Design of MVPA Studies

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Goals of this Presentation

MVPA Design

- What are requirements for the experimental design of MVPA studies?

Minimize Noise, Maximize Signal

- How can we maximize the information we extract by our experimental design?

Confounds in MVPA studies

- What are possible confounds that we have to consider?
- How can we avoid and eliminate confounds? (→ Kai Görgen's talk)

Important Notes

- How you later analyze your data can have important consequences for your design
- This presentation: strong focus on fMRI classification within subject (e.g. different conditions)
- <u>But</u>: Principles apply also to between subject classification or other modalities (e.g. EEG)

MVPA DESIGN: GENERAL

Design choices for Multivariate Decoding

Most design choices identical to univariate GLM

- duration of experiment (longer = better)
- scanner settings (TR, TE, flip angle, descending acquisition, …)
- high spatial resolution: unclear if specific benefit for multivariate

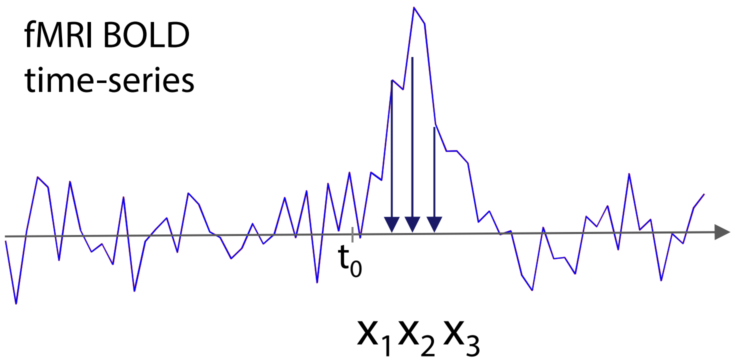
What you need to consider

- classification requires independence (or balanced dependence) of training and test data
- often data dependencies exist that invalidate this assumption
- there may be hidden confounds
- design may need special treatment whether it is a block design, slow event-related design, or fast event-related design

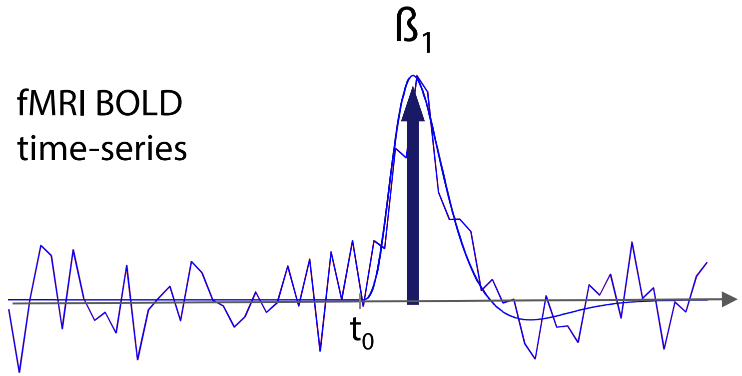
Within-subject Designs

What data enters the classifier?

single-image data

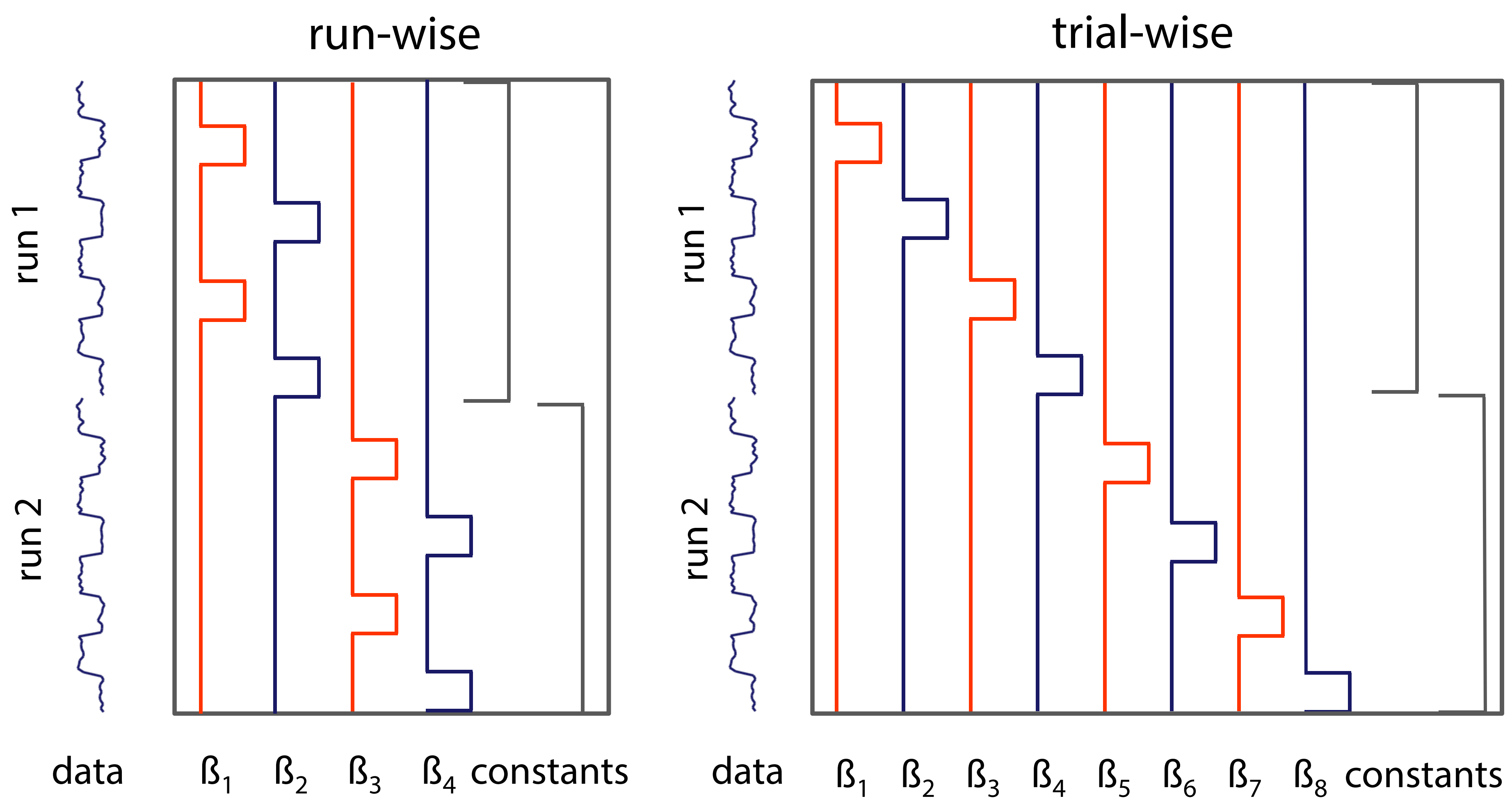


parameter estimate (beta)



- When possible: parameter estimate preferred
- Question: trial-wise or run-wise beta estimates?

Within-subject: Trial-wise or Run-wise Betas?



Within-subject: Trial-wise or Run-wise Decoding?

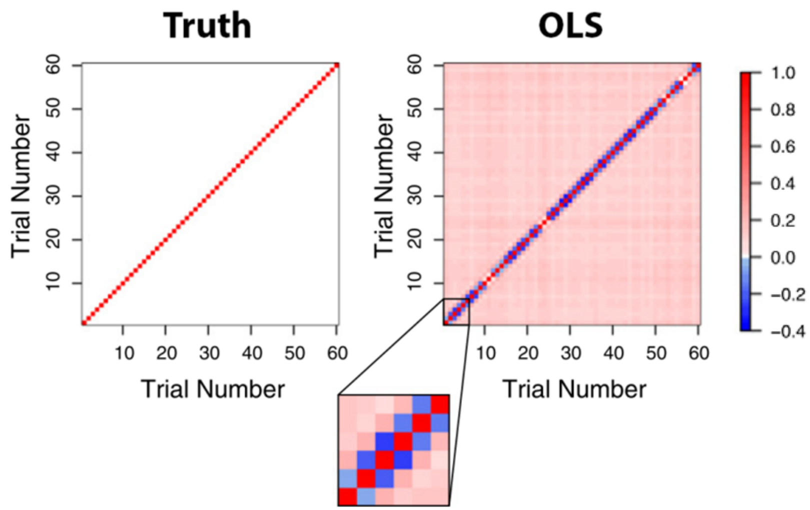
	Trial-wise	Run-wise
Training data	many samples	few samples
Data quality	noisy	stable
Consequence		
Accuracy (Ku et al., 2008)	lower, but stable	higher, but variable
Statistical Power (Allefeld & Haynes, 2014)	slightly lower	slightly higher
Speed	slow	fast
Slight imbalance	requires correction	no problem
Strong imbalance	requires correction	confound!
Statistical estimation	more samples	maybe too few samples

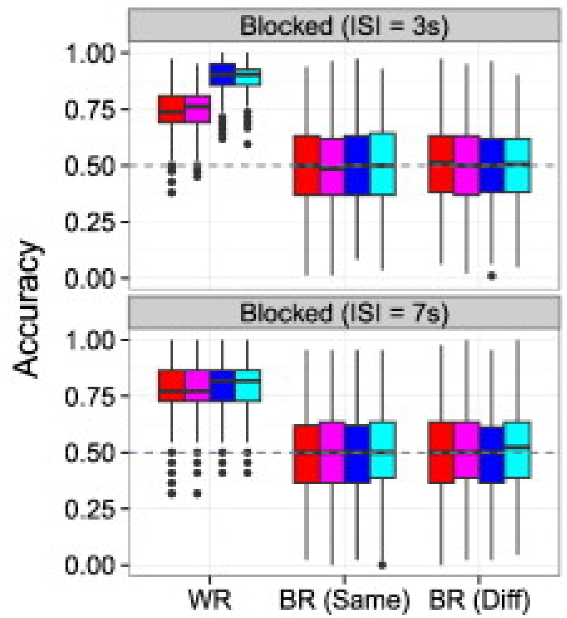
Ku et al (2008) – Magn Res Imag; Allefeld & Haynes (2014) – Neuroimage

Leave-one-run out cross-validation

Typical Analysis: Leave-one-run-out cross-validation

Reason: Non-independence within run can bias results





Mumford et al (2014) – Neuroimage

How many runs for leave-one-run out?

	Many short runs	Few long runs
Data variability	more variable	more stable
Amount of training data	more training data	less training data

→ Usually 4 to 12 runs

→ Number often determined by condition balancing within run

Coutanche & Thompson-Schill (2012) – Neuroimage

Interim Summary

- Most design choices are identical between univariate GLM and multivariate classification
- Design choice may depend on trial-wise or run-wise decoding
- Non-independence within run suggests preference for leave-one-run out classification
- Ideal number of runs unclear and probably depends on task

HOW TO MINIMIZE NOISE AND MAXIMIZE SIGNAL

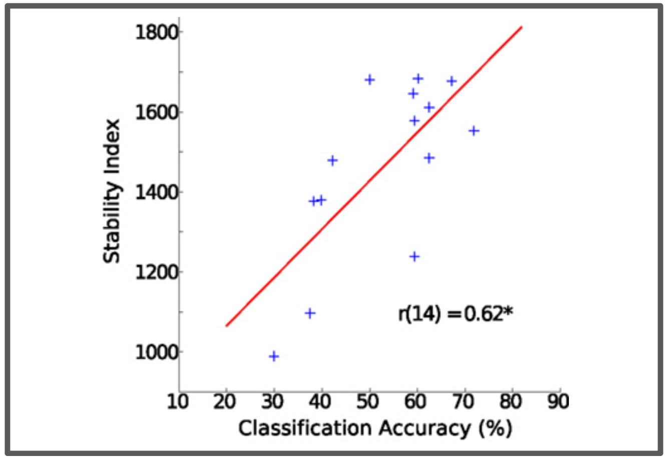
Minimize Noise

Example: Head motion vs. classification accuracy

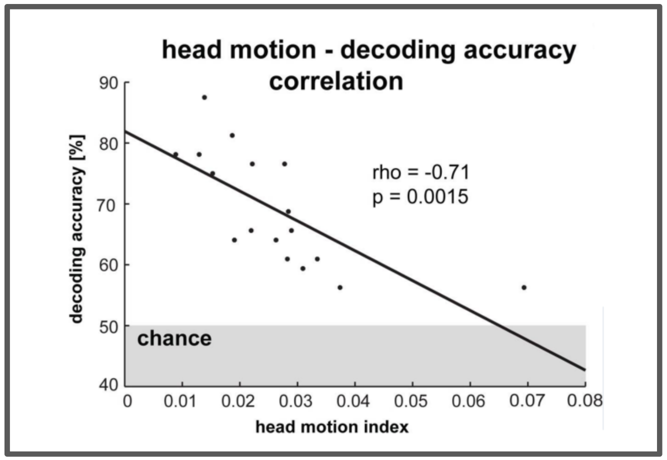
Mitchell et al (2006) – Science

test pairs across these nine participants. Accuracy across participants was strongly correlated (r = –0.66) with estimated head motion (i.e., the less the participant's head motion, the greater the prediction accuracy), suggesting that the variation in accu-

Wutte et al (2011) – Front Psych



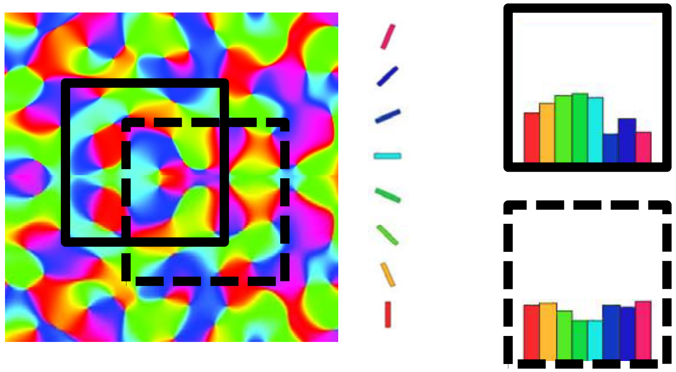
Alink et al (2013) – Front Psych



Minimize Noise

- Decoding usually done on unsmoothed data
- Reason: Part of information may lie in fine-scale patterns
- Effects of noise larger on unsmoothed data
- Most important sources of noise that affect fine-scale patterns:
  - head motion
  - physiological noise
  - scanner-related artifacts

Example: Effect of displacement on sampling of orientation columns



→ motion correction only interpolates

Swisher et al (2010) – J Neurosci; Freeman & Heeger (2011) – J Neurosci

Minimize Noise (Example: Head motion)

Solution 1: Avoid head motion

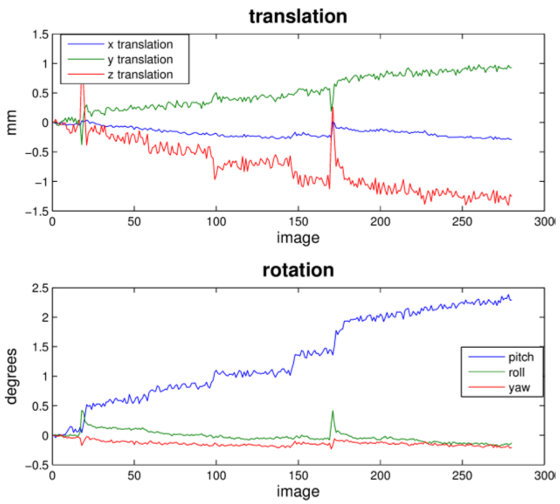
- Pad the head and instruct the subject well
- Use a bite-bar
- Use prospective motion correction (Weiskopf et al)
- Create 3D-printed version of skull (Gallant et al)

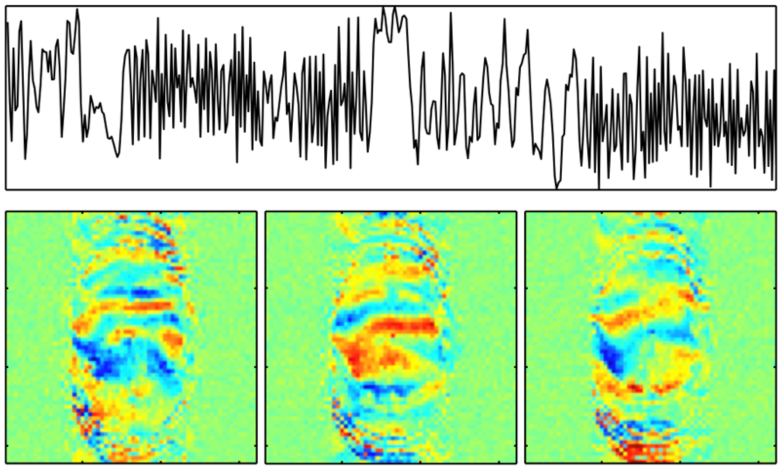
Todd et al (2015) - Neuroimage

Minimize Noise (Example: Head motion)

Solution 2: Remove head motion after acquisition

- Motion scrubbing (e.g. removing images with spikes > 0.2 mm)
- Add head motion and physiological parameters to GLM
- Use other methods for removing artifacts, e.g. MELODIC



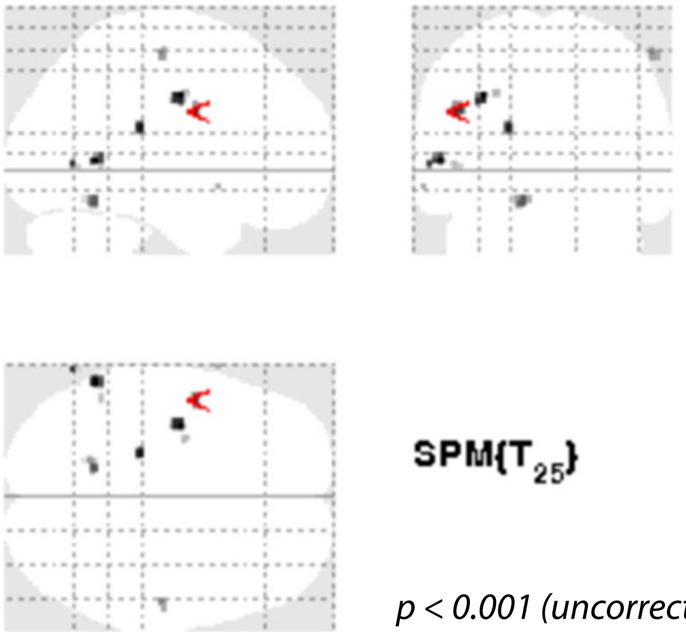


Beckmann & Smith (2004) – IEEE Trans Med Imag

Minimize Noise (Example: Head motion)

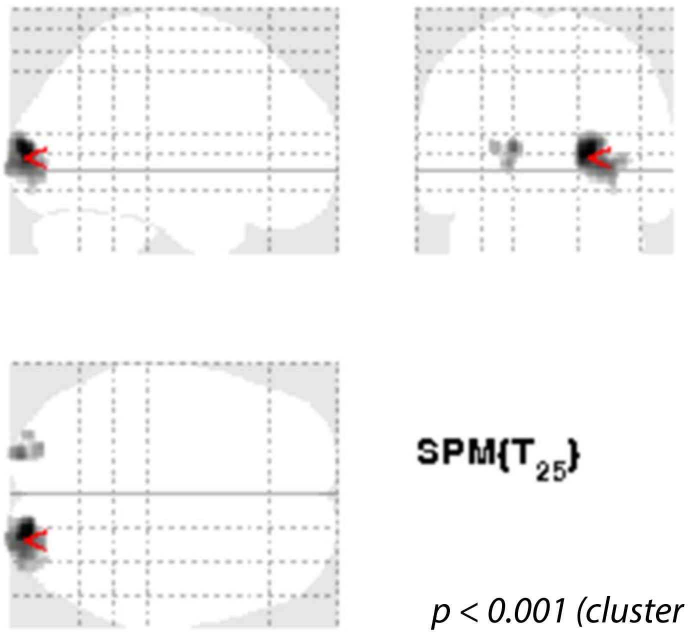
Example application of MELODIC to classification

choice (original)



p < 0.001 (uncorrected)

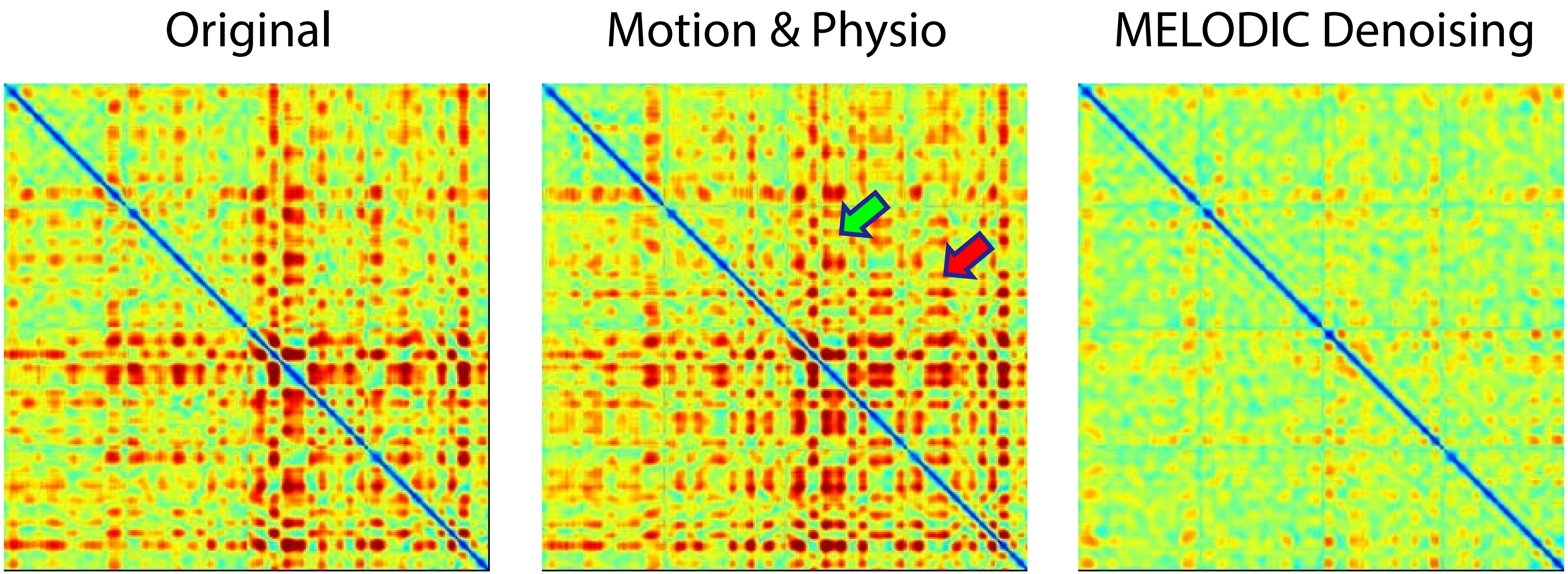
choice (denoised)



p < 0.001 (cluster corrected)

Minimize Noise (Example: Head motion)

Example application to dissimilarity matrix



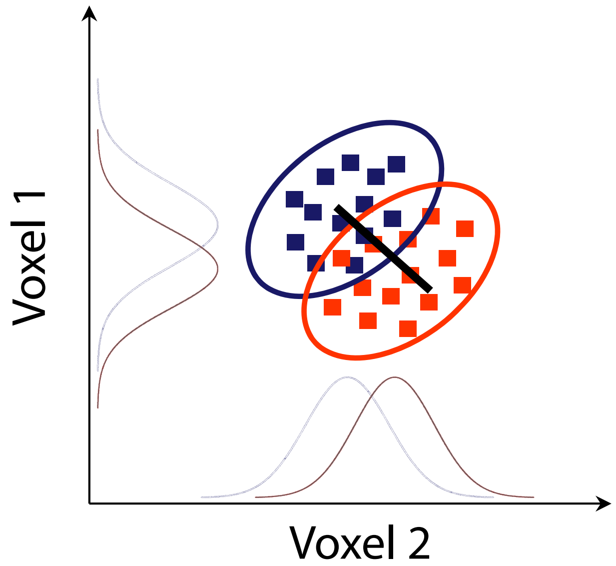
region: 251 voxel sphere in pre-SMA in one subject
dissimilarity measure: Euclidean distance (scaled between 0 and 10)
trial-by-trial dissimilarity (trials spaced regularly in steps of 2.5s)

Maximize Signal: Design Efficiency

Design Efficiency

Goal: Maximize the pattern distinctness, i.e. increase between-class scatter or decrease within-class scatter

→ Improving design efficiency of GLM for univariate contrast will maximize the distinctness before data acquisition



Maximize Signal: Design Efficiency

Design Efficiency

$$e(C,Z) = trace(C' inv(Z'Z)\ C)^{-1}$$

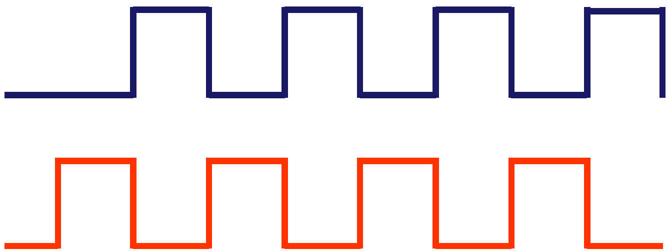
where Z is the pre-whitened and high-pass filtered design matrix X

What does this mean?

- We maximize the <u>unique</u> variance of the regressor of interest
- If we are interested in a contrast (e.g. C = [1 -1]), we maximize the variability of the *contrast* of the regressors

Example: How well can we classify betas based on such regressors?

r = -0.9



each regressor alone: terrible

classification: excellent

http://imaging.mrc-cbu.cam.ac.uk/imaging/DesignEfficiency

Maximize Signal: Design Efficiency

How do we optimize 2-class classification?

1. Create balanced randomized trial order (and possibly ISI), where $p(A|A) = p(A|B) = p(B|A) = p(B|B)$
2. Create design and apply pre-whitening
3. Calculate efficiency using contrast [1 -1]
4. Repeat and pick design with largest efficiency

Additional advice:

- For single-trial event-related analysis and short TR (< 2.5s), time-locking onsets to TR can reduce between trial variability
- Need to consider equal individual estimability, i.e. e([1 0],X) = e([0 1],X)

THE PERVASIVENESS OF CONFOUNDS IN MVPA STUDIES

Confounds

Two classes of confounds:

1. Confounds in the experimental design
2. Confounds in the results

→ Best practice is to avoid confounds before they happen

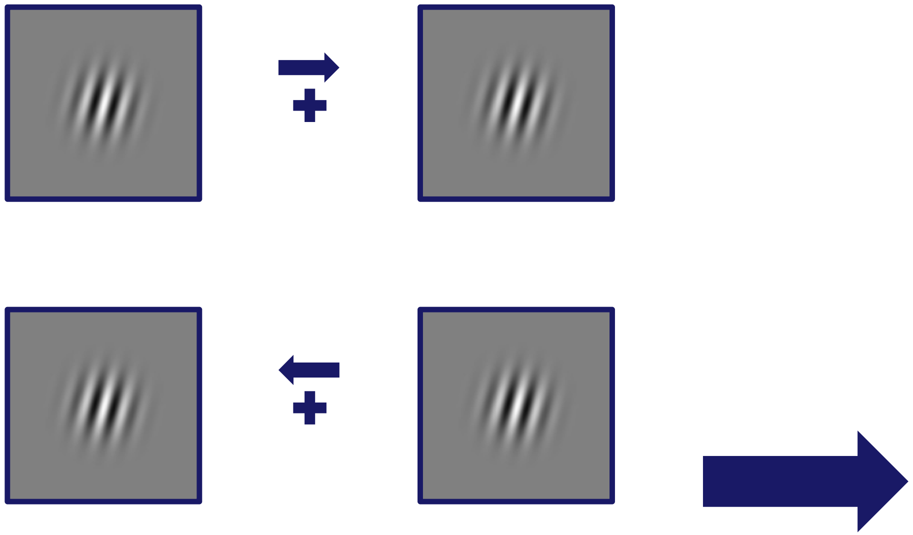
→ We can avoid confounds in experimental design

→ There are some confounds we cannot avoid, but can only control

Confounds in the Experimental Design

Typically disregarded issues can become a confound

Example: Classification of top-down visual attention

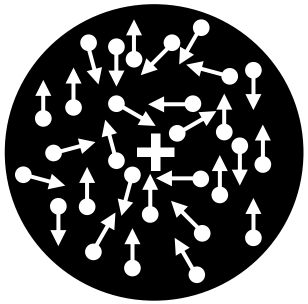


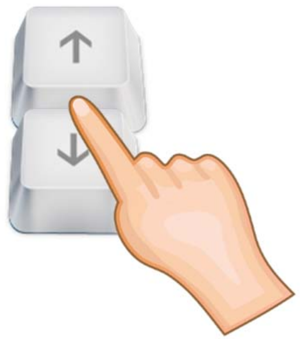
Confound: visual cue

Confounds in the Experimental Design

Typically disregarded issues can become a confound

Example: Classification of choice?





Confound: motor response

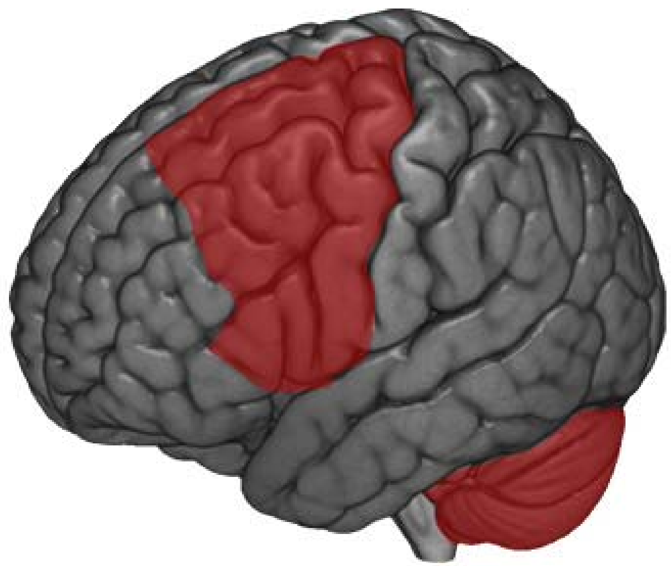
Confounds in the Experimental Design

Solution 1: Exclude brain regions that confound responds to

- For motor confound: Exclude motor-related brain regions
- For visual confound: Exclude visually responsive regions

<u>But</u>: Maybe unexpected brain region responds to confound?

<u>And</u>: Sometimes approach not possible



→ not recommended

Confounds in the Experimental Design

Solution 2: Separate confound in time or jitter

- For motor confound: Wait 20s with motor response
- For visual confound: Show cue jittered and model separately

<u>But</u>: Pattern autocorrelation can last very long

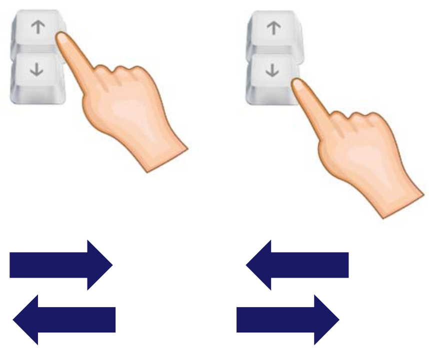
<u>And</u>: Jitter only reduces confound, never eliminates it!

→ not recommended

Confounds in the Experimental Design

Solution 3: Balance confound between runs

- For motor confound: Switch response after each run
- For visual confound: Invert cue direction



<u>But</u>: The brain may respond more to the confound in some runs or better to one version of the confound

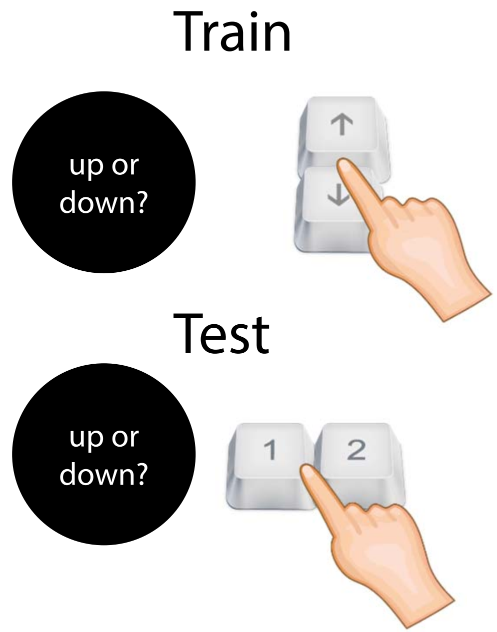
<u>And</u>: Potential bias, task-switching costs

definitely not recommended

Confounds in the Experimental Design

Solution 4: Cross-classification

- For motor confound: Switch response modality, e.g. after each run
- Train classifier on data with one confound, test on data with other
- If above chance, then classifier generalizes across confound
- For visual confound: Use different cue



<u>But</u>: Less data available for training, i.e. possibly reduced sensitivity

<u>And</u>: Possible task-switching costs

→ recommended if no better possibility

Confounds in the Experimental Design

Solution 5: Cue Trick

- For motor confound: Use response-mapping rule
- Controls for confound by balancing
- For visual confound: Not always possible

<u>But</u>: Requires training of subject

→ recommended when possible

Hebart et al (2014) – Cerebral Cortex

Summary

- Reducing noise in the acquisition can have a stronger benefit for multivariate analyses than univariate analyses
- Improving the design efficiency can improve the pattern distinctness
- Confounds are difficult to deal with
- It is not easy to follow the own intuition to avoid confounds
- We provide some recipes for avoiding or eliminating the influence of confounds
- Don’t worry: Slight confounds not always a problem

Maximize Signal

Software for Design Efficiency

- Doug Greve: OptSeq

  http://surfer.nmr.mgh.harvard.edu/optseq/

- Wager & Nichols: Genetic algorithm

  https://github.com/canlab/CanlabCore

- No optimization algorithm, but easy and more flexible method to set up design matrix:

  http://martin-hebart.de/webpages/code/matlab.html

  Suggestion: Brute-force repetition works well in general