Detecting Drug Effects in the Brain

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In the early phases of drug development, the effect of a candidate drug on the brain can be of key importance, either because the drug is specifically targeted at the brain or because of safety concerns regarding an effect on the brain. Quantitative electroencephalography (qEEG) uses multiple electrodes placed on the scalp of a subject (typically rat or human) to record the electrical activity produced by the firing of neurons within the brain. By monitoring these "brainwaves" under different treatment conditions, the effect of a candidate drug can be inferred.

qEEG produces a virtually continuous signal over time that is typically processed using a Fast Fourier Transform, producing a set of power spectra at successive time slices for each subject. The challenge is to relate these power spectra (a multivariate response representing the brain activity), to the concentration of the drug in the brain at the corresponding time. Of course, the actual concentration of the drug in the brain at a given time cannot be measured, but can be modelled using pharmacokinetic models typically with unknown parameters.

In this talk we will introduce an R package for Extended Semi-linear Canonical Correlation Analysis (ESLCCA, described in Brain et al, 2011). ESLCCA estimates the parameters of a given nonlinear pharmacometric model to maximize the correlation with a linear combination of multiple response variables (in this case, the power spectra). We shall illustrate how this method has been used to characterize brain activity under different treatment regimens in research and development projects at Pfizer.

References

Brain, P, Strimenopoulou, F & Ivarsson, M (2011). Analysing electroencephalogram (EEG) data using Extended Semi-Linear Canonical Correlation Analysis. *Submitted.*