Dynamic causal modelling in a multimodal imaging approach

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During my training stay at the Wellcome Trust Centre for Neuroimaging at the University College London, I had the unique opportunity to learn about dynamic causal modelling (DCM), a biophysical modelling approach, from leading experts in the field. Although it is most commonly applied to fMRI data, its utilization ranges from invasive to non-invasive measurements. As broad as the data modalities are that DCM is compatible with, as great is the number of research fields, in which DCM is applied. Especially cognitive neuroscience and computational psychiatry have taken advantage of the technique. Since its key paper release in 2003 more than 130 papers have been published on the topic.
In my project I used DCM to study the relation between fast electric signals and slow, lamina-specific hemodynamic signals. The aim was to establish the lamina-specificity of neuronal dynamics in early visual cortex. In this setting, lamina-specific refers to the cortical layers of origin of the different signals generated by neuronal activity. To achieve this I used concurrently measured EEG and fMRI data from a cued visual attention task([8]). DCM enabled me to infer on spectral responses at different cortical depths, which in turn I then used as regressor in a general linear model for the fMRI data. The concurrent recording of EEG and fMRI data gave me the opportunity to compare the modalities on a trial-by-trial basis.
The goal of DCM is to explain the generation of experimentally observed data features by dynamics of a network containing hidden states (i.e. not directly observable). In particular, if DCM is applied to EEG data, these networks are based on neural mass models (for example the canonical microcircuit in Figure 1) of cortical columns. This makes it possible to directly test predictions of theoretical models against the data and estimate physiologically meaningful model parameters. The temporal variation in every cell population of the neural mass model is defined by two ordinary differential equations, describing the change in voltage and current. The equations describe the transformation of the presynaptic spikes to postsynaptic output by a convolution of a synaptic alpha kernel with incoming spikes. The firing rate and hence output of single populations is approximated by a sigmoidal function. The output of the cortical column is then a weighted sum of the output of the three excitatory cell populations but is dominated by (deep and superficial) pyramidal cells.
Based on time-frequency analysis of a virtual electrode time series in early visual cortex, we assumed similar statistical feature and frequency content for the sustained gamma component, i.e. about 500ms after stimulus onset until the end of the stimulation period. This allowed us to summarize the spectral content into steady state responses that we used as features in the DCM ([6]). Using Bayesian Model Inversion we obtained the parameters of the network, such as connection strengths and synaptic time constants. This enabled us to estimate the spectral responses of different subpopulations (Figure 1), which in turn can be linked to different cortical

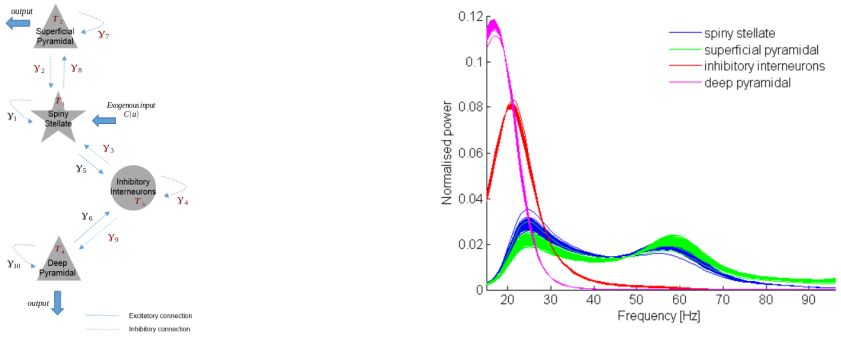

Figure 1: *Left*: Canonical Microcircuit. This neural mass model describes the dynamics in a cortical column by means of temporal variability in four cell populations, which are intrinsically connected. Exogenous input to the circuit enters through the spiny stellate cells. Due to the sensitivity of EEG to pyramidal cells, the aforementioned dominate the output of the DCM. γ_i represent connection strengths and T_i synaptic time constants, respectively. Prior believes are obtained from animal data and previous studies. The parameters that were estimated for in this analysis are marked red.
Right: DCM results for EEG. The results shown are for a single, representative subject, where single lines present spectral activity estimates per single trial. The different colors mark different cell populations.

layers. This shows that a model expressing gamma mostly in superficial pyramidal cells and beta in deep pyramidal cells can explain the observed data features. This is in line with experimental animal data ([1], [5]).
In order to link the two modalities I then used the trial-and laminar-specific spectral estimations as regressors in a general linear model for the fMRI data. The latter had been assigned to 21 cortical bins, following [3]. In particular, I used the gamma band (50-96 Hz) estimations that were mostly expressed in superficial layers in our model. This rests against the assumption that oscillations in frequencies in the gamma band are closely related to hemodynamic signals ([4], [7]). We found that indeed the variability in the gamma band is linked to the BOLD signal in all layers but correlates significantly more to superficial layers than to middle ($p = 0.0004$) or deep layers ($p = 0.0012$). This partition of the 21 cortical bins into the three functional layers was based on Haessler's proposal of functional separation in V1 ([2]).
From this research experience I benefited on one hand on a personal but mostly at a professional level. Studying the background and application of DCM, I learned an important technique that can be applied to very different scientific questions and will enable me to pursue my research goals in computational psychiatry.

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