1. Detecting brain activation using fMRI

- Functional magnetic resonance imaging (fMRI) enables to detect brain regions that become activated during specific cognitive tasks such as reading or solving equations.
- The number of fMRI studies on different cognitive functions has increased substantially. However:
  - Sample sizes are typically small
  - Reproducibility is often limited
- Understanding the brain functioning requires integration of data across studies and labs.

- Meta-analysis is promising tool to achieve this goal.

Two studies with same research question, different results?

2. Aggregating within and over studies

- At study level, estimates for the degree of activation in each brain region need to be pooled over subjects.
- These pooled estimates are further investigated in a second level group analysis.
- **Fixed pooling of subjects**: second level is ordinary average of all first level estimates (no between subject variance).
- **Mixed pooling of subjects**: second level estimates are obtained within a full Bayesian framework with non-informative priors.

- A meta-analysis aggregates different studies.
- **ALE meta-analysis** investigates the consistency of the spatial location of activation peaks in the brain.
- **ES-SDM** is a random effects meta-analysis that averages effect sizes of activation peaks over studies and takes into account within and between study variance.
- A fixed effects meta-analysis proceeds as ES-SDM but only takes into account the within study variance.

3. Goal of our study

- We study the impact of (1) the way subjects are pooled within a study and (2) the meta-analysis method for pooling studies on the false positive rate (FPR), power and spatial accuracy.
- Consider a benchmark (B) representing an area of true brain activation - depicted by the white square in the figure below.
- The black: false positives
- Gray: false negatives (i.e. lack of power)

Overlap with benchmark (i.e. accuracy):

$$V_{m,B} = V_{m} + V_{B} - V_{m,B}$$

With V=voxels that are declared significant.

4. Method and design

- Real data from the Human Connectome Project[3]: 80 subjects scanned doing a language and math task.
- We create 8 studies with respectively 7, 8, 9, 10, 11, 12 & 13 subjects by random subsampling (without replacement) from the total pool of subjects. Different methods for aggregating within and over studies are combined.
- Group analysis on all 80 subjects ⇒ benchmark.
- FPR, power and overlap are calculated on the result of each meta-analysis with the benchmark image.
- Subsampling is repeated 11 times.

5. Results

- A meta-analysis is summarizing 8 studies.
- Comparison of benchmark (B) to each meta-analysis (m). The blob represents the region of activation as detected by a meta-analysis (m).
- ALE: false positives
- ES-SDM: false negatives (i.e. lack of power)

6. Conclusion

Overall, the power and overlap is highest and FPR lowest for:

1. All meta-analyses based on pooling subjects through a mixed effects analysis.

Depending on the way subjects are pooled within study, there is an effect on the level of aggregating studies. In general we advise **not to use fixed effects pooling of subjects** unless for the purpose of pooling scanning sessions within subjects.

When pooling subjects using fixed effects, the order from best to worst performance is:

1. Random effects meta-analysis
2. Fixed effects meta-analysis
3. ALE meta-analysis

7. References

Acknowledgements: This work was carried out using the Stam Supercomputer Infrastructure at Ghent University, provided by the Flemish Supercomputer Center, funded by Ghent University, the Hercules Foundation and the Flemish Government - department EWI.

