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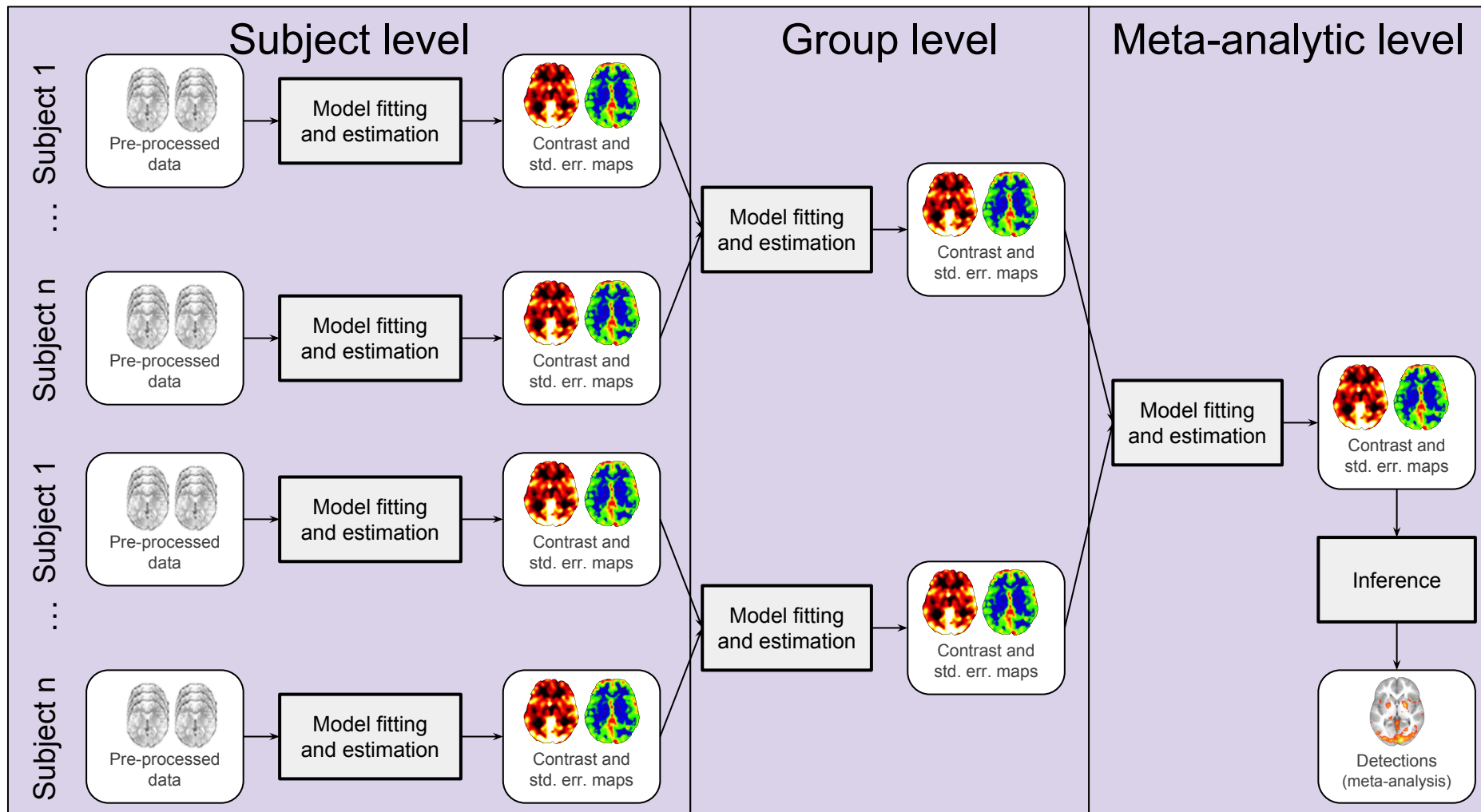


# Validity of summary statistics-based mixed-effects group fMRI

Camille Maumet and Thomas Nichols

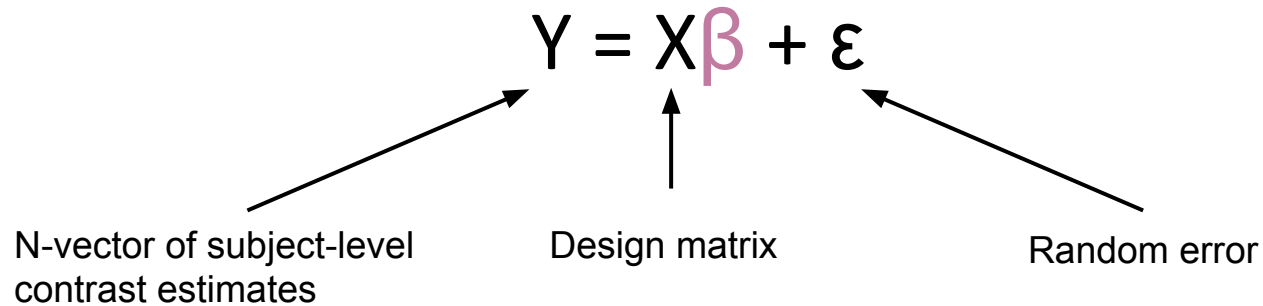
1. University of Rennes, Inria, CNRS, Inserm, IRISA, Rennes, France.
2. Oxford Big Data Institute, University of Oxford, Oxford, UK.

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

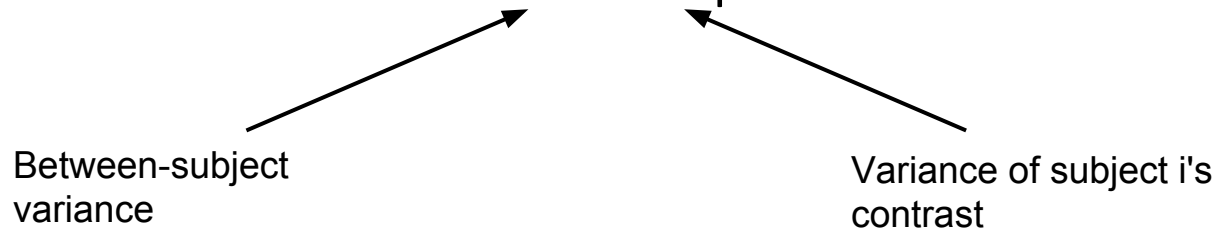


# Methods

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

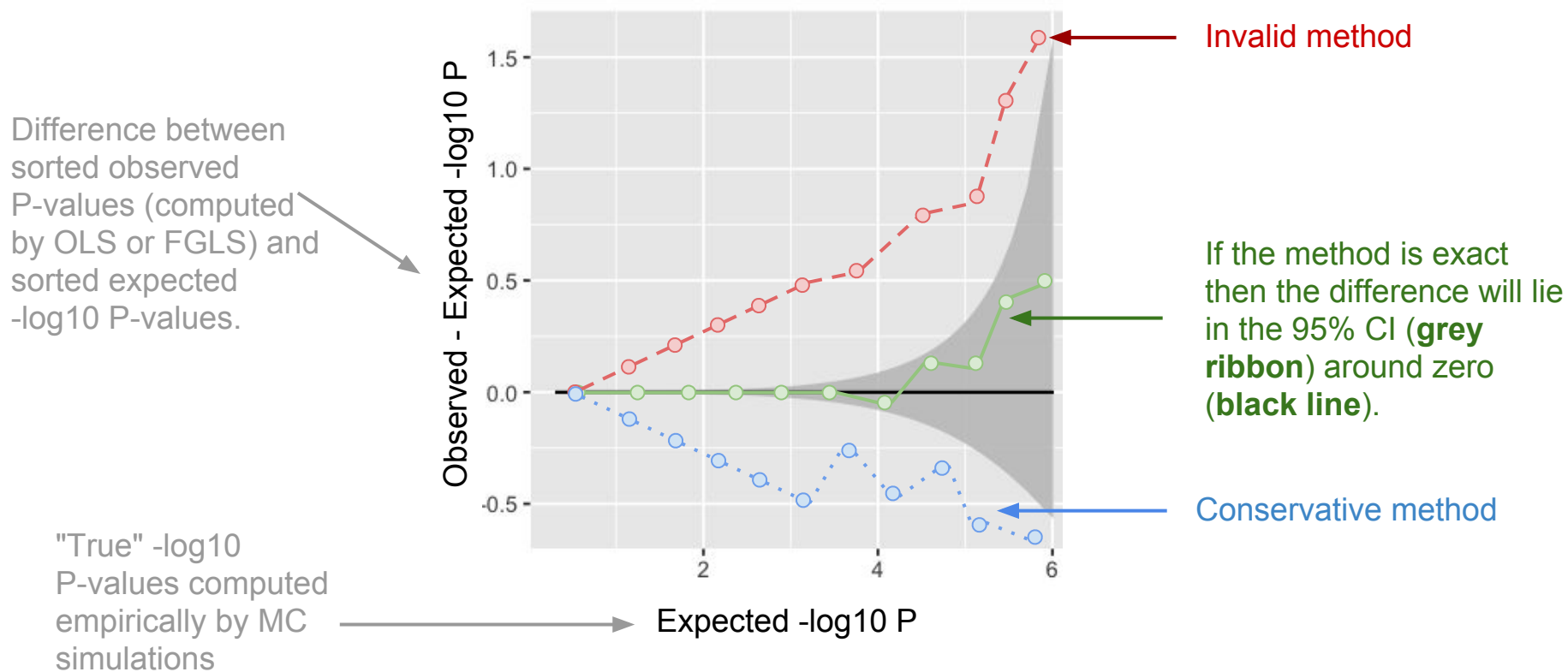
# Solving the GLM: OLS vs. FGLS

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

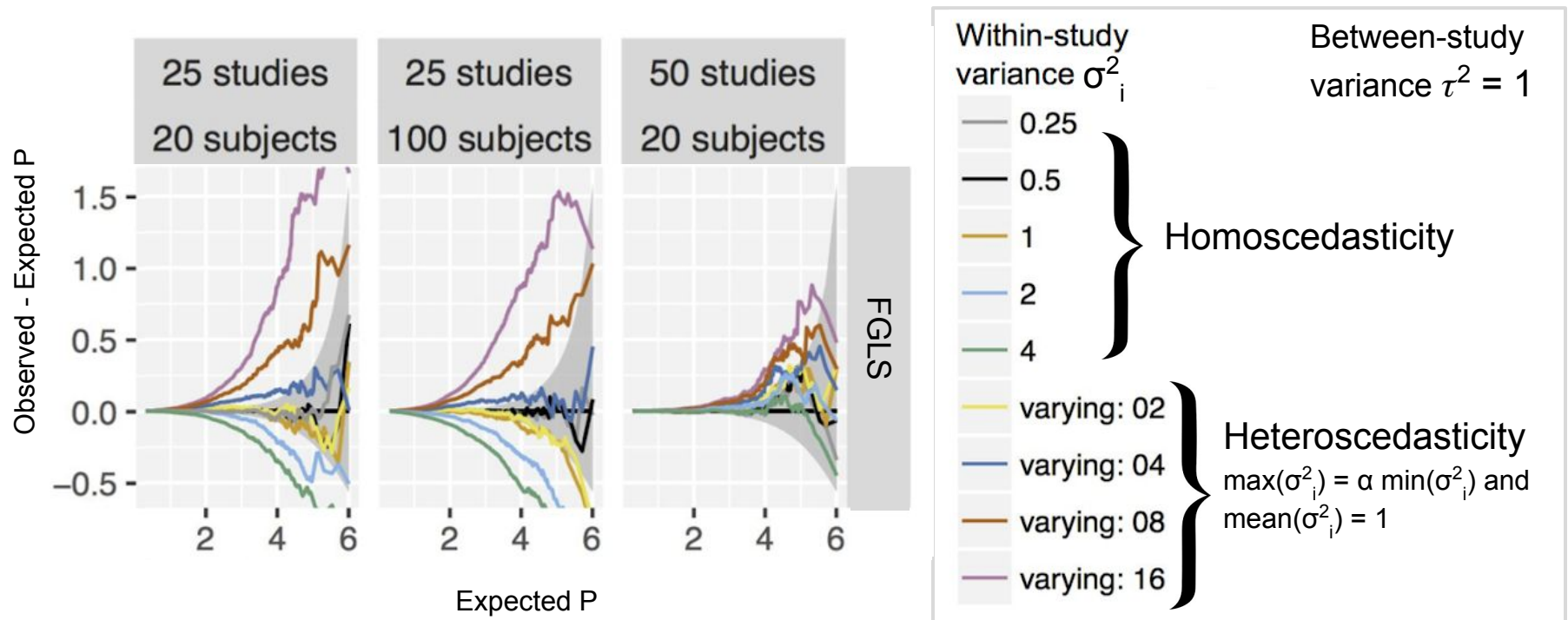


# Goal: assess the validity of OLS and FGLS under violation of their assumption

## 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 $\tau^2$	Mean $\sigma^2_{in}$	Max/Min $\sigma^2_{in}$ ratio	Mean $\sigma^2_{out}$
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	-
...	...	...	...	...	...	...
<b>Summary</b>		<b>0-15%</b>	<b>18-170</b>	<b>100</b>	<b>2-9</b>	<b>164-300</b>

# Simulation setup

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

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

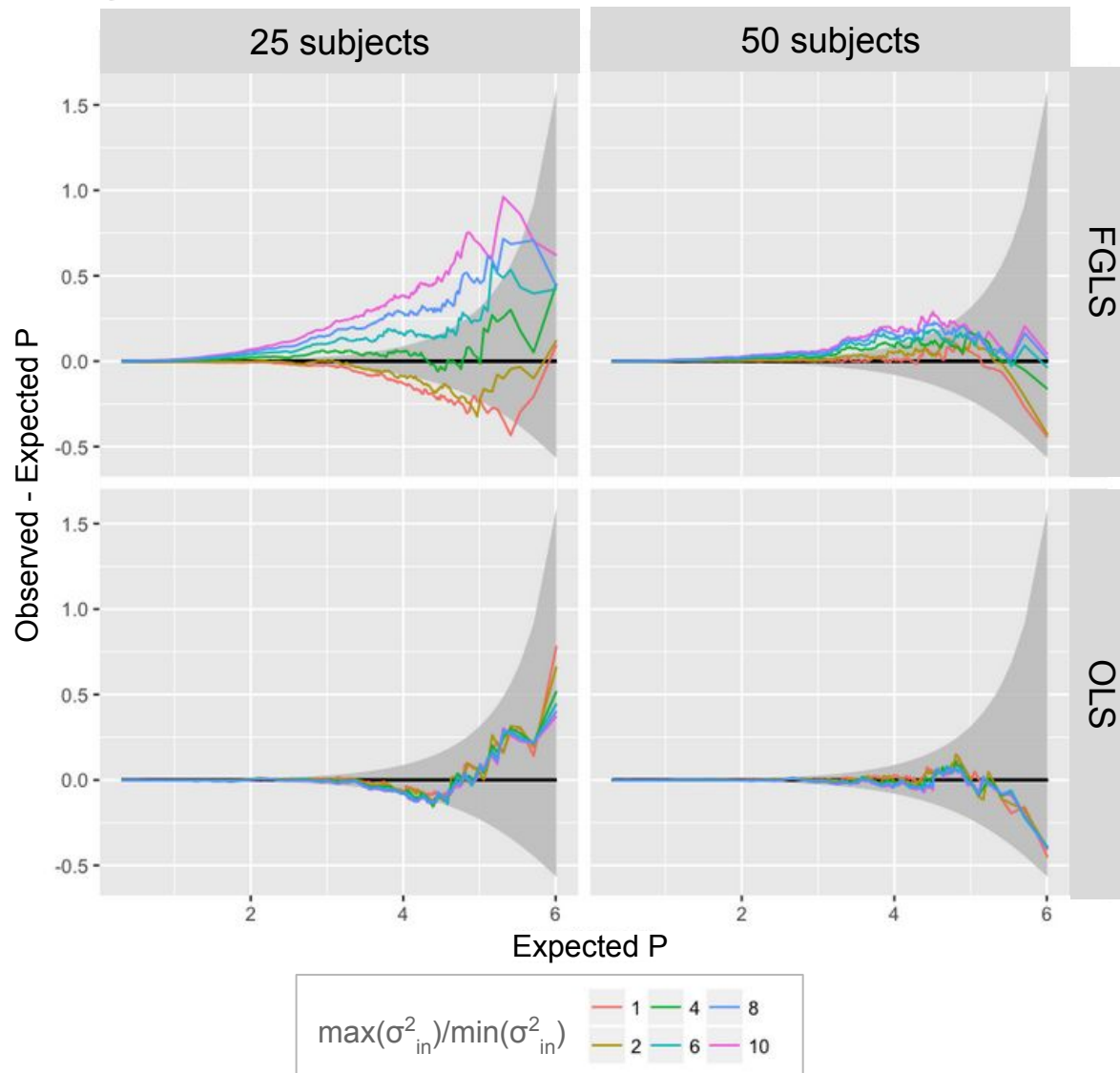
Two settings for the within-subject variance:

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

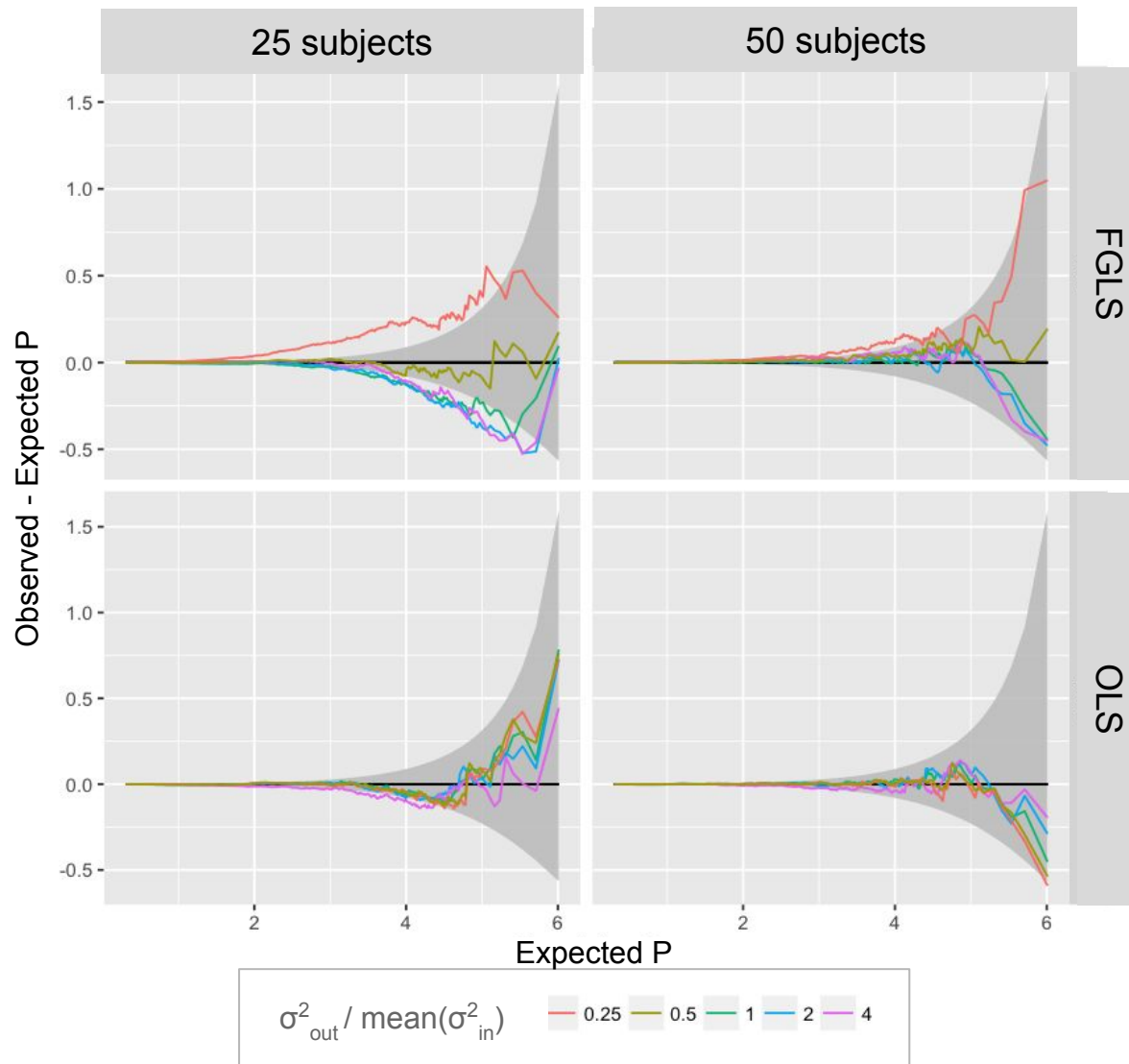
$10^6$  realisations

# Results

# Varying levels of heteroscedasticity

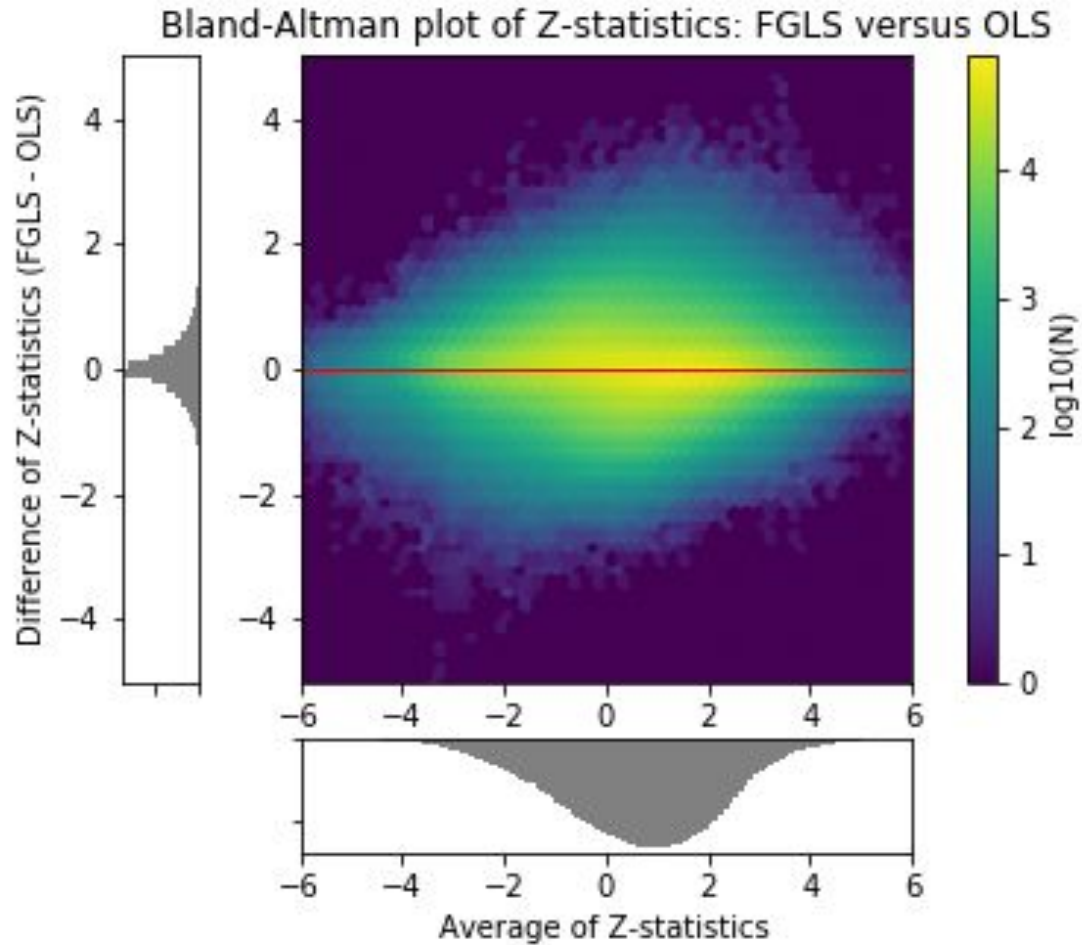


# In the presence of outliers





# 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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