Complex sensory stimuli entrain brain oscillations

Organizer: Joachim Gross

Room:# 103

Date and Time: Monday, October3 / 08:30-10:30

Entrained Brain Oscillations and the Processing of Complex Auditory or Visual Stimuli
There is a growing number of studies demonstrating a temporal reorganization of human brain oscillations in response to complex quasi-rhythmic stimuli such as speech. The reorganization is characterized by a temporal alignment of frequency-specific brain activity to stimulus features. However, the differential contributions of bottom-up and top-down processes to this alignment have remained largely unknown. Furthermore, we are just beginning to understand what physical stimulus features and what linguistic structures are entraining brain activity. Recent studies suggest that this entrainment reflects cognitive processes of temporal coding, segmentation and prediction that are orchestrated by hierarchically organized brain oscillations. In this symposium we are presenting and discussing the latest developments in this field. Specifically, we explore the role of brain oscillations in the coding and parsing of hierarchical linguistic structures and the top-down modulation of bottom-up entrainment through visual and auditory sensory channels. Through presentations and discussions our symposium aims to contribute to a better understanding of how rhythmic brain activity assists in the processing of complex, naturalistic stimuli and, ultimately, facilitates human communication.

Speakers:

- **David Poeppel** (New York Univ., USA/Max Planck Inst. for Empirical Aestetics)
  "Cortical entrainment to abstract structures in language"

  I discuss recent electrophysiological studies that focus on a general question about the neural implementation of language comprehension. Based on a set of experiments using MEG and ECoG, I develop how temporal encoding can form the basis for more abstract, structural processing. The results demonstrate that, during listening to connected speech, cortical activity of different time scales is entrained concurrently to track the time course of linguistic structures at different hierarchical levels (words, phrases, sentences). Importantly, the neural entrainment to hierarchical linguistic structures is dissociated from the neural encoding of acoustic cues as well as from processing the predictability of incoming words. These results demonstrate syntax-driven, internal construction of hierarchical linguistic structure via entrainment of hierarchical cortical dynamics. The conclusion — that language is syntactic-structure-driven — provides a new neurobiologically motivated provocation to the prevailing view that language comprehension is 'mere' statistics.

- **Hyojin Park** (Univ. of Glasgow, UK)
  "Lip movements during speech entrain observers' low-frequency brain oscillations"

  During continuous speech, lip movements contain rhythmic visual components that facilitate speech processing by the observer. Here, using MEG we investigated for the first time directly how these rhythms interact with rhythmic brain activity in participants watching movies of a speaker. Our study consisted of four main steps. First, we investigated coherence between oscillatory brain activity and speaker's lip movement and demonstrated significant entrainment in visual cortex. Second, we compared this synchronization at different levels of attention and found that enhanced attention to visual speech leads to enhanced synchronization in visual cortex. Third, we used partial coherence to remove contributions of the coherent auditory speech signal from the lip-brain. This analysis identified significant coherence between left motor cortex and lip movements. Fourth, we demonstrate that this coherence predicts

comprehension accuracy. Our results emphasize the importance of visually entrained and attention-modulated rhythmic brain activity for the enhancement of audiovisual speech processing.

- **Jonas Obleser** (Univ. of Lübeck, Germany)
"The oscillatory dynamics of auditory attention"

Listening requires us to regulate auditory attention dynamically in time and space. Listeners must be able to, on the one hand, follow the temporal structure of acoustic stimulation (i.e., "entrain" to the sensory environment) and on the other hand disengage (i.e., "functionally inhibit") brain areas processing task-irrelevant information at certain times. A guiding hypothesis of our work asserts that neural oscillatory entrainment (~1–5 Hz) index a listener's faithful tracking of acoustic stimuli, while the power of alpha oscillations (~8–13 Hz) reveals the deployment of top-down control. I will present evidence from electro-/magnetoencephalography studies showing that listeners use both mechanisms to regulate auditory attention. First, when attending to one of two concurrent speech streams, sensory entrainment and alpha power lateralization are in sync with the on-going speech stream, but lag each other. Second, individual's ability to utilize an attentional cue for improved precision in sensory memory can be predicted by the degree to which alpha power is dynamically increased in the delay period. In sum, these data demonstrate how auditory attention in time and space utilizes two complementary neurobiological mechanisms of bottom-up sensory entrainment versus top-down functional inhibition.

- **Anne Koesem & Virginie van Wassenhove** (CEA DSV/I2BM, INSERM, NeuroSpin center, France)
"Oscillatory neural activity controls the encoding of continuous speech"

During speech listening, the brain parses a continuous acoustic stream of information into computational units (e.g. syllables or words) necessary for speech comprehension. Recent hypotheses have proposed that neural oscillations contribute to speech parsing but whether they do so on the basis of acoustic cues (bottom-up acoustic parsing) or as a function of available linguistic representations (top-down linguistic parsing) is unknown. In this magnetoencephalography study, we contrasted acoustic and linguistic parsing using bistable speech sequences. While listening to speech sequences, participants were asked to maintain one of the two possible speech percepts through volitional control. We predicted that the tracking of speech dynamics by neural oscillations would not solely follow the acoustic properties but also shift in time according to participant's conscious speech percept. Our results show two dissociable markers of neural-speech tracking under endogenous control: small modulations in low-frequency oscillations and variable latencies of high-frequency activity (sp. beta and gamma bands). While changes in low-frequency neural oscillations are compatible with the encoding of pre-lexical segmentation cues, high-frequency activity specifically informed on an individual's conscious speech percept.

MEG neuroimaging of human brain development

Organizer: Blake W Johnson

Room:# 104

Date and Time: Monday, October3 / 08:30-10:30

Toward an Understanding of the Spatio-Temporal Dynamics of Human Brain Development with MEG Neuroimaging

This symposium brings together developmental MEG researchers from the US, UK, Australia, and Japan. Four of the speakers will describe their experiences using the Tristan Technologies and Yokogawa/KIT pediatric MEG systems which have recently provided new windows into brain development from infancy through the pre-school years. Two speakers will relate data from older children obtained with conventional MEG instrumentation. The talks will encompass studies of typical brain development of visual, auditory and motor processes, and studies of atypical development including fetal alcohol syndrome disorders and autism spectrum disorders. Taken together the talks of this symposium will summarize the current state of pediatric/child MEG research and illuminate future scientific and clinical directions.

Speakers:

- **Banu Ahtam** (Harvard Medical School, USA)
  "Human brain development research with MEG at Boston Children's Hospital"

  The electrophysiological aspect of brain development is studied at Boston Children's Hospital using a pediatric MEG system ("BabyMEG") (Tristan Technologies), in our new clinical MEG facility directed by Yoshio Okada. BabyMEG is a whole-head system with two layers of magnetometers: inner-layer, 270 magnetometers; and outer-layer, 35, 3-axis magnetometers; plus 9 reference magnetometers. There is an 8-9mm gap between the magnetometers and the outer surface of the helmet (sized up to 95% of boys at 36 months). The facility is equipped for studying inpatients under sedation, outpatients, and healthy children. BabyMEG is in a 2-layer MSR. Environmental noise can be rejected with noise cancellation methods (passive MSR shielding, external active shielding, signal-space projection, synthetic gradiometer). Spontaneous brain activity can be monitored in real-time (collaboration with MGH MEG Team, directed by Matti Hämäläinen). We use a closed-cycle helium recycler (Cryomech). We can perform simultaneous MEG/EEG measurements. We study epileptiform activity and localization of focal generators, and in healthy children, sleep, detailed characterization of sensory and motor areas of the cortex, and language development. We will expand our studies to other disorders such as cerebral palsy. The features of our facility expand the versatility and power of MEG for studying human brain development.

- **J Christopher Edgar** (Children's Hospital of Philadelphia, USA)
  "The maturation of auditory responses in infants and young children: a cross-sectional study from 6 to 59 months"

  An understanding of the maturation of auditory cortex responses in typically developing infants and toddlers is needed to identify auditory processing abnormalities in infants at risk for neurodevelopmental disorders. The availability of infant and young child magnetoencephalography (MEG) systems may now provide near optimal assessment of left and right hemisphere auditory neuromagnetic responses in young populations. To assess the performance of a novel whole-head infant MEG system, a cross-sectional study examined the maturation of left and right auditory cortex responses in children 6- to 59-months of age. Blocks of 1000Hz (1st and 3rd blocks) and 500Hz tones (2nd block) were presented while MEG data were recorded using an infant/young child biomagnetometer (Artemis123). Data were

obtained from 29 children (11 males; 6- to 59-months). Latency measures were obtained for the first positive-to-negative evoked response waveform complex in each hemisphere. Findings of strong age and latency associations, sensitivity to tone frequency, and good test-retest reliability support the viability of longitudinal infant MEG studies that include younger participants as well as studies examining auditory processing abnormalities in infants at risk for neurodevelopmental disorders. Building upon the above, preliminary data from a longitudinal study examining brain structure-function associations in infants (3- to-18 months) are presented.

- **Mitsuru Kikuchi** (Kanazawa Univ., Japan)
  "Atypical development of the auditory system in children with autism spectrum disorder"

  Brain responses to auditory stimuli in children with autism spectrum disorder (ASD) have been studied as a physiological indicator of language acquisition, cerebral laterality and regional connectivity. The earliest cortical component of the auditory evoked field (AEF) (i.e., the P1m) is a prominent component in 1- to 10-year-old children. Recently, a child-customized MEG device has facilitated the acquisition of bi-hemispheric recordings, even in young children. Using the child-customized MEG device, we reported that the children with ASD exhibited significantly less leftward lateralization in their P1m intensity compared with the typically developing (TD) children (2 to 5 years old). In addition, we reported that language-related performance was reflected in the dipole intensity of the P1m in TD young children (2 to 5 years old) even after controlling for confounding factors (e.g., age). Our recent study with wider age range group (3 to 10 years old) demonstrated an inverted U-shaped growth curve for the P1m dipole intensity in the left hemisphere in TD children, whereas more diversified age-related distribution was observed in children with ASD. These our results from MEG studies contribute to our understanding of diversified pathophysiological mechanisms in the central nervous systems in young children with ASD.

- **Wei He** (Macquarie Univ., Australia)
  "Effective connectivity of core brain networks for perception and cognition in preschool age children"

  Theoretical frameworks for understanding functional brain maturation suggest an increasingly fine-grained brain network including progressively specialized regional activity and more organized patterns of inter-regional connectivity during development. However, due to the practical challenges of conducting brain-imaging studies with preschool children, there is little direct evidence bearing on the development of such connections in the human brain. We measured brain activity in preschool age children with a custom-sized paediatric MEG system and examined connectivity patterns with dynamic causal modelling (DCM). Face responses (M170 and M250) were obtained in 10 children (63.6 ± 9.96 months) and auditory mismatch (MMF) fields were obtained from 25 children (51.83 ± 7.77 months). DCM results showed a forward regulation modulated by face repetitions within the immature face network that does not exist in adults, and for MMF, an extra frontal lobe connection to auditory cortex. These results are the first MEG evidence that bear directly on competing theories of human brain development in core brain networks during the preschool years.

- **Klaus Kessler** (Aston Univ., UK)
  "Local dysregulation, global hypoconnectivity, and deficient predictive coding in ASC"

  Gamma band activity (GBA) has been investigated as a proxy measure for local connectivity in order to test the hypothesis that connectivity at the local scale could be overexpressed in autism spectrum conditions (ASC), resulting in symptoms such as hypersensitivity to sensory stimulation ("the world is too intense"). However, mixed results have shown both elevated and reduced GBA in ASC. Furthermore, physiological and electrophysiological measures on ASC show that inhibitory neuron density is reduced and local cross-frequency coupling is under-expressed, suggesting that local dysregulation in form of a suboptimal balance between excitation and inhibition could provide a more plausible alternative

explanation for the apparently paradoxical coexistence of enhanced and reduced GBA and of hyper- and hyposensitivities in ASC. In conjunction with consistently reported reductions in long-range connectivity in ASC, an overall picture of local disorganisation including deficient top-down input from control areas of the brain emerges that is compatible with the notion that predictive coding might be particularly affected in ASC. In the light of these theoretical considerations we will present preliminary MEG data and analysis focussing on GBA and cross-frequency coupling.

- **Julia M. Stephen** (The Mind Research Network, USA)
  "Visual deficits in children with fetal alcohol spectrum disorder – implications for understanding normal development"

Fetal alcohol spectrum disorder (FASD) is a neurodevelopmental disorder that is defined by both structural and functional impairments associated with prenatal alcohol exposure. Initial studies implicated executive function deficits even in the absence of facial dysmorphias associated with fetal alcohol syndrome. Our recent MEG studies in adolescents (aged 12-21 years) indicate that both basic visual processing and cognitive functioning are impaired in children with FASD. Using a prosaccade task we have identified delays in visual processing in children with FASD relative to age-matched controls. Development of frontal networks was investigated using an antisaccade task with differences in the eye gaze network in children with FASD relative to healthy controls. Furthermore, our more recent studies in younger children with FASD (8-12 years) indicate that these processing delays are observed during performance of a visual go-nogo task, while additional deficits are observed in frontal cortex. Finally, our most recent results indicate that MEG differentiates children with FASD from children with attention deficit hyperactivity disorder (ADHD), despite the challenges of differentiating these groups based on neuropsychological testing. These results provide additional evidence that measurement of visual processing networks using MEG may be an important tool for early identification and classification of neurodevelopmental disorders.

Next-Generation Sensors for Neuromagnetism I

Organizers: Lauri Parkkonen and Justin Schneiderman

Room:# 105

Date and Time: Monday, October3 / 08:30-10:30

Neuromagnetic Measurements beyond Low-Tc SQUIDs: Session 1

MEG has provided significant insights into the workings of the human brain and improved our ability to treat it in disease. MEG has also been the main technology driver in the field of biomagnetism; to date, the low-Tc SQUID has remained the sensor of choice for MEG. However, the emerging new generation of magnetic sensor technologies enables finer-grained sampling of the neuromagnetic field that the head surface for on-scalp MEG and within the neural tissue for invasive magnetoneurography. By moving beyond the limitations of low-Tc SQUIDs, these new approaches hold promise for major advancements over the state of the art in neuromagnetic recordings: the substantial increase in spatial resolution and signal-to-noise ratio as well as access to neuron-scale magnetic signals may drastically change our field. This symposium will not only provide an up-to-date picture of several sensor technologies that may rival low-Tc SQUIDs in neuromagnetism but it will also illustrate the value of these novel technologies for MEG. In addition, the symposium covers the challenges in moving from demonstrations with single sensors to practical systems.

Speakers:

- **Matti S. Hämäläinen** (Boston Children's Hospital, USA)
  "Hopes and dreams for on-scalp MEG"

  Thanks to their high sensitivity, low noise, and reliable operation, low-Tc SQUIDs are employed in all present whole-head MEG systems. However, these sensors need liquid helium as a refrigerant and thus the maintenance costs are relatively high and the distance between the sensors and the head in room temperature is typically of the order of 20 mm. The newest low-Tc SQUID MEG systems, e.g., our BabyMEG device, employ closed-circuit refrigeration eliminating the need of regular helium refills. While the sensor to room temperature distance can be thus reduced to about 6 mm, the dewar is still of fixed size. If high-sensitivity sensors operating without or with simple cooling could be produced, one could imagine an MEG system with an individualized helmet hosting an array of individual MEG sensors or "magnetrodes" immediately on the scalp of the subject. Provided that the noise level of the sensors is low enough, such a system would provide clear benefits in terms of spatial resolution and ability to detect sources which are temporally coherent over only small distances on the cortex. This talk will discuss the design constraints and challenges in the operation of such a fictional system.

- **Justin F. Schneiderman** (Univ. of Gothenburg and the Inst. of Neuroscience and Physiology, Sweden)
  "High-Tc SQUIDs for on-scalp MEG"

  High-Tc SQUIDs are a promising technology for on-scalp MEG (OS-MEG) for a number of reasons. First and foremost, they can be used to sample the neuromagnetic field at a distance of less than one mm from the head surface. Micro-cryocooling systems are furthermore reaching a level of maturity that enables development of a flexible OS-MEG sensor array that would fit arbitrary head sizes and shapes while eliminating the need for liquid cryogens. The translation of existing MEG sensor control and readout hardware and software to a high-Tc SQUID-based OS-MEG system is also straightforward because the operating principles of our sensors are the same as their low-Tc counterparts. Furthermore, the noise levels of high-Tc SQUIDs are sufficient for OS-MEG, especially in the low-frequency range (< 10 Hz). In this

talk, I will present our sensor technologies, results from benchmarking experiments on somatosensory and auditory evoked fields, and progress towards a whole-head high-Tc SQUID-based OS-MEG system.

- **Jürgen Dammers** (Forschungszentrum Jülich, Germany)
"High-Tc SQUID based MEG experiments and data analysis"

The technology of high-Tc SQUID has significantly been improved in recent years. Now the magnetic field resolution of high-Tc SQUIDs is comparable to that of standard low-Tc SQUIDs, which are typically employed in modern commercial whole-head MEG systems. In particular, a higher sensitivity in the low frequency range (<10Hz) has been achieved and demonstrated for high-Tc SQUIDs to now allow for source analysis. Results from MEG recordings using high-Tc SQUID will be presented and compared to those obtained from a standard low-Tc SQUID -based MEG system. Resting state brain activity from visual areas as well as evoked magnetic fields from sensory, motor and auditory regions will be shown together with findings from time–frequency decompositions and source localizations. In this talk, I will demonstrate that results obtained with a high-Tc SQUID system are in good agreement with those obtained from a commercial low-Tc MEG system. More importantly, the results indicate that the sensitivity of high-Tc SQUIDs is ready for MEG analysis including source localization.

- **Svenja Knappe** (NIST, Univ. of Colorado, Boulder, USA)
"Small-sized OPMs for an MEG prototype array"

Optically-pumped magnetometers (OPMs) can be optimized for a variety of applications. In biomagnetism, close proximity between source and sensor is very important and should be balanced with best noise performance of the sensor. Here, we demonstrate a prototype MEG array with an OPM sensor holder inspired by stereotactic frames. The uncooled chip-scale OPMs are sufficiently small to have the sensing volume at a distance of only a few millimeters from the scalp. Operating the OPMs in a low field environment allows for the recording of the N20m in human subjects with sufficient fidelity to apply standard biomagnetic processing. Averaged responses show amplitudes in the pT-range, the well-known dipolar field structure of cortical current sources is reproduced, and the result from an estimation of the cortical current is consistent with known SQUID results. This demonstrates the potential use of OPMs for biomagnetism either complementing SQUIDs or even replacing them at least in some applications. Fortunately, the large investment in post-acquisition processing can be retained from SQUIDs.

- **Peter Schwindt** (Sandia Nat'l Laboratories, USA)
"Towards a multi-channel magnetoencephalography system using optically pumped magnetometers"

There have been several demonstrations of using optically-pumped magnetometers (OPMs) to measure magneto-encephalographic signals. Following these demonstrations, there are several groups developing multi-channel OPM arrays to localize magnetic sources within the brain. We are working to develop a complete MEG system including a person-sized magnetic shield and a 36-channel array of OPMs. The current goal is to use the array to localize the magnetic sources in the auditory and somatosensory cortices associated with auditory and median nerve stimulation, respectively. The 36-channel array will consist of nine 4-channel sensor modules where the channels within each sensor are spaced by 18 mm and each sensor covers a 40 mm by 40 mm area of the head. The sensitivity of the magnetometer channels inferred from gradiometric measurements is < 5 fT/Hz$^{1/2}$ over a frequency range of 5 to 100 Hz. We will present results on the performance our OPM array in the person-sized shield and preliminary studies with human subjects. Finally, we will highlight system-level issues encountered in the development our OPM-based MEG system.

Multimodal Insights into Neural Oscillations

Organizers: Christopher Edgar and Karim Jerbi

Room:# 104

Date and Time: Monday, October3 / 13:30-15:30

Multimodal Studies of Neural Oscillations: from Basic Systems to Pathology
Accepting the hypothesis that functional brain measures are more proximal to neurobiological mechanisms and/or pathways associated with neurologic and psychiatric disorders than overt behavioral measures, it is hoped that neuroimaging-based endophenotypes will identify biological mechanisms in these populations at the level of neural circuits. This symposium provides an overview of work in this area, with presentations first reviewing basic aspects of neural oscillatory systems, to presentations discussing how these systems can be modulated via pharmacological or cognitive treatment, to presentations reviewing studies of neural oscillations (and the ability to modulate abnormal oscillatory neural rhythms) in schizophrenia and autism. Each speaker is an expert in this area, with multiple publications over the last decade and thus with the ability to provide a broad overview of key topics in this rapidly growing area of research. A strength of the symposium is that each speaker will focus on the use of multimodal imaging to better understand normal and abnormal neural oscillatory activity. Thus, the proposed symposium showcases the increasingly sophisticated research in this area and the continued maturation of MEG psychiatry and neurology research.

Speakers:

- **Karim Jerbi** (Univ. of Montreal, Canada)
  "The curse of modality and why gamma oscillations might be a peacemaker: Bridging MEG, fMRI, intracranial EEG and GABA neurotransmission"

  Progress in monitoring und understanding brain network dynamics in health and disease draws on a wide range of neuroimaging and electrophysiological brain recording techniques. This has also resulted in parallel research fields with difficulties connecting their respective findings. Luckily, the surge in multi-modal investigations of brain function has shed light onto the links between observations made with different techniques, but addressing the same cognitive process or the same patient population. In this context, neuronal oscillations, and in particular gamma-band activity, may provide a useful framework. This talk will illustrate this using recent findings and ongoing research that connects MEG Gamma activity to GABA-A receptor density in working memory and visual processing tasks (Kujala et al. 2015). Ongoing work linking intracranially recorded gamma activity with 3T and 7T BOLD signals during visual search will also be reported. Finally, the complementary information provided by other frequency ranges of the MEG and EEG spectum will be discussed, and current/future challenges will be highlighted.

- **Krish Singh** (CUBRIC, Cardiff Univ., UK)
  "Oscillatory biomarkers in health and disease: Their use, pharmacological manipulation, and neurophysiologically informed modelling"

  It is becoming increasing clear that sensory/motor oscillatory responses, such as visual and motor gamma, may provide a new direct window onto synaptic function, providing translational biomarkers of healthy individual variability, disease state, behavioural performance and pharmacological manipulation that provide extra information that goes beyond that offered by techniques such as fMRI. Using examples from healthy control data, pharmacological studies of GABA and Glutamate modulating drugs and a recent acquired Schizophrenia cohort, this talk will illustrate the use of these measures and how modelling frameworks such as Dynamic Causal Modelling (DCM) can be used to provide

neurophysiologically relevant information that goes beyond, and is more sensitive than, the simple data features.

- **Ole Jensen** (Radboud Univ., The Netherlands)
  "Posterior alpha oscillations under top-down control are aberrant in ADHD patients"

Alpha band oscillations in sensory regions have been implicated in the routing of visual input during the allocation of attention. To identify the mechanisms of the top-down control we have conducted a set of MEG (Popov et al., submitted), TMS/MEG (Marshall et al., 2015, J Neurosci) and fMRI/EEG (Zumer et al., 2014 PLOS Biol) investigations. They point to the frontal eye-field playing an important role. A study relating the MEG to DTI (Marshall et al. 2015, PLOS Biol) implicates the superior longitudinal fasciculus in the control. We are currently investigating the contribution of the striatum (Horschig et al., 2015, PLOS One). Problems in the allocation of attention might be associated with an inability to appropriately modulate the alpha band activity. Indeed we have demonstrated that ADHD patients have a reduced ability to sustain the modulations in alpha band during the allocation of attention (terHuurne et al., 2013, Biol Psychiatry; Vollebregt et al., in press, ClinNeurophys). In future work we hope to uncover the frontal structures associated with this aberrant modulation. Furthermore we will investigate if neurofeedback training targeting alpha oscillations (Okazaki et al., 2015, Neuroimage) can be used to reduce the symptoms in ADHD.

- **J. Christopher Edgar** (Children's Hospital of Philadelphia, USA)
  "Auditory encoding in schizophrenia and unaffected relatives: low- rather than high-frequency superior temporal gyrus auditory abnormalities are primary to schizophrenia"

Studies examining superior temporal gyrus (STG) auditory encoding in schizophrenia (SZ) have observed low-frequency (alpha-to-beta) as well as 40Hz auditory steady-state abnormalities. The Edgar et al. (2013) multimodal findings suggested that disease-associated loss of left STG gray matter cortical thickness (CT) in SZ accounted for the 40Hz but not low-frequency abnormalities in SZ. Building on this study, additional analyses were performed in an expanded sample of SZ (50% increase; N=63), an expanded sample of HC (100% increase; N=63), and now also including a group of unaffected relatives (UR; N=29). Less left STG CT and lower left 40Hz steady-state inter-trial coherence in SZ and UR indicated these left STG structure and function measures as markers of genetic liability to SZ. An expected association between increased age and decreased left STG steady-state activity only in HC suggested early damage to auditory gamma circuits disrupting 40 Hz activity in SZ and family members. In contrast, higher left low-frequency (theta-to-alpha) total power and inter-trial coherence in HC and UR versus SZ indicated that left STG low-frequency abnormalities were specific to disease. Present findings are discussed within the context of other studies indicating that low-frequency rather than high-frequency STG auditory abnormalities are primary to SZ.

- **Mingxiong Huang** (Univ. of California San Diego, USA)
  "Resting-state MEG Studies of Mild Traumatic Brain Injury and Post-traumatic Brain Disorder and Relationships with Diffusion Tensor Imaging and fMRI"

Mild traumatic brain injury (mTBI) is a leading cause of physical, cognitive, and emotional deficits in military members and the general public. mTBI also substantially increases the risk of post-traumatic stress disorder (PTSD). The pathophysiology of mTBI is not completely understood, and the neuronal mechanisms by which mTBI enhances the likelihood of PTSD even less clear. This presentation reviews resting-state magnetoencephalography (rs-MEG) studies of mTBI and PTSD. Relationships between MEG findings and diffusion tensor imaging and rs-fMRI are also examined. Main findings are: 1) MEG slow-wave (delta-band, 1-4Hz) source magnitude imaging provides mTBI diagnosis on a single-subject basis, with slow-wave abnormalities due, in part, to reduced fractional anisotropy in nearby white-matter tracts.

2) Resting-state MEG functional connectivity measures reveal abnormal excitation in mTBI, with these findings consistent with reduced inhibition and over excitation in gray matter, and thus with a gray matter glutamate and GABA Imbalance after mTBI. 3) In individuals with mTBI with PTSD, MEG imaging identifies neural oscillatory dysfunction in emotion processing neurocircuitry (i.e., amygdala, ventro-medial prefrontal cortex(vmPFC), and hippocampus), with rs-MEG results consistent with resting-state fMRI default mode network findings in PTSD. Given the above, the future clinical use of MEG for mTBI and PTSD is discussed

- **Tzvetan Popov** (Univ. of Konstanz, Germany)
  "Training-induced modulation of alpha oscillations and their role in pathophysiology of schizophrenia"

Research has established an important role of brain oscillatory activity as a potential mechanism in cognitive deficits and pathophysiology in schizophrenia. We used a paired-click paradigm to study effects of cognitive training in a neuroplasticity-oriented learning protocol on induced oscillatory activity associated with a sensory gating phenomenon. Three predominant observations emerged from a series of experiments. First, stimulus processing prompts a decrease in alpha amplitude (8-14Hz) in primary sensory (auditory) and higher-order (parietal) cortices. This modulation is less pronounced in patients and is correlated with the gating deficit. Second, 4 weeks of targeted neuroplasticity-based cognitive training influence both the gating deficit and amplitude modulation of alpha oscillations. Third, gating of sensory information is not confined to sensory cortices. Spectrally resolved Granger analysis revealed that, prior to stimulus onset, primary auditory cortices are under top-down control by prefrontal cortex, realized at ~10Hz. Findings are discussed in light of theories of the role of alpha oscillations in organizing functional brain architecture and of schizophrenia conceived as a cerebrally implemented network deficiency manifesting in cognitive deficits.

Next-Generation Sensors for Neuromagnetism II

Organizers: Lauri Parkkonen and Justin Schneiderman

Room:# 105

Date and Time: Monday, October3 / 13:30-15:30

Neuromagnetic Measurements beyond Low-Tc SQUIDs: Session 2
MEG has provided significant insights into the workings of the human brain and improved our ability to treat it in disease. MEG has also been the main technology driver in the field of biomagnetism; to date, the low-Tc SQUID has remained the sensor of choice for MEG. However, the emerging new generation of magnetic sensor technologies enables finer-grained sampling of the neuromagnetic field bothat the head surface for on-scalp MEG and within the neural tissue for invasive magnetoneurography. By moving beyond the limitations of low-Tc SQUIDs, these new approaches hold promise for major advancements over the state of the art in neuromagnetic recordings: the substantial increase in spatial resolution and signal-to-noise ratio as well as access to neuron-scale magnetic signals may drastically change our field. This symposium will not only provide an up-to-date picture of several sensor technologies that may rival low-Tc SQUIDs in neuromagnetism but it will also illustrate the value of these novel technologies for MEG. In addition, the symposium covers the challenges in moving from demonstrations with single sensors to practical systems.

Speakers:

- **Visa Vesterinen** (VTT Technical Research Center of Finland, Finland)
  "The Kinetic Inductance Magnetometer"

  Commercially established technology based on low-Tc SQUID sensors has shown its strength in ultrasensitive recordings of neuromagnetic signals. The SQUIDs are based on the Josephson effect in superconducting tunnel junctions leading to a nonlinear response of magnetic signals. We present here an alternative, the kinetic inductance magnetometer (KIM), based on the intrinsic magnetic nonlinearity of the superconducting material itself [1]. A benefit is that the sensors are compatible with RF multiplexed readout. Another advantage is simplicity: the magnetometers are composed of a single thin-film layer, as opposed to 5–10 layers of commercial low-Tc superconductor (LTS) fabrication processes. Furthermore, simplicity is expected to be of particular interest in the context of high-Tc (HTS) devices. HTS SQUIDs have not reached the technological maturity needed in routine production of large sensor arrays though HTS technology has large potential in terms of simpler cryogenics such as miniaturized closed-cycle cryocoolers. In this presentation, we will show the first experimental results obtained with HTS KIMs. We will also review our previous results with LTS KIMs currently reaching electronics-limited magnetic field noise level at about 30 fT/Hz$^{1/2}$, and a dynamic range of 600 nT. We also provide an update about electronics.
  [1] J. Luomahaara et al., Nat. Commun. 5, 4872 (2014)

- **David A. Simpson** (Univ. of Melbourne, Australia)
  "Exploring magnetism in biology using defects in diamond"

  Magnetic resonance spectroscopy techniques have changed the face of biomedical research and our view of the human body to the point where electron spin resonance (ESR), nuclear magnetic resonance (NMR) and magnetic resonance imaging (MRI) now permeate most areas of clinical science and research. State-of-the-art MRI technology has recently demonstrated sub-millimetre imaging resolution, but if the sub-cellular worlds of biology and chemistry are to be fully explored, a transformative shift in technology is needed. In this presentation I will describe how an atomic-sized nitrogen vacancy (NV) defect in diamond can be used to image magnetic signals emanating from biological systems. In particular, I will detail our

journey in applying this quantum system to interesting magnetic detection problems and show how the fragile decoherence of the NV electronic spin can be exploited to detect weak magnetic fields. Finally, I will describe our recent work in scaling this technology up to image magnetic nanoparticles and the electron spin resonance signals from paramagnetic molecules in solution over wide fields of view with diffraction limited resolution.

- **Myriam Pannetier-Lecoeur** (CEA Saclay, Gif-sur-Yvette, France)
"Spintronics sensors for biomagnetism at neuron scale"

Magnetic resonance spectroscopy techniques have changed the face of biomedical research and our view of the human body to the point where electron spin resonance (ESR), nuclear magnetic resonance (NMR) and magnetic resonance imaging (MRI) now permeate most areas of clinical science and research. State-of-the-art MRI technology has recently demonstrated sub-millimetre imaging resolution, but if the sub-cellular worlds of biology and chemistry are to be fully explored, a transformative shift in technology is needed. In this presentation I will describe how an atomic-sized nitrogen vacancy (NV) defect in diamond can be used to image magnetic signals emanating from biological systems. In particular, I will detail our journey in applying this quantum system to interesting magnetic detection problems and show how the fragile decoherence of the NV electronic spin can be exploited to detect weak magnetic fields. Finally, I will describe our recent work in scaling this technology up to image magnetic nanoparticles and the electron spin resonance signals from paramagnetic molecules in solution over wide fields of view with diffraction limited resolution.

- **Elena Boto** (Univ. of Nottingham, UK)
"The Potential of Optically-Pumped Magnetometers for MEG"

MEG remains limited by low spatial resolution and sensitivity, caused by both the inherently small magnetic fields generated by the brain and the relatively large scalp-to-sensor distance. The latter is limited in current systems due to a requirement for detectors operating at low temperature. However, this could be overcome using optically-pumped magnetometers (OPMs), which have the advantage that they can be brought to within few millimetres of the scalp, thus offering increased sensitivity. In this talk I will first present the results of simulations in which we quantify the advantages of hypothetical OPM systems in terms of sensitivity, reconstruction accuracy and spatial resolution. We show that a multi-channel whole-head OPM system would offer up to an order of magnitude improvement in sensitivity for an adult brain as well as clear improvements in reconstruction accuracy and spatial resolution. However, I also show that such improvements depend critically on accurate forward models; indeed, reconstruction accuracy of the OPM system outperformed that of a SQUID only if the forward field error was less than 5%. Secondly, I will present our first experimental study, showing evidence that commercial OPMs are able to accurately characterise stimulus evoked and induced (oscillatory) changes in the human magnetoencephalogram.

- **Lauri Parkkonen** (Aalto Univ., Finland)
"From sensors to a MEG system"

Recent developments in magnetic sensing have made it feasible to record MEG signals within millimeters from the scalp and allow sensor arrays adaptable to the head size and shape of each individual and even to the research question at hand. While this flexibility may drastically improve the signal-to-noise ratio, it calls for methods to optimize the sensor locations, to accurately measure the actual sensor locations and sensitivity directions with respect to the head, and to adapt external interference suppression systems to each measurement. Here, I will discuss these aspects that need to be tackled when moving from demonstrations with single sensors to a robust multichannel system that can be operated in standard

magnetically shielded rooms. I will also present our simulations on optimizing such on-scalp arrays for picking up brain signals and for rejecting external interference.

Cutting Edge of MEG and ECoG based BMIs

Organizers: Masayuki Hirata

Room: # 103

Date and Time: Monday, October3 / 17:00-18:00

Cutting Edge of MEG and ECoG based Brain Machine Interfaces

Brain machine interface (BMI) is a promising technology for functional restoration and neurofeedback. In this symposium, 4 leading researchers present the cutting edge of BMIs using MEG and ECoG, focusing on motor and cognitive BMIs. We will clarify common and different points between MEG and ECoG in terms of BMI. Both MEG and ECoG well estimate localized oscillatory modulation, which we can use as decoding features for BMIs. MEG is noninvasive but also has high spatiotemporal resolution. They are important and appropriate factors for neurofeedback. MEG has broader spatial coverage than ECoG. This is more appropriate to estimate transcortical connectivity, which may contribute to neural decoding of higher order brain functions. MEG is inferior in the sensitivity of high frequency oscillatory activity, which contains rich neural information. In contrast, ECoG enables accurate real time control of a robotic arm by detecting high frequency oscillation in a single trial basis. By fully utilizing and improving these properties, we may light up the future perspective of MEG and ECoG based BMIs.

Speakers:

- **Ole Jensen** (Radboud Univ., The Netherlands)
  "Alpha activity modulated by attention used for MEG brain-computer interfaces and neurofeedback"

  Oscillatory activity in the alpha-band is strongly modulated by spatial attention. We investigated if these modulation can be used to control a brain-computer interface (Horschig et al., 2015, Brain Topography) using a paradigm in which subjects, on their own will, attended left or right. This allowed them to control a simple interface. Eight of eleven subjects achieved classification rates significantly above chance level. We conclude that posterior alpha power can successfully be used as a control signal in brain-computer interfaces. Next we investigated whether real-time neurofeedback training of the alpha lateralization can cause subsequent changes in visual detection (Okazaki et al. 2015, Neuroimage). The experiment consisted of assessment before and after the neurofeedback. During neurofeedback, two face stimuli superimposed with noise were presented bilaterally. The visibility of the stimuli was varied according to the momentary degree of hemispheric alpha lateralization directed by attention. We found that hemispheric alpha lateralization increased with neurofeedback. Surprisingly, comparing pre- to post-training, detection performance decreased for stimuli presented in the un-attended hemifield during neurofeedback. Thus, neurofeedback training alters alpha lateralization, which in turn decreases performances in the untrained hemifield. Our neurofeedback could be of potential use for reducing distractibility in attention deficit patients.

- **Kyousuke Kamada** (Asahikawa Medical Univ., Japan)
  "ECoG-based BCI for motor functions"

  A brain-computer-interface (BCI) allows the user to control a device with brain activity. Most of today's BCI research focuses on analyzing EEG and MEG which provide only limited signal to noise ratio. Electrocorticographic (ECoG) signals allow the investigation of spatially highly focused task-related activation within the high gamma frequency band, making the discrimination of complex grasping tasks possible. Common spatial patterns (CSP) are used for BCI systems and provide a powerful tool for feature optimization. This work focused on the discrimination of (i) three complex hand movements, (ii) hand movement and idle state. Two subjects S1 and S2 performed single 'open', 'peace' and 'fist' hand poses

and (iii) one subject S3 controlled a humanoid. Results showed for (i) an error rate of 7.22 % and 1.17 % for S1 and S2. For motor-imaginary to control the humanoid, (iii) S3 could perform such control over 4 sessions: 3 of those were performed over one day and the last one was performed two days afterwards. The performance of the classifier improved, reaching about 90% finally. This experiment showed that ECoG-based motor imagery performed well despite a short training period, providing future possibility for MEG-based BCI with higher sensitivity than present MEG sensors.

- **Jun Sic Kim** (Seoul Nat'l Univ., Korea)
  "Prediction of movement intention based on connectivity"

In most of brain-machine interface (BMI) studies for movement, the prediction models have been optimized for kinetic states. This model may not be suitable in the idle state during resting. This potential maladaptation could lead to a sudden accident or unintended movement resulting from prediction error. Thus, prediction of movement intention is needed to build a reasonable BMI system. The kinetic movement is performed through the dynamic change of brain activity such as resting, movement selection, planning, preparation, and execution. The motor network including the primary motor cortex, premotor area, supplementary motor area, and the dorsolateral prefrontal cortex is involved in these movement states. Neuronal communication would increase within the motor network in the movement state. In this study, we investigated the temporal dynamics in the motor/sensory-related networks to predict movement intention, trajectory estimation, and sensory feedback using ECoG and MEG. Movement intention was successfully predicted by connectivity analysis, and the trajectory of arm movement was also well predicted by linear regression of brain activity from motor-related regions. Furthermore sensory-related cortex would also contribute to predict trajectory prediction as much as motor cortex. These results suggest that temporal dynamics in motor-sensory networks is an excellent approach for prediction of movement and its states.

- **Masayuki Hirata** (Osaka Univ. Medical School, Japan)
  "ECoG and MEG as neural signals for BMIs"

Both ECoG and MEG are good signals for BMIs for motor and communication control. Using ECoG, we demonstrated high γ activity is useful to decode movement type and successfully controlled a robotic arm in real time. A tetraplegic patient with ALS was able to his communication support device using 'γ switch': his high γ activity in the motor area.
High γ activity is subtle but more focally distributed and better reflect functional localization than α and β activity. ECoG can stably detect this subtle high γ activity in single trial basis. This high sensitivity of ECoG in the high frequency band enables ECoG-based BMI accurate decoding. Using MEG, although its performance as a BMI signal is inferior to that of ECoG, low frequency components or powers of magnetic fields offer higher decoding accuracy than high γ activity. Low frequency components are clear and large enough to be stably detected by MEG. This robustness of low frequency components enables MEG accurate decoding. However, present MEGs are insensitive to detect high γ activity in single trial basis. Improvement of sensitivity of MEG in the high frequency band will not only improve the performance of MEG-based BMIs but also open new research fields such as cross frequency coupling between low and high frequency oscillations.

Network Disruption in Brain Disease

Organizers: Louis Lemieux and Hyang Woon Lee

Room: # 104

Date and Time: Monday, October3 / 17:00-18:00

Network Disruption in Neurological and Psychiatric Disorders
This symposium will consist of a combination of speakers in clinical neuroscience field for various neurological and psychiatric disorders. The aims of this symposium are to cover the latest topics in multimodal neuroimaging such as EEG, MEG, functional MRI, and DTI, with emphasis on connectivity mapping, provide training on the updated researches and latest methods, and provide a forum for rich discussion on more general approaches for multimodal brain mapping techniques, interpretations of the combined results, as well as future directions. Overall, studies on network properties and functional connectivity are becoming important tools for assessing abnormal brain organization in various neurological and psychiatric disorders and will help expand our understanding of identifying networks disruption in these conditions.

Speakers:

- **Louis Lemieux** (Univ. of College London, UK)
  "Multimodal functional neuroimaging in clinical neuroscience"

  As the first speaker, I will open the symposium with an overview of the role of multimodal imaging in clinical neuroscience, with emphasis on the role of synchrony of acquisitions as a function of the phenomena under study and the hypotheses being tested. I will place this discussion in the context of a more general data fusion framework. I will illustrate the points made using key examples in the investigation of a number of neurological conditions.

- **Maxime Guye** (Aix-Marseille Univ., France)
  "What can we learn from functional connectivity in neurological diseases?"

  Functional connectivity (FC) has been extensively studied in neurological disorders and showed complex and sometimes discordant results. FC measured by resting-state fMRI showed rather decreased connectivity in diseased brain networks concordant with brain network disruption due to the pathology. However, increased FC has also been evidenced at the whole-brain scale from fMRI data with the hypothesis to be linked to cognitive adaptations. By compelling multimodal connectivity data both from imaging (fMRI, DTI) and electrophysiology (EEG, MEG) we will discuss how better interpreting these FC changes in selected models of pathology encompassing: models of localized network dysfunction (partial epilepsy), models of widespread networks dysfunction affecting principally gray or white matter (Alzheimer's disease and multiple sclerosis respectively). In addition, we will discuss the fact that despite the information offered by the multimodal approach, there is a need to decipher these complex changes occurring at different time and spatial scales by measuring functional connectivity dynamics.

- **Hyang Woon Lee** (Ewha Womans Univ., Korea)
  "Network dynamics explored by functional connectivity analysis in neurological disorders"

  Examination of network dynamics can provide a better understanding of pathophysiologic mechanisms underlying various neurological disorders. Recent studies have reported various measures of connectivity using functional electrophysiologic and structural brain imaging studies to better understand the properties of brain networks involving neurological disorders. I will present recent use of various

measures for functional connectivity to assess physiologic and pathologic brain networks and their application in both clinical and research fields, especially in epilepsy, REM sleep behavior disorder with or without Parkinson's disease. In particular, functional connectivity can also identify cortical regions that are organized differently in epilepsy patients either as a direct function of the disease, or comorbid conditions such as cognitive dysfunction, or even indirect compensatory responses. Functional connectivity mapping may help identify epileptogenic tissue, whether this is a single focal location or a network of seizure-generating tissues. I will review recent studies of connectivity analysis in epilepsy especially using intracranial EEG and their clinical implications for patients with intractable epilepsy.

- **Riki Matsumoto** (Kyoto Univ., Japan)
  "Probing dynamics of cortico-cortial connectivity with direct cortical stimulation in physiological and pathologic states"

Functional brain connectivity in a broad sense is further divided into functional connectivity and effective connectivity. Effective connectivity refers to the causal influence between brain regions. There are two approaches to probe effective connectivity - non-interventional and interventional. Here, I introduce an interventional approach of cortico- cortical evoked potentials (CCEPs) that use perturbations to directly infer effective connectivity. Single pulse electrical stimulation is applied directly to the cortex and the evoked cortical potentials/induced high gamma activities are recorded directly from electrocorticogram (ECoG). We review its academic impact on understanding the functional brain networks, and clinical utility for functional 'system' mapping. With its excellent temporal resolution, CCEP could also assess dynamic alteration of cortico-cortical connectivity & excitability during physiological and pathologic states. I will introduce recent studies focusing on the dynamics of connectivity & excitability during epileptogenesis, tumor surgery and sleep.

MEG Signatures of Intrinsic Coupling: New Methods

Organizers: Laura Marzetti

Room: # 105

Date and Time: Monday, October3 / 17:00-18:00

Revealing Signatures of Intrinsic Coupling Modes by MEG: Insights from New Methods
In the last 20 years, system neuroscience has seen a paradigm shift in ongoing brain activity, moving away from considering it as an idling state towards its organization in spatiotemporal structures linked to experience. More recently, MEG functional connectivity contributed along this line by designing methods focusing on coupling of slow fluctuations (seconds) of brain activity resembling fMRI. Indeed, MEG functional connectivity studies have also shown that faster intrinsic brain activity is organized with spatio-temporal structures that only partially overlap with that of slow fluctuations, with the notion of Intrinsic-Coupling-Modes (Engel et al., 2013) providing a unifying theoretical framework for the multiple spatial and temporal scales. From a methodological standpoint, two major aspects deserve further discussion: i) approaches able to capture and integrate different aspects of such spatio-temporal structure; ii) issues of the robustness and reliability of such approaches. The aim of this symposium is to bring together experts in analysis methods to discuss these aspects with specific reference to the role of frequency, cross-frequency coupling, and coupling of slow fluctuations. Along with presenting novel methods, pitfalls and methodological issues, the speakers will cover relevance to the ICM model. The symposium will last 60 minutes and host 3 speakers.

Speakers:

- **Laura Marzetti** (Univ. G. d'Annunzio of Chieti-Pescara, Univ. G. d'Annunzio of Chieti-Pescara, Italy)
  "State of the art of methods for the study of intrinsic coupling modes by MEG."

  The notion of Intrinsic-Coupling-Modes (ICM) of brain function provides a powerful theoretical framework for addressing the dynamic coexistence of integration and segregation patterns in the brain observed at multiple spatial and temporal scales.
  Supporting such notion with further empirical evidence from MEG ongoing brain activity requires to design analysis methods able to break the barriers that currently pose a limitation in this framework. This talk will start by discussing the major factors that influence the estimation of functional connectivity from source space MEG data, with reference also to the role of forward and inverse modeling. A review of the state of the art of commonly used MEG functional connectivity methods (Imaginary Coherence, Amplitude Envelope Correlation, etc.) will be then at target with emphasis on the strengths, limitations and functional significance of the different methods. Finally, results from currently available studies will be revisited under the ICM framework.

- **Mark Woolrich** (Univ. of Oxford, United Kingdom)
  "Multi-subject MEG Connectomes"

  Modeling the strength of intrinsic coupling across cortex is a powerful approach for exploring the signatures of healthy and diseased cognition in the human connectome. Here, we assess different MEG functional connectivity metrics largely based on how well they produce consistent results over sessions, subjects and populations. We demonstrate that the performance of different metrics varies, with some struggling to provide robust estimates of connectivity, particularly at the single-subject level. The results also emphasize the importance of correcting for spatial leakage confounds, and we highlight methods for achieving this when computing parcellated connectomes. The strength of

coupling in networks covering the whole of cortex can be used to predict dysfunction and behavior, but the effectiveness of these approaches relies on generating accurate network models for each subject. We demonstrate that hierarchical models enable the sharing of information between an entire group of subjects and the individual. This has the potential to provide estimation of the intrinsic coupling within each subject, offering higher sensitivities in subsequent analyses. We illustrate the application of our techniques by analyzing the genetic influence on the amplitude coupling between intrinsic neural oscillations using data from the Human Connectome Project.

- **Guido Nolte** (Universitaetsklinikum Hamburg-Eppendorf, Germany)
  "Bicoherence. The higher harmonics strike back."

While bicoherence and cross-bicoherence are well-known measures of functional relations across frequencies, their relevance for studying e.g. the alpha rhythm is probably underestimated. This talk will start with general remarks on non-stationarities, which are necessary to understand some technicalities of bicoherence, and which are, hopefully, also of general interest. The main conclusion of this part will be that the non-stationarity of spontaneous brain activity is a myth. Bicoherence itself is a univariate measure, in general reflecting coupling between three frequencies with the constraint for stationary data that the third frequency is the sum of the first two frequencies. In real EEG and MEG data the most prominent signals are couplings between alpha and its higher harmonics. These higher harmonics are barely visible in conventional power analysis. Theoretically, it can be shown that Phase Amplitude Coupling, which attracted much attention lately, is essentially a smeared version of bicoherence, with the advantage of the latter that higher harmonics can easily be recognized as such. Finally, the more general multivariate variants, i.e. cross-bispectrum and cross-bicoherence, are discussed in the context of studying brain connectivity robust to artifacts of volume conduction.

Stimulating the brain in the MEG

Organizer: Jim Herring and Markus Butz

Room: # 103

Date and Time: Tuesday, October4 / 08:30-10:30

Entrained Brain Oscillations and the Processing of Complex Auditory or Visual Stimuli
Neurostimulation techniques including transcranial current stimulation (either direct or alternating current (tDCS/tACS)) and deep brain stimulation (DBS) allow us to directly modulate the level and timing of spontaneous neuronal activity while also producing changes outlasting stimulation. Recent methodological advancements provide the unique opportunity to directly study the effects of neuromodulation on neuronal activity and the associated changes in behaviour and disease symptoms on the neurophysiogical level using MEG. However, this is complicated by magnetic artifacts orders of magnitudes larger than the brain signal of interest.

This symposium will present both pioneering research using simultaneous tCS-MEG and DBS-MEG as well as recent advancements in artefact rejection which allow studying the effects of neurostimulation in the MEG 'online'. This symposium aims at giving further insight how neurostimulation modulates oscillatory brain activity and how MEG can be used to further our understanding of its functional relevance.

Speakers:

- **Jim Herring** (Donders Inst., The Netherlands)
  "Modulating stimulus-induced gamma-band activity with tCS in the MEG"

  Cortical alpha oscillations (8-12 Hz) are thought to support 'attentional gating' by suppressing activity from task-irrelevant regions, reflected by 'pulsed-inhibition' of gamma-band activity (40-100 Hz). However, the direct link between excitability and oscillatory activity is currently unclear. We present results from two studies where we attempted to modulate visual cortex excitability by transcranial current stimulation (tCS). In the first study we applied anodal and cathodal direct currents (tDCS) in an Oz-Cz montage while measuring whole-head magnetoencephalography (MEG). Although we were successful in reconstructing visual stimulus-induced alpha and gamma activity in the presence of strong tCS-related artifacts, tDCS did not seem to affect the measured brain activity. In a second study, we applied alternating currents (tACS) at three frequencies centered at subjects' individual alpha frequency (IAF-4 Hz; IAF; IAF+4 Hz). We found a rhythmic modulation of stimulus-induced gamma band activity by occipital tACS at IAF. Importantly, we controlled for potential retinal stimulation using a control montage closer to the eyes (Cz-FPz). Both studies show that it is possible to reconstruct source activity at the region of stimulation in the presence of strong tCS-related artifacts. Importantly, only tACS seemed to modulate gamma-band activity in phasic manner.

- **Surjo R. Soekadar** (Eberhard Karls Universität Tübingen, Germany)
  "Investigating the mechanisms underlying behavioral effects of transcranial electric stimulation (tES): current state and future perspectives"

  Transcranial electrical stimulation (tES) can affect perception, memory, motor, and cognitive function. The mechanisms underlying tES-related behavioral effects are not well understood, but recent advances in multimodal approaches allowing for simultaneous tES during assessment of brain oscillatory activity may substantially contribute to uncovering the complex interactions between externally applied currents, neurophysiology and brain function. Besides providing an introduction to various strategies for assessing neuromagnetic activity during transcranial direct or alternating current stimulation (tDCS/tACS) and their

limitations, most recent results of combined tES and MEG studies performed at the University of Tübingen will be presented. These include tES effects on slow cortical fields and reaction time, mapping of entrained brain oscillations, and purposeful phase-modulation of frontal midline theta oscillations to manipulate working memory performance. Based on insights from these studies, future perspectives, particularly implications for clinical applications, will be outlined.

- **David McGonigle** (Cardiff Univ., UK)
  "Exploring Issues of Optimisation in tES-MEG Experiments"

Transcranial Electrical Stimulation (tES) is a neuromodulation technique capable of producing prolonged, polarity-specific alterations in neuronal excitability. However, the neurobiology underlying the behavioural effects of stimulation remains uncertain, and outside of studies of motor behaviour, data often has high inter-participant variability. At present, combining stimulation and neuroimaging in neurotypical human populations represents one of the most promising routes to better understand the 'online' effects of tES, but significant challenges remain. In this presentation we will discuss recent results demonstrating how optimisation of experimental paradigms at a number of levels can assist in improving data quality when running tES-MEG experiments.

- **Toralf Neuling** (Univ. of Salzburg & Carl von Ossietzky Univ., Austria/Germany)
  "Beamforming can recover brain activity in MEG-tACS settings"

Brain oscillations are putatively crucial for normal cognitive functioning and alterations are associated with cognitive dysfunctions. This made brain oscillations a target to non-invasive brain stimulation, e.g. transcranial alternating current stimulation (tACS). The aim is to apply external rhythms to the brain to modulate internal rhythms and to test if a subsequent modulation of cognition is possible. This way, different parameters of brain oscillations (e.g., amplitude, phase, frequency) become the independent variable and behavioral measures the dependent variable, which in turn allows for causal interpretations. The combination of tACS and MEG opened up the possibility to overcome the obstacles caused by the enormous stimulation artifacts, which previously made it virtually impossible to investigate patterns of brain activity recorded *during* tACS. We present a means to overcome this limitation, showing that we are able to recover meaningful modulations of brain oscillations even at the stimulation frequency. By applying tACS in a phantom study, we can estimate the potential and the limitations of the proposed method. This work effectively opens up the black box of brain activity during tACS, enabling a more detailed understanding of this brain stimulation method with broad implications for its application in cognitive and clinical neuroscience.

- **Nima Noury** (Univ. of Tübingen, Germany)
  "Physiological processes non-linearly affect electrophysiological recordings during transcranial electric stimulation"

Transcranial electric stimulation (tES) is a promising tool to non-invasively manipulate neuronal activity in the human brain. Several studies have shown behavioral effects of tES, but stimulation artifacts complicate the simultaneous investigation of neural activity with EEG or MEG.
In this talk, I first show for EEG and MEG, that irrespective of stimulation frequency (i.e. for both tACS and tDCS) and contrary to previous assumptions, artifacts do not simply reflect stimulation currents, but that heartbeat and respiration non-linearly modulate stimulation artifacts.Second, I show that, although at first sight previously employed artifact rejection methods may seem to remove artifacts, data are still contaminated by non-linear stimulation artifacts. Because of their complex nature and dependence on the subjects' physiological state these artifacts are prone to be mistaken as neural entrainment.

- **Omid Abbasi** (Heinrich Heine Univ. Düsseldorf, Germany)
"Deeply stimulating the brain at 130 Hz and 340 Hz in the MEG scanner"

With DBS, subcortical structures are stimulated electrically by implanted macro electrodes. Recording MEG during DBS comes along with technical challenges such as DBS artefact removal as DBS distorts MEG data significantly.

We developed a method based on the combination of independent component analysis (ICA) and mutual information theory to remove DBS artefact from MEG data. We applied it on MEG data from 5 Parkinsonian patients with implanted stimulator during DBS. Patients performed an established visual attention task known to induce gamma band activity and median nerve stimulation yielding sensory evoked field. With the proposed artefact rejection approach, we could retrieve the signal of interest and reproduce the expected neurophysiological activity.

In a second study, we recorded MEG during stimulation of the subthalamic nucleus in 17 Parkinsonian patients at 130 Hz and 340 Hz using an external brain stimulator. Here, we could show that DBS at both stimulation frequencies led to widespread suppression of cortical oscillatory activity in the alpha and beta band over bilateral motor cortices. Our two studies demonstrate that (i) it is possible to remove the DBS artefact from MEG data and (ii) MEG can be used as a tool for a better understanding of DBS mechanism.

- **Jyrki Mäkelä** (HUS Medical Imaging Center, Finland)
"The effects of DBS on MEG spontaneous oscillatory activity in patients with late-phase Parkinson's disease"

We have studied the effects of bilateral electrical stimulation of subthalamic nucleus on MEG cortical spontaneous activity in patients with Parkinson's disease (PD). Large artifacts produced by deep brain stimulation (DBS) were suppressed by the tSSS algorithm. The methodology enables reliable recording of evoked fields in vast majority of PD patients and reveals slight enhancement of AEFs and SEFs when DBS on. The pericentral source strengths of oscillatory alpha and beta-band signals did not differ between the DBS on and off conditions. When DBS on, rigidity scores correlated significantly with 6-10 Hz and 12-20 Hz source strengths whilst eyes open. Corticomuscular coherence (CMC) was not systematically modified by DBS. Our most recent dataset of spontaneous oscillatory activity revealed a significant, widespread frontotemporal suppression of high alpha and low beta-band activity in the sensor space when DBS was on and eyes open in 14 out of 16 patients. Similarly distributed but less strong suppression was observed when eyes closed or during an active wrist flexion. STN DBS thus modulates cortical brain oscillations both in alpha and beta bands and some of these modulations correlate with the clinical condition of the patient.

- **Vladimir Litvak** (Univ. College London, UK)
"Simultaneous MEG and intracranial LFP recordings during Deep Brain Stimulation"

Deep Brain Stimulation (DBS) is an effective treatment for several neurological and psychiatric disorders. In order to gain insights into the therapeutic mechanisms of DBS and to advance future therapies a better understanding of the effects of DBS on large-scale brain networks is required.

We developed an experimental protocol and analysis pipeline for simultaneously performing DBS and intracranial local field potential (LFP) recordings at a target brain region during concurrent MEG measurement. A phantom setup allowed us to precisely characterise the MEG artefacts that occurred during DBS at clinical settings and show that when properly handled, they do not preclude the analysis of LFP-MEG coherence using the methodology we previously described for recordings without concurrent DBS. A group study in 15 Parkinson's disease patients stimulated at 130Hz showed that DBS selectively suppressed synchronisation of activity in the beta band between the STN and mesial premotor regions, including the supplementary motor areas. These results are in line with the previously suggested antidromic activation of the cortico-subthalamic hyperdirect pathway by DBS.

Visual Representations

Organizer: Dimitrios Pantazis

Room: # 104

Date and Time: Tuesday, October4 / 08:30-10:30

Neural Dynamics of Visual Representations

The human visual brain shows highly dynamic patterns of activity, as one transient visual representation is followed rapidly by another. This symposium focuses on several recent studies offering novel insights into the human visual brain. We show that a) MEG measurements can capture the neural signature of a perceptual Gestalt, demonstrating that differences in perceived global form are accompanied by corresponding differences in neural representations; b) conscious and unconscious perceptions share neural signatures that are initially identical and then subsequently diverge, as conscious access engages additional neural activity patterns whereas unconscious access leads to a slow decay of brain activation; c) MEG signals can capture information at spatial scales much more refined than previously believed, giving access to information encoded at the level of individual cortical columns; d) the rich content of MEG visual representations allows view-invariant decoding of human action as early as 200 ms after stimulus onset; and e) the direction of MEG source currents at fusiform cortex dissociate the feedforward and feedback inputs of the hierarchically organized visual brain. Taken together, these results exemplify the power of MEG in capturing visual representations and promise even more exciting results in the future.

Speakers:

- **Thomas Carlson** (Macquarie Univ., Australia)
  "Decoding the time varying representation of abstract visual patterns with MEG"

  Perceptual similarity is a cognitive judgment that represents the end-stage of a complex cascade of processing. Here we explore the temporal relationship between the human brain's time-varying representation of visual patterns and behavioral judgments of perceptual similarity. The stimuli were abstract patterns constructed from identical perceptual units (oriented Gabor patches) so that each pattern had a unique global form or perceptual 'Gestalt'. The stimuli were decodable from evoked neural activation patterns measured with magnetoencephalography (MEG), however, stimuli differed in the similarity of their neural representation as estimated by differences in decodability. Early after stimulus onset (from 50ms), a model based on retinotopic organization predicted the representational similarity of the visual stimuli. Following the peak correlation between the retinotopic model and neural data at 80ms, the neural representations quickly evolved so that retinotopy no longer provided a sufficient account of the brain's time-varying representation of the stimuli. Overall the strongest predictor of the brain's representation was a model based on human judgments of perceptual similarity. Our results show that large-scale brain activation patterns contain a neural signature for the perceptual Gestalt of composite visual features, and demonstrate a strong correspondence between perception and complex patterns of brain activity.

- **Lauri Parkkonen** (Aalto Univ., Finland)
  "Decoding conscious and unconscious visual percepts"

  Visual evoked responses measured by MEG carry information not only about the features and location of a stimulus in the visual field but also about whether the stimulus was consciously perceived or not. I will describe our recent study comparing the brain responses to perceived and unperceived stimuli. We pursued a novel approach, tracking the neuronal coding of consciously and unconsciously perceived

contents while keeping behavior identical. EEG and MEG were recorded while participants reported the spatial location and visibility of a briefly presented target. Multivariate pattern analysis showed that information about the spatial location of the stimulus is available in MEG/EEG also for unperceived targets but that starting about 270 ms post-onset, information unique to consciously-perceived stimuli emerges in superior-parietal and superior-frontal regions. Therefore, conscious access appears characterized by the entry of the perceived stimulus into a series of additional brain processes while the failure of such access results in the breaking of this chain and a subsequent slow decay of the lingering unconscious activity.

- **Dimitrios Pantazis** (MIT, USA)
  "Can visual information encoded in cortical columns be decoded from magnetoencephalography data in humans?"

  It is a principal open question whether noninvasive imaging methods in humans can decode information encoded at a spatial scale as fine as the basic functional unit of cortex: cortical columns. We addressed this question in five magnetoencephalography (MEG) experiments by investigating a columnar-level encoded visual feature: contrast edge orientation. We found that MEG signals contained orientation-specific information as early as approximately 50 ms after stimulus onset even when controlling for confounds, such as overrepresentation of particular orientations, stimulus edge interactions, and global form-related signals. Theoretical modeling confirmed the plausibility of this empirical result. An essential consequence of our results is that information encoded in the human brain at the level of cortical columns should in general be accessible by multivariate analysis of electrophysiological signals.

- **Leyla Isik** (Boston Children's Hospital / MIT, USA)
  "Fast, invariant representations for human action in the visual system"

  The ability to recognize the actions of others from visual input is essential to humans' daily lives. The neural computations underlying action recognition, however, are still poorly understood. We use magnetoencephalography (MEG) decoding and a computational model to study action recognition from a novel dataset of well-controlled, naturalistic videos of five actions (run, walk, jump, eat drink) performed by five actors at five viewpoints. We show that that actor- and view-invariant representations for action arise in the human brain as early as 200 ms after a video begins. We next extend a class of biologically inspired hierarchical computational models of object recognition to recognize actions from videos and explain the computations underlying our MEG findings. This model achieves 3D viewpoint-invariance by the same biologically inspired computational mechanism it uses to build invariance to position and scale. These results suggest that robustness to complex transformations, such as 3D viewpoint invariance, does not require special neural architectures, and further provide a mechanistic explanation of the computations driving fast, invariant action recognition.

- **Seppo Ahlfors** (Massachusetts General Hospital / Harvard Medical School, USA)
  "Characterizing activation patterns among hierarchically organized visual areas with MEG"

  Identifying inter-area communication in terms of the hierarchical organization of functional brain areas is of considerable interest in human neuroimaging. We have examined the hypothesis that the direction of magneto- and electroencephalography (MEG, EEG) source currents depends on whether the input into a cortical area originates from an area that is below or above in the hierarchical order of cortical areas, as defined by layer-specific connectivity patterns. The direction in MEG source currents was determined in a visual object recognition experiment in which there were specific expectations of activation in the fusiform region being driven by either feedforward or feedback inputs. The source for the early non-specific visual evoked response, presumably corresponding to feedforward driven activity, was found to point outward, i.e., away from the white matter, whereas later object-recognition related source currents, expected to be driven by feedback inputs, pointed inward. Computational modeling was used to

demonstrate a dependence between the dipole direction and the spatial pattern of synaptic inputs within the dendritic tree of pyramidal cells. Associating specific features of the MEG/EEG source waveforms to feedforward and feedback inputs could provide unique information about the activation patterns within hierarchically organized cortical areas.

Advanced Clinical Magnetocardiogram

Organizer: Hitoshi Horigome, Akihiko Kandori and Doosang Kim

Room: # 105

Date and Time: Tuesday, October4 / 08:30-10:30

In this symposium, we focused on the current status of clinical and experimental MCG study. We invite seven speakers internationally, who will present … 2) overview of current status of clinical magnetocardiography, 3) the efficacy of vector MCG for AF risk stratification, 4) the feasibility of MCG to detect left atrial dysfunction in the patients with paroxysmal AF, … This symposium will show that MCG could have a potential benefit to clarify the pathophysiology and overcome the hurdle of many cardiac diseases.

Speakers:

- **Uwe Schneider** (Univ. Hospital Jena, Germany)
  "Evaluation of autonomic nervous system of the fetus using fetal MCG"

  Fetal autonomic development follows universal principles of maturation like increasing variability, complexity and pattern formation. Autonomic aptitude is mirrored in cardiovascular regulation and the fetal heart rate (fHR) is both the major continuous regulative and access point to understand autonomic maturation. Electrophysiological methods like fetal magnetocardiography enhance the temporal monitoring acuity and enable precise beat-to-beat heart rate variability analysis (fHRV) which is of particular advantage in resolving fast vagal activity and in the analysis of complexity measures. fHR patterns change with increasing gestational age. In addition, rest/activity cycles from about 23 wks GA display progressive synchronization of neuro-behavioral variables as markers of developmental integrity. We applied basic and advanced parameters of linear and non-linear fHRV to conceive a fetal autonomic brain age score (fABAS) and tested the model for robustness between different study populations. fABAS performance depends on temporal resolution of the signal and length of the monitoring interval. During periods of fetal quiescence and active sleep, fABAS is characterized by differential properties with emphasis to confirm either fetal maturation or well-being, respectively. These phenomena qualify for further assessment of functional autonomic brain age and may be explored in clinical situations to help discriminating the impaired from the healthy fetus.

- **Eun-Seok Shin** (Ulsan Univ. Hospital, Korea)
  "Current status and Clinical Application of MCG"

  Although cardiovascular disease (CVD) is a major cause of mortality in humans, its prevention and treatment is challenging as accurate diagnosis is difficult. Moreover, despite the enhancement in coronary artery disease (CAD) or arrhythmic disease, such as non-invasive diagnostic test such as treadmill test, echocardiography, Holter monitoring, computed tomography, and magnetic resonance imaging, accurate diagnosis is still challenging. For this reason, invasive diagnostic tests such as angiography and electrophysiology are inevitable to diagnose CVD and thus the relevant complications are still concerning. Considering the characteristics of CVD, more accurate diagnosis can be made through a function-based diagnostic tool rather than image as a lot of scientific evidence supports this. Magnetocardiography (MCG) presents as an attractive alternative diagnostic tool in CAD and arrhythmias due to its non-invasive, contactless and highly sensitive nature. MCG has an ideal concept, in which it can read the information on the magnetic field that the heart creates on its own, and diagnose CVD without requiring direct patient contact or potential harm including contrast media, any drugs and radiation. Currently, the efficacy of MCG is being verified in ischemic heart disease, arrhythmic disease, and fetal

heart disease, and accordingly its indication is being expanded. The various applications of MCG as a noninvasive strategy for the diagnosis and validate in clinical cardiology seem warranted.

- **Tetsuo Sasano** (Tokyo Medical and Dental Univ., Japan)
  "Risk stratification of atrial fibrillation utilizing vector magnetocardiography"

  Atrial fibrillation (AF) is the most common arrhythmia. Since AF drastically increases the prevalence of stroke, it's important to predict the occurrence of AF. However, the risk stratification of AF has not been well established.

  A growing body of evidence indicated that 2 factors were critical for AF: a triggering activity from the myocardial sleeve surrounding pulmonary vein (PV), and a conduction disturbance in atrium. We tried to evaluate these both factors utilizing vector magnetocardiography (VMCG).

  For assessing the triggering activity, we identified the small hump representing the excitation at the PV region. All 107 AF cases showed the hump. On the other hand, the evaluation in 115 healthy subjects revealed 55% of the cases showed hump, but the remaining cases did not.

  To evaluate the conduction disturbance in atrium, we pursued the frequency analysis from the waveform obtained at both atrial regions. We established a measurement of fragmentation from the filtered waveform of VMCG recordings. AF cases showed significantly larger number of fragmentation than in healthy subjects.

  In summary, VMCG has potential to evaluate the excitation at PV and the conduction disturbance in atrium. The combination of these assessments may be useful for the risk stratification of AF.

- **Ae-Young Her** (Kangwon Nat'l Univ., Korea)
  "Magnetocardiography detects left atrial dysfunction in patients with paroxysmal atrial fibrillation: Comparison with healthy subjects"

  The aim of this study was to evaluate LA function using MCG in patients with paroxysmal AF and healthy subjects examining possible indices to diagnose PAF.

  We enrolled 70 subjects including 26 healthy volunteers and 22 marathon runners who didnot exhibit any cardiac abnormalities with sinus rhythm as controls, and 22 patients with PAF which was documented by conventional or ambulatory EKG between October 2011 and July 2014. Spatiotemporal activation graph in base-apex and left-right direction was reconstructed from the 2D-pseudo currents. Maximum value of current amplitude was measured between end of P wave and beginning of Q wave.

  LA pseudo current increase at peak exercise in PAF patients was significantly lower than healthy volunteers and marathon runners (p<0.001). The changes of grade of PQ mapping between rest and exercise using spatiotemporal activation graph in PAF patients was smaller increase than healthy volunteers and marathon runners (p<0.001). Sensitivity, specificity, and the area under the ROC curve of LA pseudo current increase at peak exercise for differentiating PAF patients from healthy subjects were 77%, 92%, and 0.898.

  MCG can provide important information in detecting LA dysfunction in patients with PAF. Therefore, MCG may help in differentiating PAF patients from healthy subjects.

- **Byeongsoo Kim** (Biomagnetik Park GmbH, Germany)
  "KE-VMCG: An Alternative Representation of Magnetocardiography Signal for Patient Positioning Offset Robustness and Device Independence"

Current diagnostic methods in magnetocardiography (MCG) are strongly dependent on measurement position and sensor configuration. This is an obstacle to overcome if MCG is to be used in daily clinical routine. We suggest a source space transformation to be used as a standard in MCG. By using direction

and magnitude information obtained by solving the inverse problem, a vector magnetocardiogram (KE-VMCG) is presented. The VMCG is system independent and easy to interpret. We present examples of VMCGs for both axial and tangential gradiometer configurations to show system independence, a feature which is important for joint effort research in MCG. We discuss a method to improve directional resolution and account for physiological variance in the heart position and apex direction of patients. A retrospective study on 98 patients with CAD is done to find diagnostic parameters of the VMCG. We have a brief discussion about the future goal of localizing ischemia and how VMCG might aid in this endeavor.

- **Xiangyan Kong** (Chinese Academy of Sciences, China)
  "Recent Progress of MCG System Development and Its Clinical Application in SIMIT"

Recently, SIMIT has development several MCG systems in different environment. According to the different environments, different SQUID gradiometer configurations have been designed and fabricated to suppress the environmental disturbance. Also, we set up the first 36 channel MCG system in China based on voltage-biased SQUID magnetometer. As for the liquid helium evaporation rate, special design of insert has been studied and the optimal insert configurations have been developed to improve the performance of MCG system. Up to now, three four-channel MCG systems have been installed in hospitals for clinical research. Some preliminary clinical results will be reported in this paper. Also, we did several demonstrations on fetal MCG measurements using new developed voltage-biased SQUID magnetometers.

- **Kuniomi Ogata** (Hitachi Ltd., Japan)
  "Magnetocardiographic vector loop and its clinical application"

Magnetocardiography (MCG) can record the magnetic fields which are generated from the cardiac electrical current (electromotive forces of the heart). It is possible to evaluate electrophysiological activities in the heart in detail (high spatial resolution) by simultaneous measurements using multi-magnetic sensors. The pseudo 2-dimensional (2-D) electrical currents in the heart (Current arrow map: CAM) is calculated from the magnetic fields. The CAM can visualize the cardiac electrophysiological activities at each sampling time. Maps of this type are providing the basis for a new method of analyzing arrhythmia, ischemic heart disease and heart failure.

When the temporal alteration of the cardiac electrophysiological activities is evaluated by the CAM, we display the time-series CAM imagery and examine the time variation of the amplitude and angle of the CAM. If the time variation of the CAM can be visualized as a single image, it will be possible to easily understand the temporal alteration of the cardiac electrophysiological activities.

Thus, we developed magnetocardiographic vector loops (MVL) which are plotted the maximal and average current vector at each sampling time onto the 2-D plane. We will apply the MVL to analyze the magnetic fields in the patient of the arrhythmia, and demonstrate its clinical values.

Functional Roles of Cross-Frequency-Coupling

Organizer: Virginie VAN WASSENHOVE

Room: # 104

Date and Time: Tuesday, October4 / 17:00-18:30

Functional Roles of Cross-Frequency-Coupling in the Neurosciences of Cognition

Cross-frequency-coupling (CFC) is used generically to indicate the inter-dependencies between low-frequency oscillations and high-frequency neural activity. Different types of oscillatory coupling have been reported and MEG is one of the best techniques to provide non-invasive characterization of CFC. This symposium aims to illustrate the possible implications of CFC in neurosciences, highlighting both state-of-the art techniques and up to date thinking on the role of CFC in perception and cognition.

Speakers:

- **Ole Jensen** (Donders Univ., The Netherlands)
  "Cross-frequency interactions route sensory information to working and long-term memory"

  Several MEG, ECoG, and monkey studies have demonstrated that the phase of alpha oscillations are coupled to gamma band activity. Importantly, we have shown that alpha oscillations in deeper layers relate to gamma activity in more superficial layers (Spaak et al., 2012, Curr Biol). In a set of MEG studies we have invested how the cross-frequency coupling relates the encoding of working and long-term memory. The working memory study showed that high alpha power is associated with weaker gamma power at the trough of the alpha cycle (Bonnefond and Jensen, 2015, PLOS One). This effect was enhanced prior to the suppression of distractors. The long-term memory study revealed that in anticipation of items to be remembered, alpha power decreased while the cross-frequency coupling increased (Park et al., submitted). A measure of directionality between alpha phase and gamma power (Jiang et al., 2015, Neuroimage) predicted the individual ability to encode memory: a relatively stronger control of alpha phase over gamma power was associated with better memory. In sum, these findings demonstrate that gating of visual information to memory is reflected by the cross-frequency interaction between alpha and gamma activity.

- **Markus Siegel** (Univ. of Tuebingen, Germany)
  "Large-scale cross-frequency phase-amplitude coupling in the mammalian brain"

  Phase-amplitude coupling between different neuronal oscillations has been implicated in neuronal coordination and encoding, but direct evidence remains sparse. I will discuss electrophysiological studies investigating this in awake behaving rats and monkeys during different visuomotor behaviors. Cortiostriatal phase-amplitude coupling in awake behaving rats suggests that neuronal coordination through coherent phase-amplitude coupling may be a general mechanism to regulate neuronal interactions between different brain regions. Furthermore, functionally specific phaseamplitude coupling along the visuomotor pathway of awake behaving monkeys suggests that large-scale phase-amplitude may establish a temporal scaffold for corticocortical interactions during spatial working memory.

- **Bernadette Van Wijk** (Univ. College, London, UK)
  "Phase-amplitude coupling: the bad guy in movement disorders?"

  Current theories suggest that phase-amplitude coupling may support cognitive functions in the healthy brain. By contrast, high-levels of phase-amplitude coupling have been found in patients with Parkinson's disease, implying that it could also impede normal functioning. Here I will present our experimental findings showing that the strength of phaseamplitude coupling between beta and high-frequency oscillations correlates with severity of motor impairment. As high-frequency oscillations typically show a movement-related increase in amplitude, this could mean that increased locking with beta band phase may hamper movement initiation. Our data set omprised an extensive number of local field potential recordings from deep brain stimulation electrodes implanted in the subthalamic nucleus. While others have also reported increased phase-amplitude coupling in ECoG recordings above motor cortex in Parkinson's patients, I will discuss the challenges we are facing to replicate this with MEG due to lower signal-to-noise levels and the multiple comparisons problem. This will trigger the debate on the appropriate use and interpretation of cross-frequency coupling measures in studying oscillatory dynamics.

- **Brett Foster** (Stanford Univ., USA.)
  "Slow fluctuations of high frequency activity reveal intrinsic network structure in human cortex"

  Spontaneous neural activity has historically been viewed as ongoing background noise, which is to be removed through experimental design and data analysis. However, over the past decade, growing evidence from human neuroimaging supports the view that spontaneous neural activity contains structured patterns that reflect the putative organization of functional networks. To explore the electrophysiological correlates of these intrinsic dynamics, we utilized intracranial recordings to study the spatio-temporal properties of spontaneous and evoked activity in the human parietal cortex. During conditions of memory retrieval subregions of the medial and lateral parietal cortex displayed increased high-frequency activity, consistent with a wealth of human neuroimaging data. In addition, we studied the spontaneous covariation of highfrequency activity across parietal cortex during resting and sleeping states. We observed that slow fluctuations (<1Hz) of spontaneous (rest & sleep) high-frequency activity recapitulated network patterns observed during memory retrieval. This covariation was also shown to closely match the network organization observed with resting state fMRI in the same subjects. These observations highlight clear electrophysiological correlates of spontaneous network patterns in resting state neuroimaging data, and link into a wide literature associating spontaneous and evoked neural dynamics.

MEG and Complex Cognitive Functions in Paediatrics

Organizer: Charline Urbain and Margot J. Taylor

Room: # 105

Date and Time: Tuesday, October4 / 17:00-18:30

MEG Applied to the Understanding of Complex Cognitive Functions in Paediatrics

MEG, with its excellent spatial and temporal resolution, is the ideal modality to assess typical and atypical development of complex cognitive abilities. Studies show tremendous changes with age not only in the localisation of function in the brain, but particularly in the timing of the processing. The challenge has been to develop age-appropriate MEG tasks that are suitable for children and across an age range, and that assess complex cognitive abilities. Also, the resulting MEG data are more complex to analyse than those from simple sensory or motor tasks, as they often contain overlapping and widespread cortical and sub-cortical sources. This field, however, is one that will have increasing importance in translational clinical work. In this symposium, we bring together researchers to present examples of MEG studies of cognitive functions in typically developing children and clinical groups – ranging from working memory to theory-of-mind to cognitive control. These aspects of cognition have protracted maturational courses, and understanding their development in both typical and atypical populations will also facilitate the understanding of these abilities and the brain-behaviour relations in adult populations.

Speakers:

- **Nicola Molinaro, Mikel Lizarazu, Marie Lallier, Mathieu Bourguignon and Manuel Carreiras** (Basque Centre on Cognition, Brain and Language, Spain)
  "Entraining to auditory stimuli in developmental dyslexia"

  It has been recently suggested that the phonological disorder in dyslexia is the result of the malfunctioning of the primary auditory regions. Taking advantage of the excellent temporal resolution of magnetoencephalography (MEG) we analyzed in two studies the functionality of the auditory system in developmental dyslexia. We studied the neural entrainment (i.e., the reactivity of a neural network to synchronize with the rhythmic properties of an external stimulus) to the multiple frequencies of both the speech and non-speech signals, i.e., delta (~1Hz), theta (~4-7 Hz) and gamma (> 30 Hz) bands oscillatory stimulation. The results mainly highlighted that: (i) dyslexic readers show an atypical specialization of the auditory cortex to both low and high frequency amplitude modulations; (ii) such specialization is related to the anatomical properties of the auditory brain regions; (iii) neural synchrony to low-frequency speech oscillations in primary auditory regions hinders higher-order speech processing steps and the sampling of high frequency speech components. Such atypical auditory entrainment has the strong potential to cause severe consequences for both phonological and reading skills. Our findings, thus, strengthen proposals assuming that low-frequency acoustic entrainment hierarchically drives processing of higher speech frequencies and its impairment contributes to the phonological disorders in developmental dyslexia.

- **Duncan Astle** (MRC Cognition and Brain Sciences Unit, UK)
  "Altering developing brain systems with cognitive training"

  Children with poor working memory skills typically suffer from educational underachievement, and high levels of inattention; poor working memory is increasingly seen as central to a number of developmental disorders, including ADHD. Despite high levels of interest in working memory training, especially in childhood, little is known about the mechanisms by which gains are achieved. I will present data from a double-blind randomised controlled training study, using the dynamic electrical activity recorded using

MEG to explore underlying neurophysiological changes following training. We used new methods to explore the spontaneous coordination of electrophysiological signals at rest. Improvements in working memory after training were significantly associated with changes in functional connectivity between areas in fronto-parietal cortex and inferior-temporal cortex. During task performance we also observed enhanced coupling between the upper alpha rhythm (at 16 Hz), recorded in superior frontal and parietal cortex, and high gamma activity (at ~ 90 Hz) in inferior temporal cortex. This is the first demonstration that this hierarchically organised neuronal coupling can be measured in childhood and is associated working memory changes following training. We are exploring the impact of psychostimulant medication on these mechanisms, in children with a diagnosis of ADHD, which I shall also discuss.

- **Marc Vander** Ghinst, Xavier de Tiege (Université libre de Bruxelles, Belgium)
  "Investigations of speech-in-noise cortical processing in healthy children and patients with Landau-Kleffner syndrome"

In a multitalker background, adults' auditory cortex follows the attended speech stream rather than the global auditory scene. Converging neurophysiological evidence shows that auditory cortex activity synchronizes with the slow modulations of the attended speaker's voice rather than with the whole acoustic input. This coupling occurs in the delta and theta frequency bands, and declines with increasing background noise level.

Since speech-in-noise and auditory attentional abilities are typically lower in children than in adults, this cortical coupling phenomenon observed in multitalker auditory scenes might be different during childhood.

In this talk, we will present neurophysiological evidence arguing for a different speech-in-noise cortical processing in children compared to adults. Recent magnetoencephalographic (MEG) data from our research group show that children exhibit significant noise-sensitive coupling only in the delta band that is significantly stronger for the whole acoustic input than for the attended speech stream. These results will be compared with those obtained in children at the recovery phase of Landau-Kleffner syndrome.

These MEG data shed light on the neural bases of children's difficulties understanding speech in noisy conditions and argues for a progressive development of speech-in-noise abilities in humans that can be altered by childhood brain disorders.

- **Charline M. Urbain, Veronica Yuk, Sarah Mossad, Rachel Leung, and Margot J. Taylor** (Hospital for Sick Children, Univ. of Toronto)
  "Temporo-spatial brain dynamics of executive functions in children with autism"

Mounting evidence suggests that autism is a network disorder, characterized by atypical brain function and connectivity, especially in the context of high level executive processes. We will review MEG from three different studies: working memory (WM), emotional inhibition and theory of mind (ToM) tasks in typically developing (TD) children and children with ASD (20-25/group, 7-12yrs). We identified reduced inter-regional alpha-band (9-15 Hz) phase synchronization in children with ASD during the WM task which encompassed fronto-temporal networks. In addition, reduced connectivity processes anchored in the right fusiform correlated with the severity of symptoms in ASD. In the ToM task, TD children activated familiar ToM regions, such as the precuneus (325-400ms) and temporo-parietal junction (325-400ms), while children with ASD relied on WM and inhibition areas, such as the right inferior parietal lobule (475-600ms) and the right inferior frontal gyrus (425-550ms). In the emotion inhibition task, emotion regulation was associated with atypical brain processes in children with ASD from 225-400ms (ps<.005), particularly during the inhibition of angry faces in fronto-temporal areas. These studies buttress the network disorder hypothesis of ASD and suggest that children with ASD have atypical modulation of cognitive processing across a number of executive domains, impacting their social-cognitive deficits.

Simultaneous recordings of MEG and intracranial EEG

Organizer: Christian-G. Bénar and Sarang Dalal

Room: # 103

Date and Time: Wednesday, October5 / 08:30-10:30

Simultaneous Recordings of Invasive and Non-Invasive Electrophysiological Data: Novel Insights into Brain Dynamics

Magnetoencephalography and electroencephalography are formidable tools that provide non-invasive access to the complex spatio-temporal dynamics of brain networks at an exquisite temporal resolution. Yet this strength comes at a high cost : Before it reaches the surface, neuronal activity needs to be summed over neuronal ensembles and propagates through large areas of hierarchically organized and connected cerebral structures. Thus, it is not clear to which extent the activity of deep sources such as amygdala, hippocampus, thalamus, basal ganglia can be reliably extracted from surface signals. The only way to elucidate the relationships between remote surface signals and actual brain activity is to simultaneously record MEG or EEG with electrodes implanted within the brain. Moreover, such recordings open a unique opportunity to perform a combined analysis at the two levels of recordings, by analyzing networks between deep structures (seen in depth recordings) and the whole cortex (seen by MEG/EEG). Combining insights from invasive and non-invasive methods is an emerging trend that will undoubtedly enhance basic neuroscience as well as clinical research. The invited experts will share past and most recent findings on this topic and will provide an overview of where the field is heading in the near future.

Speakers:

- **Jean-Michel Badier** (Aix Marseille Université. INSERM. France)
  "Simultaneous MEG and Intracerebral recordings: Technical aspects and Virtual SEEG"

  MEG and invasive Stereotaxic EEG (SEEG) record the activity from the same origin but present different sensitivity. An important question is sensitivity of MEG to deep sources as well as the capacity of signal processing techniques to infer the origin of the signal. The best strategy to answer these questions is to record simultaneously MEG with SEEG.
  We will present how we solved various technical problems linked to the constraints of simultaneous MEG and invasive recordings. Compatibility of the materials, and physical limitations of surgical equipment have been solved by appropriate electrodes and fixation techniques. Electromagnetic perturbations have been solved by the use of totally electrically insulated EEG amplifiers.

  We will then show examples of recordings where activities present in the invasive recording can or cannot be seen with MEG. Finally reconstructions of source time courses with Independent Component Analysis and Beamforming reconstructions will be compared to the invasive recordings. More studies are required for investigating influence of noise and source location. Nevertheless, we will show that it is possible, even in the absence of apparent activity on MEG signal, to reconstruct cortical activations that are comparable with the invasive recordings.

- **Stefan Rampp** (Univ. Hospital Erlangen, Germany)
  "Invasive EEG and MEG – Clinical value"

  Invasive EEG (iEEG) recordings are considered the gold standard for localization of the epileptogenic zone. However, due to the limited spatial coverage and the "tunnel view" of individual electrodes, iEEG has to focus on specific regions where it offers excellent signal to noise ratios (SNR). MEG on the other hand provides a comprehensive view on the whole cortex. While the temporal resolution is excellent, SNR is much lower in comparison to iEEG. The combination of both in either separate or simultaneous recordings offers the best of both worlds. MEG focus localization provides non-redundant evidence. Using this information for planning of iEEG optimizes coverage and chances to adequately record the seizure onset. Simultaneous recordings allow evaluation of complex propagation patterns beyond the coverage of iEEG electrodes. It also enables the evaluation of MEG sensitivity for deep sources, e.g. in mesial temporal areas and in cases of depth-of-sulcus focal cortical dysplasia. Finally, the combination of iEEG and MEG can be utilized to detect, localize and validate subtle epileptic activity, such as high frequency oscillations. The presentation reviews such advantages, opportunities and challenges of combining iEEG and MEG in a clinical context.

- **Maité Crespo García** (Univ. of Konstanz, Germany)
  "Application of a MEG-iEEG simultaneous recording helps to validate slow-theta power decreases during the encoding of item-place associations"

  Numerous MEG/EEG studies have concluded that increased hippocampal theta power is associated with better subsequent episodic memory and spatial performance. However, recent invasive studies have shown that successful encoding of items and associations are mainly characterized by broad decreases in theta activity (3-8 Hz). To investigate this issue further, we focused on theta activity time-locked to the encoding of item-place associations during virtual spatial navigation. For this purpose, we used the rare opportunity to simultaneously record MEG and iEEG from an epilepsy surgery patient who was implanted in the left parietal and temporal cortex. We found that late 2-3 Hz slow-theta power and spatial accuracy were negatively correlated in sources of hippocampal-entorhinal complex (p-cluster <0.05). Functional connectivity analyses provided crucial insights: during power decreases, slow-theta in right anterior hippocampus and left inferior frontal gyrus phase-led the left lateral temporal cortex and predicted spatial accuracy. Our study allowed us to validate our MEG results obtained in a sample of healthy participants by showing similar phase-synchronization patterns referenced to either beamforming sources or intracranial signals. Taken together, our findings suggest that decreased slow-theta activity may reflect a neural mechanism underlying the encoding of detailed spatial information and item-context associations.

- **Karim Jerbi** (Univ. of Montreal, Canada)
  "Sailing the surface or diving into the deep ? Insights from simultaneous invasive and non-invasive brain recordings"

  Understanding the organization and functional role of large-scale brain networks requires not only access to brain signals with high temporal, spectral and spatial resolution, but also adequate sampling of the involved brain circuits. While invasive electrophysiological approaches such as stereotactic-EEG (SEEG), electrocorticography (EcoG) and deep brain stimulation (DBS) recordings all provide signals with high spatio-temporal resolution, they often lack spatial coverage and the recording sites are entirely determined by clinical requirements. By contrast, non-invasive methods including MEG and EEG provide full-head coverage which allows for source-level investigations of brain network dynamics. However their resolution is inherently limited by the inverse problem and by field spread or volume conduction effects. This talk will review ongoing work that explores data acquired simultaneously with invasive and non-invasive methods in order to bridge the link between these levels of observation. In particular, joint

surface and depth recordings will be reported in patients with epilepsy and in patients suffering from bipolar disorders. Our findings advance our understanding of the relationship between surface and depth measurements of oscillatory brain dynamics, and provide potentially novel insights into the alteration of the latter in epilepsy and bipolar disorders.

- **Vladimir Litvak** (UCL Inst. of Neurology)
  "Oscillatory Cortico-Subcortical Networks: An Insight from Combined MEG, Intracranial Recordings and Deep Brain Stimulation"

  Deep Brain Stimulation (DBS) surgery affords a unique opportunity to record local field potentials (LFP) from sub-cortical structures in awake humans. Combining such recordings with MEG makes it possible to characterise the oscillatory connectivity of DBS targets with the rest of the brain and look at modulation of oscillatory activity and connectivity by tasks and treatment. Our analysis of combined LFP-MEG recordings in several different subcortical targets and several different disorders showed that oscillatory coherent cortico-subcortical networks are a ubiquitous feature in these data, suggesting that they are likely to also be present in the healthy brain. More recently we have been working on elucidating the possible computational role of these networks by combining MEG-LFP recordings with cognitive tasks tailored for each DBS target. I hope to present the first results from these projects as well as from our highly technically challenging project where we recorded LFP and MEG during clinically effective DBS in Parkinson's Disease patients.

The Dynamics of Interactions at Rest

Organizer: Stefania Della Penna

Room: # 104

Date and Time: Wednesday, October5 / 08:30-10:30

The Complex Scenario of Dynamic Large Scale Interactions at Rest
In recent years, fMRI analysis of interactions in the absence of any external stimulus (resting state) subdivided the cortex into a moderate number of functional parcels consisting of regions showing correlated activity over long periods of time (resting state networks, RSN [1]). The function of such interactions at rest and their link with the multifaceted aspects of behavior can only be explained by including the temporal dimension. As a matter of fact MEG studies on resting state interactions in spontaneous rhythmic activity of the brain suggest more complex structures of communication, involving frequency-specific interactions determining dynamic patterns of local and global integration [2-4] and spectrally-selective dynamic changes following task [5]. In this framework, the recent technical advances and the related interpretations in the dynamics of MEG resting state interactions are here reported. Results on the investigation of different aspects of architecture dynamics through linear and non linear analyses in time-frequency domain and at multiple spatio-temporal scales and the related functional role are discussed.
  [1] Power JD et al., (2014) Neuron
  [2] De Pasquale F et al., (2012) Neuron
  [3] Brookes M et al., (2011) PNAS
  [4] Hipp JF et al., (2012) Nature Neuroscience
  [5] Betti V et al., (2013) Neuron

Speakers:

- **Robert Oostenveld** (Radboud Univ., The Netherlands / NatMEG; Karolinska Inst., Sweden)
  "On the large scale of studying dynamics with MEG: lessons from the HCP"

  As part of the Human Connectome Project (HCP), which includes high-quality fMRI, anatomical MRI, DTi and genetic data from 1200 subjects, we have scanned and investigated a subset of 100 subjects (mostly comprised of pairs of twins) using MEG. The raw data acquired in the HCP has been analyzed using standard pipelines [ref1] and both raw and results at various levels of processing have been shared though the ConnectomeDB [ref2].

  Throughout the process of the HCP we have not only analyzed (resting state) MEG data, but also have developed the data analysis protocols, the software and the strategies to achieve reproducible MEG connectivity results. The MEG data analysis software is based on FieldTrip, an open source toolbox [ref3], and is shared alongside the data to allow the analyses to be repeated on independent data.

  In this presentation will outline what the HCP MEG team has learned along the way and I will provide recommendations on what to do and what to avoid in making MEG studies on (resting state) connectivity reproducible.

  1.   Larson-Prior LJ, et al., Neuroimage, 2013
  2.   Hodge MR, et al., Neuroimage, 2016
  3.   Oostenveld R, et al., Comput Intell Neurosci. 2011

- **Markus Siegel** (Univ. of Tübingen, Germany)
"BOLD fMRI Correlation Reflects Frequency-Specific Neuronal Correlation"

The brain-wide correlation of hemodynamic signals as measured with BOLD fMRI is widely studied as a proxy for integrative brain processes. However, the relationship between hemodynamic correlation structure and neuronal correlation structure remains elusive. We investigated this relation using BOLD fMRI and spatially co-registered, source-localized MEG in resting humans. We found that across the entire cortex BOLD correlation reflected the co-variation of frequency-specific neuronal activity. Resolving the relation between electrophysiological and hemodynamic correlation structures locally in cortico-cortical connection space, we found that this relation was subject specific and even persisted on the centimeter scale. At first sight, this relation was strongest in the alpha to beta frequency range (8-32 Hz). However, correcting for differences in signal-to-noise ratios across electrophysiological frequencies, we found that the relation extended over a broad frequency range from 2 to 128 Hz. Moreover, we found that the frequency with the tightest link to BOLD correlation varied across cortico-cortical space. Our work provides direct evidence for the neuronal origin of BOLD correlation structure. Moreover, our work suggests that, across the brain, BOLD correlation reflects correlation of different types of neuronal network processes and that frequency-specific electrophysiological correlation provides information about large-scale neuronal interactions complementary to BOLD fMRI

- **J. Matias Palva** (Univ. of Helsinki, Finland)
"Functional connectivity and critical dynamics are co-localized in the human brain"

The theory of critical brain dynamics predicts a relationship between neuronal interactions and scale-free dynamics. Experimentally, this would be evidenced by a correlation between functional connectivity, an elementary outcome of neuronal interactions, and indices of criticality such as avalanche dynamics and long-range temporal correlations (LRTCs). Such evidence has, however, remained scarce. We postulated that a coupling between criticality and connectivity would be reflected both in neuronal avalanches propagating preferentially along the pathways of functional connectivity and in co-localized modular structures in the networks of criticality and connectivity.
We used both intra-cranial and non-invasive resting-state human electrophysiological recordings and compared connectomes of avalanche propagation and inter-areal relationships of LRTCs with connectomes functional connectivity. After establishing that the indices of criticality and connectivity can be independently assessed, we found frequency-dependent co-localization among the strongest connections of critical dynamics and connectivity. Crucially, neuronal criticality and connectivity also had co-localized modular structures and especially for power-law distributed avalanches.

Critical dynamics is hence co-localized with functional connectivity at multiple levels of network organization, which suggests that they co-emerge in an architecture where modules characterized by internally dense connectivity, avalanche propagation, and shared dynamic states. These findings thus reveal an intimate coupling between connectivity and dynamics.

- **Matthew Brookes** (Univ. of Nottingham, UK)
  "Imaging transient networks using power envelope correlation: from methods to clinical application"

  The topic of functional connectivity in neuroimaging is expanding rapidly and many studies now focus on coupling between spatially separate brain regions. In particular, recent years have seen the introduction of a number of techniques capable of tracking the dynamics of functional networks and, with its excellent time resolution, MEG has natural advantages in this area. In this talk I will begin by outlining novel methodologies which employ MEG data, alongside power envelope correlation, to track the formation and dissolution of brain networks in real time. I will show applications in the resting state, and also how observable networks change when resting recordings are punctuated with infrequent cognitive tasks. Following this, I will introduce our recent work on in schizophrenia. I will demonstrate that the methods I describe facilitate characterisation of abnormal transient networks in the visual system in schizophrenia patients; I will explain how this fits into a broader (multimodal) picture and show that MEG offers a means predict disease symptoms, and potentially outcome. Overall my talk will show that MEG is the technique of choice for measurement of whole brain dynamic connectivity and this area has an exciting future in characterising brain function in health and disease.

- **Stefania Della Penna** (Univ. of Chieti, Italy)
  "Dynamical architecture of resting state networks reveals frequency-specific prior and idling states"

  fMRI functional connectivity over spontaneous activity subdivides cerebral cortex in a relatively small number of resting-state-networks (RSNs). According to fMRI [Spadone, PNAS 2015], RSNs represent spatiotemporal "priors" (similar connectivity patterns between rest and task) for task-networks and their modulation contributes to task-evoked responses. MEG comparisons of interactions during natural vision and rest [Betti, Neuron 2013] suggest RSNs as reflecting a state of brain "idling" (or inactivity) that must be reorganized for task-dependent interactions to emerge. Extending our previous results on the dynamical integration/segregation among RSN during rest [de Pasquale, Cerebral Cortex in press], we focus on the dynamics of betweenness centrality (BC) during natural and time-scrambled movies compared to rest. During rest, we found frequency-specific hub-clubs involving specific RSN nodes, with hubs showing joint BC fluctuations. When inspecting task-induced modulations of interaction topographies, we found that alpha and beta hub-clubs were selectively modulated by task. While in alpha the co-occurrence of hubs considerably changed during natural and scrambled movies compared to rest, in beta the dynamical co-occurrence of hubs was unaffected by movie watching but was modulated by scrambled movies. Our findings suggest that dynamics of local integration represent an idling state in alpha and a prior state in beta.

Quantitative Imaging of Magnetic Nanoparticles

Organizer: Daniel Baumgarten

Room: # 105

Date and Time: Wednesday, October5 / 08:30-10:30

Magnetic nanoparticles (MNP) open novel pathways in cancer therapy and non-invasive diagnostics. The quantitative knowledge of a magnetic anoparticle distribution inside a body is essential for the development of these diagnostic and therapeutic approaches, as the MNP distribution essentially determines drug enrichment and heat production in their application. In the last years, different MNP imaging techniques have emerged, among them Magnetic Particle Imaging (MPI), Magnetorelaxometry Imaging (MRXI) and AC susceptibility (ACS) imaging. The latter two, in particular, allow for the quantitative detection of MNP tailored to therapeutic applications in a comparably large field of view. At the same time, excitation fields can be reduced in order to avoid unintentional hyperthermia and neural stimulation during the imaging. This symposium aims at collecting current theoretical and technical developments in the exciting and rapidly expanding field of quantitative nanoparticle imaging for therapeutical and diagnostic applications. It will span a bridge from novel sensor technologies over theoretical modeling and simulations to experimental investigations and in vivo applications. Validating and Evaluating New Methods for Source Analysis

Speakers:

- **Claude Fermon** (CEA - Atomic Energy and Alternative Energies Commission, France)
  "Spin electronics devices for magnetic particle counting and imaging"

  Spin electronics based magnetic sensors may be used for the detection of magnetic nanoparticles for relaxometry or Magnetic Particle Imaging (MPI). Compared to inductive coils, they allow working at very low frequencies, still bringing a rather large sensitivity. In that case, they are coupled to uperconducting or normal flux transformers which push their sensitivity in the range of femtoTeslas. They may also be reduced down to micron size. They are then able to detect single magnetic particles either alone either used for labelling biological objects. In this talk, I shall present the bases of the technology and their use for quantitative particle counting both at large and small scale.

- **Victor Lebedev** (Univ. of Fribourg, Switzerland)
  "MPI and Imaging MRX with Atomic Magnetometers"

  Atomic magnetometers (AMs) are flexible magnetic field sensors featuring femtotesla sensitivity. Their fast frequency response and an atomic scale of sensing element allow developing instruments for dynamic measurement and high resolution spatial mapping of the magnetization of magnetic nanoparticles (MNP). Operation of atomic magnetometers is based on the optical readout of the spin precession of the spin-polarized atoms in the ambient magnetic field. Atomic vapor is localized inside the suitable glass cell, where atoms can be further immobilized by the buffer gas. We report on our progress in application of AMs to two different methods of MNP detection: magnetic particle imaging (MPI) and magnetorelaxation (MRX). Use of AMs opens up a field of the low frequency MPI with access to the first harmonic of the MNP response. Challenge of the AM-based MPI lays in the optimization of the AM performance in vicinity of the millitesla drive and selection fields. AM-based MRX was already successfully deployed for the quantitative detection of the small amounts of MNPs. Our magnetic field camera allows imaging of the MRX of the structured several centimeter large samples with sub-illimeter field mapping resolution.

- **Annelies Coene** (Ghent Univ., Belgium)
"Comparative study of particle Electron Paramagnetic Resonance and Magnetorelaxometry for quantitative magnetic nanoparticle imaging"

The imaging of magnetic nanoparticles (MNP) has become an important asset in the biomedical field; it allows to obtain the spatial MNP distribution non-invasively, which in turn aids biomedical applications such as drug targeting and disease detection to function properly. In this study we compare two MNP imaging techniques, namely Magnetorelaxometry (MRX) and particle Electron Paramagnetic Resonance (pEPR). Using sensitive magnetometers such as SQUIDs or Fluxgates, MRX measures the decaying net magnetization of a sample containing MNP after the application of a magnetizing field. In pEPR, a MNP sample is placed in a magnetic field and is then excited by a radio-frequent electromagnetic wave. The latter changes the orientation of the net magnetization, which can then be measured by a pick-up coil. Both measurement techniques require the use of an (illconditioned) inverse problem to relate the measured signal to the spatial MNP distribution. In this contribution, the advantages and disadvantages of both techniques are considered and an outlook is given on how these these techniques can be combined to overcome their weaknesses.

- **Maik Liebl** (Physikalisch-Technische Bundesanstalt, Germany)
"Feasibility and capability of magnetorelaxometry imaging as a tool for monitoring of magnetic nanoparticle based cancer therapies in humans"

The development of novel cancer therapy approaches based on magnetic nanoparticles (MNP) requires the quantitative imaging of MNP distribution inside the human body. This is provided by magnetorelaxometry (MRX) measurements mapping the specific MNP response to switched external fields. Up to now MRX has been used for noninvasive imaging of MNP distributions in the context of drug targeting and hyperthermia applications in animal models up to rabbit size. Here, we present a device configuration to extend MRX imaging to human sized objects with the aim to provide a highly sensitive imaging tool to assist the development or control the application of MNP based therapies. Key parameters as spatial resolution (cm3), measurement time (<10 min) and sensitivity (100 µg/cm3) will be addressed by our design together with patient safety considerations. The feasibility of MRX imaging in human sized objects will be demonstrated by means of computer simulations based on measurement data with respect to the above mentioned parameters. In the future, we will evaluate the design as well as its capabilities and limitations by measurements using dedicated realistic body phantoms modeling physiological and physical aspects of selected MNP based therapy scenarios.

- **Sebastian Waanders** (Univ. of Twente, The Netherlands)
"Numerical modeling and experimental evaluation of magnetic nanoparticle relaxation dynamics in nonstatic magnetic fields using a combined Brownian-Neel relaxation approach"

With the growing significance of magnetic nanoparticle-based imaging modalities, an accurate and efficient description of the magnetization dynamics governing the behavior of these particles becomes of vital importance. In this contribution, we describe the dynamics of superparamagnetic iron oxide nanoparticles (SPIONs) under varying field conditions using a combination of Brownian and Neel relaxation mechanisms, and show that the steady-state approximation of their respective time constants does not hold under nonstatic field conditions. We numerically evaluate these dynamics based on their respective Fokker-Planck equations, and show how both relaxation mechanisms can be coupled through an effective magnetic anisotropy constant. We verify the results of this method by studying the behavior of several magnetic nanoparticle species in a DiffMag magnetometer. Results indicate that our methodology accurately describes the Particle Response Functions (PRFs) of different SPIONs. Furthermore, for a certain subset of particle sizes where both Brownian and Neel relaxation occurs, a transition occurs from Brownian to Neel-dominated behavior for increasing field strengths.

Finally, we show how this approach can be used to optimize the parameters of specific nanoparticles for specific biomedical applications, illustrating the strong potential of this approach in the fields like nonlinear magnetometry (DiffMag) and Magnetic Particle Imaging.

- **Solomon G. Diamond** (Thayer School of Engineering at Dartmouth, USA)
  "Nonlinear AC Susceptibility of Magnetic Nanoparticle-Cell Interactions"

Imaging of magnetic nanoparticles (MNPs) is an emerging tool in fundamental and translational medical research. MNP tracers can be used to enhance image contrast due to their size selectivity in biological transport and can also feature surface modifications for selective binding to targeted cell types. The present work examines nonlinear AC susceptibility response characteristics of MNPs that are bound versus unbound to cells. It is demonstrated that this method is capable of determining the quantity of bound and unbound MNPs in 0.5 ml samples of two human cancer cell lines. Testing was performed over a range of five concentrations of MNPs from 0 to 80 μg /ml and five concentrations of cells from 0 to 20 million count per ml. The sensitivity of the presented method to bound MNPs is 3 μg in a 0.5 ml sample. A novel method of exploiting nonlinear AC susceptibility of MNPs to selectively amplify neural magnetic fields is also explored. Experimental results from MNPs bound to a neuronal phantom are used to demonstrate the principles involved. Methods that are capable of selectively showing contrast to cellular-bound MNPs in cancer applications and methods for amplifying neural magnetic fields add unique value to MNP imaging.

- **Oswaldo Baffa** (Universidade de São Paulo, Brasil)
  "Functional Magnetic Nanoparticle Imaging by AC Biosusceptometry"

In vivo nanoparticles detection and monitoring remains a challenge, opening the possibility for many approaches ranging from simple and low cost to more sophisticated and expensive. The AC Biosusceptometry (ACB) system was extensively employed on monitoring gastrointestinal tract physiological properties with magnetic microparticles and has been recently applied to monitor magnetic nanoparticles (MNPs) in animal models. ACB is based upon a magnetic flux transformer, which
allow us to detect and quantify magnetic samples based on the variation in magnetic inductance from an excitation pickup coil to a detection one. The time resolution is high and the spatial resolution is limited by the coils size and sensitivity. Here we describe the first *in vivo* application of the ACB system as an imaging probe for magnetic nanoparticles. A citrate coated, manganese doped, superparamagnetic iron oxide nanoparticles was used due to its good magnetic susceptibility. Five male

Wistar rats, anesthetized by urethane, were submitted to MNP intravenous injection through their femoral vein while monitored by a single and a multichannel ACB system. After all in vivo procedures, ex vivo measurements of the heart, lungs, liver, spleen and kidneys was done. All these three measurements will allow us to perform a biodistribution analysis.

Validation/Evaluation of Source Analysis Methods

Organizer: Carsten Wolters and Jens Haueisen

Room: # 104

Date and Time: Wednesday, October5 / 16:00-17:00

Validating and Evaluating New Methods for Source Analysis

In this session, new methods for EEG and MEG source analysis with regard to forward and inverse problem as well as with regard to source connectivity analysis are presented. A special focus is on validation and evaluation frameworks for these new approaches. On the lowest level, the methods are verified in computer simulations with regard to numerical errors using multi-layer sphere models and evaluations are carried out in realistic head models. Technologically, the session will introduce Whitney sources, the complete electrode model and mixed finite element methods to bioelectromagnetism. Source connectivity measures are evaluated with regard to volume conductor modeling defects. On a next higher level, rabbit measurements are used to validate and verify the methods with regard to the overall forward and inverse modeling accuracy and, more specifically, with regard to the impact of skull modeling defects. Finally, validation is brought to the new and multi-modal approaches on presurgical epilepsy diagnosis, where it will be shown, how a multi-focal epilepsy patient can be successfully diagnosed and treated using the presented state of the art methodologies. It is shown how combinations of EEG/MEG and EEG/fMRI can be carried out and that multimodal approaches outperform single modality analysis.

Speakers:

- **Sampsa Pursiainen** (Tampere Univ. of Tech., Finnland)
  "Validation of Whitney sources and evaluation of differences between the point (PEM) and the complete electrode model (CEM)"

  This presentation will concentrate on mathematically rigorous finite element modeling of EEG/MEG biopotential fields with respect to both the interior and the boundary part of the target domain. Here, the primary current distribution evoked by neuronal activity is assumed to be a divergence conforming vector field spanned by (Whitney) basis functions, which can be associated with dipolar sources. The boundary conditions are formulated via the complete electrode model (CEM). The resulting comprehensive model has certain advantages over the standard approach. Important aspects are, among other things, that it enables simulation and recovery of the primary current directly as a vector field and that it covers both stimulation and measurement electrodes. The present approach has been recently compared to the classical direct partial integration and St. Venant dipole approximation methods as well as to the point electrode model (PEM). This presentation will briefly review the theoretical basis of the CEM/Whitney model, show the connection to the classical version, and also include the central numerical comparison results.

- **Johannes Vorwerk** (Univ. of Utah, USA)
  "Avoiding Skull Leakages using Mixed-FEM approaches"

  The finite element method (FEM) allows for the easy computation of highly accurate EEG forward solutions using realistic head models. Approaches based on a conforming FEM formulation were shown to achieve high accuracies in multi-layer both sphere and realistic head models. Due to their easy generation, especially hexahedral head models are frequently used when applying FEM approaches in praxis. These have the drawback that in areas where the thickness of a conductive compartment is in the range of the mesh resolution, elements corresponding to originally separated compartments on the in- and outside might touch in single vertices. As a result, an unphysical leakage of volume currents through these vertices may appear and the numerical accuracy of the conforming FEM is decreased. This effect can, e.g., occur

for CSF or gray matter and skin elements originally separated by the skull. It can be avoided by the use of FEM approaches that explicitly control the flow of volume currents, such as discontinuous Galerkin (DG) or mixed methods. Here, a mixed finite element method (Mixed-FEM) to solve the EEG forward problem is introduced and it is shown that the Mixed-FEM effectively prevents skull leakages in both sphere and realistic head models.

- **Jae-Hyun Cho** (Max Planck Inst. for Human Cognitive and Brain Sciences, Germany)
  "An evaluation of the sensitivity of EEG and MEG connectivity measures on the source level to head volume conductor properties"

  While the comparisons of the source estimation methods or connectivity measures in EEG and MEG source connectivity analysis have been investigated, the effects of the head volume conductor properties have not been studied sufficiently.
  In the present simulation study, we investigated the influence of particular properties of the head volume conductor on source connectivity analysis using a realistic head model. We considered the distinction between white and gray matter, the distinction between compact and spongy bone, the inclusion of a cerebrospinal fluid (CSF), and a simple 3-layer model comprising the skin, skull, and brain. The finite element method was applied to solve the forward problems. A beamforming approach was used to reconstruct source time courses, and the imaginary coherence (ICoh) and the generalized partial directed coherence (GPDC) were used as a measure of connectivity.
  In both EEG and MEG, neglecting the white and gray matter distinction or the CSF causes considerable errors in source connectivity analysis, while the distinction between spongy and compact bone has less impact on the results, provided that an adequate skull conductivity value is used. Moreover, the ICoh is less affected from the crosstalk effects caused by imperfect head models, as compared to the GPDC.

- **Stephan Lau** (St. Vincent's Hospital, Univ. of Melbourne, Australia)
  "Validating and evaluating the finite element method using controlled-source MEG-EEG rabbit measurements"

  Advanced finite element (FE) approaches have been developed for the localization of neuronal activity in the brain using simulation setups. The objectives of this study are to evaluate the concordance of such FE simulations with physical measurements and to identify model qualities that are important for accurate source analysis, especially in the presence of skull defects.
  A FE simulation of an in-vivo animal experiment with a conducting skull defect above a controlled source was constructed from MRI (0.4 mm^3) and CT. A 16-channel MEG and a 64-channel EEG were forward simulated (SimBio) above intact skull and above skull defects and compared to corresponding measurements. Source analysis from the MEG and EEG measurements, respectively, was performed using the FE head model.
  The forward simulation of the MEG and EEG signals reproduced the experimentally observed ones as well as characteristic magnitude and topography changes due to skull defects. Ignoring skull defects in the head model caused location, orientation and strength errors of the reconstructed source. An exact FE model enabled source reconstruction in the presence of skull defects. Detailed FE modelling approaches were validated. Spatial sampling density, co-registration accuracy, anatomical detail, and realistic tissue conductivities are important for accurate source analysis.

- **Ümit Aydin** (Concordia Univ., Canada)
  "Multimodal (EEG/MEG, EEG/fMRI) source analysis in epilepsy and controlled tasks"

In this talk two multimodal studies will be presented. First study focuses on combined EEG/MEG source analysis (EMEG) of interictal epileptic discharges. A seven compartment finite-element head model with calibrated skull conductivity and anisotropic white-matter (derived from diffusion-tensor-imaging) was used to fully benefit from the complementary of EEG and MEG. EMEG was performed near spike onset (to minimize propagation) and ZOOMit technology was used to acquire high-resolution images (0.5×0.5×0.5mm3) within a small region-of-interest highlighted by EMEG. ZOOMit revealed a subtle focal-cortical-dysplasia that was undetectable in lower-resolutions (1mm3) and these findings were confirmed by surgery outcome.

The second study focuses on source analysis of hdEEG (high-density EEG, 256-channels) acquired simultaneously with fMRI. Combining the spatial-resolution of fMRI and temporal-resolution of hdEEG offers great benefits, however, this is not a trivial task mainly due to artefacts on hdEEG induced by MRI. In this context, benefiting from discrete wavelet decomposition to denoise the data, wMEM (wavelet-based Maximum Entropy on the Mean) source analysis showed promising results. Performance of wMEM was evaluated via simulations, with hdEEG data acquired from the same individuals and the same well-controlled tasks both inside and outside the MRI scanner, and by comparing wMEM results with the fMRI findings.

MEG-TMS Combination

Organizer: Jyrki Mäkelä

Room: # 105

Date and Time: Wednesday, October5 / 16:00-17:00

Combining MEG and Navigated TMS

Magnetic fields can be used both to obtain information from the brain function in MEG studies, and to modify the brain electric activity in transcranial magnetic stimulation (TMS). Knowledge about physical properties of the magnetic fields in the brain has enabled development of navigated TMS (nTMS), in which the location and strength of TMS can be calculated based on the model of the individual's brain. This extension has opened new clinical uses of nTMS in diagnostics as well as in therapy of neurological conditions. This symposium aims at studying the possibilities of combination of the two methods in obtaining benefits for the neurological patients and to study the questions regarding modeling of the magnetic fields relevant to both methods.

Speakers:

- **Andrew Papanicolau** (The Univ. of Tennessee, USA)
  "Combining MEG and nTMS in epilepsy surgery planning"

  Presurgical evaluation for most pediatric epilepsy and tumor patients has been carried out until recently by means of invasive procedures such as the Wada procedure for determining hemispheric dominance for language and memory and Cortical stimulation mapping for localizing the language-related cortex and another subset of patients undergo additional cortical mapping through recording of high gamma activity from subdural electrodes. Currently, however, in many neurosurgery centers, including ours, patients also undergo MEG, fMRI, and nTMS for the same purposes. The results of all the above brain mapping methods are then correlated with the ultimate aim of establishing the compatibility of the invasive and non-invasive mapping procedures and the relative efficiency of each of the non-invasive ones. In this presentation, our experience with nTMS as an efficient procedure of functional mapping (if it were to be used alone), as a procedure for securing complementary information to that of the other functional imaging procedures, especially MEG, and as a substitute for direct cortical stimulation mapping will be discussed with the aid of a series of surgical cases.

- **Jyrki Mäkelä** (HUS Medical Imaging Center, Finland)
  "Cortical excitability   estimated   by MEG and nTMS in evaluating cortical recovery and effects of rehabilitation"

  The motor system is a dynamic network of cortical and subcortical areas interacting through excitatory and inhibitory circuits and modulated by somatosensory input. The network balance is disturbed in several neurological disorders including stroke, chronic pain and Parkinson's disease. Modifications of cortical excitability enable recovery and reorganization of the motor areas both in animal models and in humans. Transcranial magnetic stimulation (TMS) and magnetoencephalography (MEG) have both been applied in neurological patients to reveal cortical excitability changes. This presentation studies the possibilities of combined MEG and nTMS recordings in evaluating the effects of recovery and effects of therapies, including navigated rapid-rate TMS, in neurological disorders.

- **Matti Stenroos**

"Improving modeling of the magnetic fields to enhance usability and precision of MEG and nTMS"

To focus TMS-induced electric field to a region of interest and to estimate the cortical source of a MEG map, we need a forward model. In nTMS, the head has been modelled locally spherical, while in MEG, either spherical or simple layered models are used. Recent studies are in favor of realistically-shaped models.

In this work, I apply computer simulations to assess the roles of a) level of detail of head model and b) accuracy of TMS coil model on TMS focusing, aiming at fast-to-solve models that are suitable for clinical nTMS use. I will also assess the possible coupling between the errors in TMS and MEG models: if the aim is to study the effect of TMS on brain activity as measured by MEG, how much will a detailed MEG model help, if nTMS is done using a simple model?

The reference computations are done using an accurate coil model and a boundary-element head model that contains the brain, realistic CSF, skull, and scalp, and test models apply various simplifications to both the head and the TMS coil model. The first results suggest that, given proper implementation, realistically-shaped models are computationally tractable in nTMS setting.

Decoding the Micro- and Macroscopic Dynamics of Neural Activity

Organizer: Eelke Spaak and Jean-Rémi King

Room: # 103

Date and Time: Wednesday, October5 / 16:00-18:10

How does the Structure of Neural Representations Unfold over Time?
Advances in the Decoding of Time-Resolved High-Dimensional Neural Data
The past few decades have seen significant advances in our understanding of which brain regions are involved in particular cognitive tasks and processes. Additionally, the fine temporal resolution offered by magneto- and electroencephalography, and invasive electrophysiology, is providing us with an ever more detailed picture of the temporal evolution of these cognitive processes. However, it is less clear exactly how the brain implements them: how are cognitive computations subserved by specific neural representations? How are these representations transformed over time? This symposium will present five lines of experimental research, showing how the decoding of micro- and macroscopic neural signals (from spikes to whole-brain MEG) allows us to dissociate and simultaneously track multiple, distributed neuronal computations. Specifically, we will demonstrate how the structure, modulation, and re-activation of neural representations can be identified with novel multivariate approaches in a variety of visual and cognitive tasks.

Speakers:

- **Eelke Spaak** (Univ. of Oxford, UK)
  "Multivariate analyses of primate prefrontal cortex activity reveal simultaneously stable and dynamic coding for working memory"

  Working memory (WM) provides the stability necessary for high-level cognition. Influential theories typically assume that WM depends on the persistence of stable neural representations, yet increasing evidence suggests that neural states are highly dynamic. Here we apply multivariate pattern analysis to explore the population dynamics in primate lateral prefrontal cortex (PFC) during three variants of the classic memory-guided saccade task (recorded in 4 animals), as well as a typical change detection task. We observed the hallmark of dynamic population coding even when the representational states remained stable. We identified two characteristics that could explain these dynamics: (1) time-varying changes in the subpopulation of neurons coding for task variables (i.e., dynamic subpopulations); and (2) time-varying selectivity within neurons (i.e., dynamic selectivity). Using a data-driven simulation, we formally demonstrate that both factors contribute to population-level dynamic coding for WM. These results indicate that even in very simple cognitive tasks, PFC neurons display complex dynamics, yet support stable representations for WM.

- **Jean-Remi King** (New York Univ., USA)
  "The selective maintenance of sensory features is dissociated from their visibility"

  Recent studies of "unconscious working memory" have challenged the notion that only visible stimuli can be actively maintained over time. In the present study, we investigated the neural dynamics of subliminal maintenance using multivariate pattern analyses of magnetoencephalography recordings (MEG). Subjects were presented with a masked Gabor patch whose angle had to be briefly memorized. We show that, while irrelevant sensory features of contrast, frequency and phase are only encoded transiently, the relevant feature of angle is encoded and maintained in a distributed and dynamically changing manner, throughout the brief retention period. Furthermore, although stimulus visibility is marked by an amplification of late neural codes, we show that unseen stimuli can be partially maintained by the corresponding neural assemblies. Together, these results invalidate several predictions of current neuronal

theories of visual awareness and suggest that visual perception relies on a long sequence of neural assemblies that repeatedly recode and maintain task-relevant features at multiple levels of processing, even under unconscious conditions.

- **Anna Jafarpour** (Univ. of California-Berkeley, USA)
  "Decoding content of working memory using MVPA"

We investigated how sequences of events are retained in working memory. In a magnetoencephalography (MEG) study, healthy human participants encoded sequences of three categorically distinct visual stimuli and maintained that information over a 5 second retention interval to answer questions about the sequence order and identity of stimuli. Multivariate pattern classifiers could discriminate the three categories at 170 ms post stimulus onset during encoding on the basis of broadband amplitude. Decoding of brain activity during retention with these classifiers revealed that one of the three stimuli dominated the content of working memory. Early (125 ms) event-related-field responses during encoding indicated that the dominating stimulus was the least attended one independent of its category and position in the encoding sequence. These findings suggest that replay in working memory benefits the retention of task-relevant but weakly attended events, possibly by reducing interference of other attended events.

- **Radoslaw Martin Cichy** (Free Univ. Berlin, Germany)
  "A spatio-temporally resolved and algorithmically explicit account combining MEG with fMRI and neural networks"

Understanding visual cognition in the brain requires answering three questions: what is happening where and when in the human brain when we see? In this talk I will present recent work that addresses these questions in an integrated analysis framework combining human magnetoencephalography (MEG), functional magnetic resonance imaging (fMRI) and deep neural networks (DNNs). The talk has three parts. In the first part, I will show how fMRI and MEG can be combined using multivariate analysis techniques (classification plus representational similarity analysis) to yield a spatio-temporally integrated view of human brain activity during object vision. In the second part I will show how DNNs can be used to understand the human visual system. In one study, we showed that DNNs predicted the spatial-temporal hierarchy of the human visual system. In another study, we showed that representations of abstract visual properties, such as scene size, find an analogue in DNNs. In the third, shorter part I will present research informing about the source of information present in MEG signals: representations encoding at the level of columnar columns may be accessible to multivariate pattern classification.

- **Nicholas Myers** (Univ. of Oxford, UK)
  "Testing sensory evidence against mnemonic templates"

Most perceptual decisions require comparisons between current input and an internal template. Classic studies propose that templates are encoded in sustained activity of sensory neurons. However, stimulus encoding is itself dynamic, tracing a complex trajectory through neural activity space. Which part of this trajectory is pre-activated to reflect the template? We recorded magneto- and electroencephalography during a visual target-detection task, and used pattern analyses to decode template, stimulus, and decision-variable representations over time. Our findings ran counter to the dominant model of sustained pre-activation. Instead, template information emerged transiently around stimulus onset and quickly subsided. Cross-generalization between stimulus and template coding, indicating a shared neural representation, occurred only briefly and weakly. Our results are thus more compatible with the proposal that template representation relies on a matched filter, transforming sensory input into task-appropriate output. This proposal was consistent with a signed difference response at the perceptual decision stage, which can be explained by a simple neural model.

Aberrant Coupling and Oscillations in Parkinson's

Organizer: Elizabeth Heinrichs-Graham

Room: # 104

Date and Time: Wednesday, October5 / 17:10-18:10

Decoding Aberrant Coupling and Oscillatory Dynamics within Motor Circuits in Parkinson's Disease
The advent of deep brain stimulation enabled researchers to directly record local-field potential (LFP) data from basal ganglia structures in humans, and recent work combining magnetoencephalography (MEG) and such LFP recordings has revolutionized our understanding of the pathophysiology that underlies Parkinson's disease (PD). In this symposium, international leaders in this field will discuss their latest findings using LFP, MEG, and LFP+MEG approaches. Specifically, the symposium opens with a discussion of frequency-specific subcortico-cortical connectivity, recorded by simultaneous LFP-MEG recordings, that distinguishes PD from other movement disorders such as dystonia. The second talk with highlight recent data connecting resting tremor to beta oscillatory activity and coherence between the subthalamic nucleus and motor cortices. Next, new data linking the severity of rigidity/bradykinesia in patients with PD to phase-amplitude coupling between ongoing beta and ultra-high frequency oscillations (150-400 Hz) will be presented. Finally, recent MEG findings will be presented that identify the physiological signature of symptom laterality in PD. Together, this series of talks will demonstrate the groundbreaking progress that has recently emerged in our understanding of the pathophysiology of PD, and will introduce critical new avenues in the search for a physiological marker of disease progression and treatment efficacy.

Speakers:

- **Wolf-Julian Neumann** (Univ. Medicine Berlin, Germany)
  "What local field potentials have taught us about the pathophysiology of movement disorders"

  Deep brain stimulation (DBS) is a highly effective treatment in movement disorders, such as Parkinson's disease (PD) and dystonia. Traditionally regarded as basal ganglia disorders, recent evidence points to more wide spread dysfunctions in these disease entities across the motor network. Therefore, both PD and dystonia are now referred to as circuit disorders. Local field potential recordings from subcortical DBS targets during and after the implantation of electrodes have revealed crucial findings that have contributed substantially to our understanding of the pathophysiology of these movement disorders. In PD subthalamic and pallidal oscillatory activity is synchronized in a beta rhythm (13 - 30 Hz) that is suppressed by dopaminergic medication and DBS in parallel with alleviation of motor symptoms in these patients. In dystonia, low frequency activity (4 - 12 Hz) is most prominent in the same structures and both, beta oscillations for PD and low frequency activity in dystonia, are hypothesized to reflect pathophysiological hallmarks of the respective disorders that may have a causal role in the development abnormal movement and posture. Parallel magnetoencephalography and local field potential recordings have now opened the window to investigate oscillatory subcortico-cortical network connectivity and studies using this innovative methodological approach further corroborate the pathophysiological role of aberrant oscillatory activity across the motor network in movement disorders. The proposed talk will give an overview on the significance of pathological oscillatory activity in the motor network.

- **Markus Butz** (Heinrich-Heine-Univ. Düsseldorf, Germany)
  "Oscillatory basal ganglia - cortex signature of Parkinsonian rest tremor"

  Motor symptoms of Parkinson's disease (PD), such as akinesia and rest tremor, seem to be associated with pathological oscillatory activity in basal ganglia and cortex. Therapeutic implantation of deep brain stimulation (DBS) electrodes into the subthalamic nucleus (STN) provides a unique opportunity to directly

measure local field potentials from the human STN. To analyse STN and cortical oscillatory power as well as coherence between STN and cortex associated with PD rest tremor we simultaneously recorded STN-LFPs, whole-head MEG, and tremor-EMG in tremor-dominant PD patients with DBS electrodes externalized after DBS surgery. We took advantage of naturally occurring spontaneous tremor fluctuations and compared oscillatory activity in the presence and absence of rest tremor. We found tremor-related oscillatory changes in distinct frequency bands: STN and cortical beta power (13-30 Hz) decreased as tremor becomes manifest. STN power at double the individual tremor frequency increased following tremor onset. Coherence between STN and cortical areas at tremor and double tremor frequency increased during tremor. The ratio between slow and fast high frequency oscillation (HFO; > 200 Hz) power in STN increased when tremor became manifest. These findings advance our pathophysiological understanding of PD rest tremor and may provide a neurophysiological marker for closed-loop DBS in tremor treatment.

- **Bernadette Van Wijk** (Univ. College London, UK)
  "High-frequency oscillations as a new window into Parkinson's disease"

The subthalamic nucleus (STN) is one of the primary targets for deep brain stimulation (DBS) treatment in Parkinson's disease. Local field potentials recorded from the STN have revealed a strong association between beta band oscillations and bradykinesia/rigidity symptoms. Both dopaminergic medication and DBS reduce beta band amplitude along with improvements in clinical motor scores. However, it remains unclear how excessive beta band oscillations mechanistically lead to motor impairment. Here, I propose that more insight into Parkinsonian neurophysiology might be obtained by focusing on another spectral peak that can frequently be observed: high-frequency oscillations (HFO) within the 150-400Hz range. Activity within this frequency range is especially relevant as it typically shows a movement-related increase in amplitude. I will present our findings indicating that HFO may express abnormally strong phase-amplitude coupling with ongoing beta band oscillations that correlates with severity of bradykinesia/rigidity. In addition, our intraoperative recordings identified that HFO and beta band oscillations are likely to arise from spatially close neural populations. Future work will be necessary to determine whether HFO can help fine-tune deep brain stimulation targeting.

- **Elizabeth Heinrichs-Graham** (Univ. of Nebraska Medical Center Omaha, USA)
  "The importance of symptom laterality in studying oscillatory patterns in Parkinson's"

Patients with Parkinson's disease (PD) initially present with unilateral motor symptoms. Importantly, the side of symptom onset has been associated with distinct symptom trajectories in PD, yet the aberrant cortical neurophysiology that underlies such symptom asymmetry has been largely overlooked. Here, I demonstrate that the side of symptom onset and degree of symptom laterality results in a distinct pattern of cortical oscillatory aberrations in PD. Using MEG and beamforming methods to examine cortical beta oscillations during a right-hand movement task in right-handed patients who exhibited either right- or left-dominant symptomatology, I show that the pattern of beta activity prior to, during, and after transient movement is significantly different between patients who exhibit right-dominant compared to left-dominant symptomatology, and that the laterality of beta activity during movement uniquely correlates with symptom laterality. This data is the first to directly probe the relationship between symptom laterality and neurophysiological laterality during movement in patients with PD, and highlights the importance of symptom variability in the search for a reliable physiological marker of disease progression on the individual patient level.

Integration and Prediction in Language

Organizer: Ole Jensen and Lin Wang

Room: # 105

Date and Time: Wednesday, October5 / 17:10-18:10

Neural Mechanisms of Language Integration and Prediction
Language comprehension relies on several brain regions interacting on a very fast time-scale in order to support the required cognitive operations. Two important processes that contribute to successful language processing are integration and prediction. Integration refers to the combination of lexical, syntactic, semantic and contextual information, whereas prediction refers to an anticipatory pre-activation of words amongst others based on contextual information. Integration serves as a basis for prediction and in turn prediction facilitates the integration of upcoming words. In order to understand the brain mechanisms involved in language processing, it is important to characterize neural activities related to integration and prediction in the brain, both in time and in space. In this symposium, speakers will present human electrophysiological data including MEG to better understand the network dynamics underlying integration and prediction in language processing.

Speakers:

- **Liina Pylkkänen** (New York Univ., USA)
  "The brain's combinatory network as revealed by MEG"

  Although our brains' ability to build complex meanings from simpler representations is fundamental to all of language, our understanding of the neurobiology of meaning composition is still grossly generic. To characterize the neural bases of semantic composition more mechanistically, a cognitive model is needed to define the space of possibilities. Our research departs from most mainstream cognitive neuroscience on semantics by taking the results of formal semantics within theoretical linguistics as the model that fundamentally guides the experimentation. Our MEG research implicates a shared combinatory network between comprehension and production comprising at least of the left anterior temporal lobe and the ventromedial prefrontal cortex. In contrast to hypotheses arising from hemodynamic literature, our MEG studies have not implicated the angular gyrus (AG) or the left inferior frontal gyrus (LIFG) as systematically sensitive to basic composition; instead, our data suggest a role in relational processing for the AG and in retrieval operations for the LIFG. To conclude, I will sketch a spatio-temporal progression of the MEG correlates of various stages of language processing as implicated by our group's work over the last 15 years, from the prediction of visual word forms to higher level integrative processes and reference resolution.

- **Ole Jensen** (Donders Institute, The Netherlands)
  "Alpha oscillations in the language network reflect prediction during reading"

  It has been demonstrated that readers and listeners actively predict upcoming words during language processing. However, it remains unclear which neural activity reflects prediction. In this talk, I will present our recent MEG data on the neural oscillatory activities associated with language prediction. We found strong alpha power suppression preceding the highly expected words were presented in both language network (left inferior frontal cortex, left superior and middle temporal region, visual word form area) as well as subcortical regions (left hippocampus and right cerebellum). In addition, there was strong alpha phase consistency in the left inferior frontal cortex and the right cerebellum when there was strong prediction of upcoming words. The involvement of the VWFA suggests that participants made predictions at the word form level. Furthermore, the left frontal, temporal language areas as well as left hippocampus and right cerebellum are likely to participate in the generations of these predictions. In addition, our study

extends previous research on the function of alpha oscillations by demonstrating that a decrease in alpha oscillations reflects the engagement of higher-level language areas. The stage is now set for investigating how the involved areas functionally interact in order to support the generation of predictions.

- **Nicola Molinaro and Mikel Lizarazu** (Basque Center on Cognition, Brain and Language, Spain)
  "The role of cortical oscillations during speech processing"

Speech comprises hierarchically organized rhythmic components that represent prosody (delta band), syllables (theta band) and phonemes (gamma band). During speech pre-processing steps, neural oscillations within a fronto-temporo-parietal network track these quasi-rhythmic modulations through different mechanisms (de-multiplexing and segmentation steps). Speech processing models associate neural computations in temporal regions to perceptual processes, while operations in frontal-parietal regions are linked to higher-order processes (attention). However, there is no comprehensive view of the neural dynamics that allow perceptual and attentional processes to interact before extracting meaning from speech. In the present study, we analyzed MEG data from 20 participants while hearing continuous speech. First, we determined how different brain areas within the fronto-temporo-parietal network deal with the de-multiplexing (Coherence analysis) and the segmentation (Phase Amplitude Coupling analysis) pre-processing steps. Then, we showed how low-frequency (delta and theta band) neural oscillations bidirectionally connect (Transfer Entropy analysis) temporal and fronto-parietal areas. Our results indicate that, during continuous speech processing, cortical oscillations represent an ideal medium to deal with perceptual and attentional neural computations, as well as to control interactions between these cognitive operations.

- **Lars Meyer** (Univ. of Potsdam, Germany)
  "Chunk, Store, and Integrate: Neural Oscillations during Sentence Comprehension"

Sentence comprehension is often conceptualized as a set of working-memory operations: Speech is chunked into phrases, which are stored for the establishment of dependencies with other phrases, and which are integrated with other phrases on dependency establishment. Prior research on speech and working memory generates hypotheses for the neural-oscillatory mechanisms behind these operations. As a first example from speech research, delta-band oscillations entrain to intonation phrases—from which I hypothesized implications for phrasal chunking. As a second example from working-memory research, alpha-band oscillations are involved working-memory storage—from which I hypothesized the alpha band's involvement in phrase storage. As a third example, long-distance theta-band synchronization underlies retrieval of items from the brain's memory systems—from which I hypothesized a role of the theta band in the integration of stored phrases. In this talk, I will present recent evidence for my hypotheses: First, phrasal chunking is predicted by delta-band phase. Second, increases in left-parietal alpha-band power accompany the storage of phrases. Third, phrase integration is accompanied by long-distance theta-band synchronization between storage and control brain regions. The functional brain network of sentence comprehension thus appears to tap into principles of information processing and transfer that are common across domains.

Ultra-Low-Field Magnetic Resonance Imaging

Organizer: John Clarke

Room: # 104

Date and Time: Thursday, October6 / 08:30-10:30

Recent Advances in Ultra-Low-Field Magnetic Resonance Imaging
In this symposium, seven speakers from five institutions will give a broad overview of recent advances in the technology of Ultra-Low-Field Magnetic Resonance Imaging (ULF MRI) and its applications. The topics will cover:

· the integration of ULF MRI and MEG using a multichannel SQUID system
· the precise elimination of eddy currents due to pre-polarization pulses
· Ultra-low-noise multichannel-SQUID-System for ULF MRI
· neuronal current imaging by ULF MRI
· study of T1 and T2 of protein gels as a function of magnetic field investigating cross-linkage
· T1 and T2 from in vivo images of the human brain and post-mortem pig brain
· portable ULF-MRI system operational without metallic shielding

The level of presentation will be accessible to a broad audience of BIOMAG attendees.

Speakers:

- **Risto Ilmoniemi** (Aalto Univ., Finland)
  "What is the intended breakthrough in MEG–MRI?"

  Hybrid MEG–MRI technology will enable the measurement of both the structure of the head (MRI) and the electrical activity of the brain (MEG) at the same time. This will improve workflow, remove the registration error, and allow new kinds of measurements such as current-density imaging (CDI). Reliable registration and CDI-enabled accurate determination of individual tissue conductivities will, for the first time, allow reliable use of geometric constraints such as the requirement that source currents may reside in gray matter only. With sufficient *a priori* information, the inverse problem will have a unique solution that can be trusted.

- **Koos Zevenhoven** (Aalto Univ., Finland)
  "Software for ULF MRI: managing the various techniques and hardware"

  As ULF MRI matures, more and more sequences and techniques are available for optimized measurements and different forms of imaging such as current-density imaging. To manage the combination of various methods with reasonable convenience while the instrumentation and techniques are changing, a robust software infrastructure is needed with appropriate abstractions and automated adjustments. As an example, it is shown how setting up DynaCan to remove eddy-current artefacts can be incorporated in the software stack as an extension module.

- **Rainer Körber** (PTB, Germany)
  "Ultra-low-noise multichannel-SQUID-System for ULF MRI"

  We discuss the design of our new multichannel-SQUID-system for ULF MRI. It is geared for ultra-low-noise performance and is based on our modular and robust 18-channel-system which was tested in a prototype. There, a central feature is the use of overlapping magnetometer pick-up coils with different dimensions

enabling maximum SNR for different source depths. Using software gradiometer we achieved a minimum noise level of 0.5 fT/√Hz. The prototype was successfully deployed for ULF NMR and MEG. As an example, the system was used to detect 1 kHz components of 1 fT peak-peak amplitude in electro-stimulated MEG signals. We will discuss the properties of the prototype and its implication for the ultra-low-noise system to be used for CDI and NCI at ULF.

- **Martin Burghoff** (PTB, Germany)
  "Neuronal current imaging by ULF MRI (NCI)"

The goal of NCI is to help overcome a long-standing barrier of the inverse problem in MEG localization, mainly the non- uniqueness of the electromagnetic inverse problem. The detection of the influence of the weak neuronal magnetic fields on an MR image contrast does not suffer from this lack of uniqueness. Phantom studies show promising results to apply this technology for long lasting neuronal activities.

- **Hui Dong** (Chinese Academy of Sciences, China)
  "ULF-NMR T1 and T2 of cross-linked proteins: Implications for brain ULF-MRI"

The slow molecular dynamics of proteins reveals important interactions of tissue surfaces such as proton and molecule exchange mechanisms. Clinical magnetic resonance imaging (MRI) machines operating in static fields B_0 of the order of tesla use the so-called $T_{1\rho}$ technique to acquire this information. This $T_{1\rho}$ method, in which a radiofrequency (RF) spin-lock field is applied with microtesla amplitude, may exceed the specific absorption rate (SAR) limit, putting subjects at risk. Ultra-low-field (ULF) MRI, based on Superconducting QUantum Interference Devices (SQUIDs), directly detects slow motions of protons at B_0 of typically 100 µT. Using our ULF MRI system at Berkeley, we systematically measured the T_1 and T_2 dispersion profiles of rotationally immobilized gels of bovine serum albumin (BSA) with variable static fields ranging from 55 to 240 µT. Comparing the ULF results with $T_{1\rho}$ dispersion obtained at 7 T, we find that the degree of protein immobilization determines the frequency-dependence of both T_1 and $T_{1\rho}$. Furthermore, scans of *ex vivo* pig brain showed similar behavior between cross-linked proteins and brain tissue. This similarity suggests that ULF MRI may be used to image stroke or traumatic brain injury (TBI) with negligible SAR.

- **Seong-min Hwang** (KRISS, Korea)
  "ULF MRI of in vivo human brain and post-mortem pig brain"

Recent animal studies with high-field MRI showed that $T_{1\rho}$, which exhibits NMR properties at spin-lock fields much lower than the static field B_0, typically several tesla, could be a good indicator of stroke onset time. ULF MRI is an ideal substitute for $T_{1\rho}$ MRI for stroke onset diagnosis since ULF-MRI measures true T_1 and T_2 at ULF rather than $T_{1\rho}$. Furthermore, ULF MRI is free from the specific absorption rate (SAR) issue unavoidable in $T_{1\rho}$ because it requires the application of a strong high-frequency spin-lock field. We have performed ULF MRI of *in vivo* human brain at B_0 between 58 µT and 235 µT using Inversion Recovery to prevent the much longer relaxation signal from cerebrospinal fluid (CSF) from contaminating T_1 and T_2 of brain tissue. We also report ULF-NMR measurements of gray and white matter taken from postmortem pig brains measured in the same B_0 range. Contrary to *in vivo* human brain, postmortem pig brain showed frequency dispersion and, more significantly, divergence of T_1 and T_2. Further studies with rotationally immobilized protein gels and Sephadex beads indicate that the frequency dispersion and the T_1/T_2 divergence may be due to interaction between localized water and surrounding matrix structures.

- **Per Magnelind** (Los Alamos National Laboratory, USA)
"Fieldable ultra-low-field MRI systems for non-traditional situations and settings"

Magnetic Resonance Imaging (MRI) is considered the best non-invasive imaging method for soft tissue anatomy and provides extraordinary diagnostic capabilities, saving countless lives each year. However, conventional MRI relies on high strength magnetic fields (> 1.5 T) with parts-per-million homogeneity, requiring very large and costly magnets that are only available in highly controlled settings in well-funded medical centers.   Traditional high-field MRI is not available in rural settings, is not deployable to emergency situations or battlefield hospitals, and is too expensive for poor and developing countries. We will present progress toward developing a portable MRI machine based on SQUID (superconducting quantum interference device) sensor technology and ultra-low-field MRI techniques. We will show brain images acquired inside a shielded room and phantom images acquired in an unshielded setting.

Resolution of Connectivity in Time and Frequency

Organizer: Stephen E. Robinson

Room: # 105

Date and Time: Thursday, October6 / 08:30-10:30

Beyond fMRI: What MEG Reveals about Functional Connectivity in the Time Domain
Brain activity is highly dynamic and is non-stationary. This fact should be obvious by observation of behavior. Functional imaging methods such as fMRI have emphasized the correlations of sub-Hertz activity. Electrophysiological methods such as MEG provide resolution of fast events in both the time and frequency domain. In this symposium we will explore how application of linear and non-linear techniques to MEG reveal the rapidly changing brain dynamics.

Speakers:

- **Mark Woolrich** (Univ. of Oxford, UK)
  "Fast transient spectrally-distinct networks"

  The importance of distributed networks in cognition is well established. In order to be able to respond to fast changing environments, the brain must be capable of coordinating networks on sub-second time-scales. While there has been some success in identifying networks using resting MEG, this has been somewhat limited to static descriptions (e.g. averaged over several seconds), and to using envelope (or power) correlations. Important questions remain unanswered: what specific mechanisms of interaction underpin these envelope correlations, and what are the dynamics of these interactions at very fast time-scales?
  In this talk, I will present an approach that can identify transient periods of distinct network dynamics, even if they persist for very short (<100ms) time-periods. Importantly, distinct networks dynamics are described using their cross-spectra, allowing for the possibility of interactions through phase locking. The approach is able to identify short-lived dynamics by recognizing when they repeat at different times, and thereby pool over them to provide good estimation of the cross-spectral patterns. Finally, I will show how the approach is providing novel insights in both task and rest data (e.g. in local field potential recordings and MEG), and in the clinical domain in psychiatric disorders.

- **Allison Nugent** (NIMH/NIH, USA)
  "Major Depressive Disorder: Disruption across the frequency spectrum"

  Major depressive disorder (MDD) is highly prevalent, frequently disabling, and sometimes fatal. Despite the severity of the public health problem, relatively little is known about the cause of MDD, and treatment is frequently inadequate. A wide array of neuroimaging techniques have been used to study MDD, including EEG and MEG. Frequently, electrophysiological studies of MDD investigate either a single frequency band of interest, or combine large groups of sensors. In our studies, we have begun to use data driven techniques to examine spatial spectral patterns of dysfunction in MDD, revealing that the abnormalities in regions known to be involved in depression, such as the amygdala, possess a complex electrophysiology. We have additionally examined cross-frequency interactions in depression, in hopes that a more comprehensive view of dysfunction in MDD may further our knowledge of this disorder and inform better treatments.

- **Michael Wibral** (Goethe Univ., Germany)
  "Tracking information transfer through cortex with (almost) single sample resolution"

  While anatomical connectivity is largely static on timescale of an experimental epoch in an MEG experiment, the information processing evolving on this fabric is highly dynamic. We have recently introduced two methods to localize information transfer in the brain in time with high resolution. First, we suggested a method based on ensembles of experimental repetitions to properly capture the time-dependent probability distributions in the data and to analyze information transfer for short time windows. Second, within such windows Lizier's method of local information dynamics that reaches all the way back to Fano's local mutual information can be used to give an informational value to every single sample of a recording, bringing the full time resolution of MEG to bear. We will demonstrate the application of these techniques to recordings from a Go/NoGO paradigm and in the investigation of information transfer through visual cortex in a closure task.

- **Matthew Brookes** (Univ. of Nottingham, UK)
  "Connectivity: It's About Time…"

  In the past decade, a vast number of neuroimaging studies have sought to elucidate networks of functional connectivity; specifically, the existence of multiple brain regions which appear to share temporal dynamics. This field has been dominated by functional magnetic resonance imaging (fMRI), however a number of recent studies have looked to MEG to elucidate the electrophysiological effects which underpin the apparent networks observed in the blood oxygenation level dependent (BOLD) haemodynamic signal. In this talk, I will summarise some of our own investigations in this area. I will begin by reviewing the relationship between networks of connectivity observed using fMRI and MEG; I will show that the two modalities are related and, most importantly, I will describe recent evidence which suggests that haemodynamic networks are not simply reflective of electrophysiological networks in isolated frequency bands, but rather are predicted by a non-linear combination of pan spectral and cross frequency electrophysiological interactions. Following this, I will move to the topic of dynamic connectivity. I will review evidence showing that connectivity is non-stationary, and I will show conclusively that, to gain a complete picture of network dynamics, one must assess connectivity on rapid timescales that are inaccessible to haemodynamic imaging.

- **Stephen E. Robinson** (NIMH/NIH, USA)
  "Frequency dependencies of information transfer"

  Transfer entropy (TE) is a non-linear measure of directional information transfer of how well knowledge of past signals from a pair of regions X and Y can predict future values of either X or Y. We have previously shown that the temporal evolution of TE can be observed using "leaky integrator" or sliding window techniques. Although it might seem that information transfer should be studied across the MEG's full range of frequencies, using data from n-back tests we have found that information transfer is not distributed uniformly across the frequency spectrum. We observe that TE is lowest and signal-to-noise is greatest at frequencies below about 50 Hz, where synchronous and rhythmic activity dominate. However, despite the poorer signal-to-noise, the magnitude of TE is generally greatest where asynchronous activity dominates above 150 Hz. These observations are general but depend upon the pair of brain regions that are selected. The frequency dependence of informational measures may provide additional markers for psychiatric disorders.

Improving EEG/MEG Source Analysis in Children

Organizers: Carsten Wolters and Robert Oostenveld

Room: # 103

Date and Time: Thursday, October6 / 13:30-14:30

Improving Source Reconstruction for MEG and EEG in Children
The European Brain Council (EBC) has recommended disorders of the brain to be prioritized for funding. One successful example of this is the Marie Curie Innovative Training Network ChildBrain (see http://www.childbrain.eu) which aims on the one hand to train young researchers and on the other hand to utilize evidence-based neuroscientific knowledge for helping children, especially those at high risk for dropout due to neurocognitive disorders, to meet future educational and societal demands.

In the ChildBrain network we develop new, innovative brain imaging-based tools in collaboration between research and industry and that can be applied by researchers and clinicians.

MEG and EEG data acquisition (movements and SNR) and modelling (volume conduction) are specifically challenging in children. In this proposed Biomag2016 session we will highlight the ChildBrain brain research methods work package. This provides not only value to the use of MEG and EEG in children, but will also contribute to improving the application in adults.

Speakers:

- **Abinash Pant** (BESA GmbH, Germany)
  "An automatic Markov Random Field-based approach for segmentation of volume conductor models of the human head"

The accurate solution of the EEG and MEG forward problem requires taking into account information about a subject's individual anatomy. This information is contained in the volume conductor model which describes the electrical properties of the subject's head. Commonly, individual models are constructed by first segmenting the head into the different tissue compartments based on the available medical image data. Next, a suitable discretization of the head domain is computed, and previously published tissue conductivities are assigned.

Here, we propose a new automatic segmentation approach for segmenting the tissues of the head. The approach is formulated in a Bayesian framework. A-priori knowledge about the anatomy is included from two sources. A Markov Random Field model encodes our knowledge about the general arrangement of the head tissues. Secondly, a custom probabilistic tissue atlas further facilitates the segmentation.

Validation studies versus CT-based and manual segmentations were performed. Results prove the accuracy and reliability of the proposed approach. Average accuracies for the skull segmentation reached values of 88%.

In the ChildBrain project an approach for segmenting volume conductor models of infant subjects and patients will be developed. An outlook will discuss the related challenges and how we are aiming to solve them.

- **Theo Papadopoulo** (INRIA, France)
  "Modeling thin tissue compartments using the immersed FEM (continuous Galerkin) "

This presentation will describe a trilinear immersed finite element method for solving the electroencephalography forward problem, which is a three-dimensional elliptic interface problem in the head geometry. The method uses hexahedral Cartesian meshes (i.e. 3D images which can be explored using standard visualization tools for MR images) independent of the interfaces between head tissues, thus avoiding the sometimes difficult task of generating geometry fitting meshes (which is exacerbated for child head volume conductors which contain close interfaces requiring a very high number of elements to obtain numerically good mesh representations). Brain interfaces are provided as level set representations, which are also 3D images. Such level set representations can directly be used in head segmentation tools but can be also easily obtained from meshes. The finite element space is locally modified to better approximate the continuity properties of the solution (continuous potential and normal currents despite a discontinuity of the conductivity). Numerical results show that this method achieves the same accuracy as the standard linear finite element method with geometry fitting meshes without the hassle of creating meshes for the complex head domain.

- **Andreas Nüßing** (Univ. of Münster, Germany)
  "The unfitted discontinuous Galerkin FEM for the EEG forward problem"

We introduce and evaluate the unfitted discontinuous Galerkin finite element method (UDG-FEM) for solving the EEG forward problem. This new approach for source analysis does not use a geometry conforming volume triangulation, but instead uses a structured mesh that does not resolve the geometry. The geometry is described using level set functions and is incorporated implicitly in its mathematical formulation. As no triangulation is necessary, the complexity of a simulation pipeline and the need for manual interaction for patient specific simulations can be reduced and is comparable with that of the FEM for hexahedral meshes. In addition it maintains conservation laws on a discrete level. We will present the theory for UDG-FEM forward modelin g, its validation using quasi-analytical solutions in multi-layer sphere models and an evaluation of the new method in a comparison with competing approaches. Results show convergence and ind icate a good overall accuracy of the UDG-FEM approach. UDG-FEM performs comparable or even better than competing approaches while providing a less complex simulation pipeline. As we will show, the new method is especially important for solving the forward problem in child brain res earch.

- **Johannes Vorwerk** (Univ. of Münster, Germany)
  "The FieldTrip-SimBio pipeline for FEM-based EEG forward computations"

For accurate EEG source analysis it is necessary to precisely simulate the electric field generated by a minimal patch of active brain tissue. This is called the forward problem of EEG. It has been shown in a variety of studies that the achieved accuracy in solving the forward problem strongly depends on an accurate representation of the conductive features of the head. Therefore, the use of realistic head models is inevitable. It can be achieved using the finite element method (FEM), which was shown to achieve high accuracies in sphere and realistic head model studies. However, despite the advantages of realistic head modeling, the generation of the necessary meshes is often considered too time consuming.

In this talk, the FieldTrip-SimBio pipeline for FEM-based EEG forward simulations is introduced. This pipeline allows for the easy generation of individual, five-compartment realistic head models and the computation of EEG forward solutions using FEM. Being included in the FieldTrip-toolbox, also tools for data preprocessing and subsequent source analysis are directly available. Besides the presentation of the

pipeline-workflow, the accuracy of the achieved segmentation is evaluated, and examplarily the results of a source analysis of somatosensory evoked potentials (SEP) using the FieldTrip-SimBio pipeline is shown.

- **Jukka Nenonen** (Elekta Oy, Finland)
  "Improving the SNR in pediatric MEG studies"

Pediatric magnetoencephalography (MEG) presents particular challenges to signal processing and source imaging.   The main difficulty is the fact that children tend to move substantially during the measurement, which sometimes compromises the quality of data. Continuous head position tracking and sensor-level movement compensation algorithms have been developed, such as data decomposition and reconstruction with the Signal Space Separation (SSS) method. However, large head movements cause increased reconstruction noise if the varying distance-related SNR is not taken into account in the SSS process. Additional difficulties arise if pediatric patients have magnetized material or implanted stimulators, causing significant movement-modulated interference.

We present novel signal processing methods for improved movement correction and for suppressing sensor noise and artifacts: 1) Improved regularization method reduces reconstruction noise associated with large head movements. 2) Cross-validation SSS model separates the spatially correlated part (brain-related signals + magnetic interference) and uncorrelated part (sensor noise and artifacts) of a multichannel MEG signal. 3) Utilization of signal and noise covariance information in SSS decomposition reduces the overall sensor noise levels through enhanced numerical stability.

We demonstrate that the new SSS workflow potentially broadens the application of pediatric MEG both in clinical and research studies.

The New MEG Frontier?

Organizer: Jing Xiang

Room: # 104

Date and Time: Thursday, October6 / 13:30-14:30

MEG Detection of Low to High Frequency Neuromagnetic Activity
Recent success in localizing low- (LFBS, 0-14 Hz) and high-frequency brain signals (HFBS, 70-2,884 Hz) opens a new window for the study of epilepsy, migraine and potentially many other disorders using magnetoencephalography (MEG). This topic is very important and interesting because both clinicians and basic researchers can benefit from it. For example: (1) localization of HFBS can increase the effectiveness of epilepsy surgery by approximately 30%. By promoting the applications of HFBS, MEG tests may result in millions of intractable epilepsy patients being seizure free. (2) By using LFBS and HFBS, MEG has revealed that migraine has abnormal cortical excitability and that medications normalizing cortical excitability can reduce the incidence of migraine attacks. (3) A discussion of LFBS and HFBS can advance our understanding of the cerebral mechanisms of multi-frequency brain activity. In addition, MEG hardware and software developers may use LFBS and HFBS to create novel solutions for diagnosis and treatment of many brain disorders.

Speakers:

- **Milena Korostenskaja** (Florida Hospital for Children, USA)
  "High Gamma Functional Mapping for epilepsy surgery"

  The essential part of epilepsy surgery is localization of eloquent cortex (responsible for motor, sensory, language, and memory functions) that must be maximally preserved while removing pathological epileptogenic substrate from the patients' brain. We have implemented innovative real-time functional mapping (RTFM) methodology based on real time detection and analysis of high gamma oscillations (70 - 110 Hz) for pre-surgical evaluation of epilepsy surgery candidates. We have validated RTFM against other functional mapping modalities, such as magnetoencephalography (MEG), electrical cortical stimulation mapping (ESM), and functional magnetic resonance imaging (fMRI). The results of our studies are highly promising and support clinical application of RTFM methodology for pre-surgical eloquent cortex localization. Moreover, we have demonstrated significant contribution of RTFM to decreasing post-surgical language morbidity. Our performed comparison between RTFM and MEG functional mapping approaches demonstrates a strong promise for the development of highly sophisticated, reliable and safe non-invasive MEG-based functional mapping procedures based on the analysis of different frequency bands, including high gamma. Inclusion the whole spectrum of frequencies (both low and high) in the analysis of functional mapping data may lead to increase in sensitivity and specificity of functional brain mapping results.

- **Kimberly A. Leiken** (Cincinnati Children's Hospital Medical Center, USA)
  "Assessment of Cortical Excitability in Migraine with Neuromagnetic High-frequency Signals"

  Reports suggest that abnormal cortical excitability may be associated with acute migraines. The present study quantitatively assesses the degree of cortical dysfunction in pediatric migraine subtypes. We investigated 27 children with chronic migraine, 27 acute and 27 controls using magnetoencephalography (MEG), recording at a sampling rate of 6000 Hz. All groups were age- and gender-matched. Neuromagnetic brain activation was elicited by a finger-tapping motor task. The spatiotemporal and spectral signatures of MEG data within a 5-2884 Hz range were analyzed using Morlet wavelet transform and beamformer analyses. Compared with controls, both migraine groups showed (i) prolonged latencies of movement-elicited magnetic fields (MEFs) 5-100 Hz; (ii) increased spectral power 100-200 Hz, and 2200-2800 Hz; and (iii) a higher likelihood of neuromagnetic activation in the ipsilateral sensorimotor cortices, supplementary

motor area, and occipital regions. Though early MEFs (< 100 ms) were identified in all groups, later MEFs (>150 ms) were only apparent in migraine groups. Between the migraine groups, chronic migraine patients showed higher odds than acute of having strong MEFs after 150 ms. Chronic migraine patients also showed higher odds than acute of having neuromagnetic activation from the deep brain areas. Results demonstrated that chronic migraine was not only different from controls, but also from acute. The chronification of migraines may be associated with delayed neural response, as well as aberrant localization of cortical activation.

- **Woorim Jeong** (Seoul Nat'l Univ. Hospital and Seoul Nat'l Univ. College of Natural Science, Korea)
  "Usefulness of multiple frequency band source localizations in ictal MEG"

  We evaluated the diagnostic value of multiple frequency band MEG source localization within a wide time window during the preictal period. Data for 13 epilepsy patients who showed an ictal event during MEG were analyzed. Several seconds of preictal data were localized in the theta, alpha, beta, and gamma bands by using wavelet transformation and the sLORETA algorithm. The same analysis was performed with narrow time and frequency band. Localization concordances to the surgically resected area were compared. Source localization in the gamma band for a 10s window before ictal onset showed best concordance to the resection cavity. Eight of 13 patients showed sub-lobar concordance in the 10s gamma band localization, whereas 3 showed concordance in the narrow time and frequency analysis. Four of 7 patients with focal cortical dysplasia (FCD) achieved seizure-free outcome, and all 4 showed sub-lobar concordance. A 10s time window gamma source localization method can be used to delineate the epileptogenic zone. The use of a long period during preictal gamma source localization has the potential to become a localizing biomarker of the epileptogenic zone in candidates for surgical intervention, especially in MRI-suspected FCD.

- **Yuping Wang** (Capital Medical Univ., China)
  "MEG low frequency activity detection for the localization of temporal lobe epilepsy"

  Epileptic discharges are of importance for the diagnosis of epilepsy and localization of epileptogenic zone. However, rhythmic oscillations are the most common electrical manifestation of epilepsy patients. Low frequency activity of cerebral cortex is related with cerebral functional changes. Depth electrode EEG can clearly show such low frequency activity in temporal lobe epilepsy (TLE) patients. Magnetoencephalography (MEG) has been used for the detection of low frequency activity in 14 TLE patients. All of them were seizure-free more than three years after the unilateral temporal resective surgery. Their MEG data were analyzed using beamformer analysis. Beamformer analysis was performed on at least two segments with spike and one segment without spike (resting state). The beamformer analysis showed time-dependent energy fluctuation in low frequency band in 11 patients (11/14, 78.6%), the energy majority was ipsilateral to the surgically treated side, irrespective of the presence or absence of spikes or MRI lesions. Delta band activity had higher lateralizing value than other frequency bands. Low frequency fluctuation in beamformer MEG source imaging was valuable for lateralizing epileptogenic zone.

- **Stefan Rampp** (Univ. Hospital Erlangen, Germany)
  "Low frequency activity in patients with focal epilepsy"

  In recent years, novel markers for the epileptic network beyond interictal spikes and ictal seizure correlates have been described. Slow activity in theta, delta and lower frequency ranges have been detected using invasive EEG and non-invasive MEG/EEG. While such activity also occurs associated e.g. with large lesions and after intracranial surgery, certain subtypes may be utilized to localize the epileptic network. The presentation will give an overview of MEG slow frequency markers in patients with focal

epilepsy. Current evidence, clinical applications and putative mechanisms are presented and illustrated with case examples.

Cognition, Computation, and Brain Diseases

Organizer: Jaeseung Jeong

Room: # 105

Date and Time: Thursday, October6 / 13:30-14:30

Cognitive and Computational Approaches to Understand Brain Diseases
This symposium discusses cognitive and computational approaches to understand neural circuits across the temporal to frontal lobe that generate flexible behaviors, thereby forming the neural basis of various brain diseases. Speakers provide a brief overview of progresses in applying advanced neural analysis techniques to brain data, such as an iEEG monitoring, a multivoxel pattern analysis, and a model-based fMRI analysis. These approaches provide effective tools for detecting impairment of neural circuits that may inform early diagnosis and systematic treatments for some brain diseases.

Speakers:

- **Yongseok Yo** (Hongik Univ., Korea)
  "Predictive Analytics for Temporal Lobe Epilepsy"

  This study investigates the sensitivity and specificity of predictive analytics for predicting temporal lobe epilepsy. A monitoring system is used to measure intracranial electroencephalography (iEEG) of epilepsy patients and applies a prediction model to generate an alarm upon detecting a precursor of as an epileptic seizure. The predictive method is evaluated by a cross-validation technique. The prediction results varied across patients. Predictive analytics based on the spectral feature of iEEG performs well for some patients but not all. This result highlights the need for patient-specific algorithms that can play a key role in predicting and ultimately preventing epileptic seizures.

- **Sue-Hyun Lee** (KAIST, Korea)
  "Decoding retrieved face information in humans"

  Despite the high similarity of human faces, we can easily discriminate and recognize face identity, and can retrieve how people look. Here, we asked how individual face information is represented in the visual cortex during perception and retrieval. To address this question, we performed an event-related functional magnetic resonance imaging (fMRI) experiment, comprising separate perception, learning and retrieval sessions. Using multivoxel pattern analyses, we found that anterior face-selective areas showed more discriminable patterns of response to individual faces during retrieval compared to those elicited during perception whereas those areas did not show any significant difference between perception and retrieval for individual shoe images. To determine whether the increased discrimination reflected a difference between perceived and retrieved face information and not an effect of learning, we conducted a similar fMRI experiment, comprising perception, learning, and the second perception sessions. Importantly, there was no difference in face discrimination between the first and second perception sessions in anterior face-selective areas. Taken together, these results suggest that retrieval of face information generates more discriminative neural responses for individual faces than that evoked by perception of the very same faces.

- **Sang Wan Lee** (KAIST, Korea)
  "Prefrontal cognitive controllability and mental disorders"

The application of computational models to functional magnetic resonance imaging (model-based fMRI) has paved the way for deciphering neural codes of higher cognitive functions within the area of the prefrontal cortex, the place where multisensory information is integrated. We begin to understand that the ventrolateral prefrontal cortex serves as a meta-controller that allocates control over behavior to brain's subsystems in a way that is optimal for the agent for the given constraints. Losing this control inevitably leads to the development of abnormal behavior patterns. Here we overview the model-based fMRI approach to elucidate the role of the prefrontal cortex in meta-control, and discuss its potential implications in metal disorders, such as addiction and obsessive compulsive disorders.

Multimodal Windows on Spontaneous Brain Activity

Organizer: Louis Lemieux

Room: # 103

Date and Time: Thursday, October6 / 14:40-15:40

MEG, EEG and fMRI at Rest: Complementary Windows on Spontaneous Brain Activity
MEG and EEG signals are both generated by primary currents within local cortical neuron populations, whereas fMRI is usually interpreted as a marker of neural function. The studies presented will show that neural and BOLD responses are two distinct measures, which can when brought together provide a more global picture of brain activity. PET and fMRI studies revealed the existence of resting-state networks, that can be relatively easily identified in individuals but remain difficult to interpret in relation to neural function. The relationship with EEG and MEG rhythms recorded during rest should therefore lead to a better understanding of these phenomena. An overview will be presented of some key findings on resting-state activity in healthy and diseased brains with special emphasis on the complementarity of various modalities, brought together through data fusion and computational modelling.

Speakers:

- **Seppo P. Ahlfors** (Massachusetts General Hospital / Harvard Medical School, USA)
  "Complementary properties of MEG, EEG, and fMRI"

  Functional MRI is well suited for localization and connectivity analyses of brain activity, including resting state networks of functionally connected areas. MEG and EEG provide powerful means for characterizing cortical activity in terms of dynamic patterns of activity, such as transient and oscillatory time courses, functional and effective connectivity, and cross-frequency coupling. For the interpretation of MEG and EEG data, however, partial cancellation of signals from simultaneous source currents is a challenge, in particular when compared or combined with fMRI data. Cancellation takes place at multiple spatial scales: at the level of synaptic and dendritic currents, local neuron populations, sulcal and gyral folding, and large-scale networks of cortical areas. The last two are perhaps of most interest in resting state analyses. At each level, different types of computational modeling are needed. For data fusion, MEG and EEG can be directly combined for estimating common sources, i.e., the primary currents. In contrast, the fusion of MEG/EEG with fMRI generally requires a model for neural activity from which both the primary current distribution and the hemodynamic effects can be derived. The complementary properties of MEG/EEG and fMRI suggest that combining data has the potential to enhance the characterization of brain processes.

- **Diego Vidaurre** (Univ. of Oxford, UK / Aarhus Univ., Denmark)
  "Large-scale resting-state networks: complementary views from different modalities"

  When we are engaged in a task, our brain recruits circuits of regions that are specialised. Strikingly, many of the networks of activity that we find in the brain in task are also observed at rest. The role of these coherent patterns of activation in unconstrained cognition has been speculated to relate to memory consolidation, planning and imagination. fMRI studies reveal the existence of these robust resting-state networks (RSNs) with very slow signatures (<0.1Hz). More recently, these networks have been also observed using MEG, seeming to indicate that resting-state fMRI connectivity is closely related to correlated modulations in the power (or amplitude) of alpha and beta-band oscillations captured with MEG. Computational modelling can offer valuable insights on this relationship.

Both fMRI and MEG offer a different view on this kind of activity, and we need methods to leverage the advantages of each modality to identify RSN at the finest possible spatial and temporal resolution. I will discuss here some of these methods and will offer hints of their interpretation with respect to behaviour.

- **Pauly P.W. Ossenblok** (Kempenhaeghe&Maastricht UMC+; Eindhoven Univ. of Tech., The Netherlands)
  "MEG vs EEG correlated functional MRI in epilepsy research"

In general it is assumed that the spatiotemporal characteristics of the activity underlying interictal epileptic discharges (IEDs) can be described by a network of brain regions as identified by either EEG, MEG or EEG correlated fMRI (EEG-fMRI) and the interactions of these regions. EEG-fMRI may yield a more realistic estimate of the spatial distribution of these epileptic networks, whereas MEG tends to localize the region within this network which is responsible for the epilepsy of the patient.

The results of these modalities will be discussed for patients who were candidate for epilepsy surgery and who underwent pre-surgical invasive recordings, i.e. either subdural grid or depth electrode EEG recordings. Network analysis is applied to evaluate whether EEG-fMRI correlation patterns indeed consist of interacting highly correlated brain regions which reflect the onset ('hub') and the propagation of the IEDs. For comparison, modelling of the network underlying the invasively recorded IEDs using the same analysis framework reveals the brain regions involved and their interactions. It will be evaluated whether the 'hub' of the epileptic network has additional value compared to interictal MEG with regard to the ability to identify the region within the network that is responsible for the epilepsy of a patient.

Language Changes in Childhood

Organizer: Elizabeth W. Pang

Room: # 104

Date and Time: Thursday, October6 / 14:40-15:40

Language Changes in Childhood: the Impact of Typical Development, Disease and Therapy
Language is a complex process that undergoes extensive changes with development, is impacted by disease in the brain, and can be rehabilitated with specific treatments. MEG, with its exquisite temporal and spatial resolution, is ideal for tracking language-specific plasticity. The speakers in this symposium will describe the use of MEG to examine these different processes. The first speaker will describe the brain oscillatory changes related to language processing in typically developing children and adolescents. The second speaker will describe a multimodal approach using MEG with fMRI to map language networks in children with epilepsy. The third speaker will present the impact of speech therapy on improving speech outcomes for young children, as captured by MEG. This symposium presents novel approaches to acquiring and analyzing MEG data in children, and emphasizes the valuable contribution of MEG to understanding language plasticity and brain networks.

Speakers:

- **Sam M. Doesburg** (Simon Fraser Univ., Canada)
  "Development of language networks in childhood"

  Synchronization of oscillations among brain areas is thought to mediate communication amongst brain networks involved in cognition, perception, and language. How task-dependent synchronization during word production develops throughout childhood and adolescence remains poorly understood. In this talk, I will present MEG data recorded from children and adolescents while they performed a verb generation task. Task-dependent increases in synchronization were observed in the theta, alpha, and beta frequency ranges, and network synchronization differences were observed between age groups. The theta band showed the strongest task-dependent synchronization and the greatest differences between age groups. Network measures were calculated for brain regions associated with verb generation and were significantly associated with both age and language abilities. These findings are the first to demonstrate an association between network synchronization and measures of individual differences in the development of language abilities. Further, these data establish the maturational trajectory of network synchronization underlying expressive language abilities throughout childhood and adolescence.

- **Darren S. Kadis** (Cincinnati Children's Hospital Medical Center, USA)
  "Multi-modal approach to language mapping in children with epilepsy"

  Children undergoing neurosurgery for treatment of intractable epilepsy are at significant risk for developing functional deficits, including post-operative aphasia. Morbidity can be minimized through careful mapping of eloquent cortex and the epileptogenic zone. Increasingly, clinicians rely on fMRI and MEG to provide presurgical functional maps, particularly for lateralization and localization of language cortex. Noninvasive neuroimaging is safe, cost effective, and repeatable (as necessary). Unfortunately, current fMRI and MEG clinical protocols lack the necessary precision to be used unambiguously in deciding resective margins. Task-related changes in BOLD signal (fMRI) or oscillatory power (MEG) inform of hemispheric or lobar involvement for language, but fail to identify the precise location of critical (i.e., vulnerable) sites from within the distributed language networks of individual subjects. Here, we describe a multimodal neuroimaging pipeline designed to identify critical language sites from patterns of information flux. We will compare maps obtained from MEG effective connectivity analyses to those derived through conventional (invasive) electrocortical stimulation mapping.

- **Vickie Y. Yu** (California State Univ., USA)
  "MEG tracks brain changes related to speech therapy in young children"

Children with childhood apraxia of speech can benefit from motor speech therapies but the brain mechanism of action has not been extensively explored. The high temporal and spatial resolution of MEG may in helpful in exploring the neural changes related to specific therapies. In this talk, I describe a study where young children, aged 4 years, diagnosed with childhood apraxia of speech were scanned in the MEG before and after an 8 week course of intensive motor speech therapy. MEG analyses identified significant post-therapy changes in brain regions related to oromotor control and speech production. In addition to the findings of the study, I will discuss the challenges of conducting neuroimaging intervention studies in young children.

Individual Differences in α Rhythm

Organizer: Rasa Gulbinaite

Room: # 105

Date and Time: Thursday, October6 / 14:40-15:40

Signal or Noise: Individual Differences in Alpha Peak Frequency

Historically, individual alpha frequency (IAF) is one of the most commonly used markers of inter-individual variations in brain rhythms, and is often considered a stable neurophysiological trait. The purpose of this symposium is to present up-to-date views on the mechanisms underlying flexibility and variability of the alpha rhythm and its functional roles, based on large-sample EEG/MEG recordings and intracranial ECoG in humans, in combination with advanced data analysis methods, and non-invasive brain stimulation protocols. In this symposium, Haegens will highlight fundamental methodological considerations related to assessment of IAF, with the emphasis both on inter-individual variability, andon intra-individual variability across brain regions. Thereafter, Gulbinaite will focus on IAF variations in the context of modern theories on the role of alpha oscillations in perception and attention. Finally, Herrmann will elucidate the conditions under which the endogenous alpha rhythm can be "hijacked" using brain stimulation and the limits of such interventions in modulating cognition. In summary, this symposium will call into question traditional ideas on the stability notion of IAF and bring discussion on how inter- and intra-individual "noise" in alpha rhythm can be turned into "signal" for studying the functional role of alpha oscillations, and frequency-band specific brain networks more generally.

Speakers:

- **Saskia Haegens** (Columbia Univ., USA)
  "Variability of the alpha rhythm across individuals, cognitive tasks and brain regions"

  Converging evidence suggests that the alpha rhythm plays an important and active role in cognitive processing. Here, we systematically studied variability in alpha peak frequency both between and within subjects. We recorded brain activity using MEG in 51 healthy human subjects under three experimental conditions – rest, passive visual stimulation and an N-back working memory paradigm, using source reconstruction methods to separate alpha activity from parietal and occipital sources.
  In both regions we observed an increase of alpha peak frequency from resting state and passive visual stimulation conditions to the N-back paradigm, with a significantly higher alpha peak frequency in the 2-back compared to the 0-back condition. Thus, alpha peak frequency increases with increasing cognitive demands. Additionally, we acquired resting state intracranial ECoG data in human patients, which allowed us to further elucidate the differences between brain regions. We found substantial variability of alpha peak frequency across brain regions within subjects.

  We conclude that alpha peak frequency varies both within and between subjects, and that the alpha rhythm operates across a wider frequency range than the 8-12 Hz band often used. Therefore, using a fixed and limited alpha frequency band for analysis might be suboptimal and lead to biased outcomes.

- **Rasa Gulbinaite and Rufin VanRullen** (Universite Paul Sabatier, France)
  "What works for you, doesn't work for me: Individual alpha frequency in perceptual and attentional processes"

  Individual alpha peak frequency (IAF) is highly heritable (80%), and has a remarkable test-retest reliability (0.75-0.9). Early studies on variations in IAF aimed at testing whether "smarter brains run faster," with some evidence for a positive relationship. However, an established role of alpha oscillations in visual perception and attention raises a more fundamental question: "Is there a link between perceptual/attentional processes and IAF?" In the first study, we focused on IAF and illusory perception by using the triple-flash illusion (the occasional perception of three flashes when only two veridical ones are presented). We demonstrated that the probability of third-flash perception is correlated with task-related IAF at parietal but not occipital alpha sources, and that the inter-flash interval that maximizes illusory perception is strongly correlated with the period of subject-specific "perceptual echoes" [VanRullen & Macdonald, 2012]. In the second study, we used a causal approach and tested the interaction between exogenous and endogenous alpha rhythms. Here, we showed that visual stimulus flicker modulates the effectiveness of spatial attention in a frequency-dependent manner: The strength of modulation depends on the correspondence between the flicker frequency and IAF. These results indicate that individual alpha tempo is important, yet faster is not necessarily better.

- **Christoph S. Herrmann and Annika Notbohm** (Carl von Ossietzky Univ., Germany)
  "Entrainment of human alpha rhythm modulates cognition"

  Many aspects of human cognition depend upon parameters of the ongoing alpha activity such as amplitude, frequency, and phase. Here, we demonstrate how sensory driving with flickering light and transcranial stimulation with alternating currents can entrain the human alpha rhythm and thus modifythe above-mentioned parameters. We have used EEG and MEG to monitor how the alpha activity changes during such stimulation protocols. In turn, this results in a modulation of cognitive processes such as visual perception, mental rotation, and short term memory capacity. We will review the physical properties of brain entrainment which require an adaptation of the stimulation frequency to the individual alpha frequency.