Accurate autocorrelation modeling substantially improves fMRI reliability

A journal club about “sphericity” when the word appears nowhere in the whole article.

Article:
https://www.nature.com/articles/s41467-019-09230-w

Supplementary:
https://static-content.springer.com/esm/art%3A10.1038%2Fs41467-019-09230-w/MediaObjects/41467_2019_9230_MOESM1_ESM.pdf

Code:
https://github.com/wiktorolszowy/fMRI_temporal_autocorrelation

Peer-review:
https://static-content.springer.com/esm/art%3A10.1038%2Fs41467-019-09230-w/MediaObjects/41467_2019_9230_MOESM3_ESM.pdf

My code about it:
https://github.com/Remi-Gau/talk_sphericity_correction

Why talk about this?

- NARPS fMRI data
  - low repetition time (“high temporal resolution”).
- For me (and you?)
  - better understand sphericity-correction.
- Peek under the hood
  - make SPM less of a black box.

- What is sphericity?

- How does SPM deal with non-sphericity when it runs a GLM?

- The part where I talk about the paper

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```

Sphericity, Sphericity… If you say sphericity one more time...

What in the name of sanity is sphericity anyway?

Sphericity - a long intro

General linear model:

$$\mathbf{Y = X\,\beta + \varepsilon}$$

$$\mathbf{\varepsilon \sim N(0, \sigma^2\, I)}$$

Ordinary least square estimators (OLS) are the best* linear **unbiased** estimator (BLUE) IF errors are **uncorrelated** with **mean zero** and **homoscedastic** with finite variance.

* "best" means giving the lowest variance of the estimate, as compared to other unbiased, linear estimators.

Gauss-Markow theorem
Simple linear regression
Multiple linear regression with matrices

Sphericity - a long intro

General linear model: $Y = X\beta + \varepsilon$

What do we want? We want the best model!

Why? Unmodelled things hurt our t-value! #PoorTValue.

$$\mathbf{beta = (X'\,X)^{-1}\,X\,y\;;}$$

$$\mathbf{sigma^2 = \; e\,e' / (N - p)}$$

$$\mathbf{t = c\,(X'X)^{-1}\,X'\,y \,/\, sigma\,(c(X'X)^{-1}\,c')^{.5}}$$

$$\mathbf{t = c\;beta \,/\, sigma\,(c(X'X)^{-1}\,c')^{.5}}$$

$$t = \frac{Z}{s} = \frac{\bar{X} - \mu}{\widehat{\sigma}/\sqrt{n}}$$

Gauss-Markow theorem
Simple linear regression
Multiple linear regression with matrices

Sphericity - a long intro

General linear model: $Y = X\beta + \varepsilon$

We want the best model!

- Block design (using data from auditory regions of SPM auditory data set)
- Convolve with HRF
- Convolve with HRF at higher resolution
- Model out other effects (“noise”):
    - linear drift - low frequencies
        - High pass filtering: linear regressor
        - HPF à la SPM: Discrete cosine transform (SPM.xX.K.X0)
    - Motion regressors (or other data: physiological).

DEMO

Sphericity - a long intro

General linear model: $Y = X \beta + \varepsilon$

What else do we want? $\varepsilon \sim N(0, \sigma^2 I)$

"errors are **uncorrelated** with **mean zero** and **homoscedastic** with finite variance".

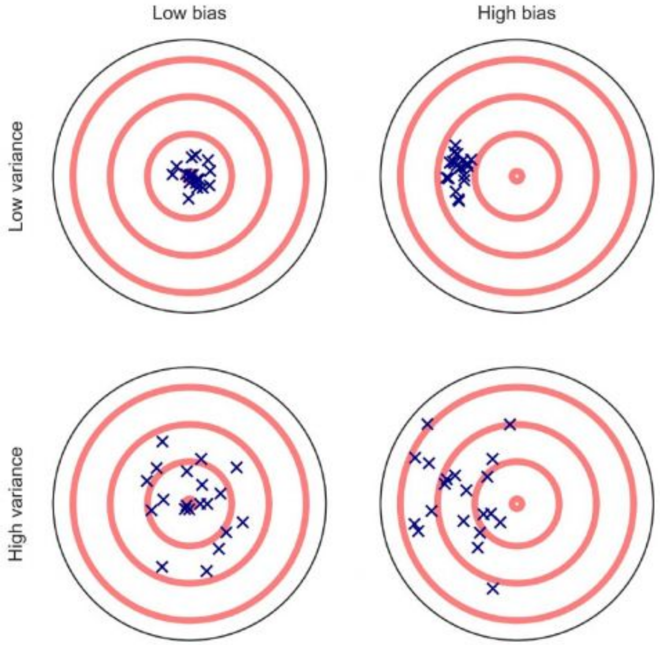
When the assumptions about **ε** breakdown

Errors with mean not equal to 0:

- bias

If unequal variance or correlation:

- increased variance



Choosing Prediction Over Explanation in Psychology: Lessons From Machine Learning

Sphericity refers to the uncorrelated bit

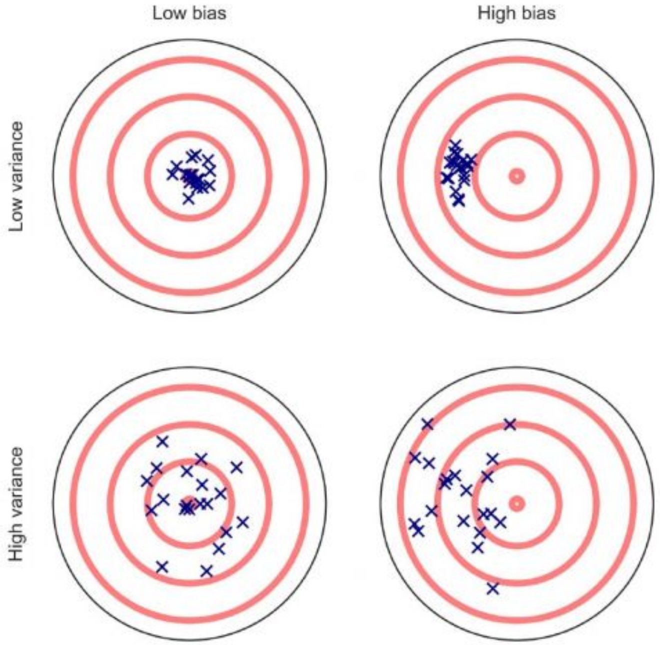
Sphericity - a long intro

General linear model: $Y = X\beta + \varepsilon$

What else do we want? $\varepsilon \sim N(0, \sigma^2 I)$

“errors are **uncorrelated** with **mean zero** and **homoscedastic** with finite variance”.

Sphericity is about to the uncorrelated bit.



[Choosing Prediction Over Explanation in Psychology: Lessons From Machine Learning]

Sphericity - a long intro

Sphericity violations occur when $\boldsymbol{\varepsilon \sim N(0, \sigma^2 V)}$ instead of **$\boldsymbol{\varepsilon \sim N(0, \sigma^2 I)}$**

- $N(0, \sigma^2 I)$ and $N(0, \sigma^2 V)$. What does this look like? DEMO
- White residuals means this $N(0,\sigma^2 I)$. What does it look like? DEMO

Sphericity - a long intro

How do we typically deal with this? (e.g repeated measure ANOVAs)

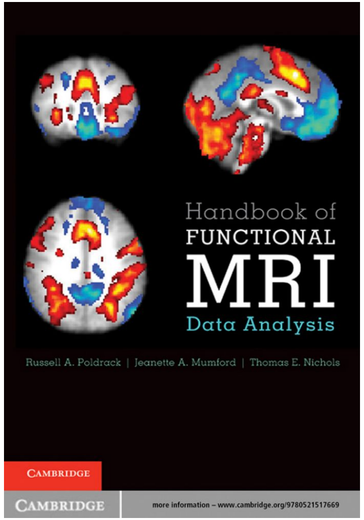
- Greenhouse-Geiser correction
- Huynh and Feldt correction

Estimate how far V is from I and reduce the degrees of freedom.

Sphericity - a long intro

References for non-sphericity correction / pre-whitening in neuroimaging

What the “bible” has to say about it. Page 90 and 195



Jeanette Mumford

- Youtube
- Course
- Slide

SPM course (minute 32)
SPM slides

Andy Field’s book “discovering statistices” is awesome: His bluffer’s guide to sphericity

Sphericity in neuroimaging

$\boldsymbol{\varepsilon \sim N(0, \sigma^2 V)}$ but we want $\boldsymbol{\varepsilon \sim N(0, \sigma^2 I)}$

$$\mathbf{W\,V\,W' = I}$$

W is a whitening matrix.

$$\mathbf{W\,Y = W\,X\,\beta + W\varepsilon}$$

Premultiply data and design matrix by W.

$$\mathbf{var(WY) = var(W\varepsilon) = \sigma^2\;W\,V\,W' = \sigma^2\;I}$$

Woohoo!

Sphericity in neuroimaging

In practice: We need to estimate W. Need to be done from data.

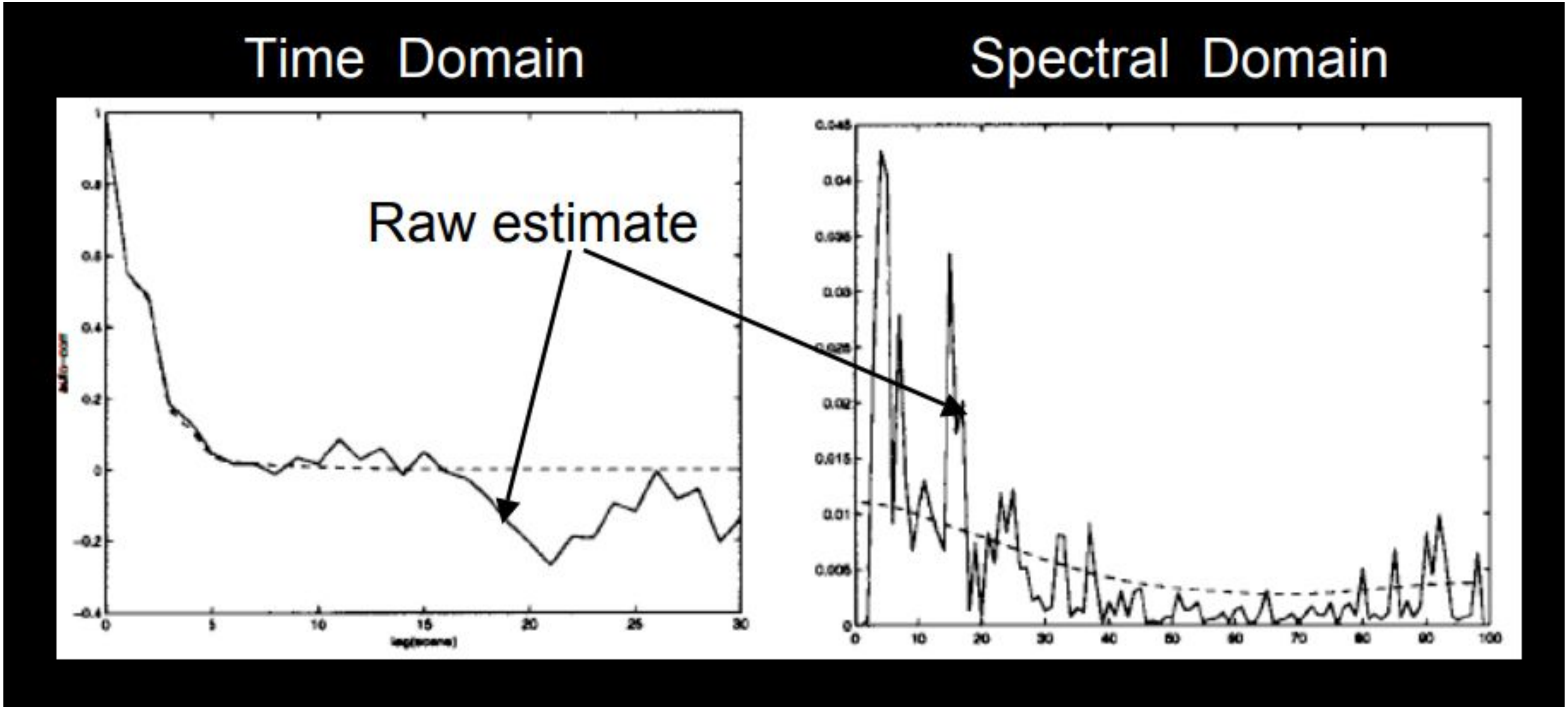
- Run GLM without worrying about autocorrelation (OLS)
- Get residuals from this to estimate W (that’s the crux)
- Create whitened model.

Sphericity in neuroimaging

Bias / variance trade off: hard to estimate W in an unbiased way.

Different ways to to go around it.

- Voxel wise: More variance. Less bias.
    - FSL: Tukey taper is used to smooth the spectral density estimates. These smoothed estimates are then additionally smoothed within tissue type.
- Voxel wise but fewer things (hyperparameters) to estimate: Less variance. Less bias.
    - AFNI: an autoregressive-moving-average ARMA(1,1) model is estimated


Time Domain
Spectral Domain
Raw estimate

Sphericity in neuroimaging

Bias / variance trade off: hard to estimate W in an unbiased way.

Different ways to to go around it.

- Global approach: Less variance. More bias.
    - SPM: Same W for the whole brain, but get more stable estimate because we can pool over voxels
        - autoregressive (AR) + white noise model.
        - FAST.
            - I tried to understand the paper but it was written in Fristonian.

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```

What’s in SPM.mat?
[Check here]

Calculating globals with spm_global.

Will be used to create the inclusive mask where the GLM will be run.

See also threshold used to define inclusive mask.

matlabbatch.spm.stats.fmri_spec.mthresh = 0.8;

Default is 0.8 and it can be changed.

Create a spm_my_defaults based on spm_defaults

defaults.mask.thresh   = 0.8;

```
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```

spm_spm is the heart of the SPM package.

```
%-Get non-sphericity (xVi), otherwise assume i.i.d.
%----------------------------------------------------------------------
if isfield(SPM,'xVi')
   xVi        = SPM.xVi;
else
   xVi        = struct('form', 'i.i.d.',...
                   'V',    speye(nScan,nScan));
end

%-Evoke ReML for hyperparameter estimation
%----------------------------------------------------------------------
if ~isfield(xVi,'V')
   SPM.xY.VY  = VY;
   SPM.xM     = xM;
   SPM.xX.K   = xX.K;
   [xVi, am]  = spm_est_non_sphericity(SPM);
   mask       = mask & am;
   spm('FnBanner',mfilename,SVNid);
end
```

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```

spm_est_non_sphericity

% In a first pass, voxels over which non-sphericity will be estimated are
% selected using an 'effects of interest' F-contrast (can be specified in
% SPM.xVi.Fcontrast) and critical threshold taken from SPM defaults
% stats.<modality>.UFp.

Check hyperparameters in “Review design”

```
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```

Spatial non-sphericity.

For MVPA check RSA toolbox

```
function
[u_hat,resMS,Sw_hat,beta_hat,shrinkage,trRR]=noiseNormalizeB
eta(Y,SPM,varargin)

% function
[u_hat,Sw_hat,resMS,beta_hat]=rsa_noiseNormalizeBeta(Y,SPM,v
arargin)
% Estimates beta coefficiencts beta_hat and residuals from
raw time series Y
% Estimates the true activity patterns u_hat by applying
noise normalization to beta_ha
```

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Wanna speed things up?

Reduce the number of chunks by changing memory usage defaults.

defaults.stats.maxmem = 2^29;

```
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The part where I talk about the paper...

About time if you ask me.

Note:

- Glaring absence of p-values in the whole paper
- Statistical test: IOTT (IntraOcular Trauma Test)

“Plot the data. If the result hits you between the eyes, then it's significant.”

Data

Table 1 Overview of the employed datasets

Study	Experiment	Place	Design	No. subjects	Field [T]	TR [s]	Voxel size [mm]	No. voxels	Time points
FCP	Resting state	Beijing	N/A	198	3	2	3.1 × 3.1 × 3.6	64 × 64 × 33	225
	Resting state	Cambridge, US	N/A	198	3	3	3 × 3 × 3	72 × 72 × 47	119
NKI	Resting state	Orangeburg, US	N/A	30	3	1.4	2 × 2 × 2	112 × 112 × 64	404
	Resting state	Orangeburg, US	N/A	30	3	0.645	3 × 3 × 3	74 × 74 × 40	900
CRIC	Resting state	Cambridge, UK	N/A	73	3	2	3 × 3 × 3.8	64 × 64 × 32	300
neuRosim	Resting state	(Simulated)	N/A	100	NA	2	3.1 × 3.1 × 3.6	64 × 64 × 33	225
NKI	Checkerboard	Orangeburg, US	20 s off + 20 s on	30	3	1.4	2 × 2 × 2	112 × 112 × 64	98
	Checkerboard	Orangeburg, US	20 s off + 20 s on	30	3	0.645	3 × 3 × 3	74 × 74 × 40	240
BMMR	Checkerboard	Magdeburg	12 s off + 12 s on	21	7	3	1 × 1 × 1	182 × 140 × 45	80
CRIC	Checkerboard	Cambridge, UK	16 s off + 16 s on	70	3	2	3 × 3 × 3.8	64 × 64 × 32	160
CamCAN	Sensorimotor	Cambridge, UK	Event-related	200	3	1.97	3 × 3 × 4.44	64 × 64 × 32	261

For the enhanced NKI data, only scans from release 3 were used. Out of the 46 subjects in release 3, scans of 30 subjects were taken. For the rest, at least 1 scan was missing. For the BMMR data, there were 7 subjects at 3 sessions, resulting in 21 scans. For the CamCAN data, 200 subjects were considered only

FCP Functional Connectomes Project, *NKI* Nathan Kline Institute, *BMMR* Biomedical Magnetic Resonance, *CRIC* Cambridge Research into Impaired Consciousness, *CamCAN* Cambridge Centre for Ageing and Neuroscience

Analysis

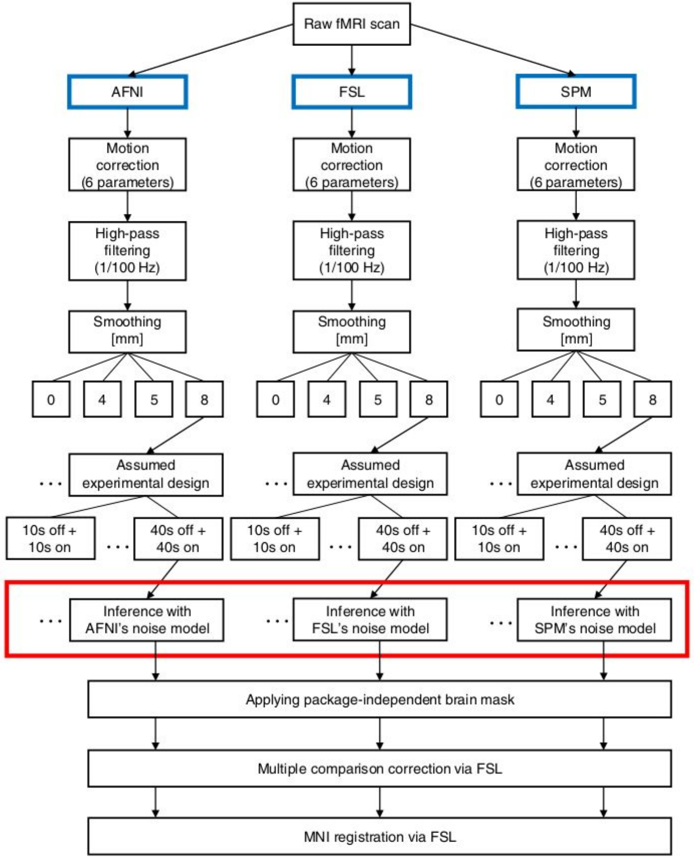


Fig. 4 The employed analyses pipelines. For SPM, we investigated both the default noise model and the alternative noise model: FAST. The noise models used by AFNI, FSL, and SPM were the only relevant difference (marked in a red box)

Analysis

Dummy design approach:

take resting state MRI data and fit a GLM on it as if it were task fMRI

H0:

any activation you see is a false positive

Advantage:

using real data with real underlying noise structure

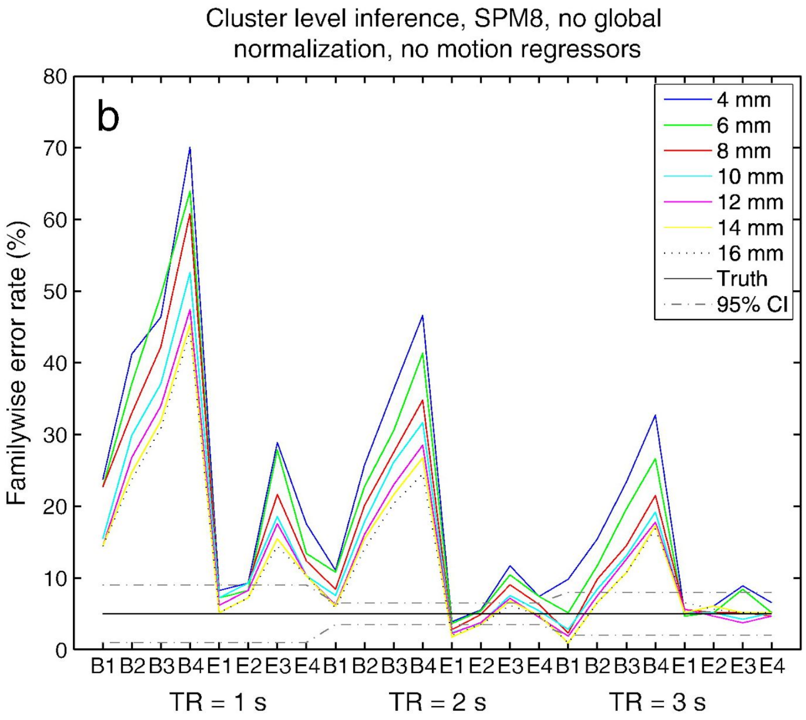
Analysis

See Eklund's papers

- SPM
- SPM, AFNI, FSL subject level
- Cluster F...

TLDR: Neuroskeptics posts about it

- Post 1
- Post 2
- Post 3
- Post 4



Analysis

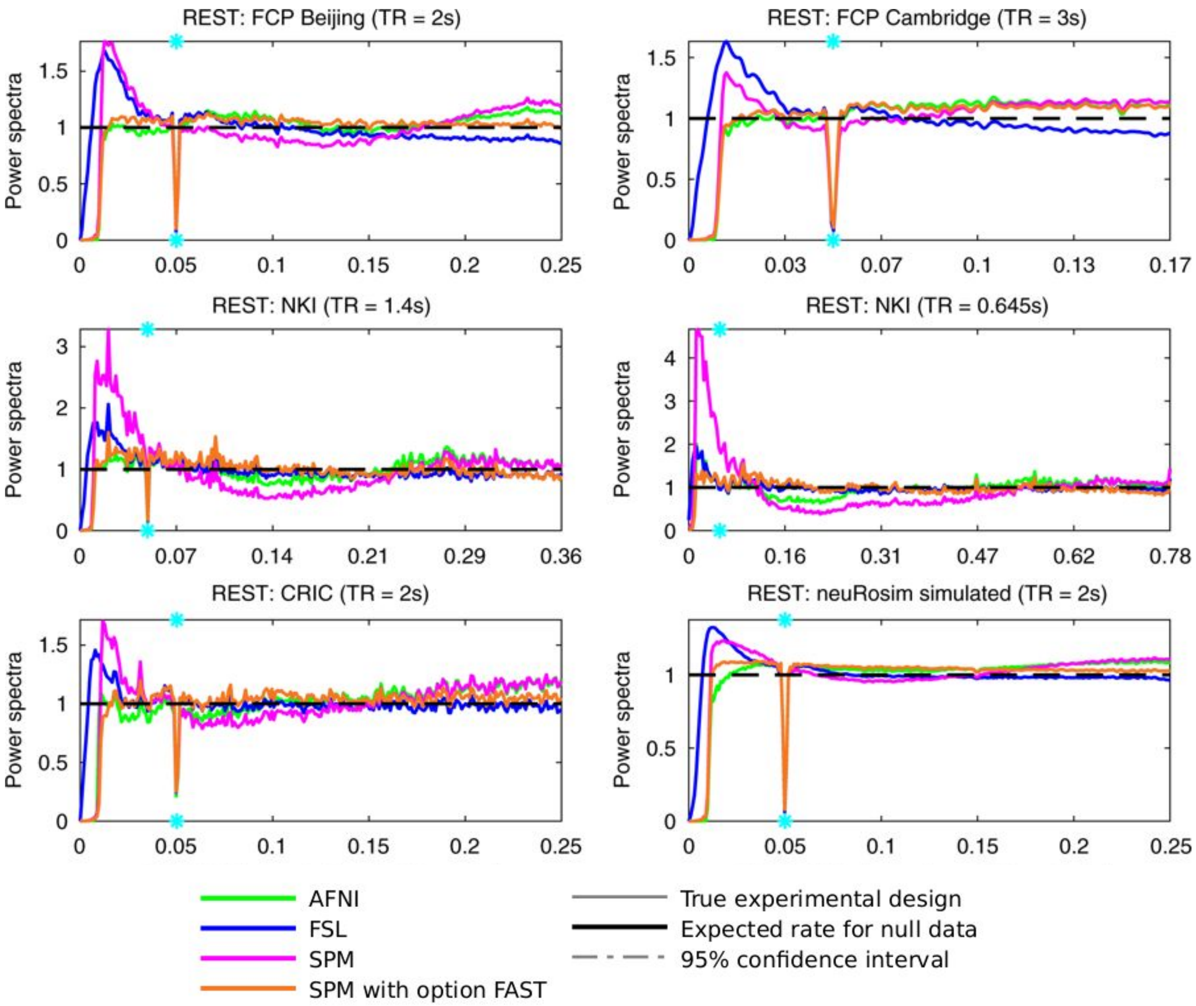
(1) the power spectra of the GLM residuals: should be flat

(2) the spatial distribution of significant clusters

(3) the average percentage of significant voxels within the brain mask

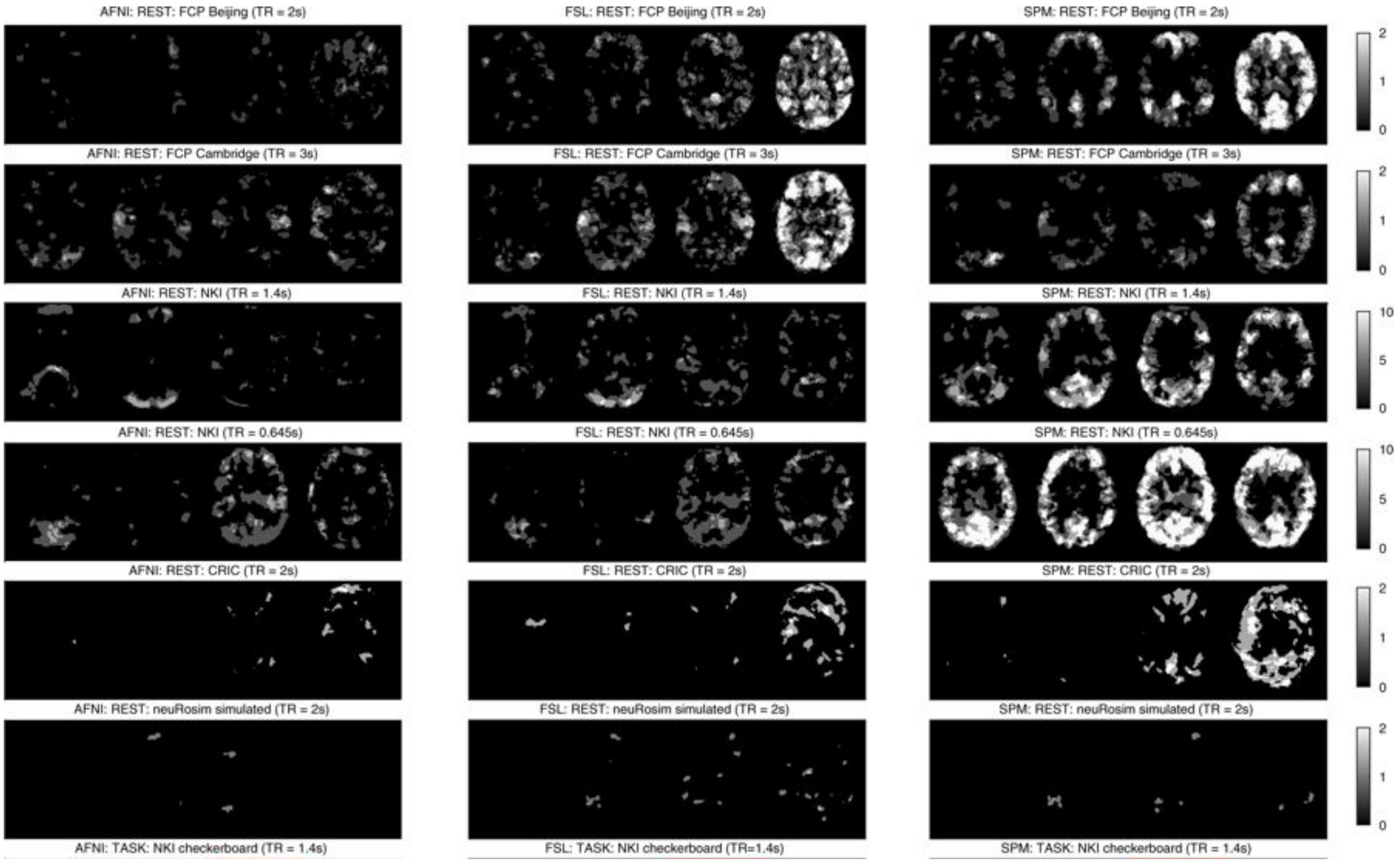
(4) the positive rate: proportion of subjects with at least one significant cluster

Results

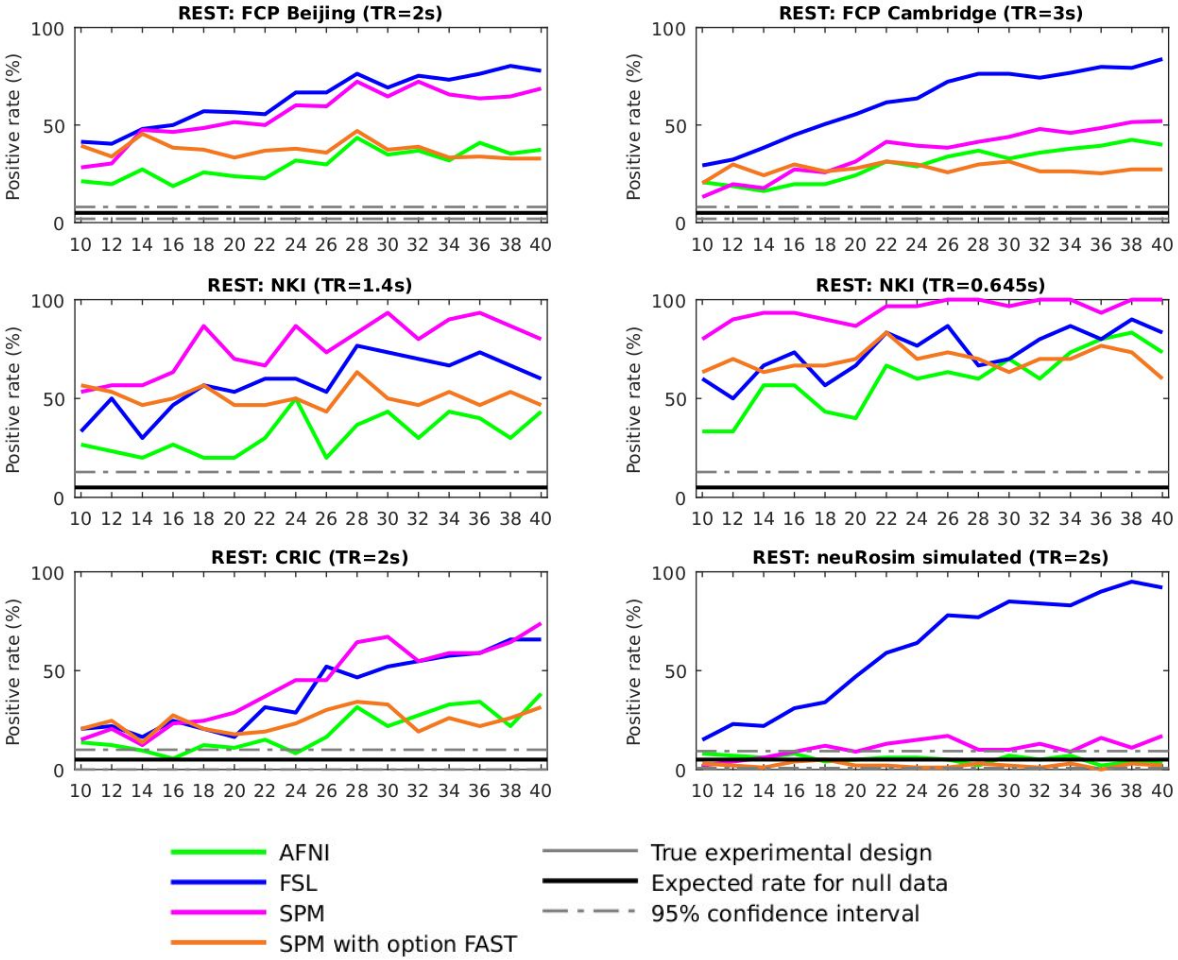


REST: FCP Beijing (TR = 2s)
REST: FCP Cambridge (TR = 3s)
REST: NKI (TR = 1.4s)
REST: NKI (TR = 0.645s)
REST: CRIC (TR = 2s)
REST: neuRosim simulated (TR = 2s)
Power spectra
AFNI
FSL
SPM
SPM with option FAST
True experimental design
Expected rate for null data
95% confidence interval

Results


AFNI: REST: FCP Beijing (TR = 2s)
FSL: REST: FCP Beijing (TR = 2s)
SPM: REST: FCP Beijing (TR = 2s)
AFNI: REST: FCP Cambridge (TR = 3s)
FSL: REST: FCP Cambridge (TR = 3s)
SPM: REST: FCP Cambridge (TR = 3s)
AFNI: REST: NKI (TR = 1.4s)
FSL: REST: NKI (TR = 1.4s)
SPM: REST: NKI (TR = 1.4s)
AFNI: REST: NKI (TR = 0.645s)
FSL: REST: NKI (TR = 0.645s)
SPM: REST: NKI (TR = 0.645s)
AFNI: REST: CRIC (TR = 2s)
FSL: REST: CRIC (TR = 2s)
SPM: REST: CRIC (TR = 2s)
AFNI: REST: neuRosim simulated (TR = 2s)
FSL: REST: neuRosim simulated (TR = 2s)
SPM: REST: neuRosim simulated (TR = 2s)
AFNI: TASK: NKI checkerboard (TR = 1.4s)
FSL: TASK: NKI checkerboard (TR=1.4s)
SPM: TASK: NKI checkerboard (TR = 1.4s)
2
1
0
10
5
0

Results



REST: FCP Beijing (TR=2s)
REST: FCP Cambridge (TR=3s)
REST: NKI (TR=1.4s)
REST: NKI (TR=0.645s)
REST: CRIC (TR=2s)
REST: neuRosim simulated (TR=2s)
Positive rate (%)
0
50
100
10 12 14 16 18 20 22 24 26 28 30 32 34 36 38 40
AFNI
FSL
SPM
SPM with option FAST
True experimental design
Expected rate for null data
95% confidence interval

Results

Do problem at the first level spread at the group level?

Results at group level compared summary statistics approach and mixed effect.

“*FWER for the mixed effects analyses was almost twice higher than FWER for the summary statistic analyses.*

The use of AFNI’s pre-whitening led to highest FWER (????), while FAST led to lower FWER than the SPM’s default approach.”

Conclusion

When using SPM go FAST… Or go home.

Check your residuals: authors provide function on github repo (sort of works)

Check model fit and compare models: MACS toolbox