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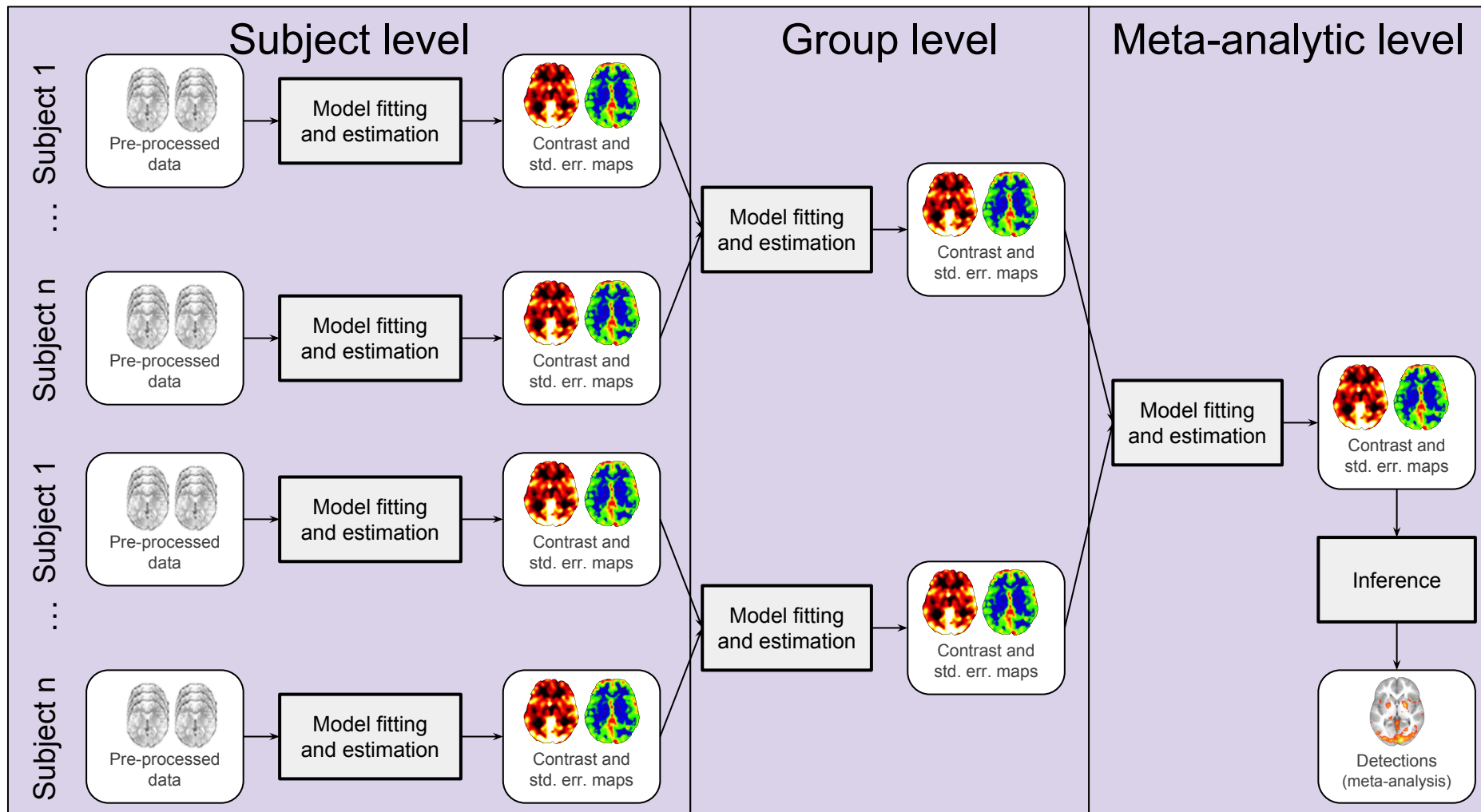


Validity of summary statistics-based mixed-effects group fMRI

Camille Maumet and Thomas Nichols

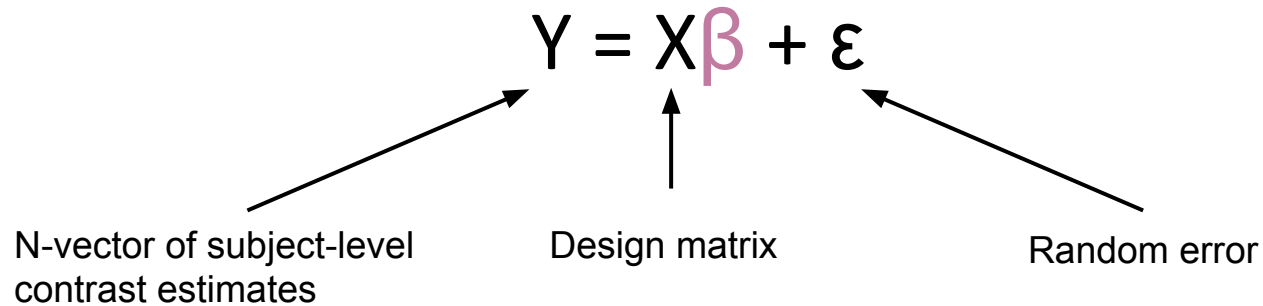
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2. Oxford Big Data Institute, University of Oxford, Oxford, UK.

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

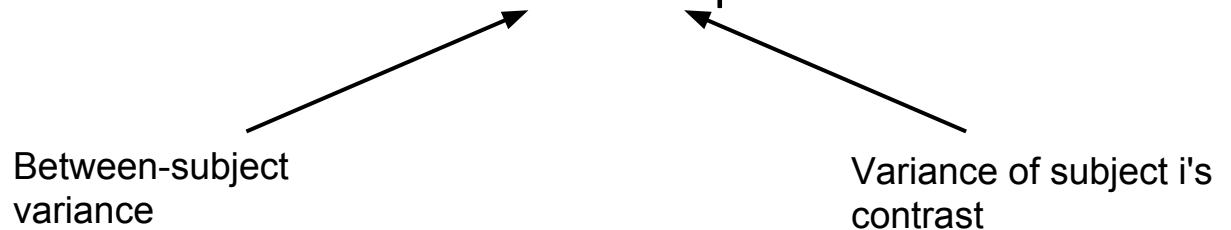


Methods

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.

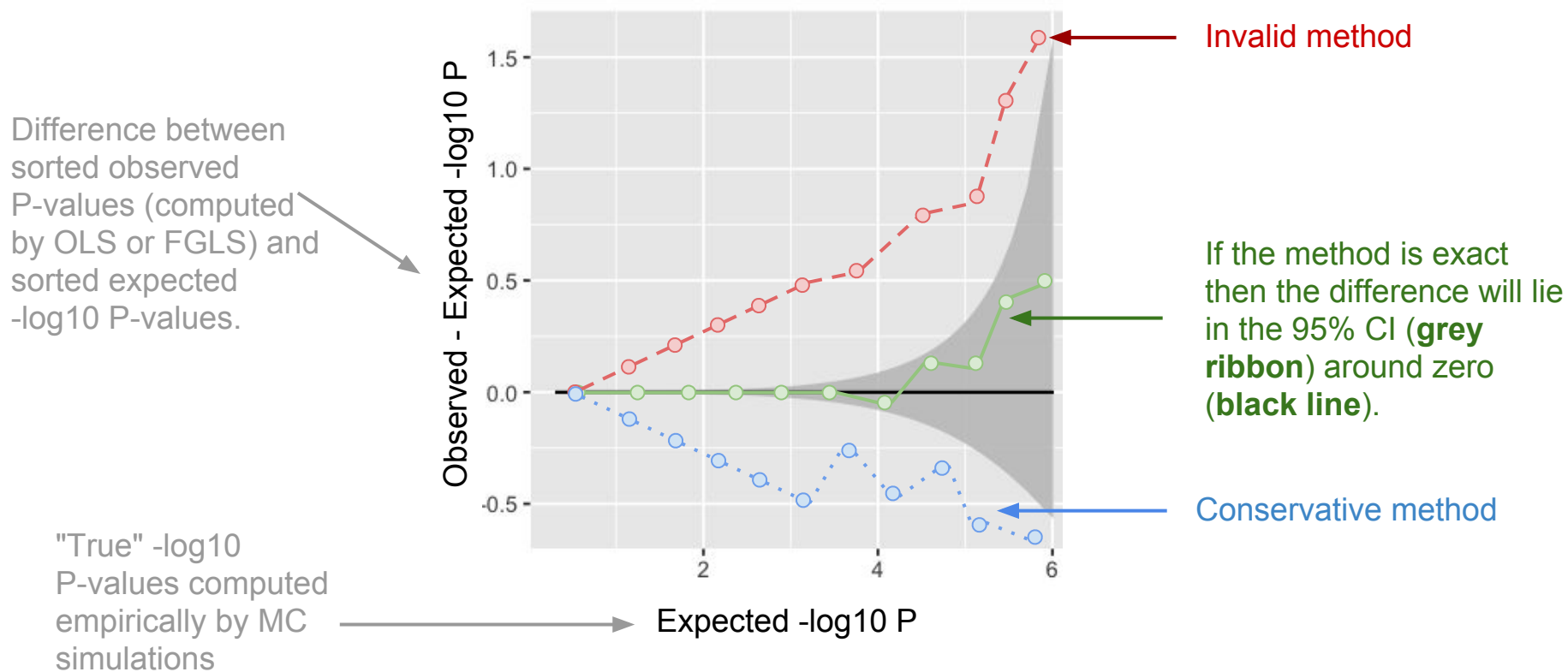
In large samples, under H_0 : $T \sim \mathcal{T}_{N-1}$

Solving the GLM: OLS vs. FGLS

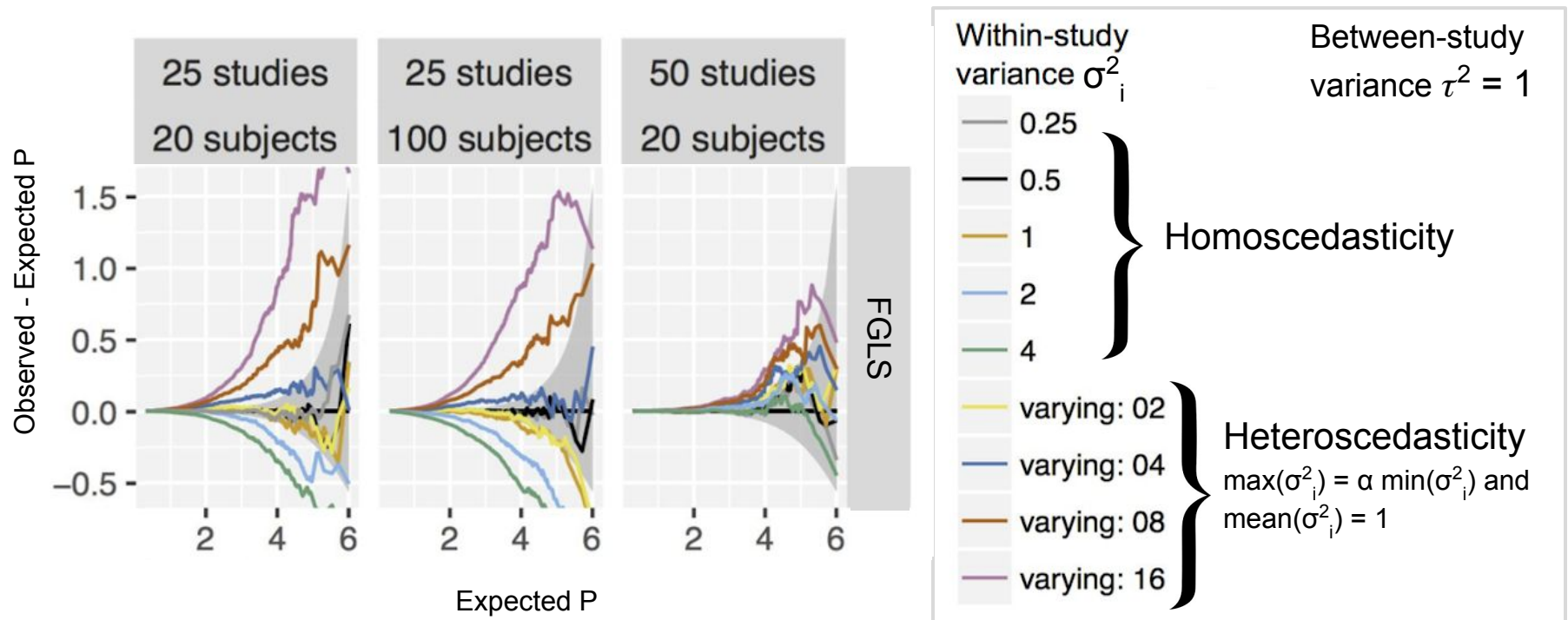
	Statistic	Assumptions	Implementation
OLS	$T = \left(\sum_{i=1}^N \frac{Y_i}{\sqrt{N}} \right) / \widehat{\sigma}_C^2$	$\tau^2 + \sigma_i^2$ constant	 'One-sample t-test' (default)  'Mixed effects: Simple OLS'  3dttest++
FGLS	$T = \left(\sum \kappa_i Y_i \right) / \sqrt{\sum_{i=1}^N \kappa_i}$	Large samples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



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

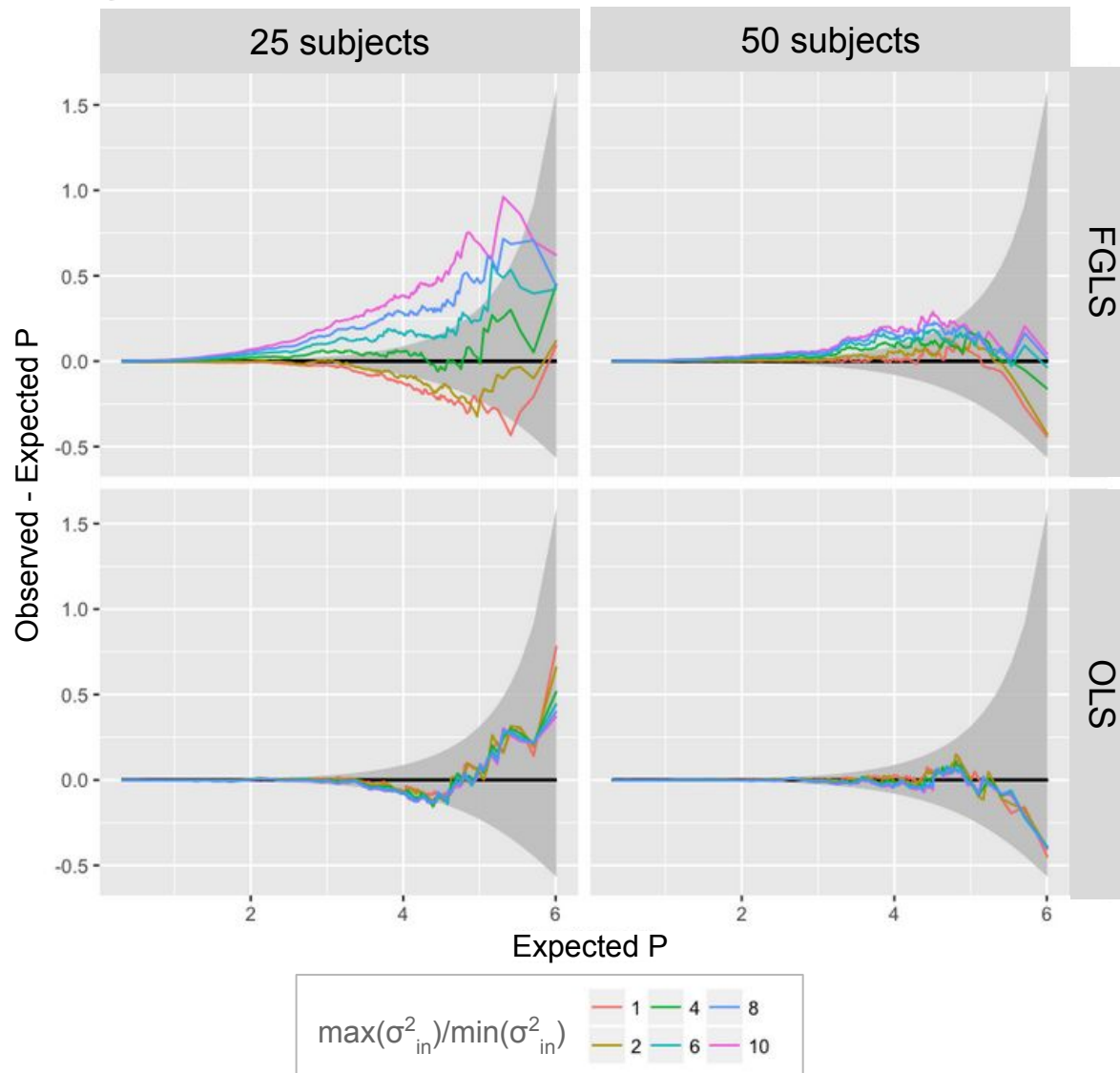
Two settings for the within-subject variance:

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

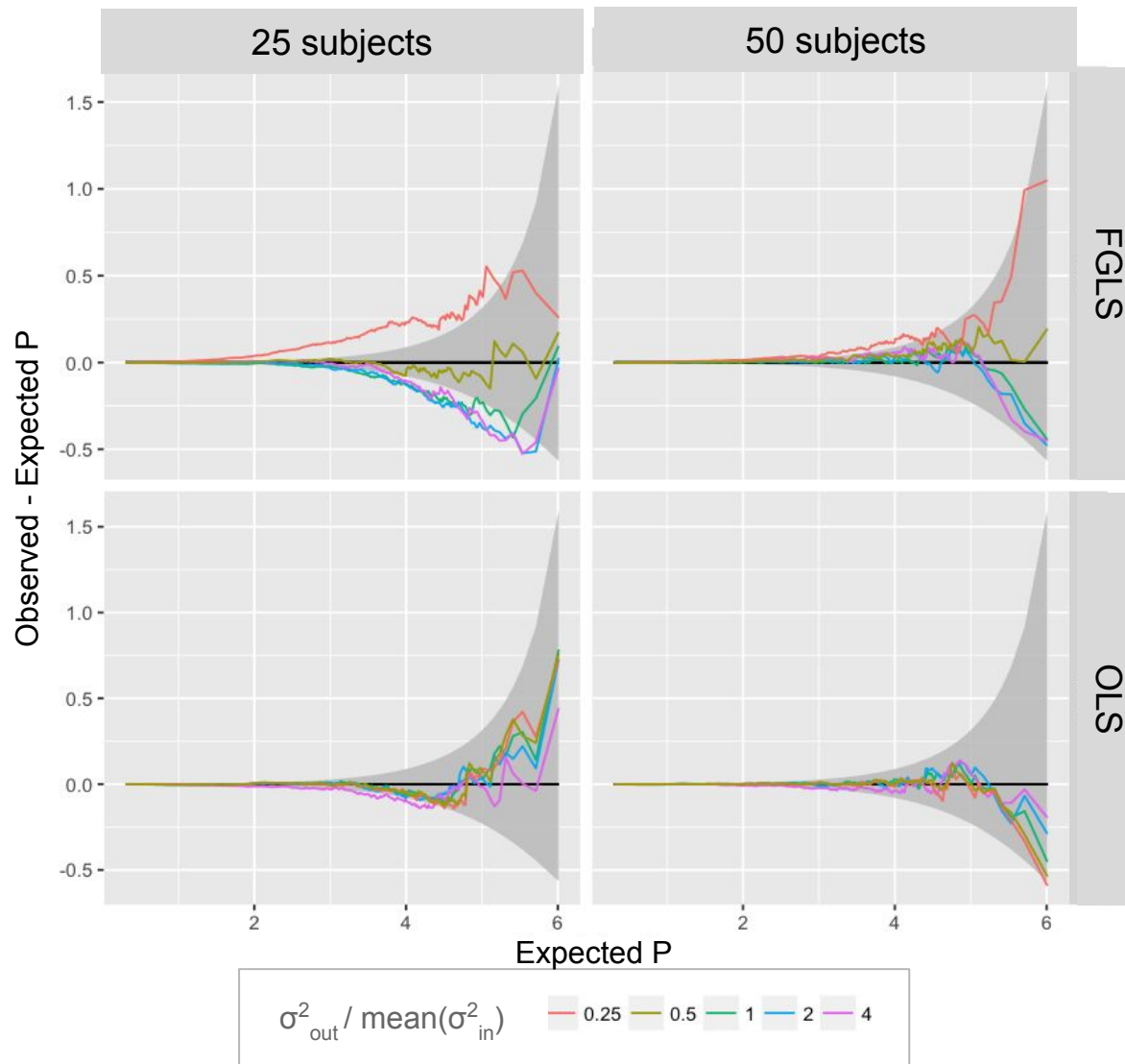
10^6 realisations

Results

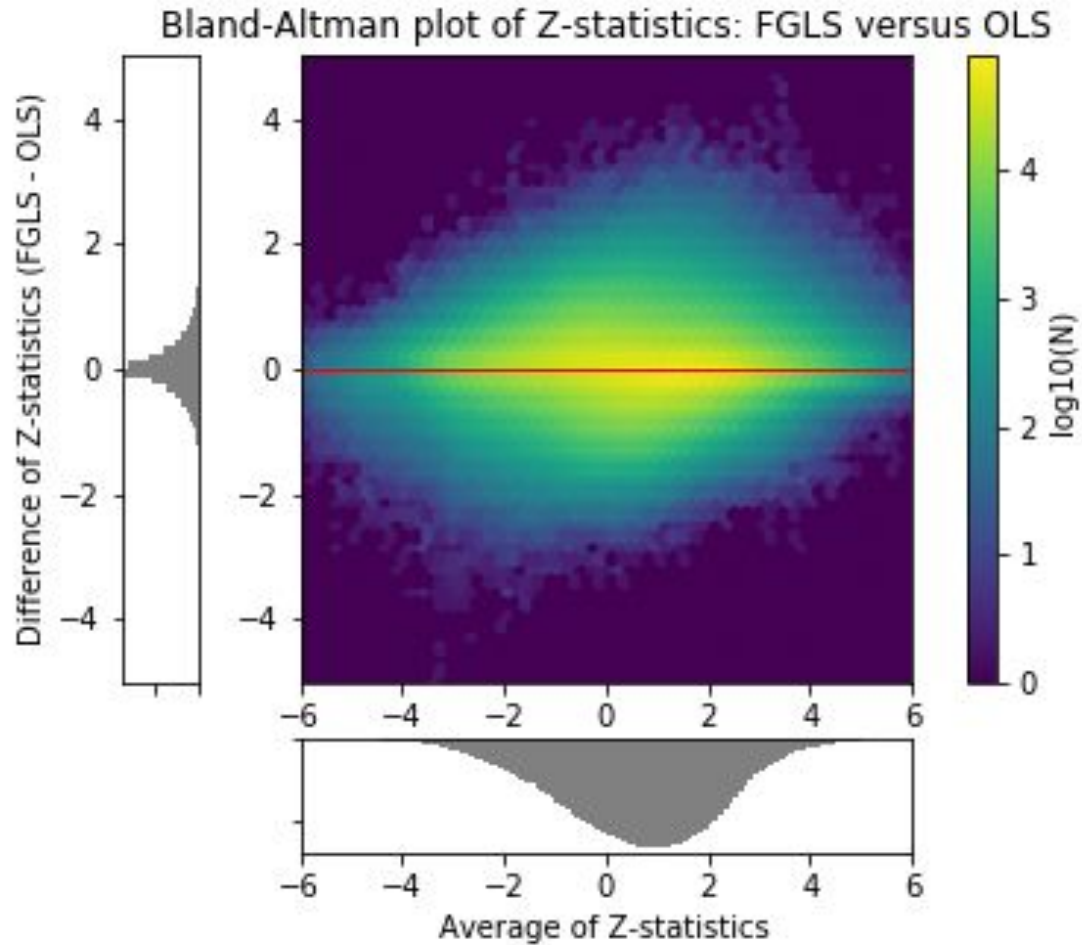
Varying levels of heteroscedasticity



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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