Ongoing processes account for a large fraction of the brain activity observed in functional imaging. The study of this intrinsic, or spontaneous, activity is currently a major field of research in neuroscience, as it opens the door to fundamental insights on brain architecture and can be applied to severely impaired patients for the study of pathologies. However, unlike with evoked activity, there is no universally-accepted standard analysis framework for group inference. This symposium will present latest progress in statistically-principled methods for inter-subject comparisons of ongoing activity. It will feature different approaches used to test for differences in spontaneous brain activity between subjects or populations with neuroscientifically-relevant results, such as ICA or graphical models, and will focus on the statistics and interpretation issues raised by the inter-subjects comparisons.

Learning Objectives: Having completed this workshop, participants will be able to:
1. Understand and apply different state-of-the-art modeling strategies for group inference on ongoing activity;
2. Interpret the differences detected by various methods in terms of functional connectivity; and
3. Devise and carry out functional-imaging experiments to highlight differences in on-going activity.

Robust and Unbiased Multi-Subject RSN Analysis Using ICA and Dual Regression
Christian Beckmann, Department of Medicine, Imperial College London, London, UK

Independent Component Analysis and related techniques have been used extensively to estimate patterns of resting functional connectivity. While early work concerned the characterization of these effects at the single group level, increasingly-often researchers now use such tools in order to characterize the differences between groups of subjects. This talk will present a review of the methods most commonly applied in this rapidly advancing field, such as seed-based correlation analysis and independent component analysis, along with examples of their use at the individual subject and group analysis levels and a discussion of practical and theoretical issues. We describe the similarities and differences across these varied statistical approaches to processing resting-state functional magnetic resonance imaging signals. In particular, we will focus on the issue of biased between-group analysis and discuss the biased nature of group inferences derived both in the context of a seed-based analysis and an ICA/PCA.

Graph Theoretical Analysis of Brain Networks in Clinical States
Ed Bullmore, University of Cambridge, Cambridge, UK

Graph theoretical analysis is a promising emerging tool [1] which can be used to understand the collective organization of functional relationships in the human brain in both resting and task conditions [2], and provide valuable insights into the dynamic effects of disease. Using neuroimaging data across multiple modalities, we have characterized network, i.e. graph, architecture in people with schizophrenia in comparison to healthy matched controls: using magnetoencephalography we have shown that cost-efficient architecture of high frequency functional networks predicts performance during a working memory task [3]; using resting-state functional magnetic resonance imaging, we have shown that intrinsic connectivity is less integrated, and more diverse in probands [4]; and using structural morphometric networks we have shown that heteromodal association cortex displays an altered hierarchical structure in a patient population [5]. In this series of clinical studies and in graph analysis in general, the ability to compare network results -between two individuals, two groups, or two brain states or between the cortical network and a benchmark null model network is imperative. Several methods have recently been proposed in the literature for the comparison of graphs including group averaging [6], bootstrap methods, and non-parametric permutation-based methods [5], each with specific advantages and disadvantages. However, the statistical significance and appropriate interpretation of apparent differences between graphs are further constrained by several factors including the properties of the graphs themselves [7], the variance of the metrics under study, and methodological choices made in the construction of the graphs [8].
awareness and understanding of these methods and issues are imperative for successful statistical testing of differences in graph topology between groups.


Comparison of Multi-Subject ICA Methods for Analysis of fMRI Data: Consistency and Variability of Intrinsic Networks in the Healthy and Diseased Brain

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Spatial independent component analysis (ICA) applied to functional magnetic resonance imaging (fMRI) data identifies functionally-connected networks by estimating spatially-independent patterns from their linearly-mixed fMRI signals. Several multi-subject ICA approaches estimating subject-specific time courses (TCs) and spatial maps (SMs) have been developed, however there has not yet been a full comparison of the implications of their use. In this talk, we provide extensive comparisons of four multi-subject ICA approaches in combination with data reduction methods for simulated and fMRI task data. We pay particular attention to the accuracy with which group ICA methods preserve individual variations demonstrated in extensive simulations as well as application to real data. We then demonstrate our approach applied to a large (N>1000) study of intrinsic fMRI networks collected on the same MRI scanner from individuals who are healthy as well as those with different brain disorders including schizophrenia, bipolar disorder and nicotine and alcohol dependence.

The ubiquitous nature of functional connectivity networks combined with the many new studies showing variations in these networks due to brain disorders suggests the possibility of using these networks to differentiate the healthy brain from the diseased brain. However it is not yet known the degree to which resting state networks actually vary or are sensitive or specific to brain disorders. Resting state networks are first estimated from the data using group independent component analysis and subject specific images and time courses are reconstructed. We then evaluate the similarities and differences of multiple resting state networks among a large number of subjects using a variety of features including the spatial pattern, the frequency content of the time courses, and the functional connectivity between networks. These metrics are compared also as a function of brain disorder, functional domain (as assessment by neuropsychological scores), as well as age and sex.

Functional-Connectivity Group Inference on Correlation Matrices with Application to Strokes

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On-going activity is often observed in fMRI as large distributed networks comprised of several brain region regions with correlated time course. The study of correlations in on-going activity recorded from these regions provides insights on intrinsic brain functional architecture [1] and can provide markers of cognitive processes [2]. However, estimation and comparison of correlation matrices from the observations is challenging from a statistical point of view, as the different parameters of a correlation matrix cannot be considered as statistically independent.
I will present recent results on principled group comparison of correlation matrices [3]. Using a group-variability model for correlation matrices, we infer subject-specific differences in between-region functional connectivity. This statistical framework is applied to stroke patients for the study of post-stroke recovery markers in resting-state fMRI.

In most fMRI study there is a limited amount data available to estimate single-subject correlation matrices. As a result, large-scale correlation matrices used in graph-theoretical approaches are noisy estimates as the number of available samples is small compared to the number of coefficients to estimate. On the other hand, concatenating data from multiple subjects to increase sample size does not allow a proper modeling of subject-to-subject variability. I will present a penalized covariance estimator to set a population prior on the estimation of correlation matrices by learning which regions of the brain are independent at the group level [4]. Cross-validation studies demonstrate that it estimates correlation matrices that match better subject-specifics. Using this estimator on a resting-state study comprising 20 subjects, we show that the segregated communities introduced in graph-theoretical studies correspond to known functional networks.