NetSci 2015

BRAIN NETWORKS SATELLITE

Book of Abstracts

ZARAGOZA. SPAIN. June 1-5, 2015

BRAIN NETWORKS.
NETSCI 2015. SATELLITE. 1-2 JUNE. ZARAGOZA. SPAIN.

Organizing Committees

Session I

Danielle Basset. University of Pennsylvania, USA
Qawi K. Telesford. University of Pennsylvania, USA
Robin W. Wilkins. University of North Carolina-Greensboro, USA

Session II

Raffaella Burioni. Universita di Parma, Italy
Guido Caldarelli. IMT - Institute for Advanced Studies, Lucca, Italy
Andrea Gabrielli. Istituto dei Sistemi Complessi (ISC) - CNR, Rome, Italy
Tommaso Gili. IRCCS Fondazione "Santa Lucia", Rome, Italy

Session III

Javier. M. Buldú. URJC & Center for Biomedical Technology, Madrid, Spain
Mario Chávez. CNRS & Institut du Cerveau et de la Moelle Épinière, France
Fabrizio de Vico Fallani. Inria&Institut du Cerveau et de la Moelle Épinière, France
Johann. H. Martínez. UPM & Universidad del Rosario, Bogotá, Colombia
David Papo. LPC Institute & Center for Biomedical Technology, Madrid, Spain
Martijn van den Heuvel. Brain Center Rudolf Utrecht, Utrecht, The Netherlands

BRAIN NETWORKS SATELLITE

Characterizing how the brain organizes its activity to carry out complex tasks is highly non trivial. While early neuroimaging and electrophysiological studies of brain structure and function, typically aimed at identifying patches of task-specific activation or local time-varying patterns of activity, there has soon been consensus that activity has a temporally multiscale spatially extended character, as transient networks of coordinated brain areas are continuously being created and destroyed. The complex networks approach to functional neuroimaging represents a conceptual revolution, not just an incremental refinement of existing techniques. It offers a qualitatively different view of brain activity and brain-behaviour mapping (shifting from a computer-like to a complex system vision of the brain), where networks are endowed with properties, which stem in a non-trivial way from those of their constituents nodes.

The aim of this Satellite is to explore how network science methods can be successfully applied to neuroimaging data. Vital to these studies is the development of methods and algorithms for understanding the distinct properties of brain-based graphs. This workshop will provide a review of the current techniques used in network neuroimaging studies, and a description of emerging analysis methods designed to understand underlying structures and relationships in the brain. Attendees of this workshop will gain an understanding of the field of network neuroscience.

The organizers

ZARAGOZA. SPAIN. JUNE 1st 2015.

NetSci 2015: SATELLITE SYMPOSIUM.

Brain Networks (I) | 1 June 2015 | 9:00 – 13:00

Opening Remarks: TBA [9:00 – 9:10]

1. Speaker: Qawi Telesford | [9:10 – 9:45]

University of Pennsylvania, USA

Title: An Introduction to the Network Science in the Brain

2. Speaker: Richard Betzel | [9:45 – 10:20]

University of Pennsylvania, USA

Title: Generative models of the human connectome

The configuration of connections in the human connectome, the "wiring map" of an organism's neural system, is thought to arise from a drive to reduce the total cost of wiring while simultaneously promoting efficient information processing. We attempted to disentangle the contributions made by these components by incorporating geometric (spatial) and topological information into the wiring rules of network generative models for the human connectome.

Across three independently acquired human MRI datasets (N=380 participants in total), we found that generative models where connection formation was based solely on spatial proximity were unable to produce realistic synthetic networks. Specifically, such models underestimate the number of long-range connections and fail to reproduce the distance-dependent degree assortativity that characterize empirical human connectomes.

On the other hand, models whose wiring rule included both spatial and topological information were able to match these properties and others. Of this class of models, we found that the best-fitting model combined a topological parameter for homophily, calculated as the similarity of connectivity profiles, and a geometric parameter that penalized the formation of long-distant connections. Fitting these models to the connectomes of a cohort whose ages ranged from 7-85 years, we find that the homophily parameter remains constant with age, whereas there was a monotonic reduction of the geometric parameter, suggesting that "older" networks penalize long-distance connections proportionally less.

3. Speaker: Paul Brodersen [10: 20 – 10:55]

University of Oxford, UK

Title: How does the topology of neuronal network change during spatial learning?

Paul Brodersen (1,2), Mason Porter (1,3), Colin Akerman (2), David Dupret (2,4)
(1) Department of Mathematics, (2) Department of Pharmacology, (3) CABDyN Complexity Centre, (4) MRC Brain Networks Dynamics Unit, University of Oxford

The manner in which information is processed and stored in the brain is determined by networks of functionally interconnected neurons. Understanding how these networks are organised and how

they might change over time are fundamental challenges for neuroscience. For instance, we know that during learning processes the strength or 'weight' of connections between pairs of neurons can increase or decrease, yet we understand very little about how this scales to larger networks of neurons. It is not known whether topological features of networks change in a consistent manner across different individuals undergoing the same learning process. Nor is it known how different subsets of neurons contribute to learning-associated changes in networks.

To address these questions, we are investigating changes in neuronal networks in the dorsal hippocampus of mice. The hippocampus is involved in the encoding and processing of spatial information, and so we recorded with multi-electrodes the spiking activity of hippocampal neurons as the animals explored novel and familiar environments. We then inferred the connectivity between neurons recruited in each environment and determined how different aspects of the network topology changed during exploration.

In the talk, I will first discuss some simple but effective methodological improvements that we have made in the inference of connections between neurons from spike trains. I will then present some preliminary results on how the topology of neuronal networks in the hippocampus changes during learning.

- **Coffee Break (Refreshments Served) [10:55-11:10]**

4. Speaker: Matthias Ekman [11:10 – 11:45]

Donders Center Cogn. The Netherlands

Title: Determinants of Dynamic Reconfigurations in Human Brain Networks

Human brain networks underlie constant reconfigurations, even in the absence of specific task demands. These changes are believed to reflect the system's capacity to explore its various configurations. However, little is known about mechanisms governing the transitions between different brain states. In this talk, I will introduce a dynamical network framework which tracks changes of brain states over time in a so-called state-space. Graph theoretical analysis of the network formed by state transitions revealed that brain regions differ in their multitude of realized states. Although state transitions occurred spontaneously, I will show that the network formed by these state transitions displays a characteristic, non-random structure with a preference for transient high-integration states. Building on this framework, I will link network dynamics to biophysical models of brain functioning and explore various determinants of dynamic network reconfigurations and their implications for human behavior.

5. Speaker: Joaquín Goñi [11:45 – 12:20]

Indiana University, USA

Title: Modeling resting-state functional brain networks: from population data to individual subjects

Resting-state is a widely used approach in functional brain imaging. Here, subjects are asked not to perform an explicit task, hence favoring the emergence of spontaneous (low frequency) neural activation patterns consequence of mind wandering related processes. This is the most frequent experiment employed to model and assess the human brain as a functional network, and has allowed the identification of well characterized resting-state networks (RSN). Resting-state functional

connectivity (rsFC) is usually measured by quantifying the level of coupling between pairs of time-series that reflect the activity of different brain regions along time, as measured by blood-oxygen-level dependent (BOLD). I will revise and present a number of processing aspects (namely based on cohort characteristics, scrubbing of volumes, principal components analysis and outliers detection) that may impact the modeling of FC networks and subsequent network measures (such as those related to integration and segregation), especially when assessing individual subjects as opposed to obtaining group-averages of functional connectomes. Interestingly, these steps may be seen as post-processing from the scanner acquisition point of view, or as pre-processing from the network modeling point of view.

6. Speaker: Ruben Schmidt [12:20 – 13:00]

Univ. Med. Cent. Utrecht. The Netherlands

Title: The connectome as an underlying infrastructure of disease propagation

In recent years the connectome has become the subject of investigations into its role as a possible anatomical substrate for spread of pathology in neurodegenerative diseases, with the aim to better understand the pathogenic mechanisms involved. In this exciting new field within connectomics, macroscale connectivity is being linked to disease effects at the neuronal level by combining diffusion imaging with histological observations. In my talk I will discuss the work on connectome-based simulation and prediction models in disease.

- **Dismissed for Lunch [13:00 – 15:00]**

Brain Networks (II) | 1 June 2015 | 15:00 – 19:00

Opening: Andrea Gabrielli [15:00 – 15:10]

7. Speaker: Tommaso Gilil | [15:10 – 15:30]

Istituto dei Sistemi Complessi (ISC) - CNR, Rome, Italy

Title: Routes to adaptation in functional brain networks

The human brain is able to functionally reorganize in order to adapt to neuronal challenges. External intervention both on healthy and injured brains can induce collective processes able to alter the functional architecture of neuronal interaction. The global functional reaction to an enduring external stimulation can be easily investigated if human brain is considered as a large-scale complex network. A quantitative analysis of the complex brain networks, largely based on graph theory analysis, is typically achieved through all major magnetic resonance imaging (MRI) modalities. Under this framework, resting-state functional MRI (fMRI), a non-invasive way of measuring the spontaneous neural activities in the human brain, has been widely proven to catch the fundamental topological organization of brain networks. In addition, resting-state fMRI has been used to elicit the association between topological reorganization of complex brain networks and cognitive load, loss of consciousness, psychiatric or neurologic brain disorders. Here we present some complex network analyses on both healthy and diseased

brains, that react to external forcing agents, showing how functional nodes are able to change the role of their connectedness respect with the baseline condition.

8. Speaker: Johanna Meijer [15:30 – 16:00]

Leiden University. Netherlands

Title: Networks of the biological clock

Proper theoretical network models of the brain are in need of well-characterized brain areas that are preferably described at a multi-scale level. The suprachiasmatic nucleus (SCN) is the master clock in the mammalian brain and consists of 20,000 individually oscillating cells. Each cell contains a molecular feedback loop that produces an endogenous rhythm with its own intrinsic frequency. In order to obtain a robust and coherent 24-h rhythm that can drive other circadian rhythms in our body, the SCN cells synchronize to each other as a result of neural coupling. In addition to the internal synchronization, the SCN synchronizes to external cycles, such as to the 24-h light-dark cycle and to seasonal cycles. The network structure of the SCN results in a system that shows a balance between robustness on the one hand and flexibility on the other hand.

In our lab we perform electrophysiological recordings from single neurons and from populations of about 100 neurons. Furthermore transgenic luciferase expressing mice are used to simultaneously measure the rhythms in gene expression at single cell level. Finally we record electrical activity from populations of neurons with implanted electrodes in freely moving animals. In this preparation, the recorded neurons of the central clock are interacting with other brain areas.

We have observed that temporal behavioral patterns and the central clock show scale invariant behavior. With disease and aging, scale invariance is lost, and also in a brain slice preparation when the clock is not communicating with other brain areas, scale invariance is absent. We conclude that scale invariance emerges at the integrated network level. Understanding how neurons and brain regions communicate, coordinate, synchronize, and collectively respond to signals and perturbations is one of the most intriguing, yet unsolved problems in neuroscience. As the output of the SCN is unambiguously measurable in terms of phase and period, the measurements from the different levels of organization, i.e., the molecular level, the cellular level, the organ level and the behavioral level, can be compared. Current studies are aimed at bridging scales, from the micro to the macro level and vice versa, thereby understanding how properties emerge at each of these levels.

9. Speaker: Lucilla De Arcangelis [16:00 – 16:30]

2nd University Naples. Italy

Title: Criticality and correlations in neuronal networks

Neuronal avalanches are a novel mode of spontaneous brain activity, experimentally found in vitro and in vivo, which exhibits a robust critical behaviour. Avalanche activity can be modelled within the self-organized criticality framework, including threshold firing, refractory period and activity-dependent synaptic plasticity. The size and duration distributions confirm that the system acts in a critical state, whose scaling behaviour is in agreement with experimental data. Interestingly, the critical behaviour is robust with respect to network features but shows interesting features on modular networks.

The temporal organization of neuronal avalanches can be characterized by the distribution of waiting times between successive events. Experimental measurements in the rat cortex in vitro exhibit a

non-monotonic behavior, not usually found in other natural processes. Numerical simulations provide evidence that this behavior is a consequence of the alternation between states of high and low activity, leading to a dynamic balance between excitation and inhibition. This behavior has been verified on a larger scale, i.e., on fMRI data from resting patients, where activity variations with opposite sign are correlated over a temporal scale of few seconds, suggesting a critical balance between activity excitation and depression in the brain.

10. Speaker: Hernan Makse [16:30 – 16:50]

City College NY. USA

Title: Percolation and cascading in a brain network of networks

The human brain is organized in functional modules. Such an organization presents a basic conundrum: Modules ought to be sufficiently independent to guarantee functional specialization and sufficiently connected to bind multiple processors for efficient information transfer. It is commonly accepted that small-world architecture of short paths and large local clustering may solve this problem. However, there is intrinsic tension between shortcuts generating small worlds and the persistence of modularity, a global property unrelated to local clustering. Here, we present a possible solution to this puzzle. We first show that a percolation process defines a brain network of networks of hierarchical self-similar modules made of strong links interconnected via weak ties. Weak ties are precisely organized as predicted by theory maximizing information transfer with minimal wiring cost. Such a design suggests a natural solution to the paradox of efficient information flow in the highly modular structure of the brain. We test our theoretical predictions in functional brain networks (in task and resting state). Furthermore, weak interconnecting ties are provided by network hubs implying that the resulting system of correlated networks is stable and robust to failure in contrast to NoN theoretical predictions in uncorrelated systems with one-to-one interdependencies.

- **Coffee Break (Refreshments Served) [16:50-17:10]**

11. Speaker: Tiziano Squartini [17:10 – 17:30]

ISC-CNR Rome. Italy

Title: Detecting cluster structure of resting state fMRI brain networks of mice: percolation and modularity features

Although the brain has been an object of study for a long time, its working principles are still largely unknown. Its highly, non-trivially connected structure shapes a functional network whose activation and synchronization mechanisms represent a major challenge for scientists belonging to different disciplines, from neuroscience to complex system theory.

This talk is a contribution to the study of the brain from the perspective of complex network theory. Specifically, resting state functional connectivity networks from 41 mouse brains were measured by functional MRI and analyzed applying clustering algorithms, community detection methods and percolation analysis to gain insight into their modular structure. Statistically significant partitions of functionally connectivity networks from different methods were identified and compared, thus enabling the identification of a set of functionally segregated sub-networks.

This study suggests that analytical tools provided by network theory may provide novel insight

into the structure of the brain, highlighting non-trivial topological relations between different areas.

12. Speaker: Miguel A. Munoz [17:30 – 18:00]

Universidad de Granada. Spain

Title: A novel brain partition highlights the modular skeleton shared by structure and function

Elucidating the intricate relationship between brain structure and function, both in healthy and pathological conditions, is a key challenge for modern neuroscience. Recent progress in neuroimaging has helped advance our understanding of this important issue, with diffusion images providing information about structural connectivity (SC) and functional magnetic resonance imaging shedding light on resting state functional connectivity (rsFC). Here, we adopt a systems approach, relying on modular hierarchical clustering, to study together SC and rsFC datasets gathered independently from healthy human subjects.

Our novel approach allows us to find a common skeleton shared by structure and function from which a new, optimal, brain partition can be extracted. We describe the emerging common structure-function modules (SFMs) in detail and compare them with commonly employed anatomical or functional parcellations. Our results underline the strong correspondence between brain structure and resting-state dynamics as well as the emerging coherent organization of the human brain.

13. Speaker: Raffaella Burioni [18:00 – 18:30]

University of Parma. Italy

Title: Average synaptic activity and neural networks topology: a global inverse problem

By a heterogeneous mean--field approach to neural dynamics on random networks, we provide an effective description of microscopic and large scale temporal signals in a leaky integrate-and-fire model with short term plasticity, featuring a complex dynamical phase diagram with quasi-synchronous events and locking. Within this framework, we obtain a set of self consistency equations that allow to formulate and solve a global inverse problem: reconstructing the in-degree distribution from the knowledge of the average activity field. The method is very general and applies to a large class of dynamical models on massive and sparse random networks, with excitatory and inhibitory components.

14. Speaker: Angelo Bifone [18:30 – 19:00]

IIT - Rovereto (TN). Italy

Title: The modular structure of brain networks and the resolution limit

The modular organization of brain networks has been widely investigated using Modularity, a fitness function introduced by Newman to find the optimal partition of a graph. However, despite its popularity and merits, Newman's approach presents some important limitations. Indeed, Modularity-based methods were shown to suffer from a resolution limit, as they fail to identify modules that are smaller than a scale that depends on the size of the overall network. As a consequence, even unambiguously defined modules, like complete sub-graphs or cliques, may be unduly merged into larger communities when they are too small compared to the size of the network. Here we explore the effects of this limitation on the study of brain connectivity networks. We demonstrate that the resolution limit prevents detection of important details of the brain modular structure, thus hampering the ability to appreciate differences between networks and to assess the topological roles of nodes. We discuss the

important implications of these findings for the identification of the brain structures responsible for the integration of brain connectivity, and argue that current models of the brain modular architecture suffer from the detrimental effects of the resolution limit and should be revisited.

Brain Networks (III) | 2 June 2015 | 9:00 – 13:00

Opening: J. M. Buldú – M. Chavez [9:00 – 9:10]

15. Speaker: C. Hilgetag | [9:10 – 9:50]

UKE Hamburg. Germany

Title: Excitable Neural Dynamics Based on Topological Features of Brain Networks

Brain connectivity is characterised by a number of distinctive topological features, such as a heterogenous degree distribution with hubs, hierarchically organised modules, as well as a characteristic spectrum of motifs and cycles. These features have consequences for different aspects of brain dynamics such as self-sustained network activity, the wave-like propagation of activity as well as correlations and anti-correlations of activity patterns. We have investigated the relation between neural network topology and dynamics with the help of a general excitable model (a cellular automaton) which allows a mechanistic understanding of the contribution of different topological features.

16. Speaker: M. Kaiser | [9:50 – 10:30]

Newcastle University. UK

Title: The Human Connectome in Health and Disease: Organization and Development of Hierarchical Brain Networks

Using routines from physics and the social sciences, neuronal networks were found to show properties of scale-free networks exhibiting hubs and rich-club connectivity while also showing a modular and small-world organization. Developmental brain diseases such as epilepsy and schizophrenia as well as network diseases of old age such as dementia show characteristic changes in these network properties. I will describe novel results concerning the hierarchical and modular organisation of neural networks using standard and high-resolution networks. Second, I show how this organisation changes during brain development in healthy subjects in childhood and early adulthood and how the network deteriorates at old age for Alzheimer's disease and Lewy Body Dementia patients. Finally, I will describe network growth approaches that can generate a hub, rich-club, and modular structural connectivity.

17. Speaker: P. Vertes | [10:30 – 11:00]

University of Cambridge. UK

Title: The organization of brain networks during normal and abnormal development

Adolescence is a time of enormous changes in the cognitive, social, sexual and economic repertoires of most humans. It is also the time-window for the highest rates of incidence of many psychiatric disorders. In this talk I will describe our recent work as part of the NSPN consortium on the structural and functional changes in brain organization which underpin this important decade of human

life. I will also show how the observed brain network changes can be related to genetic drivers of differential brain development. Finally, I will discuss how this work sets the stage for a more focussed investigation of alternative developmental trajectories in psycopathology.

- **Coffee Break (Refreshments Served) [11:00-11:30]**

18. Speaker: J. Garcia-Ojalvo | [11:30 – 12:10]

UPF, Barcelona. Spain

Title: Dynamical organization of neural activity in brain networks

For its correct operation, the brain relies on an exquisite organization of its dynamics in space and time. We will show that a complex network of neural mass models exhibits mesoscopic segregation of excitation and inhibition, with some cortical columns acting mainly in an excitatory manner while some others have a predominantly inhibitory effect on their neighbors. The character of the each column depends on its local topology within the network: hubs are preferentially inhibitory, while nodes with small degree are mainly excitatory. These results suggest that the excitation-inhibition balance is organized mesoscopically in brain networks.

19. Speaker: J. Soriano | [12:10 – 12:50]

University of Barcelona. Spain

Title: Exploring effective connectivity in neuronal cultures. Applications to medicine

In several neurological disorders the deterioration of brain's functionality and cognition has been ascribed to the loss of specific connectivity pathways or a change in the topological properties of the brain's circuits. To deepen in the understanding of the dynamics-connectivity relation, neuronal cultures have emerged as remarkable systems given their accessibility and easy manipulation [1]. Additionally, recent advances in bioengineering and genetics have allowed for the preparation of neuronal cultures with specific disorders, such as Sanfilippo or Huntington. These resources are helping to uncover, as model systems in vitro, the deterioration of neuronal network circuitry upon disease. Our group has specialized in such experimental preparations. In our measurements we monitor spontaneous activity using calcium fluorescence imaging, which allows the detection of neuronal firing events with both high temporal and spatial resolution [2,3]. The detailed analysis of the recorded activity in the context of network theory, information theory and non-linear physics allows for the quantification of important properties, most notably the repertoire of activity patterns [2,3] and functional connectivity [3], as well as their alteration upon disease. The talk will illustrate the potential of using several interdisciplinary tools to model brain networks in vitro, and how they can be further exploited to develop therapeutic strategies for Sanfilippo's syndrome.

20. Speaker: Gorka Zamora | [12:50 – 13:20]

Center for Brain and Cognition, Universitat Pompeu Fabra, Barcelona, Spain.

Title: The link between the structural and the functional connectome

Beyond the specialization of brain regions to process and store information related to particular functions, proper brain function also requires of the cross-talk between them. Investigation of the

anatomical communication patterns (the structural connectome) help us better understand how information is organised, shared and integrated within the brain. Although necessary, good knowledge of this structural connectome is insufficient to explain the emergence of collective dynamics in the brain which are characterised by transient associations of regions that synchronise and desynchronise over time. In this talk we will summarise our efforts to model the resting-state dynamics, based on knowledge of the anatomical connectivity, and we will try to identify the missing ingredients to acqurately reproduce the empririically observed brain dynamics.

Concluding Remarks: F. De Vico Fallani – D. Papo [13:20 – 13:30]

Poster Session: Brain Networks | 1 June 2015 | All Day

1. Multilayer Motifs in Brain Networks

Federico Battiston(1), Mario Chavez(2), Vincenzo Nicosia(1), Vito Latora(1)
(1) School of Mathematical Sciences, Queen Mary University of London, UK.
(2). CNRS UMR-7225, Hôpital de la Pitié-Salpêtrière. Paris, France

In complex network analysis, a motif is a small subgraph that is statistically over-represented with respect to a given null model [1]. The abundance of such subgraphs seems to be related to the robustness of the system or to the stability of the dynamical or signalling circuit they represent [1, 2]. Empirical studies have lead to the hypothesis that brain (dys)-functions rely on the (lack of) coordination of a scattered mosaic of distant brain regions, forming a non-random network [3]. Although a small set of motifs have been found in both neuroanatomical and functional brain data sets [2], and are considered central to information processing in the brain, the interplay between structural and functional motifs is still not well understood.

The present contribution sheds some light on this relationship, by casting the problem in the multiplex network formalism. We considered two-layer multiplex networks constructed from structural and functional brain information on 21 healthy subjects, respectively obtained by Diffusion Tensor Imaging (DTI) and resting-state functional MRI (rs-fMRI). In these networks, nodes are defined as Regions of Interest of the brain (ROIs). The edges of the structural (DTI) layer represent the average probabilistic white matter connection between any pair of ROIs, while links in the functional network indicate functional correlations between the fMRI time-series of the two corresponding ROIs (see Panel (a)).

We started by analysing the simplest multiplex motif, namely all the different configurations of the multi-edge connecting two ROIs. Since the correlation fij between the fMRI activity of two ROIs i an j can be either positive (+), or negative (-) or non-significative (0), and a structural edge between two ROIs might either exist (Y) or not (N), we have in total six possible elementary multi-edge motifs, namely +Y , -Y , 0Y , +N , -N and 0N.

We report in panel (b) the Z-score $Z\ (p_\alpha) = \frac{p_\alpha - \mu_\alpha}{\alpha}$ of the frequency (p_α) of each of these six motifs, with respect to a multiplex null-model where we kept fixed the structural layer and performed a (signed) configuration model on the functional layer (μ_α and σ_α are mean and standard deviation of the

motif abundances in the null-model, and the reported results are aggregated over the 21 subjects). Interestingly, the motif +Y (corresponding to the concurrent presence of a positive fMRI correlation and of a direct connection in the DTI layer) is significantly over-represented, while +N (positive correlation and absence of edge) is markedly under-represented. This means that the significant functional positive links are definitely correlated with the structural network. Conversely the motif -Y is as likely in real data as in the random model.

For a more in-depth analysis of the relationship be- tween functional and structural connections, we measured the probability P (fij $>$ th) that there exists a strong positive correlation between two ROIs in the functional layer as a function of the weight dij of their connection in the structural layer [top figure in panel (c)], and the dual probability P (dij $>$ 0) that a structural link between two ROIs exists as a function of the strength of the correlation of their fMRI activity. The results, shown in panel (c), indicate that the functional coordination of human brain dynamics at rest is non-trivially constrained by its underlying anatomical net- work, and suggest that structural connections might be necessary but not su_cient for the existence of positive functional correlations between two regions of the brain.

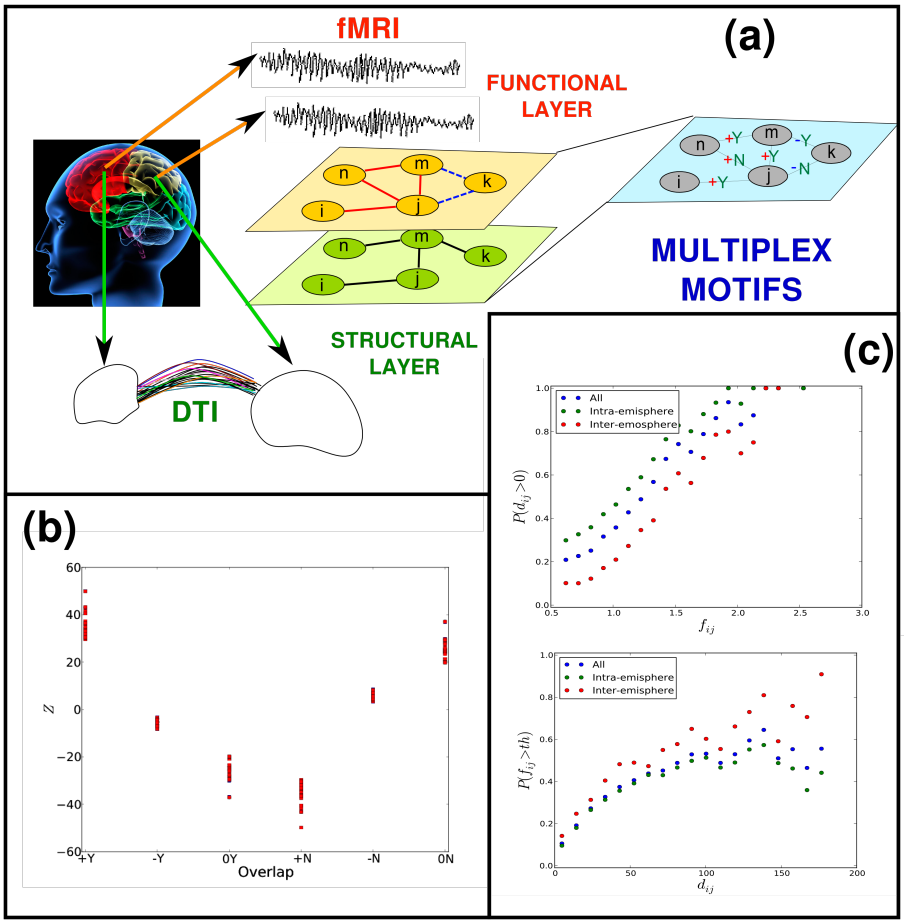

Figure 1: (a) The human brain can be naturally mapped into a duplex network whose layers respectively encode the structural (DTI) and functional (fMRI) relationships among Regions of Interests (ROIs). As a result, six elementary multi-edge motifs can be defined. (b) The over-abundance of the +Y motifs confirms the high correlation between positive functional links (+) and the presence of a physical connection between two ROIs. (c) The marginal probabilities of observing an edge on one layer given its existence and weight on the other confirms that structural connections are not sufficient for the presence of functional correlations.

2. Influence of bilingual exposure in the developing brain networks

B. Blanco
Basque Center on Cognition, Brian and Language. Spain

During the first months of life the language and auditory networks are two of the functional brain networks that experience the fastest development (Dubois et al., 2014; Gao et al., 2014). The bidirectional interaction between experience and brain development is especially relevant for the configuration of these networks during the first postnatal months. As it has been previously observed that different brain regions are involved during speech processing across monolingual and bilingual 4-month-old infants (Molnar et al., 2014), it is a possibility that bilingual exposure, as a long-term environmental factor, affects the developing language neural circuitry. This work aims to investigate how the development of synchronized spontaneous activity of spatially distant areas in the infant brain during resting state is modulated by the early exposure to one versus two languages. A 52-channel near-infrared spectroscopy system was used to measure spontaneous brain activity in 4-month-old Spanish monolingual (n=16) and Basque-Spanish bilingual (n=16) infants. Functional brain connectivity was evaluated by computing the correlation between hemoglobin time series of each measurement channel for each participant. Intrahemispheric and interhemispheric connectivity were then evaluated by means of a network based statistics approach (Zalesky et al., 2010) to reveal potential differences in the connectivity patterns between groups. Overall, the results suggest that an early and continued exposure to a bilingual environment leads to changes in the configuration and the development of resting state functional brain networks that are detectable as early as 4 months of age.

3. Bridging the gap between structure and function in the human brain

A. Messé
Department of Computational Neuroscience. Universitätsklinikum Hamburg-Eppendorf

Introduction

Magnetic resonance imaging (MRI) has been able to provide relevant information regarding the human brain structure and function, leading to a central and very active topic in neuroscience: the "connectomics". In order to bring together the structural and functional connections, some studies have used computational models, with apparently similar performance despite great differences in models definition [Deco et al. 2013]. The absolute and relative explanatory power and the properties that actually drive that performance remain insufficiently characterized. We here perform an extensive comparison of mainstream models in their ability to predict empirical functional connectivity (FC) [Messé et al. 2014, 2015].

Materials and methods

Data resting state fMRI data and DTI images were acquired from 21 healthy volunteers. Anatomical parcellation was performed to define sets of regions of interest, from low to high resolution [Fischl et al. 2004]. FMRI time series were correlated between ROIs, defining FC. Structural connectivity (SC) was then set as the proportion of fibers connecting two given ROIs using probabilistic tractography [Behrens et al. 2007]. Computational models The individual SC matrices were finally fed to seven generative models possessing various levels of complexity and realism. Comparison Statistical analyses were performed on predictive powers (ie. the correlation between simulated and empirical FCs). We also applied graph theory in order to further characterize the relationships between the models and the MRI

data.

Results

We found that: (i) there were significant effects of scale and model on predictive power; (ii) among all models, the simplest model, the SAR, was found to consistently perform better than the other models; (iii) the SAR also appeared more 'central' from a graph theory perspective; (iv) empirical FC only appeared weakly correlated with simulated FCs, and was featured as 'peripheral' in the graph analysis.

Conclusions

To conclude, the computational models we compared, which display oscillatory behaviors and dynamics that can be quite different, nevertheless mostly differ in aspects that have little impact on their overall predictive power, over the range of parameters explored. Beyond their basic differences, their ability to predict FC from SC appears to mostly reduce to a simple core (stationary) linear process that is explicitly embodied by the SAR model. This, along with the models' limited predictive power with respect to empirical FC, demonstrates the limited value of such modeling approaches in their current form for predicting observed functional connectivity.

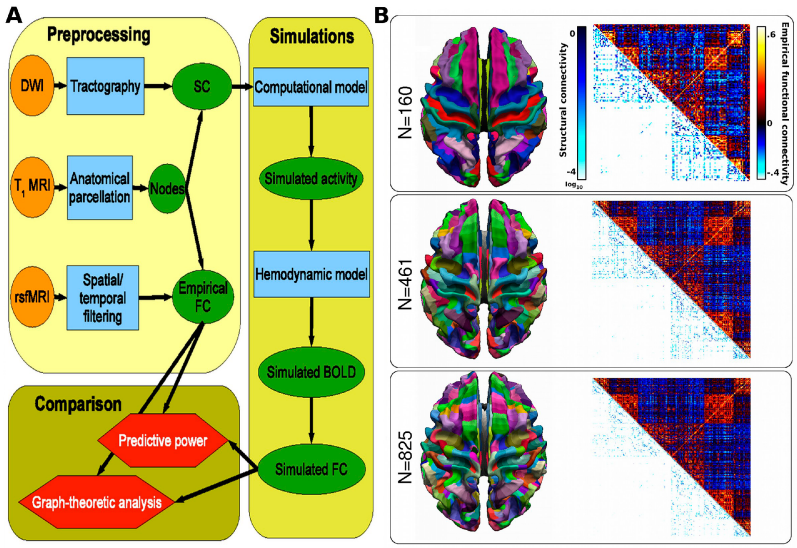

Figure 1: Flowchart illustrating the processing pipeline and empirical data. (A) From the raw MRI data to the comparison of simulated FC. (B) Brain parcellations and corresponding averaged SC (lower) and empirical FC (upper) for increasing spatial scales.

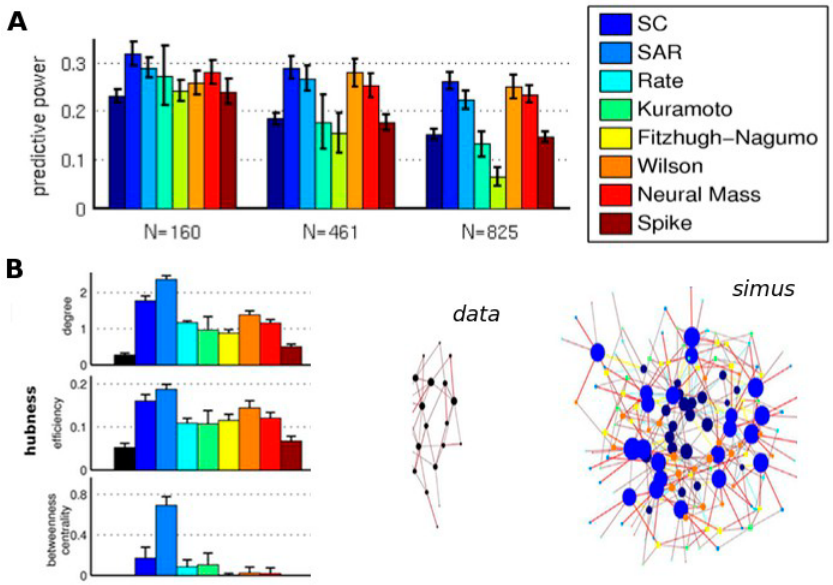

Figure 2: (A) Predictive power. (B) Graph theoretic comparison, backbone layout of the partial correlation between FC patterns, from there we clearly observe a split between empirical ('data') and simulated ('simus') FCs as well as the predominant position of the SAR model (right) and the associated hubness metrics (left).

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4. Multilayer functional connectivity of human brain

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Complex network approaches have successfully characterized informational attributes of the functional connectivity network of the human brain. The majority of studies on this type of networks have used functional magnetic resonance imaging (fMRI) to estimate the functional connectivity,

especially with signals measured during resting state of individuals.
Recently, it has been demonstrated that there are frequency-specific functional connectivity topologies obtained from fMRI with distinct capacities of integration and segregation [1], suggesting that the human brain exhibits intrinsic frequency-dependent functional organization. Each frequency-dependent network defines a functional layer with a characteristic topology, therefore it is natural to represent the whole set of graphs as a multilayer network [2].

Of course, such a modeling raises new intriguing questions. For instance, it is not known how these multiple layers interact each other to generate the brain function as a whole. In this study, we tackle this issue by employing multilayer analysis and modeling of complex networks [3 , 4]. Multilayer tools allow the analysis of all functional networks simultaneously within a consistent mathematical framework by exploiting the intrinsic interconnectivity of layers. More specifically, from the analysis of structural reducibility [5] and versatility [6], we show that the multilayer modeling is necessary and that any network aggregation leads to misleading results. From the analysis of correlations [7 , 8], structural reducibility [5] and mesoscale structure of the multilayer network { employed by means of multi-slice modularity maximization [9] and information flow compression [10] we show that it is possible to discriminate between healthy and schizophrenic individuals.

For instance, the quantum Jensen-Shannon distance [5] matrix J (s) among all layers is built for each healthy and schizophrenic individual in our data set, and, for each group, the average over all subjects is calculated. For each pair of layers α and β the inverse of the coefficient of variation, i.e. $\langle J_{\alpha\beta}\rangle / var(J_{\alpha\beta})$, is calculated, and the relative difference between the values obtained from healthy and schizophrenic subjects is reported in Fig. 1 . The results suggest that this descriptor is sensitive to the difference between healthy and schizophrenic subjects, with differences of up to 30% in absolute value. Finally, we discuss how the multiplexity of the functional connectivity network contributes to the brain function in terms of integration and segregation.

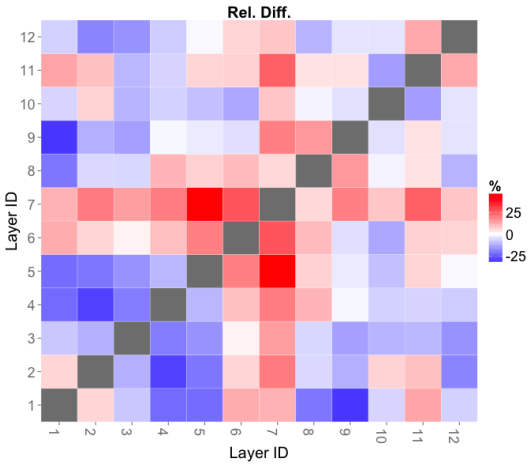

FIG. 1. Reducibility analysis of the brain multilayer network in healthy and schizophrenic individuals.

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5. How spatial smoothing affect fMRI brain networks?

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Since the rise of connectomics, modeling the human brain as a complex network has gained an everincreasing popularity (Sporns 2013). Nowadays, network-based methods belong to the standard set of tolos in the analysis of fMRI data. However, collection and preprocessing of the data are rarely optimized for network analysis and the effects that traditionally used preprocessing methods have on the network structure are only partially known (Aurich et al. 2015). In the present work, we address two questions concerning the effects of spatial smoothing of fMRI data. First, we investigate how spatial smoothing affects how the network structure is propagated from the voxel to the region-of-interest (ROI) level, where the time series of each ROI is defined as an average of the time series of the voxels belonging to the ROI. Second, we ask if smoothing changes which of the network nodes are hubs.

Spatial smoothing is commonly used to increase the signal-to-noise ratio of fMRI data and to decrease inaccuracies caused by anatomical differences between subjects (Bennett & Miller 2010). In the smoothing process, the time series of each voxel is redefined as the convolution of the data and a (Gaussian) smoothing kernel placed on the voxel. Thus, smoothing increases correlations between close voxels, in particular between neighboring voxels. In the simple and widely used correlation-based network-building approach, such correlations directly define the weights of the network links between the respective nodes. Our results show that spatial smoothing increases the internal coherence of the ROIs and thereby reduces the information loss between the voxel and ROI level networks. Smoothing increases both voxel-voxel and ROIROI correlations in a uniform manner and thus it does not add spurious links to the network that is obtained by thresholding, i.e. discarding a fraction of weakest links. Further, although smoothing increases the strength of the nodes, i.e. their total correlations with other nodes, it has only a minor effect on the degree distribution of the network. Thus, spatial smoothing does not change the identity of the network hubs (when defining hubs by degree). The impact of the present work is two-fold. First, we show that spatial smoothing has no fatal effects on fMRI resting state networks and the use of this common fMRI preprocessing method in network analysis is justified. Second, by illustrating changes in the network structure, starting from a full voxel-level network, our work lays foundations for deeper understanding of the effects of spatial smoothing on network-level metrics. More generally, our work contributes to an increase in the awareness of what functional brain networks actually measure and depict.

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6. A closer look at the apparent correlation between structural and functional connectivity in brain networks

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Department of Computational Neuroscience. Universitätsklinikum Hamburg-Eppendorf

Introduction

The relationship between the structural connectivity (SC) and functional connectivity (FC) of neural systems is a central focus in brain network science. As it seems that the specific dynamic models used for replicating empirical FC do not matter [Messé 2014, 2015], it is an open question how strongly the SC-FC relationship depends on the characteristic topological features of brain networks. Using a basic model of discrete excitable units that follow a susceptible-excited-refractory dynamic cycle (SER), we analyzed how FC is shaped by the modularity of a neural network. We compared the results obtained by the SER model with corresponding simulations by another well established dynamic mechanism, the Fitzhugh-Nagumo model, in order to explore general features of the SC-FC relationship.

Materials and methods

Network topology Simulations were performed on a synthetic undirected flat modular network. To investigate the effect of topology on the relationship between simulated FC and underlying SC, the original modular graph was randomized at various proportions from 0%, the original graph, to 100%, the completely randomly rewired network. Randomized networks were generated using a Markov switching algorithm that randomly swapped pairs of edges [Maslov and Sneppen, 2002]. The set of randomized networks was degree-matched (both in- and out-degree), and statistical assessment was performed by exploring 50 randomization of the original network for each proportion.

Models

We used a cellular automaton model of excitable dynamics, the SER model, representing a stylized biological neuron or neural population [Garcia et al, 2012]. The SER model operates in discrete time and employs the following synchronous update rules: a transition from susceptible (S) to excited (E) occurs when at least one neighbor is active, or with a spontaneously probability of f. After one time step in the E state, a node enters the refractory state (R). The transition from R to S occurs stochastically with the recovery probability p. FC was computed as the averaged number of coactive nodes. Additionally, we used the well-known Fitzhugh-Nagumo model [Fitzhugh, 1961; Nagumo et al, 1962]. FC was defined as correlation between simulated time series. Moreover, in order to reconcile the FHN model with the SER model, FHN time-series were discretized, spikes detected and the FC computed from co-activations, as for the SER model.

Results

Initially, comparing the behavior of the SER and the FHN models in Figure 1A, we observed a striking discrepancy: The FHN produced high correlations between SC and FC with only little impact of the global topological feature of modularity. By contrast, the SER model is highly sensitive to the topological feature of modularity, as the SC-FC correlation vanishes with increasing network randomization. To reconcile the models, we, first, discretized the FHN dynamics, in order to be in line with the discrete nature of the SER, and, second, in both models varied the time window from which co-activationsmwere drawn for the calculation of FC. Re-analyzed in such a way, the behavior of the FHN model closely resembled that of the SER model (Figure 1B). When considering very short time

integration windows the FHN model behaved very similarly to the SER model; specifically, destroying network modularity abolished the SC-FC correlation.

Conclusions

By comparing two different models of excitable neural nodes across a range of network architecture from modular to random wiring, we gathered insights into the effects of network topology underlying FC. We showed that apparent discrepancies between the results produced by the two models can be resolved by adjusting the time integration window of coactivations from which the FC is derived, providing a clearer distinction between co-activations and sequential activations. Thus, network modularity appears as an important factor shaping the FC-SC relationship across different dynamic models [Messé et al, 2015b].

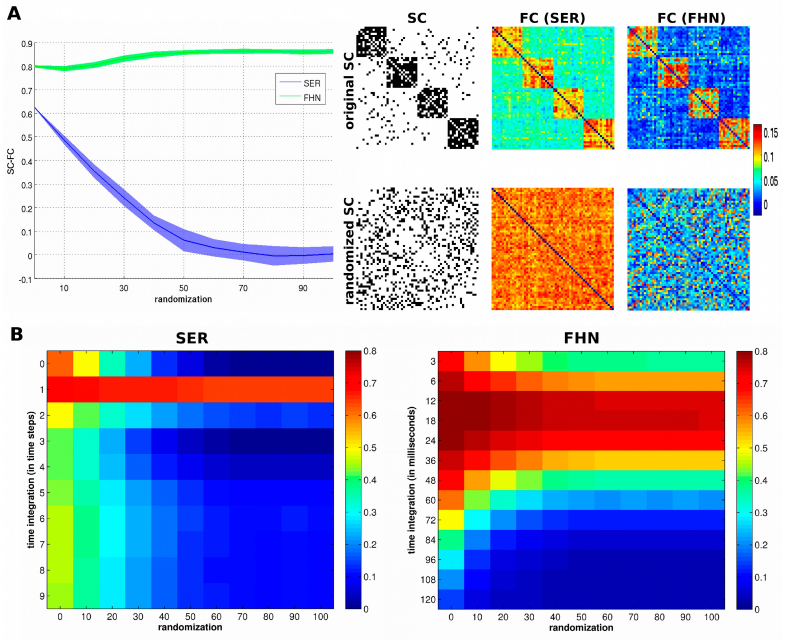

Figure 1: (A) Illustration of the SC-FC relationship in the SER and FHN model. (Left) SC-FC correlation across the range of randomization in both models. (Right) Illustration of the SC patterns (binary, black entries denote the presence of connections) and FC patterns (weighted, colors code for the strength of FC, see associated color bar) for the two extreme cases of network organization (i.e., original modular SC, top, and its fully randomized version, bottom). (B) Effect of time integration windows. (Left) SC-FC correlations from the SER with various time integration step windows. (Right) SC-FC correlations from the FHN with SER-like co-activation FC as a function of time integration window length.

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7. Cross-subject and empirical variability of human brain connectivity: how averaging of connectivity data biases network properties

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Neuroimaging techniques such as DTI/DSI allow to explore the complex architecture characterising the anatomical brain structure, the structural connectivity (SC), and are at the foundations of a growing number of empirical and theoretical studies linking such structure with emergent functional properties both at rest or during different tasks, in healthy and in impaired subjects. However, a systematic exploration of the reliability of SC data obtained through tractography is still lacking. For network analysis, the errors in the SC data lead to biased interpretation of its topology whereas for modelling, it is critical that the weighted information of the links truly represent the strength of the connections between regions, e.g. the actual number of axons from one region to another. Apart from the natural cross-subject differences, empirically induced variability is large in SC datasets. Usually the weights of the links span over orders of magnitude but unfortunately, those are not comparable across studies because the different tractography methods applied by different laboratories imply that the physical meaning of those weights are incompatible.

In an attempt to uncover the "grand-average" of human structural connectivity we investigate the variability of SC data. First, we find that the simple average of SC matrices over subjects introduces fundamental biases in the topology of the "average brain" as compared to the connectivity of individual subjects. On the other hand, we find that only 20%–30% of the links are prevalent across all subjects and the rest are prone to variability. A major challenge is to discern how much of that variability is due to empirical errors or natural cross-subject differences. Although stronger links seem to be more resilient across subjects and weaker links exhibit larger inter-subject variability, we show that such pattern is mainly due to technical constraints, such as the resolution of the measurements. For example, we show how the sampling resolution substantially biases the observed variability of the weights. Finally, we propose a method to average connectivity datasets which avoids those biases and corroborate that dynamical models of resting-state activity reproduce better the empirically observed functional connectivity when based on the corrected average SC.

8. Emergent Dynamical-Structural Interdependencies in Hippocampus Cultures

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Hippocampus is a well known structure of the mammals limbic system, which is associated to physiological responses from afferent emotional stimuli as well as memory and space orientation. Several studies have shown similar emergent properties in experiments with in vitro and in vivo cultures. Based on that, we have investigated the dynamical and topological properties of functional complex networks of several hippocampus cultures from 18-days rat embryos, aiming to identify the interplay between them. To do that, Six Multi Electrode Array experiments were designed in order to record the spikes dynamics from spontaneous activated neurons. Specifically, we study how neural networks evolve and mature (from 7 to 26 days in vitro). From the dynamical point of view, we obtain the ordinal patterns of Inter Spike Intervals (ISIs) of the cultures. With this data, we compute their respective normalized permutation Shannon's entropy, the disequilibrium and its statistical complexity. In addition, Kuramoto order parameter was computed to capture the emergence of the synchronous behaviour of the cultures. Pearson correlation parameter between neuron phases along culture maturation is used to determine the weight of the functional connections between neurons, altogether leading to a complex functional network whose topology evolves in time. Thus, complex networks parameters such as strength, weighted clustering, local efficiency, global efficiency, averaged shortest path, and eigenvector centrality were computed to topologically characterize the evolution of the cultures. Our results revealed two different stages in the evolution of the hippocampus cultures: a growing stage and a mature demeanor. Also, due to their inherent spontaneous generation of spikes, the growing scenario depicts a high phase synchronization, which evolves to an asynchronous regime. On the other hand, networks metrics show differences correlated with the culture growth. Interestingly, we found correlations between two specific topological and dynamical metrics: the higher (lower) the clustering, the lower (higher) the entropy of the whole culture.

9. An Algebraic Topological Method for Multimodal Brain Networks Comparisons

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Understanding brain connectivity has become one of the most important issues in neuroscience. But connectivity data can reflect either the functional relationships of the brain activities or the anatomical properties between brain areas. Although one should expect a clear relationship between both representations it is not straightforward. Here we present a formalism that allows for the comparison of structural (DTI) and functional (fMRI) networks by embedding both in a common metric space. In this metric space one can then find for which regions the two networks are significantly different. Our methodology can be used not only to compare multimodal networks but also to extract statistically significant aggregated networks of a set of subjects. Actually, we use this procedure to aggregate a set of functional (fMRI) networks from different subjects in an aggregated network that is compared with the anatomical (DTI) connectivity. The comparison of the aggregated network reveals some features that are

not observed when the comparison is done with the classical averaged network.

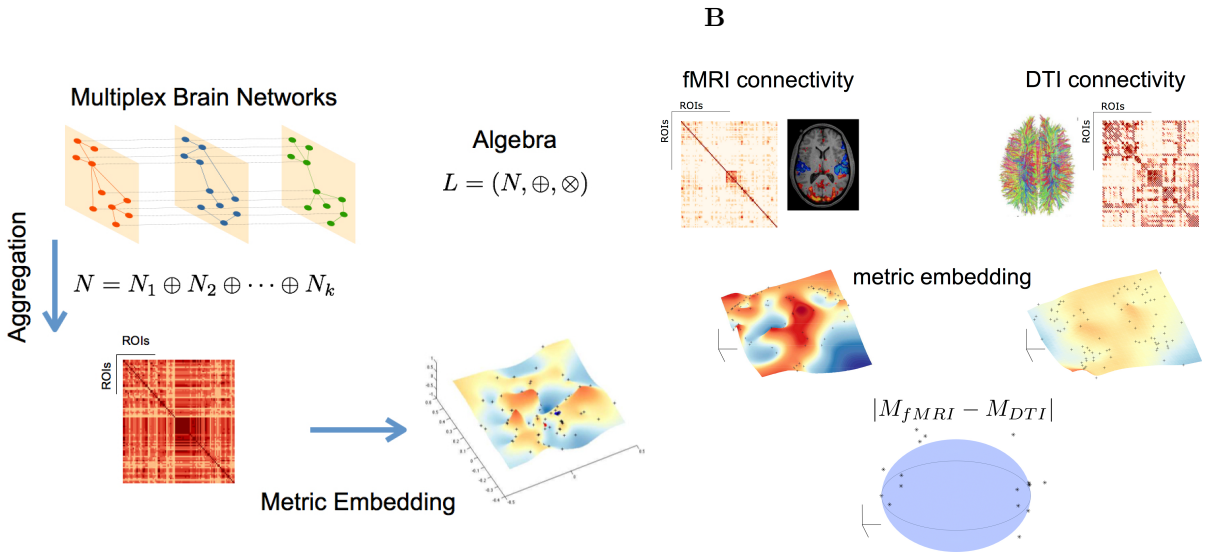

Figure – (1) (A) Schematic Representation of the main steps for the described networks aggregation and metric embedding (defined here for the algebra L) (B) and Topological Algebraic networks comparison. Connectivity From different modalities (here fMRI and DTI) Are firstly embedded (black dot points on the manifolds indicate the brain nodes) and then compared in a low-–dimensional space. Black Points outside the sphere correspond to nodes with a topological difference (at a given threshold) in the two modalities.

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10. Structural constraints to information flow: a TMS-EEG/DTI study

Enrico Amico, Daniele Marinazzo and Steven Laureys
Ghent University

Transcranial magnetic stimulation (TMS) has been used for more than 20 years to investigate connectivity and plasticity in the human cortex. By combining TMS with high density electroencephalography (hd-EEG), one can stimulate any cortical area and measure the effects produced by this perturbation in the rest of the cerebral cortex. The purpose of this paper is to investigate changes of information flow in the brain after TMS from a functional and structural perspective, using multimodal modeling of source reconstructed TMS/hd-EEG recordings and DTI tractography. The assumptions behind the scope of this work, gathered from the existing literature to date, are: 1) that the extent to which information transfer changes in a cortical region, as a consequence of the induced perturbation, is related to the number of fiber pathways passing through it [1]; 2) the temporal variability of the response to TMS has specific spectral signatures (i.e. "natural frequencies' [2]); 3) these "natural frequencies" play a primary role in the flow spread during TMS and in the structure-function relationship [2], [3]. We evaluated TMS effective connectivity over 13 healthy subjects (area of TMS stimulation: precuneal

(PCC)) using a multivariate model of spectral coefficients. Specifically, in order to cope with the non-stationary nature of the signals under study, we adopted the spectrum-weighted adaptive directed transfer function (swADTF), which has been successfully used for connectivity modeling of epileptic intracranial EEG data [4][5]. Then, for each subject, we correlated the effective connectivity pattern with the structural connectome obtained by determining the fiber density between any two regions of the AAL parcellation, as in [6]. We show how brain dynamics induced by TMS is constrained and driven by its structure, at different spatial and temporal scales, especially when considering cross-frequency interactions. These results shed light on the function-structure organization of the brain network at the global level, and on the huge variety of information contained in it.

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Monday 1st June	1. Brain Networks (I)
09:00 - 09:10	Opening Remarks
09:10 - 09:45	An introduction to network science in the brain (Qawi Telesford)
09:45 - 10:20	Generative models of the human connectome (Richard Betzel)
10:20 - 10:55	How does the topology of neuronal network change during spatial learning? (Paul Brodersen)
10:55 - 11:10	Coffee Break
11:10 - 11:45	Determinants of dynamic reconfigurations in human brain networks (Matthias Ekman)
11:45 - 12:20	Modeling resting-state functional brain networks: from population data to individual subjects (Joaquín Goñi)
12:20 - 12:55	The connectome as an underlying infrastructure of disease propagation (Ruben Schmidt)

Monday 1st June	1. Brain Networks (II)
3.00pm - 3.10pm	Opening (A. Gabrielli)
3.10pm - 3.30pm	Routes to adaptation in functional brain networks (T. Gili)
3.30pm - 4.00pm	Networks of the biological clock (J. Meijer)
4.00pm - 4.30pm	Criticality and correlations in neuronal networks (L. De Arcangelis)
4.30pm - 4.50pm	Percolation and cascading in a brain network of networks (H. Makse)
4.50pm - 5.10pm	Coffee break
5.10pm - 5.30pm	Detecting cluster structure of resting state fMRI brain networks: percolation vs modularity features (T. Squartini)
5.30pm - 6.00pm	A novel brain partition highlights the modular skeleton shared by structure and function (M. A. Muñoz)
6.00pm - 6.30pm	Average synaptic activity and neural networks topology: a global inverse problem (R. Burioni)
6.30pm - 7.00pm	The modular structure of brain networks and the resolution limit (A. Bifone)

Tuesday 2nd June	1. Brain Networks (III)
09:00 - 09:10	Opening (J.M. Buldu - M. Chávez)
09:10 - 09:50	Excitable neural dynamics based on topological features of brain networks (C. Hilgetag)
09:50 - 10:30	The Human Connectome in Health and Disease: Organization and Development of Hierarchical Brain Networks (M. Kaiser)
10:30 - 11:00	The organization of brain networks during normal and abnormal development (P. Vertes)
11:00 - 11:30	Coffee break
11:30 - 12:10	Dynamical organization of neural activity in brain networks (J. Garcia-Ojalvo)
12:10 - 12:50	Exploring effective connectivity in neuronal cultures. Applications to medicine (J. Soriano)
12:50 - 13:20	The link between the structural and the functional connectome (Gorka Zamora)
13:20 - 13:30	Concluding remarks (F. De Vico Fallani - D. Papo)

POSTER SESSION @BrainNetwork Satellite

Accepted Posters

F. Battiston, et al, (UK). ***Multilayer Motifs in Brain Networks***

B. Blanco, (Spain). ***Influence of bilingual exposure in the developing brain networks***

A. Messé, (Germany). ***Bridging the gap between structure and function in the human brain***

M. de Domenico, et al, (Spain). ***Multilayer functional connectivity of human brain***

O. Korhonen, et al, (Finland). ***How spatial smoothing affect fMRI brain networks?***

A. Messé, (Germany), ***A closer look at the apparent correlation between structural and functional connectivity in brain networks***

G. Zamora-López, et al, (Spain). ***Cross-subject and empirical variability of human brain connectivity: how averaging of connectivity data biases network properties***

J. H. Martínez, et al, (Colombia). ***Emergent Dynamical-Structural Interdependencies in Hippocampus Cultures***

T. Simas, et al, (UK). ***An Algebraic Topological Method for Multimodal Brain Networks Comparisons***

E. Amico, et al, (Belgium). ***Structural constraints to information flow: a TMS-EEG/DTI study***