Computational Neurology
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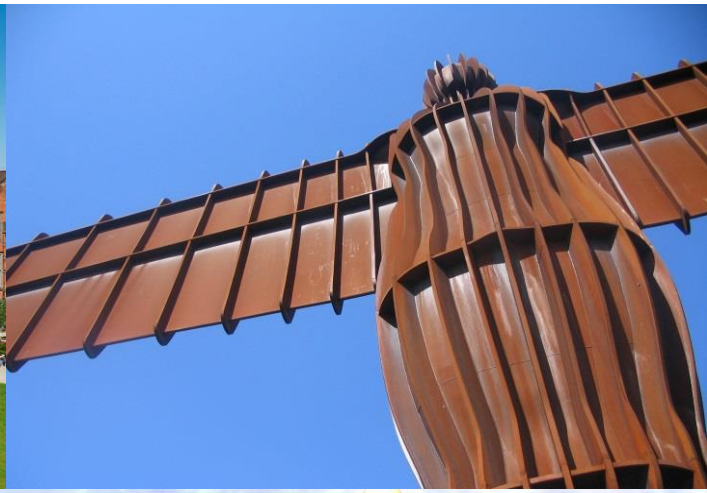
Bridging computer science, neuroscience,
imaging, modelling and neurology

Book of Abstracts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Detecting, modelling and manipulating good and bad oscillations in the brain

Prof Dimitri M Kullmann

Institute of Neurology, University College London, UK

Neural population oscillations have been proposed to serve many roles including flexible communication among anatomically connected regions. Several diseases, most notably epilepsy, are characterized by pathological oscillations. I shall provide an overview of recent efforts in my laboratory to understand the dynamical properties of gamma oscillations by a combination of modelling, ex vivo electrophysiology and optogenetics. I shall also discuss the challenge of real-time and off-line detection of seizures in experimental epilepsy models. This work aims to develop closed-loop anti-epileptic strategies for clinical translation.

How neurons form memories: Single-unit recordings in the human temporal lobe during perception and memory

Prof Florian Mormann

Epileptologische Klinik, University of Bonn, Germany

The human medial temporal lobe contains neurons that respond to the semantic contents of a presented stimulus. These "concept cells" may respond to very different pictures of a given person and even to their written or spoken name. Their response latency is far longer than necessary for object recognition, and they are found in brain regions that are crucial for declarative memory formation. It has thus been hypothesized that they may represent the semantic "building blocks" of episodic memories.

In this talk I will present data from single unit recordings in the hippocampus, entorhinal cortex, parahippocampal cortex, and amygdala during paradigms involving encoding and consolidation of episodic memories in order to characterize the role of concept cells in these cognitive functions.

Translational Neuroscience: from bifurcations to epilepsy

Prof Viktor Jirsa

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Aix-Marseille University, France

Over the past decade we have demonstrated that the fusion of subject-specific structural information of the human brain with mathematical dynamic models allows building biologically realistic brain network models, which have a predictive value, beyond the explanatory power of each approach independently. The network nodes hold neural population models, which are derived using mean field techniques from statistical physics expressing ensemble activity via collective variables. This approach has been successfully applied to the modelling of the resting state dynamics of individual human brains, as well as clinical situations including stroke and epilepsy research. In epilepsy, we reconstruct personalized connectivity matrices of human epileptic patients using Diffusion Tensor weighted Imaging (DTI). Subsets of brain regions generating seizures in patients with refractory partial epilepsy are referred to as the epileptogenic zone (EZ). During a seizure, paroxysmal activity is not restricted to the EZ, but may recruit other brain regions and propagate activity through large brain networks, which comprise brain regions that are not necessarily epileptogenic. The identification of the EZ is crucial for candidates for neurosurgery and requires unambiguous criteria that evaluate the degree of epileptogenicity of brain regions. Stability analyses of propagating waves provide a set of indices quantifying the degree of epileptogenicity and predict conditions, under which seizures propagate to nonepileptogenic brain regions, explaining the responses to intracerebral electric stimulation in epileptogenic and nonepileptogenic areas. We demonstrate the predictive value of our seizure propagation model by validating it against empirical patient data. In conjunction, our results provide guidance in the presurgical evaluation of epileptogenicity based on electrographic signatures in intracerebral electroencephalograms.

The role of networks in seizure generation

Dr Marc Goodfellow

University of Exeter, UK

Epilepsy is characterised by the repeated occurrence of seizures, which are periods of pathological brain activity that arise spontaneously from a predominantly healthy functional state. Since the goal of epilepsy treatment is to abolish or reduce the tendency of the brain to transition into seizures (its ictogenicity), it is important to better understand these transitions, and how we might interact with the brain to abate them. However, seizure dynamics emerge in, and affect, large-scale brain networks, and the network paradigm for ictogenesis introduces new challenges and new opportunities to understand epilepsy.

In this talk I will review mathematical modelling approaches that can help us understand the generation of seizures in networks and quantify their ictogenicity. I will demonstrate how these approaches can be used to quantify differences in brain networks between patients with generalised epilepsies and healthy controls. I will also describe how we can extend this approach to quantify the contribution of each component of a network to seizure generation. This quantification is based upon the effect that a treatment specific perturbation, for example node removal in epilepsy surgery, has on network ictogenicity.

I will demonstrate a validation of this approach analysing electrocorticogram (ECoG) recordings from 16 patients who had undergone epilepsy surgery, and for whom both outcome and location of resection was known. When post-operative outcome was good, model predictions for optimal strategies aligned better with the actual surgery undertaken than when post-operative outcome was poor. The accuracy of our approach was found to be close to 90% in terms of predicting good versus poor responders. Crucially, I will demonstrate that this approach allows the prediction of optimal surgical strategies and the provision of quantitative prognoses for patients undergoing epilepsy surgery.

The Human Connectome: Linking Brain Network Features to Healthy and Pathological Information Processing

Prof Marcus Kaiser

**School of Computing Science / Institute of Neuroscience,
Newcastle University, UK**

Our work on connectomics over the last 15 years has shown a small-world, modular, and hub architecture of brain networks [1,2]. Small-world features enable the brain to rapidly integrate and bind information while the modular architecture, present at different hierarchical levels, allows separate processing of various kinds of information (e.g. visual or auditory) while preventing wide-scale spreading of activation [3]. Hub nodes play critical roles in information processing and are involved in many brain diseases [4].

Nonetheless, general observations of human brain connectivity, or of patients at the group-level, have so far had little impact on understanding cognition, or deficiencies in cognition, in individual subjects. As a result, human connectome information is not used as a biomarker for diagnosis or a predictor of the most suitable treatment strategy. After discussing the organisation of brain networks, we will show how connectivity can be used to determine the disease type of individual dementia patients. An important aspect of these brain networks is their spatial organisation in terms of the length of fibre tracts and the location of brain regions [5]. However, simply observing connectivity is insufficient as small changes in network organisation might lead to large changes in network behaviour (dynamics) [6]. We therefore show how simulations can be applied to predict regions that are involved in pathological processes [7]. We conclude with the role of simulations in understanding the developmental origin of diseases as determining these origins will again inform diagnosis and treatment (http://www.greenbrainproject.org/).

These are first steps towards using connectome-based computer simulations as a tool to understand normal and pathological processing in individuals. Developing models that are based on anatomical information will be crucial to define the most suitable intervention [8].

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Beyond classical connectivity analysis: Inspecting temporal variability in brain functional connectivity

Dr Javier Escudero

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The study of the human brain has benefited enormously from functional connectivity estimations and network theory, which emphasise the dependency of the information processed in diverse brain regions. Functional connectivity analysis enables a deeper understanding of brain activity and it has shown promise to transform clinical care, for example in epilepsy. However, current methods are inherently limited when trying to inspect the presence of dynamic changes in functional connectivity. To overcome these limitations, we build on recently emerging signal processing areas, such as tensor factorisations and signal processing on graphs, to develop approaches able to exploit the temporal variability of functional connectivity for more insightful analyses of task-related recordings. We focus on two recently developed approaches: 1) a complex tensor factorisation (based on PARAFAC-2) to decompose electroencephalogram (EEG) signals into scalp components described by their frequency, spatial and trial profiles for a reduced cross-talk between them; and 2) graph functions which allows for a novel temporal probing of the connectivity information in short EEG time series. We present the basic concepts behind these developments and illustrate them with simulated data and in real-world task-related EEG activity.

Multielectrode-array applications to investigate retinal function in health and disease

Dr Evelyne Sernagor

Institute of Neuroscience, Newcastle University, UK

Vision begins with photoreceptors converting light from different parts of the visual scene into electrical signals, compressing our visual world into a parsimonious code of spikes at the retinal output level, the retinal ganglion cells (RGCs). The brain then recreates images from interpreting these highly compressed “barcodes” or trains of spikes.

RGCs reside in a monolayer, the innermost cellular layer of the retina. This two-dimensional configuration is particularly amenable to recordings using planar multielectrode arrays (MEAs) which come in direct contact with the RGC layer, allowing us to undertake population recordings of the retinal output to the brain.

In this talk, I will introduce various projects from our group investigating retinal function and plasticity in health and disease using MEA recordings from the RGC layer. First, I will present our findings about developmental changes in the spatiotemporal properties of spontaneous waves that spread across the RGC layer in the neonatal retina. These waves are important for guiding the development of visual connectivity both at the level of the retina and in retinal central projections. Using the active pixel sensor MEA, a large-scale, high-density MEA consisting of 4,096 electrodes covering most of the neonatal mouse retina, we were able to detect and characterise profound developmental changes in wave dynamics that may underlie various critical periods during wiring of the visual system. Using the same recording system, we found that the maturation time course of RGC light responses is not homogeneous across the mouse retina, suggesting that there are ecological requirements that favour earlier maturation of the dorsal retina. I will then present our recent studies showing that RGCs use a population approach to decode visual stimuli, including complex visual scenes, and that their performance is significantly improved when images undergo transformations, a very important issue for the development of retinal prosthetics. I will then discuss recent projects from our group on strategies for regaining visual function in photoreceptor dystrophies. These include direct optogenetic stimulation of RGCs. Dystrophic retinas are characterised by prominent pathological oscillations in the RGC layer. These strong oscillations pose a serious challenge for efficient RGC stimulation because they reduce the signal-to-noise ratio of the responses. Blockade of these oscillations vastly improves the performance of optogenetic stimulation. Finally, I will discuss the choice of electrode material for electrical retinal prosthetic devices. We have used MEAs with electrodes made of carbon nanotubes (CNTs) to stimulate RGCs in a mouse model of photoreceptor dystrophy. Based on electrophysiological and ultrastructural findings, we found that CNTs allow better coupling between RGCs and the stimulating device, offering promising perspectives for the development of a new generation of retinal implants.

Relating firing rate codes and oscillations to the function and pathology of neural circuits

Prof Mathew Nolan

Centre for Integrative Physiology, University of Edinburgh, UK

Neural circuits in the medial entorhinal cortex (MEC) play key roles in spatial cognition by providing the hippocampus and other brain structures with estimates of location. The MEC is also clinically important. It is likely to be contribute to early cognitive deficits in Alzheimer's disease, is a locus for some types of epileptic seizures, and shows evidence for circuit reorganisation in schizophrenia. To begin to understand how the MEC estimates location, and how pathology in the MEC leads to clinical symptoms, we have developed, based on the circuitry of the MEC, models that account for its spatial computations and network activity. Our investigation of these models has general implications for disorders. First, cognitive functions encoded by neuronal firing rate may be relatively insensitive to changes in overall synaptic strength, whereas functions that relay on oscillatory activity are likely to be much more sensitive. Second, while network oscillations are often used to index elements of cognitive function, they may not be a reliable index of computations encoded by neural firing rates. Third, noise in neural circuits may paradoxically be important for stabilisation of activity and suppression of seizures. Our results indicate that relationships between cognitive functions and easily measurable phenomena such as synaptic strength and oscillatory activity are not necessarily straightforward, and suggest that circuit-based mechanistic models will be important for identifying and understanding cognitive deficits in clinical disorders.

Oscillations and Neuronal Dynamics in Schizophrenia: The Search for Basic Symptoms and Translational Opportunities

Dr Peter Uhlhaas

Institute of Neuroscience and Psychology
University of Glasgow, UK

A considerable body of work over the last 10 years combining non-invasive electrophysiology (electroencephalography/magnetoencephalography) in patient populations with preclinical research has contributed to the conceptualization of schizophrenia as a disorder associated with aberrant neural dynamics and disturbances in excitation/inhibition (E/I) balance parameters. Specifically, I will propose that recent technological and analytic advances in MEG provide novel opportunities to address these fundamental questions as well as establish important links with translational research. We have carried out several studies which have tested the importance of neural oscillations in the pathophysiology of schizophrenia through a combination of MEG-measurements in ScZ-patients and pharmacological manipulations in healthy volunteers which target the NMDA-receptor. These results highlight a pronounced impairment in high-frequency activity in both chronic and unmedicated patients which could provide novel insights into basic circuit mechanisms underlying cognitive and perceptual dysfunctions. Our recent work has employed MEG to understand the developmental trajectory of neural oscillations during adolescence and the possibility to develop a biomarker for early detection and diagnosis of ScZ. We found marked changes in the amplitude of high-frequency oscillations and synchrony that were particularly pronounced during the transition from adolescence to adulthood. Moreover, data from participants meeting ultra-high risk criteria for psychosis suggest that signatures of aberrant neuronal dynamics are already present prior to the onset of psychosis, highlighting the importance of advancing biomarkers for early intervention and diagnosis.

Cortical dynamics in health, disease and anaesthesia

Dr Gregory Scott

Imperial College London, UK

An important challenge is to relate brain structural connectivity, neural dynamics, and behaviour. Traumatic brain injury (TBI) is a structural disconnection disorder whereby traumatic axonal injury damages large-scale structural connectivity, producing characteristic cognitive impairments including reduced cognitive flexibility, which may be a result of disrupted neural dynamics. I will discuss our empirical and computational approaches in TBI to investigate how the dynamical property of metastability arises from a healthy structural connectome and relates to cognitive performance.

Cortical neuronal networks often exhibit activity patterns in which all spatiotemporal scales are represented. Such “scale-free” cortical dynamics manifest as cascades of activity with cascade sizes that have power-law form. Theory and in vitro experiments suggest that information transmission among cortical circuits is optimized by scale-free dynamics. I will discuss our work in mice using voltage indicator imaging, which measures cortex-wide electrical activity at high spatiotemporal resolution. As mice recovered from anesthesia, scale-invariant spatiotemporal patterns of neuronal activity gradually emerged. We found cortical information capacity increased alongside increasing information transmission between cortical regions. Our results demonstrate that both information capacity and information transmission are maximized in the awake state in cortical regions with scale-free network dynamics.

Computational neurology: not just moonshots, but clinical impact

Dr Marco Manca

Medical Applications CERN, Genève, Switzerland

Progresses in IT have had a huge impact on science and its lifecycle, and so they have impacted neurosciences greatly, empowering researchers to new forms of investigations.

Rather than focusing on the stars of big science, during this lecture we would like to pay heed to all the scales of research that often starts with a single investigator crafting some code to explore her/his hypothesis, and walks up the ladder all the way before feeding into the ecosystem of big science. How can contemporary IT improve this practice, and accompany the investigators as they scale up their effort? How to support both creativity and reproducibility thrive in the same ecosystem? Here comes a short story about BioDynamo, a developmental neurology simulation suite that was born from the idea that researchers should be able to quickly test the implications of their theories and prepare for better experiments. This simple thought opened a long list of computational challenges, but offers the promise of a tool closing the loop of research to inform pre-clinical and clinical trials. What is the current state of the art?

Invited Talks

Dynamic mode decomposition of resting state EEG data - a dynamical systems approach to identifying epilepsy characteristics

Karin Mora

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Time series of neural activity recorded by 10-100s of electrodes over several minutes are large scale data. Either their temporal or spatial properties can be analysed by current methods such as discrete Fourier transform or principal component analysis, respectively. We, however, employ a more recently developed method called dynamic mode decomposition (DMD) to capture the spatio-temporal dynamics and patterns of such high dimensional data, and demonstrate its novel application to electroencephalography (EEG) data. EEG is commonly used to record electrical neural activity to then diagnose epilepsy. However, such diagnoses are at best di_cult unless the EEG is performed during or shortly after an epileptic seizure. Recent studies have suggested that the functional connectivity in the resting state is altered in patients with temporal lobe epilepsy (TLE). Motivated by these findings we relate the spatio-temporal characteristics of the dynamical system extracted with DMD to the electrode topology and thus to the functional network. We show how from such an analysis novel numerical indicators can be derived to identify network di_erences and hence distinguish between TLE patients and controls.

This is joint work with Michael Dellnitz, Solveig Vieluf, and Claus Reinsberger (University of Paderborn, Germany).

Controlling Abnormal Network Dynamics using Optogenetics (CANDO)

Andrew Jackson

Institute of Neuroscience, Newcastle University, UK

Epilepsy affects over 600,000 people in the UK and uncontrolled seizures have devastating effects on patients' lives. Nearly a third of cases fail to respond to conventional drug treatments and may require surgical removal of the seizure focus. However, surgery may not be suitable for all patients due to irreversible damage to necessary brain functions. Brain stimulation has been proposed as an alternative treatment option in such cases.

The CANDO project (Controlling Abnormal Network Dynamics using Optogenetics) aims to develop such a brain stimulation device for epilepsy patients. Specifically, it is a multi-site, cross-disciplinary project to develop a cortical implant for optogenetic neural control. The goal is to create a first-in-human trial in patients with focal epilepsy.

In this talk, I will give an overview of the CANDO project in terms of its goals, and the interdisciplinary collaborations within the project. The project aims not only to develop the hardware and software of the cortical implant, but also test the implant in a range of animal models. Furthermore, multimodal data will be acquired from a patient cohort to establish suitable parameters for the cortical implant, and to screen for suitable candidate subjects.

Learning how to see the invisible - using machine learning to find underlying abnormality patterns in reportedly normal MR brain images from patients with epilepsy

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The visual identification of subtle abnormalities in MR brain images that underlie focal epilepsies is a challenging problem. If a focal abnormality that is concordant with clinical and EEG data can be located, then resection of this region has a high probability of bringing about seizure remission.

There are many cases in which covert abnormalities are not detected visually by a radiologist. In this study, we used machine learning techniques to reveal patterns of abnormality that exist within reportedly normal MR brain images from 17 patients with refractory temporal lobe epilepsy. We trained random forest classifiers on features from these images and then performed feature importance measurements within these trained forests. This demonstrated where information necessary to locate abnormalities within the temporal lobe was generally coming from.

Our results demonstrated that abnormalities exist in MR images reported to be normal by a human reader, and that these abnormalities existed in a different spatial pattern to that seen in visually apparent cases. We obtained novel insights into why visual assessment may be ineffective in visually normal cases and provide suggestions on how to improve this situation. In particular, we demonstrated that most of the hippocampal volume and signal changes associated with hippocampal sclerosis are absent in these cases. Instead, abnormalities were detected in a number of other areas, particularly the amygdala, suggesting that visual assessment could be improved by focusing attention on these other areas.

A computational approach for neurosurgical planning in focal epilepsy

Nishant Sinha[1,2], Justin Dauwels[3], Marcus Kaiser[1,2], Sydney S Cash[4], Brandon Westover[4], Yujiang Wang[2], Peter N Taylor[1,2]

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A third of patients with epilepsy are refractory to anti-epileptic drug treatment. For some of these patients with focal epilepsy, better seizure control can be achieved by surgical intervention in which the seizure focus is localised and resected. A key challenge is to predict the likelihood of seizure reduction following the resection of particular areas. In this study, we use a dynamical network model of transitions to seizure-like dynamics. The connectivity of the model is underpinned by patient data. We simulate the model and predict the regions with high seizure likelihood. In some patients, these regions correspond with those identified by clinicians as the site of surgical resection. We then re-simulate the model with the resection of specific regions and quantify the reduction in simulated seizure likelihood. This enables in predicting the likelihood of a surgical success upon resection of specific brain tissues. The methods presented here may aid clinicians to investigate various cortical tissues for surgical intervention for achieving maximum seizure control while avoiding the eloquent brain tissues.

Re-establishment of local E/I balance by homeostatic plasticity provide a recovery mechanism after a variety of lesions: A computational framework

Dr Dipanjan Roy

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Computational modelling of the spontaneous dynamics over the whole brain provides a critical window in understanding the spatiotemporal brain dynamics that unfolds on a given anatomical connections. These connections in the healthy brain exhibits gradual deterioration or dysfunction of structure (e.g. in diseased states, aging, across individuals). Recent, experimental evidence further suggests that the adverse effect of such dysfunction is clearly visible on spontaneous dynamics characterized in particular by changes in resting state functional connectivity and its graph theoretical properties (e.g. modularity, hub classification, rich club index). These changes originate from altered neural dynamics in individual brain areas that are otherwise poised towards a homeostatic equilibrium to maintain a stable excitatory and inhibitory activity. Using a mean-field network model that operates close to criticality we show excitation-inhibition (E/I) balance (that is the local Glutamate/GABA ratio) has the potential to provide substantial recovery and restore the functional connectivity in the higher order neurocognitive networks. Further, recent findings suggest that these cognitive networks e.g. Saliency network (SN), Default Mode Network (DMN) and Dorsal Attention Network (DAN) are hubs of the brain and important for cognitive functions. Their dysfunction also lead to a variety of neurological disorders and pathological spatiotemporal brain dynamics. We show that local homeostatic plasticity provides a functional recovery by re-establishing excitation–inhibition balance in all areas that are affected by lesion. We systematically compare the extent of recovery in the primary hub areas and demonstrate that stability, richness similar to normal resting state is achievable.

Keywords— Structural Connectivity, Functional Connectivity, Hub Classification, DMN, DAN, Glutamate/GABA ratio, (E/I) balance

Neurocomputational modelling of decision making in schizophrenia and obsessive-compulsive disorders

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Decision making is an accumulation process of evidence about the state of the world and the utility of possible outcomes. The antisaccade paradigm, a fruitful experimental approach to understand how humans and animals make decisions, requires subjects to suppress an erroneous saccade towards a peripheral stimulus and instead make an eye movement to an equidistant position in the opposite hemifield. Subjects make errors in this paradigm when they look toward the peripheral stimulus instead of performing the antisaccade. Healthy participants typically fail to suppress erroneous prosaccades toward the target on about 20–25% of trials, before correctly saccading toward the mirror image location. However, patients suffering from schizophrenia and OCD make more antisaccade errors and their antisaccade and corrected antisaccade response times are more variable within and across subjects. The antisaccade performance deficit is usually reported to be a deficit in top–down inhibition control of the erroneous response.

I will present neurocomputational models of the antisaccade performance in schizophrenia and OCD suffering participants. In contract to popular belief local competition between competing decision processes and not a third top-down inhibitory signal that suppresses the erroneous response can account for the antisaccade performance of both subject groups. Answers as to why are the antisaccade performances of subjects with schizophrenia and OCD so poor, why are antisaccade and corrected antisaccade medians greater in subjects with schizophrenia and OCD than in controls, and why are latencies more variable and errors greater in patients with schizophrenia and OCD will be provided.

Poster Presentations

Not just theory: the role of computational neuroscience in clinical neurophysiology

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Neurocomputational modelling has the ultimate goal of enhancing the understanding of the behavior of neural cells and circuits. This aim is usually reached by starting from the experimental phenomena, then by postulating hypotheses or conceptual models of the biophysical events, and finally by transforming them in computational models. The conversion of experimental data in neurocomputational models takes mainly advantage of two well established mathematical theories: the cable conductor theory and the Hodgkin-Huxley equations. In this study the considered experimental phenomena are represented by the axon-somatic back-propagation and the recurrent discharge, which are the basis of a clinical test known as the F wave. This is a neurophysiological test commonly used to assess the motor conduction along the most proximal segments of the peripheral axons, a portion of nerves otherwise poorly accessible to the electrophysiological examination. The F wave arises from the backfiring (recurrent discharge) of antidromically activated spinal motoneurons. Until recently the test has been also used as a measure of motoneuronal excitability in experimental studies. By modelling the axon-somatic back-propagation and the recurrent discharge and by showing their dependance from the biophysical properties of the transition zone between axonal initial segment (AIS) and soma of the spinal motoneurons, a clearer insight is gained about the relations between the F wave and the spinal excitability. The modelling study appears able to provide both a clearer interpretation of the electrophysiological interplay between motoneuronal regions of high morphological inhomogeneity, and a novel demonstration of the flawed role of F-wave recordings in estimating the motoneuronal excitability.

A multi-scale network model for afterdischarges in humans

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Epileptiform afterdischarges are a conspicuous but poorly understood rhythmic response of human neocortex to electrical stimulation. They were long thought to represent a marker for the onset regions of focal-onset epileptic seizures, yet the evidence to support this assumption is poor. A major problem is the response variability, potentially based on too naive assumptions about the non-epileptic background state. We address the afterdischarge as a spatio-temporal transient induced in a noisy excitable medium with irregular deterministic pattern formation.

Recent investigations specifically highlight the importance of the background state at the moment of stimulation as a variable that has mostly been neglected in previous attempts to explain the highly variable cortical responses. In our computational approach, the electrical brain signals are modelled as local mesh works of oscillatory elements that connect over large distances to form extended after discharge networks with patient-specific Fourier spectral components. In addition, we try to account for recent observations of focal seizure onset dynamics as recorded simultaneously by macro and micro electrodes. Multivariate data analysis is used to compare simulation output to clinical recordings.

The computational work suggests candidates for interictal markers of predicted stimulation response. These may be used to predict the outcome of clinical stimulation guided by real-time feature selection. However, the connection between afterdischarges and epileptic seizure rhythm might be more complex than previously thought.

Combining Connectomics with Gene Expression Data

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Assessing brain connectivity becomes more and more important for diagnosis, pathophysiology and treatment of neurologic and psychiatric diseases. Graph theory is the standard method to analyse brain connectivity quantitatively [1], however, graph theoretical measures describe the network as a whole but not individual connections. The cause of brain diseases can in many cases be attributed to alterations in specific connections [2] but available tools so far provide little support for clinicians and scientists for connectivity analysis. We used the knowledge management platform BioXM™ (Biomax Informatics AG, Planegg), so far widely used in genomics and proteomics, to organize and store connectivity matrices from DTI and fMRI imaging and link this data to gene expression in post-mortem brain tissue from the Human Allen Brain Atlas [3]. We took fMRI and DTI example data sets from the Human Connectome Project [4]. We are convinced that linking gene expression data to neuroimaging data enable new integrated analysis of the patients' connectome and a better understanding of brain disorders.

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Next generation neural mass modelling

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In electrophysiological recordings of the brain, the transition from high amplitude to low amplitude signals are most likely caused by a change in the synchrony of underlying neuronal population firing patterns. Classic examples of such modulations are the strong stimulus-related oscillatory phenomena known as the movement related beta decrease (MRBD) and post-movement beta rebound (PMBR). A sharp decrease in neural oscillatory power is observed during movement (MRBD) followed by an increase above baseline on movement cessation (PMBR). MRBD and PMBR represent important neuroscientific phenomena which have been shown to have clinical relevance. In this talk I will present a parsimonious model for the dynamics of synchrony within a synaptically coupled spiking network that is able to replicate a human MEG power spectrogram showing the evolution from MRBD to PMBR. Importantly, the high-dimensional spiking model has an exact mean field description in terms of four ordinary differential equations that allows considerable insight to be obtained into the cause of the experimentally observed time-lag from movement termination to the onset of PMBR (~ 0.5 s), as well as the subsequent long duration of PMBR (~ 1 - 10 s). Our model represents the first to accurately predict these commonly observed and robust phenomena and represents a key step in their understanding, in health and disease.

Computational modelling of ganglion cells growth in the retina

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Being part of the central nervous system, the development of the retina is governed by complex and dynamic rules that allow the formation of a coherent and functional organ. The cellular organisation is guided by chemical signals, but also by physical interactions between cells (e.g. competition and electrical communication). A better understanding of how retinal neurons develop and what the essential requirements from the local environment are would be of great benefit for clinical applications using stem cells.

Here, we use the simulation framework Cx3D (Zubler and Douglas 2009), to computationally model the development of retinal ganglion cells. These neurons play a key role in the retina, as they are the only retinal neurons that send information to the brain. They also play a crucial role in the development of other retinal as well as cortical neurons, e.g. through retinal waves. A large number of the morphologies of ganglion cells have been reconstructed and are publicly available.

In this work, we investigated the spatial growth of such neurons, and compared simulated morphologies with real ganglion cells present in the neuromorpho database (http://neuromorpho.org). This comparison is based on measures that indicate patterns of branching and arborisation. Moreover, we demonstrate that our approach provides a platform for the generation of experimentally verifiable hypotheses, in particular on the contribution of inter-cellular interactions.

Zubler F, Douglas R. 2009. A framework for modeling the growth and development of neurons and networks. Front Comput Neurosci. 3:25.

Structure-function clustering in multiplex brain networks

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A key question in neuroscience is to understand how a rich functional repertoire of brain activity arises within relatively static networks of structurally-connected neural populations: elucidating the subtle interactions between evoked 'functional connectivity' and the underlying 'structural connectivity' has the potential to address this. These structural–functional networks (and neural networks more generally) are more naturally described using a multilayer or multiplex network approach, in favour of standard single-layer network analyses that are more typically applied to such systems. We address such issues by exploring important structure-function relations in the Macaque cortical network by modelling it as a duplex network that comprises an anatomical layer (describing the known macro-scale network topology of the Macaque monkey) and a functional layer derived from simulated neural activity. We investigate and characterize correlations between structural and functional layers by varying system parameters which govern neural activity and employing recently described multiplex network measures. Moreover, we propose a novel measure of multiplex structure-function clustering which allows us to (i) investigate the emergence of functional connections that are distinct from the underlying cortical structure and (ii) to highlight the dependence of multiplex structure on the neural dynamical regime.

A multifractal analysis of seizure emergence in human intracranial electroencephalographic signals

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PURPOSE: A deeper understanding of the genesis of the ictal state could improve current therapeutic techniques for drug resistant epilepsy patients. We aim to study intracranial EEG recordings and look for markers of ictogenesis based on multifractal theory concepts. Such markers may provide a measure of the possible pro-ictal state.

METHODS: Intracranial Electroencephalographic (EEG) signals were evaluated in a search for changes that occur prior to the seizure. Data was collected from three patients with epilepsy undergoing pre-surgical evaluation. The signals were analysed based on the Chhabra-Jensen multifractal approach resulting in a spectrum one every 2 seconds in a non-overlapping window. The width and height of the spectra were evaluated, resulting in a measure for each channel in each two second window. The values were then averaged across all channels and smoothed based on the Savitzky–Golay polynomial filter.

RESULTS: A multifractal behaviour was observed in all recordings. In 1/3 patients, a stereotypical pattern of seizure emergence on both width and height quantities is found 20 minutes prior to onset.

DISCUSSION: The results of the analysis show the method may be able to provide markers on the seizure emergence and could lead to the conception of a pro-ictal state index.

Functional connectivity of lower visual processing in Lewy body dementia

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Dementia with Lewy bodies is characterized by attentional dysfunction, parkinsonian features and impairments in visual processing. Previous studies suggest that the latter might not originate from deficits in the lower visual areas, but might be rather a product of dysfunctional interaction of the ventral or dorsal visual stream. Therefore, we aimed to examine underlying network dysfunction involved in passive visual processing in Lewy body dementia (LBD) and compare that with Alzheimer‘s disease (AD) and healthy subjects.

18 patients with LBD, 14 patients with AD and 19 healthy controls participated in a passive visual task in a 3T MRI scanner, where they were required to look at a screen with flashing checkerboards (checker condition), alternating with a blank screen (baseline condition). After image preprocessing, we estimated functional networks that were active during that task using an independent component analysis. The timeseries of each network were extracted using dual regression and split into conditions (checkerboard and baseline condition) and then correlated with each other during each condition, resulting in a covariance matrix of functional networks. The correlations were normalized and corrected for multiple comparisons. We also performed exploratory correlations with several variables depicting cognition, visual function, hallucinations and fluctuations.

Our data showed that there was increased connectivity in LBD compared to HC between the dorsal attentional network and the left ventral attentional network during the checkerboard condition which was not present during the baseline condition. Compared to AD, there was increased connectivity in LBD between the dorsal attentional network and the right ventral attentional network. We did not find any difference in connectivity between AD and healthy controls.

All in all, we did not find any deficit in the connectivity of the occipital network with other regions in LBD. However, the increased functional connectivity between the dorsal and the ventral attentional network might suggest either intensified bottom-up transfer of visual information leading to disturbed visual processing or increased network interactions reflecting a subtle underlying attentional dysfunction.

The significance of network topology in epilepsy surgery

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Epilepsy is a chronic neurological disorder that is characterized by recurrent seizures. In around one third of cases, epilepsy is not controlled by drugs, and these patients are potential candidates for surgery. The current paradigm for surgery is to remove as completely as possible the brain tissue responsible for generating seizures, which is assumed to correspond to a localized abnormality. However, epilepsy surgery is not always successful: around one half of the patients is no longer seizure free one year after surgery. A confounding factor that may explain these poor success rates is that seizures are now acknowledged to arise in large-scale brain networks, and consequently localized abnormalities are neither a necessary nor sufficient condition for the development of seizures. It remains unclear how different network structures cause emergent seizures, and whether certain network structures would be more or less amenable to a surgical approach.

To address this, we use mathematical models of seizure generation in brain networks and evaluate the emergent dynamics in different synthetic networks. In each case we quantify the contribution of each node to the propensity of the network to seize (ictogenicity) and study how this correlates with node properties and network topology. We find that the node topological properties can account for its ictogenicity, and the emergence of seizures depends on the topology of the network.

Modelling Seizure Self-Prediction

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Evidence suggests that patients have some awareness of their risk of an upcoming seizure and gain a degree of predictive ability from this information. Here we investigate the implications for seizure self-prediction. The extent of predictive ability is dependent on the underlying distribution of seizure risk, and the accuracy of the patient's estimate of risk. Monte Carlo simulation of seizure occurrence and prediction suggest study lengths of greater than a year would be required to reliably detect all patients who have significant predictive ability and thus we may be dramatically underestimating this capability within the population of patients with epilepsy (PWE). In addition utilising a classifier to predict seizures on the basis of predictive information can dramatically improve performance, suggesting there is scope for improving seizure prediction on the basis of patient derived information, and that this may be applicable to an appreciable proportion of PWE.

Speed of brain dynamics: comparison between autistic and healthy individuals using fMRI data

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Past research suggests that various psychiatric disorders involve aberrant neural dynamics in the brain. Different data-driven approaches such as fractal and chaotic time series analysis, oscillation and synchronisation analysis, and more recently developed signal variability analysis have characterised how brain dynamics alters in specific psychiatric disorders.

Here we hypothesise that the speed of brain dynamics is different between individuals with such neuropsychiatric disorders and controls. To test this hypothesis, we compared the area under the curve (AUC) of the autocorrelation function of resting-state fMRI signals between high-functioning autistic adults and sex-/IQ-/age-matched neurotypical participants. A large AUC value corresponds to slow dynamics at a ROI. We found that the AUC value for autistic adults was smaller (i.e., faster brain dynamics) than that for controls in some sensory brain networks. Moreover, the AUC value was negatively correlated with severity of socio-communicational symptoms of autism.

Brain Connectivity Alteration in Neurological Diseases Explored by Resting-State fMRI

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Dementia describes a group of symptoms affecting thinking and social abilities severely enough to interfere with daily human behavior. It is related with at least two brain functions: memory loss and impaired judgment or language, and the inability to perform some common activities. Brain's energy is largely consumed at rest during spontaneous neuronal activity (~20%), while task-related increases in metabolism energy are minor (<5%). About 50% of people above the age of 85 experience cognitive impairments or dementia. Spontaneous low-frequency fluctuations in BOLD rsfMRI signals are temporally coherent among brain areas that are structurally connected and functionally related. Several cognitive functions such as learning and memory depend on normal communication between the hippocampus and prefrontal cortex. There is evidence that disruption to communication channels in these two areas of the brain contribute to symptoms in psychiatric disorders. Connectivity studies using functional neuroimaging data have increased the understanding of the organization of large-scale structural and functional brain networks. It has been shown that nonlinear analyses employing concepts such as entropy, fractality, and predictability provide significant diagnostic and prognostic information in a large number of pathologies. The contribution aims to identify specific changes in the resting-state networks univocally related to certain forms of dementia and/or dementia phases. The goal is to review and evaluate the most current approaches for early detection and classification of cognitive impairments and dementia, particularly among syndromes with relatively similar behavioral effects, on the basis of alterations in brain connectivity explored by real-time fMRI during rest.

Lithium imaging in bipolar disorder

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Lithium is used as a treatment for bipolar disorder but despite its efficacy, the mechanism of action remains unknown. It is only effective in approximately 1 in 3 patients; the reason for which is also unknown. The present study aimed to use the recently developed ability to image lithium in vivo using Magnetic Resonance Imaging to examine the distribution of lithium within the brains of patients currently taking lithium and their response. A region of interest analysis was performed using data obtained from subjects currently responding well to lithium. The results from this appear to show greater lithium signal in white matter than grey matter and also show very high levels of signal within the eyes and lateral ventricles. The signal to noise ratio for lithium was also calculated across the whole brain for each patient. The results from this appear to show a common trend between signal to noise ratio, lithium response, and serum lithium concentration; namely, increases in lithium signal appears to correspond with increases in concentration of lithium in the blood and subject responsivity to lithium as indicated using the ALDA scale. Further analyses of this kind may enable the identification of a biomarker able to predict responsiveness to lithium. This would prove to be a valuable tool for clinicians during the prescription of medication for bipolar patients. Further studies may also lead to further insights regarding how lithium works during bipolar disorder.

Multi-scale computational modelling of neuronal dynamics in genetic epilepsies

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There has been a recent increase in our ability to identify "epilepsy genes". Yet even in well-delineated genetic epilepsies, such as those associated with mutations in *SCN1A*, or *GRIN2A*, the link between the molecular disruption and the phenotype is often not well understood. Computational modelling allows *in silico* simulations of specific abnormalities at different spatial and temporal scales. Using case studies, we illustrate how modelling can be used to identify neuronal dysfunction in the context of an epilepsy syndrome with known molecular cause.

In the first, "bottom-up" example, we focus on a specific *SCN1A* mutation causing a temperature-sensitive epilepsy in the Dravet-syndrome spectrum. Using patch-clamp recordings at different environmental temperatures, we identify specific gating abnormalities introduced by the mutation. A computational model of the neuronal membrane is used to show how these gating abnormalities allow abnormal tolerance to high input currents, thus linking molecular abnormality with the observed phenotype (Peters et al. 2016).

The second, "top-down" example explores abnormal sleep dynamics in a child with a *GRIN2A* mutation and an epilepsy-aphasia phenotype. Using dynamic causal modelling of sleep-EEG, observed spectral changes are modelled as fluctuations in neuronal coupling and synaptic dynamics. The electromagnetic model is then used to identify changes in thalamaocortical coupling underlying observed sleep abnormalities using Bayesian model comparison.

These examples illustrate contrasting, but complementary approaches to using computational modelling techniques in identifying pathophysiological mechanisms in genetic epilepsies. They allow for the integration of existing knowledge and empirical evidence to develop a patient-specific understanding of neurological abnormalities.

Peters C, Rosch RE, Hughes E, Ruben PC (2016) Temperature-dependent changes in neuronal dynamics in a patient with an SCN1A mutation and hyperthermia induced seizures. *Sci Rep* 6, 31879.

Convergent Evidence of Brain connectivity patterns in higher order resting networks for Children with Autism?

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Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder, brain connectivity studies have been particularly useful in understanding the differences between high functioning autistic children compared to typically developed ones. Autism spectrum disorder (ASD) affects 1 in 50 children between the ages of 6 and 17 years. Although, the etiology of Autism Spectrum Disorder (ASD) is not precisely known, a large number of investigations in ASD have been associated with primarily under-connectivity, default mode segregation, functional pathology associated with default mode midline core—medial prefrontal cortex–posterior cingulate cortex leading to social-cognitive impairment in ASD. In this study, to check the reproducibility of the developmental disconnection hypothesis of ASD which posits that shorter connections become overly well established with development in this disorder, at the cost of long-range connections, we use age matched cohort that was obtained from open access dataset available at umcd.humanconnectomeproject.org. The research carried out here attempts to gain insights of ASD using network analysis of resting state functional connectivity as well as structural/anatomical connectivity. Differences were found predominantly in the default mode networks which is supposed to play a crucial role in self-referential thinking and theory of mind (TOM). As expected, structural under-connectivity was observed and functional connectivity (FC) exhibited both under-connectedness and hyper-connectedness. Such abnormalities in connections could possibly lead to explain the varied behavior exhibited by autistic individuals and help in their diagnosis.

Keywords—Autism Spectrum Disorder, Structural Connectivity, Functional Connectivity.

Phase reorganization leads to diverse transient β-LFP spatiotemporal wave patterns in motor cortex during steady movement preparation

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Transient LFP oscillations in the beta band (~20 Hz, β-LFP) are a prominent feature of motor cortex, and abnormalities in β-LFP oscillations are seen in movement disorders. Motor cortex β-LFP exhibits traveling waves, but the significance of these waves and their relationship to single-unit activity remains obscure. We examine spatiotemporal β-LFP waves during steady-state movement preparation in a cued grasping task with instructed delays, and assess three scenarios: (1) spatial patterns arising from conduction delays, (2) traveling waves through an excitable medium, and (3) phase reorganization in coupled neural oscillators. We find that diversity in spatiotemporal waves cannot be fully explained by fixed anatomical patterns. We compare the statistics of spatiotemporal activity to optogenetically-induced traveling waves, and find that the spatiotemporal β-LFP activity is inconsistent with traveling waves in an excitable medium. In particular, transient spatial pattern reorganizations are rapid, and apparent wavelength correlates with amplitude. These features indicate wave activity representing phase reorganization in coupled oscillators. Indeed, oscillatory β-rhythmic single-unit activity is widespread during movement preparation. Despite this, single-unit phase coupling to β-LFP is weak. Importantly, changes in single-unit firing rates encode task-related information during movement preparation, limiting single-neuron phase coupling to a single coherent LFP oscillation. β-LFP transients are, therefore, likely due to fast transient relative-phase reorganization among oscillators at slightly different frequencies. These results clarify the origins of spatiotemporal β-LFP activity, and emphasize the importance of phase and frequency diversity in the generation of β-LFP in motor cortex and in maintaining of preparatory motor states.

The bridge between exploratory and confirmatory analysis of fMRI data sets

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We are in a big changes period in terms of deciphering the secrets of all the sciences, especially physics, biostatistics and neuroscience. Which is why the purpose of this paper is to make a comparison between two methods of statistical analysis of fMRI *(functional Magnetic Resonance Imaging)* data, because the fMRI can study brain activity, non-invasive, based on the contrast offered by the oxygenation of blood BOLD (Blood Oxygenation Level Dependent). This study increases interest because this imaging method is successfully used both in clinical practice and research.

In this paper we chose the design model type Event-Related and a statistical analysis is essential in interpreting the experimental paradigms were behind large data sets. Thus, we have to find the bridge between statistical confirmatory factorial analysis (CDA – *Confirmatory Data Analysis*) and exploratory (EDA – *Exploratory Data Analysis*), by processing the collected data in a visuomotor experiment. EDA is implemented by independent component analysis (ICA), while CDA using generalized linear model (GLM) of the Statistical Parametric Mapping software package for SPM (Statistical Parametric Mapping).

In conclusion we noticed that these two methods EDA and CDA are two methods that allow increasing complementarity and decreasing the competitiveness.

Network topology determines seizure generation in generalized epilepsy

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We introduce a modular network model of phase-coupled oscillators that gives a phenomenological description of the emergent electrographical activity of the cerebral cortex at rest as well as during epileptic seizures. This model is used to generate both focal and generalized model seizures in neural networks that are derived from electrophysiological data from subjects with epilepsy as well as healthy control subjects. This model presents a novel, computationally efficient approach to study epileptogenic activity in networks.

Parameters that define the network structure, and parameters that define the model dynamics are derived from resting-state EEG, thus there is no need to observe seizures from electrophysiological recordings. We apply this model to two different scenarios: Firstly, we study the global mechanisms of seizure generation in epilepsy in comparison to healthy controls. We demonstrate that networks from subjects with epilepsy have a statistically higher propensity to generate seizures than healthy controls [1].

Secondly, we demonstrate that this model-based approach can be used as diagnostic tool for epilepsy. By generating localized model seizures and recording the resultant activity in the network, we identify optimal sites and tuning parameters to distinguish between healthy subjects and drug-naïve subjects who were recently diagnosed with generalized epilepsy. We find that a reliable diagnosis of epilepsy (i.e. excluding the possibility of false-positives) can be given in more than half of all cases [2].

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Within- and between-network functional connectivity changes in dementia with Lewy bodies and associations with core clinical symptoms

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Dementia with Lewy bodies (DLB) is the second most common form of degenerative dementia and is characterized by core symptoms of cognitive fluctuations, visual hallucinations, and Parkinsonism. The objective of this study was to investigate how changes in functional connectivity within and between several resting state networks (RSNs) relate to clinical symptoms in DLB.

To this end, we studied resting state fMRI data from 30 DLB patients and 31 healthy controls (HC) matched by age and gender. 24 RSNs were identified from group independent component analysis on time-concatenated data from the HC group. Dual regression, FSLnets and randomise were used to assess between-group differences in connectivity within and between the 24 RSNs. Additionally, correlations between within- and between-network connectivity and core clinical scores were tested in the DLB group.

Aberrant connectivity in DLB was observed mainly within and between networks related to motor function, including basal ganglia, primary motor, and cerebellar networks. In addition, clusters of disrupted connectivity associated with non-motor networks (visual, prefrontal, insular, and thalamic networks) were mainly located in motor areas such as different parts of the basal ganglia and primary motor cortex. The strength of connectivity in several motor clusters was related to the severity of Parkinsonism in DLB. Non-motor related changes in connectivity were observed for the default mode, visual, and insular networks. This study emphasizes the importance of disrupted connectivity within motor, and between motor and non-motor networks in DLB, suggesting a role in the aetiology of Parkinsonian symptoms.

A Novel Scheme for the Validation of an Automated Classification Method for Epileptic Spikes by Comparison with Multiple Observers and the use of Information Theory

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PURPOSE: To better understand the region responsible for the generation of interictal epileptiform discharges (IEDs), it is important to classify IEDs consistently. In this study we propose and apply a statistical framework to validate an automated neuronal spike classification algorithm, Wave_clus (WC), applied to IEDs detected in human intracranial EEG data.

METHODS: IEDs were detected and marked by an expert human observer in icEEG data recorded in 5 patients with drug-resistant epilepsy undergoing invasive presurgical monitoring. A set of 100 randomly chosen IED from each patient recording was used for this study. Three human (H) EEG reviewers and WC classified the IEDs, with the option of re-labelling events as non-IED. To assess whether the results of automated classification fall within inter-human classification variability, we calculated the distance between classification (using the concept of variation of information (VI)) pairs. We then compared the individual IED labels (IED vs non-IED and IED classes) to calculate sensitivity and classification overlap.

RESULTS: IED were classified into between 3 and 7 classes. The percentage overlap between human and automated classification results was >58% for all 5 patients. The sensitivity of spike identification was high for WC and all human observers (>70%). There was a good visual and quantitative similarity between WC and human observers.

CONCLUSION: Wave_clus based IED classification is indistinguishable from that of humans. Automated classification algorithms have the potential to label epileptic spikes in a naturalistic and less subjective way. The statistical methods presented here can be used as a general framework for automated spike classification validation.

Assessment of cell types using kernel density estimation

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It is generally accepted that brains contain many types of neurons and that brain functions are likely to be determined by specific interactions between different neuron types. However, objective statistical criteria for defining neuronal types are lacking. Here, we address this problem by focusing on neurons in superficial layers of the medial entorhinal cortex (MEC). Superficial populations of MEC neurons have been extensively investigated and include neurons with well-defined grid-like spatial firing patterns. Theorising a network architecture capable of producing observed grid fields remains difficult and is limited by an incomplete definition of superficial layer cell subpopulations and their electrophysiological characteristics. Our aim here was to develop an objective electrophysiological assessment of stellate cell population structure in layer 2 of the MEC (L2SCs). We used a data set of patch-clamp recordings made from 1228 L2SCs. Passive and active cell properties from raw current clamp data were automatically extracted using custom MATLAB scripts. We apply advanced statistical methods developed in machine learning and computer vision fields to assess the significance of modes in the probability distribution function of these extracted features. Assessment of L2SC distributions is undertaken in both single electrophysiological parameter space and principal component space. Our approach provides a potentially valuable tool in the classification of neurons without relying on assumptions presented by other parametric or Euclidean-distance based clustering frameworks.

TD-source: a tool to estimate EEG source localization guided by time varying fMRI source covariance derived from tensor decomposition technique

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Currently there has been increased interest in investigating possible alterations in EEG brain networks at source level using source reconstruction in patients with epilepsy. The source localization technique is considered an ill-posed problem with no unique solution. However, if the source covariance matrix is known, one can reconstruct the signals in the source space directly (Dale and Sereno 1993, Nguyen et al. 2015). Functional Magnetic Resonance Imaging (fMRI) is an imaging technique with high spatial resolution, which is well suited for estimating the source covariance matrix. Traditionally, the source covariance matrix can be estimated from a correlation between fMRI time courses within a sliding window. Here we propose using tensor decomposition to estimate an instantaneous source covariance matrix at each TR (Ponce-Alvarez et al 2014). This would preserve the temporal resolution of the fMRI. For this we developed a tool "TD-source" in MATLAB. This tool includes two main functions: (1) a Tensor decomposition of fMRI, and (2) an EEG source reconstruction. As proof of concept, we applied this toolbox to surrogate data and found high concordance between the reconstructed and the original signals when the source covariance matrix is known. In conclusion, this tool offers a possibility to perform source reconstruction guided by fMRI with higher temporal resolution. In the future, we will test this tool with empirical simultaneous EEG/fMRI data in patients with epilepsy.

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Influence of pre-TMS brain activity on post-TMS brain activity in context of visual hallucinations

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Visual Hallucinations (VH) are common in several psychiatric and neurological diseases including Lewy Body Dementia (LBD). The pathophysiology and treatment mechanisms of VH are still largely unknown. Non-invasive brain stimulation carries potential studying the mechanisms of VH pathways as well as treatment options. In this study, transcranial magnetic stimulation (TMS) was applied to the occiput to elicit a subjective phenomena called phosphenes, during concurrent electroencephalography (EEG) in a group of n=20 healthy controls and n=20 patients with Parkinson's disease dementia (PDD), while the VH was assessed using the clinical questionnaires: the Neuropsychiatric Inventory (NPI) and the North-East Visual Hallucinations Interview (NEVHI). A number of rTMS studies demonstrate a functional connection between executive cortices (fronto-parietal) and occipital/parietal cortices through modulation of the posterior occipital alpha rhythm in response to rTMS. Intact alpha rhythm is a measure of attention and visual perception in healthy controls and is reported to dysfunction in PDD. Alpha phase prior to TMS has also shown promise as a marker of phosphene perception in previous control studies. Preliminary results indicate association between VH severity and phosphene thresholds. We will further investigate the spatio-temporal characteristics of TMS evoked potentials and examine the influence of top-down expectancies which are posited to be central in VH aetiology by examination of the pre-TMS phase state and its connectivity (posterior and frontal) as a marker of perception.

Efficient simulation platform for the cerebral cortex

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Explicit models and their numerical simulations are necessary to understand the function or malfunction of complex systems. For the cerebral cortex, various simulation platforms have emerged recently, aimed either at extreme speed, translational aspects, or at detailed replication of the cortical physiology. Because it is unclear which biological processes have significant effect on behavior, an intent to include all of them calls for a biophysically detailed model. Unfortunately, such detailed models comprise large parameter spaces and are computationally intensive. Our work follows the detailed model of Markram et al. (Cell 163 (2015) 456—492) with the specific aim to experiment with reduced complexity and parameter space in an efficient platform. We operate on the python-based Brian2 simulator and our platform supports Brian's stand-alone code generation for C++ as well as GPU acceleration via GeNN simulator. Connections between our 16 cell groups were mapped from the Markram et al. 55 morphological cell groups, resulting in 239 connection types between groups. We could replicate the dynamics of the 32k neurons, including a visible onset response riding on spontaneous activity for four cell groups while the others were non-responsive for the stimulus. In addition, relative shift in excitatory-inhibitory balance resulted in qualitatively similar shift between asynchronous and synchronous activation. Our model is open for experimentation with various biological details, such as distinct dendritic compartments and plasticity. In the future, such simulations may target disease models, as long as the pathophysiology affecting the neuronal membrane potential has been characterized.