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Speaker Abstract Collection
Alphabetical order according to presenting author

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List of Abstracts (in alphabetical order)

Excitation - Inhibition interplay in the modelling of epileptic seizures

Alain Destexhe
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This lecture will overview data about the role of excitation-inhibition interplay in the normal brain activity, and how it can divert into seizures. Micro-electrode recordings in humans can be used to record up to about 100 neurons, and it is possible to formally identify some of these neurons as excitatory or inhibitory. This allows one to follow the two populations of neurons across all states of the brain, such as wakefulness, sleep and pathological activities such as seizures. It is seen that seizures correspond to a complete break-down of the balance between excitatory and inhibitory neurons. These data provide very tight constraints to the modeling of seizure dynamics.

Biomarkers for whole-brain dynamics estimated from fMRI data: Toward clinical applications

Matthieu Gilson
Unviersitat Pompeu Fabra

Connectivity analysis has become a cornerstone in neuroscience following the recent progress in neuroimaging techniques to interpret brain activity. Recent methods have been developed to characterize the functional, structural and effective connectivities: these measures are biomarkers of the brain dynamics, which allows a quantitative comparison between subjects' conditions. Here we present recent developments with some example applications to neural pathologies:

– brain connectome and functional connectivity: uncovering patterns in the interconnectivity between the brain regions with different functions hints at the distributed information scheme in the brain; graph theory provides the tools (e.g., community and hub detection) to study those brain networks.

- whole-brain dynamic modeling to interpret fMRI data: these models are fit to data to capture the statistics of observed fMRI signals; their estimated effective connectivity describes the transition of fMRI activity between brain regions and can be interpreted to describe the communication flow between brain regions (typically 100) and how it changes across tasks and pathological conditions.

- on the technical side: we develop methods to classify the (pathological/non-pathological) conditions of single subjects from fMRI measurements, as a first step toward clinical diagnostic; statistical methods (e.g., Granger causality) need to be adapted in the case of large networks to extract significant interactions between brain regions.

Modelling specific circuit deficits underlying genetic epilepsies

John Huguenard
Stanford University

Epileptic seizures arise as a modal switch in CNS network behavior. Many rodent models of genetic epilepsies have been developed and these are associated with specific defects in cells, synapses, and networks. From these we have learned of the control mechanisms that have evolved within neural networks whose purpose appears to be to keep the network in a proper operational state. When these control mechanisms fail, seizure susceptibility increases, and breakthrough epileptic seizures occur. Understanding the dynamics and efficacy of these control mechanisms is a fundamentally important issue, and we are just beginning to approach such issues. Several mouse models of genetic generalized (absence) seizures will be discussed, including GABAB3, stargazer, gria4, and dbi, and the specific cellular/synaptic defects in each that increase seizure susceptibility.

Modelling stroke and rehabilitation in mice using large-scale brain networks

Spase Petkoski
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Stroke, and subsequent motor learning and recovery, induce changes in the structural and functional connectivity of the brain. Their consequences are accessible to modeling and empirical data collection on various levels of organization including the meso, macro and behavioral level. Mesoscale brain network model is thus a useful paradigm, allowing for multi-scale integration.

Individualized connectomes are so far not available in the mouse data of the stroke study. For this reason we use the generic Allen Mouse Atlas data. For validation we used another data set of healthy mice, in which individual structural and functional data were complete and available, and performed a systematic comparative analysis of simulated functional mouse network data based on 1) individual DTI-based mouse connectome, 2) averaged DTI-based mouse connectome, 3) Allen Mouse Connectome and various other surrogates. The results of this study demonstrate that the simulations based on the Allen Atlas Connectome compare best with empirical functional data and thus justifies its use in the modeling of the stroke data set.

The stroke is followed by period of motor learning and recovery, during which the changes of the functional connectivity are compared for calcium imaging data of the cortex in stroke versus control mice. The brain network model thus captures structural alterations caused by the stroke, and the recovery, in order to predict their impact on the functional data between different brain regions.

Alzheimer’s Disease biomarkers

Alberto Redolfi
IRCCS Fatebenefratelli

Magnetic resonance imaging (MRI) is extensively used in clinical routine and research field. It is essential to our understanding of the pathophysiology of neurodegenerative disorders, such as Alzheimer's disease (AD). Aims of this speech is to provide a comprehensive overview of the main findings in AD over the past twenty years, focusing on the patterns of gray and white matter changes assessed in vivo using MRI.

Major progresses in the field concern the segmentation of the hippocampus with automatic segmentation approaches (such as: Adaboost, Freesurfer, etc..). Advancements in quantification of hippocampal volumetry might pave the way to its broader use as outcome marker in AD clinical trials.

Patterns of cortical atrophy have been shown to accurately track disease progression and seem promising in distinguishing among AD subtypes. Disease progression has also been associated with changes in white matter tracts. Future integration of different MRI modalities may further advance the field by providing more powerful biomarkers of disease onset and progression.

Rehabilitation-induced cortical plasticity after stroke

Francesco Resta
CNRS

Neuro-rehabilitation is one of the most effective treatment for recovering motor deficits in stroke patients. Nevertheless, the neural basis of recovery associated with rehabilitative intervention is debated. We are interested in studying cortical remodeling induced by rehabilitative treatment based on physical training and brain stimulation. By longitudinal wide-field fluorescence imaging of cortical activity while training, we address the recovery of motor representation in the peri-infarct area. Coupling of the spared cortex to the injured hemisphere is investigated by an all-optical approach that combines calcium imaging and optogenetic neuronal activation. In addition, by using two-photon microscopy both in vivo and ex vivo on cleared cortices, we analyze how vascular remodeling accompanies synaptic plasticity. In this seminar I will show how the impact of rehabilitation on cortical plasticity can be dissected at multiple scales by combining optical tools of visualization and manipulation of neuronal activity.

Pathological sleep-like activity in brain-injured patients

Mario Rosanova
University of Milan

Despite being active and reactive, the brain of most severely brain-injured, non communicating patients is stuck in a low-complexity state. Indeed, as revealed by recent electrophysiological studies in unconscious patients diagnosed with an Unresponsive Wakefulness Syndrome (UWS), previously known as Vegetative State (VS) cortical networks fail to engage into complex interactions when directly perturbed (Casali et al., Science Translational Medicine 2015; Casarotto et al., Annals of Neurology 2016). Why is this so? How low complexity and consciousness are linked?

Stemming from recent intracranial studies (Pigorini et al., Neuroimage 2015), we hypothesized that the cerebral cortex of UWS patients is pathologically bistable, as in physiological NREM sleep. In other words, when directly perturbed cortical circuits in UWS patients would tend to fall into a period of neuronal silence (OFF periods) preventing the build up of complex interactions, which is a necessary requirement for consciousness.

To test this hypothesis we employed TMS/EEG in low-complexity UWS patients. In these patients TMS evoked simple slow waves, which strongly resemble the ones evoked in NREM sleep (Rosanova et al., Brain 2012). The analyses of TMS/EEG measurements in the time-frequency and phase domains revealed a significant suppression of high-frequency EEG oscillations associated with a slow, positive-to-negative sleep-like response to TMS and a short-living phase locking. These results indicate that cortical circuits in low-complexity VS/UWS patients invariably fall into an OFF period, which never occurred in healthy awake subjects.

Most important, the occurrence of TMS-evoked cortical OFF periods terminated the build up of complexity within cortical circuits and eventually resulted in low levels of the Perturbational Complexity Index (PCI), a metric which is based on TMS/EEG measurements and is specifically designed to measure cortical complexity. Overall, our findings strongly suggest that due to cortical bistability structurally preserved portions of the cerebral cortex of most UWS can react to a direct perturbation, yet do not engage into global complex interactions, which is a theoretical prerequisite for consciousness.

Notably, we have found similar results when applying TMS/EEG in perilesional areas of patients affected by cortical strokes. However, in these patients, who are fully conscious, TMS/EEG revealed the occurrence of OFF periods that remain local and do not affect overall brain complexity.

Neuronal and network mechanisms sustaining sleep-like cortical bistability in UWS and stroke will be discussed as well as critical methodological aspects to reliably apply TMS/EEG in brain-injured patients.

Therapeutic approaches for stroke and Alzheimer using largescale brain network models

Ana Solodkin
UC Irvine

The neuroscience community is immersed in the collecting of large datasets to provide greater sensitivity for understanding brain function and dysfunction. Such initiatives span normal function (Human connectome project), development (NIH pediatric Database), brain disorders such as Alzheimer's disease (ADNI) and psychiatry (RDoC: Research Domain Criteria Project). While these initiatives provide the necessary empirical foundation, what are lacking are the quantitative tools to link these multiple datasets to "reconstruct" the brain, provide the link between these data and those from a single person (precision medicine) and to translate these approaches to the evaluation and management of neurological patients.

To achieve these quantitative goals, we take a connectivity-based multi-scale approach built on the theoretical and practical framework embodied by *The Virtual Brain* (TVB). TVB uses empirical neuroimaging data to create dynamic models of the human brain. The models contain the anatomical connectivity between parts of the brain and the dynamics of local neural populations. TVB uses structural MRI data to create the custom brain surface, diffusion-weighted MRI data to infer the anatomical connections between brain areas, and then functional MRI data as target to modify the parameters of the model to reproduce the observed functional data. The neuroinformatics architecture houses a library of models, which catalogues the biophysical parameters that produce different empirical brain states. These biophysical parameters are invisible to brain imaging devices, thus TVB acts as a "computational microscope" that allows the inference of internal states and processes of the system. Determining these parameters, validating them, and applying them as individualized predictive biomarkers, has enormous potential to change acute and chronic neurological care of neurological patients.

The central idea in this presentation is to demonstrate how to utilize this unifying computational framework to integrate neuroscience "big data" across multiple scales to identify general principles determining brain dynamics as they occur in two contrasting clinical scenarios: chronic stroke and Alzheimer's disease.

In this work, we will our current investigatigations of the impact of vascular lesions and neurodegeneration on the structural connectome and their consistent effects in various multi-scale dynamical properties. The premise of this presentation will focus on the importance of morphing the modeling process to adapt to the particular neuropathology of each disease.

Our long-term goal with this work is to develop multi-scale precision biomarkers with strong biophysical grounding that can serve as the basis for personalized prognosis and/or therapeutic selection.

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Stimulation in large-scale brain network models

Andreas Spiegler
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Brain stimulation techniques such as transcranial direct-current stimulation (tDCS) are potential adjunct therapy in many psychological and neurological disorders. When the brain is stimulated, also by self-paced or cue-based tasks, the brain initially responds with activities in specific areas. The subsequent pattern formation of functional networks is constrained by the structural connectivity. The extent to which stimulus-induced brain activity spreads and information is processed over short- or long-range connections is unclear. This talk discusses the effects of structural connectivities on the network response to stimulation in whole-brain models of humans and mice. The results suggest that the stimulus-induced brain activity, which may indicate information and cognitive processing, follows specific routes imposed by the network structure explaining the emergence of functional networks. The results also show how tDCS can alter the network and its functional connectivity.

Structural and functional connectivity-based macroscopic modelling in epilepsy

Peter Taylor
Newcastle University

Computational models have shown great promise in helping to understand aspects of brain function and dysfunction. Models are composed of parameters (which do not change, or change very slowly), and variables (which are a property of interest that can change over time). In this lecture I will present some recent studies showing how models can be constructed to reproduce a property of interest, then constrained by data to make predictions. I will demonstrate specific examples in the context of epilepsy.

Models of interacting brain regions at cellular resolution

Sacha van Albada
FZ Jülich

In this lecture, I will go into neural network simulations of interacting brain regions, the reasons for performing them, and possible applications to clinical topics. Examples of such neural network simulations from the literature will be given, as well as an overview of a multi-area spiking model of vision-related cortex relating its structure to its dynamics at multiple scales. This model can serve as a prototype for cellular-level models of interacting cortical areas more generally. It is implemented with the simulation tool NEST, which specializes in networks consisting of simple neuron models. To close, I will provide a brief introduction to this simulation tool.

Data-driven disease progression modelling

Alexandra Young
University College London

Data-driven disease progression models are a new set of machine learning tools that reconstruct how a disease evolves over time from diverse medical datasets. This reconstruction can be used to gain insight into the underlying biological process, and to provide fine-grained staging and stratification systems for clinical trials and healthcare.

In this talk I will first discuss how quantitative models of disease progression can facilitate precision medicine, with a particular focus on neurodegenerative disease applications. I will highlight the key challenges in mapping out quantitative pictures of how neurodegenerative diseases progress, and discuss why traditional statistical and machine learning tools fail to meet these challenges. I will introduce the concept of data-driven disease progression modelling, explain how these models overcome these difficulties, and summarise the current state of the art. Finally I will discuss opportunities for future enhancements to data-driven disease progression models.