FMRI group analysis

• Overview
• Fixed versus mixed effects
• Multiple sessions per subject
Similarities across modalities

1. Data acquisition
2. Data preprocessing
3. Single-subject analysis
4. Group-level analysis
5. Statistical inference

Same across modalities
Different across modalities
A simple example

Does the group activate on average?
A simple example

Does the group activate on average?
A simple example

Does the group activate on average?

\[ Y_k = X_k \beta_k + \epsilon_k \]

First-level GLM on Mark’s 4D FMRI data set
A simple example

Does the group activate on average?

\[ Y_k = X_k \beta_k + \epsilon_k \]
A simple example

Does the group activate on average?

\[ Y_k = X_k \beta_k + \epsilon_k \]

Mark’s within-subject variance
A simple example

Does the group activate on average?

\[ Y_k = X_k \beta_k + \epsilon_k \]

All first-level GLMs on 6 FMRI data set
Single Group Average

*Does the group activate on average?*
Single Group Average

Does the group activate on average?
Fixed versus mixed effects
Fixed-Effects Analysis

Do these exact 6 subjects activate on average?

- Consider only these 6 subjects
- estimate the mean across these subject
- only variance is within-subject variance

\[ Y_K = X_K \beta_K + \epsilon_K \]

\[ \beta_K = X_g \beta_g \]

Fixed Effects Analysis:
Mixed-Effects Analysis

Does the population activate on average?

- Consider the 6 subjects as samples from a wider population
- estimate the mean across the population
- between-subject variance accounts for random sampling

Mathematical model:

\[ Y_K = X_K \beta_K + \epsilon_K \]
\[ \beta_K = X_g \beta_g + \epsilon_g \]

Mixed-Effects Analysis:
Multiple sessions per subject
All-in-One Approach

- Could use one (huge) GLM to infer group difference
- difficult to ask sub-questions in isolation
- computationally demanding
- need to process again when new data is acquired
Summary Statistics Approach

In FEAT estimate levels one stage at a time

- At each level:
  - Inputs are summary stats from levels below (or FMRI data at the lowest level)
  - Outputs are summary stats or statistic maps for inference
  - Need to ensure formal equivalence between different approaches!
Unpaired Two-Group Difference

- We have two groups (e.g. 9 WashU, 7 Oxford) with different between-subject variance

*Is there a significant group difference?*

- estimate means
- estimate std-errors (FE or ME)
- test significance of difference in means
Unpaired Two-Group Difference

Is there a significant group difference?
Unpaired Two-Group Difference

Is there a significant group difference?
FLAME
FMRIB’s Local Analysis of Mixed Effects

- Fully Bayesian framework
  - Input COPES, VARCOPES & DOFs from lower-level
  - estimate COPES, VARCOPES & DOFs at current level
  - pass these up
- Infer and threshold at top level (Z-stat)
- Equivalent to All-in-One approach
FLAME Inference

- Default is:
  - FLAME1: fast approximation for all voxels

- Optional slower, slightly more accurate approach:
  - FLAME1+2:
    - FLAME1 for all voxels, FLAME2 for voxels close to threshold
    - FLAME2: MCMC sampling technique
Choosing Inference Approach

1. Fixed Effects
   Use for intermediate/top levels

2. Mixed Effects - OLS
   Use at top level: quick and less accurate

3. Mixed Effects - FLAME 1
   Use at top level: less quick but more accurate

4. Mixed Effects - FLAME 1+2
   Use at top level: slow but even more accurate
FLAME vs. OLS

- allow different within-level variances (e.g. patients vs. controls)
- allow non-balanced designs (e.g. containing behavioral scores)
- allow un-equal group sizes
FLAME vs. OLS

- Two ways in which FLAME can give different Z-stats compared to OLS:
  - *higher Z* due to increased efficiency from using lower-level variance heterogeneity
FLAME vs. OLS

- Two ways in which FLAME can give different Z-stats compared to OLS:
  - *Lower Z* due to higher-level variance being constrained to be positive (i.e. solve the implied negative variance problem)
Multiple Group Variances

- can deal with multiple group variances
- separate variance will be estimated for each variance group (be aware of #observations for each estimate, though!)
- EVs can only have non-zero values for a single group
Paired T-test
Paired T-Test

- 8 subjects scanned under 2 conditions (A,B)

*Is there a significant difference between conditions?*
Paired T-Test

First, let’s try an unpaired T-test
Paired T-Test

subject mean accounts for large prop. of the overall variance
Paired T-Test

- Paired T-Test
- Data: subject vs. effect size
- De-meaned data: subject vs. effect size
- Subject mean accounts for large prop. of the overall variance
- $>0$?
Paired T-Test

Model out each subject’s mean
Group average with covariate
Group average with covariate

- Additional measurements (e.g. age; disability score; behavioral measures like reaction times)
- Use covariates to ‘explain’ variation
Group average with covariate

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Group average with covariate

Need to demean covariates
Break Time!