Cross-term deprived covariance (CTDC) approach for non-invasive detection of non-linearly coupled cortical sites

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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 (up to 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.

The extensions of the proposed technique include the Fast CTDC (F-CTDC) approach that uses singular values decomposition for express detection of interacting topographies as well as recursively applied and projected CTDC (RAP-CTDC) that allows for effective model-based management of the observed local maxima in case when multiple pairs of sources are interacting.

Simulation study illustrates that the proposed approach is extremely robust and capable of successful operation in very noise environements. 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 physiologically 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.