

FMRI group analysis

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- Overview
- Fixed versus mixed effects
- Multiple sessions per subject





The GLM for group analysis



COPE from single subject analysis (Subject 1)

OUTPUTS from single subject analysis are INPUT for group analysis



a voxel across subjects

Design Matrix







Does the group activate on average?

For a specific PE/contrast from the first level analysis, which part of the brain were significantly activated across all subjects?





Does the group activate on average?







Does the group activate on average?

$$Y_k = X_k \beta_k + \epsilon_k$$

First-level GLM on Mark's 4D FMRI data set







Does the group activate on average?

 $Y_k = X_k \beta_k + \epsilon_k$ Mark's effect size





Does the group activate on average?

$$Y_k = X_k \beta_k + \epsilon_k$$

$$Mark'$$

$$Mark'$$
within-sul





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?

General Linear Model
EVs Contrasts & F-tests
Number of EVs 1
Number of groups
Group EV1
Input 1 1 1
Input 2 1 1 1 Input 3 1 1 1 Input 4 1 1 1 Input 5 1 1 1 Input 6 1 1 1 Input 7 1 1 1
Input 3 1 🚔 1 🚔
Input 4 1 🗍 1
Input 5 1 🗍 1 🚔
Input 6 1 🗍 1 🗐
Input 2 1 </td
Input 8 1 2 1
View design Sovariance Done



Single Group Average

Does the group activate on average?

General Linear Model	General Linear Model
EVs Contrasts & F-tests	EVs Contrasts & F-tests
Number of EVs 1	Contrasts 1 🚔 F-tests 0
Number of groups 1	Title EV1
Group EV1	C1 🗖 group mean 1
Input 1 1 1 1	
Input 2 1 🛔 1 🚔	
Input 3 1 🛔 1 🚔	
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Fixed versus mixed effects

Fixed-Effects Analysis

Do these exact 6 subjects activate on average?







Mixed-Effects Analysis

Does the population activate on average?



Mixed-Effects Analysis:

• Consider the 6 subjects as samples from a wider population estimate the mean across the population



• between-subject variance accounts for random sampling





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!

Group difference Group Subject Session



Unpaired Two-Group Difference

subject variance

Is there a significant group difference?

- estimate means
- estimate std-errors (FE or ME)
- test significance of difference in means

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





Unpaired Two-Group Difference

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Number o	Number of groups 2								
	Group	EY	EV2						
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Input 3	1	1							
Input 4	1 3	1							
Input 5	1 1	1							
Input 6	1_1	1							
Input 7	1	1							
Input 8	1	1							
Input 9		1							
Input 10	2	0							
Input 11	2	0							
Input 12	2	0	1						
Input 13	2	0							
Input 14	2	0							
Input 15	2	0							
Input 16	2	0	1						
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Is there a significant group difference?





Unpaired Two-Group Difference

Is there a significant group difference?

General	Linear M	lodel					Ger			
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Input 3	1	1	-	 ▼						
Input 4	1	1	-0	 ▼						
Input 5	1	1	0	A		L				
Input 6	1	1	10	- 		L				
Input 7	1	1	10	- 		L				
Input 8	1	1	10	- -		L				
Input 9			10	-		L				
Input 10	1	0	-	- -		L				
Input 11	2	0	-	- -		L				
Input 12	2	0	- 1	-		L				
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FLAME FMRIB's Local Analysis of Mixed Effects

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

Group difference Group Subject Session



- 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

FLAME Inference



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

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	Mixed effects: FLAME 1 🛛 🗕	>		
	Model setup wizard			
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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

- - heterogeneity



Two ways in which FLAME can give different Z-stats compared to OLS:

• higher Z due to increased efficiency from using lower-level variance



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)





- can deal with multiple group variances
- #observations for each estimate, though!)
- EVs can only have non-zero values for a single group



• separate variance will be estimated for each variance group (be aware of



1	-	1.0 🚔	1.0 🚔
1	-	1.0 🚔	1.0 🚔
1	-	1.0 🚔	1.0 🚔
2	-	1.0 🔎	-1.0 🚔
2	-		-1.0 🚔
2	-		-1.0 🚔





• 8 subjects scanned under 2 conditions (A,B) Is there a significant difference between conditions?





First, let's try an unpaired T-test





data



accounts for large prop. of the overall variance

de-meaned data





data



accounts for large prop. of the overall variance

de-meaned data





Model out each subject's mean

Gen	eral	Line	ar No	del					1	10.5							227					 18	0	Ger	era	Linear	Mode1		
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Input	3	1	1	1		0	_	0	1	1		0		0		0	-	0		0									
Input	4	1	1	1		_		0	1	0		1	1	0		ln.	_	0	_	0	3								
Input	5	1	1	1		0		0	1	0	1	0	1	1	-	0	_	0	_	0									
Input	6	1	1	1	1	-	1	0	1	0		0	-	0		1	_	0		0	1								
Input	7	1	1	1		0		0	1	0	10 mil	0	~	0		0	_	1	later -	0									
Input	8	1	1	1		0		0	1			0	~	0		0	~	0	1	1									
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- Additional measurements (e.g. ag like reaction times)
- use covariates to 'explain' variation

• Additional measurements (e.g. age; disability score; behavioral measures





- Additional measurements (e.g. ag like reaction times)
- use covariates to 'explain' variation

• Additional measurements (e.g. age; disability score; behavioral measures







Need to demean covariates

General Linear Model	General Linear Model
EVs Contrasts & F-tests	EVs Contrasts & F-tests
Number of EVs 2	Contrasts 2 🚔 F-tests 0
Number of groups 1	Title EV1 EV2
Group EV1 EV2	C1 🗖 group mean 1 🚔 0 🚔
Input 1 1 1 24	C2 🗖 reaction time 0 🚔 1 🚔
Input 2 1 1 1 -18	
Input 3 1 1 7 4	
Input 4 1 1 5	
Input 5 1 1 -4 -4	
Input 6 1 1 6	
Input 7 1 1 1-6	
View design Covariance Done	View design Covariance Done

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C1	group mean	1	0
C2	reaction time	0	1



Break Time!

