21st EEGLAB Workshop Thursday 7th April 2016 Santa Margherita Ligure, Italy



Hierarchical Linear Modelling for EEG data

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Context

- In all cases, data collection consists in recording electromagnetic events over the whole brain and for a relatively long period of time, with regards to neural spiking.
- In the majority of cases, data analysis consists in looking where we have signal and restrict our analysis to these channels and components.
- Are we missing the forest by choosing working on a single (or a few) tree?
- By analysing where we see an effect, we increase the type 1 FWER because the effect is partly driven by random noise (solved if chosen based on prior results)

Rousselet & Pernet – It's time to up the Game Front. Psychol., 2011, 2, 107

Context

- Most often, we compute averages per condition and do statistics on peak latencies and amplitudes
- Several lines of evidence suggest that peaks mark the end of a process and therefore it is likely that most of the interesting effects lie in a component before a peak
- **Neurophysiology**: whether ERPs are due to additional signal or to phase resetting effects a peak will mark a transition such as neurons returning to baseline, a new population of neurons increasing their firing rate, a population of neurons getting on / off synchrony.
- **Neurocognition**: reverse correlation techniques showed that e.g. the N170 component reflects the integration of visual facial features relevant to a task at hand (Schyns and Smith) and that the peak marks the end of this process.

Rousselet & Pernet – It's time to up the Game Front. Psychol., 2011, 2, 107

Context

 Most often, we compute averages per condition and do statistics on peak latencies and amplitudes

Univariate methods extract information among trials in time and/or frequency across space

Multivariate methods extract information across space, time, or both, in individual trials

Averages don't account for trial variability, fixed effect can be biased – these methods allow to get around these problems

Pernet, Sajda & Rousselet – Single trial analyses, why bother? Front. Psychol., 2011, 2, 322

Overview

- \rightarrow Setting up a study (again)
- Fixed, Random, Mixed and Hierarchical
- A extreme example
- GLM overview
- Weighted Least Squares for EEG (not covered in the talk but you have it here anyway)
- → Review results / set 2nd level
- A word on designs



STUDY

The Steinberg Experiment

Quick overview

- Sternberg working memory task
- Ignore/Memorize \rightarrow Maintain \rightarrow Probe
- 8 items each time \rightarrow variable load to memorize
- Load your study from yesterday
- Precompute single trials
- If ICA, do the clustering
- Create a design and run it through the LIMO EEG toolbox

EEGLAB v14.x (dev)		
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ISSUE: Make sure the condition names
are the same for all subjects
(case sensitive)

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Page 1

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Update dataset info - datasets stored on disk will be overwritten (unset = Keep study info separate).

Delete cluster information (to allow loading new datasets, set new components for clustering, etc.)

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Ok



Save current study as

Currently a small bug, there is no name saved (ie 'save current study' doesn't work and nothing is saved by default)

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saves .daterp files = single trials

Pre-compute channel measures for STUDY 'Steinberg'								
V	Spherical interpolation of missing channels (performed after optional ICA removal below)							
	Remove ICA artifactual components pre-tagged in each dataset							
	Remove artifactual ICA cluster or clusters (hold shift key)							
List	of measures to pre	compute						
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	Total size (Mb)	174.2		

Linear MOdeling of EEG data pop_limo()	
Linear MOdeling of EEG data (Use STUDY design interface to	of design1 switch to a different design)
Input data to use for the GLM	ERP
Options	'timelim'
Optimization method	OLS 🔽
Erase previous model for this	design and measure
	Cancel Ok

Currently little bug – 'timelim' or 'freqlim' don't actually trim the data (will be fixed obviously)

LIMO stats without study

🛃 limo_	batch_gui		
	L	LIMO EEG: 1st LEVEL BATCH	
Da	ta Import		- Specify
	Import subjects' se	et	Specify the categorical variables
	ERP (analysis in time)	•	full factorial
	Starting time (ms)		Specify continuous variables
	Ending time (ms)		o not z-score regressors
	Starting frequency (Hz)		Analysis
	Ending frequency (Hz)		✓ scalp data
			Mass-univariate VLS
	Done	Quit	Bootstrap data add TFCE
	Ending frequency (Hz) Ending frequency (Hz) Done	Quit	Analysis Scalp data Component data Mass-univariate Bootstrap data dd TFCE

Needs a single .set Lists of text files

- Sets
- Categorical variables (conditions)
- Continuous varfiables

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Fixed, Random, Mixed and Hierarchical

Fixed effect: Something the experimenter directly manipulates

y=XB+e	data = beta * effects + error
y=XB+u+e	data = beta * effects + constant subject effect + error

Random effect: Source of random variation e.g., individuals drawn (at random) from a population. **Mixed effect**: Includes both, the fixed effect (estimating the population level coefficients) and random effects to account for individual differences in response to an effect

Y=XB+Zu+e data = beta * effects + zeta * subject variable effect + error

Hierarchical models are a mean to look at mixed effects.

Fixed vs Random

Fixed effects: Intra-subjects variation suggests all these subjects different from zero

Random effects: Inter-subjects variation suggests population not different from zero



Hierarchical model = 2-stage LM

Single subject Each subject's EEG trials are modelled Single subject parameter estimates



Single subject parameter estimates or combinations taken to 2nd level

Group/s of subjects

For a given effect, the whole group is modelled Parameter estimates apply to group effect/s



Group level of 2nd level parameter estimates are used to form statistics

Fixed effects



Only source of variation (over trials) is measurement error True response magnitude is *fixed*

Random effects



Two sources of variation

- measurement error
- response magnitude (over subjects)

Response magnitude is random

• each subject has random magnitude

Random effects



Two sources of variation

- measurement error
- response magnitude (over subjects)

Response magnitude is random

- each subject has random magnitude
- but note, population mean magnitude is *fixed*

An extreme example

<u>Example</u>: present stimuli from intensity -5 units to +5 units around the subject perceptual threshold and measure RT

 \rightarrow There is a strong positive effect of intensity on responses



Fixed Effect Model 1: average subjects



Fixed effect without subject effect \rightarrow negative effect

Fixed Effect Model 2: constant over subjects



Fixed effect with a constant (fixed) subject effect \rightarrow positive effect but biased result

HLM: random subject effect



Mixed effect with a random subject effect \rightarrow positive effect with good estimate of the truth

MLE: random subject effect



Mixed effect with a random subject effect \rightarrow positive effect with good estimate of the truth

Hierarchical Linear Model for MEEG



The General Linear Model

What is a linear model?

- An equation or a set of equations that models data and which corresponds geometrically to straight lines, plans, hyperplans and satisfy the properties of additivity and scaling.
- Simple regression: $y = \beta 1x + \beta 2 + \epsilon$
- Multiple regression: $y = \beta 1x1 + \beta 2x2 + \beta 3 + \epsilon$
- One way ANOVA: $y = u + \alpha i + \epsilon$

• ...

• Repeated measure ANOVA: $y=u+\alpha i+\epsilon$

What is the GLM?

- <u>Model</u>: assign to the data different effects / conditions ... All we have to do is find the parameters of this model
- <u>Linear</u>: the output is a function of the input satisfying rules of scaling and additivity (e.g RT = 3*acuity + 2*vigilance + 4 + e)
- <u>General</u>: applies to any known linear statistics (ttest, ANOVA, Regression, MANCOVA), can be adapted to be robust (ordinary least squares vs. weighted least squares), and can even be extended to non Gaussian data (Generalized Linear Model using link functions)

GLM examples

• EEG amplitude is modulated by the stimulus intensity:

Y1 = X1*B1+B2+e Y2 = X2*B1+B2+e Y3 = X3*B1+B2+e Y4 = X4*B1+B2+e

*e*1 X *Y*2 *X*2 *e*2 Y3 *X*3 *e*3 *Y*4 X4*B*1 *e*4 *B*2 • • ٠ • en

 \rightarrow Y = XB+e

Yn = Xn*B1+B2+e

GLM examples

• EEG amplitude is modulated by the stimulus conditions (A vs B):

Y1 = 1*B1+0*B2+B3+e Y2 = 1*B1+0*B2+B3+e Y3 = 0*B1+1*B2+B3+e Y4 = 0*B1+1*B2+B3+e

$Yn = X_{1}n*B_{1}+X_{2}n*B_{2}+B_{3}+e$

 \rightarrow Y = XB+e

General Linear model



N: number of trials p: number of regressors Model is specified by 1. Design matrix *X*

2. Assumptions about ε

Linear Algebra and Statistics

Y = 3 observations X = 2 regressors Y = XB+E -->Y^=XB



SS total = variance in Y SS effect = variance in XB SS error = variance in E R2 = SS effect / SS total F = SS effect/df / SS error/dfe

Linear Algebras: Projections



 $y^{A} = \beta x$ x'(y- \beta x) = 0 $\beta x'x = x'y$ $\beta = x'y / x'x$

 $y^{=}(x'y / x'x)x$ $y^{=} Py \rightarrow P = xx' / x'x$

Why project? XB = Y may have no solution, the closest solution is a vector located in X space that is the closest to Y. In N dimensions: P = X inv(X'X) X'B = inv(X'X) X'Y



Projection and Least squares



 $y = \beta x + c$ P projects the points on the line Minimizing the distance (^2) is projecting at perpendicular angles



Y = y^+e y^ = PY e = (I-P)Y An 'effect' is defined by which part of X to test (i.e. project on a subspace)

Ro = I - (Xo*pinv(Xo)); P = Ro - R; Effect = (B'*X'*P*X*B);

Weighted Least Squares

The LIMO EEG approach: a single weight per trial

Mathematical issues

- Least Squares requires the error covariance to have 0 off diagonal ie Cov(e) = $\sigma^2 I$
- Deviations from that assumption can lead to substantial power reduction and increase in false positive rate
- Weighted Least Squares is the solution to these problems allowing $Cov(e) = \sigma^2 V_{I}$ with V a diagonal matrix

$$y = X \beta + e, \quad E(e) = 0, \quad Cov(e) = \sigma^2 V$$

Wy = WX \beta + We,
$$E(e) = 0, \quad Cov(e) = \sigma^2 I$$

 $\hat{\beta} = (X^T W X)^{-1} X^T W y$

How to apply weights?

- Weight reflect outlying data does it make sense to be for some time frames and/or frequency bin?
- Noise + signal model → unlikely to have a background neural synch higher than signal
- Noise + signal model

 unlikely to a single frame outlier, this an autoregressive process, many frames must be outlying
- Phase reset model → either a trial is out of phase or it as amplitude difference, in both cases many frames must be outlying



A trial can be both good and bad ? What about information accumulation?

Weighted least squares in LIMO EEG

- Principal Component Projection method:
- PCA
- outlier detection on projected data points (Filzmoser et al., 2008)
- 1 weight per trial



Weighted least squares in LIMO EEG

LIMO EEG data set → limo_CheckWeight.m.



Subject 2 electrode 41

good trials vs bad trials

Bias between conditions

Review results

What has been computed

- Input files: .set listing to single trial files generated using eeglab
- Yr the data for the design considered
- Yhat the modelled data
- Res thr residuals
- Condition and covariates effects
- Betas files
- Con files

 \rightarrow only use betas and con for 2nd level

Now 2nd level

- Think of your betas are equivalent of your mean
- Cleaner because only show condition effect accounting of the variance between trials
- Now we use eg paired t-test ignore vs memorize
- → Create of working directory paired_ttest
- →Call limo_eeg
- \rightarrow Select random effect
- \rightarrow Input neighbouring matrix
- \rightarrow do the paired t test (set bootstrap to o): select beta list and select [1 2]

Now 2nd level

Electrodes

• You can also check what is going on raw data ! using summary stats



'Make and Plot a difference'



DESIGNS

So what now that we have a HLM?

EEG signals are idiosyncratic

Gaspar et al. 2011 Reliability of ERP and single-trial analyses NeuroImage 58

Test-retest of ERPs



- ERPs are highly reliable within subjects
- xcorr >0.90 with ~4/6 ms lag

Grand averages do not reflect ERP dynamics



- Because ERPs are highly reliable within subjects, grand averages are also highly reliable.
- However, this 'within-subject' reliability also means that grand averages ERPs are significantly different from individual subjects' ERPs.
- Plots of grand average can be misleading

Grand averages do not reflect ERP dynamics



Single subjects or group analysis

What is the question?

- If the question pertains to dynamic analyses (when things happen) and/or quantitative aspects (how much this variable explains of the data), then single subjects analyses make more sense given the idiosyncratic nature of EEG.
- Yet some group stats are needed for inference e.g. average cluster onset, average number of subject showing an effect, etc .. + derive group level effect sizes
- If the question is general in nature (is there a measurable difference between these conditions) or pertains to group differences and/or attributes, then group analyses makes sense.

How task constraints modulate the ERP response?





Rousselet et al. Front Psy 2011

How task constraints modulate the ERP response?



At the group level, ERP sensitivity to phase noise was reduced between about 140 and 300 ms when stimulus phase information was task irrelevant.

we observed a significant task effect in only 60% of subjects, and at any time point only 31% of subjects showed results consistent with group analyses

Rousselet et al. Front Psy 2011

MEG of acoustic properties in affective vocalizations



Salvia et al. Front Neurosc 2014

MEG of acoustic properties in affective vocalizations



Simple model: for each sound, input the arousal and valence value - Combined model: valence, arousal, and 2 components of a PCA (72% var) from six acoustic parameters: mean/ SD of fo, HNR and percentages of unvoiced frame, jitter and shimmer.

Early effects are largely driven by acoustical variations Once the variance explained by acoustic properties is accounted for, the remaining effects of emotionalv variables (especially valence) are mostly observed at late stages (\sim 400–600 ms).



Categorical designs

Factorial Designs: 3*3

Amplitude spectrum



For group analyses, all you need is an estimate for each condition per subject Level 1: Y = XB1 \rightarrow 6, each beta is a mixture of the factors at that stage, but estimate the condition Level 2: Y = XB1 \rightarrow 12, the beta of the 1st level are now split into factors (3*3) and interaction (6)

Factorial Designs: N*N*N*...

<u>Amplitude spectrum</u>



For single subject analyses, you need all effects Level 1: Y = XB1 \rightarrow 12, the data of each subject are split into factors (3*3) and interaction (6) Level 2: nothing left to explain (stats on attributes)

Bienek, et al (2012). Phase vs Amplitude Spectrum. Journal of Vision 12

Continuous designs

Regression based designs – 1st level



Split continuous variables like factors to control low level physical properties

Bienek, et al (2012). Phase vs Amplitude Spectrum. Journal of Vision 12

Regression based designs – 2nd level



study the effect of stimulus properties within subjects effect of aging between subjects

Rousselet, et al. (2010). Aging and face perception. Front Psy