Nonlinear dynamics in mixed inverse problems

Questions
- The inverse problem for data fusion. The mammoth time-space autoregression problem: the use of sparseness, clusters and ROI hypothesis. Exploring causality and self-dynamics robustly: the concept of innovations for model fitting in time series analysis and the AIC
- Parametric models, inference and statistics tests. Introducing neuronal models to account for large-scale brain causal relationships in electrophysiological, vascular, and metabolic signals

Chair:

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I present an approach to identifying dynamic input-state-output systems. Identification of the parameters proceeds in a Bayesian framework given the known, deterministic inputs and the observed responses of the [neuronal] system. We develop this approach for the analysis of effective connectivity in the brain, using experimentally designed inputs and fMRI and EEG responses. In this context, the parameters correspond to effective connectivity and, critically, changes in coupling induced by inputs. The ensuing framework allows one to characterize experiments, conceptually, as an experimental manipulation of integration among brain regions (by contextual or trial-free inputs, like time or attentional set) that is perturbed or probed using evoked responses (to trial-bound inputs like stimuli). As with previous analyses of effective connectivity, the focus is on experimentally induced changes in coupling (c.f. psycho-physiologic interactions). However, unlike previous approaches to connectivity in neuroimaging, the causal model ascribes responses to designed deterministic inputs, as opposed to treating inputs as unknown and stochastic. The issues here are (i) the central role of generative models in analysis of distributed responses; (ii) the nature of the models (e.g., Dynamic vs. Static, Deterministic vs. Stochastic); (iii) the techniques available for model inversion and (iv) finally framing hypotheses in terms of Bayesian model selection.
**Granger Causality on Spatial Manifolds: Applications to Neuroimaging**

The (discrete time) vector Multivariate Autoregressive (MAR) model is generalized as a stochastic process defined over a continuous spatial manifold. The underlying motivation is the study of brain connectivity via the application of Granger Causality measures to functional Neuroimages. Discretization of the spatial MAR (sMAR) leads to a densely sampled MAR for which the number of time series $p$ is much larger than the length of the time series $N$. In this situation usual time series models work badly or fail. Previous approaches, reviewed here, involve the reduction of the dimensionality of the MAR, either by the selection of arbitrary regions of interest or by latent variable analysis. An example of the latter is given using a multi-linear reduction of the multichannel EEG spectrum into atoms with spatial, temporal and frequency signatures. Influence measures are applied to the temporal signatures giving an interpretation of the interaction between brain rhythms. However the approach introduced here is that of extending usual influence measures for Granger Causality to sMAR by defining "influence fields", that is the set of influence measures from one site (voxel) to the whole manifold. Estimation is made possible by imposing Bayesian priors for sparsity, smoothness, or both on the influence fields. In fact, a prior is introduced that generalizes most common priors studied to date in the literature for variable selection and penalization in regression. This prior is specified by defining penalties paired with a priori covariance matrices. Simple pairs of penalties/covariances include as particular cases the LASSO, Data Fusion and Ridge Regression. Double pairs encompass the recently introduced Elastic Net and Fussed Lasso. Quadruples of penalty/covariance combinations are also possible and used here for the first time. Estimation is carried out via the MM algorithm, a new technique that generalized the EM algorithm and allows efficient estimation even for massive time series dimensionalities. The proposed technique performs adequately for a simulated "small world" cortical network with linear dynamics, validating the use of the more complex penalties. Application of this model to fMRI data validate previous conceptual models for the brain circuits involved in the generation of the EEG alpha rhythm.
Brain Connectivity Inferred from In-Vivo Functional Measurements of Local Field Potential Responses to Sensory Stimuli

I will present a novel approach to the inverse problem of determining the interactions among structures that may have caused a set of functional observations. This approach uses fundamental neuroanatomical and biophysical constraints to find simultaneously optimal anatomical models and physiological parameter sets for large-scale brain interactions. The method rests on a linear system of delayed inputs for each functional measurement site, whose equations are independently solved by simulated annealing, an optimization procedure derived from statistical physics. Since the output at each site is derived from the observed data at all other sites we avoid the non-linear deviations typical of cascaded forward models and achieve excellent approximations of the functional observations as well as structural and effective connectivity estimates for the full functional connectivity matrix. Evaluation against CoCoMac, a database of established anatomical connections, specifies the degree of functional expression and predicts previously unknown projections. The method was tested with a well known set of simultaneous intracortical LFP recordings in monkeys performing a visually cued go/no-go paradigm. We suggest that it could have useful applications in the analysis of event-related activity in the human brain and the estimation of effective network influences in conditions of health and disease.
The treatment of "heteroscedasticity" (time inhomogeneous noise variance) and the state space modeling with "unobserved variables" are essential for the modelling and analyzing the causality of non-stationary time series data recorded from the brain in vivo with non-invasive measurement techniques. Recently several methods for modelling heteroscedastic time series have been developed in financial time series analysis. The difficulty of applying these methods to neuroscience data comes from the fact that important neural or vascular variables in the models are often not directly observable as the financial time series model case. In the present talk, we will show that this problem can be solved using the state space modelling approach, and will show how the important but unobservable variables in the model are estimated together with the time-varying system noise variance of the state variable in the heteroscedastic situations. Immediate advantage of the present method over the conventional methods is shown using some of the following 6 examples: 1) Dynamic Inverse Solution of EEG, 2) Dynamic ICA of EEG and ECG, 3) Real time detection of rise and fall of delta rhythm in the EEG of an anaesthesized patient, 4) Causality detection between two or more subjects from their gaze time series, 5) Causality detection of right hemisphere and left hemisphere from the finger motion of the both hands and 6) Causality detection between V1, V5 and PP from the fMRI time series recorded in the visual experiment.