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Inferential Brain Mapping

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Overview

- **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 deriving estimates and testing hypotheses.

1. Deriving estimates from the GLM
2. Design considerations for correct inference
3. Multivariate hypotheses

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	$A_{tvs}=\gamma_0+e_{0s}+e_{0vs}+X_{pts}\gamma_p+X_{pts}e_{ps}+X_{pts}e_{pvs}+e_{tvs}$	

Deriving estimates from the GLM

MODELLING TRIALS

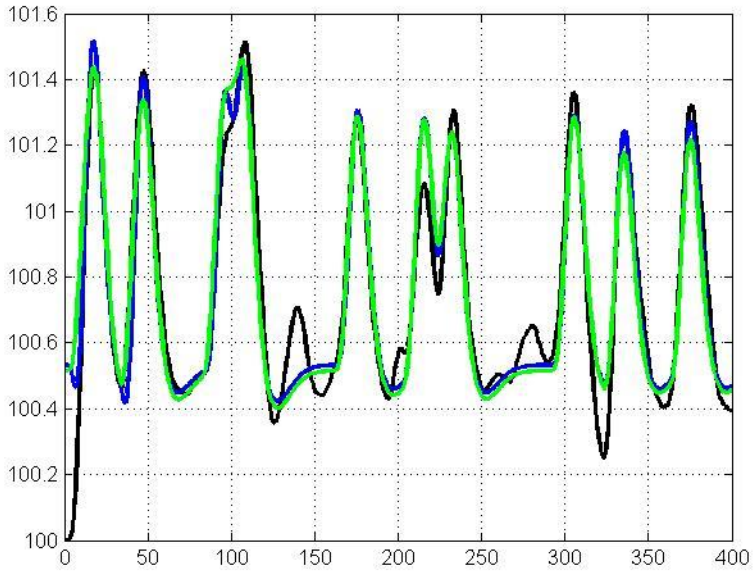
Accounting for neural differences

- In many tasks, subject have to take a decision
- Neurophysiological work points 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, which also differs from regions which do not have such dynamic.

- 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, and it is not adequate for multiple conditions/categories.

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)

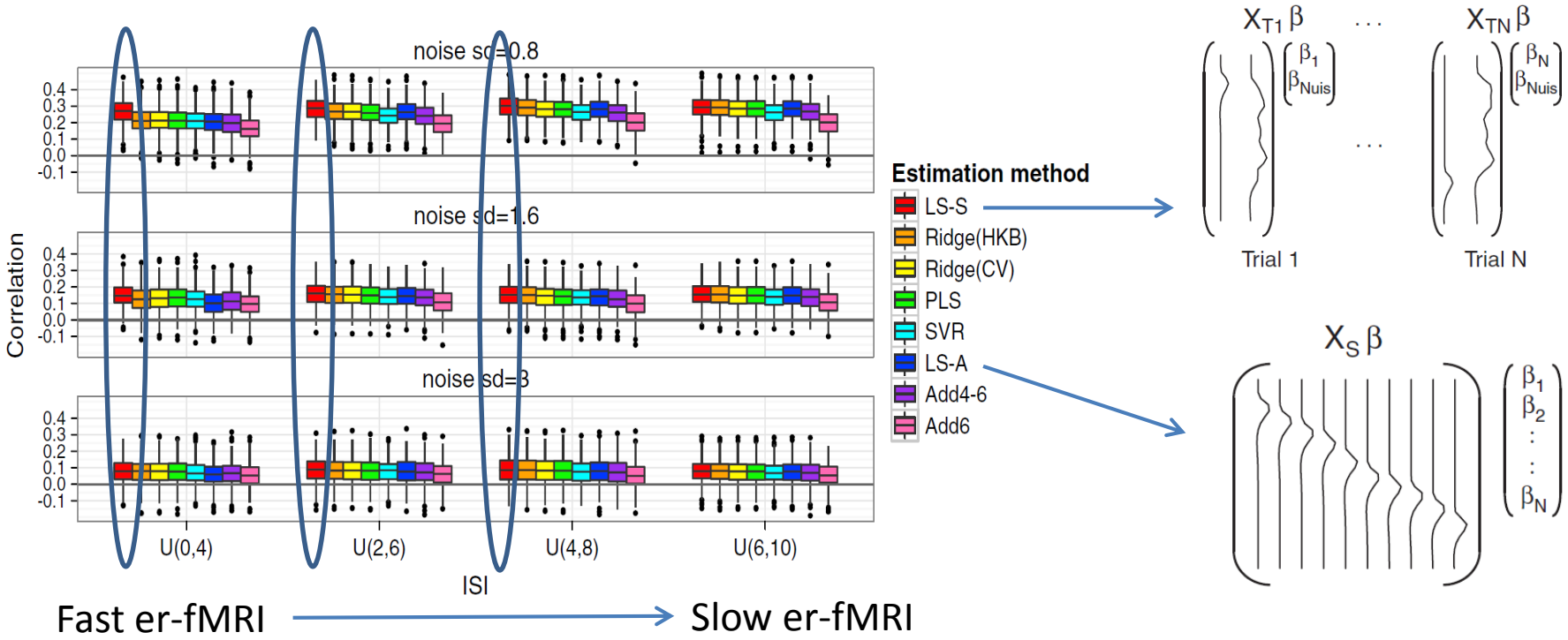
hrf using RT (variable epoch)

hrf and deriv with mean RT + param reg

Pernet HBM 2015

Estimating single trials

- Slow event related design are inefficient (1) for GLM (2) because the number of stimuli is limited (3) because it is not 'natural' for subjects. Mumford et al. (2012) showed that modelling all+1 (LSS) always gives better estimates.



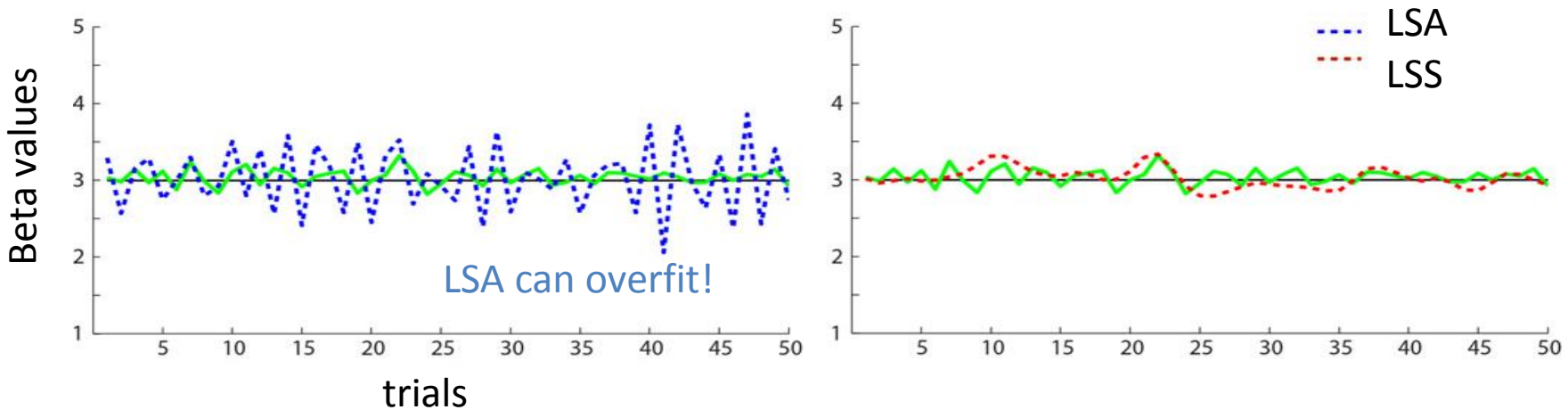
Estimating the mean via single trials

- Abdulrahman & Henson (2016) showed that different models works for different designs (SoA, as Mumford et al. 2012), level of noise and questions (univariate, multivariate, connectivity).

- *Univariate analysis (mean response)*: standard GLM (LSU) works fine down to SoA 6sec to simple effects and 8sec for contrasts (the more trial variance, the trials are needed = shorter SoA better) BUT if high trial variance (more than scan) LSA > LSU at short SoA

Estimating single trials in a voxel

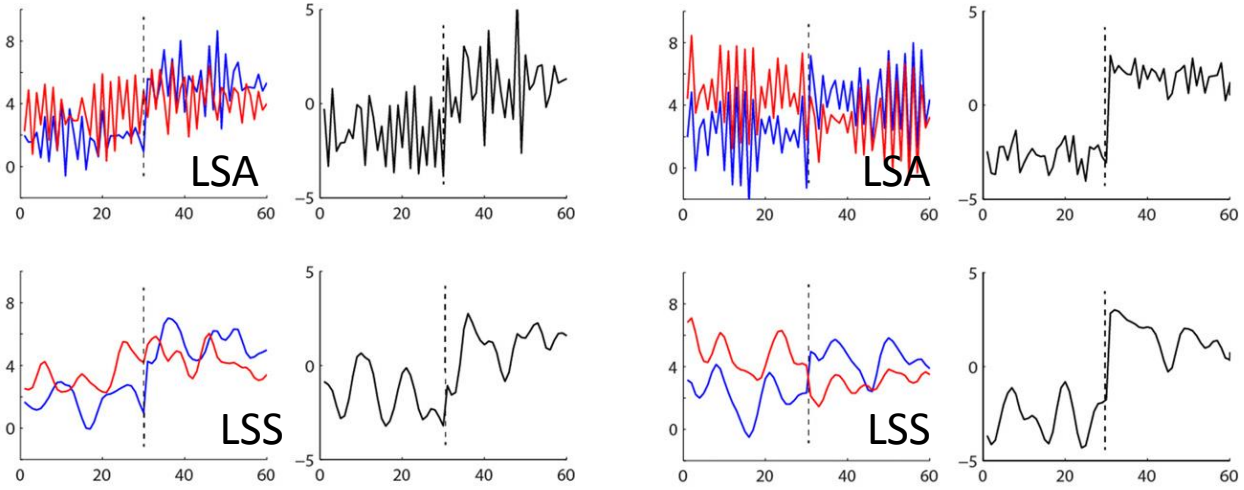
- *Beta series (single trials in a voxel):* LSA (one design) is best for all SoA (down to 6sec) BUT LSS-LSN (one design per trial) is better when trial variance is low (i.e. trial variance < scan variance i.e. difficult to distinguish)



We can expect 1.5T to have higher scan variance than 3T, i.e. might need to switch method depending on the scanner you use

Estimating single trials over voxels

- *MVPA (pattern of single trials):* SoA 6-7sec works fine for LSA-LSS-LSN but assumption about noise matter. For coherent noise (voxel in the same region?) → LSA (one design) is better, for incoherent noise (voxels from different regions?) → LSS is better (one design per trial) (never LSN = MVPA bias).



Incoherent scan noise

Coherent scan noise

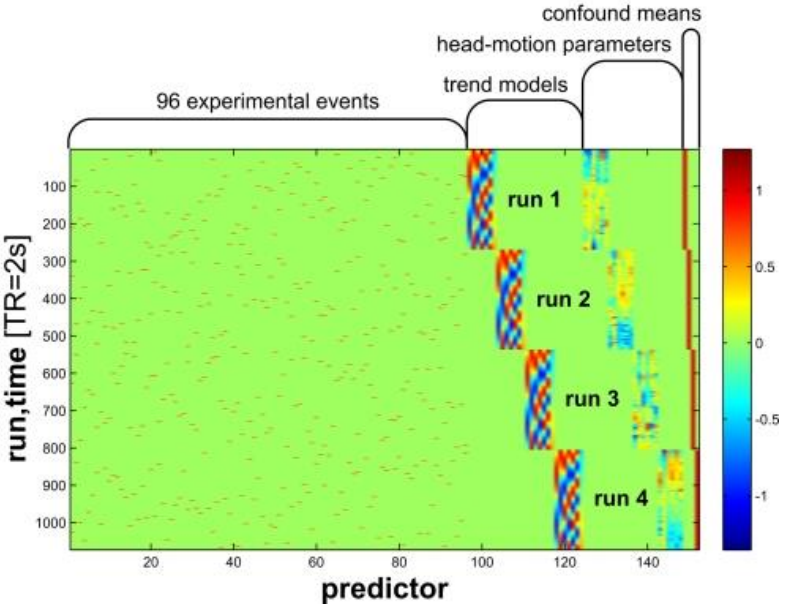
Design considerations for correct inference

INFERENCIAL ERRORS BY DESIGN

How many stimuli ?

- **Classifications (SVM) are more accurate with limited number of classes.** Multiple exemplars per class/category with the same number of stimuli to avoid bias toward most frequent stimuli.

- **RSA necessitate stimulus rich designs but is not limited to the number of classes.** Numerous, non-repeated stimuli (Kriegeskorte 2008)



Which order for my stimuli ?

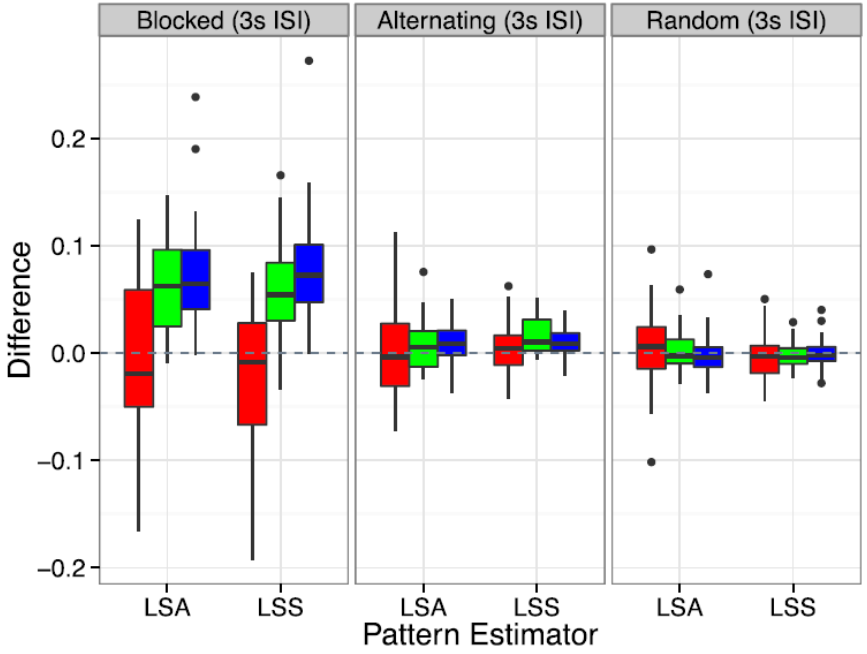
- For univariate analysis, dynamic stochastic designs (pseudo-random) offers the maximum power (Friston et al., 1999).

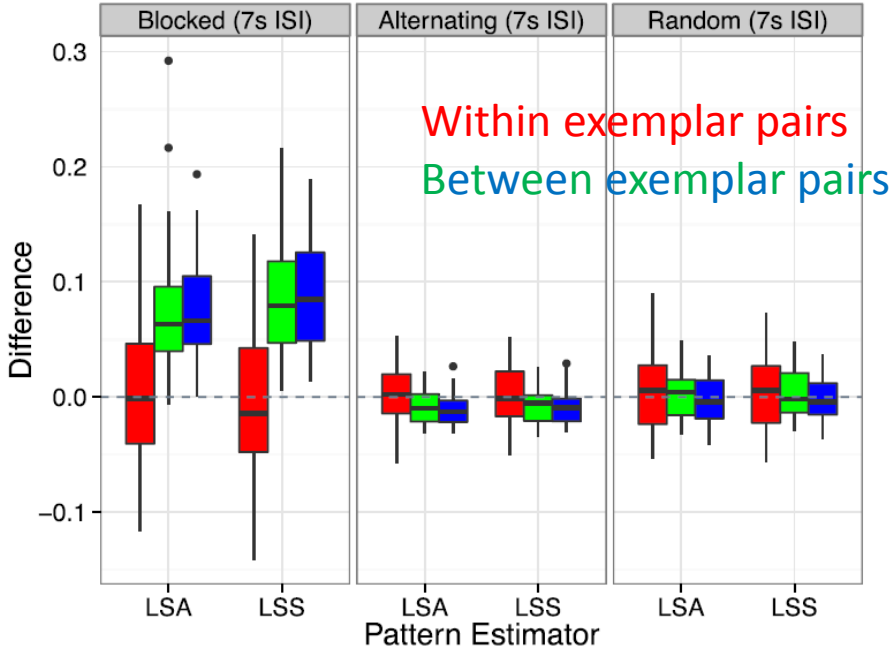
- One issue is that with large number of classes, the spacing becomes large – i.e. gets close to the noise.
- Mumford et al. (2014) showed that for multivariate analysis, only randomized designs are appropriate. Importantly, to avoid a bias due to collinearity and autocorrelation, the randomization must be performed across subjects as well.

→ **Optimal univariate and multivariate designs have different requirement.**

Which order for my stimuli ?

- Mumford et al. 2014.

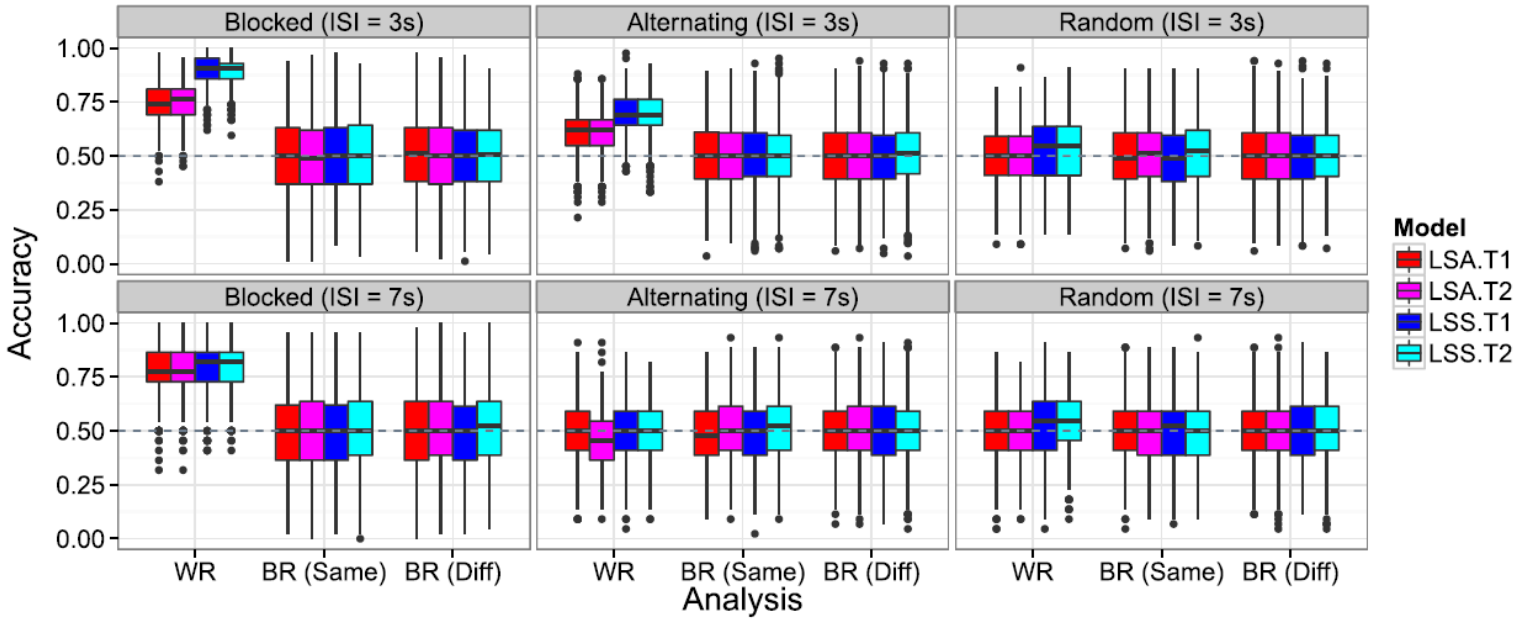




For RSA, pseudorandom designs lead to artificial differences. Alternating and random design are better, no matter the ISI (doesn't need to be slow !)

How many runs?

- Any collinearity and autocorrelation bias the results of MVPA.
- Correlations and cross-validation between runs are better.



- Better to get 4*100 volumes in 4 sessions than 1x400 volumes (Courtanche 2013, Mumford, 2014) – opposite for vanilla univariate GLM.

Multivariate Confound

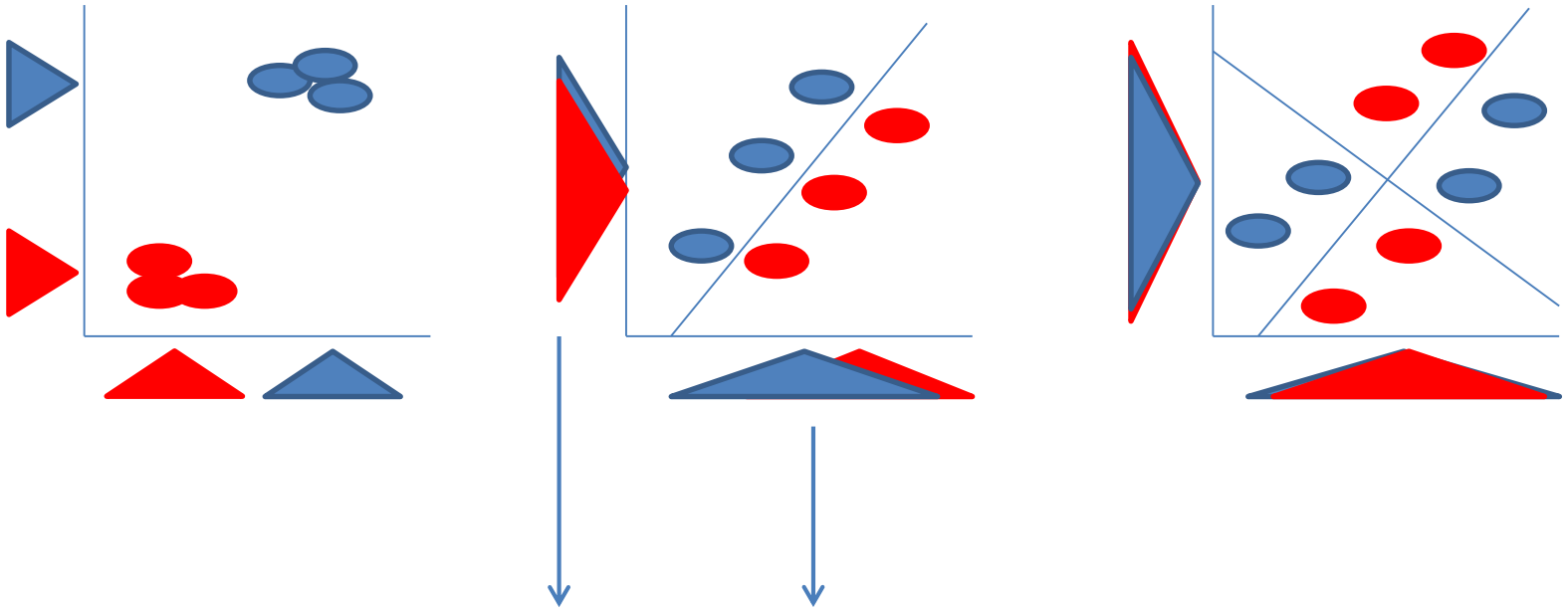
- Counterbalance assumes multi-directional effects. For instance learning effect in the sequence of tasks ABC is balanced with CBA.
- In univariate analyses, testing for A≠C is not confounded with learning because it is cancelled out averaging estimates across subjects. In multivariate analyses where 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.

Interpretation errors

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.



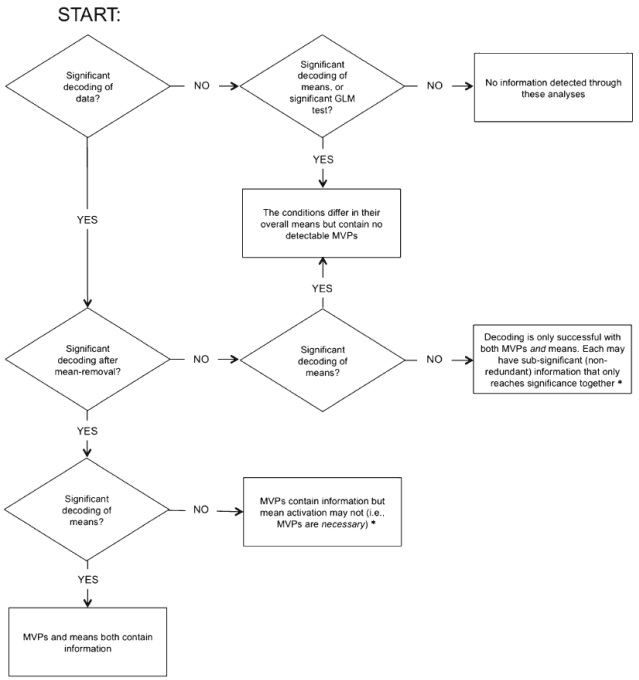
A linear classifier can take advantage of the small, yet consistent differences in mean activations

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:

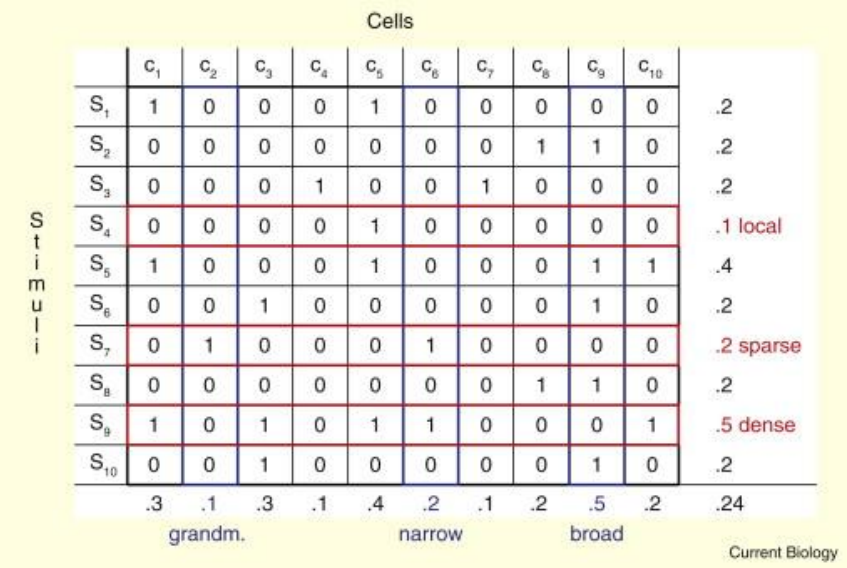
➢ remove across voxel means at each time point to ensure the response is driven by the variance (no mean diff)

➢ 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, whilst sparseness is an encoding property relative to stimuli.



The same rule applies to voxels: having heavy weighting on one or a few voxels doesn't mean they are selective to some features – but the 'code' is more likely local or sparse.

Take Home Message

- Modelling (GLM) is not trivial, mis-modelling can lead to create or obscure differences (use mean RT, parametric, BF + separate models per trial).
- What is your research question? Which method would address this best? → Optimize designs (stimuli, runs, order)
- Carefully interpret results using additional tests for dimensionality, sparsity, selectivity

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