Non-invasive imaging of non-linear interactions

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Interactions between neuronal assemblies form a basis for the mechanism of functional integration that underlies most of our actions. Studying these interactions is important for understanding the principles of brain operation. However, such neuronal communications are hallmark of a living brain and therefore it is of paramount importance to develop tools for imaging of these interactions on the basis of **non-invasively** collected data.

The interactions manifest themselves in synchrony of activity of neuronal assemblies. Recent years demonstrated a dramatic increase in the number of studies dealing with synchrony detection and analysis on the basis of EEG and MEG data. Several reliable algorithms have been developed, **however very few studies dealt with the task of source-space analysis of non-linear (cross-frequency) interactions on the basis of non-invasive data.**

Validation of real data analysis results are complicated due to the difficulty of establishing the gold standard as the interaction picture may differ from subject to subject. One way to approach this problem is to do validation of the new techniques for imaging of synchrony in application to simultaneously recorded ECoG and EEG/MEG datasets.

Synchrony detection methods should either be built based on statistical considerations or should be followed by a statistical testing step. It is important that **such tests include physiologically plausible models** balancing the accuracy and the relatively low level of spatial details yielded by EEG and MEG measurements.

Titles of talks and abstracts

Network identification and characterization methods from human electrophysiological data – an overview (Richard Greenblatt)

The characterization of large scale transient networks plays an increasingly prominent role in the study of the dynamical neural systems on the centimeter length scale and millisecond time scale. The properties of these networks may be inferred from structural imaging, functional imaging and electrophysiological measurements. In this overview presentation, I will compare a number of linear, bilinear, and nonlinear methods in both the time and time-frequency domains. These include MVAR, coherence, phase synchrony, mutual information, and transfer entropy, which have been used to infer network geometries and topologies from EMEG and ECoG (local field potential) data. Domains of applicability and the relative strengths and limitations of various methods will be considered. Algorithmic descriptions of the methods will be discussed in the common context of a random variable estimation framework, and application examples from experimental data will be presented.

Reconstructing phase dynamics of oscillator networks (Michael Rosenblum)

We consider the problem of reconstruction of phase dynamics of coupled oscillators from data. The crucial issue of our approach is distinction between phase estimates, obtained, e.g., via the Hilbert transform, and hereafter denoted as protophases, and true phases, used in the theory of coupled oscillators. We present a transformation from protophase to phase, which allows us to reconstruct the phase dynamics equations of coupled oscillators in an invariant way, i.e. to a large extend independently of the observables, used for reconstruction. We start by the case of two coupled systems and illustrate it with numerical examples as well as with real data. We present examples, demonstrating importance of the protophase to phase transformation for a correct quantification of the strength and directionality of coupling. We proceed by consideration of small networks of coupled periodic units. Starting from the multivariate time series, we first reconstruct genuine phases and then obtain the coupling functions in terms of these phases. The partial norms of these coupling functions quantify directed coupling between oscillators. We illustrate the method by different network motifs for three coupled oscillators and for random networks of five and nine units. We also discuss effects of non-pairwise coupling.

Cross-frequency phase and amplitude interactions among human cortical oscillations. (Matias Palva)

Oscillatory interactions and synchronization may be a key mechanism for coordinating scattered neuronal activity into transient neuronal assemblies to serve coherent action and perception at the systems level. How is the co-operation of oscillatory assemblies in distinct frequency bands regulated? Two distinct forms of cross-frequency (CF) phase interactions, phase-phase and phase-amplitude coupling, are in a position to mechanistically underlie such cross-spectral coordination, but their prevalence and phenomenology in cognitive tasks has remained unclear.
Neuronal synchronization in the human brain can be investigated non-invasively with millisecond-range temporal resolution by using magneto- (MEG) and electroencephalography (EEG) but it is essential to incorporate source reconstruction methods into M/EEG data analyses to recover and disentangle information about the underlying cortical sources. In this presentation, I discuss framework for integrated mapping of within- and cross-frequency phase interactions in M/EEG data. I first review a family of interaction metrics and discuss the favourable and less favourable properties of three established circular statistics; phase-locking value, pairwise-phase consistency, and mutual information, and also present a novel method for estimating causal directionality in phase interactions. I then demonstrate how the predominant confounding factors inherent to M/EEG, e.g., signal mixing, signal-to-noise ratio dynamics, and evoked activity, bias the interaction statistics and how these biases could be compensated for. Finally, I will describe the cross-frequency phase interaction networks for the coupling among theta-, alpha-, and beta-frequency band oscillations during visual working memory. In line with prior observations, these data suggest that cross-frequency phase interactions may indeed support cross-spectral functional integration.

DICS variations for non-invasive cross-frequency coupling detection. The method and preliminary results. (Alex Ossadtchi)

Synchronization of activity between distinct cortical regions underlies the mechanism of functional integration that forms a foundation of all our actions. Recently, the role of non-linear interactions manifested in cross-frequency(across scale) synchronization has been emphasized as facilitating the exchange of information between cell assemblies. Such synchronization has been found in many experimental paradigms and is currently under active study. Unfortunately spatially and temporally precise analysis available only in a limited number of cases corresponding to neurological patients with implanted cortical grids. In order to provide the flexibility in experimental designs and allow for more specific studies tools for analysis of such non-linear synchronizations are to be developed. Instrumentally, MEG is a unique technology that allows for mapping of cortical activations and provides high temporal resolution. The use of beamformers supported by sufficiently accurate forward models allows for reasonable (0.5 cm) spatial resolution. The time frequency representation of MEG signals is natural and captures the nature of MEG observed cortical activity as consisting of short time narrow-band bursts.

In this work our goal was to combine the above and develop a signal processing method for identification of the cortical spatial structure of cross-frequency coupling between the oscillations in the two non-overlapping time-frequency windows. Our method is a statistical test contrasting the results of adaptive beamformer based inverse mapping obtained using the original and cross-term deprived time-frequency domain data covariance matrices by calculating the ratio of the two inverse values. We use multiple comparison corrected randomization statistical tests for identification of significant source space coupling.

Application of the method to an event-related MEG dataset from a single subject (imagined hand rotation) yielded plausible results with interacting pairs falling into physiologicsally plausible cortical sites. We observed beta-gamma coupling between frontal and parietal-occipital regions, consistent with published signal space analysis. We also observed beta-gamma prefrontal/frontal and alpha-gamma temporal/frontal couplings.

Studying neuronal n:m phase synchronization with the frequency-shift approach (Vadim Nikulin)

Neuronal synchronization has been hypothesized to be the mechanism through which efficient communication between the neurons can be achieved. In addition to conventional interactions at the same frequency range, phase synchronization between different frequency ranges has been demonstrated recently. Such cross-frequency phase synchronization is usually studied in a sensor space or with computationally demanding beamformer techniques, leading to a very large number of statistical comparisons. Here we present a novel method for the extraction of neuronal components showing cross-frequency phase synchronization. The method allows a compact representation of the sets of interacting components (along with their spatial patterns) without the need to perform inverse modeling. In general it works for the detection of phase interactions between components with frequencies n and kn, where n and k are integers. This class of interactions includes 1:2 and 1:3 synchronization frequently observed in EEG and MEG recordings. We refer to the method as Cross-Frequency Decomposition (CFD), which consists of the following steps: a) extraction of n-oscillations with spatio-spectral decomposition algorithm (SSD); b) frequency-shift transformation of the oscillations obtained with SSD, and c) finding kn–oscillations synchronous with n-oscillations using least-squares estimation. Our simulations showed that CFD was capable of recovering interacting components even when the signal-to-noise ratio was as low as 0.1. An application of CFD to the real EEG data demonstrated that cross-frequency phase synchronization between alpha and beta oscillations can originate from the same or remote neuronal groups. While interactions occurring at the same spatial location can potentially indicate quasi-sinusoidal waveform of neuronal oscillations, the synchronization between spatially remote populations is likely to be a marker of genuine neurophysiological coupling between different oscillations.

Testing for nested oscillation in source and sensor space (Will Penny)

One neuroscientifically important category of cross-frequency interactions are the nested oscillations, otherwise referred to as phase-amplitude coupling, where the amplitude of a faster rhythm is coupled to the phase of a slower rhythm. In previous work we have proposed a simple method based on the General Linear Model (GLM) for detecting nested oscillations. We have shown, using empirical data from Electrocorticography and simulated data from hippocampal interneuron networks, that the GLM approach is superior to other methods including (i) the modulation index, (ii) phase-locking value and (iii) envelope to signal correlation. In this talk I will show how the GLM approach can be extended to the analysis of noninvasive EEG and MEG data. I will use data from an MEG study of visual working memory to show how activity in sensor space over a range of frequencies is phase-amplitude coupled to sources of theta activity in frontal and temporal lobe regions. Statistical inference is implemented using sensor-by-frequency maps of F-statistics testing for group-level effects, and corrections for multiple comparisons are made using random field theory. The significant higher frequency sensor space activity can then be source reconstructed in the usual way

Relevant papers

1. Palva JM, Monto S, Kulashekhar S, Palva S (2010) Neuronal synchrony reveals working memory networks and predicts individual memory capacity. Proc Natl Acad Sci U.S.A. 107: 7580-5. 2. Palva S, Monto J and Palva JM (2010). Topological properties of synchronized cortical networks during working memory maintenance. Neuroimage 49: 3257-68. 3. Dennis J.L.G. Schutter , Claudia Leitner , J. Leon Kenemans, Jack van Honk, Electrophysiological correlates of cortico-subcortical interaction: A cross-frequency spectral EEG analysis, Clinical Neurophysiology 117 (2006) 381–387 4. F. Darvas, J.G. Ojemann, L.B. Sorensen, Bi-phase locking — a tool for probing non-linear interaction in the human brain, NeuroImage 46 (2009) 123–132 5. Vadim V. Nikulin, Guido Nolte, Gabriel Curio, A novel method for reliable and fast extraction of neuronal EEG/MEG oscillations on the basis of spatio-spectral decomposition,NeuroImage 55 (2011) 1528–1535 6. B. Kralemann, A. Pikovsky, and M. Rosenblum,Reconstructing phase dynamics of oscillator networks,Chaos, xx, p. xxxx, 2011, submitted. 7. A. Ossadtchi, R.E. Greenblatt, V.L. Towle, M.H. Kohrman, K. Kamada, Inferring Spatiotemporal Network Patterns from Intracranial EEG Data, Clin, Neurophysiology, June 2010 ; 121(6):823-35

Workshop format

The workshop consists of 7 presentations of 30 minutes each plus 10 minutes for questions/discussion. A final session of 45 minutes is planned for the final discussion.