Modeling Group fMRI Data

UCLA Advanced NeuroImaging
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Overview

• What is a mixed effects model
  – Fixed effects
  – Random effects
• 2-stage summary statistics approach
• How do different software packages work?
• Overview FSL modeling options
Mixed Model Motivation

• Start with a simple ANOVA example
• Study: How does a college student’s opinion about a political party change after viewing a tv commercial?
Data: Scenario 1

- 60 students were randomly sampled from all universities in the US
Data: Scenario 2

- Correction: 60 students were randomly sampled from 3 universities in the US
Are the data scenarios different?

• Data points are *exactly* the same
• Data collection technique changes the interpretation
  – Scenario 1: 60 independent measurements from total student population distribution
  – Scenario 2: Measurements within university are related…intuitively only 3 measurements
Fixed vs random effects: When is it an issue?

- Patients grouped by hospital
- Students grouped by university
- Observations grouped by subject
Fixed and Random Effects

- Fixed effect:
  - Models the mean
Fixed and Random Effects

• Fixed effect:
  – Models the mean

3 University means
Fixed and Random Effects

• Fixed effect:
  – Models the mean

Population mean
Fixed and Random Effects

- **Fixed effect:**
  - Models the mean

- **Random effect:**
  - Models the variance
  - Random university effect

Within university
Between university
Fixed and Mixed

• Fixed effects model
  - Fixed effects only (with error variance)

• Mixed effects model
  - Fixed and random effects (with error variance)
Fixed or random?

Were all groups sampled?

- No
- Yes

Interested in group effects?

- Fixed effects only
Fixed or random?

- Were all groups sampled?
  - no
  - Interested in group effects?
    - no
    - Apply inference to sampled groups?
      - no
      - Fixed effects only
      - yes
      - Fixed effects only
  - yes
    - Fixed effects only
Fixed or random?

Were all groups sampled?
- no
- yes

Interested in group effects?
- no
- yes

Apply inference to sampled groups?
- no
- yes

Random group effect
- Fixed effects only

Fixed effects only
Wrong data description: Fixed effects model

\[
\begin{pmatrix}
Y_{1,1} \\
\vdots \\
Y_{1,20} \\
Y_{2,1} \\
\vdots \\
Y_{3,20}
\end{pmatrix} = \begin{pmatrix} 1 & 1 & 1 & \cdots & 1 \end{pmatrix} \beta_g + \begin{pmatrix} \epsilon_{1,1} \\
\epsilon_{1,2} \\
\epsilon_{1,3} \\
\epsilon_{2,1} \\
\vdots \\
\epsilon_{N,3} \end{pmatrix}, \quad \epsilon_{i,j} \sim N(0, \sigma_{win}^2)
\]
Mixed Effects Model

Stage 1

\[ Y = X\beta + \epsilon \]

\[
\begin{pmatrix}
Y_{1,1} \\
\vdots \\
Y_{1,20} \\
Y_{2,1} \\
\vdots \\
Y_{3,20}
\end{pmatrix} =
\begin{pmatrix}
1 & 0 & 0 \\
\vdots & \vdots & \vdots \\
1 & 0 & 0 \\
0 & 1 & 0 \\
\vdots & \vdots & \vdots \\
0 & 0 & 1
\end{pmatrix}
\begin{pmatrix}
\beta_1 \\
\beta_2 \\
\beta_3
\end{pmatrix} +
\begin{pmatrix}
\epsilon_{1,1} \\
\epsilon_{1,2} \\
\epsilon_{1,3} \\
\epsilon_{2,1} \\
\vdots \\
\epsilon_{N,3}
\end{pmatrix}, \epsilon_{i,j} \sim N(0, \sigma^2_{\text{win}})
\]

Stage 2

\[ \beta = X_g \beta_g + \eta \]

\[
\begin{pmatrix}
\beta_1 \\
\beta_2 \\
\beta_3
\end{pmatrix} =
\begin{pmatrix}
1 \\
1 \\
1
\end{pmatrix} \beta_g +
\begin{pmatrix}
\eta_1 \\
\eta_2 \\
\eta_3
\end{pmatrix}, \eta_i \sim N(0, \sigma^2_{\text{btwn}})
\]
Mixed Effects Model

Stage 1

\[ Y = X\beta + \epsilon \]

\[
\begin{pmatrix}
Y_{1,1} \\
\vdots \\
Y_{1,20} \\
Y_{2,1} \\
\vdots \\
Y_{3,20}
\end{pmatrix} =
\begin{pmatrix}
1 & 0 & 0 \\
\vdots & \vdots & \vdots \\
1 & 0 & 0 \\
0 & 1 & 0 \\
\vdots & \vdots & \vdots \\
0 & 0 & 1
\end{pmatrix}
\begin{pmatrix}
\beta_1 \\
\beta_2 \\
\beta_3
\end{pmatrix} +
\begin{pmatrix}
\epsilon_{1,1} \\
\epsilon_{1,2} \\
\epsilon_{1,3} \\
\epsilon_{2,1} \\
\vdots \\
\epsilon_{N,3}
\end{pmatrix}, \epsilon_{i,j} \sim N(0, \sigma^2_{\text{within}})
\]

Stage 2

\[ \beta = X_g\beta_g + \eta \]

\[
\begin{pmatrix}
\beta_1 \\
\beta_2 \\
\beta_3
\end{pmatrix} =
\begin{pmatrix}
1 \\
1 \\
1
\end{pmatrix}\beta_g +
\begin{pmatrix}
\eta_1 \\
\eta_2 \\
\eta_3
\end{pmatrix}, \quad \eta_i \sim N(0, \sigma^2_{\text{between}})
\]

Random effect
Mixed Effects Model: All-In-One

\[
Y = X X_g \beta_g + X \eta + \epsilon
\]

\[
\begin{pmatrix}
Y_{1,1} \\
\vdots \\
Y_{1,20} \\
Y_{2,1} \\
\vdots \\
Y_{3,20}
\end{pmatrix}
= \begin{pmatrix}
1 \\
1 \\
1 \\
\vdots \\
1
\end{pmatrix}
\beta_g + \begin{pmatrix}
1 & 0 & 0 \\
\vdots & \vdots & \vdots \\
1 & 0 & 0 \\
0 & 1 & 0 \\
\vdots & \vdots & \vdots \\
0 & 0 & 1
\end{pmatrix}
\begin{pmatrix}
\eta_1 \\
\eta_2 \\
\eta_3
\end{pmatrix}
+ \begin{pmatrix}
\epsilon_{1,1} \\
\epsilon_{1,2} \\
\epsilon_{1,3} \\
\vdots \\
\epsilon_{N,3}
\end{pmatrix}
\]

Variance Terms
Wrong model leads to wrong conclusion

- Scenario 1: Fixed effects model (wrong)
  - Mean difference=9.41 (se=1.54), p<0.0001
  - Strong evidence of positive opinion change
Wrong model leads to wrong conclusion

- Scenario 1: Fixed effects model (wrong)
  - Mean difference=9.41 (se=1.54), \( p<0.0001 \)
  - Strong evidence of positive opinion change

- Scenario 2: Mixed effects model (right)
  - Mean difference=9.41 (se=5.22), \( p=0.07 \)
  - Change not statistically different than 0
  - Standard error increases due to between-university variance
Mixed Model Comments

• If you fail to include a random effect when there is one
  – Results only apply to that data sample
  – P-values are smaller than mixed model p-values
How does this relate to fMRI?

Each time series is a collection of data grouped by subject.

A random subject effect is necessary to apply inference to total population.
Mixed Model for fMRI Data

- fMRI data are more complicated than the student opinion example
  - Not typically estimating an intercept
  - Time series are temporally autocorrelated
  - Time series can be quite long
- Let’s take a look at the model!
  - A study with 2 stimuli of interest
Subject 1

Subject 2

Subject N

\[ \begin{align*}
\text{Var}(\eta_{i,1}) &= \sigma_{btwn_1}^2 \\
\text{Var}(\eta_{i,2}) &= \sigma_{btwn_2}^2
\end{align*} \]

\[ \begin{pmatrix}
\beta_{g_1} \\
\beta_{g_2}
\end{pmatrix} \]

\[ \begin{pmatrix}
\epsilon_1,1 \\
\epsilon_1,T \\
\vdots \\
\epsilon_N,1 \\
\epsilon_N,T
\end{pmatrix} \]

\[ \text{Cov} \begin{pmatrix}
\epsilon_{i,1} \\
\epsilon_{i,2} \\
\vdots \\
\epsilon_{i,T}
\end{pmatrix} = \sigma_{win_i}^2 V_i \]
Yuck!

- Computationally intensive
  - Large matrices that need to be inverted
- What if we add another subject?
  - Must estimate *whole* model for all subjects
Recall the two stages

Stage 1

\[
Y = X \beta + \epsilon
\]

\[
\begin{pmatrix}
Y_{1,1} \\
\vdots \\
Y_{1,20} \\
Y_{2,1} \\
\vdots \\
Y_{3,20}
\end{pmatrix}
= \begin{pmatrix}
1 & 0 & 0 \\
\vdots & \vdots & \vdots \\
1 & 0 & 0 \\
0 & 1 & 0 \\
\vdots & \vdots & \vdots \\
0 & 0 & 1
\end{pmatrix}
\begin{pmatrix}
\beta_1 \\
\beta_2 \\
\beta_3
\end{pmatrix}
+ \begin{pmatrix}
\epsilon_{1,1} \\
\epsilon_{1,2} \\
\epsilon_{1,3} \\
\epsilon_{2,1} \\
\vdots \\
\epsilon_{N,3}
\end{pmatrix}, \epsilon_{i,j} \sim N(0, \sigma_{\text{win}}^2)
\]

Stage 2

\[
\beta = X_g \beta_g + \eta
\]

\[
\begin{pmatrix}
\beta_1 \\
\beta_2 \\
\beta_3
\end{pmatrix}
= \begin{pmatrix}
1 \\
1 \\
1
\end{pmatrix}
\beta_g + \begin{pmatrix}
\eta_1 \\
\eta_2 \\
\eta_3
\end{pmatrix}, \eta_i \sim N(0, \sigma_{\text{btwn}}^2)
\]
Two-Stage Summary Statistics

Stage 1

\[
\begin{align*}
\begin{pmatrix}
Y_{1,1} \\
\vdots \\
Y_{1,20}
\end{pmatrix}
&= 
\begin{pmatrix}
1 \\
\vdots \\
1
\end{pmatrix}
\beta_1 + 
\begin{pmatrix}
\epsilon_{1,1} \\
\vdots \\
\epsilon_{1,20}
\end{pmatrix} \\
\begin{pmatrix}
Y_{2,1} \\
\vdots \\
Y_{2,20}
\end{pmatrix}
&= 
\begin{pmatrix}
1 \\
\vdots \\
1
\end{pmatrix}
\beta_2 + 
\begin{pmatrix}
\epsilon_{2,1} \\
\vdots \\
\epsilon_{2,20}
\end{pmatrix} \\
\begin{pmatrix}
Y_{3,1} \\
\vdots \\
Y_{3,20}
\end{pmatrix}
&= 
\begin{pmatrix}
1 \\
\vdots \\
1
\end{pmatrix}
\beta_3 + 
\begin{pmatrix}
\epsilon_{3,1} \\
\vdots \\
\epsilon_{3,20}
\end{pmatrix}
\end{align*}
\]

\[\epsilon_{i,j} \sim N(0, \sigma_{win}^2)\]
Two-Stage Summary Statistics

Stage 1

\[
\begin{pmatrix}
Y_{1,1} \\
\vdots \\
Y_{1,20}
\end{pmatrix} = \begin{pmatrix} 1 \\ \vdots \\ 1 \end{pmatrix} \beta_1 + \begin{pmatrix} \epsilon_{1,1} \\
\vdots \\
\epsilon_{1,20} \end{pmatrix}
\]

\[
\begin{pmatrix}
Y_{2,1} \\
\vdots \\
Y_{2,20}
\end{pmatrix} = \begin{pmatrix} 1 \\ \vdots \\ 1 \end{pmatrix} \beta_2 + \begin{pmatrix} \epsilon_{2,1} \\
\vdots \\
\epsilon_{2,20} \end{pmatrix}
\]

\[
\begin{pmatrix}
Y_{3,1} \\
\vdots \\
Y_{3,20}
\end{pmatrix} = \begin{pmatrix} 1 \\ \vdots \\ 1 \end{pmatrix} \beta_3 + \begin{pmatrix} \epsilon_{3,1} \\
\vdots \\
\epsilon_{3,20} \end{pmatrix}
\]

\[\epsilon_{i,j} \sim N(0, \sigma_{win}^2)\]

Stage 2

\[
\begin{pmatrix}
\hat{\beta}_1 \\
\hat{\beta}_2 \\
\hat{\beta}_3
\end{pmatrix} = \begin{pmatrix} 1 \\ 1 \\ 1 \end{pmatrix} \beta + \begin{pmatrix} \eta_1^* \\
\eta_2^* \\
\eta_3^* \end{pmatrix}, \quad \text{Var}(\eta_i^*) = \frac{\sigma_{win}^2}{W} + \sigma_{btwn}^2
\]

Use first stage estimates
Two-Stage Summary Statistics

Stage 1

\[
\begin{pmatrix}
Y_{1,1} \\
\vdots \\
Y_{1,20}
\end{pmatrix} = 
\begin{pmatrix}
1 \\
\vdots \\
1
\end{pmatrix} \beta_1 + 
\begin{pmatrix}
\epsilon_{1,1} \\
\vdots \\
\epsilon_{1,20}
\end{pmatrix}
\]

\[
\begin{pmatrix}
Y_{2,1} \\
\vdots \\
Y_{2,20}
\end{pmatrix} = 
\begin{pmatrix}
1 \\
\vdots \\
1
\end{pmatrix} \beta_2 + 
\begin{pmatrix}
\epsilon_{2,1} \\
\vdots \\
\epsilon_{2,20}
\end{pmatrix}
\]

\[
\epsilon_{i,j} \sim N(0, \sigma^2_{\text{win}})
\]

\[
\begin{pmatrix}
Y_{3,1} \\
\vdots \\
Y_{3,20}
\end{pmatrix} = 
\begin{pmatrix}
1 \\
\vdots \\
1
\end{pmatrix} \beta_3 + 
\begin{pmatrix}
\epsilon_{3,1} \\
\vdots \\
\epsilon_{3,20}
\end{pmatrix}
\]

Stage 2

\[
\begin{pmatrix}
\hat{\beta}_1 \\
\hat{\beta}_2 \\
\hat{\beta}_3
\end{pmatrix} = 
\begin{pmatrix}
1 \\
1 \\
1
\end{pmatrix} \beta_g + 
\begin{pmatrix}
\eta_1^* \\
\eta_2^* \\
\eta_3^*
\end{pmatrix}, \quad \text{Var}(\eta_i^*) = \frac{\sigma^2_{\text{win}}}{W} + \sigma^2_{\text{btwn}}
\]

within \hspace{2cm} between
Two-Stage Model

- Stage 1
  - Means
Two-Stage Model

- Stage 1
  - Means
  - $\sigma^2_{win}$
    (same across subjects here)
Two-Stage Model

- **Stage 1**
  - Means
  - $\sigma^2_{\text{win}}$
    (same across subjects here)

- **Stage 2**
  - $\sigma^2_{\text{btwn}}$
Two-Stage Model

- **Stage 1**
  - Means
  - $\sigma_{win}^2$
    (same across subjects here)

- **Stage 2**
  - $\sigma_{btwn}^2$
  - $\sigma_{mix}^2 = \frac{\sigma_{win}^2}{20} + \sigma_{btwn}^2$
    - 20/university
Two-Stage Model

- **Stage 1**
  - Means
  - $\sigma_{win}^2$
    (same across subjects here)

- **Stage 2**
  - $\sigma_{btwn}^2$
  - $\sigma_{mix}^2 = \frac{\sigma_{win}^2}{20} + \sigma_{btwn}^2$
    - 20/university

- Pop mean
Two-Stage Model

\[ T = \frac{\sqrt{N} \hat{\beta}}{\sqrt{\sigma_{win}^2/W + \sigma_{btwn}^2}} \]

- \( N = \) # universities
- \( W = \) # within university

- If new data is added, only run first stage for new data
Two Stage Model fMRI

Stage 1
- Estimate N subject models

Stage 2
- Estimate between subject variance, combine with Stage 1 results

\[ \hat{c\beta_1} \quad \text{Cov}(c\hat{\beta}_1) \]
\[ \hat{c\beta_2} \quad \text{Cov}(c\hat{\beta}_2) \]
\[ \ldots \]
\[ \hat{c\beta_N} \quad \text{Cov}(c\hat{\beta}_N) \]

\[ \hat{\beta}_g \quad \text{Cov}(\hat{\beta}_g) \]
Stage 1: Subject Model

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

\[ \text{Cov}(\epsilon_k) = \sigma_k^2 V_k \]

\[ H_0 : \beta_{k1} - \beta_{k2} = 0 \]
Stage 1: Estimation

- $W_k$ such that $W_k V_k W_k' = I_T$
Stage 1: Estimation

• $W_k$ such that $W_k V_k W_k^T = I_T$
• Whitened model
  
  $W_k Y_k = W_k X_k \beta_k + W_k \epsilon_k$
  $Y_k^* = X_k^* \beta_k + \epsilon_k^*$
Stage 1: Estimation

- $W_k$ such that $W_k V_k W'_k = I_T$
- Whitened model
  - $W_k Y_k = W_k X_k \beta_k + W_k \varepsilon_k$
  - $Y^*_k = X^*_k \beta_k + \varepsilon^*_k$
- Use OLS on whitened model
  - $c \hat{\beta}_k = \left( X^*_k X^*_k \right)^{-1} X^*_k Y^*_k$
  - $\overline{\text{Cov}}(c \hat{\beta}_k) = \hat{\sigma}^2_k \left( X^*_k X^*_k \right)^{-1}$
Stage 2: Group Model

\[
\hat{\beta}_{cont} = X_g \beta_g + \epsilon_g
\]

\[
\text{Cov}(\epsilon_g) = V_g = \left( \sigma^2 c(X_1^{*'} X_1^*)^{-1} c' \right) + \sigma_g^2 I_N
\]
Stage 2: Estimation

- \( W_g \) such that \( W_g V_g W'_g = I_N \)
Stage 2: Estimation

- $W_g$ such that $W_g V_g W'_g = I_N$
- $W_g \hat{\beta}_{cont} = W_g X_g \beta_g + W_g \epsilon_g$
- $\hat{\beta}^*_{cont} = X^*_g \beta_g + \epsilon^*_g$
Stage 2: Estimation

• $W_g$ such that $W_g V_g W_g' = I_N$

• $W_g \hat{\beta}_{cont} = W_g X_g \beta_g + W_g \epsilon_g$
  $\hat{\beta}_{cont}^* = X_g^* \beta_g + \epsilon_g^*$

• $\hat{\beta}_g = \left( X_g^* X_g^* \right)^{-1} X_g^* \hat{\beta}_{cont}^*$
  $\text{Cov}(\hat{\beta}_g) = \left( X_g^* X_g^* \right)^{-1}$
Stage 2: Estimation

- $W_g$ such that $W_g V_g W_g' = I_N$
- $W_g \hat{\beta}_{cont} = W_g X_g \beta_g + W_g \epsilon_g$
  \[ \hat{\beta}^*_\text{cont} = X_g^* \beta_g + \epsilon_g^* \]
- $\hat{\beta}_g = \left( X_g^* X_g \right)^{-1} X_g^* \hat{\beta}^*_\text{cont}$
- $\hat{\text{Cov}}(\hat{\beta}_g) = \left( X_g^* X_g \right)^{-1}$
- $T = \frac{\hat{\beta}_g}{\sqrt{\hat{\text{Cov}}(\hat{\beta}_g)}}$
How is the model estimated?

- Depends on software
  - SPM: Does not estimate $\sigma^2_g$
    - Due to a set of assumptions, estimation of $\sigma^2_g$ is unnecessary
  - FMRIstat: Restricted maximum likelihood (ReML) approach to estimating $\sigma^2_g$
  - FSL: Bayesian approach to estimating $\sigma^2_g$
SPM2

- Does not estimate $\sigma_g^2$
  - Assumes homoscedastic variance across subjects
  - Assumes first level design is same across subjects

$$\hat{\sigma}_{win_{all}}^2 = \hat{\sigma}_1^2 c \left( X_1^* X_1^* \right)^{-1} c' = \ldots = \hat{\sigma}_N^2 c \left( X_N^* X_N^* \right)^{-1} c'$$

$$V_g = \sigma_{win_{all}}^2 I_N + \sigma_g^2 I_N = \sigma_{g*}^2 I_N$$

OLS can be used
SPM2: Single contrast per subject

\[
\begin{pmatrix}
  \hat{c}\beta_1 \\
  \hat{c}\beta_2
\end{pmatrix} = \begin{pmatrix}
  1 \\
  1 \\
  1 \\
  1 \\
  1 \\
  1 \\
  1 \\
  1
\end{pmatrix} \beta_g + \epsilon_g \\
\epsilon_g \sim N(0, \sigma^2_g * I_N)
\]

A one-sample T-test!
SPM2: Multiple contrasts per subject

\[ \hat{\beta}_{1,1} \]
\[ \hat{\beta}_{1,2} \]
\[ \hat{\beta}_{2,1} \]

\[
\begin{bmatrix}
\beta_{g1} \\
\beta_{g2}
\end{bmatrix}
\]

\[ = \begin{bmatrix}
1 & 0 \\
0 & 1 \\
1 & 0 \\
0 & 1 \\
1 & 0 \\
0 & 1 \\
0 & 1 \\
0 & 1 \\
0 & 1 \\
0 & 1
\end{bmatrix}
\]

\[ + \epsilon_g \]

\[ \epsilon_g \sim N(0, \sigma^2_{g*} V_{g*}) \]

Global correlation estimate
SPM2 : Summary

• Multiple contrasts per subject can enter second level
  – Contrasts can be correlated
  – T and F-tests are possible

• Special case
  – One contrast per subject…Reduces to T-test!
SPM2

• **Pros**
  – Model is easy to estimate
  – Model is easy to understand
  – Multiple contrasts can enter the group model and are *not* considered independent

• **Cons**
  – Global covariance estimate (same across voxels)
  – Assumes variance is homogeneous across subjects
FMRIstat

- Estimates $\sigma_g^2$ using Restricted Maximum Likelihood (ReML)
  - Likelihood: $P(Y|\beta_g, \sigma_g^2)$
  - Treats $\beta_g$ as a nuisance then maximizes likelihood to estimate $\sigma_g^2$
  - Degrees of freedom for $\sigma_g^2$ are typically low
FMRIstat

• Regularization step
  – Fixed effects variance higher degrees of freedom
  – “Borrows” precision from a fixed effects variance estimate
    • $\hat{\sigma}^2_{g_{\text{final}}} = \text{smooth} \left( \frac{\hat{\sigma}^2_{g_{\text{ReML}}}}{\hat{\sigma}^2_{\text{fixed}}} \right) \times \hat{\sigma}^2_{\text{fixed}}$
  • Smooth to reach desired degrees of freedom
– Details
FSL: FMRIB Software Library

- Bayesian approach to estimating model
- Inference is based on *posterior* distribution of the data
  
  \[ P(\beta_g, \sigma_g^2, \nu_g | Y) \]
  
  - Parameters of interest are treated as random
FSL : Second Level Estimation

• Flame 1: Maximum a posteriori (MAP) estimate of $\sigma_g^2$ found iteratively
  – Assumes degrees of freedom, $\nu_g = N - p$
• Flame 2: Slower MCMC method of estimation
  • Applied to voxels close to threshold in step 1
  • Fine tunes estimates of $\beta_g, \sigma_g^2, \nu_g$
• Details
FSL and FMRIstat

• **Pros**
  – When single contrast is taken to the second level, equivalent to all-in-one model
  – Within-subject variances are carried to the second level
    • Heterogeneity across subjects is modeled

• **Cons**
  – Multiple contrasts in the group model are assumed to be independent
Which software?

- FSL and FMRIstat best for heteroscedastic variances
  - Different number of trials per subject
- SPM best for multiple correlated contrasts at group level
- Other differences in first level modeling may sway users one way or another
FSL Group Model Options

FEAT - FMRI Expert Analysis Tool - v5.88

Mixed effects: FLAME 1+2
FSL Group Model Options

• Fixed effects
  – Only uses w/in sub variance

• Simple OLS
  – Assumes w/in sub variances are equal

• Flame 1& 2
  – w/in sub var and btwn sub var
**W_g Matrix**

- Recall we pre-multiply by $W_g$ so our errors are uncorrelated and constant variance.

$$W_g \hat{\beta}_{cont} = W_g X_g \beta_g + W_g \epsilon_g$$
Fixed effects analysis
- Only appropriate for intermediate levels
- Assumes the between-run variability=0

Why would we do this?
- What if df are low?
  - $\hat{\sigma}_g^2$ has high variance
  - If $\hat{\sigma}_g^2$ is too large, it will override differences in $\hat{\sigma}_{\text{win}_k}^2$

$V_g = \begin{pmatrix} \sigma_{\text{win}_1}^2 & \cdots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \cdots & \sigma_{\text{win}_N}^2 \end{pmatrix}$
MFX*  FFX
SD=0.6962  SD=1.4289

*Assuming overestimate of $\hat{\sigma}_g^2$
Fixed Effects

• Use to improve your mean estimates
  – eg correct trials
• Since variance is underestimated, you *must* only run this at an intermediate level
  – Higher level analysis soaks up rest of variance
Fixed Effects

• Which is better FE or Flame with pooled variance?
  – Flame usually pools estimate, $\hat{\sigma}_g^2$, over subjects to increase DF
  – FSL folks currently advise to use FE for intermediate levels

• If you have low DF, FE is your only choice
  – If it is a top level analysis and you have very low DF, you can’t estimate OLS or Flame models
FSL Group Model Options

• **OLS**
  - Assumes $\hat{\sigma}_{win_k}^2$ is the same across subjects
  - Like SPM2

• **Flame 1 and 2**
  - Estimates $\hat{\sigma}_g^2$
  - Flame 2 has more refined estimates

\[
V_g = \begin{pmatrix}
\sigma_g^2 & 0 \\
0 & \sigma_g^2
\end{pmatrix}
\]

\[
V_g = \begin{pmatrix}
\sigma_{win_1}^2 + \sigma_g^2 & 0 \\
0 & \sigma_{win_N}^2 + \sigma_g^2
\end{pmatrix}
\]
3rd Level Analysis Results

- OLS L3, Flame L2
- Flame L3, Flame L2
- Flame L3, FE L2
- FE L3, Flame L2

thresh=3.5
Third Level Analysis

• Typically Flame and OLS have similar results
  – Flame is probably the best choice, since it adjusts for heteroscedastic variance
  – OLS runs faster
  – OLS stats can be larger or smaller than Flame stats

• FE at level 3 is bad
  – Variance is underestimated
  – High risk of false positives
Concluding Remarks

• Mixed models are appropriate for fMRI data
  – Include between-subject variance
  – Allows inference to be applied to entire population

• The two-stage summary statistics model
  – Computationally easier to estimate
  – Easier to add new subjects

• Software packages use the same basic model, but estimate $\sigma_g^2$ differently

• Use FE at intermediate levels and Flame at the top level in FSL