceptual scheme of a project on decision making that links cognitive variables and respective computations in the neural system by combining the experimental study of behaviour, normative approaches (classic decision theory, melioration, game theory) and neuroscientific methods.

### Scholarships:

2003 - 2004: Stipend International Max Planck Research School **Honors/Awards:** 

1997/1998: German Maths/Informatics Competition - Special Merit Award

# SCIENTIFIC INTERESTS AND GOALS:

My present interests tend to cognitive neuroscience, especially in the area of learning, reasoning, and decision-making. Thereby my overall goal is to understand the neural basis of thought and behavior. I seek to contribute to our understanding of the relation between the mind and the central nervous system to expand the current concepts of cognitive theories with the underlying neural functioning.



First Name: Klaus

Last Name: Wunderlich

Date of birth: 22 January 1980

> **Country:** Germany

### Le Xiao



First Name: Le

Last Name: Xiao

Date of birth: 10 September 1980

Country: P.R. China

# EDUCATION

College / University: 1998 - 2003: Chongqing University of Medical Science, P.R.China Highest Degree:

Bachelor of Medicine Major Subjects: Clinical medicine

### Lab Experience:

October - December 2001: The anti-tumor effect of Tetramethylprazine (TMP) and its relationship with inhibiting angiogenesis. July - August 2002: Possible interaction between an anti-tumor drug and apoptosis-inducing gene therapy **Scholarships:** 1999 - 2000 and 2000 - 2001: Excellent College Student in Chongqing City 2002 - 2003: National Scholarship of College Students 2003 - 2004: Stipend International Max Planck Research School

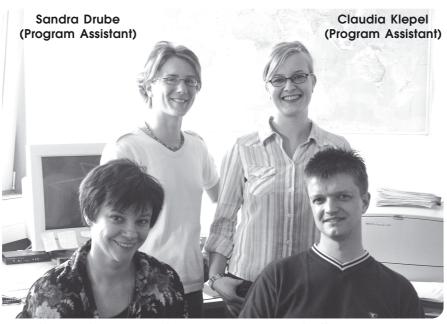
# SCIENTIFIC INTERESTS AND GOALS:

I want to concentrate on the molecular events in degenerative diseases. While normally a neuron can survive for many years, how does it trigger its own suicide in degenerative diseases such as Parkinson's and Alzheimer's disease?

### Graduate Program Committee

Prof. Dr. Eberhard Fuchs Prof. Dr. Ralf Heinrich Prof. Dr. Willhart Knepel Dr. Christian Rosenmund Prof. Dr. Dr. Detlev Schild Prof. Dr. Walter Stühmer PD Dr. Heinrich Terlau Dr. Swen Hülsmann Dr. Jürgen Klingauf Dr. E. Ponimaskin Klaus Wunderlich Manuela Schmidt

### **Program Coordination**



Dr. Simone Cardoso de Oliveira (Program Coordinator)

Dr. Steffen Burkhardt (Program Coordinator)

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### **Further Information:**

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## Faculty

(Senior Faculty, Group Leaders, Lecturers)

Mathias Nils Edgar Nicole Norbert Wolfgang Gabriele Jens Eberhard Ralf Sven Herbert Reinhard Hubertus Bernhard Jürgen Willhart Reiner Kerstin Reinhard Gerd Markus Tobias Klaus-Armin Erwin Harald Walter Evgeni Thomas Diethelm W. Michael Christian E. Marian Eckart Detlev Ralf Friedrich-Wilhelm Stephan Anastassia Walter Andreas Heinrich Stefan Michael Fred Wolfgang Weigi Annette

Bähr U Göttingen Neurology Brose Molecular Neurobiology MPI em Brunner **Medical Statistics** U Göttingen Dünker Neuroanatomy U Göttingen Elsner Neurobiology U Göttingen Engel Human Genetics U Göttingen Flügge Neurobiology DPZ Frahm Biomedical NMR Research / Physical Chemistry MPI bpc Fuchs Animal Physiology / Neurobiology DPZ Heinrich Neurobiolgy U Göttingen Hülsmann Neuro- and Sensory Physiology U Göttingen Jäckle Molecular Developmental Biology MPI bpc Jahn Neurobiology MPI bpc Clinical and Experimantal Endocrinology U Göttingen Jarry Keller Neuro- and Sensory Physiology U Göttingen Klingauf Membrane Biophysics MPI bpc Knepel Molecular Pharmacology U Göttingen Kree **Theoretical Physics** U Göttingen Krieglstein Neuroanatomy U Göttingen Lakes-Harlan Neurobiology U Göttingen Lüer Psychology U Göttingen Missler Neuro and Sensory Physiology U Göttingen Moser U Göttingen Otolaryngology Nave **Neurogenetics** MPI em Neher Membrane Biophysics MPI bpc Neumann Neuroimmunology ENI Paulus Clinical Neurophysiology U Göttingen Ponimaskin Neuro- and Sensory Physiology U Göttingen Rammsaver Psychology U Göttingen Richter Neuro and Sensory Physiology U Göttingen Rickmann Neuroanatomy U Göttingen Rosenmund Membrane Biophysics MPI bpc Roussa U Göttingen Neuroanatomy Rupnik Neuroendocrinology ENI Rüther Psychiatry U Göttingen Schild Molecular Neurophysiology U Göttingen Schneggenburger Membrane Biophysics MPI bpc Schürmann Cell Biology U Göttingen Sigrist Neuroplasticity ENI Stoykova Molecular Cell Biology MPI bpc Stühmer Molecular Biology of Neuronal Signals MPI em U Göttingen Stumpner Neurobiology Terlau Molecular and Cellular Neuropharmacology MPI em DPZ Treue Cognitive Neuroscience and Biological Psychology Waldmann Psychology U Göttingen Wouters **Cellular Biophysics** ENI Wuttke Clinical and Experimental Endocrinology U Göttingen Zhang Neuro- and Sensory Physiology U Göttingen Zippelius **Theoretical Physics** U Göttingen

### Mathias Bähr

### **Professor of Neurology**

1985 MD, University of Tübingen Medical School, Training in Neurology at University Hospitals in Tübingen and Düsseldorf

DFG and Max-Planck Fellow at the Max Planck Institute for Developmental Biology Tübingen and at the Department of Anatomy and Cell Biology, Washington

University St.Louis Schilling-Foundation Professor for Clinical at

Schilling-Foundation Professor for Clinical and Experimental Neurology, University of Tübingen

Director at the Department of Neurology, University of Göttingen since 2001

# Major Research Interests:

We are interested to understand 2 basic questions in cellular and molecular neurobiology:

1. Which factors support survival of adult CNS neurons?

2. What kills these cells under pathological conditions?

Up to now, only little is known about the mechanisms that support survival of a postmitotic cell like a human neuron for eventually more than 100 years under physiological conditions. However, by examining the molecular regulation of cell survival and cell death during development and in the lesioned adult CNS, one may get some clues to answer this question.

In our group, several in vitro and in vivo model systems are used which allow examination of neuronal de- and regeneration. Our basic model is the rodent retino-tectal projection. Here, we can study development, de- and regeneration of the respective projection neurons, the retinal ganglion cells (RGCs) in single cell cultures, explants or in vivo. Transection or crush-axotomy of the optic nerve induces retrograde death more than 80% of RGCs within two weeks. This secondary cell loss is mainly apoptotic and involves specific changes in gene expression pattern of transcription factors (e.g. c-jun or ATF-2), pro- and anti-apoptotic genes (e.g. bcl-2 or bax) and growth-associated genes (like GAP-43). Thus, long term survival and initiation of regeneration programmes of RGCs critically depends on inhibition of apoptotic cell death. To that end, we have used a variety of techniques to interfere with the cell death cascades that follow lesions of the optic nerve in adult rats. Inhibition of neuronal apoptosis can be afforded by pharmacological administration of trophic factors or by gene therapy approaches using adenovirus vectors that can deliver neurotrophic factors directly into neurons or into surrounding glial cells. These, and other new strategies like using transduction-domains to deliver anti-apoptotic proteins across the blood-brain-barrier are now used to develop new experimental therapy strategies in animal models of human neurological disorders like stroke, trauma, multiple sclerosis od neurodegenerative diseases (e.g. Alzheimer 's or Parkinson's disease).

### Selected Recent Publications:

Meyer R, Weissert R, de Graaf K, Diem R, Bähr M (2001) Acute neuronal apoptosis in a rat model of multiple sclerosis. J Neurosci 21: 6214-6220

Dietz GPH, Kilic E, Bähr M (2002) Inhibition of apoptosis *in vitro* and *in vivo* using TAT-mediated protein transduction. Mol Cell Neurosci 21 (1): 29-37

Kilic E, Dietz GPH, Herrmann DM, Bähr M (2002) Intravenous TAT-BcI-XL is protective when delivered before and after middle cerebral artery occlusion in mice. Ann Neurol 52(5) 617-22

Kilic E, Herrmann DM, Kügler S, Kilic Ü, Holzmüller H, Schmeer C, Bähr M (2002) Adenovirus-mediated Bcl-XI expression using a neuron-specific promoter protects against disseminated neuronal injury and brain infarction following focal cerebral ischemia in mice. Neurobiol Dis 11: 275-284

Kügler S, Kilic E, Bähr M (2003) Human synapsin 1 gene promoter confers highly neuron specific long-term transgene expression from an adenoviral vector in the adult rat brain depending on the transduced area. Gene Therapy 10(4): 337-47

Diem R, Hobom M, Maier K, Weissert R, Storch MK, Meyer R, Bähr M (2003) Methyprednisolone increases neuronal apoptosis during autoimmune CNS inflammation by inhibition of an endogenous neuroprotective pathway. J Neurosci 23(18): 6993-7000



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### **Further Information:**

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### **Nils Brose**



# Address

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phone: +49-551-38 99725 fax: +49-551-38 99707

### **Further Information:**

http://www.em.mpg.de/User/ Brose/index.html

# Professor, Director at the Max Planck Institute for Experimental Medicine

Dr. rer. nat. (Ph.D.) 1990, Ludwig Maximilians University Munich Appointed as Director at the Max Planck Institute for Experimental Medicine 2001

### Major Research Interests:

Research in the Department of Molecular Neurobiology focuses on the molecular mechanisms of synapse formation and function in the vertebrate central nervous system. Typically, synapses are formed between cellular processes of a sending and a receiving nerve cell. They are the central information processing units in the vertebrate brain where some 10<sup>12</sup> nerve cells are connected by 10<sup>15</sup> synapses to form an elaborate and highly structured neuronal network that is the basis for all forms of behaviour. Signal transmission at synapses is mediated by the regulated release of signal molecules (neurotransmitters) which then diffuse to the receiving nerve cell and change its physiological state. In the Department of Molecular Neurobiology, we combine biochemical, morphological, mouse genetic, behavioural, and physiological methods to elucidate the molecular basis of synapse formation and transmitter release processes. Our synaptogenesis research concentrates on synaptic cell adhesion proteins of the Neuroligin family and their role in synapse formation. Studies on the molecular mechanisms of neurotransmitter release focus on components of the presynaptic active zone (Munc13s, RIM, Complexins) and their regulatory function in synaptic vesicle fusion.

### Selected Recent Publications:

Augustin I, Korte S, Rickmann M, Kretzschmar H A, Südhof T C, Herms J W, Brose N (2001) The cerebellum-specific Munc13 isoform Munc13-3 regulates cerebellar synaptic transmission and motor lerning in mice. J Neurosci 21: 10-17

Reim K, Mansour M, Varoqueaux F, McMahon HT, Südhof TC, Brose N, Rosenmund C (2001) Complexins regulate a late step in Ca<sup>2+</sup>-dependent neurotransmitter release. Cell 104: 71-81

Betz A, Thakur P, Junge H J, Ashery U, Rhee J S, Scheuss V, Rosenmund C, Rettig, J Brose N (2001) Functional interaction of the active zone proteins Munc13-1 and RIM1 in synaptic vesicle priming. Neuron 30: 183-196

Rhee J S, Betz A, Pyott S, Reim K, Varoqueaux F, Augustin I, Hesse D, Südhof TC, Takahashi M, Rosenmund C, Brose N (2002)  $\beta$  Phorbol ester- and diacylglycerol-induced augmentation of transmitter release is mediated by Munc13s and not by PKCs. Cell 108: 121-133

Varoqueaux F, Sigler A, Rhee JS, Brose N, Enk C, Reim K, Rosenmund C (2002) Total arrest of spontaneous and evoked synaptic transmission but normal synaptogenesis in the absence of Munc13-mediated vesicle priming. Proc Natl Acad Sci USA 99: 9037-9042

### **Edgar Brunner**

### **Professor of Medical Statistics**

Student: WS 64/65 - SS 69, Technical University of Aachen Diploma: April 1969, Mathematics Promotion: 12. May 1971, (Dr. rer. nat.), Technical University of Aachen Title: Eine Beziehung zwischen dem Holm-Test und dem Kolmo-gorov-Smirnov-Test (A Relation between Holm's Test and the Kolmogorov-Smirnov-Test) Habilitation: 11.11.1973, Medical Statistics Professor: 01.01.1976 University of Göttingen, Dept. of Medical Statistics, 01.03.1976 Head of the Department



### **Nonparametric Statistics**

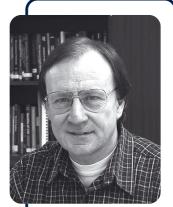
- Asymptotic distribution of rank statistics
- Multi-factor designs
- Adjustment for covariates

### Longitudinal data

Ordered categorical data

Design and analysis of diagnostic trials

Statistical methods for the analysis of microarray data



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### **Further Information:**

http://www.ams.med. uni-goettingen.de/

### Selected Recent Publications:

Brunner E and Langer F (2000) Nonparametric Analysis of Ordered Categorical Data in Designs with Longitudinal Observations and Small Sample Sizes. Biom J 42: 663-675

Brunner E, Munzel U and Puri ML (2001) The multivariate nonparametric Behrens-Fisher-Problem. J Statist Plann and Inf 108: 37-53

Brunner E, Domhof S and Langer F (2002) Nonparametric Analysis of Longitudinal Data in Factorial Designs. Wiley: New York

Brunner E und Munzel U (2002) Nichtparametrische Datenanalyse. Springer: Heidelberg

Brunner E and Puri M L (2002) A class of rank-score tests in factorial designs. J Statist Plann and Inf 103: 331-360

### Nicole Dünker



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Center of Anatomy Department of Neuroanatomy University of Göttingen Kreuzbergring 36

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### Privatdozent, Neuroanatomy

1998: Dr. rer. nat./ PhD, Department of Zoology, University of Darmstadt1998: University of California, Department of Integrative Biology, Berkeley1999: University of Michigan, Department of Molecular, Cellular and DevelopmentalBiology

1999 - 2002: Department of Anatomy and Cell Biology, University of Homburg 2003: Habilitation (PD) for anatomy at the anatomical faculty of the University of Göttingen

Current position: senior postgraduate researcher at the Center for Anatomy, Department of Neuroanatomy, University of Göttingen

### Major Research Interests:

- I Role of extracellular signaling molecules in mediating neural and non- neuronal programmed cell death
- II Interaction of pro-and anti-apoptotic extracellular signaling molecules like Transforming growth factor beta (TGF-ß), tumor necrosis factor alpha (TNF(), bone morphogenetic protein (BMP) or insulin in mediating programmed cell death
- III Role of extracellular signaling molecules in the establishment and maintenance of axonal projections
- IV Possibilities of clinical application of extracellular signaling molecules in treatment of neurodegenerative diseases and cancer

# Selected Recent Publications:

Krieglstein K, Richter S, Farkas L, Schuster N, Dünker N, Oppenheim RW, Unsicker K (2000) Reduction of endogenous transforming growth factors beta prevents ontogenetic neuron death. Nat Neurosci 3: 1085-90

Dünker N, Schuster N, Krieglstein K (2001) TGF- $\beta$  modulates programmed cell death in the retina of the developing chick embryo. Development 128: 1933-1942

Dünker N, Schmitt K, Schuster N., Krieglstein K (2002) The role of Transforming growth factor beta 2 and 3 in mediating apoptosis in the murine intestinal mucosa. Gastroenterol 122: 1364-1375

Dünker N, Schmitt K, Krieglstein K (2002) TGF- $\beta$  is required for programmed cell death in interdigital webs of the developing mouse limb. Mech Dev 113: 111-120

Farkas LM, Dünker N, Roussa E, Unsicker K, Krieglstein K (2003) TGF-βs are essential for the development of midbrain dopaminergic neurons *in vitro* and *in vivo*. J Neurosci 23: 5178-5186

Dünker N, Krieglstein K (2003) Reduced programmed cell death in the retina and defects in lens and cornea of Tgf $\beta 2^{-/-}$  Tgf $\beta 3^{-/-}$  double deficient mice. Cell Tiss Res 313: 1-10

### **Professor of Zoology**

Dr. rer. nat. University of Cologne 1967 PostDoc: Makerere University College, Kampala (Uganda) 1968 Department of Zoology, University of Copenhagen (Denmark) 1971 Department of Biology, University of Oregon (USA) 1972 Habilitation (Zoology) University of Cologne 1974 Professor of Zoology, University of Göttingen 1978 Head of the Department of Neurobiology

### Major Research Interests:

The common research topic of the department is Neuroethology of acoustic communication in singing insects. This involves as main fields of interest neuronal basis of song production and song recognition, neuropharmacology of motor actions, interdependence of singing and hearing, evolution of acoustic communication, bioacoustic and sensory ecology in the lab and in the field, and development and regeneration of components of the auditory system.

The songs of insects are produced as fixed action patterns. Single cell recordings, behaviour following lesions and electric or pharmacologic stimulation of the brain help to identify single elements and networks in the CNS producing the innate song patterns. Application of neuroactive substances to the brain aim to identify mechanisms like second messenger cascades involved in production of these motor programs (Heinrich).

A song only makes sense when it is heard by a potential partner. Song parameters and song recognition behaviour are studied with a focus on bushcrickets (Stumpner). The function of sensory cells and auditory interneurones in various insects is investigated by means of extra- and intracellular recordings, neuroanatomy and immunohistochemistry. The relevant questions are: to what degree are hearing systems specialized to species-specific needs, how is song recognition realized on the level of single interneurones, or: what are the potential predecessor structures or systems in the evolution of audition? For the latter, various sensory organs are in the focus of research - neuroanatomically, functionally and their ontogenesis (Lakes-Harlan, Stumpner).

Singing and hearing, of course, are highly interdependent, on the one hand by interference of movements with the ability to hear (studied e.g. by laser-vibrometry), on the other hand by biophysical constraints limitating the detection of parameters in the field (studied e.g. by sound analysis and behavioural tests) (Elsner).

Very helpful and sometimes surprising data are gained from developmental studies. This involves regeneration of behaviour and neuronal structures, molecular mechanisms in early development and regeneration as well as cell cultures with neurones identified as parts of the auditory system (Lakes-Harlan).

### Selected Recent Publications:

Heinrich R, Elsner N (1997) Central nervous control of hindleg coordination in stridulating grasshoppers. J Comp Physiol A 180: 257-269

Heinrich R, Jacobs K, Lakes-Harlan R (1998) Tracing of a neuronal network in the locust by pressure injection of markers into a synaptic neuropile. J Neurosci Meth 80: 81-89

Heinrich R, Rozwod K, Elsner N (1998) Neuropharmacological evidence for inhibitory cephalic control mechanisms of stridulatory behaviour in grasshoppers. J Comp Pysiol A 183: 389-399

Lakes-Harlan R & Pfahlert C (1995) Regeneration of axotomized tympanal nerve fibres in the adult grasshopper *Chorthippus biguttulus* (L.)(Orthoptera: Acrididae) correlates with regaining the localization ability. J Comp Physiol A 176: 797-807

Jacobs K & Lakes-Harlan R (1997) Lectin histochemistry of the metathoracic ganglion of the locust, *Schistocerca gregaria*, before and after deafferentation. J Comp Neurol 387: 255-265

Lakes-Harlan R, Stölting H & Stumpner A (1999) Convergent evolution of an insect ear from a preadaptive structure. Proc R Soc Lond B 266: 1161-1167

Stölting H, Stumpner A (1998) Tonotopic organization of auditory receptorcells in the bushcricket *Pholidoptera griseoaptera* (Tettigoniidae, Decticini). Cell Tissue Res 294: 377-386

Stumpner A (1998) Picrotoxin eliminates frequency selectivity of an auditory interneuron in a bushcricket. J Neurophysiol 79: 2408-2415

Stumpner A (1999) An interneurone of unusual morphology is tuned to the female song in the bushcricket *Ancistrura nigrovittata* (Orthoptera: Phaneropteridae). J Exp Biol 202: 2071-2081

# Norbert Elsner



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# Wolfgang Engel



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### **Professor of Human Genetics**

Dr. med., Universität Freiburg, 1967 Physician, Hospital Schorndorf, 1966 - 1968 Postdoc, Institute of Human Genetics and Anthropology, Universität Freiburg, 1968 - 1977 Habilitation (Human Genetics), Universität Freiburg, 1974 Professor of Human Genetics and Director of the Institute, Universität Göttingen, 1977

### Major Research Interests:

Our research is focussed on the molecular analysis of normal human variability and genetic disturbances of development and differentiation.

Isolated genes are being analysed in detail with respect to their functional properties by animal models (transgenic and knock-out-mice). For suitable genetic diseases therapeutic strategies (substitution; gene therapy) are being developed and initial evaluation of such strategies is done in the mouse. We are working on the genotype – phenotype correlations in neurological and cardiovascular diseases (e. g. Spastic paraplegia, Rett syndrome, mental retardation by subtelomeric microdeletions, molybdenum cofactor deficiency; cardiomypathies, Noonan syndrome) and several genetically determined malformation syndromes (e.g. Townes-Brocks syndrome, Okihiro syndrome, Morbus Osler). We are also engaged in the molecular and cellular basis of initiation events of cancer, specifically in prostate cancer, medulloblastoma and rhabdomyosarcoma. One main interest in our institute is the analysis of structure, expression and function of genes involved in differentiation of male gametes. The knowledge of the function of those genes can help us to clarify the genetic causes of male infertility.

# Selected Recent Publications:

Trappe R, Laccone F, Cobilanschi J, Meins M, Huppke P, Hanefeld F, Engel W (2001) MECP2 mutations in sporadic cases of Rett-syndrome are almost exclusively of paternal origin. American Journal of Human Genetics 68: 1093-1101

Pires-daSilva A, Nayernia K, Engel W, Torres M, Stoykova A, Chowdhury K, Gruss P (2001) Mice deficient for spermatid perinuclear RNA-binding protein show neurologic, spermatogenetic, and sperm morphological abnormalities. Developmental Biology 233: 319-328

Lee H-J, Adham IM, Schwarz G, Kneussel M, Sass JO, Engel W, Reiss J (2002) Molybdenum cofactor-deficient mice resemble the phenotype of human patients. Human Molecular Genetics 26: 3309-3317

Böhm D, Schwegler H, Kotthaus L, Nayernia K, Rickmann M, Köhler M, Rosenbusch J, Engel W, Flügge G, Burfeind P (2002) Disruption of PLC -b1-mediated signal transduction in mutant mice causes age-dependent hippocampal mossy fiber sprouting and neurodegeneration. Molecular and Cellular Neuroscience 21: 584-601

Sauter S, Miterski B, Klimpe S, Bönsch D, Schöls L, Visbeck A, Papke T, Hopf H C, Engel W, Deufel T, Epplen JT, Neesen J (2002) Mutation analysis of the Spastin gene (SPG4) in patients in Germany with autosomal dominant hereditary spastic paraplegia. Human Mutation 20: 127-132

### Gabriele Flügge

### Privatdozent, Experimental Neuroscience

Dr. rer. nat., University of Munich, 1979 Senior Scientist at the German Primate Center

### Major Research Interests:

In humans, stressful or traumatic life events such as death of a close relative often represent a chronic psychological load that can lead to central nervous diseases such as depression. We are investigating central nervous processes that occur in the course of chronic psychosocial stress in animals that show similar symptoms as depressed patients.

Changes in neurotransmitter systems, receptors, transporters and other molecules are investigated using molecular biology methods to quantify expression of genes in combination with *in situ* hybridization and immunocytochemistry to localize the changes in distinct neurons of the brain. The effects of antidepressants are investigated with the same tools to elucidate mechanisms that underlie the beneficial effects of these drugs. In conjunction with behavioral studies we are able to find neuromolecular factors that contribute to emotional behavior in the animals.

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### **Further Information:**

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### Selected Recent Publications:

Flügge G (2000) Regulation of monoamine receptors in the brain: dynamic changes during stress. Int Rev Cytology 195: 145-213

Isovich I, Mijnster MJ, Flügge G, Fuchs E (2000) Chronic psychosocial stress reduces the density of dopamine transporters. Eur J Neurosci 12: 1071-1078

Meyer H, Palchaudhuri M, Scheinin M, Flügge G (2000) Regulation of alpha<sub>2A</sub>-adrenoceptor expression by chronic stress in neurons of the brain stem. Brain Research 880: 147-158

Flügge G, Kramer M, Fuchs E (2001) Chronic subordination stress in male tree shrews: replacement of testosterone affects behavior and central alpha<sub>2</sub>-adrenoceptors. Physiol. Behav 73: 293-300

Fuchs E, Flügge G (2002) Social stress in tree shrews. Effects on physiology, brain function, and behavior of subordinate individuals. Pharmacol Biochem Behav 73: 247-58

Flügge G, van Kampen M, Meyer H, Fuchs E (2003) Alpha2A and alpha2C-adrenoceptor regulation in the brain: alpha2A changes persist after chronic stress. Eur J Neurosci 17:917-928

### Jens Frahm



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### **Further Information:**

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### **Professor of Physical Chemistry**

Director of 'Biomedizinische NMR Forschungs GmbH' - Biomedical Nuclear Magnetic Resonance -

### Major Research Interests:

### Methodology

- development and application of spatially resolved NMR
- magnetic resonance functional neuroimaging
- localized magnetic resonance neurospectroscopy

### **Brain Research**

- noninvasive neurobiology, human neuroscience
- structural, metabolic, and functional studies of the central nervous system
- functional mapping of neuronal activation, cognitive information processing in humans
- brain disorders in childhood
- animal models, transgenic mice

# Selected Recent Publications:

Natt O, Watanabe T, Boretius S, Radulovic J, Frahm J, Michaelis T (2002) High-Resolution 3D MRI of Mouse Brain Reveals Small Cerebral Structures *In Vivo*. J Neurosci Methods 120: 203-209

Watanabe T, Natt O, Boretius S, Frahm J, Michaelis T (2002) *In Vivo* 3D MRI Staining of Mouse Brain After Subcutaneous Application of MnCl<sub>2</sub>. Magn Reson Med 48: 852-859

Merboldt KD, Baudewig J, Treue S, Frahm J (2002) Functional MRI of Self-Controlled Stereoscopic Depth Perception. Neuroreport 13: 1721-1725

Wilken B, Dechent P, Brockmann K, Finsterbusch J, Baumann M, Ebell W, Korenke GC, Pouwels PJW, Hanefeld FA, Frahm J (2003) Quantitative Proton Magnetic Resonance Spectroscopy of Children with Adrenoleukodystrophy Before and After Hematopoietic Stem Cell Transplantation. Neuropediatrics 34: 1-10

Dechent P, Frahm J (2003) Functional Somatotopy of Finger Representations in Human Primary Motor Cortex. Hum Brain Mapp 18: 272-283

### **Eberhard Fuchs**

### **Professor of Animal Physiology**

1977: Dr. rer. nat., University of Munich 1996 - 2000: Professor (Animal Physiology), University of Karlsruhe 2000 - 2003: Professor for Animal Physiology, University of Göttingen since 2003: Professor for Neurobiology, Department of Neurology, Medical School, University of Göttingen



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### Major Research Interests:

We are an interdisciplinary research laboratory using functional neuroanatomical, neuropharmacological, behavioral and molecular techniques to investigate functioning of the brain in animal models of psychiatric and neurodegenerative diseases. The aim of our work is to elucidate brain structures, circuits, pathways and mechanisms that underlie normal and pathological behavior. This work integrates inputs from other research fields with the ultimate aim of developing new therapeutic strategies for psychiatric and neurodegenerative disorders.

The laboratory specializes in the development, validation and investigation of animal models to detect abnormal cognitive, motor and emotional expressions of brain pathology. Currently, we are engaged in the investigation of central nervous and behavioral phenomena associated with stress, depression and aging. In addition, there are initial studies in the areas of Parkinson's disease and Multiple Sclerosis.

### Selected Recent Publications:

Keuker J, Luiten PGM, Fuchs E(2003) Preservation of hippocampal neuron numbers in aged rhesus monkeys. Neurobiol Aging 24: 157-165

van der Hart MGC, Czéh B, de Biurrun G, Michaelis T, Watanabe T, Natt O, Frahm J, Fuchs E (2002) Substance P receptor antagonist and clomipramine prevent stress-induced alterations in cerebral metabolites, cytogenesis in the dentate gyrus and hippocampal volume. Mol Psychiat 7: 933-941

Fuchs E, Flügge G (2002) Social stress in tree shrews: effects on physiology, brain function and behavior of subordinate individuals. Pharmacol. Biochem Behav 73: 247-258

Kole MHP, Swan L, Fuchs E (2002) The antidepressant tianeptine persistently modulates glutamate receptor currents of the hippocampal CA3 commissural-associational synapse in chronically stressed rats. Europ J Neurosci 16: 807-816

Bartolomucci A, de Biurrun G, Czéh B, van Kampen M, Fuchs E (2002) Selective enhancement of spatial learning under chronic psychosocial stress. Europ J Neurosci 15: 1863-1866

Czéh B, Michaelis T, Watanabe T, Frahm J, de Biurrun G, van Kampen M, Bartolomucci A, Fuchs E (2001) Stress-induced changes in cerebral metabolites, hippocampal volume and cell proliferation are prevented by antidepressant treatment with tianeptine. Proc Natl Acad Sci USA 98: 12796-12801

Lucassen P, Vollmann-Honsdorf GK, Gleisberg M, de Kloet ER, Fuchs E (2001) Chronic psychosocial stress differentially affects apoptosis in hippocampal subregions and cortex of the adult tree shrew. Europ J Neurosci 14: 161-166

### **Ralf Heinrich**



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### Juniorprofessor, Molecular Neuropharmacology of Behavior

Dr. rer. nat., University of Göttingen, 1995 Postdoctoral fellow, Harvard Medical School, Boston, USA, 1997 - 1999

### Major Research Interests:

Invertebrate preparations can offer unique advantages over more complex nervous systems of vertebrates and especially mammals, such as a smaller total number of neurons in the CNS, the concept of individually identifiable neurons and rather limited repertoires of behaviors composed of genetically determined and stereotype components.

Behavior is the product of complex interactions between various types of neurons. We are especially interested in the central nervous mechanisms underlying the selection and adaptation of actions that are most appropriate for a particular behavioral situation an animal encounters. Our neuroethological studies focus on two systems:

1) The acoustic communication behavior of insects: Pharmacological interference with transmitter- and second messenger-systems in identified brain areas aims to characterize the signaling pathways that contribute to general motivation, initiation of communication behaviors and the selection/composition of behaviorally meaningful song patterns. Our studies on intact and behaving preparations allow to link natural sensory stimuli to physiological changes in the brain and to analize their modulatory effects on the subsequent behavior of the animal.

2) Aggressive behavior of crustaceans: In essentially all species of animals, including man, 5HT is important in aggression, which is a quantifiable behavior in crustaceans. In lobsters and crayfish, enhanced serotonergic function is linked to increased aggression and dominance, while octopamine (the invertebrate analogue of norepinephrine) antagonizes these effects. Pharmacological and physiological studies aim to find out where and how these amine-releasing neurosecretory systems change during a fight to establish stable hierarchies and allow experience to alter the subsequent fighting behavior.

### Selected Recent Publications:

Heinrich R, Cromarty S I, Hörner M, Edwards D H and Kravitz E A (1999) Autoinhibition of serotonin cells: an intrinsic regulatory mechanism sensitive to the pattern of usage of the cells. Proc Nat Acad Sci USA 96: 2473-2478

Heinrich R, Bräunig P, Walter I, Schneider H and Kravitz E A (2000) Aminergic neuron systems of lobsters: Morphology and electrophysiology of octopamine-containing neurosecretory cells. J Comp Physiol A 186: 617-629

Heinrich R, Wenzel B and Elsner N (2001) A role for muscarinic excitation: Control of specific singing behavior by activation of the adenylate cyclase pathway in the brain of grasshoppers. Proc Nat Acad Sci USA 98: 9919-9923

Wenzel B, Elsner N and Heinrich R (2002) mAChRs in the grasshopper brain mediate excitation by activation of the AC/ PKA and the PLC second-messenger pathways. J Neurophysiol 87: 876-888

Heinrich R (2002) Impact of descending brain neurons on the control of stridulation, walking and flight in orthoptera. Microscopy Research and Technique 56: 292-301

### Swen Hülsmann

### Group leader at the Department of Neurophysiology

### Dr. med., University of Münster

Postdoctoral fellow, University of Münster Dept. of Neurosurgery, 1995 - 1996 Postdoctoral fellow, University of Göttingen, Dept. of Neurophysiology, 1996 - 2001 Group leader (Wissenschaftlicher Assistent) Neurophysiology, since 2001 Principle Investigator at the DFG Research Center for Molecular Physiology of the Brain (CMPB) since 2002



The majority of cells in the human brain are glial cells, outranging the number of neurons by a factor of 10. However, most behavioral aspects of life are attributed to neurons, leaving a rather white spot of knowledge about the function of the different types of glial cells.

Our group aims to identify and clarify the mechanisms that allow glial cells, e.g. astrocytes to modulate and stabilize the most vital behavior of breathing.

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### Selected Recent Publications:

Hülsmann S, Mußhoff U, Madeja M, Fischer B, Speckmann E-J (1998) Characterization of transmembraneous ion currents elicited by a stream of fluid during spontaneous and ligand-induced chloride-current oscillation in *Xenopus laevis* oocytes. Pflügers Arch 436: 49-55

Hülsmann S, Greiner C, Köhling R, Wölfer J, Moskopp D, Riemann B, Lücke A, Wassmann H, Speckmann E-J (1999) Dimethyl sulfoxide increases latency of anoxic terminal negativity in hippocampal slices of guinea pig *in vitro*. Neurosci Lett 261: 1-4

Hülsmann S, Oku Y, Zhang W, Richter D W (2000) Metabotropic glutamate receptors and blockade of glial Krebs cycle depress glycinergic synaptic currents of mouse hypoglossal motoneurons. Eur J Neurosci 12: 239-246

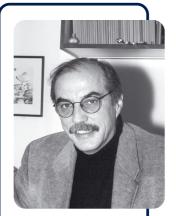
Hülsmann S, Oku Y, Zhang W, Richter D W (2000) Metabolic coupling between glia and neurons is necessary for maintaining respiratory activity in transverse medullary slice of neonatal mouse. Eur J Neurosci 12: 856-862

Gomeza J, Ohno K, Hülsmann S, Armsen W, Eulenburg V, Richter DW, Laube B, Betz H (2003) Deletion of the mouse glycine transporter 2 results in a hyperekplexia phenotype and postnatal lethality. Neuron (in press)

Gomeza J\*, Hülsmann S\*, Ohno K, Eulenburg V, Szöke K, Richter DW, Betz H (2003) Inactivation of the glycine transporter 1 gene discloses vital role of glial glycine uptake in glycinergic inhibition. Neuron (in press), \*Equal contribution



### Herbert Jäckle



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# Professor, Director at the Max Planck Institute for Biophysical Chemistry

Faculty member at the EMBL, Heidelberg (1980 - 1982) Head of the group (associate professor), Max Planck Institute for Developmental Biology, Tübingen (1982 - 1988) Professor and Chairman, Dept. of Genetics and Microbiology, Univ. of Munich (1988 - 1991)

### Major Research Interests:

How is the embryo generated from a single cell, the egg? We address this question by using the *Drosophila* embryo as an experimental system, applying the combined tools of classical embryology, genetics, molecular biology and biochemistry. We have focussed our efforts to isolate and characterize the factors underlying early pattern formation along the anterior-posterior axis of the embryo. We sought to unravel their mode of action und the molecular mechanism in which they function.

Many of the factors required to establish the basic body plan are also necesssary for organ formation, a process which involves local inductive interactions between groups of cells and/or epithelial cell layers. We have started to identify the genetic components and regulatory circuitries involved in organogenesis as well as in neural conductivity and function. We also use the fly to identify the components of novel biochemical pathways and cellular key components that control and maintain homeostasis and energy balance, and we initiated a gene discovery program to systematically characterize the function of genes on the *Drosophila* X-chromosome.

# Selected Recent Publications:

Schöck F, Reischl J, Wimmer E, Taubert H, Purnell B A and Jäckle H (2000) Phenotypic supression of *empty spiracles* is prevented by buttonhead. Nature 405: 351-354

Piepenburg O, Vorbrüggen G, and Jäckle H (2000) *Drosophila* segment borders result from unilateral repression of hedgehog activity by Wingless signaling. Molecular Cell 6: 203-209

Niessing D, Sprenger F, Driever W, Taubert H, Jäckle H and Rivera-Pomar R (2000) Homeodomain position 54 specifies transcriptional versus translational control by Bicoid. Mol Cell 5: 595-401

Linder B, Gerlach N and Jäckle H (2001) The *Drosophila* homolog of the human AF10 is a HP1-interacting suppressor of position effect variegation. EMBO reports 2: 211-216

Benos P V *et al.* (2001) From first base: The sequence of the tip of the *X*-chromosome of *Drosophila melanogaster*, a comparison of two sequencing strategies. Genome Research 11: 710-730

#### **Reinhard Jahn**

#### Professor, Director at the Max Planck Institute for Biophysical Chemistry

Dr. rer. nat. (Ph.D.) 1981, University of Göttingen

Professor (since 1997 Adjunct Professor) of Pharmacology, Yale University School of Medicine

Appointed as Director at the Max Planck Institute for Biophysical Chemistry 1997



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### Major Research Interests:

Our group is interested in the mechanisms of membrane fusion, with the main emphasis on regulated exocytosis in neurons. Since recent years it is known that intracellular membrane fusion events are mediated by a set of conserved membrane proteins, termed SNAREs. For fusion to occur, complementary sets of SNAREs need to be present on both of the fusing membranes. The neuronal SNAREs are among the best characterized. They are the targets of the toxins responsible for botulism and tetanus. To understand how these proteins make membranes fuse, we studied their properties in detail using biochemical and biophysical approaches. We found that they assemble into a tight complex which ties the membrane closely together and thus probably initiates bilayer mixing.

In our current approaches, we study membrane fusion at the level of isolated proteins as well as in semi-intact and intact cells. Thus, we are investigating conformational changes of the SNARE proteins before and during fusion. Furthermore, we use reconstitution of membrane fusion in cell-free assays and in proteoliposomes. Other projects of the group include the study of neurotransmitter uptake by synaptic vesicles and the function of Rab-GTPases in neuronal exocytosis.

### Selected Recent Publications:

Takamori S, Rhee JS, Rosenmund C, Jahn R (2000) Identification of a vesicular glutamate transporter that defines a glutamatergic phenotype in neurons. Nature 407: 189-194

Lang T, Bruns D, Wenzel D, Riedel D, Holroyd P, Thiele C, Jahn R (2001) SNAREs are concentrated in cholesteroldependent clusters that define docking and fusion sites for exocytosis. EMBO J 20: 2202-2213

Antonin W, Fasshauer D, Becker S, Jahn R, Schneider TR (2002) Crystal structure of the endosomal SNARE complex reveals common structural principles of all SNAREs. Nature Struct Biol 9: 107-111

Fasshauer D, Antonin W, Subramaniam V, Jahn R (2002) SNARE assembly and disassembly exhibit a pronounced hysteresis (2002) Nature Struct Biol 9: 144-151

Jahn R, Grubmüller H (2002) Membrane fusion. Curr Opinion in Cell Biology 14: 488-495

Lang T, Margittai M, Hölzler, H, Jahn R (2002) SNAREs in native plasma membranes are active and readily form core complexes with endogenous and exogenous SNAREs. J Cell Biol 158: 751-760

#### Bernhard U. Keller



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#### Professor of Neurophysiology

Dr. rer. nat., University of California, San Diego / University of Göttingen, 1986 Postdoctoral fellow, Max-Planck-Institute for biophysical Chemistry, Göttingen, 1987 Staff Scientist, Max-Planck-Institute for biophysical Chemistry, Göttingen, 1989 Heisenberg - Stipend, 1995

Extraordinary Professor (apl.), Neurophysiology, University of Göttingen, 2001

### Major Research Interests:

Calcium signals represent a key information processing system in the central nervous system, and defined changes in cytosolic calcium levels have been associated with multiple neuronal processes including learning, memory, synaptic plasticity and neurodegenerative disease. While the last years have provided significant information about the molecular elements that control calcium signals in identified cells, little is known about how Ca-dependent signal cascades are processed, superimposed and integrated in a functionally intact neuronal net.

Based on a functionally intact neuronal network that controls rhythmic-respiratory activity in the brain stem of mice, we have addressed three questions:

i ) which molecular elements control Ca-dependent signal cascades underlying rhythmic-respiratory activity in identified brain stem neurones ?

ii) how does the spatio-temporal profile of cytosolic Ca signaling modulate neuronal activity in this interconnected neuronal net ?

iii) how are cytosolic Ca signals affected in transgenic mouse models of human neurodegenerative disease (e.g. SOD1 G93A mouse model of human amyotrophic lateral sclerosis) that specifically affect brain stem neurones ?

In our present research, we address these questions by a combined research approach. For example, we employ techniques from molecular biology and classical electrophysiology like patch clamp recordings from slice preparations and combine these recordings with up-to date imaging techniques including fast CCD imaging and IR-laser based multiphoton measurements. Accordingly, the central focus of our research is to increase our understanding of Ca signaling in a functionally intact neuronal system, and achieve a better understanding of the disruptions of Ca-dependent signal cascades characteristic for human neurodegenerative disease.

# Selected Recent Publications:

Lips M B and Keller B U (1998) Endogenous calcium buffering in motoneurones of the nucleus hypoglossus from mouse. J Physiol 511 (1): 105-117

Palecek J, Lips M B and Keller B U (1999) Calcium dynamics and buffering in motoneurones of the mouse spinal cord. J Physiol 520 (2): 485-502

Lips M and Keller B U (1999) Activity-related calcium dynamics in motoneurones of the nucleus hypoglossus from mouse. J Neurophysiol 82 (6): 2936-2946

Paarmann I, Frermann D, Keller B U and Hollmann M (2000) Expression of fifteen glutamate receptor subunits and various splice variants in tissue slices and single neurones of brainstem nuclei, and potential functional implications. Journal of Neurochemistry 74 (4): 1335-45

Ladewig T and Keller B U (2000) Simultaneous patch clamp recording and calcium imaging in a rhythmically active neuronal network in the brain stem slice preparation from mouse. Pflügers Arch 440: 322-332

Vanselow B and Keller B U (2000) Calcium dynamics and buffering in oculomotor neurones from mouse, that are particularly resistant during amyotrophic lateral sclerosis (ALS)-related motoneuron disease. J Physiol 525: 433-445

Ladewig T, Kloppenburg P, Lalley P, Zipfel W, Webb W and Keller BU (2003). Spatial profiles of store-dependent calcium release in motoneurones of the nucleaus hypoglossus from newborn mouse. J Physiol 547: 775-787

### Jürgen Klingauf

# Research Group Leader at the Max Planck Institute for Biophysical Chemistry

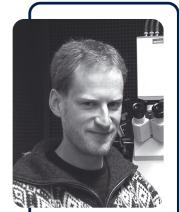
Research fellow, Dept. of Molecular & Cellular Physiology, Stanford University, Ca, 1996 - 1998.

Dr. rer. nat. (Ph.D.) 1999, University of Göttingen.

Since 2000 junior group leader at the Max Planck Institute for Biophysical Chemistry.



The focus of our research is the study of synaptic transmission, with the emphasis on presynaptic mechanisms. At the synapse, neurotransmitter is rapidly released from small vesicles which are triggered to fuse with the plasma membrane by the entry of  $Ca^{2+}$  ions. The maintenance of synaptic transmission requires that these vesicles be retrieved by a reverse process, i.e. endocytosis. How is this endocytic activity and subsequent formation of fusion-competent vesicles coupled to exocytosis? To delineate the mechanisms by which synaptic vesicles can be retrieved we employ high-resolution imaging techniques, like two-photon laser scanning and total internal reflection microscopy, electrophysiology, as well as biochemical approaches. By transfection of neurons in primary cell culture or the usage of knock-out models we can target or modulate specific proteins thought to be pivotal in synaptic vesicle endocytosis. Currently, we are mainly studying synapses of rodent hippocampus, down to the level of single fluorescently labeled vesicles in cultured or freshly isolated synaptic boutons. By making use of fluorescent styryl dyes with different kinetic properties we found that in central nervous synapses at least two kinetically distinct modes of endocytosis co-exist. We are now trying to characterize the respective molecular events underlying those different mechanisms using genetically encoded fluorescent probes.



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### Selected Recent Publications:

Klingauf J, Kavalali ET, Tsien RW (1998). Kinetics and regulation of fast endocytosis at hippocampal synapses. Nature 394: 581-585

Kavalali ET, Klingauf J, Tsien RW (1999). Properties of fast endocytosis at hippocampal synapses. Phil Trans R Soc Lond B 354: 337-346

Kavalali ET, Klingauf J, Tsien RW (1999). Activity-dependent regulation of synaptic clustering in a hippocampal culture system. Proc Natl Acad Sci USA 96: 12893-12900

Choi S, Klingauf J, Tsien RW (2000). Postfusional regulation of cleft glutamate concentration during LTP at 'silent synapses'. Nature Neurosci 3: 330-336

Bruns D, Riedel D, Klingauf J, Jahn R (2000). Quantal release of serotonin. Neuron 28(1): 205-220

### Willhart Knepel



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#### Professor of Molecular Pharmacology

Dr. rer. nat., University of Freiburg i. Br., Germany, 1980 Habilitation, University of Freiburg i. Br., Germany, 1985 Research Fellow, Laboratory of Molecular Endocrinology, Harvard Medical School, Boston, MA, USA, 1987 - 1990 Joined Medical Faculty of the University of Göttingen 1991

### Major Research Interests:

The main interest of the laboratory is in the molecular mechanisms of gene transcription. Transient transfections of reporter fusion genes, transgenic mice, and other molecular biology techniques are used to study the mechanisms of cell-specific and signal-induced gene transcription, and how drugs interfere with these mechanisms to produce pharmacological effects. 1. The pancreatic islet hormone glucagon is a biological antagonist of insulin and regulates blood glucose levels. Enhanced synthesis and secretion of glucagon contributes to increased hepatic glucose output and hyperglycemia in diabetes mellitus. We study the mechanisms which activate the glucagon gene in pancreatic islet a cells as well as signaling pathways to the glucagon gene induced by cAMP, membrane depolarization, and insulin. 2. We study the regulation of glucagon gene transcription by the new group of oral antidiabetic drugs, the thiazolidinediones. These so-called 'insulin sensitizers' may improve insulin action in part through an effect on glucagon. 3. The ubiquitously expressed, cAMP- and calcium-regulated transcription factor CREB is affected by several classes of drugs. We study how the immunosuppressive drugs cyclosporin A and FK506 (tacrolimus) inhibit CREB-mediated transcription. This effect may underlie their pharmacological effects, both desired and undesired. Using transgenic mice and an animal model of depression, we also study whether treatment with antidepressants alters CREB-mediated transcription in order to better understand the molecular mechansims of action of antidepressant drugs.

# Selected Recent Publications:

Beimesche S, Neubauer A, Herzig S, Grzeskowiak R, Diedrich T, Cierny I, Scholz D, Alejel T, Knepel W (1999) Tissuespecific transcriptional activity of a pancreatic islet cell-specific enhancer sequence/Pax6-binding site determined in normal adult tissues *in vivo* using transgenic mice. Mol Endocrinol 13: 718-728

Siemann G, Blume R, Grapentin D, Oetjen E, Schwaninger M, Knepel W (1999) Inhibition of cyclic AMP response elementbinding protein/cyclic AMP response element-mediated transcription by the immunosuppressive drugs cyclosporin A and FK506 depends on the promoter context. Mol Pharmacol 55: 1094-1100

Herzig S, Füzesi L, Knepel W (2000) Heterodimeric Pbx-Prep1 homeodomain protein binding to the glucagon gene restricting transcription in a cell type-dependent manner. J Biol Chem 275: 27989-27999

Grzeskowiak R, Amin J, Oetjen E, Knepel W (2000) Insulin responsiveness of the glucagon gene conferred by interactions between proximal promoter and more distal enhancer-like elements involving the paired-domain transcription factor Pax6. J Biol Chem 275: 30037-30045

Schinner S, Dellas C, Schröder M, Heinlein C, Chang C, Fischer J, Knepel W (2002) Repression of glucagon gene transcription by peroxisome proliferator-activated receptor  $\gamma$  through inhibition of Pax6 transcriptional activity. J Biol Chem 277: 1941-1948

### Kerstin Krieglstein

#### Professor of Anatomy/Neuroanatomy

Dr. rer. nat., University of Gießen, Germany, 1990 Postdoctoral fellow, University of California, Irvine, 1990 - 1992 Professor of Anatomy, University of Saarland, 1999 - 2001 Appointed 2001 as head of the Department of Anatomy/Neuroanatomy, University of Göttingen



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#### Major Research Interests:

The nervous system is a complex network of billions of neurons building appropriate connections and transmitting the information required. Although the nervous system has a lifelong synaptic plasticity, it is essentially built just once with very little regenerative capacity, meaning that neurons have to survive and function for lifetime. Loss of neurons will eventually lead to functional impairments such as those found in Alzheimer's, Parkinson's or ALS patients.

We are interested in the understanding of the regulation of neuronal survival and death. Recent advancements in the field have provided clear evidence that neuronal survival is caused by synergistic actions of neurotrophic factors along with other cytokines most prominently from the TGF- $\beta$  superfamily. Synergisms of TGF- $\beta$  in combination with neurotrophic factors, like GDNF or NGF, will be studied to establish their role in nervous system development and their therapeutic potential in brain repair. Specifically, we shall investigate such synergisms by utilising mouse mutants to understand the developmental role and by emplying genomic screens to identify new target genes for the establishment of new therapeutic strategies for human neurodegenerative disorders. Furthermore, as growth factors function not only in the decision of neuron survival or death, we shall explore their morphogenetic and differentiation capacities employing the powerful potential of embryonic (ES) and CNS stem cells.

### Selected Recent Publications:

Krieglstein K, Henheik P, Farkas L, Jaszai J, Galter D, Krohn K and Unsicker K (1998) GDNF requires TGF-B for establishing its neurotrophic activity. J Neurosci 18: 9822-9834

Schober A, Hertel R, Arumäe U, Farkas L, Jaszai J, Krieglstein K, Saarma M, Unsicker K (1999) GDNF rescues targetdeprived spinal cord neurons but requires TGF-B as co-factor *in vivo*. J Neurosci 19: 2008-2015

Krieglstein K, Richter S, Farkas L, Schuster N, Dünker N, Oppenheim R W, Unsicker K (2000) Reduction of endogenous transforming growth factor beta prevents ontogenetic neuron death. Nature Neuroscience 3: 1085-1091

Peterziel H, Unsicker K, Krieglstein K (2002) TGFbeta induces GDNF responsiveness in neurons by recruitment of GFRalpha1 to the plasma membrane, J Cell Biol 159: 157-167

Farkas L, Dünker N, Roussa E, Unsicker K, Krieglstein K (2003) Transforming growth factor-beta(s) are essential for the development of midbrain doparninergic neurons *in vitro* and *in vivo*. J Neurosci 23: 5178-5186

#### **Reinhard Lakes-Harlan**



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#### **Professor of Zoology**

Dr. rer. nat., University of Marburg, Germany, 1988 Postdoctoral fellow, McGill University Montreal, Canada 1989 - 1990 Since 1991 at the Faculty of Biology, University of Göttingen, Germany

### Major Research Interests:

Hearing organs are extremely sensitive to mechanical stimulation and provide the organism with crucial information for communication and survival. The information processing in the central nervous system requires highly specific synaptic connections. All this is especially interesting for the small ears of insects. The smallness causes special problems, like that of directionality, but also provides the opportunity to work with individually known cells. The function, development and evolution of these sophisticated systems are in focus of our research.

We investigate the development of the sensory organ, especially that of the sensory cells in respect to soma position, axogenesis and synaptogenesis. These primary sensory cells establishing a topographic order which is a prerequisite for precise information processing. The rules underlying this process are analysed on a cellular and molecular level. After the embryonic development, developmental processes are repeated during regeneration. During regeneration the formation of individual synapses for behavioural recovery can be followed. The function of sensory cells are investigated *in vivo* and *in vitro*. The main keywords are the biophysics, the peripheral modulation via second messengers and the sensory transduction of the auditory organs. The functional analyses include experiments with a systems approach: investigations of behaviour and of the sensory ecology reveal the evolutionary selection pressures which resulted in the specific properties of the sense organs.

### Selected Recent Publications:

Lakes-Harlan R, Stölting H & Stumpner A (1999) Convergent evolution of an insect ear from a preadaptive structure. Proc B Roy Soc 266: 1161-1167

Jacobs K & Lakes-Harlan R (1999) Axonal degeneration within the tympanal nerve of *Schistocerca gregaria*. Cell Tiss Res 298: 167-178

Jacobs K & Lakes-Harlan R (2000) Pathfinding, target recognition and synapse formation of single regenerating fibres in the adult grasshopper *Schistocerca gregaria*. J Neurobiol 42: 394-409

Köhler U & Lakes-Harlan R (2001) Auditory behaviour of a parasitoid fly (Emblemasoma auditrix, *Sarcophagidae, Diptera*) J Comp Physiol A 187: 581-587

Schäffer S & Lakes-Harlan R (2001) Embryonic development of the central projection of auditory afferents (*Schistocerca gregaria*, Orthoptera, Insecta) J Neurobiol 46: 97-112

#### Gerd Lüer

#### **Professor of Psychology**

Diploma in Psychology at the University of Hamburg, Germany (1963) Dr.rer.nat. (1966) and Habilitation (1971) at the Christian Albrechts University at Kiel, Germany Professor of Psychology at the Universities Kiel (1973), Düsseldorf (1974 - 1978) (chairman), Aachen (1979 - 1982) (chairman), and Göttingen (since 1982) (chairman)

# Major Research Interests:

Experimental psychology; Cognitive psychology: Problem solving; Memory: Working memory; Iconic memory. Language and language disturbance (aphasia); Eye movement research, visual perception and mental imagery; Word recognition in different writing systems (cross-cultural approach): Language and memory; Spatial cognition.

#### **Further Information:**

http://www.psych.unigoettingen.de/abt/2

### Selected Recent Publications:

Lüer G, Becker D, Lass U, Fang Y, Chen G & Wang Z (1998) Memory span in German and Chinese: Evidence for the phonological loop. European Psychologist 3: 102-112

Werner S, Saade Chr & Lüer G (1998) Relations between the mental representation of extrapersonal space and spatial behavior. In Chr. Freksa, Chr. Habel & K. F. Wender (Eds.), Spatial Cognition (Pp. 107-127). Berlin: Springer

Lass U, Fang Y, Chen G, Becker D & Lüer G (1999) Is memory for shapes subject to language-specific effects? An experimental study of memory span in German and Chinese subjects. - Zeitschrift für Sprache & Kognition 18: 136-145

Lass U, Lüer G, Becker D, Fang Y, Chen G & Wang Z (2000) Kurzzeitgedächtnisleistungen deutscher und chinesischer Probanden mit verbalen und figuralen Items: Zur Funktion von phonologischer Schleife und visuell-räumlichen Notizblock. Zeitschrift für Experimentelle Psychologie 47: 77-88

Elsner N & Lüer G (Hrsg.) (2000) Das Gehirn und sein Geist. Göttingen: Wallstein

Kluwe R, Lüer G & Rösler F (Eds.) (2003) Principles of Human Learning and Memory. Basel: Birkhaeuser



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#### **Markus Missler**



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#### Research Group Leader at the Center for Physiology

Dr.med. (M.D.), University of Göttingen, 1992 Graduate College (DFG), Göttingen, 1992 - 1994 Postdoctoral fellow, UTSW & HHMI, Dallas, 1994 - 1999 Research Group Leader (SFB 406), since 1999

### Major Research Interests:

Synapses of the nervous system combine two different aspects: From a structural point of view, they represent a specialized form of cell-cell adhesion/recognition sites, and functionally they maintain neurotransmission, thereby sustaining the flow of information from one neuron to the next. Our group is particularly interested in studying the question of whether these two aspects of synapses are related to each other. To address this question we have studied the role of candidate molecules. In a recent major finding, we demonstrated that a family of cell adhesion molecules (neurexins) is indeed essential for efficient regulated exocytosis and is therefore required for a successful communication between neurons. We were able to show that (i) neurexins are presynaptically localized, and (ii) they regulate the activity of presynaptic as well as postsynaptic high-voltage activated calcium channels - the latter via a hitherto unknown transsynaptic signalling pathway.

Further activities in the laboratory include functional analysis of neurexophilins, a secreted ligand of  $\alpha$ -neurexins. Expression patterns of neurexophilins show an extremely localised distribution pattern in specific subpopulations of neurons, which may utilize neurexophilins to modulate the  $\alpha$ -neurexin function. In addition, we have started a screening test to identify novel genes involved in synaptogenesis using a so-called differential display approach to examine differentially expressed mRNAs at chracteristic stages of development. Our investigations rely on molecular biological, neurogenetic, morphological and (in our collaborations) electrophysiological methods.

### Selected Recent Publications:

Missler M, Südhof T C (1998) Neurexins: three genes and 1001 gene products. Trends Genet 14: 20-26 (review)

Missler M, Südhof T C (1998) Neurexophilins form a highly conserved family of neuropeptide-like glycoproteins. J Neurosci 18: 3630-3638

Missler M, Hammer R E, Südhof T C (1998) Neurexophilin binding to  $\alpha$ -neurexins: A single LNS-domain functions as independently folding ligand-binding unit. J Biol Chem 273: 34716-34723

Verhage M, Maia A S, Plomp J J, Brussard A B, Heeroma J H, Vermeer H, Toonen R F, Hammer R E, van den Berg T K, Missler M, Geuze H J and Südhof T C (2000) Synaptic assembly of the brain in the absence of neurotransmitter secretion. Science 287: 864-869

Safavi-Abbasi S, Wolff J R, Missler M (2001) Rapid morphological changes in astrocytes are accompanied by re-distribution but not quantitative changes of cytoskeletal proteins. Glia 36: 102-115

Missler M (2003) Synaptic cell adhesion goes functional. Trends Neurosci 26: 176-178

Missler M, Zhang W, Rohlmann A, Kattenstroth G, Hammer RE, Gottmann K, and Südhof TC (2003) α-Neurexins couple Ca<sup>2+</sup>-channels to synaptic vesicle exocytosis. Nature 423: 939-948

#### **Tobias Moser**

#### Group Leader at the Department of Otolaryngology

Dr. med. (M.D.) 1995, University of Jena, Habilitation for Otolaryngology 2003 Postdoctoral fellow with E. Neher at the MPI for biophysical Chemistry, 1994 - 1997 Group leader at the Department of Otolaryngology, University of Göttingen since 1997



The main focus of our group is the synaptic function and dysfunction of cochlear inner hair cells (IHCs), which transform sound-induced mechanical signals into auditory nerve activity by Ca<sup>2+</sup> triggered exocytosis of neurotransmitter. We use cell-physiological techniques: patch-clamp, uncaging of caged signal molecules and fluorimetric imaging to study hair cell ion channels, synaptic exocytosis and endocytosis in inner hair cells. Our current and future research aims on an improved understanding of normal presynaptic hair cell function, including the characterization of the molecular players e.g. by investigation of IHCs from mouse mutants for synaptic proteins. In addition, we try to identify pathomechanisms of deafness by investigating different aspects of hair cell function in mouse models of human deafness. Here, we focus on mouse models of human auditory neuropathy, which is caused by defects central to the mechanically amplifying outer hair cells.



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#### Selected Recent Publications:

Moser T und Beutner D (2000) Kinetics of exocytosis and endocytosis at the cochlear inner hair cell afferent synapse of the mouse. Proc Natl Acad Sci USA, 97: 883-888

Beutner D, Voets T, Neher E and Moser T (2001) Calcium dependence of exocytosis and endocytosis at the cochlear inner hair cell afferent synapse. Neuron 29: 681-90

Beutner D and Moser T (2001) The Presynaptic Function of Mouse Cochlear Inner Hair Cells during Development of Hearing. J Neurosci 2001 21: 4593-4599

Fuchs P, Glowatzki E, Moser T (2003) The afferent synapse of cochlear hair cells. Curr Opin Neurobiol 13(4): 452-8

Brandt A, Striessnig J, Moser T CaV1.3 Channels are essential for Development and Presynaptic Activity of Cochlear Inner Hair Cells (in press in J Neurosci)

### **Klaus-Armin Nave**



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#### **Further Information:**

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#### Professor of Molecular Biology, Director at the Max Planck Institute of Experimental Medicine

PhD 1987, University of California, San Diego, Postdoc, The Salk Institute, La Jolla, California

1991 Junior Group Leader, ZMBH,University of Heidelberg 1998 Professor of Molecular Biology, ZMBH

2000 Director, Department of Neurogenetics Max Planck Institute of Experimental Medicine, Göttingen and Adj. Professor of Molecular Biology, Heidelberg

# Major Research Interests:

Transgenic and natural mouse mutants are useful tools to study human genetic diseases. Focussing on the nervous system, we are interested in diseases involving myelinforming glial cells. These highly specialized cells enwrap neuronal axons with multiple layers of membranes and provide the electrical insulation that is necessary for rapid impulse propagation. We are studying the principles of these neuron-glia interactions and the genes that are required for normal myelin assembly and maintenance. One gene of interest encodes PMP22 (a myelin membrane protein of Schwann cells) and is frequently duplicated in patients with Charcot-Marie-Tooth disease. Mutations of another myelin protein gene, termed PLP, underlie Pelizaeus-Merzbacher disease, a lethal white matter disease. A third neurological disorder under study is adrenoleukodystrophy, caused by a dysfunction of peroxisomes. We have generated mouse mutants that accurately model these human diseases to study disease mechanism at the cellular levele and to explore possible treatment strategies

#### **Future Projects and Goals**

Identification of disease modifier genes; epigenetic factors of disease expression; novel transgenic strategies to obtain conditional mouse mutants;

Mechanisms of neuron-glia signalling; transcriptional control genes of neuronal differentiation

# Selected Recent Publications:

Griffiths I, Klugmann M, Anderson T, Yool D, Thomson C, Schwab M H, Schneider A, Zimmermann F, McCulloch M, Nadon N and Nave K-A (1998) Axonal swellings and degeneration in mice lacking the major proteolipid of myelin. Science 280: 1610-1613

Schwab M H, Bartholomä A, Heimrich B, Feldmeyer D, Druffel-Augustin S, Goebbels S, Naya F J, Frotscher M, Tsai M-J, and Nave K-A (2000) Neuronal bHLH proteins (NEX and BETA2/NeuroD) regulate terminal granule cell differentiation in the hippocampus. J Neuroscience 20: 3714-3724

Niemann S, Sereda M W, Suter U, Griffiths I R and Nave K-A (2000) Uncoupling of myelin assembly and Schwann cell differentiation by transgenic overexpression of PMP22. J Neuroscience 20: 4120-4128

Werner H, Dimou L, Klugmann M, Pfeiffer St, Nave K-A (2001) Multiple splice isoforms of proteolipid M6B in neurons and oligodendrocytes. Mol Cell Neurosci. 18: 593-605

Lappe-Siefke C, Göbbels S, Gravel M, Nicksch E, Lee J, Braun P E, Griffiths I, Nave K-A (2003) Disruption of Cnp1 uncouples oligodendroglial functions in axonal support and myelination. Nature Genetics 33: 366-374

Sereda MW, Meyer zur Hörste G, Suter U, Uzma N, Nave K-A (2003) Therapeutic administration of anti-progesterone in a PMP22-transgenic model of Charcot-Marie-Tooth disease (CMT1A). Nature Medicine (in print)

#### **Erwin Neher**

#### Professor, Director at the Max Planck Institute for Biophysical Chemistry

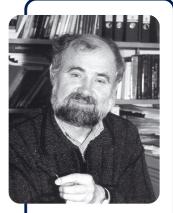
M.Sc. (Physics), University of Wisconsin, (1967)
Ph.D. (Physics), Institute of Technology, Munich (1970)
Research associate at the Max Planck Institute for Biophysical Chemistry in
Göttingen, Germany (1972 - 1975 and 1976 - 1982) and as a guest in the laboratory
of Dr. Ch.F. Stevens at Yale University, Dept. of Physiology, New Haven, Conn.
(1975 - 1976)
Fairchild Scholar, California Institute of Technology; Pasadena, USA (1989)

Director of the Membrane Biophysics Department at the Max Planck Institute for Biophysical Chemistry, Göttingen, Germany, since 1983

#### Major Research Interests:

#### Molecular Mechanisms of Exocytosis, Neurotransmitter Release, and Short Term Synaptic Plasticity

In order to understand how the brain handles its information flow and adjusts synaptic connections on the second and subsecond timescale, one has to understand all aspects of synaptic transmission ranging from availability of vesicles for exocytosis, presynaptic electrophysiology, Ca<sup>++</sup> signalling, the process of exocytosis, and postsynaptic neurotransmitter action. Our work concentrates on presynaptic aspects. We study the basic mechanisms of exocytosis, using adrenal chromaffin cells as a model system and the patch-clamp method. This work, in which intracellular Ca<sup>++</sup> is manipulated (caged Ca<sup>++</sup>) and measured on the single cell level aims at understanding the role of specific synaptic proteins in the maturation and exocytosis of secretory vesicles. We use neuronal cell cultures and brain slices for studying mechanisms of short term plasticity, such as depression and paired pulse facilitation. The Calyx of Held, a specialized synapse in the auditory pathway, offers unique possibilities for simultaneous pre- and postsynaptic voltage clamping. This allows a quantitative analysis of the relationship between [Ca<sup>++</sup>] and transmitter release.



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### Selected Recent Publications:

Klingauf J and Neher E (1997) Modeling buffered Ca<sup>2+</sup> diffusion near the membrane: Implications for secretion in neuroendocrine cells. Biophys J 72: 674-690

Neher E (1998) Vesicle pools and Ca<sup>2+</sup> microdomains: new tools for understanding their roles in neurotransmitter release. Neuron 20: 389-399

Rettig J and E Neher (2002) Emerging roles of presynaptic proteins in Ca\*+-triggered exocytosis. Science 298: 781-785

Sakaba T and E Neher (2003) Direct modulation of synaptic vesicle priming by GABAB receptor activation at a glutamatergic synapse. Nature 424: 775-778

Schneggenburger R and Neher E (2000) Intracellular calcium dependence of transmitter release rates at a fast central synapse. Nature 406: 889-893

Soerensen J, Nagy G, Varoqueaux F, Nehring RB, Brose N, Wilson MC and E Neher (2003) Differential control of the releasable vesicle pools by SNAP-

Voets T, Moser T, Lund P-E, Chow R H, Geppert M, Suedhof T C and Neher E (2001) Intracellular calcium dependence of large dense-core vesicle exocytosis in the absence of synaptotagmin I. PNAS 98: 11680-11680

#### Harald Neumann



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#### Group Leader at the European Neuroscience Institute Göttingen

1990 'Approbation' in Medicine, University Würzburg and University (LMU) Munich 1991 M.D., University of Würzburg

1998 'Habilitation' in Neuroimmunology, Technical University, Munich Positions held

1990 - 1992 Internship, Department of Neurology, University Ulm (Germany) 1992 - 1994 DFG Scholarship (postdoctoral fellow), Max-Planck-Institute of Psychiatry, Martinsried (Germany)

1994 - 2001 Research associate and group leader, Department of Neuroimmunology, Max Planck-Institute of Neurobiology, Martinsried (Germany) since 2001 Group leader, Neuroimmunology, European Neuroscience Institute Göttingen

### Major Research Interests:

The immunoprivileged status of the central nervous system (CNS) is conditional. In the healthy organism, immune responsiveness of the brain tissue is kept to a minimum. However, under pathological conditions, genes are turned on which change non-reactive CNS tissue to a pro-inflammatory milieu supporting bi-directional interactions between CNS and immune cells. Striking examples are disorders as diverse as CNS auto-immune diseases, injury and neurodegenerative diseases.

Our group has demonstrated that neuronal lesions recruit inflammatory cells to the pathologically changed tissue. Furthermore, neurons are stimulated by inflammatory cytokines to express MHC (major histocompatibility complex) class I molecules and are susceptible to cytotoxic attack by T lymphocytes. In particular, neurites are highly susceptible to T lymphocyte cytotoxicity.

Our group is currently interested in the role of the innate immune response in neurodegenerative and neuroinflammatory diseases such as multiple sclerosis. We are analyzing the cytotoxic and growth inhibitory effects of activated murine microglia and macrophages on neurites. In particular, we are studying the immune-mediated modulation of the axonal transport of synaptic molecules by time-lapse confocal microscopy.

Furthermore, we are assessing the use of the genetically modified hematopoietic precursor and stem cells as a new therapy in animal models of neuroinflammatory diseases. Bone marrow derived hematopoietic stem cells and mesenchymal cells will be modified by retroviral vectors to express chemokine receptors for attraction to lesioned brain tissue and release of growth factors after differentation into resident brain cells.

### Selected Recent Publications:

Medana I, Martinic MMA, Wekerle H and Neumann H (2001) Transection of major histocompatibility class I-induced neurites by cytotoxic T lymphocytes. Am J Pathol 159: 809-815

Medana I, Li Z, Flügel A, Tschopp J, Wekerle H, and Neumann H (2001) Fas Ligand (CD95L) protects neurons against perforin-mediated T lymphocyte cytotoxicity. J Immunol 167: 674-681

Neumann H, Medana I, Bauer J, Lassmann H (2002) Cytotoxic T lymphocytes in autoimmune and degenerative CNS diseases. Trends in Neurosci 25 (6): 313-319

Neumann H, Schweigreiter R, Yamashita T, Rosenkranz K, Wekerle H and Barde Y-A (2002) Tumor necrosis factor inhibits neurite outgrowth and branching of hippocampal neurons by a Rho-dependent mechanism. J Neurosci 22. 854-862

Neumann H (2003) Molecular mechanisms of axonal damage in inflammatory central nervous system diseases. Curr Opin Neurology 16. 267-273

#### **Walter Paulus**

#### Professor of Clinical Neurophysiology

Dr. med., University of Düsseldorf, 1978 Training in Neurology at the Universities of Düsseldorf, UCL London and Munich Habilitation (Neurology and Clinical Neurophysiology) in Munich Prof. and Head of the Department of Clinical Neurophysiology 1992

#### Major Research Interests:

Neuroplastic changes are defined as any enduring changes in the organization of the central nervous system such as the strength of connections, representational patterns, or neuronal properties, either morphological or functional. At present we study how to induce and control plasticity in the human nervous system, and to derive new therapeutic strategies from this research.

Present research focuses on transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (TDCS). TMS induces a short electric current in the human brain. It may be used to measure excitability changes in the motor cortex or alterations in visual perception thresholds. It may also induce plastic changes of excitability when used repetitively (rTMS). At present a multicenter blinded rTMS protocol is applied in epilepsy patients. TDCS offers the prospect of inducing LTD and LTP like effects in the human brain when applied at least with a stimulation duration of 3 minutes. We investigate underlying mechanisms both in human and animal experiments. TDCS induced changes in motor cortex excitability may be detected by functional MR imaging. Other functional imaging studies trace the epileptic focus in epileptic patients in space and time. We extended our research field to dopaminergic cell replacement strategies in animal models in collaboration with PD. Dr. Ahmed Mansouri (MPI biophysikalische Chemie) and Prof. Fuchs (German Primate center).

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#### **Further Information:**

http://www.neurologie.unigoettingen.de/ neurophysio.htm

#### Selected Recent Publications:

Ziemann U, Tergau F, Wassermann E M, Wischer S, Hildebrandt J and Paulus W (1998) Demonstration of facilitatory I wave interaction in the human motor cortex by paired transcranial magnetic stimulation. J Physiol 511: 181-190

Nitsche M A and Paulus W (2000) Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. J Physiol 527: 633-639

Nitsche MA, Paulus W (2001) Sustained excitability elevations induced by transcranial DC motor cortex stimulation in humans. Neurology 57: 1899-1901

Liebetanz D, Nitsche MA, Tergau F, Paulus W (2002) Pharmacological approach to the mechanisms of transcranial DCstimulation-induced after-effects of human motor cortex excitability. Brain 125: 2238-2247

Sommer M, Koch MA, Paulus W, Weiller C, Buchel C (2002) Disconnection of speech-relevant brain areas in persistent developmental stuttering. Lancet 360: 380-383

Nitsche MA, Schauenburg A, Lang N, Liebetanz D, Exner C, Paulus W, Tergau F (2003) Facilitation of implicit motor learning by weak transcranial direct current stimulation of the primary motor cortex in the human. J Cogn Neurosci 15: 619-626.

Nitsche MA, Fricke K, Henschke U, Schlitterlau A, Liebetanz D, Lang N, Henning S, Tergau F, Paulus W (2003) Pharmacological modulation of cortical excitability shifts induced by transcranial DC stimulation. J Physiol in press

### Evgeni Ponimaskin



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#### Group Leader at the Centre for Molecular Physiology of thr Brain

1994 Dr. rer. nat., Free University of Berlin, Germany 1994 - 2000 Postdoctoral training within the special research unit (Sonderforschungsbereich) "Cellular signal recognition and signal transduction" 2000 - 2002 Faculty member and group leader at the Departments of Neuro and Sensory Physiology, Medical School at the University of Göttingen Since October 2002 Tenure Track position within the Centre for Molecular Physiology of the Brain (ZMPG)

# Major Research Interests:

Our scientific activities are centered on the understanding of the time- and spacedependent interactions between different signalling proteins (in particular G-Protein Coupled Receptors and their downstream effectors), leading to the specific actions within the cell. As model system we use the serotonergic signaling, which is critically involved in regulation of different neuronal processes. This project addresses following aspects:

- Dynamic distribution and clustering of defined serotonin receptors (5-HTR) in different cell types. To study the activation-dependent changes in receptor distribution, individual receptor are coupled with fluorescence proteins (GFP, CFP, YFP) and analysed by confocal as well as 2-photon microscopy. We also analyse oligomerization state of different receptors by biochemical methods as well as by molecular imaging (i.e. FRET, single-cell FRET)

- Determination of G-proteins as well as downstream effectors specifically interacting with individual serotonin receptors. Cross-talk between GPCRs and specific effectors. To identify specific downstream effectors we apply biochemical, biophysical and electrophysiological methods. To get dynamic biochemical information we are establishing molecular imaging of high spatial and temporal resolution (single-cell FRET, fluorescence lifetime imaging microscopy (FLIM)). Combination of this nanotomographic fluorescence imaging with various forms of "patch clamping" will also be used for the parallel on-line measurement of physiological parameters in whole cell function. Using "patch-clamp" method will also allow the quantitative analysis of the transcription level for individual signalling molecules by using single-cell RT-PCR and TaqMan techniques, which are presently established in our lab.

- Functional role of post-translational protein modifications on G protein-coupled 5-HTR. Differential expression of receptors during development und after chronic application of drugs.

# Selected Recent Publications:

Ponimaskin E, Schmidt M F, Heine M, Bickmeyer U and Richter D W (2001) 5-Hydroxytryptamine 4(a) receptor expressed in Sf9 cells is palmitoylated in an agonist-dependent manner. Biochemical Journal 353: 627-634

Ponimaskin E and Schmid M F G (2001) Fusogenic viral envelopes as potent vehicles for gene transfer. Current Genomics 2: 261-267 Review

Heine M, Ponimaskin E, Bickmeyer U and Richter D W (2002) 5-HT-receptor-induced changes of the intracellular cAMP level monitored by a hyperpolarization-activated cation channel. Pflügers Archive European Journal of Physiology 443: 418-426

Ponimaskin E, Heine M, Joubert L, Sebben M, Bickmeyer U, Richter D W and Dumuis A (2002) The 5-hydroxytryptamine(4a) receptor is palmitoylated at two different sites and acylation is critically involved in regulation of receptor constitutive activity. Journal of Biological Chemistry 277: 2534-2546

Ponimaskin E, Profirovic J, Vaiskunaite R, Richter D W and Voyno-Yasenetskaya T (2002) 5-hydroxytryptamine(4a) receptor is coupled to Galpha subunit of heterotrimeric G13 protein. Journal of Biological Chemistry 277: 20812-20819

### Thomas H. Rammsayer

#### **Professor of Psychology**

1988 - 1989 Postdoctoral Fellow, Department of Pharmacology, Thomas Jefferson University, Philadelphia, Pa.

1989 - 1995 Assistant Professor, Department of Psychology, University of Giessen 1995 - 1997 Associate Professor, Institute for Psychology, University of Jena since 1997 Professor of Psychology, Georg Elias Müller Institute for Psychology, University of Göttingen



#### Biological and experimental personality research:

Biological basis of extraversion Neuropharmacology of individual differences Pharmacopsychological approaches to personality Elementary cognitive tasks and mental ability Behavioral sex differences

#### Temporal information processing in humans:

Neurobiological approaches to timing systems in humans Perceptual and cognitive mechanisms in human timing and time perception Time psychophysics

#### Cognitive neuroscience:

Neurochemistry of declarative and procedural memory functions Cognitive inhibition in humans

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### Selected Recent Publications:

Rammsayer T H (1998) Extraversion and dopamine: Individual differences in responsiveness to changes in dopaminergic activity as a possible biological basis of extraversion. European Psychologist 3: 37-50

Rammsayer T (1999) Neuropharmacological evidence for different timing mechanisms in humans. Quarterly Journal of Experimental Psychology, Section B: Comparative and Physiological Psychology 52: 273-286

Rammsayer T H (2001) Effects of pharmacologically induced changes in NMDA-receptor activity on long-term memory in humans. Learning and Memory 8: 20-25

Rammsayer T & Ulrich R (2001) Counting models of temporal discrimination. Psychonomic Bulletin & Review 8: 270-277

Rammsayer T H, Rodewald S & Groh D (2000) Dopamine-antagonistic, anticholinergic, and GABAergic effects on declarative and procedural memory functions. Cognitive Brain Research 9: 61-71



### **Diethelm Richter**



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#### Professor of Physiology Chairman of the II. Department of Physiology, University of Göttingen Deputy Speaker of the European Neuroscience Institute Göttingen

Wiss. Angestellter, I. Physiol. Inst., Univ. Saarland, 1969 - 1970
Wiss. Assistent, I. Physiol. Inst., Univ. Saarland, 1970 - 1972
Wiss. Assistent, I. Physiol. Inst., Univ. Munich, 1972 - 1974
1974 Universitätsdozent, I. Physiol. Inst., Univ. Munich, 1974
Universitätsdozent, I. Physiol. Inst., Univ. Heidelberg, 1975 - 1976
C-3 Professor, I. Physiol. Inst., Univ. Heidelberg, 1976 - 1988
C-4 Professor, II. Physiol. Inst., Univ. Göttingen, 1988

# Major Research Interests:

Neurotransmitters, neuromodulators, and peptide hormones are known to activate metabotropic receptor proteins that control ion channels or second messenger cascades. These receptors regulate an intracellular network of interacting signal transduction pathways by means of G-proteins. Thus, receptors transmit extracellular signals to intracellular proteins and other chemical factors. These signals are normally not transduced in a stereotype manner, but they are integrated in a space- and time-dependent manner, resulting in highly dynamic and variable cellular responses. The specific nature of the cellular response depends on individual cell types that may differ in the expression pattern of receptor subtypes or of intracellular signaling factors. Our research group concentrates on the spatial organization of various subtypes of

Sour research group concentrates on the spatial organization of various subtypes of serotonin receptors and targets an understanding of the highly localized regulation of molecular interactions occurring simultaneously at many sites of a neuron. The goal is to achieve a refined understanding of the parallel signal processing within networks of chemical signal pathways and to clarify their effects on the properties of the neuron as a whole.

# Selected Recent Publications:

Hülsmann S, Oku Y, Zhang W, Richter D W (2000) Metabotropic glutamate receptors and blockade of glial Krebs cycle depress glycinergic synaptic currents of mouse hypoglossal motoneurons. Europ J Neurosci 12: 239-246

Mironov S L, Richter D W (2001) Oscillations and hypoxic changes of mitochondrial variables in neurons of the brainstem respiratory center. J Physiol 533: 227-236

Ponimaskin E G, Schmidt M F G, Heine M, Bickmeyer U, Richter D W (2001) 5-Hydroxytryptamine 4(a) receptor expressed in Sf9 cells is palmitoylated in an agonist-dependent manner. Biochem J 353: 627-634

Heine M, Ponimaskin E, Bickmeyer U, Richter DW (2001) 5-HT-receptor-induced changes of the intracellular cAMP level monitored by a hyperpolarization-activated cation channel. Europ J Physiol DOI 10: 1007

Manzke T, Günther U, Ponimaskin EG, Haller M, Dütschmann M, Schwarzacher S, Richter DW (2003) 5-HT<sub>4ca1</sub> Receptors avert opioid-induced breathing depression without loss of analgesia. Science 301: 226-229

### **Christian Rosenmund**

#### Group Leader at the Max Planck Institute for Biophysical Chemistry

PhD Neurosciences, Vollum Institute, Portland, OR, USA 1993 Postdoctoral fellow Salk Institute, La Jolla, CA, USA 1993 - 1995 Helmholtz fellow, MPI biophysikalische Chemie 1995 - 1997 Heisenberg fellow and independent group leader, Dept. Membranbiophysik at the Max Planck Institute for Biophysical Chemistry, since 1998



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#### Major Research Interests:

Neurotransmission at the central synapse involves a series of functional highly coordinated steps. On the presynaptic site, synaptic vesicles tether, prime to fusion competence, and fuse Ca<sup>2+</sup> triggered with the plasma membrane to release the neurotransmitter in the synaptic cleft. Postsynaptically, ionotropic receptors respond to binding of the neurotransmitter with distinct conformational steps that shape the postsynaptic response. We characterize synaptic properties with standard patch-clamp electrophysiology and optical techniques from cultured primary hippocampal neurons of transgenic mice that bear deletions or mutations of pre- or postsynaptic proteins. We have identified and/or characterized the vesicular neurotransmitter transporters VGLUT and VGAT, the vesicle priming factor Munc13, and the core complex associated proteins synaptotagmin 1 and complexin. Furthermore, knock-out mice are used to examine protein-domain and -residue function by gain of function rescue experiments by viral overexpression of wildtype and mutant proteins. Postsynaptically, we examine structural principles that control the gating properties of AMPA-type glutamate receptors.

### Selected Recent Publications:

Takamori S, Rhee JS, Rosenmund C, Jahn R (2000) Identification of a vesicular glutamate transporter that defines a glutamatergic phenotype in neurons. Nature 407: 189-94

Mansour M, Nagarajan N, Nehring R, Clements J, Rosenmund C (2001) Heteromeric AMPA receptors assemble with a preferred subunit stoichiometry and spatial arrangement. Neuron 32: 841-853

Rhee JS, Betz A, Pyott S, Reim K, Varoqueaux F, Augustin I, Hesse D, Südhof TC, Takahashi M, Rosenmund C, Brose N: β-phorbol ester- and diacylglycerol-induced augmentation of neurotransmitter release from hippocampal neurons is mediated by Munc13s and not by PKCs. Cell 108: 121-133

Rosenmund C, Sigler A, Augustin I, Reim K, Brose N, Rhee JS (2002) Differential control of vesicle priming and short term plasticity by Munc13 isoforms. Neuron 33: 411-424

Varoqueaux F, Sigler A, Rhee SJ, Brose N, Enk C, Reim K, Rosenmund C (2002) Total arrest of spontaneous and evoked synaptic transmission but normal synaptogenesis in the absence of Munc13 mediated vesicle priming. PNAS 99: 9037-9042

### Marjan Rupnik



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# Research Group Leader at the European Neuroscience Institute Göttingen

Ph.D. 1996, University of Ljubljana Assistant Professor of Pathophysiology and Physiology, 1997 Junior group leader since 2000, European Neuroscience Institute Goettingen

# Major Research Interests:

During embryonic stages there is not much need for a functional endocrine secretion due to domination and hyperactivity of maternal endocrine glands. However, after birth a body of a newborn mammal has to activate various endocrine systems and later establish neuronal control over them. The main focus of our group is to characterize the Ca<sup>2+</sup>-dependent secretory activity in cells composing a pancreatic neuroendocrine system during early postnatal life.

We developed a tissue slice preparation of rodent pancreas, a novel approach to *in situ* characterization of secretory activity from pancreatic cells, both endocrine and exocrine, as well as neurons. The slice preparation is particularly advantageous due to its short preparation time, lack of chemical disturbance, preserved paracrine inputs and relative longevity in organotypic culture.

The techniques we apply are whole-cell patch-clamp for channel and membrane capacitance measurements, Ca<sup>2+</sup> photometry and imaging, confocal and multi-photon microscopy, immunocytochemistry and a series of cell biology techniques.

Our studies aim to provide important information about innervation of different cell types found in pancreas and their physiology. In addition we want to establish how the malfunction of the interplay between the cells in this neuroendocrine system contributes to the pathophysiology of Diabetes mellitus.

### Selected Recent Publications:

Rupnik M, Zorec (1995) Intracellular Cl<sup>-</sup> modulates Ca<sup>2+</sup>-induced exocytosis from rat melanotrophs through GTP binding proteins. Pflugers Arch - Eur J Physiol 431(1): 76-83

Kreft M, Gasman S, Chasserot-Golaz S, Kuster V, Rupnik M, Sikdar SK, Bader M, Zorec R (1999) The heterotrimeric Gi(3) protein acts in slow but not in fast exocytosis of rat melanotrophs. J Cell Sci 112: 4143-4150

Rupnik M, Kreft M, Sikdar SK, Grilc S, Romih R, Zupancic G, Martin TF, Zorec R (2000) Rapid regulated dense-core vesicle exocytosis requires the CAPS protein. Proc Natl Acad Sci USA 97(10): 5627-5632

Poberaj I, Rupnik M, Kreft M, Sikdar SK, Zorec R (2002) Modeling excess retrieval in rat melanotroph membrane capacitance records. Biophys J 82(1 Pt 1): 226-232

Speier S, Rupnik M (2003) A novel approach to *in situ* characterization of pancreatic B-cells. Pflugers Arch - Eur J Physiol 446: 553-558

#### **Eckart Rüther**

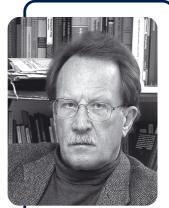
#### **Professor of Psychiatry**

Dr. med. LMU Munich Prof. of Psychiatry LMU Munich Dept. of Psychiatry Univ. Munich

### Major Research Interests:

Psychopharmacology Sleep Medicine Dementia PTSD Schizophrenia Biological Psychiatry

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### Selected Recent Publications:

Wiltfang J, Otto M, Baxter H C, Bodemer M, Steinacker P, Bahn E, Zerr I, Kornhuber J, Kretzschmar H A, Poser S, Rüther E, Aitken A (1999) Isoform pattern of 14-3-3 proteins in the cerebrospinal fluid of patients with Creutzfeldt-Jakob disease. J Neurochem 73,6: 2485-2490

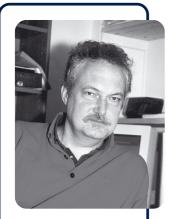
Bandelow B, Wedekind D, Pauls J, Brooks A, Hajak G, Rüther E (2000) Salivary cortisol in panic attacks. Am J Psych 157 (3): 454-456

Moll G H, Mehnert C, Wicker M, Bock N, Rothenberger A, Rüther E, Huether G (2000) Age-associated changes in the densities of presynaptic monoamine transporters in different regions of the rat brain from early juvenile life to late adulthood. Dev Brain Res 119: 251-257

Rüther E and Glaser A (2000) A prospective PMS study to validate the sensitivity for change of the C-Scale in advanced stages of dementia using the NMDA-antagonist memantine. Pharmacopsychiatry 33: 1-6

Rüther E, Ritter R, Apecechea M, Freytag S, Gmeinbauer R, Windisch M (2000) Sustained improvements in patients with dementia of Alzheimer's type (DAT) 6 months after termination of Cerebrolysin therapy. J Neural Trans 1-15

#### **Detlev Schild**



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#### **Professor of Physiology**

1979 Diplom in Physics, Univ. Göttingen
1982 M.D., Univ. Göttingen
1985 Dr. rer.nat., Univ. Göttingen
1987 Dr. med., Univ. Göttingen
1997 Appointed head of the Department of Molecular Neurophysiology in the Center of Physiology and Pathophysiology, Medical School, Georg August University
Göttingen

### Major Research Interests:

The olfactory system is able to detect and distinguish thousands of molecules in our environment. Receptor neurons are endowed with hundreds of different receptors to bind odorants and transduce the chemical signal into an electrical one. The receptor neurons convey their information onto the olfactory bulb where a neuronal image of odorants is generated. Using a combination of electrophysiological and high resolution imaging techiques, we are studying

- the biophysical details of the primary transduction processes,
- the synaptic transmission in the olfactory bulb,
- the generation of the neuronal chemotopic map and
- the mechanism of odor learning

# Selected Recent Publications:

Gennerich A, Schild D (2000) Fluorescence correlation spectroscopy in small cytosolic compartments depends critically on the diffusion model used. Biophys J 79: 3294-3306

Czesnik D, Nezlin L, Müller B, Rabba J, Schild D (2001)  $\alpha_2$  - receptors modulate glutamatergic synaptic transmission in the olfactory bulb of *Xenopus laevis* tadpoles. Eur J Neuroscience 13: 1093-1100

Gennerich A, Schild D (2002) Anisotropic diffusion in mitral cell dendrites of *Xenopus laevis* tadpoles Biophys J 83: 510-522

Manzini I, Rössler W, Schild D (2002) cAMP-independent responses of olfactory neurons in *Xenopus laevis* tadpoles and their projection onto olfactory bulb neurons J Physiol 545: 475-484

Czesnik D, Rössler W, Kirchner F, Gennerich A, Schild D (2003) Neuronal representation of odorants in the olfactory bulb of *Xenopus laevis* tadpoles. Eur J Neurosci 17: 113-118

Manzini I, Schild D (2003) Multidrug resistance transporters in olfactory receptor neurons of *Xenopus laevis* tadpoles. J Physiol 546: 375-385

Nezlin LP, Heerman S, Schild D, Rössler W (2003) Organisation of glomeruli in the olfactory bulb of *Xenopus laevis* tadpoles. J Comp Neurol 464: 257-268

Manzini I & Schild D (2003) cAMP-independent olfactory transduction of amino acids in *Xenopus laevis* tadpoles. J Physiol 551: 115-123

#### Ralf Schneggenburger

# Research Group Leader at the Max Planck Institute for Biophysical Chemistry

Dr. rer. nat. (PhD) 1993, University of Göttingen 1994 - 1996 Postdoctoral fellow at the Neurobiology Laboratory, Ecole Normale Supérieure, Paris 1996 - 2000 Research Assistant at the Max Planck Institute for Biophysical Chemistry, Göttingen since 2001 Heisenberg fellow and leader of the Research Group "Synaptic

Dynamics and Modulation" at the Max Planck Institute for Biophysical Chemistry

### Major Research Interests:

Fast communication between nerve cells in the brain is mediated by chemical synaptic transmission. During this process, a presynaptic action potential is translated via Calcium dependent membrane fusion of small synaptic vesicles into the release of neurotransmitter substances. Interestingly, upon repeated presynaptic activity, the responses in most postsynaptic cells show a pronounced dynamic behavior. The strength of synaptic responses either grows, or declines with time, and this short term synaptic plasticity is expected to modulate the information flow in neural networks.

We study a synapse in the auditory pathway which has an unusually large presynaptic terminal with hundreds of active zones. This synapse is unique because patch-clamp recordings can be made directly from the presynaptic terminal. This allows us to apply Calcium imaging and Calcium uncaging methods directly to the presynaptic nerve terminal. We have shown that the sensitivity of the vesicle fusion reaction for intracellular Calcium ions is significantly higher than previously assumed. This has direct consequences for our understanding of different forms of synaptic plasticity, such as facilitation and depression. In collaborative studies, we also use gene knock-out approaches to analyze the precise role of proteins in presynaptic Calcium signalling and plasticity of transmitter release.

# Selected Recent Publications:

Schneggenburger R, Sakaba T & Neher E (2002) Vesicle pools and short-term synaptic depression: lessons from a large synapse. Trends in Neurosci 25: 206-212

Schneggenburger R, Neher E (2000) Intracellular calcium dependence of transmitter release rates at a fast central synapse. Nature 406: 889-893

Wölfel M and Schneggenburger R (2003) Presynaptic capacitance measurements and Ca<sup>2+</sup> uncaging reveal sub-millisecond exocytosis kinetics and characterize the Ca<sup>2+</sup> sensitivity of vesicle pool depletion at a fast CNS synapse. J Neuroscience 23: 7059-7068

Felmy F, Neher E, and Schneggenburger R (2003) Probing the intracellular Calcium sensitivity of transmitter release during synaptic facilitation. Neuron 37: 801-811



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# Friedrich-Wilhelm Schürmann



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#### **Professor of Zoology**

1967 Doctor rer.nat., University of Münster)
1967 - 1970 Research Fellow (Assistent) at the Max Planck Institute of Brain Research, Department of General Neurology/ Köln
1970 - 1977 Research Assistant at the Institute of Zoology, Department of Experimental Morphology, University of Köln
1975 - 1976 Visiting Fellow at the Research School of Biological Sciences, Department of Neurobiology, Australian National University, Canberra, Australia)

1977 Professor and Head of the Department of Cell Biology at the Zoological Institute, University of Göttingen

#### Major Research Interests:

Neurobiology of invertebrate nervous systems, mainly central nervous system of insects; work on insects, crayfish, earthworms and onychophora. Cellular neurobiology: Structure and function of interneurons, giant fibre systems, synaptic networks, neuroactive compounds with emphasis on biogenic amines in crickets and bees; olfactory brain systems in *Drosophila* wild type and mutants; electrophysiological and behavioural studies: walking and escape behaviour of crickets and cockroaches.

Currently used techniques in the department:Neurocytology, Neuroanatomy, Immunocytology, Electron microscopy, Electrophysiology, Tissue culture of identified neurons, Setups for quantitative registration of behaviours.

# Selected Recent Publications:

Schürmann F-W, Ottersen O P, Honegger H-W (2000) Gluatamate-like immunoreactivity marks compartments of the mushroom bodies in the brain of the cricket. J comp Neurol 418: 227-239

Watson A H D, Schürmann F-W (2002) Synaptic structure, distribution, and circuitry in the central nervous system of the locust and related insects. Microsc Res Technique 56: 210-226

Yasuyama K, Meinertzhagen J A, Schürmann F-W (2002) Synaptic organisation of the mushroom body calyx in *Drosophila melongaster*. J comp Neurol 445: 211-226

Yasuyama K, Meinertzhagen J A, Schürmann F-W (2003) Synaptic connections of cholinergic antennal lobe relay neurons innervating the lateral horn neuropile in the brain of *Drosophila melanogaster*. J comp Neurol 466: 299-315

### Stephan J. Sigrist

# Research Group Leader at the European Neuroscience Institute Göttingen

Dr. rer. nat (PhD) 1997, University of Tübingen Since 2001 Independent group leader position group located at the European Neuroscience Institute Göttingen (ENI-G), Max Planck Society 1997 - 2001 Postdoc with Christoph Schuster at Friedrich Miescher Laboratory in Tübingen (Germany), Max Planck Society 1993 - 1997 Ph.D. with Christian F. Lehner at Friedrich Miescher Laboratory in Tübingen (Germany), Max Planck Society

### Major Research Interests:

Synaptic strengths change as neuronal circuits develop and are modified by experience, providing a cellular basis for the correct development of neuronal systems as for higher brain functions (e.g. learning and memory). Model system for our studies is the developing larval neuromuscular junction (NMJ) of Drosophila, offering access for physiological, ultrastructural and biochemical methods as well as for the powerful molecular-genetic and genetic approaches typical for Drosophila. Moreover, the optical transparence of the larva opens the way for the *in vivo* imaging of plasticity relevant processes using genetically encoded GFP-sensors.

At the NMJ, we have recently demonstrated the existence of large aggregates of translation factors very close to the synaptic sites. Increasing this subsynaptic translation stimulated synaptogenesis, neurotransmission as well as morphological outgrowth of the developing NMJ. Postsynaptic translation we found to provoke this substantial long-term strengthening by increasing the synaptic levels of a particular glutamate receptor subunit, DGluR-IIA.

In our ongoing work, mechanisms underlying synapse formation and growth at the Drosophila NMJ are characterized further. On one hand, newly designed genetic screens and a molecular analysis of the translational control mechanisms throughout plasticity will be the basis to identify molecules that regulate synaptic growth and function. Moreover, synaptic protein synthesis, glutamate receptor dynamics and synaptic growth are visualized live in developing larvae, using lines transgenic for GFP-tagged marker proteins in combination with confocal and 2-photon microscopy. Moreover, the fact that learning and memory paradigms are well established for adult Drosophila flies offers the possibility to assess the relevance of junctional plasticity-mechanisms for central synapses and brain functions in general.

# Selected Recent Publications:

Sigrist S J, Ried G, Lehner C F (1995a) *Dmcdc2* kinase is required for both meiotic divisions during *Drosophila* spermatogenesis and is activated by the twine/cdc25 phosphatase. Mech of Dev 53: 247-260

Sigrist S J, Jacobs H, Stratmann R, Lehner C F (1995b) Exit from mitosis is regulated by *Drosophila* fizzy and the sequential destruction of cyclins A, B and B3. EMBO J 14(19): 4827-38

Sauer K, Weigmann K, Sigrist S J, Lehner C F (1996) Novel members of the *cdc2*-related kinase family in *Drosophila*: cdk4/6, cdk5, PFTAIRE, and PITSLRE kinase. Mol Biol Cell: 1759-69

Sigrist S J and Lehner C F (1997) *Drosophila* fizzy-related down-regulates mitotic cyclins and is required for cell proliferation arrest and entry into endocycles. Cell 1997 (4): 671-81

Sigrist S J, Thiel P R, Reiff D, Lachance P E, Lasko P and Schuster C M (2000) Postsynaptic translation affects the morphology and efficacy of neuromuscular junctions. Nature 405 (6790): 1062-1065



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### Anastassia Stoykova



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#### Privatdozent, Developmental Biology

1972 Medical Doctor (M.D.), Bulgarian Medical Academy 1973 - 1988 Research Associate in Neurochemistry; Regeneration Research Laboratory, Bulgarian Academy of Sciences, Sofia 1985 PhD; Bulgarian Academy of Sciences, Sofia 1989 Habilitation (Neurobiology) and Assistant Research Professor at the Institute of Molecular Biology, Bulgarian Academy of Sciences 1980 -1981 and 1988-1989: Guest investigator as Alexander von Humboldt grant holder at the Max Planck Institute of Experimental Medicine and Max-Planck Institute for Biophysical Chemistry, Göttingen 1991 -2002 Staff Research Scientist at the Max Planck Institute for Biophysical Chemistry; Department Molecular Cell Biology, Göttingen 2002 Habilitation (Developmental Biology); Faculty of Human Medicine, University of Göttingen 2002 -present Research Group Leader at the Max Planck Institute for Biophysical Chemsitry; Department Molecular Cell Biology, Göttingen Lecturer at the International Max Planck Research School, Program Neurosciences

### Major Research Interests:

In the mammalian cortex billions of neurons are organized in six layers and numerous functional domains that process different kinds of sensory information. Our recent efforts are focused on the identification and functional analysis of genes involved in the arealization and layer formation of the developing cortex, using the mouse as a model system. As a result of microarray assays performed through the Affymetrix chip technology, we obtained a collection of genes and ESTs that are differentially expressed in distinct domains of the embryonic cortex. Currently we are in a process of creating and analyzing knockout mouse mutants for selected genes. The morphological, expression and behavioural phenotypic analysis of the generated loss-of-function mutants will be supplemented by gain-of-function assays through somatic electroporation *in vitro* (whole embryo cultures or isolated brains) and *in vivo* (*in utero*) in the brain of developing embryos. Some of these mutants may represent models for human neurological diseases thus providing in the long term some basis to understand the relationship between the genetic regulation of cortical development and cortical dysfunctions in man.

Furthermore, we are analyzing the role of the transcription factor Pax6 in mammalian corticogenesis, which function is abolished in the human disease *Aniridia*. Evidences from our and other laboratories show that Pax6 is intrinsic determinant of the cortical multipotent progenitors (the radial glial cells) and is also involved in the cortical arealization. By using the Cre-LoxP recombination system for *in vivo* conditional inactivation and overexpression, we are studying the function of Pax6 on progenitor proliferation, regionalization, cell fate specification, functional arealization and layer formation. We will also attempt to identify downstream gene targets for the two Pax6 isoforms that are active in vertebrates and possibly involved in a specific cell fate pathway.

# Selected Recent Publications:

Götz M, Stoykova A and Gruss P (1998) Pax6 controls radial glia differentiation in the cerebral cortex. Neuron 21: 1031-1044

Stoykova A, Treichel D, Hallonet M and Gruss P (2000) *Pax6* modulates the patterning of the mammalian telencephalon. J Neuroscience 20 (21): 8042-8050

Tarabykin V, Stoykova A, Usman N and Gruss P (2001) Cortical upper layer neurons derive from the subventricular zone as indicated by *Svet1* gene expression. Development 128(1): 1983-1993

Muzio L, DiBenedetto B, Stoykova A, Boncinelli E, Gruss P, Mallamaci A (2002) Conversion of cerebral cortex into basal ganglia in *Emx2-/- Pax6*<sup>sey/sey</sup> double-mutant mice. Nature Neuroscience 5: 737-745

Muzio L, DiBenedetto B, Stoykova A, Boncinelli E, Gruss P, Mallamaci A (2002) *Emx2* and *Pax6* control regionalization of the pre-neuronogenic cortical primordium. Cerebral Cortex 12(2): 129-139

Stoykova A, Hatano O, Gruss P and Götz M (2003) Increase in reelin-positive cells in the marginal zone of *Pax6* mutant mouse cortex. Cerebral Cortex 13(6): 560-571

#### Walter Stühmer

#### Professor of Neurophysiology, Director at the Max Planck Institute for Experimental Medicine

1978 - 1980 PhD with Dr. F. Conti in Camogli, Italy1980 - 1983 Post Doc in the Department of Physiology and Biophysics in Seattle, USA, with Dr. W. Almers

1983 - 1992 group leader at the Max Planck Institute for Biophysical Chemistry in Göttingen with Dr. E. Neher

1992 - present Director of the Department Molecular Biology of Neuronal Signals at the Max Planck Institute for Experimental Medicine in Göttingen

### Major Research Interests:

The principal aim of the department "Molecular Biology of Neuronal Signals" is the study of signaling within cells and between cells. To this end, molecular biology, genetics and electrophysiology are used to elucidate structure-function relationships of membrane-bound proteins, expecially ion channels and receptors. Specific tools such as antibodies and toxins are developed and used to interfere with signaling pathways relevant for cell cycle control, ion selectivity and the secretion of cells in culture and in primary cells.

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# Selected Recent Publications:

Pardo L A, Brüggemann A, Camacho J and Stühmer W (1998) Cell-cycle related changes in the conducting properties of r-eag K<sup>+</sup> channels. J Cell Biol 143: 767-775

Pardo L A, del Camino D, Sánchez A, Alves F, Brüggemann A, Beckh S and Stühmer W (1999) Oncogenic potential of EAG K<sup>+</sup> channels. EMBO J 18: 5540-5547

Niemeyer BA, Mery L, Zawar C, Suckow A, Monje F, Pardo LA, Stühmer W, Flockerzi V and Hoth M (2001) Ion channels in health and disease. EMBO Rep 2: 568-573

Loerke D, Stühmer W and Oheim M (2002) Quantifying axial secretory-granule motion with variable-angle evanescentfield excitation. J Neurosci Methods 119: 65-73

Jenke M, Sánchez A, Monje F, Stühmer W, Weseloh RM and Pardo LA (2003) C-terminal domains implicated in the functional surface expression of potassium channels. EMBO J 22: 395-403

Becherer U, Moser T, Stühmer W and Oheim M (2003) Calcium regulates exocytosis at the level of single vesicles. Nature Neurosci 6: 846-853

#### **Andreas Stumpner**



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#### Assistant Professor of Neuroethology

Dr. rer. nat., University of Erlangen, Germany, 1988 Postdoctoral fellow, Andrews University, Berrien Springs, USA, 1990 - 1991 Habilitation, University of Göttingen, 1997 Guestprofessor, University of Zürich, Switzerland, 2002 - 2003

### Major Research Interests:

My research focuses on how a small nervous system recognises specific frequencies and temporal patterns (in the context of acoustic communication in insects, mainly in Orthoptera). Understanding these processes bears implications also for understanding function and evolution of the same performances of the vertebrate brain. I see the strength of the acoustic and invertebrate system *a*) in the precise temporal and spectral stimuli one can deliver and the clear (innate) responses on the behavioural and neuronal level, *b*) in the comparative potential (song recognition in groups of related species and differences in neuronal layout to related non-singing or non-hearing groups) allowing to understand what mechanisms might have played a role in evolution and how evolution of songs and recognition systems depend on each other, *c*) in the identified neuroneapproach allowing to find homologous neurones in related species and indicating evolutionary changes on the cellular level and *d*) the potential to directly test hypotheses in behavioural experiments.

Recent findings from intracellular studies in bushcrickets are: Central neurons receive lateral frequency-dependent inhibitions. After blocking such inhibitions the frequency tuning broadens considerably. Species-specificity of a neuron in related species depends on specific inhibitions, not on specific excitations. And homologous neurons in more distantly related species may differ considerably in their properties.

### Selected Recent Publications:

Stumpner A (1998) Picrotoxin eliminates frequency selectivity of an auditory interneuron in a bushcricket. J Neurophysiol 79: 2408-2415

Rust J, Stumpner A, Gottwald J (1999) Singing and hearing in an ancient bushcricket. Nature 399: 650

Stumpner A (1999) Comparison of morphology and physiology of two plurisegmental sound-activated interneurones in a bushcricket. J Comp Physiol A 185: 199-205

Stumpner A, von Helversen D (2001) Evolution and function of auditory systems in insects. Naturwiss 88: 159-170

Stumpner A (2002) A species-specific frequency filter through specific inhibition, not specific excitation. J comp Physiol A 188: 239-248

#### **Heinrich Terlau**

#### Research Group Leader at the Max Planck Institute for Experimental Medicine

Dr. rer. nat. (Ph.D.) 1990, University of Tübingen Group leader at the Max Planck Institute for Experimental Medicine since 1999

### Major Research Interests:

The research of our group focuses on the identification and characterization of pharmacological active substances interacting with ion channels. A biophysical description and the investigation of the potential physiological implications of this interaction is performed by using mainly electrophysiological techniques and expression systems. Due to the key role of ion channels in different physiological processes, substances interacting with these proteins may have a great variety of possible pharmacological or even clinical implications. The main focus of our research is the analysis of the interaction of conotoxins with certain ion channels. Conotoxins are neurotoxic peptides from the venoms of the predatory cone snails. These cysteine rich peptides are usually between 10 to 30 amino acids long. Conotoxins are heavily used in neuroscience research and are known to be highly selective and specific for their target molecules. Due to these properties conotoxins are also used for trying to understand the structure and function of ion channels.



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# Selected Recent Publications:

Terlau H, Bocaccio A, Olivera BM and Conti F (1999) The block of Shaker K<sup>+</sup> channels by  $\mu$ -conotoxin PVIIA is state dependent. J General Physiology 114: 125-140

Jacobson RB, Koch ED, Lange-Malecki B, Stocker M, Verhey J, Van Wagoner RM, Vyazovkina A, Olivera BM and Terlau H (2000) Single amino acid substitutions in µ-conotoxin PVIIA disrupt interaction with the Shaker channel. J Biological Chemistry 275: 24639 - 24644

Ferber M, Sporning A, Jeserich G, DeLaCruz R, Watkins M, Olivera BM and Terlau H (2003) A novel Conus peptide ligand for K<sup>+</sup> channels. J Biological Chemistry 278: 2177-2183

Terlau H and Olivera BM Conus venoms: A rich source of novel ion channel-targeted peptides. Physiological Reviews, in press

### **Stefan Treue**



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#### Professor, Director of the German Primate Center

Head of the Cognitive Neuroscience Laboratory
Ph.D. 1992, Massachusetts Institute of Technology
Postdoctoral Fellow, MIT, 1992 - 1993
Postdoctoral Fellow, Baylor College of Medicine, Houston, Texas, 1993 - 1995
Work Group Leader, Laboratory of Cognitive Neuroscience, Univ. of Tübingen, 1995 - 2001
Professor of Animal Physiology, Univ. of Tübingen, 2000 - 2001
Professor of Cognitive Neuroscience and Biological Psychology, Univ. of Göttingen, 2001

# Major Research Interests:

Research at the Cognitive Neuroscience Laboratory is aimed at understanding the neural basis of visual perception. Vision is an active process that is far more than a passive registration of our environment. Rather, on its way from the eyes to and through the cortex, visual information is modulated by numerous processes that enhance some aspects while diminishing others. One of these processes is attention, i.e. the ability to filter out unwanted information and concentrate the brain's processing abilities on relevant information.

The accurate representation of visual motion in the environment is one of the most important tasks of the visual system. Correspondingly research in the laboratory concentrates on this ability as a model for sensory information processing in general.

We use various techniques. While our emphasize is on electrophysiology, i.e. the recording of the activity of neurons in the visual cortex of macaque monkeys and measuring human perceptual abilities with psychophysical methods we also use theoretical approaches and are planning to use functional brain imaging in the future. Using these techniques, we have been able to elucidate how motion information is represented in primate cortical area MT and how attention changes that representation and correspondingly the percept of the visual environment.

### Selected Recent Publications:

Treue S and Maunsell J H R (1996) Attentional modulation of visual motion processing in cortical areas MT and MST. Nature 382 (6591): 539-541

Treue S and Martinez Trujillo J C (1999) Feature-based attention influences motion processing gain in macaque visual cortex. Nature 399 (6736): 575-579

Treue S, Hol K and Rauber H J (2000) Seeing multiple directions of motion - Physiology and psychophysics. Nature Neuroscience 3 (3): 270-276

Martinez-Trujillo J C and Treue S (2002) Attentional modulation strength in cortical area MT depends on stimulus contrast. Neuron 35: 365-370

Hol K and Treue S (2001) Different populations of neurons contribute to the detection and discrimination of visual motion. Vision Research 41(6): 685-689

Treue S (2001) Neural correlates of attention in primate visual cortex. Trends in Neurosciences 24 (5): 295-300

### Michael R. Waldmann

#### **Professor of Psychology**

1988 Ph.D. at the University of Munich
1987 - 94 Teaching and research positions at the Universities of Frankfurt and Tübingen
1988 - 90 Postdoctoral research at the University of California, Los Angeles(UCLA); collaboration with Keith Holyoak
1995 Habilitation at the University of Tübingen
1994 - 98 Senior research scientist at the Max Planck Institute for
Psychological Research
since 1998 Professor of Psychology (C3) at the University of Göttingen

### Major Research Interests:

#### **Causal learning**

Our general approach is to study the interaction of top-down knowledge about abstract characteristics of causality and bottom-up contingency learning. The majority of current learning theories view learning as a purely data-driven, associative process ("bottom up"). In contrast, our theory ("causal-model theory") assumes that the processing of the learning input is partly determined by domain knowledge. We are particularly interested in the role of abstract knowledge about causality, such as knowledge about causal directionality, causal relevance, causal structures, and causal interventions. In a number of studies we have shown that this kind of knowledge may dramatically affect learning despite the fact that the learning input was kept constant. Currently we are planning to explore the neural basis of associative as opposed to causal learning processes.

#### Categorization and Induction

In this project we are interested in the interplay between alternative categorial frameworks and induction. The traditional approach to categorization claims that categories mirror the correlational structure of the environment. By contrast, we argue that in many domains there are alternative ways of categorizing the world. For example, human behavior may either be explained by functional, cognitive or by neuropsychological theories. We are interested in factors determining the way domains are categorized, and in the influence of alternative categorial schemes on subsequent induction processes.



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# Selected Recent Publications:

Waldmann M R & Holyoak K J (1992) Predictive and diagnostic learning within causal models: Asymmetries in cue competition. Journal of Experimental Psychology: General 121: 222-236

Waldmann M R, Holyoak K J & Fratianne A (1995) Causal models and the acquisition of category structure. Journal of Experimental Psychology: General 124: 181-206

Waldmann M R (1996) Knowledge-based causal induction. In D. R. Shanks, K. J. Holyoak, & D. L. Medin (Eds.), The psychology of learning and motivation, Vol. 34: Causal learning (pp. 47-88). San Diego: Academic Press

Waldmann M R & Hagmayer Y (1999) How categories shape causality. In M. Hahn & S. C. Stoness (Eds.), Proceedings of the Twenty-first Annual Conference of the Cognitive Science Society (pp. 761-766). Mahwah, NJ: Erlbaum

Waldmann M R (2000) Competition among causes but not effects in predictive and diagnostic learning. Journal of Experimental Psychology: Learning, Memory, and Cognition 26: 53-76

#### **Fred Wouters**



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# Group Leader Cell Biophysics Group at the European Neuroscience Institute

Dr. (Ph. D.) 1997, Faculty of Chemistry, University of Utrecht, The Netherlands Postdoctoral fellow, Imperial Cancer Research Fund (ICRF), London UK, 1997 - 2000

Postdoctoral fellow, European Molecular Biology laboratory (EMBL), Heidelberg, 2000 - 2001

Appointed as group leader at the European Neuroscience Institute, Göttingen 2001.

# Major Research Interests:

The focus of our research is the regulation and role of the neuronal cytoskeleton in the modulation of neuronal shape and motility during chemotactic processes. The growing neuronal growth cone probes its environment for the chemical composition of its substrate and the presence of neighbouring cells. The former information is sampled by cell adhesion receptors in focal adhesion structures that, next to their sensing function also perform a structural function in that they provide the cell with a means to exert force on its substrate. We are primarily interested in the signal transduction processes that regulate these effects and the cross-talk between the different motility systems.

The main interest areas in this question are; 1. The role and molecular mechanism of lipid raft-resident cell adhesion molecules in the remodelling of the membrane cytoskeleton, 2. Dynamic control of growth cone protein content by local proteolysis and chaperone function during chemotactic responses, 3. Role and mechanism of the neuronal exocyst complex as critical landmarks for dendritic/axonal neuritogenesis.

Our group has a related interest in the pathophysiological mechanism of neurodegeneration by intracellular aggregation of the tau protein, as occurs in Alzheimer's disease. As tau is an intrinsically unstructured protein that can undergo remarkable conformational changes upon binding to microtubules and in the Alzheimerrelated aggregation condition, it presents an ideal model system for the biophysical analysis of protein conformational change and protein interactions.

Our research depends on the development and application of advanced microscopy techniques, primarily; fluorescence lifetime imaging microscopy (FLIM), and Förster resonance energy transfer (FRET) microscopy, in combination with a range of GFPbased optical biosensors and novel bioconjugation approaches for organic dyes, and protein biochemical/molecular biological techniques to resolve and quantify biochemical reactions and conditions in living cells.

### Selected Recent Publications:

Wouters F S, Bastiaens P I H, Wirtz K W A & Jovin T M (1998) FRET microscopy demonstrates molecular association of non-specific lipid transfer protein (nsL-TP) with fatty acid oxidation enzymes in peroxisomes. EMBO J 17: 7179-7189

Wouters F S. & Bastiaens P I H (1999) Fluorescence lifetime imaging of receptor tyrosine kinase activity in cells. Curr Biol 9: 1127-1130

Wouters F S, Verveer P J, Reynolds A R & Bastiaens P I H (2000) Quantitative imaging of lateral ErbB1 receptor signal propagation in the plasma membrane. Science 290: 1567-70

Harpur A, Wouters F S & Bastiaens P I H (2001) Imaging FRET between spectrally similar GFP molecules in single cells. Nat Biotechnol 19: 167-9

Wouters F S, Verveer P J & Bastiaens P I H (2001) Imaging biochemistry inside cells. Trends Cell Biol 11: 203-11

#### Wolfgang Wuttke

#### Professor of Clinical and Experimental Endocrinology

Dr. med. 1967 Post-doc, Michigan State University and UCLA, 1969 - 1971 Habilitation (Physiology) 1972 Apl. Professor 1976 Professor of Clinical and Experimental Endocrinology 1985

### Major Research Interests:

The proper function of the GnRH pulse generator ist essential for reproduction of all mammals studied so far. GnRH pulses are a prerequisite for proper pituitary gonadotropin release. The neurochemical mechanisms leading to pulsatile GnRH release involve norepinephrine and gamma amino butyric acid (GABA) as most important neurotransmitters. In addition, other catecholamines, amino acid neurotransmitters and neuropeptides play a modulatory role in the function of the GnRH pulse generator. Many of the GABAergic neurons in the hypothalamus are estrogen-receptive. The mechanisms by which the estrogen receptors of the alpha and beta subtype regulate gene and protein expression of neurotransmitter-producing enzymes are at present a prime focus of interest.

Induction of puberty is not a gonadal but a hypothalamic maturational process. The initiation of proper GnRH pulse generator function is the ultimate trigger signal for puberty which is currently investigated.

Ageing involves also neuroendocrine mechanisms. The GnRH pulse generator function deteriorates in aged rats, mechanisms which involve a variety of catecholamines and amino acid neurotransmitters which are currently investigated.

Steroidal feedback signals (of estradiol, progesterone, and glucocorticoids) are crucial for the development and proper function of the adult hypothalamus of which the molecular and neurochemical mechanisms are studied with cell biological and animal experimental tools. Proper function of the GnRH pulse generator is also of crucial importance for initiation of puberty and maintenance of normal menstrual cycles in women. Many of hitherto unexplained infertilities can be explained of malfunctioning GnRH pulse generators which are studied in a series of clinical experiments.

#### Selected Recent Publications:

Roth C, Jung H, Kim K, Arias P, Moguilevsky J, Jarry H, Leonhardt S, Wuttke W (1997) Involvement of gamma amino butyric acid (GABA) in the postnatal function of the GnRH pulse generator as determined on the basis of GnRH and GnRH-receptor gene expression in the hypothalamus and the pituitary. Exp Clin Endocrinol Diab 105: 353-358

Cho S, Han J, Sun W, Choi D, Kwon H B, Jarry H, Wuttke W, Kim K (1997) Evidence for autocrine inhibition of gonadotropinreleasing hormone (GnRH) gene transcription by GnRH in hypothalamic GT1-1 neuronal cells. Mol Brain Res 50: 51-58

Roth Ch, Leonhardt S, Theiling K, Lakomek M, Jarry H, Wuttke W (1998) Ontogeny of the GNRH-, glutaminase- and glutamate decarboxylase-gene expression in the hypothalamus of female rats. Developmental Brain Research 110: 105-114

Leonhardt S, Shahab M, Luft H, Wuttke W and Jarry H (1999) Reduction of luteinizing hormone secretion induced by longterm feed restriction in male rats is associated with increased expression of GABA-synthesizing enzymes without alterations of GnRH gene expression. Journal of Neuroendocrinology 11: 613-619

Kang S S, Kim S R, Leonhardt S, Jarry H, Wuttke W, Kim K (2000) Effect of Interleukin-1ß on Gonadotropin-Releasing Hormone (GnRH) and GnRH Receptor Gene Expression in Castrated Male Rats. J. Neuroendocrinol. 12:421-429

Leonhardt, S., Böning, B., Luft, H., Wuttke, W., Jarry, H. (2000) Activation of Gene Expression of the -Aminobutyric Acid Rather than the Glutamatergic System in the Preoptic Area during the Preovulatory Gonadotropin Surge of the Rat. Neuroendocrinology 71: 8-15



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### Weiqi Zhang



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#### Privatdozent, Neurophysiology

#### Dr. med. (M. D.) University of Bonn, 1987

Intership, Department of Neurology, University of Bern, Switzerland, 1988 Postdoctoral fellow, Department of Physiology, University of Bern, Switzerland, 1989 - 1992

Postdoctoral fellow, Department of Physiology, University of Oxford, UK, 1993 Postdoctoral fellow, The Nobel Institute of Neurophysiology, Karolinska Institute, Stockholm, Sweden, 1994 - 1996

Research Group Leader, Center of Physiology, University of Göttingen, since 1997

### Major Research Interests:

The modulation of synaptic activity represents one of the essential feature of neuronal network, which empowers the networks to keep their plasticity. The modulatory processes change the dynamic range of synaptic activity from milliseconds to hours and days depending the requirements of the network. Such modulatory processes involve ligand- and G-protein-mediated regulation of ion channel activity, regulation of neurotransmitter release machinery, regulation of receptor targeting and internalisation, and regulation of intracellular RNA- and protein-synthesis. We currently use a combination of electrophysiological, immunocytochemical and molecular biological methods to investigate the molecular mechanisms responsible for GABA<sub>B</sub>-receptor-mediated modulation of GABA<sub>B</sub>-receptor targeting and internalisation in a functional brainstem respiratory network. Furthermore, knock-out mice are used to directly examine the synaptic function of membrane-binding proteins and protein-protein interactions.

### Selected Recent Publications:

Zhang W, Pombal M A, El Manira A and Grillner S (1996) Rostrocaudal Distribution of 5-HT Innervation in The Lamprey Spinal Cord and Differential Effects of 5-HT on Fictive Locomotion. Journal of Comparative Neurology 374 (2): 278-290

Zhang W, Elsen F, Barnbrock A and Richter D W (1998) Postnatal development of GABA<sub>B</sub> receptor-mediated modulation of voltage-activated Ca<sup>2+</sup> currents in mouse brain stem neurones. European Journal of Neuroscience 11 (7): 2332-2342

Ritter B, Zhang W (2000) The GABA<sub>A</sub>-mediated inhibition matures during first postnatal week in brain stem of mouse. European Journal of Neuroscience 12: 2975-2984

Zhang W, Barnbrock A, Gajic S, Pfeiffer A and Ritter B (2002) Differential ontogeny of GABA<sub>B</sub> receptor-mediated pre- and postsynaptic modulation of GABA and Glycine transmission in respiratory rhythm-generating network of mouse. The Journal of Physiology 540 (2): 435-446

Missler M, Zhang W, Rohlmann A, Kattenstroth G, Hammer R, Gottmann K and Südhof TC (2003)  $\alpha$ -Neurexins are Required for Coupling Ca<sup>2+</sup>-Channels to Synaptic Vesicle Exocytosis. Nature 423: 939-948

### Annette Zippelius

#### **Professor of Theoretical Physics**

Dr. rer. nat., Technical University of Munich, 1977 Postdoctoral Fellow, Universities of Harvard and Cornell, 1978 - 1981 Habilitation at the Technical University of Munich, 1982 Research Associate, Forschungszentrum Jülich, 1983 - 1988 Professor at the Institute of Theoretical Physics, University of Göttingen, since 1988

#### Major Research Interests:

A semi-microscopic model of synaptic transmission and plasticity A stochastic model of synaptic transmission has been designed on the basis of electrophysiological experiments and is currently analysed with help of Monte Carlo simulations. The transmission process is decomposed into three steps: 1) release of neurotransmitter from presynaptic vesicles, 2) diffusion of transmitter molecules in the cleft, and 3) kinetics of postsynaptic receptors.

The model of presynaptic vesicle dynamics has been designed on the basis of experimentally observed patterns of synaptic depression (and facilitation) at the Calyx of Held in the mammalian auditory pathway and comprises recruitment and calcium related release of vesicles. Transmitter dynamics within the cleft can be effectively modeled by a two-dimensional diffusion process, where absorbing boundary conditions reflect the effect of transmitter uptake by transporters and diffusion into extra-synaptic space. On the postsynaptic membrane the neurotransmitter interacts with individual spatially distributed receptors, which are included in the model on the basis of kinetic Markov models. The modeling steps of presynaptic vesicle dynamics, transmitter motion in the cleft and its interaction with postsynaptic receptors are combined to create a model of a single synaptic connection between two neurons. Postsynaptic responses are studied as function of input-frequency and possible physiological determinants. It is shown that the specific combination of release-probability, receptor desensitization and presynaptic release-machinery determines whether synaptic connections facilitate or depress and sets the range of input-rates, i.e. frequencies, that can be transmitted towards the postsynaptic side.

# Selected Recent Publications:

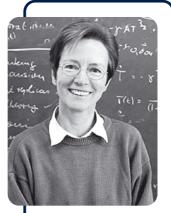
Marienhagen J, Keller B U and Zippelius A (1997) Kinetic model of excitatory synaptic transmission to cerebellar Purkinje cells. J Theor Biology 188: 227

Broderix K, Goldbart P M and Zippelius A (1997) Dynamical signatures of the vulcanisation transition. Phys Rev Lett 79: 3688

Trommershäuser J, Marienhagen J and Zippelius A (1999) Stochastic model of central synapses: slow diffusion of transmitter interacting with spatially distributed receptors and transporters. J Theor Biol 198: 101

Broderix K, Löwe H, Müller P and Zippelius A (1999) Shear viscosity of a crosslinked ploymer melt. Europhys Lett 48: 421

Trommershäuser J, Titz S, Keller B and Zippelius A (2001) Variability of excitatory currents due to single channel noise, receptor number and morphological heterogeneity. J Theor Biol 208



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