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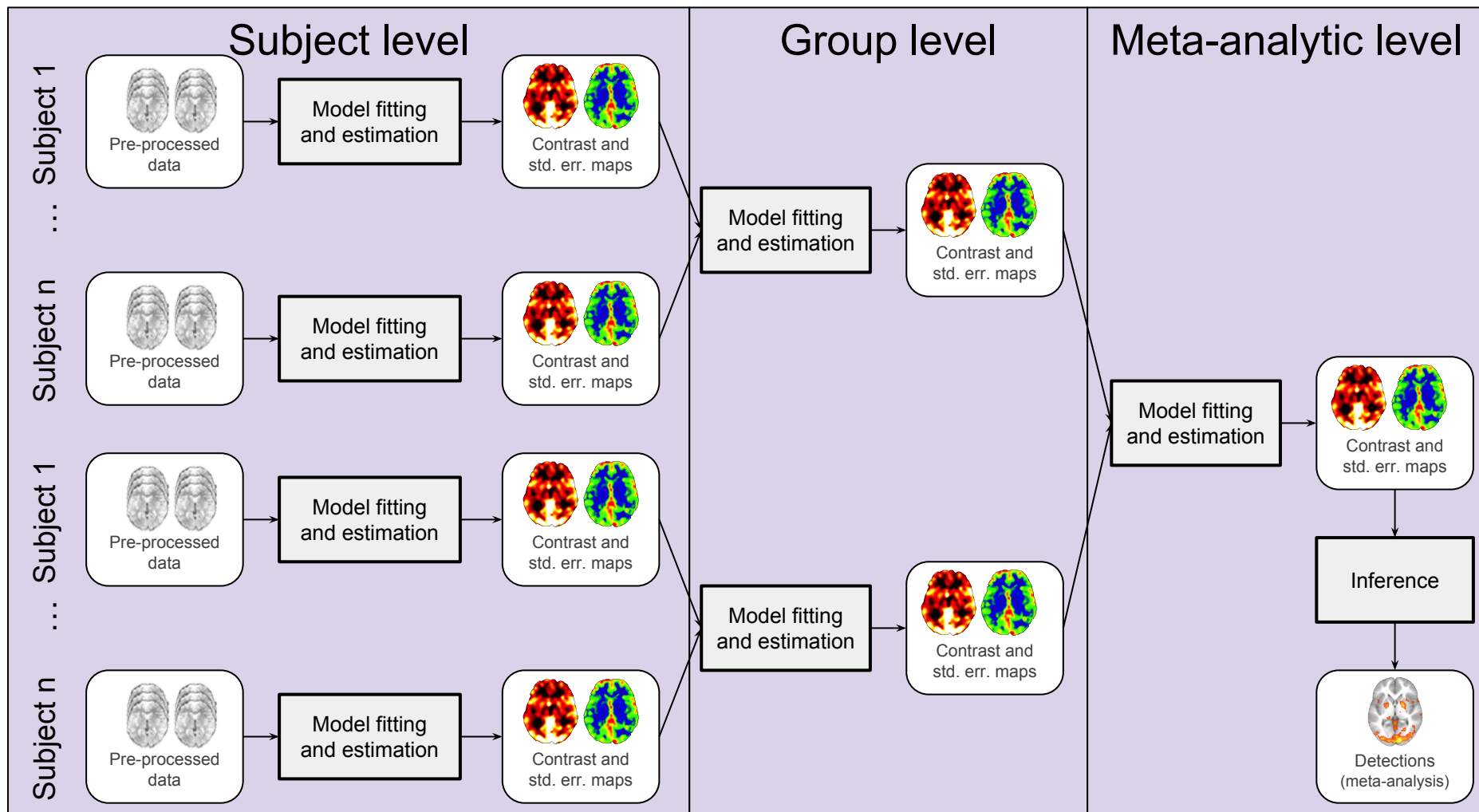


Validity of summary statistics-based mixed-effects group fMRI

Camille Maumet and Thomas Nichols

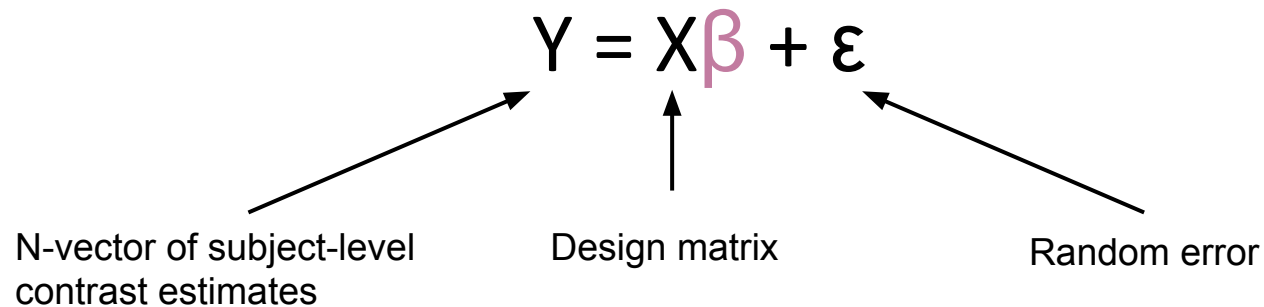
1. University of Rennes, Inria, CNRS, Inserm, IRISA, Rennes, France.
2. Oxford Big Data Institute, University of Oxford, Oxford, UK.

What is the link between meta-analysis and group fMRI?

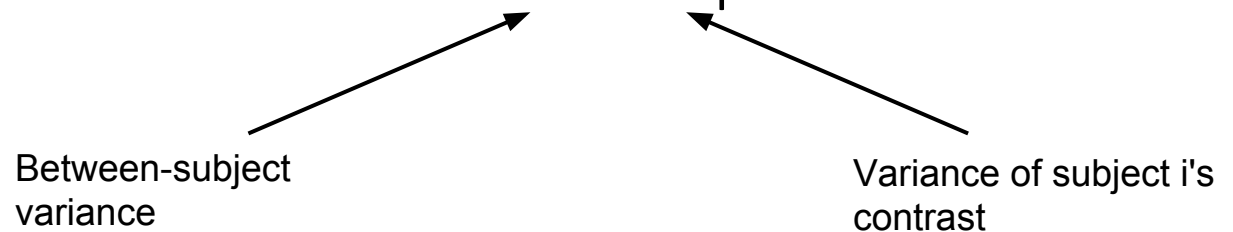


Methods

GLM for group fMRI



$$\text{where } \varepsilon \sim N(0, \tau^2 + \sigma_i^2)$$



Solving the GLM: OLS vs. FGLS

$$Y = X\beta + \varepsilon, \quad \text{where } \varepsilon \sim N(0, \tau^2 + \sigma^2_i)$$

Assuming $\tau^2 + \sigma^2_i$ constant, **Ordinary Least Squares (OLS)** gives the following group statistic estimate:

$$T = \left(\sum_{i=1}^N \frac{Y_i}{\sqrt{N}} \right) / \widehat{\sigma}_C^2$$

where $\widehat{\sigma}_C^2$ is the usual one-sample variance.

$$\text{Under } H_0: T \sim \mathcal{T}_{N-1}$$

Solving the GLM: OLS vs. FGLS

$$Y = X\beta + \varepsilon, \quad \text{where } \varepsilon \sim N(0, \tau^2 + \sigma^2_i)$$







Feasible Generalised Least Squares (FGLS) gives the following group statistic estimate:

$$T = \left(\sum \kappa_i Y_i \right) / \sqrt{\sum_{i=1}^N \kappa_i} \quad \text{where } \kappa_i = 1/(\hat{\tau}^2 + s_i^2)$$

where s_i^2 is the study i 's sampling variance.

In large samples, under H_0 : $T \sim \mathcal{T}_{N-1}$

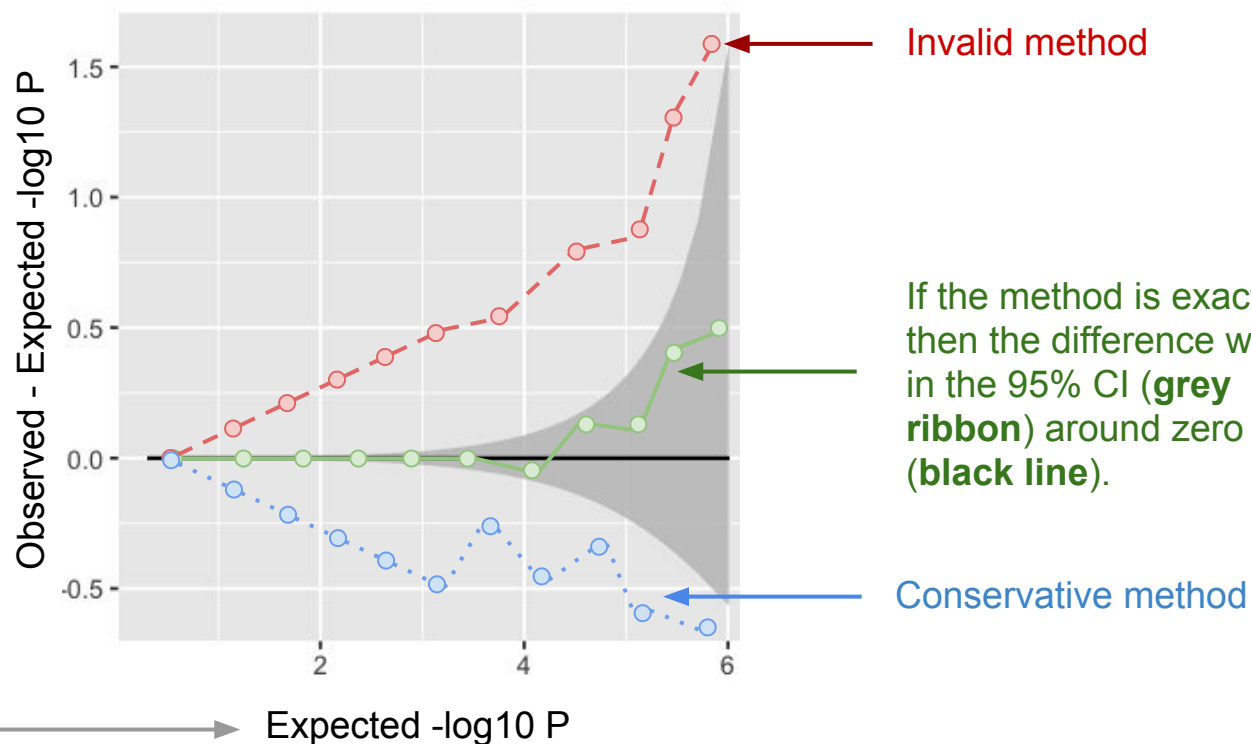
Solving the GLM: OLS vs. FGLS

	Statistic	Assumptions	Implementation
OLS	$T = \left(\sum_{i=1}^N \frac{Y_i}{\sqrt{N}} \right) / \widehat{\sigma}_C^2$	$\tau^2 + \sigma_i^2$ constant	 'One-sample t-test' (default)  'Mixed effects: Simple OLS'  3dttest++
FGLS	$T = \left(\sum \kappa_i Y_i \right) / \sqrt{\sum_{i=1}^N \kappa_i}$	Large samples	 'Mixed-effects analysis'  'Mixed effects: FLAME1' (default)  3dMEMA

Goal: assess the validity of OLS and FGLS under violation of their assumption

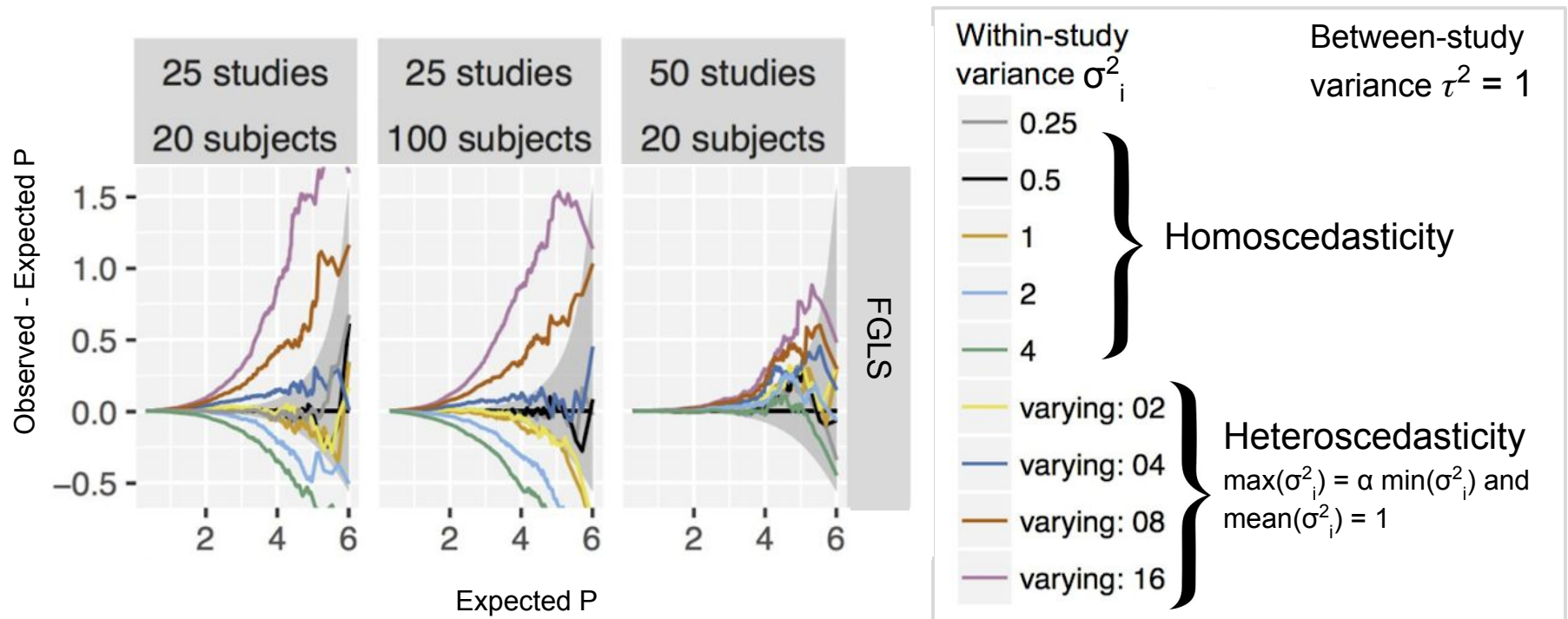
Method: Monte Carlo simulations

Difference between sorted observed P-values (computed by OLS or FGLS) and sorted expected $-\log_{10}$ P-values.



"True" $-\log_{10}$ P-values computed empirically by MC simulations

And in meta-analyses?



Question: Does this issue also affects group fMRI studies?

Simulations

Between- and within-subject variances in real fMRI data

21 studies investigating pain

Study	# subjects	# outliers	Mean τ^2	Mean σ^2_{in}	Max/Min σ^2_{in} ratio	Mean σ^2_{out}
01	25	2	354	100	4	282
02	25	1	680	100	5	317
03	20	2	800	100	5	281
04	20	3	886		9	347
05	9	0	1802		3	-
...
Summary		0-15%	18-170	100	2-9	164-300

Simulation setup

$N \in \{ 25, 50 \}$ subjects

$\tau^2 = 1$ and $\text{mean}(\sigma^2_{\text{in}}) = 1$

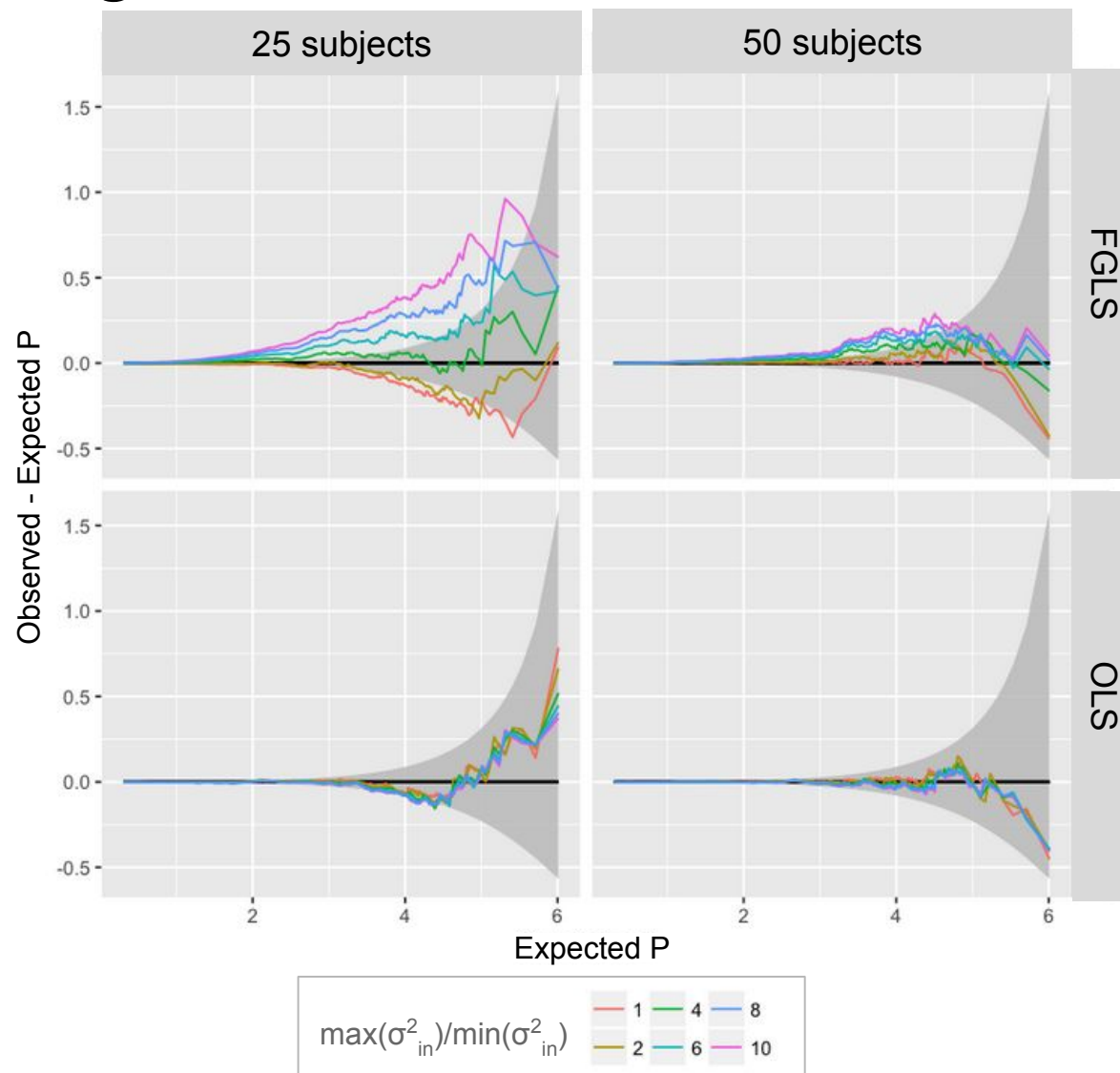
Two settings for the within-subject variance:

- $\max(\sigma^2_{\text{in}}) / \min(\sigma^2_{\text{in}}) \in \{ 1, 2, 4, 6, 8, 10 \}$
- 16% of outliers with $\sigma^2_{\text{out}} \in \{ 0.25, 0.5, 2, 4 \}$

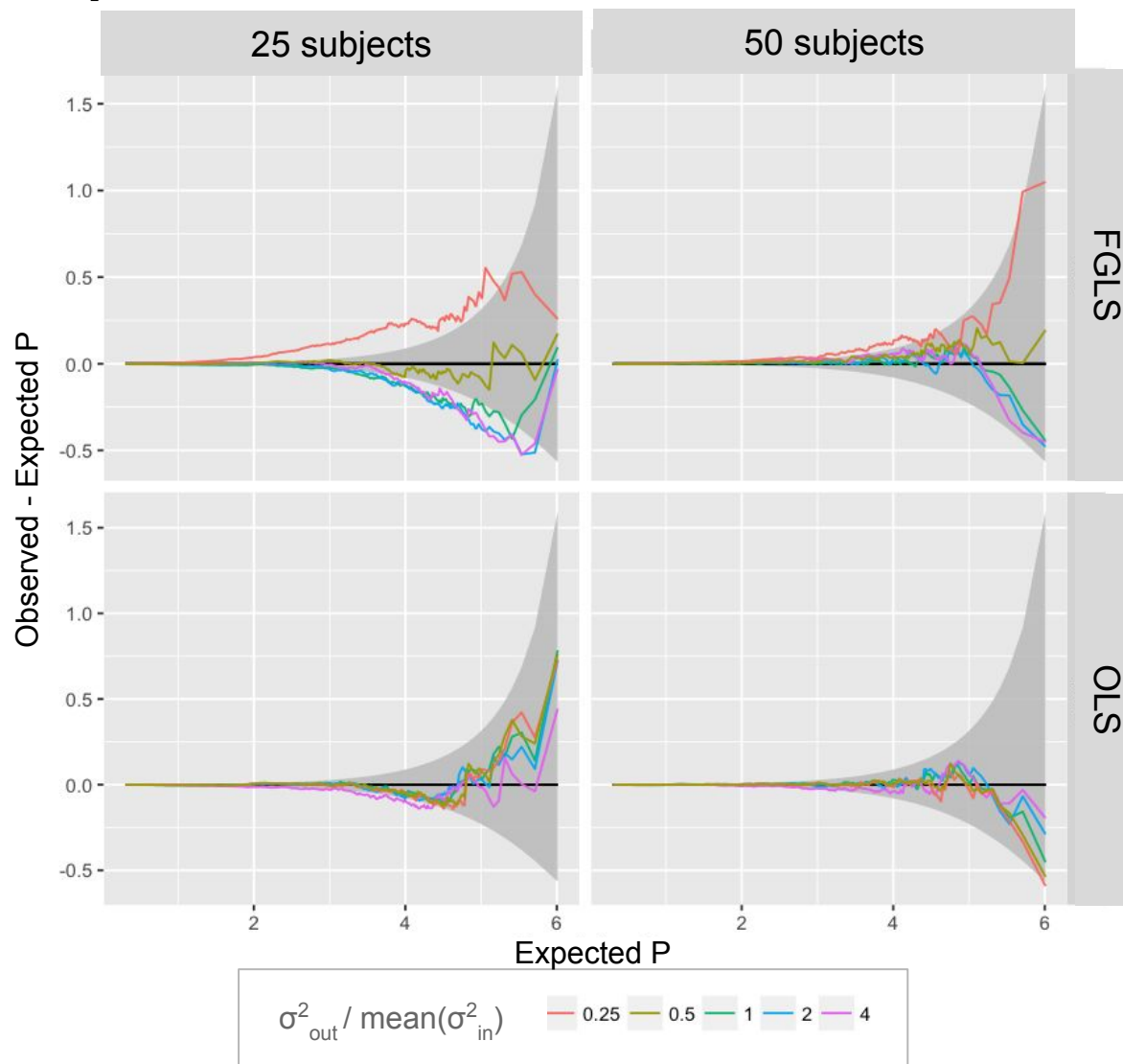
10^6 realisations

Results

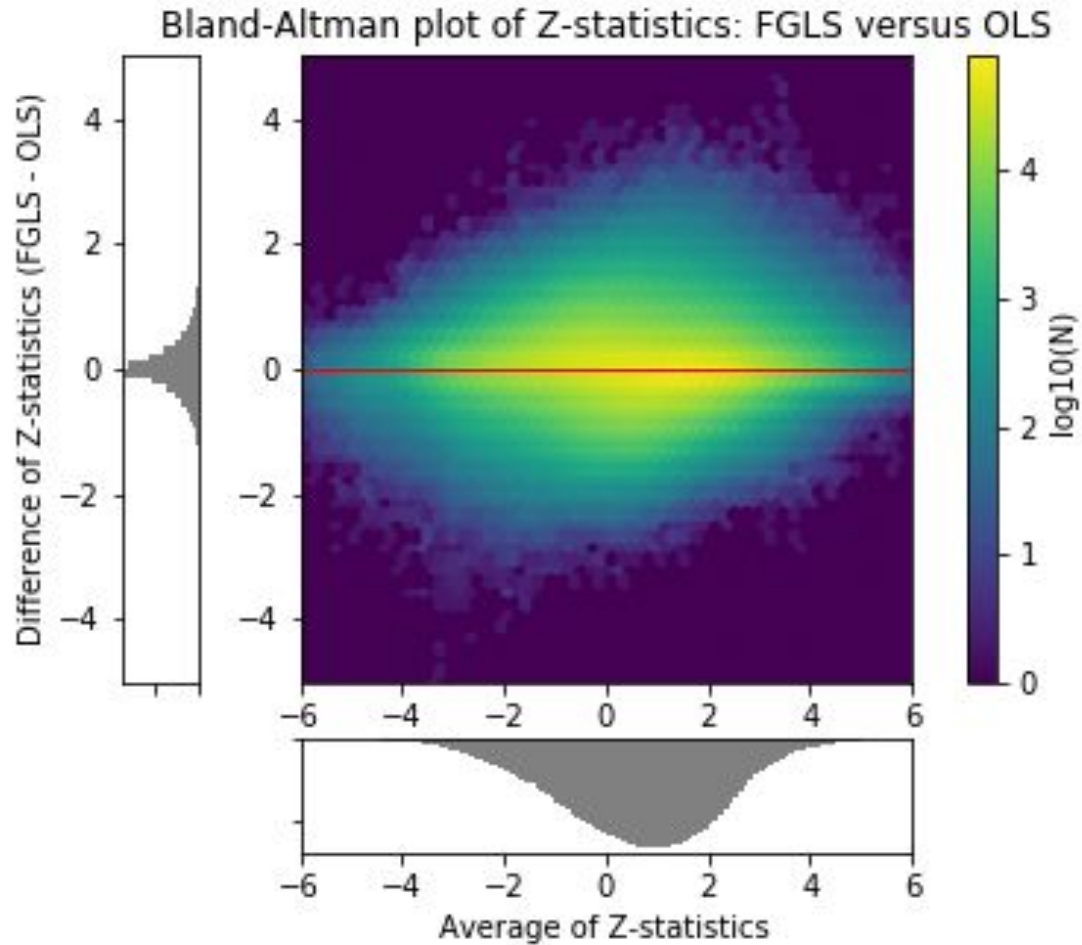
Varying levels of heteroscedasticity



In the presence of outliers



Real data



Conclusions

FGLS can be invalid in small samples, especially in the presence of **strong heteroscedasticity** or **'low variance' outliers**.

RFX remained valid in all studied settings.

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