# *Wednesday June 22 - Tutorial lectures*

9.00 - 10.15 - *Registration + coffee*

10.15 - 10.30 - *Welcome*

**SESSION 1.1 -** *Chair: Aileen McGonigal (AMU, INS and AP-HM, Marseille, France)*

10.30 - 11.30

## Jorge GONZALEZ-MARTINEZ

*(Epilepsy Center, Cleveland Clinic, Cleveland, OH)*

## Functional Anatomy of Perisylvian Areas

11.30 - 12.30

## Stephan VAN GILS

*(Applied Mathematics, University of Twente, Enschede, The Netherlands)*

## Measures for brain networks

It is a crucial task to determine abnormal brain regions in patients with focal epilepsy. We compare in some detail two methods both based on intracranial EEG. A non-directional network can be constructed based on cross-correlations between nodes during inter-ictal epochs. Alternatively, a bi-directional network can be constructed, based on Single Pulse Evoked Stimuli (SPES), where brief local electrical stimulations are applied to the brain that yield both physiological and pathological responses elsewhere.
We find that the network of strong correlations is a subnetwork of the SPES network. Strong correlations are mostly found between topographically nearby electrodes. Dynamics comes into play when when the nodes of the network are replaced by neural masses and should indicate which regions are pathological. The strength of the connections in the network determine the strength of the coupling between the neural masses. We find that SPES responses (in silico) reproduce the connectivity in the network faithfully. We compare the dynamics of both the SPES-network and the correlation-network with the actual inter-ictal brain dynamics for one specific patient.
This content of the talk is based on joint research between the Department of Neurology of the University Medical Centre Utrecht (Dorien van Blooijs, Geertjan Huiskamp, Frans Leijten) and the Applied Analysis group of the University of Twente (Stephan van Gils, Jurgen Hebbink en Hil Meijer).

12.30 - 14.00
LUNCH BREAK

**SESSION 1.2 -** *Chair: Christian Bénar (AMU, INS, Marseille, France)*

14.00 - 15.00

## Marc GOODFELLOW

*(Centre for Biomedical Modelling and Analysis,*
*University of Exeter, United Kingdom)*

## The role of networks in seizure generation

Epilepsy is characterised by the repeated occurrence of seizures, which are periods of pathological brain activity that arise spontaneously from a predominantly healthy functional state. Since the goal of epilepsy treatment is to abolish or reduce the tendency of the brain to transition into seizures (its ictogenicity), it is important to better understand these transitions, and how we might interact with the brain to abate them. However, seizure dynamics emerge in, and affect, large-scale brain networks, and the network paradigm for ictogenesis introduces new challenges and new opportunities to understand epilepsy.
In this talk I will review mathematical modelling approaches that can help us understand the generation of seizures in networks and quantify their ictogenicity. I will demonstrate how these approaches can be used to quantify differences in brain networks between patients with generalised epilepsies and healthy controls. I will also describe how we can extend this approach to quantify the contribution of each component of a network to seizure generation. This quantification is based upon the effect that a treatment-specific perturbation has on network ictogenicity. Using exemplar networks I will explore how the apparent ictogenicity of nodes can vary according to network structure and the presence or absence of "pathological" nodes (seizure foci). I will explain how this approach can potentially provide an insightful and principled way to interpret and describe generalised or focal seizure dynamics, and may enhance our strategies for the classification and treatment of epilepsies.

15.00 - 16.00

## Esther KROOK-MAGNUSON

*(Department of Neuroscience,*
*University of Minnesota, Minneapolis, MN)*

## Optogenetics: timely illumination of neuronal circuitry

Optogenetics allows selective control of elements in neuronal circuits with unprecedented precision. This tutorial will cover the basics of optogenetics, fun new tools in the optogenetic toolbox, and the power of on-demand applications. Recent gains in our understanding of neuronal circuits in normal physiology and pathophysiology, including epilepsy, achieved through optogenetic techniques will be highlighted.

16.00 - 16.30
COFFEE BREAK

**SESSION 1.3 -** Chair: Andrea Brovelli (MU, INT, Marseille, France)

16.30 - 17.30

## Karl FRISTON

(Wellcome Trust Centre for Neuroimaging,
University College London, United Kingdom)

### Dynamic causal modelling and canonical microcircuits

The past decade has seen tremendous advances in characterising functional integration in the brain. My talk will focus on the application of dynamic causal modelling to evoked and induced brain responses. I will review recent developments in modelling distributed neuronal responses – and how this modelling rests upon hierarchical processing in the brain. I hope to illustrate the use of dynamic causal modelling in studies of predictive coding, with a special focus on canonical microcircuits and laminar specific message passing in cortical hierarchies.

17.30 - 18.30

## Michael WIBRAL

(MEG Unit, Brain Imaging Center,
Goethe University, Frankfurt am Main, Germany)

### Neural information dynamics in predictive coding - from synapses to systems

Predictive coding has become a dominant candidate theory for cortical function. Yet, current efforts to validate or refute this theory largely depend on an experimenter's opinion of what a neural structure should predict in her or his experiment - sometimes leading to a circular approach. We introduce an information theoretic framework that can identify predictions and the computation of matches or prediction errors based on neural data alone, i.e. without the need for an experimenter's opinion. This is important as it extends our efforts to validate predictive coding theories and their universal claim about brain function to those 99% of experiments that were not planned as tests for the theory, and to species where our intuitions about the things their brains predict are weak, and even to individual cells. We will demonstrate the use of this framework with human MEG data recorded in a priming task, and with paired single cell recordings from the cat retina and the lateral geniculate nucleus.

19.00 - 21.00
WELCOME RECEPTION
Restaurant “Le Chalet du Pharo”

# *Thursday June 23 - Thematic sessions I*

9.00 - 9.15 - *Welcome*

**KÖTTER LECTURE**
sponsored by EPJ NBP "Nonlinear Biomedical Physics" (Springer Verlag)

*Chair: Viktor Jirsa (AMU, INS, Marseille, France)*

9.15 - 10.00

## Michael BREAKSPEAR

*(Systems Neuroscience Group,*
*QIMR Berghofer Medical Research Institute, Brisbane, Australia)*

## Brain Waves

Complex network topology in the brain occurs against the backdrop of a spatially invariant, isotropic connectivity kernel. The former arises through specific topological rules of connectivity whereas the latter reflects the brain's spatially embodied geometry. For strong dynamic interactions, the local kernel yields large-scale waves of activity - scroll waves, breathers and travelling waves- that are broken up by the long-range interactions into brief metastable patterns. For weak coupling, the background coupling dominates and leads to the intermittent expression of spatially dispersed clusters. I will argue that these observations provide an explanatory framework for healthy and pathological brain activity as well as a unifying perspective on neural field versus neural mass models of brain activity.

10.00 - 10.30
COFFEE BREAK

**SESSION 2.1 -** *Chair: Ingo Bojak (University of Reading, United Kingdom)*

10.30 - 11.15

## Claudius GROS

*(Institute for Theoretical Physics,*
*Goethe University, Frankfurt am Main, Germany)*

## Short-term synaptic plasticity, attractor relicts and robot motion

Short term synaptic plasticity (STSP) is a transient form of mostly presynaptic plasticity resulting typically in an initial increase of the synaptic efficiency followed then by a decrease of the synaptic strength for up to a few hundred milliseconds. STSP is thought to be important for (transient) forms of short term memories, with the involved timescales being however also important for other cognitive tasks, like motor sequence generation. We point out that STSP often results in autonomously ongoing dynamics for a wide range of neural networks, transforming in particular preformed attractors into attractor relicts. The inclusion of STSP may hence change substantially the resulting dynamical state. We do in particular simulate sphere-shaped autonomous robots, within the LPZrobots simulation package, containing three weights moving along orthogonal internal rods. The position of a weight is controlled by a single neuron receiving excitatory input from the sensor measuring its actual position and inhibitory inputs from the other two neurons. The inhibitory connections are plastic according to standard STSP rules, as measured in mammalian neural circuits.
We find that short term synaptic plasticity is prone to generate movements. For the simulated robot a wide palette of self-organized motion patterns are observed, including various meandering forward and circular motions, together with chaotic and hence explorative trajectories. The observed locomotion is robust with respect to noise and to additional interactions with obstacles.

11.15 - 12.00

## Olaf SPORNS

*(Computational Cognitive Neuroscience Laboratory,*
*Indiana University, Bloomington, IN)*

## Modeling Communication Dynamics in the Brain

Neurons and brain regions continually exchange signals that travel along axonal (structural) connections. Dynamic patterns of brain activity are in part an expression of these complex patterns of neuronal communication. How should we model such patterns, and can models of communication dynamics provide insight into the functioning of brain networks?

12.00 - 14.00
LUNCH BREAK

**SESSION 2.2 -** *Chair: Pascale Quilichini (AMU, INS, Marseille, France)*

14.00 - 14.45

## Randy McINTOSH

*(Rotman Research Institute, Baycrest Centre, University of Toronto, ON, Canada)*

### Time will tell if your brain is healthy or not

The network architecture of the brain is such that communication between regions shows differing time delays dependent on distance and myelination. These time delays, considered in the context of the spatial distribution of regions establish a space-time structure that characterizes the potential network dynamics that can be supported by a given brain. We have shown that information processing, measured with multiscale entropy, shows a principled evolution during maturation and senscence. Clinical studies suggest that if such a shift in preferred timescales does not happen cognitive dysfunction ensues. These studies reinforce the need to carefully consider brain dynamics as a more sophisticated index of brain health and dysfunction.

14.45 - 15.30

## Lionel NACCACHE

*(ICM, Brain and Spine Institute, Paris, France)*

### Probing conscious states and conscious contents with measures of brain functional connectivity

15.30 - 16.00
COFFEE BREAK

**SESSION 2.3 -** *Chair: Demian Battaglia (AMU, INS, Marseille, France)*

16.00 - 16.45


## Charles GRAY

*(Department of Cell Biology and Neuroscience, Montana State University, Bozeman, MT)*


## Distributed Cortico-cortical Interactions Underlying Visual Working Memory

Cognitive processes, such as working memory, engage large neuronal populations spanning widespread cortical and subcortical areas. To further understand the task dependence, and the spectral, temporal and spatial organization of these activity patterns, we designed a large-scale recording system that enables the chronic implantation of 256 independently movable microelectrodes spanning an entire cerebral hemisphere in macaque monkeys. We implanted this system in two animals and recorded neuronal activity from more than 60 separate cortical areas while the animals performed an object-based, visual delayed match-to-sample task and a set of control tasks. Analysis of the unit activity revealed a widespread distribution of task dependent and content specific cellular responses, concentrated in multiple areas of the prefrontal, premotor, posterior parietal and visual cortices. Analysis of the local field potential (LFP) revealed striking regional variations in the distribution of spectral power and coherence. These signals displayed a mixture of increases and decreases in magnitude during the task. Coherence and phase-locking analyses revealed widespread, task-dependent patterns of correlated activity that varied in frequency and phase. These studies provide the first analysis of the temporal and spectral patterns of cortical neuronal activity spanning a cerebral hemisphere in macaque monkeys performing a cognitive task.

16.45 - 17.30


## Kenneth KNOBLAUCH

*(INSERM U1208, Stem Cell and Brain Research Institute, Bron, France; University Lyon 1, Lyon, France)*


## Distance, Weight and Hierarchy: Universal Constraints on Cortical Connectivity

The mammalian order shows a massive 5-order magnitude variation in brain size. Scaling factors have been shown to vary considerably in rodent and primate classes. Here we explore organizational differences in a large, folded primate brain (macaque) and a small smooth rodent brain (mouse). In both species, inter-areal connectivity profiles extracted from track-tracing experiments display high graph densities (>65%). Such high densities exclude popular topological graph models of cortical organization, such as small worlds and rich clubs, as being of particular interest.

By contrast, both data sets show a spatial embedding as manifested in a weight-distance relation, in which the probability distribution of inter-areal connection lengths is described by an Exponential Distance Rule (EDR), scaled for brain size (Szobalcs et al., 2016). The EDR predicts a surprising number of features of connectivity across both macaque and mouse cortex, including optimal areal placement minimizing wire length and a dense core defined by large cliques. Laminar patterns of inter-areal connectivity conjectured to represent feedback/feedforward relations indicate an order relationship between cortical areas that can be used to construct a structural inter-areal hierarchy (Markov et al., JCN 2014). Electrophysiological recordings in macaque (Bastos et al., 2015, Neuron) demonstrate a functional hierarchy based on laminar-specific frequency interactions that mirrors the structural hierarchy. Similar functional hierarchies have been identified in human using MEG (Michalareas et al, 2016, Neuron). These results point to universal features in cortical organization across species with brain volume varying over several orders of magnitude.

17.30 - *Closing remarks*

**Starting from 19.00**

GALA DINNER
*Fort Ganteaume*

*with an informal speech by*
**Patrick CHAUVEL**
*(AMU, INS, Marseille, France)*
*about*
*"From Jackson, Cajal and Sherrington to French Connection"*
*(unofficial title)*

*and musical animation by*
**"Yetem" (& friends)**

# *Friday June 24 - Thematic sessions II*

9.00 - 9.15 - *Welcome*

**SESSION 3.1** - *Chair: Maxime Guye*
*(AMU, CRMBM and AP-HM, Marseille, France)*

9.15 - 10.00

**Martin HOFMANN-APITIUS**
*(Department of Bioinformatics, Fraunhofer Institute for Algorithms and Scientific Computing - SCAI, Sankt Augustin, Germany)*

## The AETIONOMY Project: Embedding biological mechanisms in the connectome context

The AETIONOMY project aims at generating a "mechanism-based taxonomy" of neurodegenerative diseases, focusing on Alzheimer's Disease and Parkinsonism. The concept of biological mechanisms goes way beyond the common understanding of "pathways"; in fact, the modeling and mining approaches in AETIONOMY deliver multiscale and multimodal mechanisms that e.g. link genetics to imaging readouts.
Mechanistic context at cellular and whole organ level - essentially linking anatomical and physiological information in cause-and-effect models - is currently an emerging focus in our project. In my talk, I will present general modeling and mining strategies in AETIONOMY and shed light on the current mechanism representation and mining strategies for cellular micro-circuitry and connectome information.

10.00 - 10.30
COFFEE BREAK

**SESSION 3.2 -** *Chair: Mireille Bonnard (AMU, INS, Marseille, France)*

10.30 - 11.15

## Vince CALHOUN

*(Medical Image Analysis Lab, The Mind Research Network and University of New Mexico, Albuquerque, NM)*

### The chronnectome, signal or noise?

11.15 - 12.00

## Gregor THUT

*(Institute of Neuroscience and Psychology, University of Glasgow, United Kingdom)*

### Using non-invasive brain stimulation (NIBS) to interact with network activity and associated functions: Targeting brain oscillations as a promising strategy?

Brain oscillations reflect interactions between neuronal elements which functionally assemble into networks through synchronization in specific frequency bands, and which can be measured by encephalography (EEG/MEG). NIBS on the other hand can be used to stimulate cortical areas rhythmically at frequencies that characterize EEG/MEG-signals. This raises a series of intriguing questions: Could frequency-tuned NIBS be used to transiently entrain oscillatory network activity? Could this enhance the specificity of established NIBS interventions by adding a temporal to the customary spatial dimension of targeting? And may this promote associated functions? This talk will cover experiments that used frequency-tuned rhythmic TMS or tACS, combined with EEG/MEG recordings, to guide and document the effects of transcranial stimulation, with an emphasis on the visual/attention system. This has been used to address whether brain oscillations merely reflect correlates of the neuronal processes implementing brain functions (are inevitable side-products) or may also have explanatory power as to how the brain operates, and by extension may serve as targets for experimental and clinical interventions.

12.00 - 14.00
LUNCH BREAK

**SESSION 3.3 -** *Chair: Monique Esclapez (AMU, INS, Marseille, France)*

14.00 - 14.45

**Pierre LUPPI**
*(UMR 5292 CNRS/U1028 INSERM, Université Lyon I, Lyon, France)*

## Cortical activation during paradoxical (REM) sleep and its implication in learning and memory

Recent studies strongly support a role of the two states of sleep, slow wave (SWS) and paradoxical sleep (PS) in learning and memory consolidation. However, the mechanisms underlying the beneficial effect of both states of sleep on learning and memory have not yet been identified. To this aim, we recently identified at cellular level the populations of cortical neurons activated and displaying plasticity during PS hypersomnia by means of functional neuroanatomy. Their mapping clearly shows for the first time that only a small number of limbic structures are activated during PS in contrast to waking. Among them, the dentate gyrus (DG) is the only cortical region that display more activated neurons during PS hypersomnia than waking. Further, combining retrograde tracing, neurotoxic lesion and FOS immunostaining, we showed that neurons from the lateral part of the supramammillary nucleus (SuML) projecting to the DG, are responsible for the activation of DG granule cells during PS. These surprising results pointed out for the first time that the SuML/DG pathway activates DG granule cells specifically during PS. We propose that such activation might play a key role in the previously reported beneficial effect of PS on learning and memory. Indeed, many studies clearly indicate that PS is instrumental for memory consolidation. Further, it has recently been shown that PS deprivation in rats impairs consolidation of contextual fear conditioning. In parallel, it has also been recently demonstrated that granule cells play a key role in the formation of the contextual component of fear memories.

14.45 - 15.30

**Ivan SOLTESZ**
*(Stanford Neurosciences Institute, Stanford University, Stanford, CA)*

## Spatiotemporal Organization of Hippocampal Circuits

Distinct interneuronal subtypes deliver GABA to specific spatial domains of principal cells at particular times during behaviorally relevant network oscillations in cortical circuits. Recent results from awake mice have revealed emerging novel principles of the temporal ordering of interneuronal discharges during network oscillations in the hippocampus. I will discuss new evidence showing the highly non-homogeneous organization of inhibitory-excitatory microcircuits in the hippocampus is highly selective with respect to the long-distance projection patterns of the heterogeneous pyramidal cell populations. Next, the question of principal cell type-specific neuromodulation will be addressed. Finally, I will discuss results from data-driven, full-scale (1:1) computational models of the hippocampus that give us quantitative insights into the roles of the constituent cell types in ensemble network activities.

15.30 - 16.00
COFFEE BREAK

**SESSION 3.4 -** *Chair: Christophe Bernard (AMU, INS, Marseille, France)*

16.00 - 16.45

## William STACEY

*(Departments of Neurology and Biomedical Engineering, University of Michigan, Ann Arbor, MI)*

## Signal detection and synchrony in the noisy brain

Principle cells in the brain are faced with the daunting task of integrating thousands of inputs in an extremely noisy environment. However, under certain conditions that noise is beneficial to signal detection, and can be the underlying force generating coherent oscillations. This has important implications to normal and pathological brain function. Using computational, in vitro, and in vivo data, we show that synaptic noise plays an important role in detection of subthreshold signals and in generation of both normal and abnormal oscillations. The physical mechanisms of stochastic resonance and coherence resonance describe and quantify these effects. However, physiological neural networks deviate from those theories when highly active: they can generate coherent oscillations even with disrupted or completely absent connectivity between cells. Thus, one of the natural states of large neural networks– regardless of connectivity–is to oscillate. From these results, we hypothesize that synaptic noise is integral to tuning individual signal detection, generating fast oscillations, and is one potential trigger for seizures.

16.45 - 17.30

## Fabrice BARTOLOMEI

*(Aix-Marseille University, Institute for Systems Neuroscience, and Clinical Neurophysiology and Epileptology, AP-HM, Marseille, France)*

## Networks in Epilepsy: a clinical utility?

Focal epilepsies are increasingly recognized as disease affecting large scale brain network. In comparison with other brain diseases, this involvement is characterized by specific dynamic (interictal/ictal states) affecting brain rhythms. Different approaches (EEG, SEEG, MEG, fMRI, structural MRI) have been used to this aim. The clinical consequences are however disputable. Many clinicians in the field of the epilepsies still consider that focal epilepsies are focal diseases. In this talk we will discuss the role of network approaches in our understanding and in our management of these diseases.

17.30 - *Closing remarks*