Issue November 2014

Neurex Newsletter n°29

Strasbourg

Freiburg

Basel

Contents

Edito

During the recent neurogenomic training at the LSTF Basel, the geneships' leader *Affymetrix* company described the recent tools developed to explore transcriptomics. On the 1st and 2nd of December, scientists from companies will interact with academics to address the fundamental basis and clinical relevance of fighting neuroinflammation/rebuilding myelin as an additional therapeutic strategy to the immunomodulatory treatments of Multiple Sclerosis. On Dec 4th, scientists from Roche will interact with researchers from Neurex and all over the world during a first web-conference on Translational Imaging for Psychopharmacology. In Strasbourg, the company *Axilum Robotics* was created in 2011 to design a robot to automate TMS treatment.

These initiatives illustrate the growing interactions of academic researchers with industry, which should undoubtedly profit to the enhancement of translational research and favour drug & neurotechnology development. Such positive consequences of networking were among the aims of Prof Heinrich Reichert in 2001 when he raised the first important source of financial support which launched the development of Neurex. More than ten years later, we must acknowledge that this challenge was a real success for the benefit of the community. See you the 23rd of January 2015 for a farewell symposium in his honor during which we will celebrate his brilliant career and devotion to Neuroscience. Mark your calendar! ■ P.P.

neurex
neuroscience·upper·rhine·network

FROSTY SHOWER FOR A HOT CAUSE

Obviously, the weather was more generous back in September when members of the lab of Luc Dupuis in Strasbourg decided to take up the coolest challenge of the moment and dumped buckets (or more precisely, lab polystyrene boxes) of ice water on their heads. But still, they did it.

If the Inserm U1118 lab decided to take part to this now world-renowned action, it is not only because they are brave and fearless but also because they know more than anyone that funding for research on ALS is necessary.

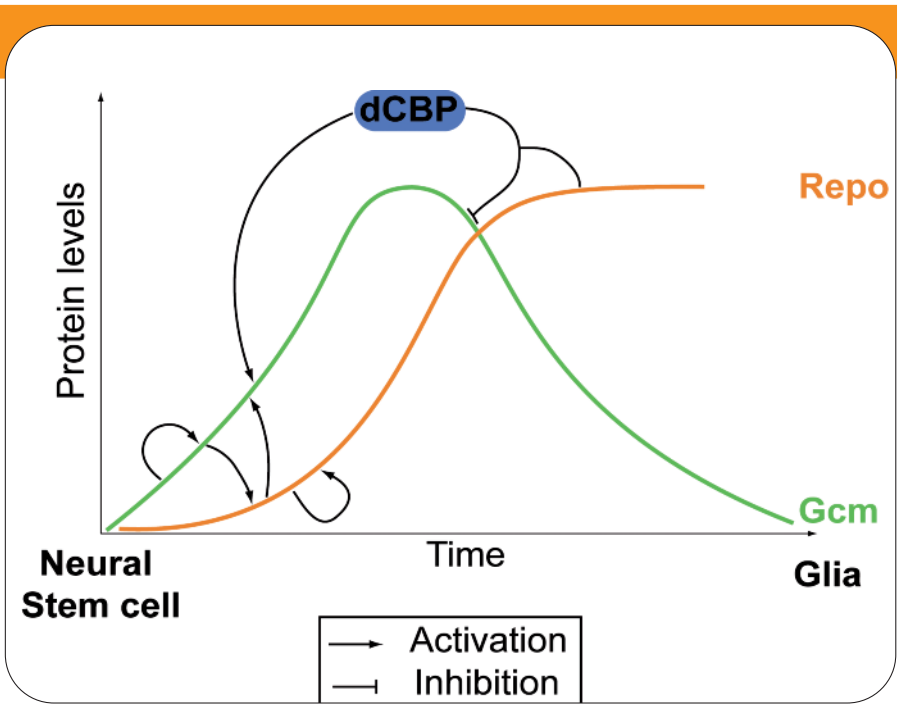
Luc Dupuis has been working for more than 15 years on Amyotrophic Lateral Sclerosis, a deadly disease which represents the 3rd neurodegenerative disease after Alzheimer and Parkinson. "In France, the number of patients dying from this disease is very close to the number of persons dying in a car crash" indicates Luc. Despite these dramatic figures, the disease and its mechanisms are still poorly known and, prior to the challenge, public awareness of the disease was relatively limited. This is why the group of Luc Dupuis had decided to take up the challenge and proudly participate to this "collective and smart" campaign raised for a cause they believe in.

After the Ice Bucket Challenge went viral on social media, charitable donations to the ALS associations soared. Along with them, a number of criticisms have arisen accusing the action to be self-congratulatory and promote waste of water. For Luc Dupuis, these criticisms are not grounded and he suggests to the persons who take up the challenge "to consider the ice water as a metaphor of an ALS diagnosis" with a life expectancy of 2-3 years, a gradual paralysis leading to a respiratory failure and virtually no possibility of curative treatment available.

The video of the Ice Bucket Challenge of the Inserm U1118 lab is available on **YouTube at www.youtube.com/watch?v=ESBW-KaNFyv4**. For this special occasion, members of the lab were wearing T-shirts customized with logo of the organizations funding their research, NeuroTime and Neurex among others. ■ D.B.

Images: courtesy of Yannick von Grabowiecki

Cell specification or the hidden face of plasticity



Stem cells play a fundamental role in building the harmonious architecture of our organism. Their high plasticity raises questions on the mechanisms involved in the control of the absolute number of differentiated cells, on the ratio between the cell types that make our organs and finally on the way by which distinct cell types are maintained on a lasting scale. Some answers to these questions have been obtained using the *Drosophila* genetic model.

Glial cells, the caretakers of the nervous system, are in fixed number and depend on the Glide/ Gcm transcription factor, which dictates the choice of identity between neuron and glial cells within the neural stem cell population.

Angela Giangrande's team (IGBMC) just demonstrated the existence of a temporal sequence of regulatory loops that acts just like a detonator with a timer. Glide/Gcm controls its own level of expression. As soon as the threshold necessary to trigger gliogenesis is reached, one of its targets starts to degrade Glide/Gcm in order to allow lineage progression and the stable differentiation of the glial cell.

Moreover, the study shows that, if this « feed forward » mechanism is deficient, then the neuron/ glial cell ratio is altered and some cells remain blocked in an intermediate state of neuroglial differentiation.

Such behavior strangely reminds us of the one of cancer cells. This analysis thus brings a new perspective on the bases of cell specification, as well as on the physiopathological mechanisms of metastatic processes. This work was just presented in an article published in the prestigious review Nature Communication. ■ A.G.

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Welcome to...

Prof. Ilka Diester

who recently (Oct. 2014) joined the Brain Links-Brain Tools Research Centre of the University of Freiburg. Zoom on her research interest.

Ilka Diester is a professor for optophysiology, a new field in neuroscience, at the University Freiburg where she conducts research on the neural correlates of movement control. In October 2014 she left the Ernst Strüngmann Institute in Cooperation with Max Planck Society for Neuroscience in Frankfurt am Main where she was head of the «Optogenetics group» in the department of Pascal Fries. Her lab aims at understanding how motor control arises from neural activity in the brain. To tackle this central question in neuroscience she employs a combination of optogenetic, electrophysiological, and behavioral techniques in rodents.

Most animals are blessed with the ability to move seemingly effortlessly through their environment. What looks simple on the first glance, is based on complex neural circuits. The simplest versions are already developed in invertebrates and mainly rely on reflexes while more involved patterns are emerging in vertebrates and climax in mammals. The more automatic movements can be generated with basic and well conserved circuits across the mammalian realm. However, if planning of complex movements with specific timing is required, the neocortex comes into play. It is this brain structure which lies in the focus of Ilka Diester's research group. In particular, the lab investigates subsections of the cortex which are associated with movement planning and generation (motor cortex) or cognitive tasks (prefrontal cortex). For that, modern approaches like high dimensional neural recordings with multi-electrode arrays and optogenetic manipulation techniques are combined with behavioral assays which allow establishing a correlative and causal role of brain areas, pathways and neural subpopulations. At the heart of this approach stands the key technique «optogenetics». Optogenetics is based on light sensitive membrane proteins – so called opsins – derived from microorganisms like algae or archaebacterial. With genetic tricks, these opsins can be integrated into mammalian cells and act there as ion channels or pump which open upon illumination with the correct wavelength. This makes the neurons controllable with light: they can get activated or silenced. The opsin genes are delivered via viral vectors or transgenic techniques. Since the opsin genes are controlled by specific promoters, the expression of the opsins can be restricted to cellular subpopulations. Based on these techniques four synergistic projects are currently running in Ilka Diester's lab.

Perturbation resistant neural networks in motor cortex

Motor cortex is the main output structure of the mammalian brain. What goes out to spinal cord will influence our movements. To prevent involuntary movements, neural activity in motor cortex is under tight control of local microcircuits which determine whether a signal propagates further and eventually evokes a movement. How these control mechanisms are realized is not entirely clear. How does motor cortex deal with inappropriate input and how does it overcome disruptions? To what extent does the spread of activation depend on the particular network structure of the brain, or the connections between nerve cells? How do the mechanisms differ between species?

An adequate experimental setup in combination with a model of network dynamics is needed to investigate these questions. To address these questions, Prof. Diester's lab uses multi-electrode arrays for the recordings of neural population responses and optogenetic and electrical stimulation methods for the stimulation of neural populations.

3D reconstruction of motor behavior allows capturing and parameterizing the movements and correlating these parameters with the recording and stimulation signals. In order to organize the obtained results, a theoretical framework is required which allows filling in data bit by bit and thus systematically solving the puzzle. Small-world-like networks have been chosen as such a framework due to their features which resemble anatomical and functional connectivity of the brain.

With this approach the lab aims to reveal key features of organization and computational power of motor circuits. This project is funded by the Bernstein Award (BMBF).

Optogenetic dissection of motor cortex dynamics and pathways

Cortical computation develops as interplay between neuronal dynamics and structural connectivity which is used for simultaneous communications with several targets. Within a densely interconnected network, selectivity can be achieved only if neuronal inputs and outputs are functionally segmented and if only one segment is selected for a given time and neural population. Ilka Diester's lab focuses on this process in the primary motor cortex (M1) which projects to a variety of brain structures involved in motor generation and suppression as well as somatosensory perception. The lab investigates what kind of information is sent to two of M1's main target brain areas – striatum and primary somatosensory cortex (S1) by separate or partially overlapping neural subpopulations. To dissect the two pathways, new optogenetic projection and stimulation strategies are combined with controlled behavior and electrophysiological recordings. The goal is to neurophysiologically characterize the two populations in a specially designed Go/NoGo task with tactile component and understand their functional relevance for motor behavior. To define the most effective optical stimulation frequencies, the group capitalizes on consistently reported oscillations in the sensorimotor system. In particular, the lab investigates how manipulating ongoing beta and gamma band oscillations impact behavior. Both frequency bands have been assigned importance in complementary tasks: beta band activity has been mainly associated with the suppression of movements, with postural maintenance, and with sensorimotor integration and planning; elevated gamma band activity has been reported often during movement initiation and has been attributed a role in attention. A double dissociation paradigm is used to test whether the two neural populations can be manipulated differentially with the two frequency bands. A key hypothesis is that the best suited resonance frequencies differ between the two neuron populations and might change across trial phases. For causally defining the optimal frequencies for a specific task period and neural population, real-time feedback based on ongoing oscillatory patterns are employed to enhance or phase shift the synchronized activity. This project is funded by an ERC Starting Grant.

Cell-type specific optogenetic manipulation for characterizing the role of inhibitory interneurons in motor cortex of non-transgenic animals

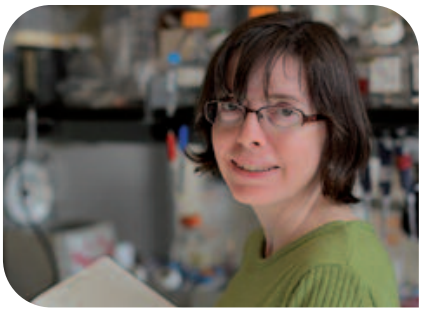
The role for local circuit inhibitory interneurons in shaping the timing and excitability of cortical circuits is well established. Inhibitory interneurons control cellular and network synchronization and output by dictating and coordinating action potential generation. Given the central role for interneurons in the function of the central nervous system it comes as no surprise that loss or dis-regulation of this important cell type has been implicated in cognitive and motor defects. So far, it has only been possible to reliably target genetic modifications to inhibitory interneurons by applying transgenic animals. Recent progress in gene transfer vector technology has made gene delivery more efficient and also more cell type specific. In collaboration with Hannah Monyer (DKFZ), Christian Buchholz (Paul-Ehrlich-Institute), and Pascal Fries (Ernst Strüngmann Institute), the lab aims at generating recombinant viruses that will deliver genes precisely to inhibitory neurons with a special focus on parvalbumin and somatostatin positive neurons. This will make optogenetic manipulations of specific cell types available for non-transgenic animals. Equipped with this new targeting method the role of inhibitory neurons in generating neural oscillations and controlling movements can be investigated. This project is funded by the DFG in the framework of the Priority Program 1665.

Optogenetic dissection of prefrontal circuits for impulse control

The ability to control impulsive behavior and respond adequately to the environment is an important component of goal-directed behavior. Both humans and animals learn to adapt to their surroundings by suppressing maladaptive behavioral impulses. This process is thought to depend on the top-down modulation by the prefrontal cortex over lower-order circuits. The neural circuits involved are complex and often anatomically intermixed, which has prevented a full characterization with common technologies. This project which is conducted in collaboration with Over Yizhar (Weizmann Institute), aims to use advanced projection-based optogenetic manipulation to establish the functional connectivity that supports two distinct types of impulse control: proactive and reactive stopping of an ongoing behavior. Prof. Diester's lab uses in vivo approaches to dissect the projection pathways from the prefrontal cortex to the basal ganglia and establish the neural basis for impulse control. In awake behaving animals, neural activity which is associated with the stopping behavior is recorded and causally probed. Specifically, the lab is interested in how incoming prefrontal input modulates this activity. For that, the stopping commands are traced into the basal ganglia and up to the neural responses in motor cortex.

All of the projects are directed at widening our basic understanding of the brain and the intricate sensorimotor circuits. The lab's ultimate vision is that one day the acquired knowledge will help improving bidirectional neural prostheses for a simultaneous writing in and reading out of neural signals. ■ I.D.

Welcome to...



Prof. Fiona Doetsch

(University of Basel) recently joined the Biozentrum in September 2014. She and her research team are interested in the study of neural stem cells and the development of the Nervous System.

Prof. Kelly Tan

(University of Basel) arrived at the Biozentrum in October 2014. Her research team is interested in the physiopathology of basal ganglia neuronal subcircuits.

Further details about their research groups in the next newsletter.
Welcome to them !

A new Neurex board's member for Basel

We are pleased to welcome Prof. Christian Cajochen (UPK, University Psychiatry Clinic, Basel) who joined the Neurex scientific board last Summer.

Prof. Christian Cajochen heads the Centre for Chronobiology at the University of Basel. He received his PhD in natural sciences from the ETH in Zürich, Switzerland, followed by a 3-y postdoctoral stay at the Harvard Medical School in Boston, USA. The major research interests in his lab include investigative work on the influence of light on human cognition, circadian rhythms and sleep, circadian related disturbances in psychiatric disorders, and age-related changes in the circadian regulation of sleep and neurobehavioral performance. He has held a number of honours and has authored more than 120 original papers and reviews in his career. ■ C.C.

Funding attributed to the BCF (Bernstein Center Freiburg)

In November 2014, the German Academic Exchange Service (DAAD) launched the project "IPID4all" (International Promovieren in Deutschland - for all) The Bernstein Center Freiburg was successful with its application for the new PhD program BrainDisC ("International PhD program in Computational Neuroscience of Brain Disease"). It will be fully integrated into the center's new focus on Computational Neuroscience of Brain Disease. For at least the next three years, BrainDisC will allow the BCF to recruit excellent graduates for PhD studies, and aid German and international PhD students to qualify for a career within an international environment. This activity is funded by the Federal Ministry of Education and Research (BMBF). ■ G.G.

The Carl Zeiss Foundation supports the Bernstein Center Freiburg (BCF) at the University of Freiburg in developing and implementing new research approaches that employ computer-based and mathematical methods to gain a better understanding of the neuronal mechanisms of neurological and psychiatric diseases. Funds amounting to 750,000 € will allow the scientists to carry out important build-up work over the next four years. The Carl Zeiss Foundation will enable the BCF to fund staff who support the scientists indirectly and thus participate in the full establishment of the center's new research focus. ■ G.G.

Welcome to the new NeuroTime students!

We recently had the pleasure to welcome in Strasbourg the 5 new doctoral students who had been selected NeuroTime Erasmus+ Joint Doctorate program.

Our program which is now starting its 3rd Edition was initially initiated by Neurex and accepted in 2011 by the European Executive Agency of the European Commission (EACEA). The new comers are from Argentina, China, Serbia and Turkey and a sixth student from Mexico had soon joined the group recently.

New doctoral students will all be registered at the University of Strasbourg and at a partner University (Freiburg, Amsterdam or Basel) and will work on their PhD project under the joint supervision of scientists of the Institute of Cellular and Integrative Neurosciences (INCI), in Strasbourg and of a partner lab: Netherlands Institute for Neuroscience (NIN), in Amsterdam; or Uniklinik in Freiburg or the Friedrich Miescher Institute (FMI) in Basel.

A total of 21 students are now enrolled in the NeuroTime program and dispatched at the 6 partner Universities. Several of them were present to welcome their new mates and share tips on how to live (and survive!) in Strasbourg.

Applications for the 4th Edition of the program (starting Oct. 1st 2015) are open and interested candidates can now apply on the website at **http://www.neurotime-erasmus.org/**. ■ D.B.

1st web-conference on Translational Imaging for Psychopharmacology

We are pleased to announce the 1st web-conference on Translational Imaging for Psychopharmacology that will be held on the 4th of December 2014 at the University of Basel (Kollegiengebaüde, Room 114).
A web-conferencing formula will be in place during this event in order to allow remote attendance to the conference in parallel to local attendance.

The theme of this first symposium will focus on MRI based methodology not only to understand the effect of psychotropic drugs on the brain of humans and animals, but also to help translational research. As the ultimate goal is to enhance drug design and development, representatives from the pharmaceutical industry will come to define the needs and share their experience with academics.

There will be one session dedicated to human pharmacological MRI (phMRI), another one dedicated to animal phMRI, and a session dedicated to the integration of the two in a translational perspective using the pharmacology of pain as an example. Last, a round table will close the conference. It aims at discussing the needs, technological bottleneck, pitfalls and perspectives in the field. We hope that provisional guidelines on the paradigm and imaging techniques will emerge. Last further actions in the field shall be discussed in a much opened manner.

Beyond the sharing of knowledge, this conference seeks to gather the community interested in this subject. Accordingly, we invite all the researchers around the world to contact us and to attend for free. We will do our best to allow remote attendees to interact with the panel. ■ J.C.

We would like to express our gratefulness to the organizer of the event, Dr Jack Foucher (Icube laboratory, Strasbourg, France), as well as to all the scientists who kindly accepted to participate in the event.
We hope that many of you will join us and are looking forward to meeting you at this event. ■ P.P.

NEUREX MEETING

FIRST WEB-CONFERENCE ON TRANSLATIONAL IMAGING FOR PSYCHOPHARMACOLOGY

04 | 12 | 2014
Kollegiensgebaüde
Room 114

Basel

We are pleased to announce the **1st web-conference on Translational Imaging for Psychopharmacology** which will focus on MRI based methodology not only to understand the effect of psychotropic drugs on the brain of humans and animals, but also to help translational research. As the ultimate goal is to enhance drug design and development, representatives from the pharmaceutical industry will come to define the needs and share their experience with academics.

Although physically located at the University of Basel, the web-conferencing formula will also allow remote attendance to the conference. Beyond the sharing of knowledge, this conference seeks to gather the community interested in this subject. Accordingly, we invite all the researchers around the world to contact us and to attend for free. We will do our best to allow remote attendees to interact with the panel.

Illustration : Fotolia

Organizer: Jack Foucher
Registration and more info on www.neurex.org
or contact: Pascale.Piguet@unibas.ch

PROGRAM

09.00 - 09.15 Welcome address

DEFINING THE NEEDS

09.15 - 10.00 **Fabio Sambataro**, ROCHE, Basel, Switzerland
Needs and expectations in translational pharmacological imaging

HUMAN PHARMACOLOGICAL MRI

10.00 - 10.45 **Mitul Mehta**, Institute of Psychiatry, London, United Kingdom
Human pharmacological imaging: approaches, pitfalls and utility

10.45 - 11.15 Coffee break

11.15 - 12.00 **Joop van Greven**, Centre for Human Drug Research, Leiden, Netherlands
Pharmacology of resting state imaging in human

12.00 - 12.30 **Jack Foucher**, Icube laboratory, Strasbourg, France
A resting state ASL-BOLD study of methylphenidate

12.30 - 13.30 Lunch Break

ANIMAL PHARMACOLOGICAL MRI

13.30 - 14.00 **Alessandro Gozzi**, Istituto Italiano di Tecnologia, Rovereto, Italy
Functional and pharmacological MRI of the mouse brain

14.00 - 14.30 **François Dauphin**, EA 4259, Caen, France
Central effects of the modulation of 5-HT6 receptors: a Pharmacological MRI study

14.30 - 15.15 **Markus von Kienlin**, ROCHE, Basel, Switzerland
Reference System of fMRI Activation Patterns induced by Psychoactive Treatments in Rat

15.15 - 15.45 Coffee Break

TRANSLATIONAL PERSPECTIVES

15.45 - 16.45 **Lino Becerra**, PAIN group, Boston, United States of America
Translational imaging for pain pharmacology

16.45 - 17.30 **Round table**
Defining the needs, technological bottleneck, pitfalls and perspectives in the field. Provisional guidelines on the paradigm and imaging techniques.

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European Regional Development Fund

Partners: Program Interreg IV Upper Rhine "Transcending borders with every project", CNRS, INSERM, Université de Strasbourg, Région Alsace, Département du Bas-Rhin, Département du Haut-Rhin, Communauté Urbaine de Strasbourg, Bernstein Center Freiburg, Universität Freiburg, Universität Basel, Kanton Basel-Stadt, Kanton Basel-Landschaft, Confédération Helvétique.

Prof Heinrich Reichert
Biozentrum, UniBasel:
Farewell symposium on January 23rd, 2015

Euros für Neuros: Basel profitiert

Mit wegbereitenden Erfolgen arbeiten Neurofachschaften in der trinationalen Region zusammen. EU-Gelder aus dem Interreg-Programm fördern die Kooperation. Vorerst profitieren vor allem Doktorierende.

Über die Grenzen hinausdenken.

Trinationale Plattform

Gemeinsame Interessen

Zirkus und Wissenschaft

On the 23rd of January 2015, a farewell symposium in the honour of Prof. Heinrich Reichert will take place at the Pharmazentrum Basel. Heinrich Reichert will retire in Spring 2015 after a fruitful career as Professor and Director of the Division of Molecular Zoology at the Biozentrum of the University of Basel. Heinrich Reichert received his Doctorate at the University of Freiburg and did his postdoctoral work at Stanford University. Following a period back at the University of Basel where he got his habilitation, he held faculty positions at the University of Geneva, after which he came back to the University of Basel where he became a Full Professor.

Pioneer for Neurex …

In parallel to a brillant scientific career, Heinrich Reichert has devoted much of his time and energy to the Neurex network which is really indebted to him. Thus, in 2001, then member of the scientific board of Neurex, he raised a Swiss funding of 1.88 million CHF then called the ELTEM (Eucor Learning & Teaching Mobility) program, subsidized by CUS (Conférence Universitaire Suisse).

Together with the support of the University of Basel, this first important source of money for the network (which was then amounting to a group of motivated researchers of the Upper Rhine region meeting once a year) allowed the development of many actions, the list of which has grown since then with several Interreg programs.

Among them, it is important to cite the numerous workshops & meetings which give researchers of our trinational region the possibility to meet each other and invite experts and colleagues from throughout the world.

Several long-lasting and fruitful collaborations have emerged from such stimulated interactions (see for example page 3 of the newsletter). Moreover, the funding of PhD students and postdoctoral fellows by Neurex has allowed the development of collaborative research projects between the universities of Basel, Freiburg and Strasbourg. Such collaborations have led to the defense of joint PhDs between 2 universities, called PhDs in "co-tutelle".

The first Neurex newsletter was published in 2003, reinforcing the links between researchers of the 3 universities. Created in 2005, a joint Master enrolled the first students in 2006 and was attributed the Bartholdi price in 2010. This joint Master now welcomes every year

Prof. Heinrich Reichert,
Division of Molecular Zoology, Biozentrum, University of Basel

students from all over the world in a joint research program that includes lectures at our 3 universities. In 2011, Neurex obtained an Erasmus Mundus funding for a scientific project called NeuroTime, involving the university of Basel, Strasbourg, Freiburg, together with the University of Amsterdam, the Hebrew University of Jerusalem (Israel) and the university of Bangalore (India). We must remember that such successes have their source in the opportunity that was offered to our network thanks to the original efforts of Prof Reichert who dedicated his time and energy for the neuroscience community.

A name in developmental neuroscience …

Heinrich Reichert's lab uses *Drosophila* melanogaster as a model system to analyze the developmental mechanisms that generate neural stem cells and transform their progeny into complex brain circuitry. Moreover, his lab also studies how genetic defects in neural stem cell proliferation can lead to lethal brain tumors in this genetic model. His recent work has shown that many of the molecular genetic control processes that operate in the developing fly brain are evolutionarily conserved and involved in the development of the mammalian brain.

Farewell symposium

In line with his research interests, the symposium that will take place on the 23rd of January will address the Nervous System Development in Invertebrates. During that day, former colleagues and friends of Prof Reichert will present some part of their scientific work, sometimes done in collaboration or under the supervision of Heinrich. Finally, a dinner will bring together Heinrich and some colleagues of the University of Basel, among which the Neurobiology Department of the Biozentrum.

Always available for helping, generous and dynamic: that is the image that Heinrich Reichert's friends and colleagues have from him. We will of course regret our interactions with him, but wish him a very nice retirement: for those who know him, we are quite sure that he will again make perfect use of his time and energy for other good causes. And who knows? We might have the pleasure to meet Heinrich in one of our future meetings. Interest in brain function never really fades… Thanks, Heinrich, and have a great time! ■ P.P.

NEUREX MEETING

Farewell Meeting **Heinrich Reichert** **Nervous System development in Invertebrates**

01 | 23th | 2015

Location:
Hörsaal 1,
Pharmazentrum,
Basel

MARK YOUR CALENDAR!

PROGRAM

Organizers : Angela Giangrande & Pascale Piguet
Registration and more info on www.neurex.org or contact: Pascale.Piguet@unibas.ch

09.00 - 09.15 Introduction

SESSION 1

09.15 - 09.35 **Straussfeld Nicholas**, Tucson, AZ, United States
Tripartite Brains and Deep Time: Fossil Brains

09.35 - 9.55 **Volker Hartenstein**, LA, United States
Assembly of a central circuit in the Drosophila larval brain: neuroblasts, genes and lineage-dependent neuronal wiring

09.55 10.15 **Markus Affolter**, Basel, Switzerland
From genes to proteins: Organogenesis in living organisms»

10.15 - 10.45 Coffee Break

10.45 - 11.05 **Angela Giangrande**, IGBMC, Strasbourg, France
Cell specification or the dark side of plasticity

11.05 - 11.25 **Vijay Raghavan**, NCBS, Bangalore, India
Brain, Brawn, Basel and Bangalore: How cells and circuits make a fly

11.25 - 11.45 **Boris Egger**, Fribourg, Switzerland
Cell intrinsic and environmental control of neural stem cell states

11.45 - 14.20 Lunch break

SESSION 2

14.20 - 14.40 **Karl Friedrich Fischbach**, Freiburg, Germany
I have seen the light. About eyes and beyond

14.40 - 15.00 **Simon Sprecher**, Fribourg, Switzerland
Seeing with simple eyes: Vision in Drosophila larvae

15.00 - 15.30 **Jan Pielage**, Basel, Switzerland
Controlling taste behaviour

15.30 15.50 **Frank Hirth**, London, United Kingdom
Evolutionary conserved neural circuitry for the selection and maintenance of behavioural activity

15.50 - 16.20 Coffee Break

16.20 - 16.40 **Katsu Furukubo-Tokunaga**, University of Tsukuba, Japan
Genetic Dissection of Schizophrenia in Fruit Flies

16.40 - 17.00 **George Boyan**, LMU, München, Germany
Station to station: encounters with H.R.

17.00 17.30 **Heinrich Reichert**, Basel, Switzerland
Farewell lecture

European Regional Development Fund

Partners: Program Interreg IV Upper Rhine "Transcending borders with every project", CNRS, INSERM, Université de Strasbourg, Région Alsace, Département du Bas-Rhin, Département du Haut-Rhin, Communauté Urbaine de Strasbourg, Bernstein Center Freiburg, Universität Freiburg, Universität Basel, Kanton Basel-Stadt, Kanton Basel-Landschaft, Confédération Helvétique.

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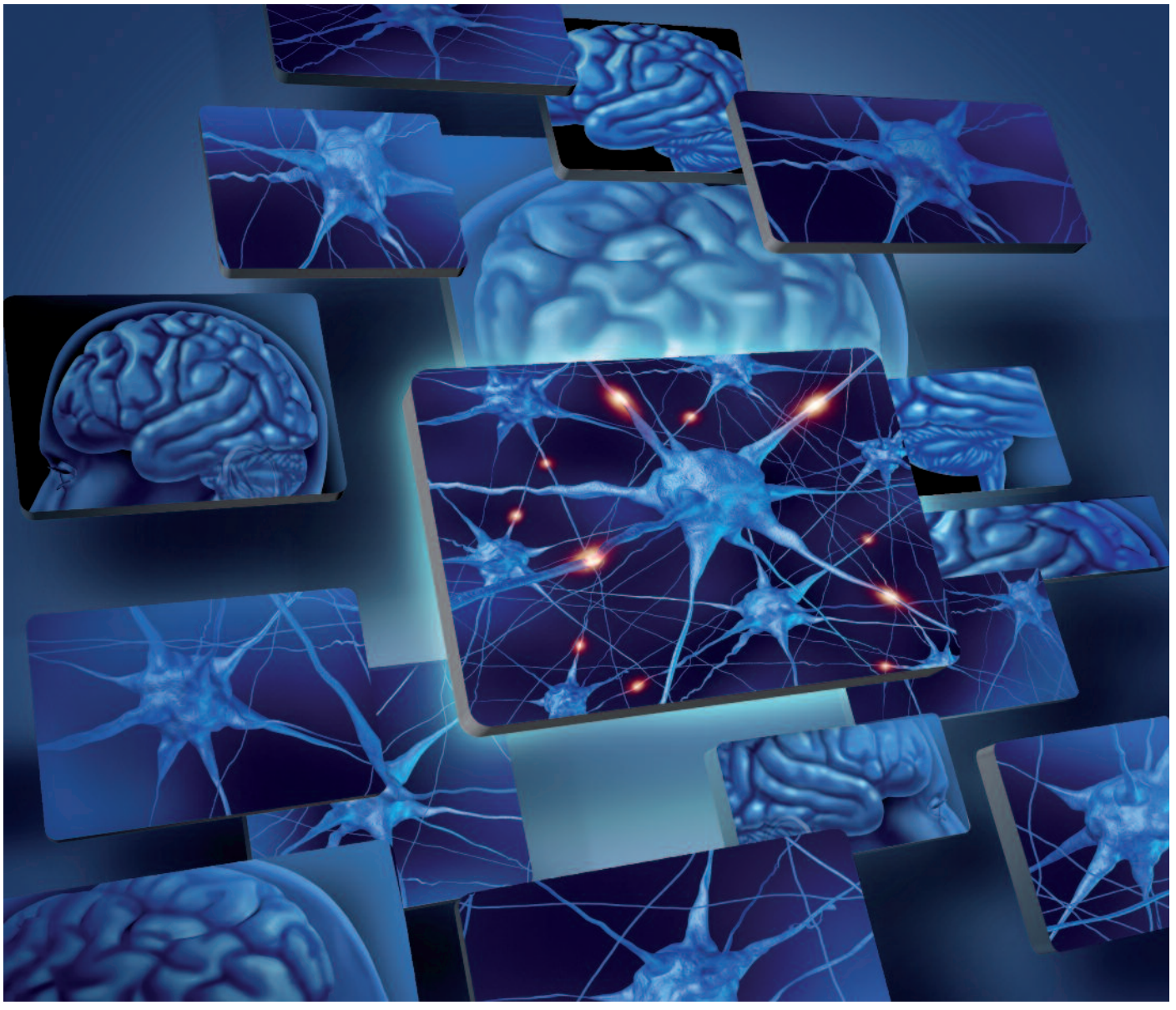
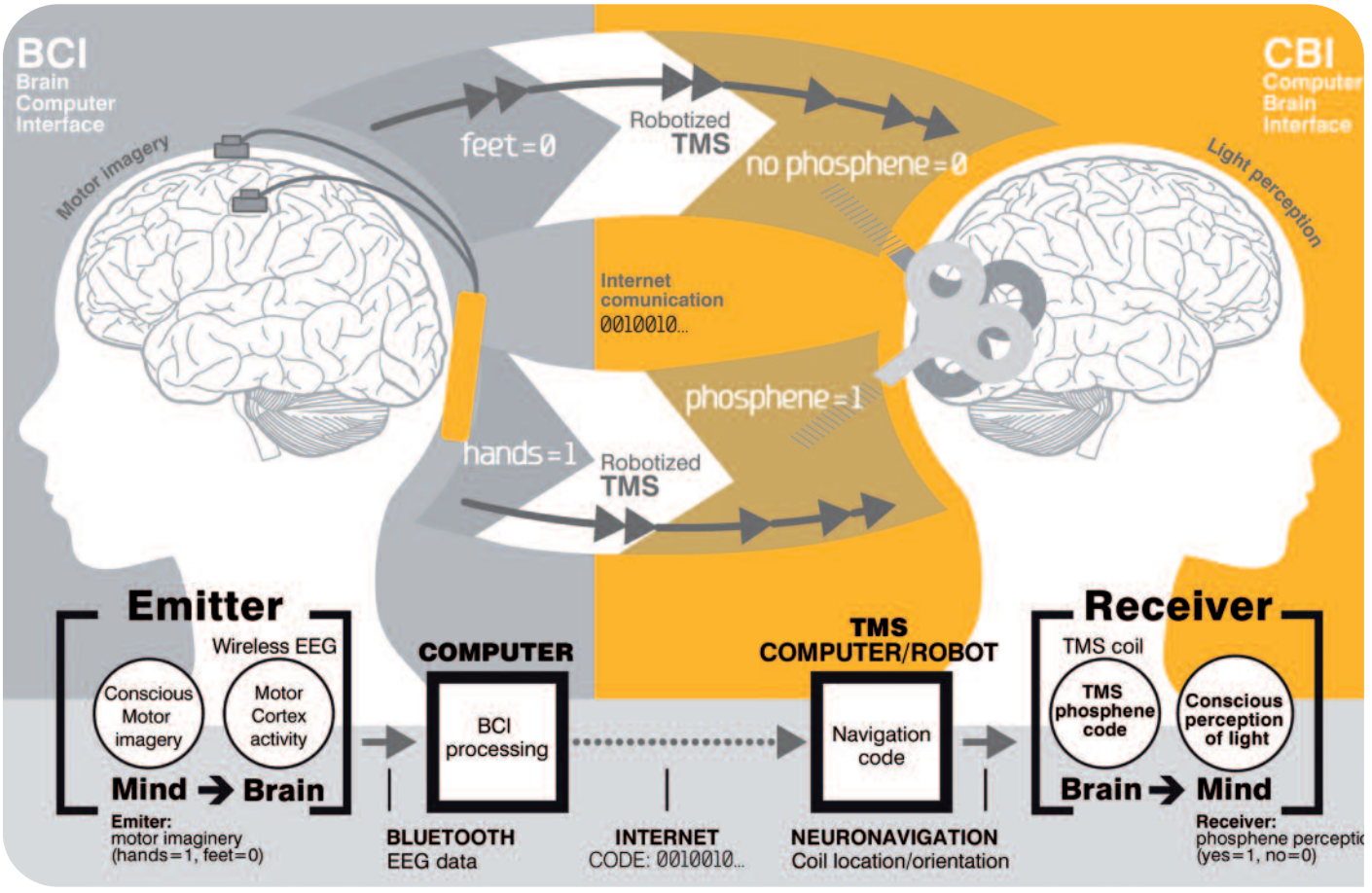
Axilum Robotics / Strasbourg

Axilum Robotics TMS-Robot, first robot specifically designed for Transcranial Magnetic Stimulation (TMS)



On the 28th of March 2014, a brain-to-brain transmission of words was successfully performed between a human emitter (at the laboratory of Thiruvananthapuram, India), and human receiver (Strasbourg, France).This experiment, a collaboration between a Spanish team (Barcelona university and Starlab company), a French team (Axilum Robotics, Strasbourg) and an American group (Harvard Medical School) was recently published in PLOS One. >>>

Axilum Robotics / Strasbourg



Legend Fig.1: Brain to brain communication system overview. In a first step, the words ("hola" and "ciao") had to be coded into binary code, and then emailed from India to France.
The coding of words made use of a BCI communication system which converted conscious voluntary motor imagery into brain activity changes that could be captured non-invasively (using EEG) as physical signals conveying information. The CBI subsystem relied on biphasic TMS pulses – performed thanks to a robotized TMS equipment (the Axilum Robotics robot)– to encode information (Figs. 2-5).
The subjects experienced this as phosphenes, flashes of light in their peripheral vision. The light appeared in numerical sequences that enabled the receiver to decode the information in the message, and while the subjects did not report feeling anything, they did correctly receive the greetings

The brain-to-brain communication was made possible by combining a Brain Computer Interface (BCI) based on voluntary motor imagery-controlled electroencephalographic (EEG) changes with a Computer Brain Interface (CBI) inducing the conscious perception of phosphenes (light flashes) with special care taken to block sensory (tactile, visual or auditory) cues (Fig.1).

In this experiment, phosphenes were induced thanks to a neuronavigated, robotized transcranial magnetic stimulation system from Axilum Robotics, Strasbourg (http://www.axilum robotics.com/fr/), who developped the robot, to automate the TMS procedure (Fig. 2).

Legend Fig.2: Axilum Robotics TMS-Robot is the first robot specifically made for TMS. It offers a solution to the challenge of guarantying both precision and reproducibility of stimulations (some 30 stimulations may be needed in the course of one therapeutic treatment). It includes a 7 degree-of-freedom robotic arm and a 2 degree-of-freedom, computer-controlled patient seat. *Image: courtesy of Axilum Robotics.*

This groundbreaking experiment rapidly draw the attention of journalists who reported this first successful brain to brain communication experiment in several national and international popular work articles. For the research community, this demonstration not only is a critically important proof-of-principle for the feasibility of developing brain-to-brain communications, but it is also a step forward in the use of robotized TMS equipment. Transcranial magnetic stimulation (TMS) is a neurostimulation and neuromodulation technique, based on the principle of electromagnetic induction of an electric field in the brain. It consists of stimulating the brain non-invasively using high-intensity brief magnetic pulses applied through a coil positioned near the skull of the subject. Repetitive transcranial magnetic stimulation (rTMS) has been found to be a promising non-invasive treatment for a variety of neuropsychiatric conditions, among which notably depression, hallucinations and pain syndromes, such as neuropathic pain, visceral pain or migraine. In earlier experiments and clinical studies, TMS was performed using "manual" location of the equipment. However, the reproducibility of the results is relatively low, owing to a too approximate precision in location of the TMS pulses.

The need of robotized TMS was expressed in 2004 to Pr Michel de Mathelin, former head of the medical robotics research group of ICube (Laboratoire des Sciences de l'Ingénieur, de l'Informatique et de l'Imagerie), a Research Unit of the University of Strasbourg, CNRS, ENGEES & INSA), by Dr Jack Foucher, (UMR_S Inserm 1114, Strasbourg), one of the pioneers of TMS in France. Facing the double challenge to ensure precision of stimulation and to reproduce identical procedures by patients who need sometimes up to 30 sessions, Dr Foucher was seeking a solution to automate the stimulation procedure. Axilum Robotics was founded in April 2011 by a team composed of researchers, robotics engineers and a physician with business experience: Bernard Bayle, Michel Berg, Michel de Mathelin, Romuald Ginhoux, Benjamin Maurin and Pierre Renaud. This spin-off company from ICube developed the first robot specifically designed for TMS, based on a proof of concept of ICube.

The automated TMS procedure offers many advantages including precision, repeatability of TMS sessions, compensation of patient's motions, ease of use, operator safety and comfort, patient safety, access to large stimulation areas and permanent contact between the patient's head and the coil monitored by force sensors (Figs. 3 & 4).

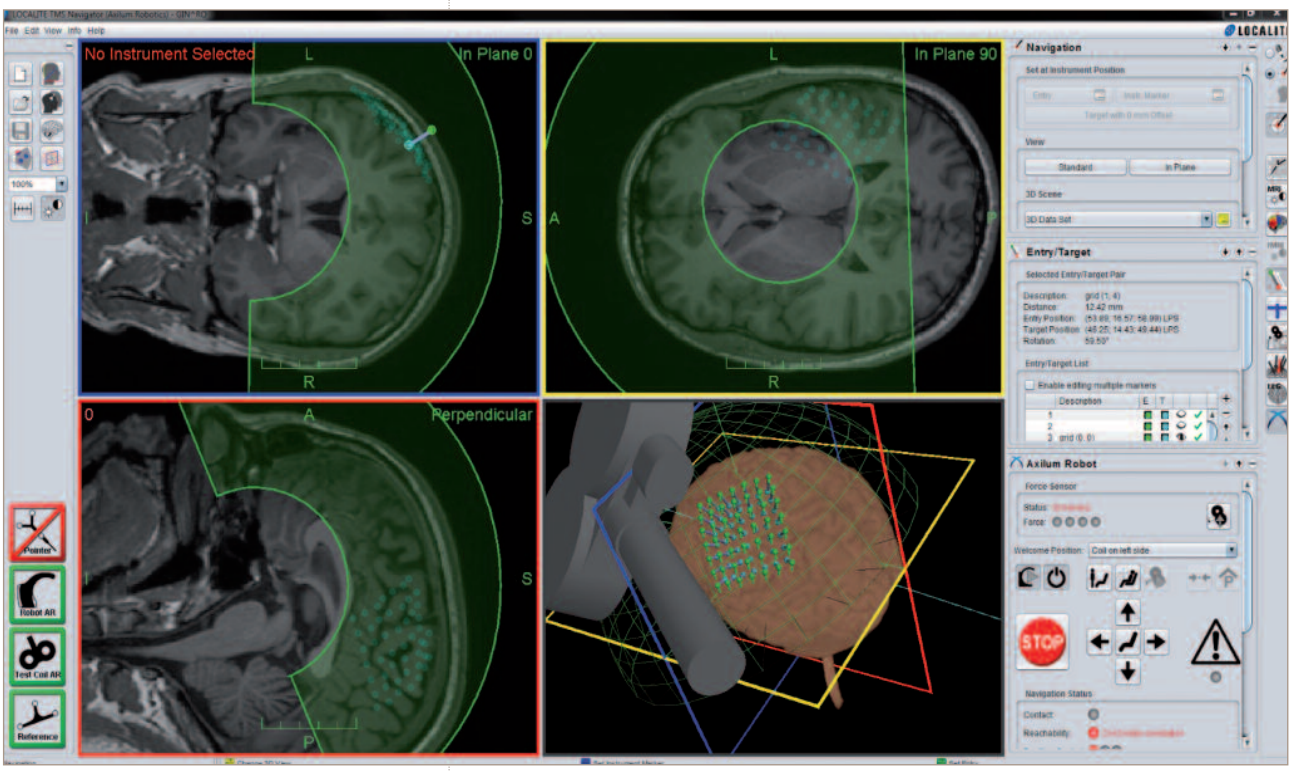
The R&D project was an award winner at the national contest for creation of innovative technology companies organized by the French Ministry of Research (2009 & 2010) and has been certified through the Life Science cluster Alsace Biovalley in 2011.

The Quality Management System of Axilum Robotics has been certified to match the requirements of UKAS and SCC ISO 13485 standard by the Notified Body SGS 0120. This certification confirms that the company fulfills the requirements applicable in Europe and Canada to organizations manufacturing and commercializing medical devices.

Axilum Robotics / Strasbourg

Legend Fig.3: Dr Romuald Ginhoux, Product Director at Axilum Robotics, performing a demonstration of the Axilum Robotics TMS robot. The patented hemispherical shape of the robotic arm allows the positioning of the coil's stimulation hot spot around a hemisphere. This architecture enables access to all stimulation areas while the head is located inside the work hemisphere. The computer-controlled patient seat facilitates the adjustment of the patient head inside the workspace. In combination with compatible equipement (neuronavigation system & coil connected to its own stimulator), the robot allows the automatic execution of an image-guided TMS session planned in advance. Once the stimulation targets and coil self-rotation have been defined in the neuronavigation system, Axilum Robotics TMS-Robot positions the coil tangentially at these targets, ensures contact between coil and head, and compensates for any head movements during the session, keeping the coil position and orientation with respect to the brain. This protocol allows not only a precise, but reproducible stimulation. *Image: courtesy of Axilum Robotics.*

Legend Fig.4: Dr Michel Berg, CEO at Axilum Robotics testing the conditions (absence of sensory inputs) which allow to perform a TMS experiment while not relying on peripheral nervous system (PNS) cues that could be used by the subject to guess the position of the coil. In order to avoid the identification of the coil orientation using auditory information, the subject wears earplugs and the robot moves the coil between TMS pulses towards an intermediate site. The robot thus realizes a movement of same duration and same noise levels for all bit transmission events, irrespective of coil orientation. Visual cues are blocked by having subjects close their eyes and wear an eye mask. A flat force sensor (non-sensitive to the magnetic field) lies on the inferior surface of the TMS coil to assess the contact between the coil and the head. The robot's embedded software controls the applied force in real time so that it does not exceed the coil's own weight. Therefore, stimulations can be delivered only when the coil is touching the head. *Image: courtesy of Axilum Robotics.*



Legend Fig.5: The LOCALITE neuronavigation system (LOCALITE GmbH, Sainkt Augustin, Germany) monitors the coil position and orientation in real time to compensate for any movement of the head measured by its 3D optical tracking system during the stimulation. The position of the arm is represented by the green area over the brain of the subject. The location and orientation of the hot spot for stimulation is overlaid on the MRI image of the head (top left, short line between blue & green circle). A 3-D picture (bottom right) illustrates the position of the coil and the underlying stimulated area. *Image: courtesy of Axilum Robotics.*

Axilum Robotics TMS-Robot is a CE marked Class IIa medical device and has received a Health Canada licence in 2013.

There is growing evidence about clinical benefits of TMS, particularly in diseases like major depression or chronic pain (Lefaucheur et al., in Clinical Neurophysiology, 2014). Using TMS since 2007 at hôpital Ambroise Paré (Boulogne-Billancourt, APHP, France) in trials for the treatment of chronic pain, the team of the local Pain Center is currently evaluating a robotized TMS protocol in patients suffering from chronic neuropathic pain. Axilum Robotics has also installed last March its robot at the Berenson Allen Center for Noninvasive Brain Stimulation (directed by Pr Alvaro Pascual-Leone, Professor of Neurology at Harvard Medical School, co-author of the PLOS One article) at the Beth Israel Deaconess Medical Center. A full image guided robotic system built around the robot will allow implementing an automated TMS procedure in a new research study.

Axilum Robotics offers to health professionnals and researchers different robotic solutions for TMS, adapted to various needs, from research to therapeutics. It commercializes the robot and organizes demonstrations of robotized TMS. More information on **http://www.axilumrobotics.com/en/**

No doubt that with its unique robot, this company -located within the Neurex network- will develop interactions with our researchers and clinicians interested in TMS !

We would like to express our gratefulness to Romuald Ginhoux for his precious collaboration and support. ■ P.P.

Multiple sclerosis: fighting neuroinflammation & rebuilding the myelin

Certainties, illusions and expectations

On the 1st and 2nd of December 2014, a meeting co-organized by Dr Said Ghandour (UMR_S 1119 Inserm unit, University of Strasbourg) and by Prof Jérôme De Sèze (Head of the Clinical Investigation Centre of the Strasbourg university hospital & UMR_S 1119 Inserm unit, University of Strasbourg) will address the fundamental basis and therapeutic relevance of fighting neuroinflammation and rebuilding myelin for the treatment of MS.

During that event, miscellaneous aspects of this multifaceted disorder will be presented, with a special focus on the demyelination process. This chronic inflammatory demyelinating disorder of the CNS is characterized by infiltration of immune cells and progressive damage to myelin sheaths and neurons. It was however shown during the last decades that direct axonal damage as well as neuronal injury resulting from chronic demyelination are essential contributors to the development of long-term disability in patients. Viewing MS as both inflammatory and neurodegenerative has significant implications for treatment: thus, the remyelination of denuded axons in order to protect neurons from damage is nowadays regarded as a potential therapeutic complementary approach in addition to controlling inflammation.

The etiopathogenesis of MS will also be addressed during this event: an update will be made on the role of vitamin D (the deficiency of which has been suspected for long to play a role because of an elevated risk of MS in Northern countries). Moreover, the putative involvement of viral infections will be discussed together with recent hypotheses on the role of the gut microbiome and dysfunction of the gut brain axis in the development of the disease.

What is the rationale for the gender differences observed in the prevalence of MS? The influence of sex setroids will be discussed in the session 3 of this event, followed by a session on the genetics of MS and markers of the disease.

The event will terminate by a session dedicated to clinical aspects & therapeutic approaches of MS discussed above.

We would like to express our gratefulness to the organizers of the event, Dr Ghandour and Prof De Sèze, as well as to all the scientists who kindly agreed to participate in this meeting. ■ P.P.

The Neurex research force working in the field of Multiple Sclerosis is very strong:
in Strasbourg, it is represented by the team "Biopathology of Myelin, Neuroprotection & Therapeutic Strategies" led by Prof Mensah-Nyagan (UMR_S 1119 Inserm unit, University of Strasbourg) and by the Clinical Investigation Centre of the Strasbourg university hospital (led by Prof Jérôme De Sèze, organizer of the December event).
In Basel, fundamental and clinical research on MS is performed by the Neurobiology research laboratory (Department of Biomedicine, DBM DBM) led by Prof Nicole Schaeren-Wiemers, the Clinical Neuroimmunology laboratory (DBM) led by Tobias Derfuss & Raija Lindberg and the Department of Neurology led by Prof Ludwig Kappos.
In Freiburg, the laboratory led by Prof Marco Prinz at the Neurozentrum (Uniklinik Freiburg) investigates the role of innate immunity in MS and autoimmune diseases. Due to the multifaceted aspect of the disease, such research is complemented by the contribution of additional disciplines such as immunology or microbiology which address various features of MS, questioning its etiopathogenesis in particular. This multidisciplinary research stimulates horizontal interactions between disciplines and paves more and more the way for collaborative studies.

NEUREX MEETING

MULTIPLE SCLEROSIS: FIGHTING NEUROINFLAMMATION & REBUILDING THE MYELIN

Certainties, illusions and expectations

European Regional Development Fund

Partners: Program Interreg IV Upper Rhine "Transcending borders with every project", CNRS, INSERM, Université de Strasbourg, Région Alsace, Département du Bas-Rhin, Département du Haut-Rhin, Communauté Urbaine de Strasbourg, Bernstein Center Freiburg, Universität Freiburg, Universität Basel, Kanton Basel-Stadt, Kanton Basel-Landschaft, Confédération Helvétique.

Organizers: Said Ghandour, Jérôme De Sèze, Pascale Piguet & Stéphanie Klipfel
Registration and more info on www.neurex.org or contact: Pascale.Piguet@unibas.ch

PROGRAM

Monday December 1st

09.15 - 09.45 Registration and welcome Coffee
09.45 - 10.00 Welcome Address / **Said Ghandour** (Strasbourg, France)

SESSION 1 — **VIEWS & NEWS IN MULTIPLE SCLEROSIS & DEMYELINATION**
Discussion leaders: Stefan Gold (Hamburg, Germany) & Michael Schumacher (Paris, France)

10.00 - 10.30 **Bruce Trapp** (Cleveland, Ohio, USA)
Cortical demyelination in MS

10.30 - 11.00 **Robin Franklin** (Cambridge, UK)
Remyelination and the regenerative medicine of MS

11.00 - 11.30 Coffee break

11.30 - 12.00 **Hauke Werner** (Göttingen, Germany)
Proteomic approaches to myelin-related pathology

12.00 - 12.30 **Robert Skoff** (Detroit, Michigan, USA)
The relationship between proteolipid protein, mitochondrial abnormalities, and myelin in white matter disorders

12.30 - 14.00 Lunch break

SESSION 2 — **ETIOPATHOGENESIS OF MULTIPLE SCLEROSIS**
Discussion leaders: Bruce Trapp (Cleveland, USA) & Marco Prinz (Freiburg, Germany)

The gut brain axis and the role of gut microbiome in MS

14.00 - 14.30 **Gilles Mithieux** (Lyon, France)
Microbiota-generated metobolites and brain-gut neural circuit

14.30 - 15.00 **Hartmut Wekerle** (Martinsried, Germany)
The intestinal origins of autoimmune demyelination

Vitamin D and MS

15.00 - 15.30 **Peter Sundstrom** (Umeå, Sweden)
The status of vitamin D in MS

15.30 - 16.00 Coffee break

Viruses and MS

16.00 - 16.30 **Pamela Knapp** (Richmond, VA, USA)
Viruses and CNS neuropathology: A role in Multiple Sclerosis?

16.30 - 17.00 **Daniel Pinschewer** (Basel, Switzerland) & **Doron Merkler** (Geneva, Switzerland)
Virus-triggered immunopathology in the CNS

18.30 Dinner

Tuesday December 2nd

SESSION 3 — **SEX HORMONES & MS**
Discussion leaders: Robin Franklin (Cambridge) & Kevin Da Silva (USA)

09.00 - 09.30 **Tomáš Paus** (Toronto, Canada)
Sex differences in the growth of white matter and the role of testosterone and androgen receptor

09.30 - 10.00 **Michael Schumacher** (Paris, France)
Significance and therapeutic relevance of steroid hormones for myelin regeneration

10.00 - 10.30 **Stefan Gold** (Hamburg, Germany)
Therapeutic potential of sex steroids in multiple sclerosis

10.30 - 11.00 **Sandra Vukusic** (Lyon, France)
Pregnancy and post-partum: a particular period in MS life

11.00 - 11.30 Coffee Break

SESSION 4 — **GENETICS, IMMUNOLOGY& IMAGING**
Discussion leaders: Ludwig Kappos (Basel, Switzerland) & Patrick Vermersch (Lille, France)

11.30 - 12.00 **Alastair Compston** (Cambridge,UK)
MS and genetics

12.00 - 12.30 **Tobias Derfuss** (Basel, Switzerland)
Immunological markers in neuroinflammatory diseases

12.30 - 13.00 **Bruno Stankoff** (Paris, France)
New markers for in vivo imaging

13.00 - 14.30 Lunch break

SESSION 5 — **MS NEWS: TREATMENT AND DIAGNOSIS**
Discussion leaders: Alastair Compston (Cambridge, UK) & Jérôme de Sèze (Strasbourg, France)

14.30 - 14.45 **Alastair Compston** (Cambridge,UK)
Introductory remarks: The basis of MS treatments

14.45 - 15.15 **Patrick Vermersch** (Lille, France)
Current therapeutic strategies in MS: induction or escalation

15.15 - 15.45 **Gilmore O'Neill** (Boston, Massachusetts, USA)
Moving remyelination therapy from the laboratory to the clinic

15.45 - 16.15 **Paul Smith** (Basel, Switzerland)
Therapeutic approaches across the MS clinical subtypes

16.15 - 16.45 **David Leppert** (Basel, Switzerland)
B-cell therapy in MS

16.45 **General Discussion**
Concluding remarks
A.G. Mensah-Nyagan (Strasbourg, France)

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Bi-annual.

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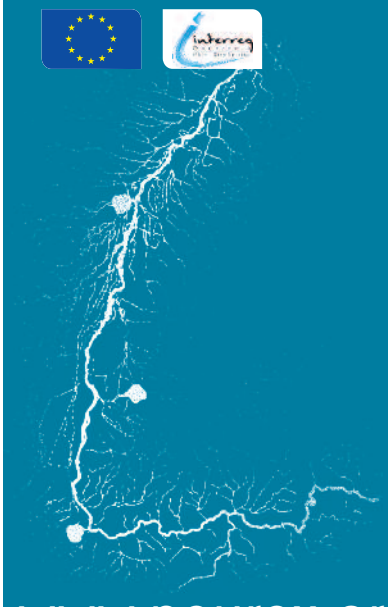

www.neurex.org

Coming events

DECEMBER 2014

- 1st-2nd - Neurex Meeting
  «Fighting Neuroinflammation: Certainties and illusions & Rebuilding the Myelin: Expectations and hopes»
  Strasbourg, France
- 4th - Neurex Meeting & web conference
  «Translational Imaging for Psychopharmacology»
  Basel, Switzerland

JANUARY 2015

- 20th-22nd - Erasmus Mundus NeuroTime Meeting
  Basel, Switzerland
- 23rd - Farewell symposium in the honour of Prof Heinrich Reichert's retirement
  «Nervous System development in Invertebrates»
  Basel, Switzerland

SPRING 2015

- Neurex Event
  «Neurex Annual Meeting »
  Freiburg, Germany

MARCH 2015

- 9th-10th - Neurex Workshop
  «Neuronal oscillations: from mechanisms to functions»
  Strasbourg, France

This description is not definitive, but lists the events which are ready or in preparation. Please check again on www.neurex.org or in the next newsletter for additional events.

Info & links

NEUROSCIENCE FEDERATIONS & LABORATORIES IN THE UPPER RHINE VALLEY

The Neurex network includes the 3 neuroscience federations of Basel (NNB, Neuroscience Network Basel), Freiburg (Neurag) and Strasbourg (Neuropôle) plus additional research units performing research in the NS. For a detailed description of the institutes making up the neuroscience landscape in Neurex, you may download our supplement to newsletter 26 on www.neurex.org.

- Neuropôle
  http://neurochem.u-strasbg.fr
- NEURAG
  http://www.neurag.uni-freiburg.de
- NNB
  http://www.neuronetwork.unibas.ch

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