Edinburgh 2015: biennial SPM course

Advanced Data Modelling & Inference

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Modelling?

- Y = XB + e

here is my model

- B might be biased due to signal shifts
- The accuracy and precision of B estimates depends on what is included in X and how trials are modelled

- Impact on fMRI univariate analysis
- Impact on multivariate classification and similarity analyses that uses B and/or T values

Inference?

- **Statistical inference** is the process of deducing properties of an underlying distribution by analysis of data. Inferential statistical analysis infers properties about a population: this includes testing hypotheses and deriving estimates.

- What you think you observed might be wrong.
- What can you say from your results.

Overview

- Variance Components
- Modelling and inference
- Multivariate inference
- Confounds

Variance components

A full model of variance

Following Davis et al. (2014) we can distinguish

- variations from trial to trial → modelling issues
- variations between voxels → MVPA and connectivity issues due to spatial covariance
- variations between subjects → random sampling and directionality of effects

Trial Level	$A_{tvs}=\alpha_{0vs}+X_{pts}\alpha_{pvs}+e_{tvs}$	$e_{tvs}\sim N(0,\sigma^2)$
Voxel Level	$\alpha_{0vs}=\beta_{0s}+e_{0vs}$ $\alpha_{pvs}=\beta_{ps}+e_{pvs}$	$e_{vs}\sim N(0,\tau)\quad \tau=\begin{bmatrix}\tau_0^2 & 0\\ 0 & \tau_p^2\end{bmatrix}$
Subject Level	$\beta_{0s}=\gamma_0+e_{0s}$ $\beta_{ps}=\gamma_p+e_{ps}$	$e_s\sim N(0,\Sigma)\quad \Sigma=\begin{bmatrix}\Sigma_0^2 & 0\\ 0 & \Sigma_p^2\end{bmatrix}$
Combined	$A_{tvs}=\gamma_0+e_{0s}+e_{0vs}+X_{pts}\gamma_p+X_{pts}e_{ps}+X_{pts}e_{pvs}+e_{tvs}$	

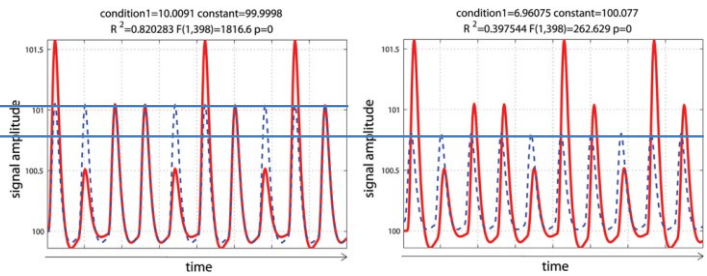
Modelling

Accounting for hemodynamic differences

- It is well known that the hdr varies not only between subjects but also within subject for different brain regions (Aguirre et al., 1998, Buckner 1998).
- The problem is that mis-modelling leads to inappropriate estimates of the 'true' response ; which impact on both univariate and multivariate methods that rely on beta estimates.

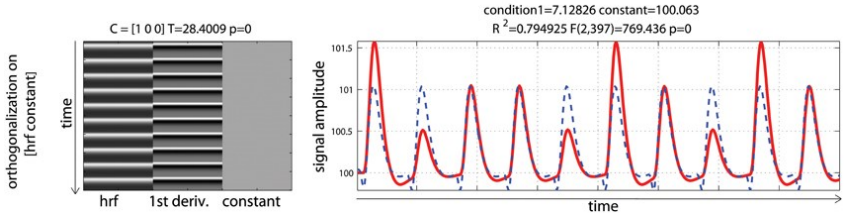
data model

Timing error =
reduced B estimates



Accounting for hemodynamic differences

- A well known solution is to use basis functions: for instance include derivatives in the model.



- This only solves partially the problem, the model is accurate but B estimates are still biased – fortunately there is a simple correction factor we can apply (Pernet 2014)

$$H = \sqrt{\widehat{\beta}_1^2 \sum_1^N x1^2 + \widehat{\beta}_2^2 \sum_1^N x2^2} * \frac{\widehat{\beta}_1}{|\widehat{\beta}_1|}$$

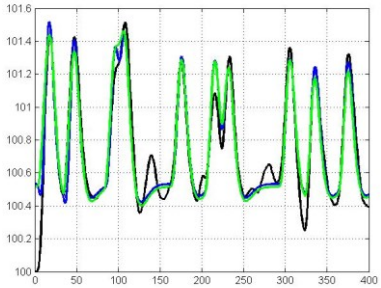
Accounting for neural differences

- Another issue relates to tasks – whatever subject have to do, there is a decision to take; and recent data point to accumulation models in which neurons fire until enough information is accumulated. This implies that decision related areas have different neural dynamics from trial to trial.

- Grinband et al. (2008) makes a distinction between *variable impulse* model (GLM with parametric modulation) and *variable epoch* model (GLM with the stimulus duration equal to RT).
- One issue with the variable epoch model, is mis-modeling of regions show no trial-to-trial variations !

Accounting for neural differences

- The best way to model such variations trial-to-trial is (1) use the mean RT across all trials/conditions for each regressor and (2) add a parametric modulation (Mumford, 2014).
- If we add also basis functions, we can capture all variations and have 'better' beta estimates once corrected.



response with variable neural duration

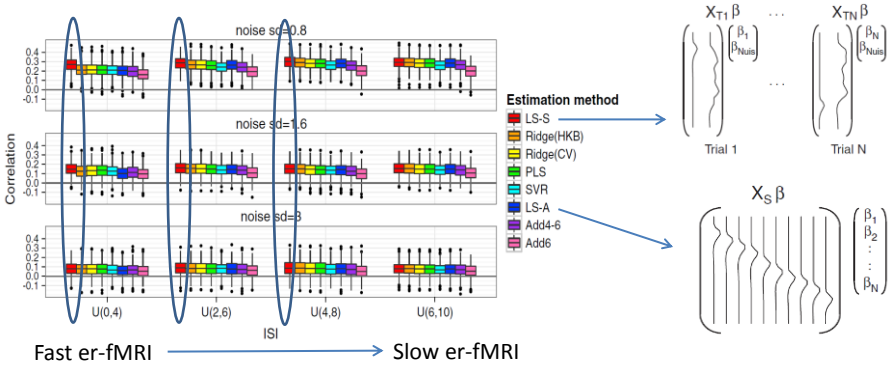
hrf + param reg (variable impulse)

hrf using RT (variable epoch)

hrf and deriv with mean RT + param reg

Estimates of single trial

- Slow event related design are inefficient (1) for GLM (2) for the number of stimuli (3) for subjects
- Mumford et al. (2012) showed that modelling all+1 gives better estimates



Inference

- Mis-modelling leads to the wrong B estimates (and therefore wrong T values)
- Ensuring proper timing and duration in the model (and possibly correction of beta values) can improve univariate and multivariates results
- Collinearity leads to unstable estimates – single trial estimates for fast er-fMRI design should be modelled specifically.

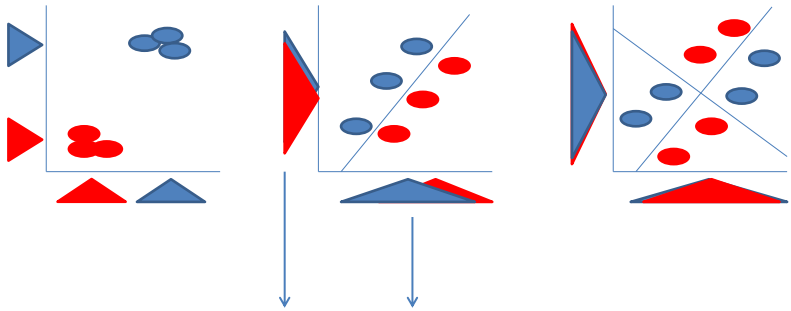
Inference

- Comparing controls to patients or young and old participants: there are many reasons to believe the hdr will vary between groups and observed differences can relate to modelling issues rather than true differences between groups (being mean activations or patterns)
- Comparing two conditions: when differences are subtle, this can easily be related to hdr differences in amplitude like in timing or shape due to differences in neural firing rate or neural duration.

Multivariate inference

Testing for patterns

- If all voxels show a small effect A>B, MVPA will be significant.
- Yet this is not a 'pattern' as one might understand it.



A linear classifier can take advantage of the small, yet consistent differences in mean activations

Inference

- Pattern differences = distributed processes?
- Davis et al. (2014) showed that MVPA strives on variations between voxels even for unidimensional differences
- Coutanche (2013) propose a series of steps to test dimensionality for SVM:
  - ➢ remove across voxel means at each time point to ensure the response is driven by the variance (no mean diff)
  - ➢ Compare results with/without the mean

Inference

- sparse ≠ selective
- Assuming the multidimensional nature of a signal in the set of regions, Foldiak (2009) remind us that selectivity is a property of neurons and sparseness of a set of neurons. The same applies to voxels:

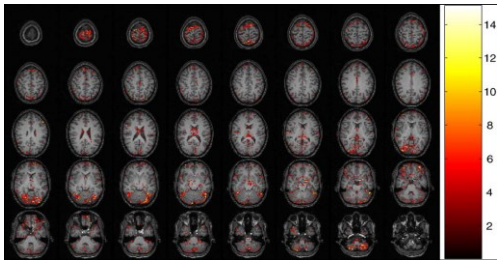
	v1	v2	v3	v4	v5	v6	v7	v8	
S1	0	0	0	0	0	0	0	1	local response (1/8)
S2	1	0	1	1	1	1	0	1	dense response (6/10)
S3	0	1	0	0	1	1	0	1	sparse response (4/8)
	selective voxels				narrow voxels			broad voxel	

Confounds

Motion

- In univariate analyses, motion is known to elicit activations everywhere but is predominant at tissue interfaces.
- Motion has also been shown (in resting state studies) to add spurious variance that tends to cluster – creating spurious distance-dependent correlations.
- The local spatial variance increase can also influence data fit (and thus GLM/MVPA).

Lund et al. 2006



Experimental confounds

- We often use tasks to assure vigilance (catch trials, questions, 1-back repetition detection)
- Button responses can be included as nuisance regressors but (1) it must be balanced across classes and runs (2) it must not systematically vary with conditions (e.g., always use same response hand) as this can bias classifiers

Multivariate Confound

- Counterbalance assumes multi-directional effects. For instance learning effect in the sequence of tasks ABC is balanced with CBA.
- In univariate analyses, testing for A≠C is not confounded with learning because it is cancelled out averaging estimates across subjects.
- In multivariate analyses where we use mean accuracy or correlation, it is confounded: the effect is there for each subject and not cancelled because the direction of the effect is not present in those measures (Todd et al. 2013).
- In RSA, we need to ensure full design balance (ABC, ACB, BAC, BCA, CAB, CAB) as symmetric designs can lead to symmetric RSM.
- Group belonging can be regressed out voxel-wise before entering MVPA (like in GLM)

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