FEAT 3 - Advanced FMRI Analysis

高级fMRI分析

Pipeline overview

处理流程概述

Advanced preprocessing steps

高级预处理步骤

- Motion artefact correction

  头动矫正

- Physiological noise correction

  生理噪音矫正

Demeaning EVs

EVs去均值

Advanced designs:

- Parametric designs and F-tests 参数设计和F检验
- Factorial designs and interactions

  因子设计和交互作用

  - Contrast masking

    对比mask

- Correlated EVs
  - Design efficiency

    设计效应量

  - F-test F检验

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Pipeline overview

流程概述

Generic blueprint

1. Data acquisition 数据获取

2. Data preprocessing 数据预处理

3. Single-subject analysis 单个被试的分析

4. Group-level analysis 组水平分析

5. Statistical inference 统计推断

Generic blueprint

Aims:

- Obtain good quality and consistent data
  获取高质量一致性的数据
- Optimise SNR
  优化SNR

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

Keep in mind:

- Many trade-offs 许多权衡
- Consider drop-out and distortions
  考虑信号丢失和失真
- What are the most important regions?
  最重要的脑区是什么

Generic blueprint

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

Aims:

- Reduce noise in data 减少噪声
- Prepare data for analysis
  准备数据分析
- Prepare data for group comparison
  为组水平比较准备数据

Keep in mind:

- Requires careful checking
  需要仔细检查
- Can add additional steps if necessary
  如有必要，可添加其他步骤

Generic blueprint

1. Data acquisition
2. Data preprocessing
3. Single-subject analysis
   单个被试的分析
4. Group-level analysis
5. Statistical inference

Aims:

- Obtain measure of interest for each subject (often an image)
  获取每个被试感兴趣的指标

Keep in mind:

- Differs considerably between modalities
  不同模态的差别

Generic blueprint

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

Aims:

- Compare single-subject results across group
  比较组间单个被试的结果
- Group mean/ t-test/ correlation
  组均值/T检验/相关

Keep in mind:

- Can have additional layer to average over sessions 可以使用其他的图层平均session间的结果
- Account for confounding variables
  解释混淆变量

Generic blueprint

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

统计推断

Aims:

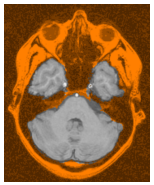
- P-values P值
- Reliability of results
  结果的可靠性
- Generalise to population
  结果的生态效度

Keep in mind:

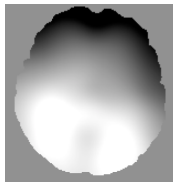
- Need enough subjects to have power 需要足够的被试才能有较强的统计检验力
- Cannot interpret null results
  不能解释不显著的结果

What we covered so far

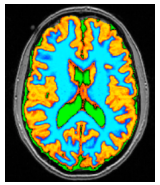
Structural data:
结构数据



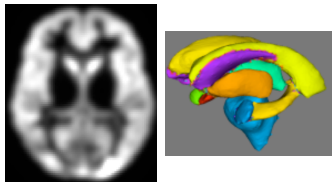
Brain extraction
脑提取



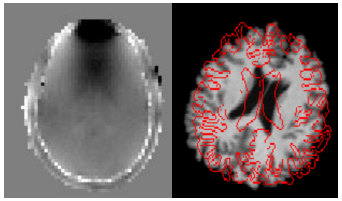
Bias field correction
偏场校正



Segmentation
分割

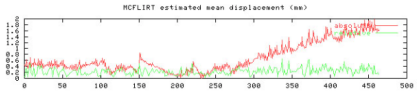


VBM or vertex analysis
VBM分析

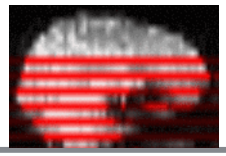


Registration & unwarping
配准&变换

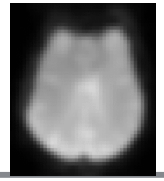
Functional data:
功能数据



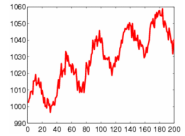
Motion correction
头动矫正



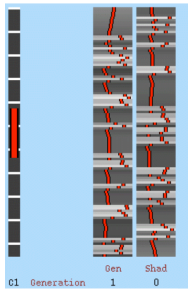
Slice timing correction
层间时间矫正



Spatial filtering
空间滤波

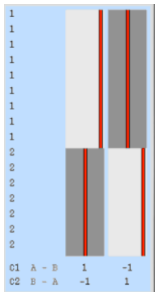


Temporal filtering
时间滤波



Regressors & contrasts
回归&对比

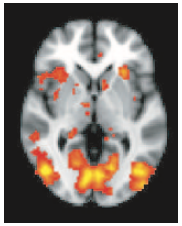
First level GLM
第一水平的GLM



Regressors & contrasts
回归&对比

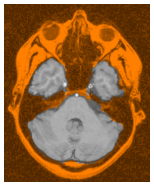
Group level GLM
组水平GLM

Thresholding & correction
阈限和矫正

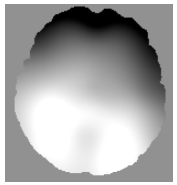


Preprocessing

Structural data:
结构数据



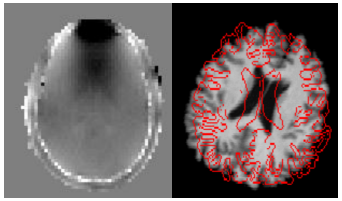
Brain extraction
脑提取



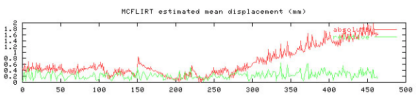
Bias field correction
偏场校正

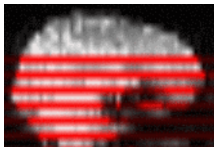
Segmentation

VBM or vertex analysis



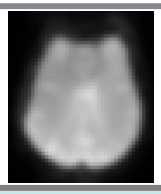
Registration & unwarping
配准&变换



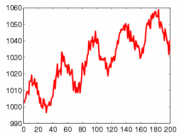


Motion correction
头动矫正

Slice timing correction
层间时间矫正



Spatial filtering
空间滤波



Temporal filtering
时间滤波

Functional data:
功能数据

Regressors & contrasts

First level GLM

Regressors & contrasts

Group level GLM

Thresholding & correction

Structural preprocessing summary

结构像预处理概述

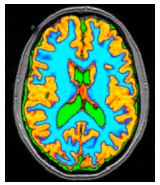
Brain extraction 脑提取	Remove non-brain tissue to help with registration. Needs to be very precise. 移除非脑组织，这一步需要非常小心
Bias field correction 偏场矫正	Corrects for B1 inhomogeneities 矫正上一步结果的非同质性
Registration 配准	Put images into same space (standard space for group analysis) 将图像放到同一个标准空间，为之后的组分析做准备

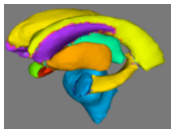
fMRI preprocessing summary

功能像预处理概述

Brain extraction 脑提取	Remove non-brain tissue to help with registration移除非脑组织帮助配准
Motion Correction 头动矫正	Get consistent anatomical coordinates (always do this) 获取一致性的结构坐标
Slice Timing 层间时间矫正	Get consistent acquisition timing (use temporal derivative instead) 获取一致性的时间位置
Spatial Smoothing 空间平滑	Improve SNR & validate GRF 提高信噪比&验证高斯随机场分布
Temporal Filtering 时间滤波	Highpass: Remove *slow* drifts 移除慢波信号
Registration & unwarping 配准&变换	Unwarping corrects for B0 inhomogeneities. Registration images into same space (standard space for group analysis)校正B0不均匀性，将图像配准到同一空间（用于组分析的标准空间）

Single-subject analysis单被试分析





Structural data:
结构数据

Brain extraction
脑提取

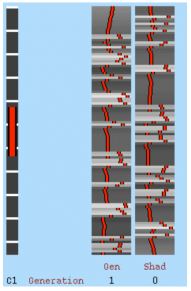
Bias field correction
偏场校正

Segmentation
分割

VBM or vertex analysis
VBM分析

Registration & unwarping
配准&变换

Functional data:
功能数据



Motion correction
头动矫正

Slice timing correction
层间时间矫正

Spatial filtering
空间滤波

Temporal filtering
时间滤波

Regressors & contrasts
回归&对比

First level GLM
第一水平的GLM

Regressors & contrasts

Group level GLM

Thresholding & correction

Structural single-subject summary

结构像单被试处理概述

Segmentation 分割	Tissue-type segmentation (FAST), sub-cortical segmentation (FIRST), white matter hyperintensities (BIANCA) 组织类型分割、皮质下结构分割、白质信号增强
Voxel-based morphometry 基于体素的形态测量	To detect differences in local grey matter volume. Jacobian modulation and spatial smoothing. 检测局部灰质的差异，Jacobian调整和空间平滑
Vertex analysis 峰值分析	To run shape analysis on subcortical structures. *first_utils* uses bvars output from FIRST to perform vertex analysis (4D output image of all subject meshes) 为了进行皮层下的形状分析，首先使用FIRST中的结果来进行峰值分析

fMRI single-subject summary

功能像单被试处理概述

EVs/ regressors 实验变量/回归因子	Design matrix: model of predicted responses based on stimuli presented at each time point 设计矩阵，基于刺激呈现的时间点的对响应变量的预测模型
GLM 一般线性模型	Estimate parameter estimates for each EV so that the linear combination best fits the data 对每个EV的估计参数（其线性组合可以最好的拟合数据）
Contrasts (F or t) 对比（F检验或T检验）	Maths on parameter estimates to ask research questions. Result is a COPE image per contrast 对研究问题的参数估计，其结果为脑区（每个比较都有一个）

Group-level analysis组水平分析

Structural data:
结构数据

Brain extraction
脑提取

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偏场校正

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VBM or vertex analysis
VBM分析

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配准&变换

Functional data:
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Motion correction
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Slice timing correction
层间时间矫正

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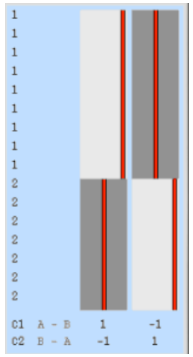
空间滤波

Temporal filtering
时间滤波

Regressors & contrasts
回归&对比

First level GLM
第一水平的GLM



Regressors & contrasts
回归&对比

Group level GLM
组水平GLM

Thresholding & correction

Group-level analysis summary组水平分析概述

EVs/ regressors 实验变量/回归因子	Design matrix: one entry per subject. Can describe subject groups, confounds etc 设计矩阵：每个被试有一个输入，可以描述被试的组信息
GLM 一般线性模型	*Structural*: inputs are smoothed, modulated GM volumes (VBM) or single subject subcortical meshes (vertex analysis) 结构：输入的图像被平滑，调整灰质或者单个被试的皮层下结构 *fMRI*: inputs are first-level COPE and VARCOPE images. fMRI：输入的是first-level的cope/varcope结果
Contrasts (F or t) 对比（F检验或T检验）	*Structural*: tests differences in GM density or shape 结构：检测灰质密度和形状的差异 *fMRI*: Each group-level contrast is tested for each of the subject-level contrasts fMRI：对单被试水平的比较结果进行组水平比较

Statistical inference 统计概述

Structural data:
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脑提取

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偏场校正

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分割

VBM or vertex analysis
VBM分析

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配准&变换

Functional data:
功能数据

Motion correction
头动矫正

Slice timing correction
层间时间矫正

Spatial filtering
空间滤波

Temporal filtering
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Regressors & contrasts
回归&对比

First level GLM
第一水平的GLM

Regressors & contrasts
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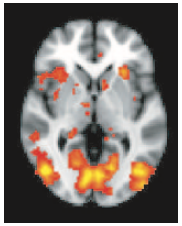
Group level GLM
组水平GLM

Thresholding & correction



Statistical inference summary

Fixed effects vs mixed effects 固定效应VS混合效应	Averaging across multiple sessions Generalisation to population
OLS vs FLAME vs Randomise	Quick, doesn't use VARCOPEs Uses COPEs & VARCOPEs Non-parametric
Multiple comparison correction (FWE/ FDR)	Gaussian Random Field (voxel or cluster based) TFCE

What we covered so far

Structural data:
结构数据

Brain extraction
脑提取

Bias field correction
偏场校正

Segmentation
分割

VBM or vertex analysis
VBM分析

Registration & unwarping
配准&变换

Preprocessing

Functional data:
功能数据

Motion correction
头动矫正

Slice timing correction
层间时间矫正

Spatial filtering
空间滤波

Temporal filtering
时间滤波

Regressors & contrasts
回归&对比

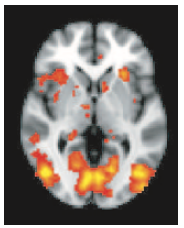
First level GLM
第一水平的GLM

Single-subject analysis

Regressors & contrasts
回归&对比

Group level GLM
组水平GLM

Thresholding & correction



Group-level analysis

Statistical inference

Looking ahead:

resting state 静息态

diffusion 弥散

arterial spin labeling

血管标记成像

Generic blueprint

1. Data acquisition 数据获取

2. Data preprocessing 数据预处理

3. Single-subject analysis 单个被试的分析

4. Group-level analysis 组水平分析

5. Statistical inference 统计推断

Resting state analysis静息态分析

1. Data acquisition数据获取 → Consider using multiband
   考虑使用多频段MB序列
2. Data preprocessing数据预处理
3. Single-subject analysis单被试分析
4. Group-level analysis组水平分析
5. Statistical inference统计推断

Resting state analysis静息态分析

1. Data acquisition数据获取 → Consider using multiband
2. Data preprocessing数据预处理 → Need to apply extra noise-reduction steps (ICA)
需要利用额外的去躁步骤（独立成分分析）
3. Single-subject analysis单被试分析
4. Group-level analysis组水平分析
5. Statistical inference统计推断

Resting state analysis静息态分析

1. Data acquisition数据获取 → Consider using multiband
2. Data preprocessing数据预处理 → Need to apply extra noise-reduction steps (ICA)
3. Single-subject analysis单被试分析
4. Group-level analysis组水平分析
5. Statistical inference统计推断

→ Group ICA+dual regression/ Network analysis (FSLnets)
组分析ICA+双回归/网络分析

Diffusion analysis弥散分析

1. Data acquisition数据获取 → Diffusion directions弥散朝向
   Blip-up/blip-down向上/向下编码方向
   Multi shell多层
2. Data preprocessing数据预处理
3. Single-subject analysis
   单被试分析
4. Group-level analysis组水平分析
5. Statistical inference统计推断

Diffusion analysis弥散分析

1. Data acquisition数据获取 → Diffusion directions
Blip-up/blip-down
Multi shell

2. Data preprocessing数据预处理 → Need to correct for eddy currents
需要对涡流矫正

3. Single-subject analysis

单被试分析

4. Group-level analysis组水平分析

5. Statistical inference统计推断

Diffusion analysis弥散分析

1. Data acquisition数据获取 → Diffusion directions
Blip-up/blip-down
Multi shell

2. Data preprocessing数据预处理 → Need to correct for eddy currents

3. Single-subject analysis → Fractional anisotropy/ mean diffusivity/ tractography
部分各异向性/平均扩散率/纤维束追踪

单被试分析

4. Group-level analysis组水平分析

5. Statistical inference统计推断

ASL analysis

1. Data acquisition数据获取 → label and control images 标记和控制图像
   background suppression 背景压制
   calibration image 校准图像
2. Data preprocessing数据预处理
3. Single-subject analysis
   单被试分析
4. Group-level analysis组水平分析
5. Statistical inference统计推断

ASL analysis

1. Data acquisition数据获取 → label and control images
background suppression
calibration image

2. Data preprocessing数据预处理 → label-control subtraction
标记-控制图像差值

3. Single-subject analysis
单被试分析 label-control subtraction

4. Group-level analysis组水平分析

5. Statistical inference统计推断

ASL analysis

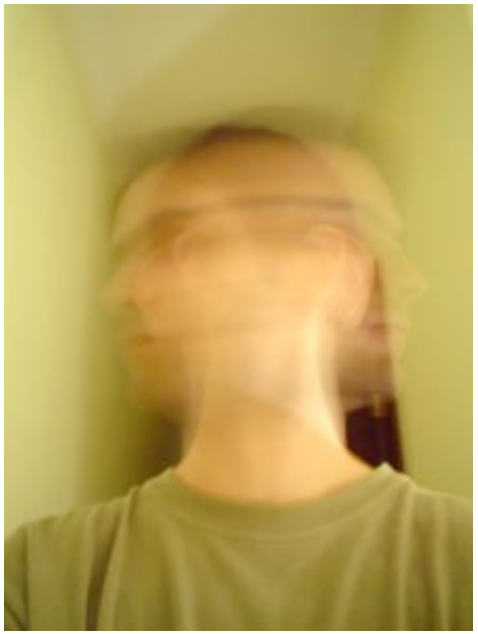
1. Data acquisition数据获取 → label and control images
   background suppression
   calibration image
2. Data preprocessing数据预处理 → label-control subtraction
3. Single-subject analysis
   单被试分析 → Perfusion weighted image 灌注加权磁共振成像
   Absolute perf. measurements 绝对灌注测量
   Partial volume correction 部分体积修正
4. Group-level analysis组水平分析
5. Statistical inference统计推断

Advanced preprocessing

进阶预处理

Case Study: Motion Artefacts

案例学习：头动伪影



Scenario:

Young/elderly/sick subjects that move a lot during an FMRI study

年轻人/老年人/病人在fMRI中头动较多

Problem:

Motion correction does not fully correct for excessive motion 对于过多的头动，仅仅头动矫正是不够的。

Sudden motion creates massive distortion (>12 DOF)

突发性的头动会造成大量的信号干扰 （大于12个自由度的运动）

Smaller, slower motion induces intensity changes due to physics effects (e.g. spin history) and interpolation

小的、慢的头动导致信号密度发生变化，由于物理成像因素（比如自旋轨迹）和插值

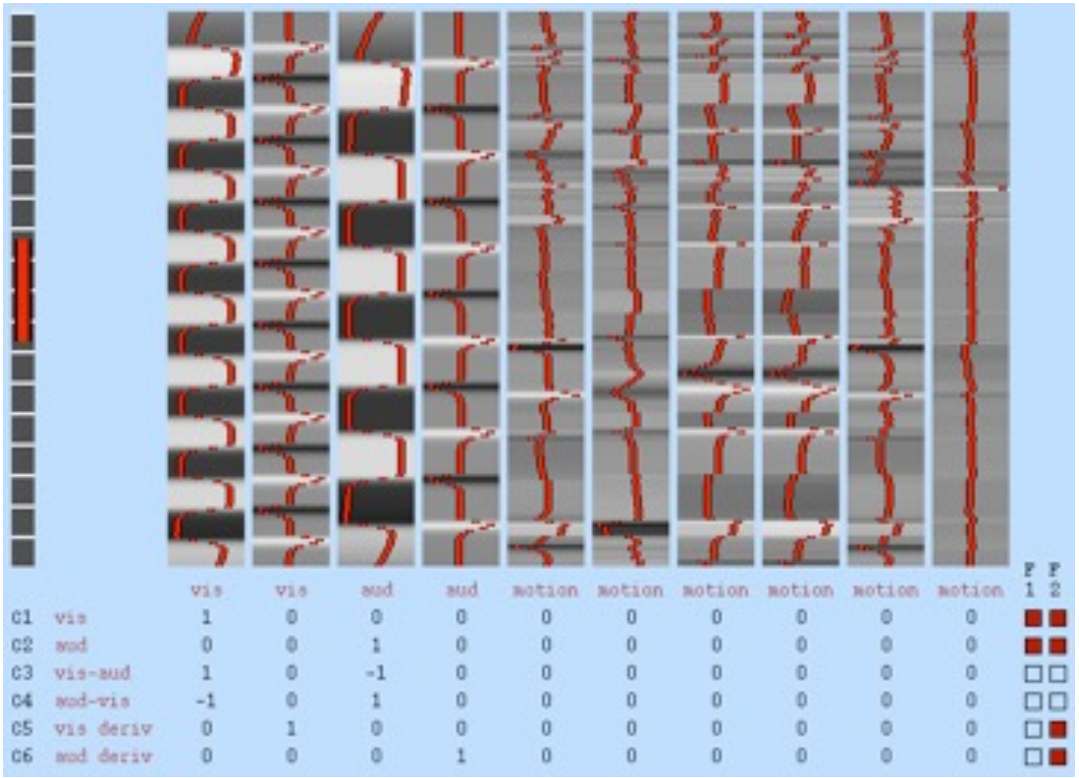
Solution:

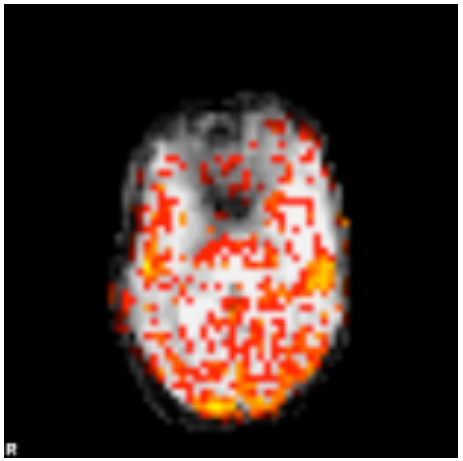
Remove or compensate for motion artefacts 移除或者补偿头动

Motion Artefact Correction头动伪影校正

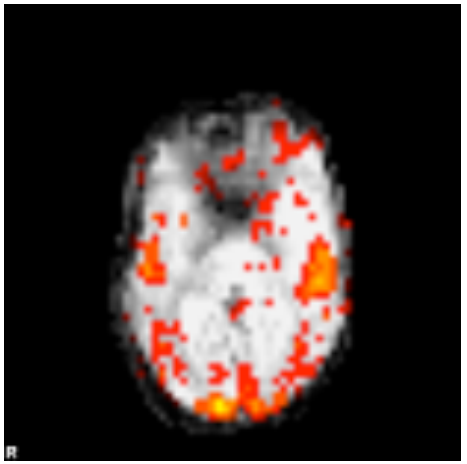
Options for motion artefact correction:

1. Add motion parameters as confound EVs 增加头动参数作为协变量
2. Detect "outlier" timepoints and remove them via confound EVs
   检测这些异常值，并且移除
3. Use ICA (MELODIC) denoising for cleanup 使用ICA去除噪音





Without motion parameter EVs
无头动协变量的结果



With motion parameter EVs
有头动协变量的结果

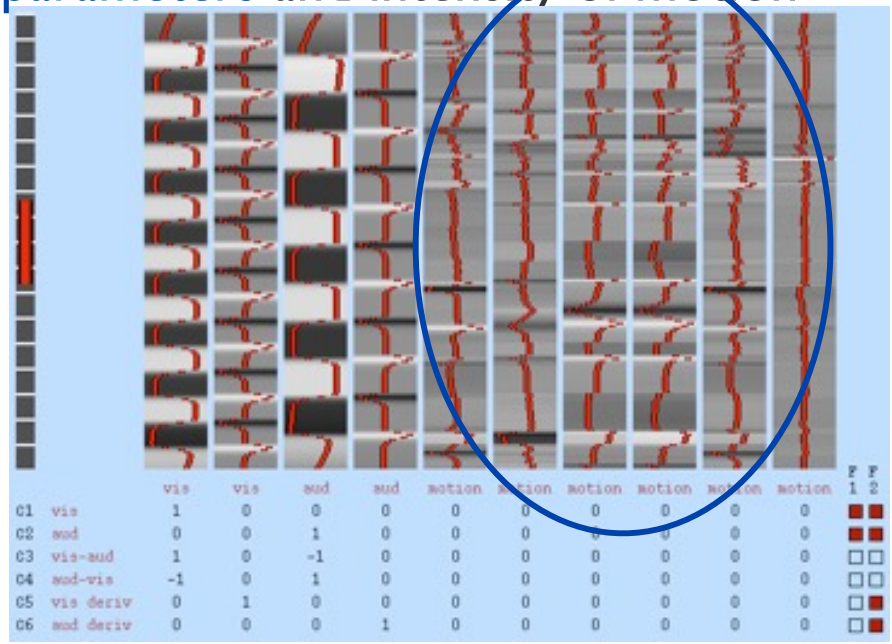
Motion Parameter Confounds

Add the 6 parameters (rotations and translations) as measured by MCFLIRT to the GLM as *confounds* - simple button in FEAT 增加6个头动参数到GLM中

- Removes any correlated signals (since they are confounds) 移除任何相关的信号
- Assumes a linear relationship between motion parameters and intensity of motion artefact

  假设头动参数和头动密度之间存在线性关系
- Assumes that MCFLIRT estimation is accurate 假设MCFLIRT估计是正确的
- Problematic if motion parameters and EVs of interest are highly correlated (stimulus-correlated motion)

  如果头动参数和感兴趣的激活相关，那么数据可能存在问题
  - can result in loss of activation 会造成激活损失
  - orthogonalising EVs does not change result 对EVs的正交分析不会影响结果



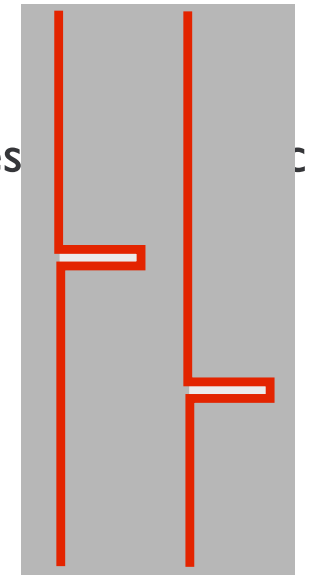
- Also possible to include non-linear (e.g. squared) parameters 也可能包含非线性的参数

Outlier Timepoint Detection

Use *fsl_motion_outliers* to detect timepoints that display large intensity differences to the reference timepoint (after motion correction)
使用fsl头动模块来检测与参考点信号密度差异较大的时间点

- Removes ***all*** influence of the timepoints declared as outliers but does ce any bias (unlike "deleting" timepoints from data)
  移除异常值时间点的影响，但是不产生其他干扰

- Uses one extra confound regressor per outlier timepoint
  每个异常值时间点用一个协变量表示
  - the regressor is zero at all timepoints except the outlier
    该协变量上，出了异常值以外的赋值都为0



Confound matrix with 2 outlier timepoints

- Implemented via confound matrix in the GLM GLM中使用协变量矩阵
  - another simple button in FEAT 另一个简单的FEAT按钮

- Does not assume that MCFLIRT is accurate 并不假设MCFLIRT是准确的
  or that the effect is linear 或影响是线性的

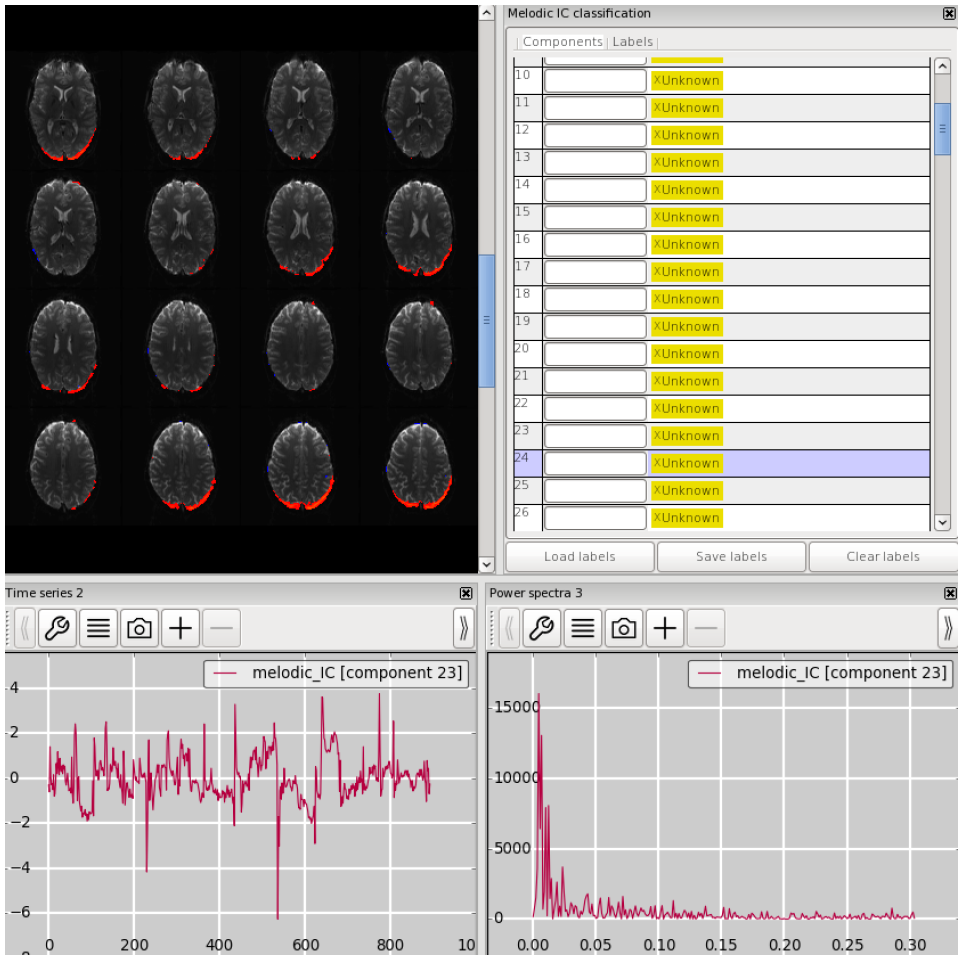
- Can cope with very extreme motion effects 能够处理非常极端的头动影响
  but leaves other timepoints uncorrected 但是会留下一些时间点是没有矫正过的

- Can be combined with other correction methods 可以和其他矫正方法结合

ICA denoising ICA去躁

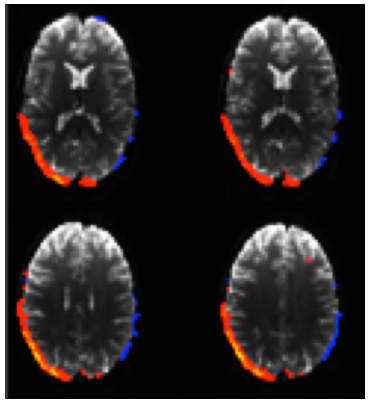
Use ICA (MELODIC) on individual runs to identify components related to motion artefacts and remove these from the 4D data 对个体使用ICA分析确认和头动有关的成分，并且剔除

- Requires identification of components
  需要确认这些成分
  - manual classification 手工确认
  - (semi-) automated classification (FIX/ AROMA) （半）自动分类
- Can also be combined with other cleanup techniques 可以和其他处理方法共同使用
  - ICA denoising should be done first ICA去噪应该首先做
- Can also be used to identify and remove structured noise that is not related to motion
  也可以被用来确认和移除和头动无关的噪音结构



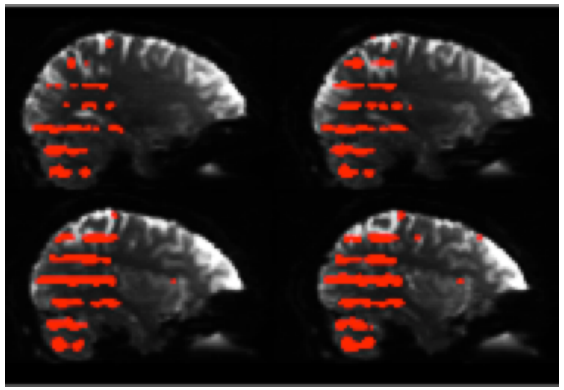
ICA denoising ICA去躁

- Typical motion components display ringing around brain edge 典型的头动成分发生在头部边缘
- Can also note sharp effects in timecourses 时间点上也会出现效应
- There are typically a large number of noise components (70-90%) 存在大量的噪音成分



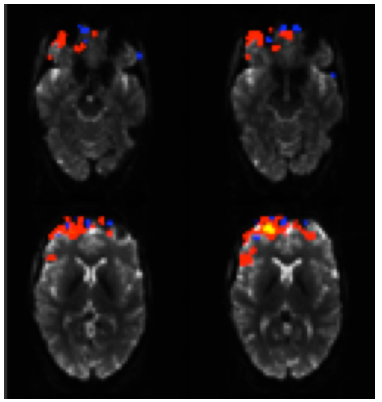
Classic motion

经典头动



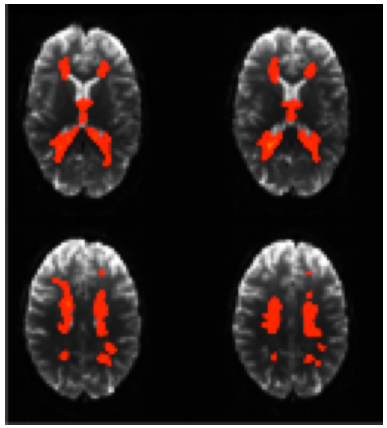
Multiband motion

MB序列中头动

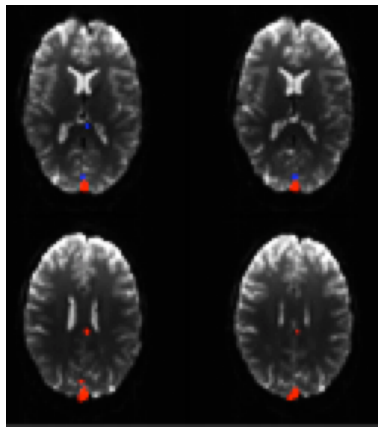


Susceptibility motion

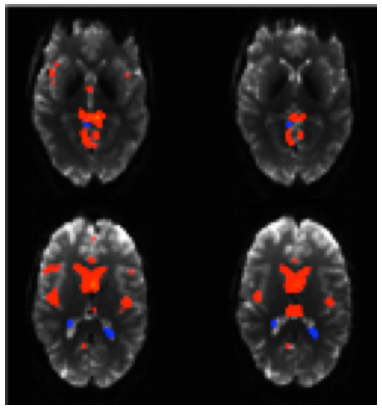
受磁率相关头动



White matter白质

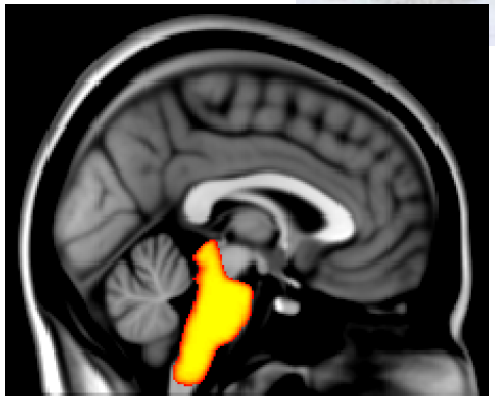


Sagittal sinus 矢状窦



Cardiac/CSF 心跳

Case Study:
Physiological Noise Correction
生理噪音矫正



Scenario:

FMRI study of the brainstem 脑干的研究

Problem:

High levels of pulsatility and respiratory effects in the brainstem and in other inferior areas

脑干及其其他下部脑区的影响

Solution:

Use Physiological Noise Model (PNM) to correct for physiological noise 使用生理噪声模型PNM矫正噪音

Requires independent physiological measurements

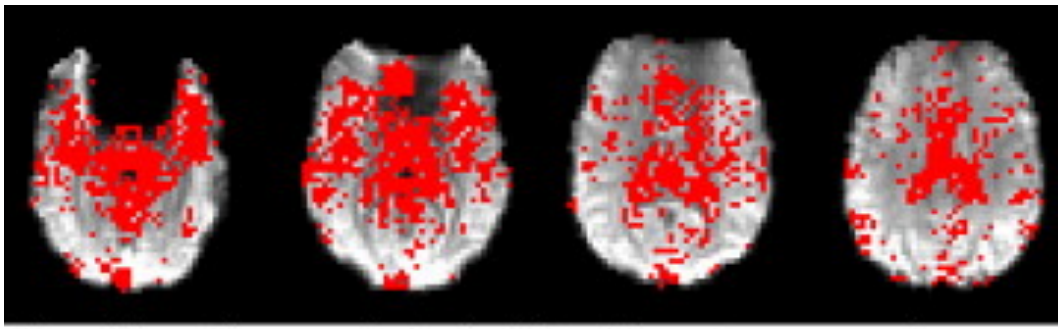
需要独立的生理指标

Location of Effects

Cardiac effects typically occur:

- near vessels and areas of CSF pulsatility (e.g. brainstem, ventricles) 心脏有关的效应发生在血管和CSF区域附近

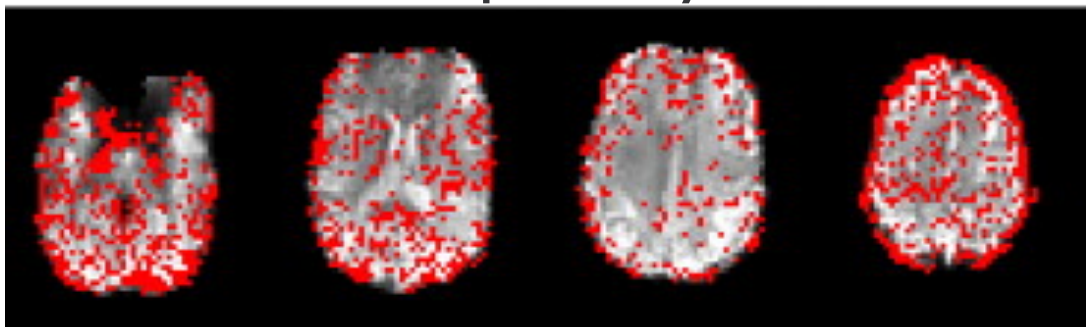
Cardiac



Respiratory effects typically occur:

- in inferior areas (where the induced B0 field changes due to lung volume changes are highest) 下部脑区
- near image edges (due to geometric shifts/distortion by B0 causing large intensity changes) 靠近图像边缘
- throughout the grey matter (due to oxygenation changes) 穿过灰质

Respiratory



Bright & Murphy, NeuroImage, 2013

Physiological Measurements

Need to measure cardiac and respiratory cycles.
需要测量心跳和呼吸循环数据

Several options available - the easiest are: 一些可以采取的简便措施

Pulse Oximeter 指脉

Respiratory Bellows 呼吸腰带

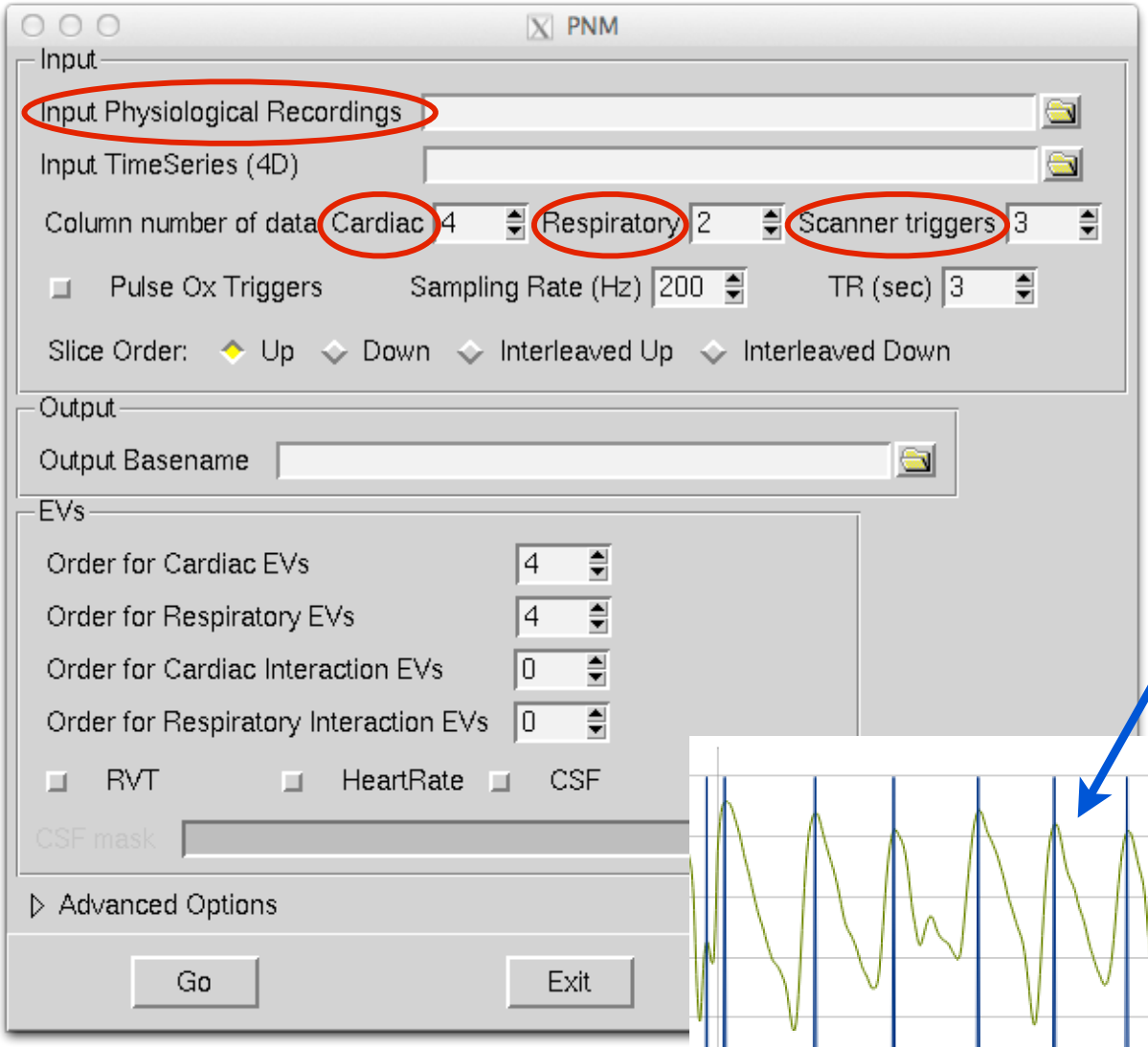
Also ***record scanner triggers*** from the scanner console
同步记录磁共振扫描仪触发点

Triggers are essential for accurate timing over the course of the experiment. Beware of standard scanner recordings and timing drift or rescalings. trigger
对于准确的时间定位非常有必要。注意扫描和时间定位的标准

PNM

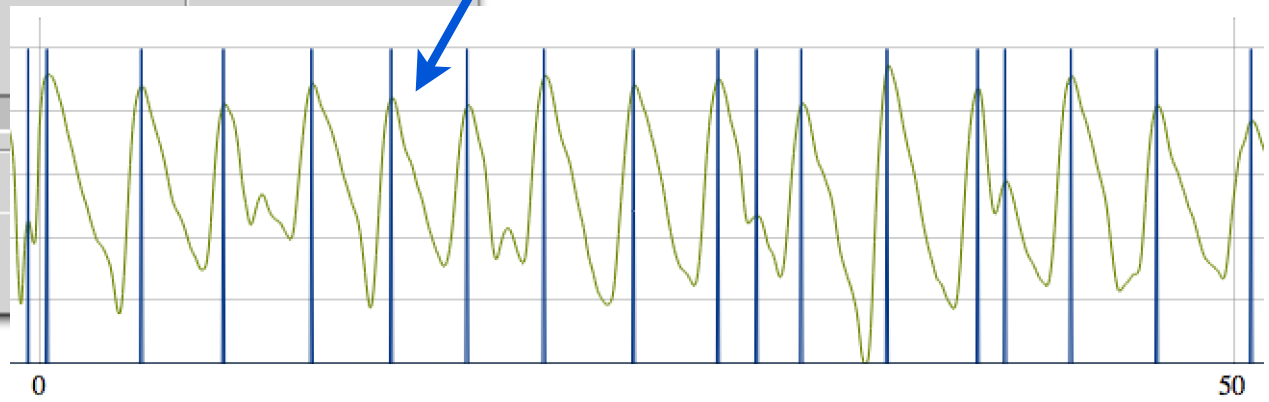
生理噪声模型

Physiological Noise Model (GUI)



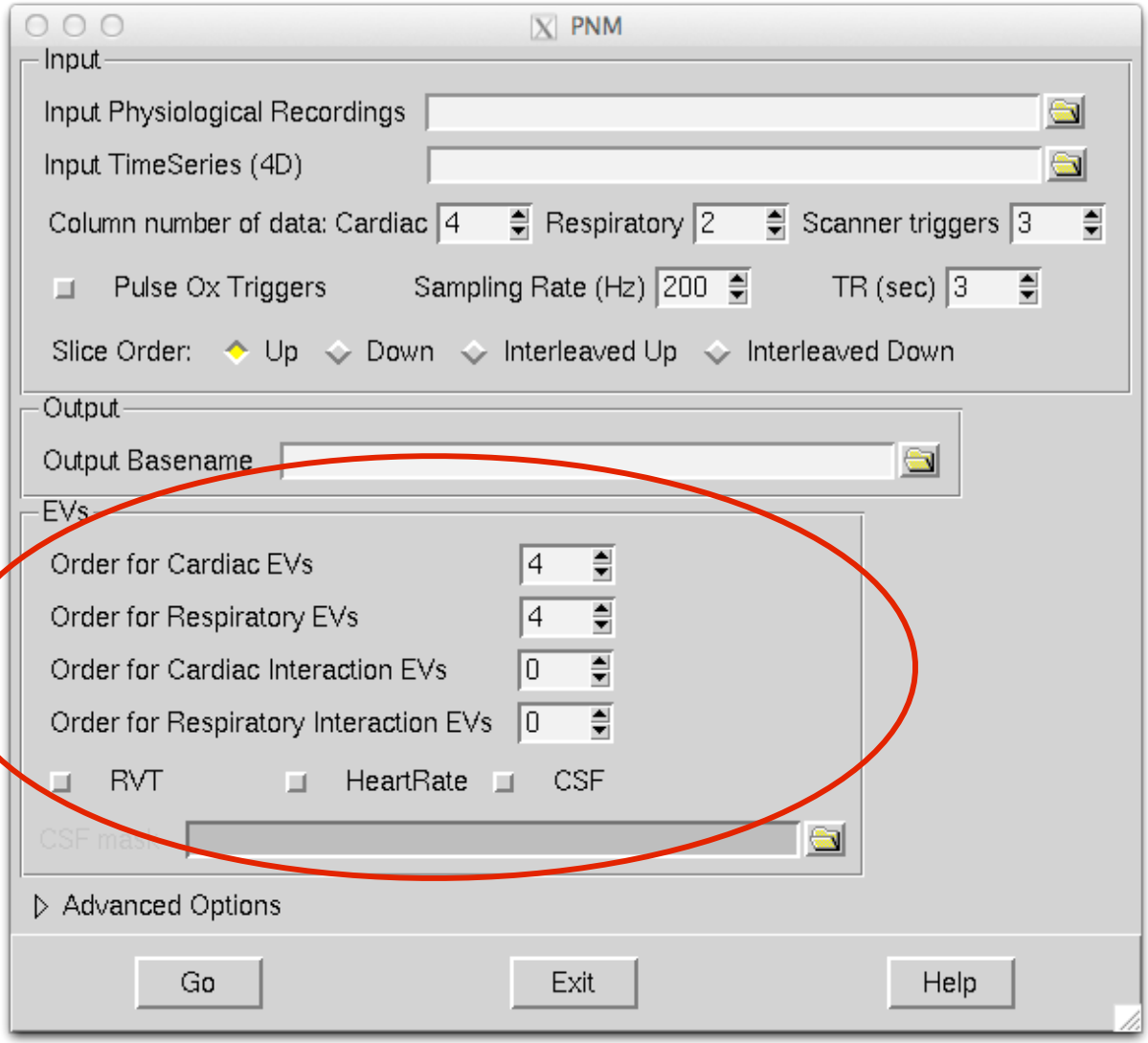
Requires text file with physiological recordings (cardiac, respiratory, triggers) 需要记录生理信号的文件（包括心跳、呼吸、扫描触发点）

Peak detection in physiological trace needs manual checking via webpage
生理信号中的峰值检测需要通过网页进行手动检查



PNM

Physiological Noise Model (GUI)



Need to specify what type of corrections: 需要确认什么类型的矫正

- Fourier series 傅里叶级数
  (harmonics / shape) 谐波和形状

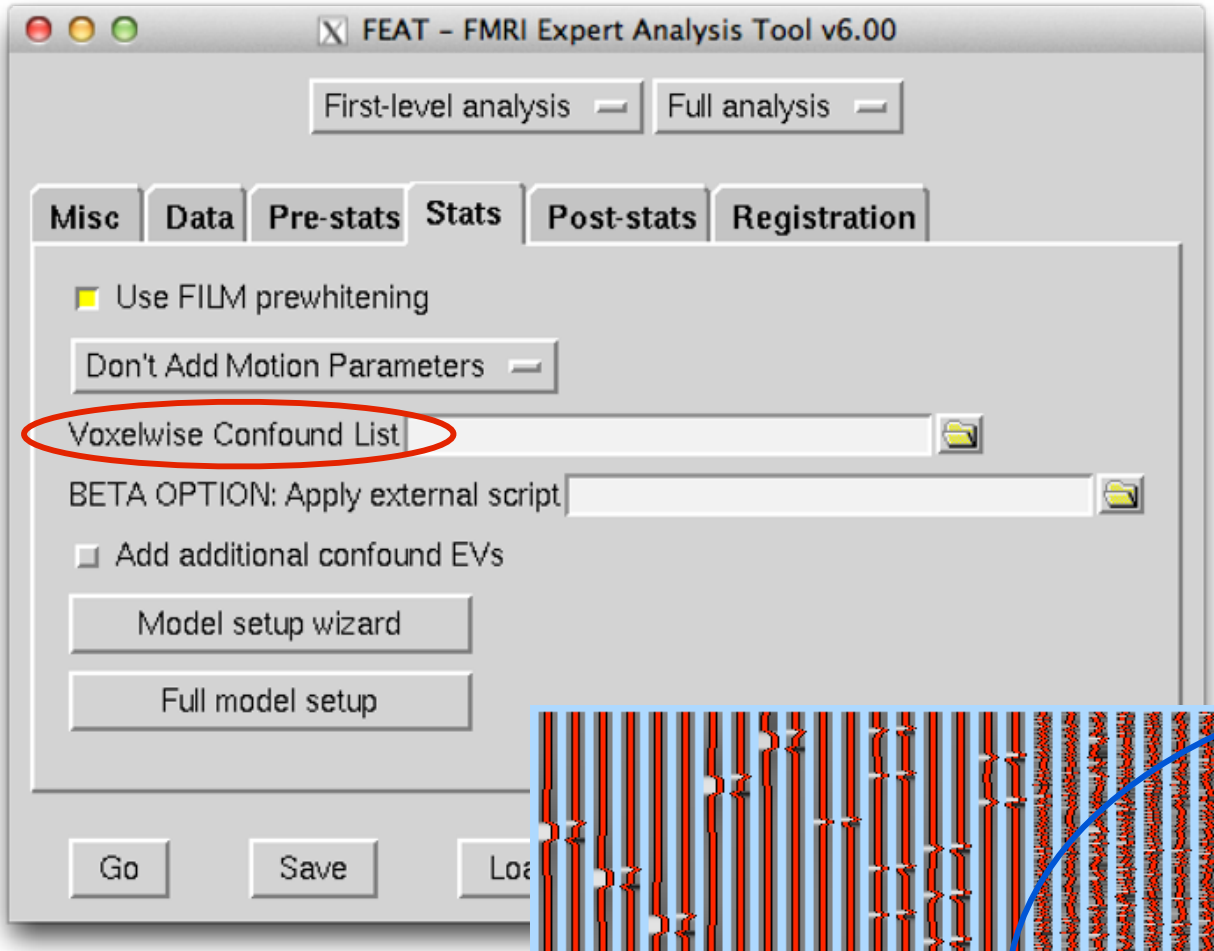
- Interactions 交互
  (resp x cardiac)

NB: higher orders = better fit to shape, but many more EVs and so less DOF
更高阶=更好的拟合形状，但会增加很多*EV*从而降低模型自由度

- RVT
  (resp volume per time) 呼吸体积频率

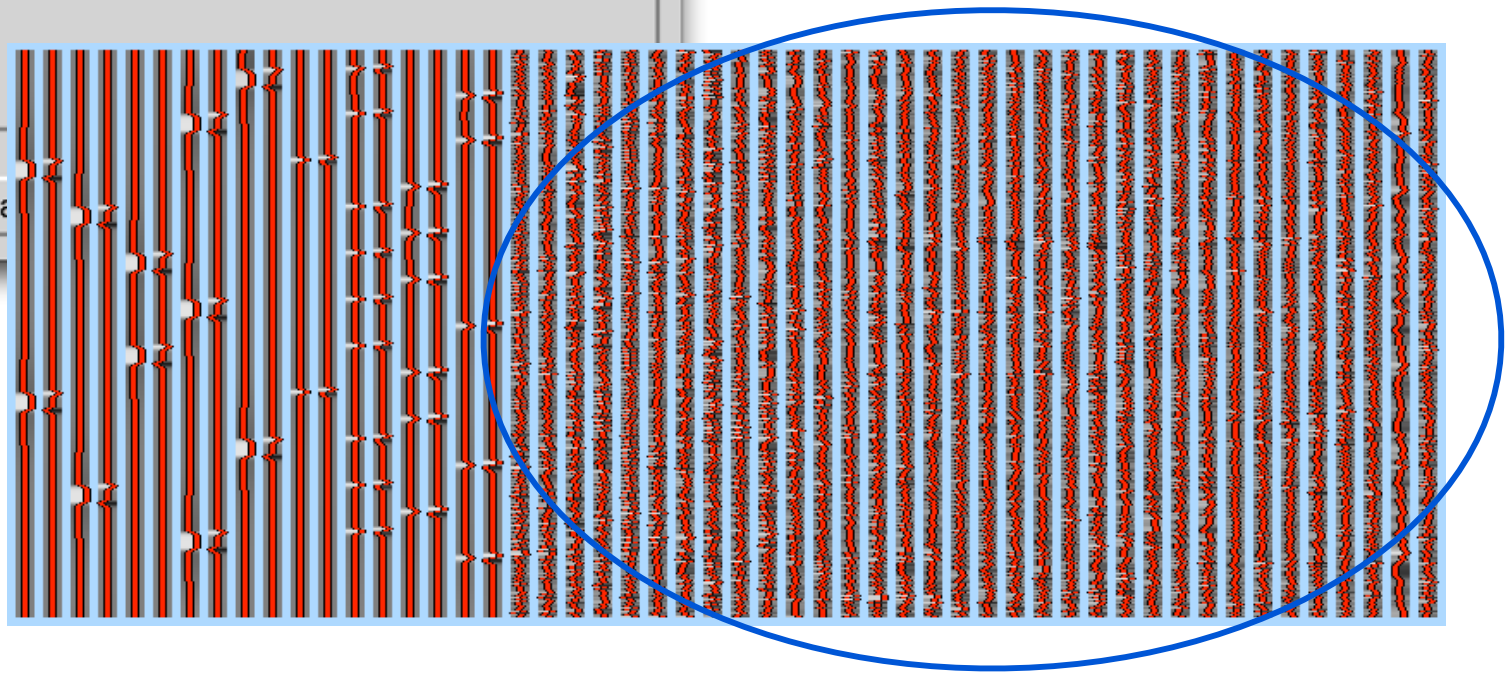
- HeartRate 心率
- CSF 脑脊液

Use in FEAT



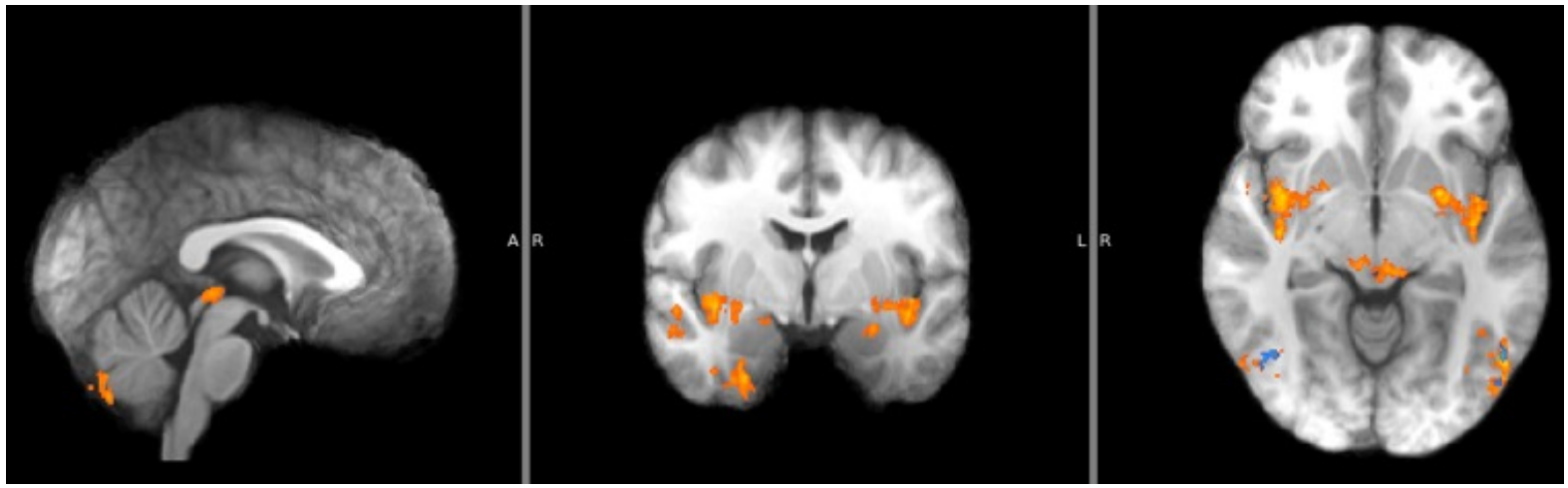
PNM GUI creates a set of files suitable for use as ***Voxelwise Confounds*** in FEAT

PNM图形界面创建适用于单体素协变量模型的一系列文件



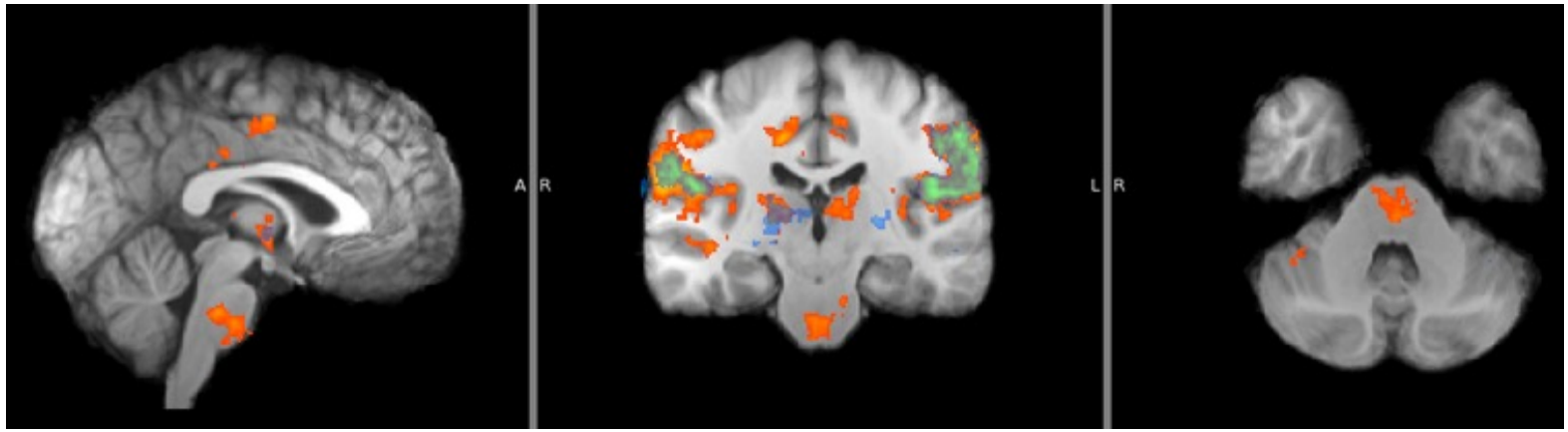
Results: Pain-punctate arm

结果实例：机械刺痛手臂实验



AXIAL

N=6, Group mean (Fixed effects), Z=1.8 p<0.05



CORONAL

With PNM
使用生理噪声模型

Without PNM
未使用生理噪声模型

Both
重叠

Demeaning EVs

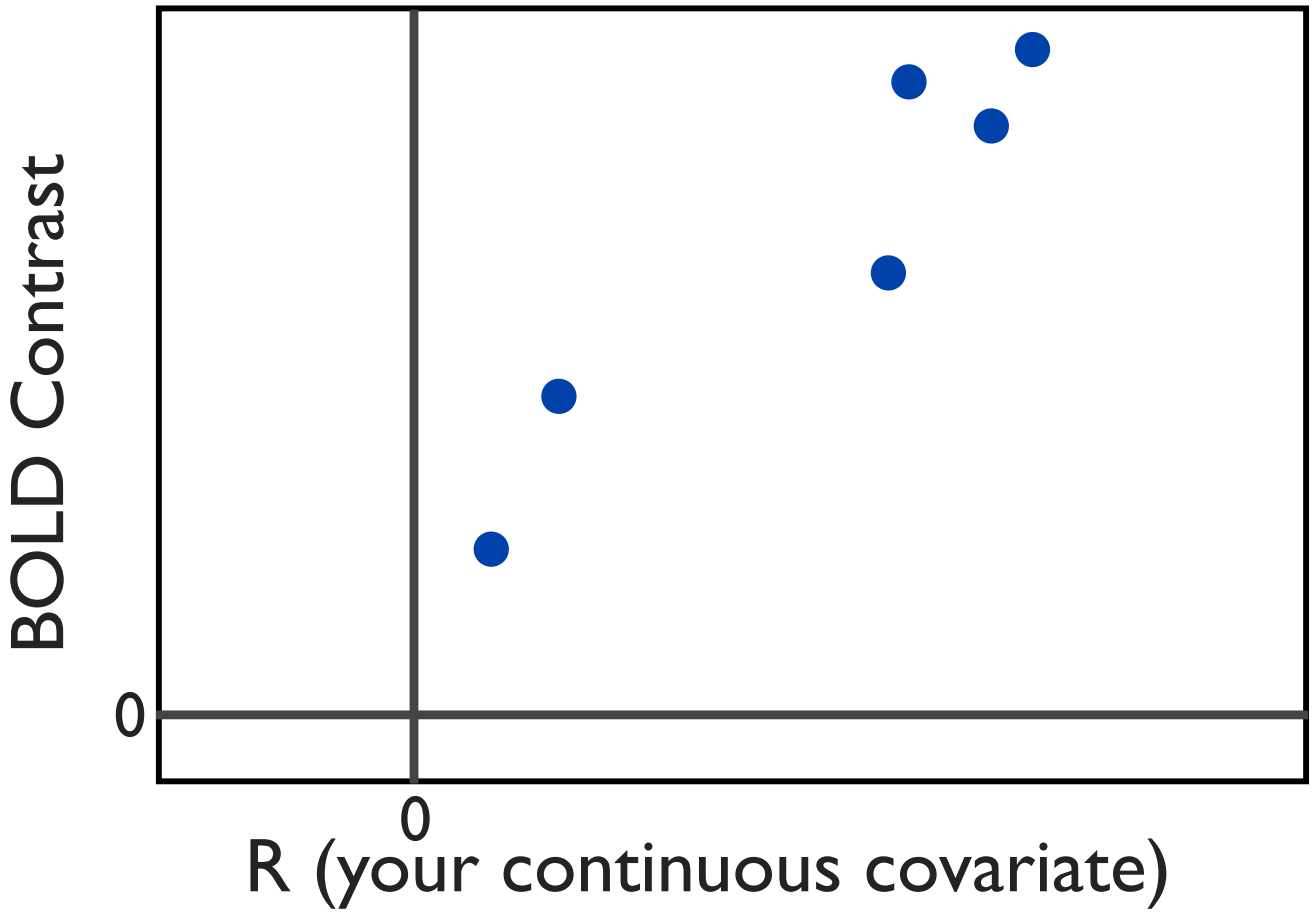
对EV去均值化

Demeaning at the group level

mumford.fmripower.org/mean_centering/

$$\begin{pmatrix} 1 & r_1 \\ 1 & r_2 \\ 1 & r_3 \\ 1 & r_4 \\ 1 & r_5 \\ 1 & r_6 \end{pmatrix}$$

组水平去均值化



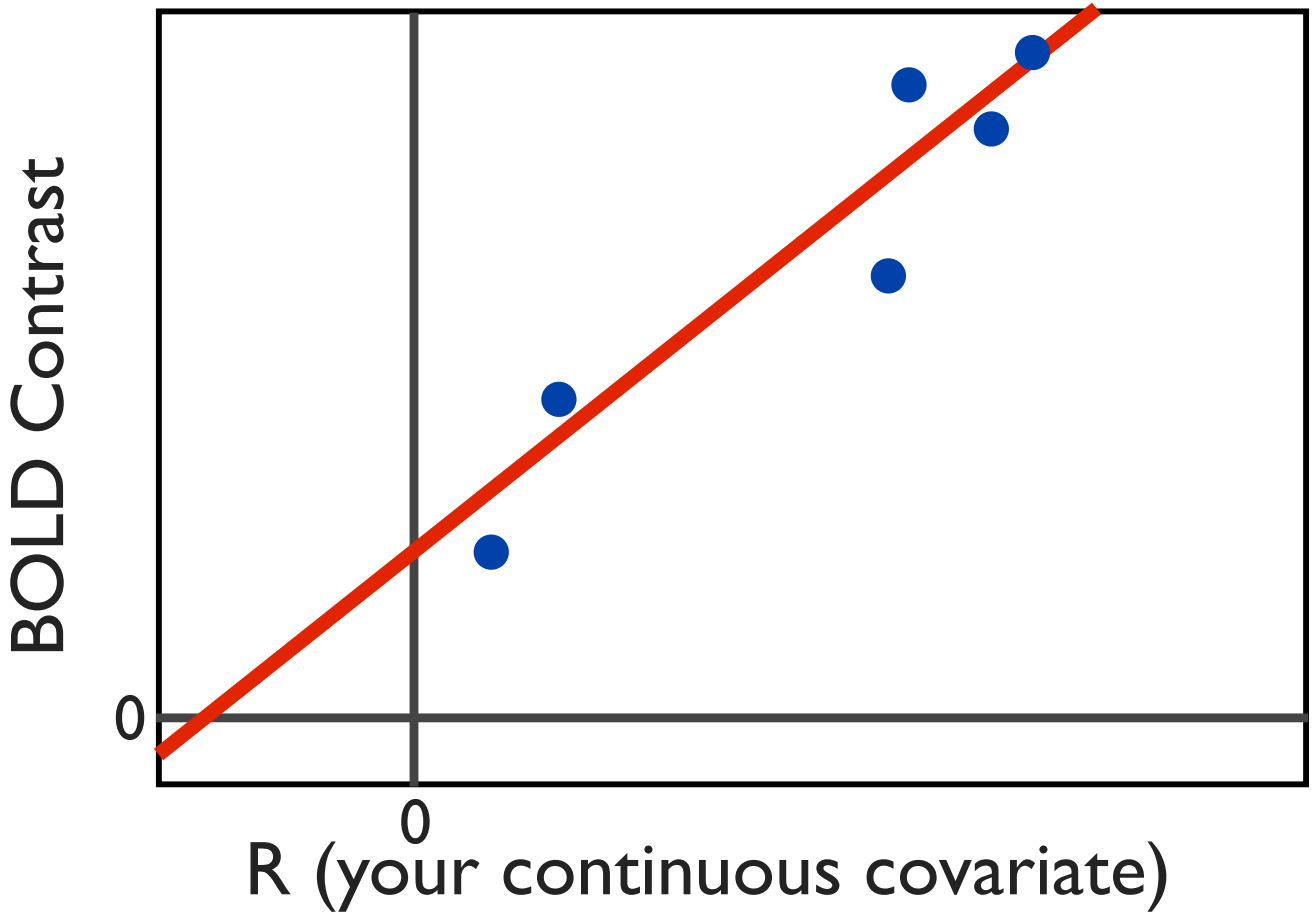
连续型协变量

e.g. reaction time 反应时

mumford.fmripower.org/
mean_centering/

Demeaning

去均值化



e.g. reaction time 反应时

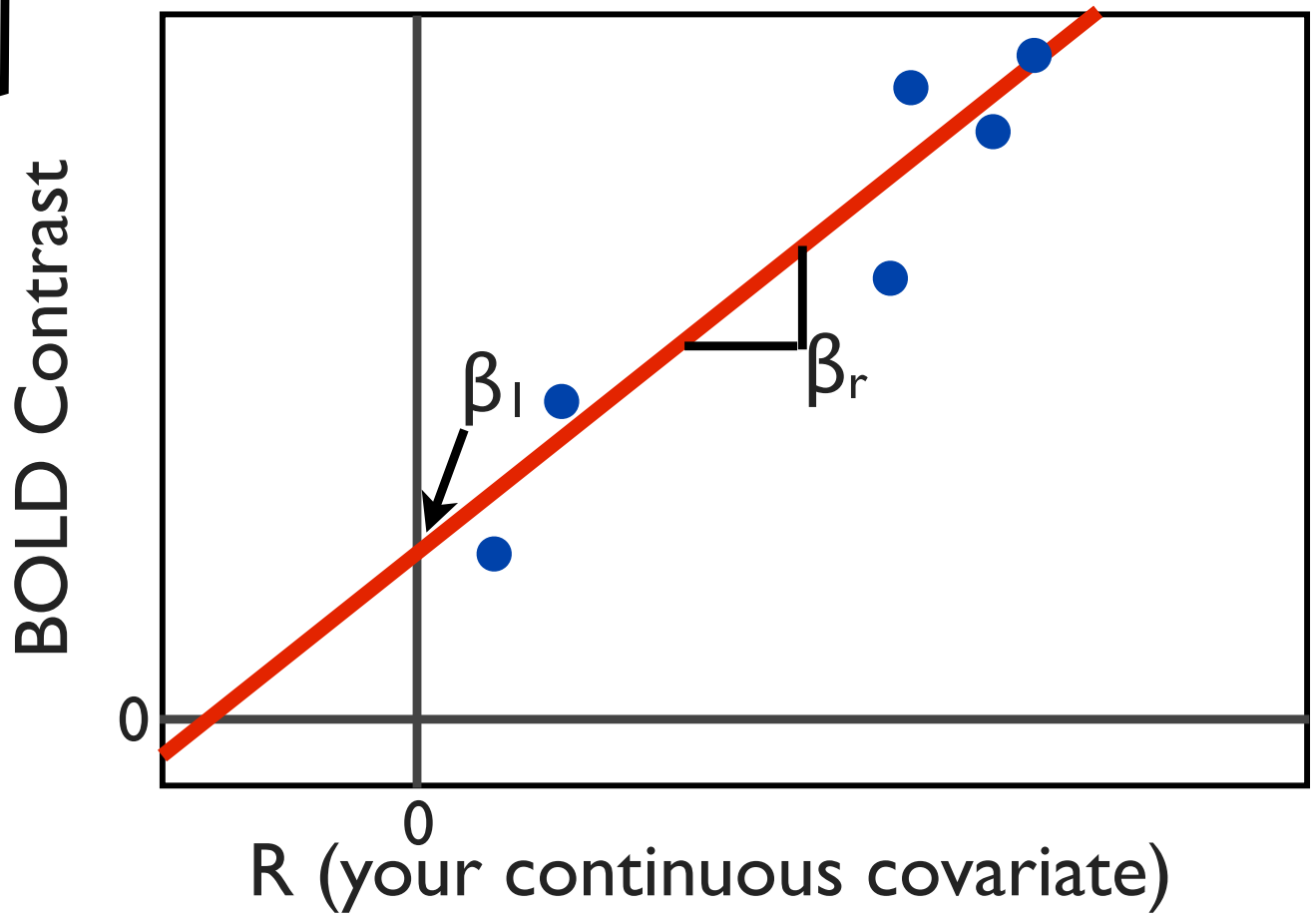
Demeaning

去均值化

mumford.fmripower.org/mean_centering/

$$\begin{pmatrix} 1 & r_1 \\ 1 & r_2 \\ 1 & r_3 \\ 1 & r_4 \\ 1 & r_5 \\ 1 & r_6 \end{pmatrix} \begin{pmatrix} \beta_1 \\ \beta_r \end{pmatrix}$$

$$[\,1 \quad 0\,]$$



e.g. reaction time 反应时

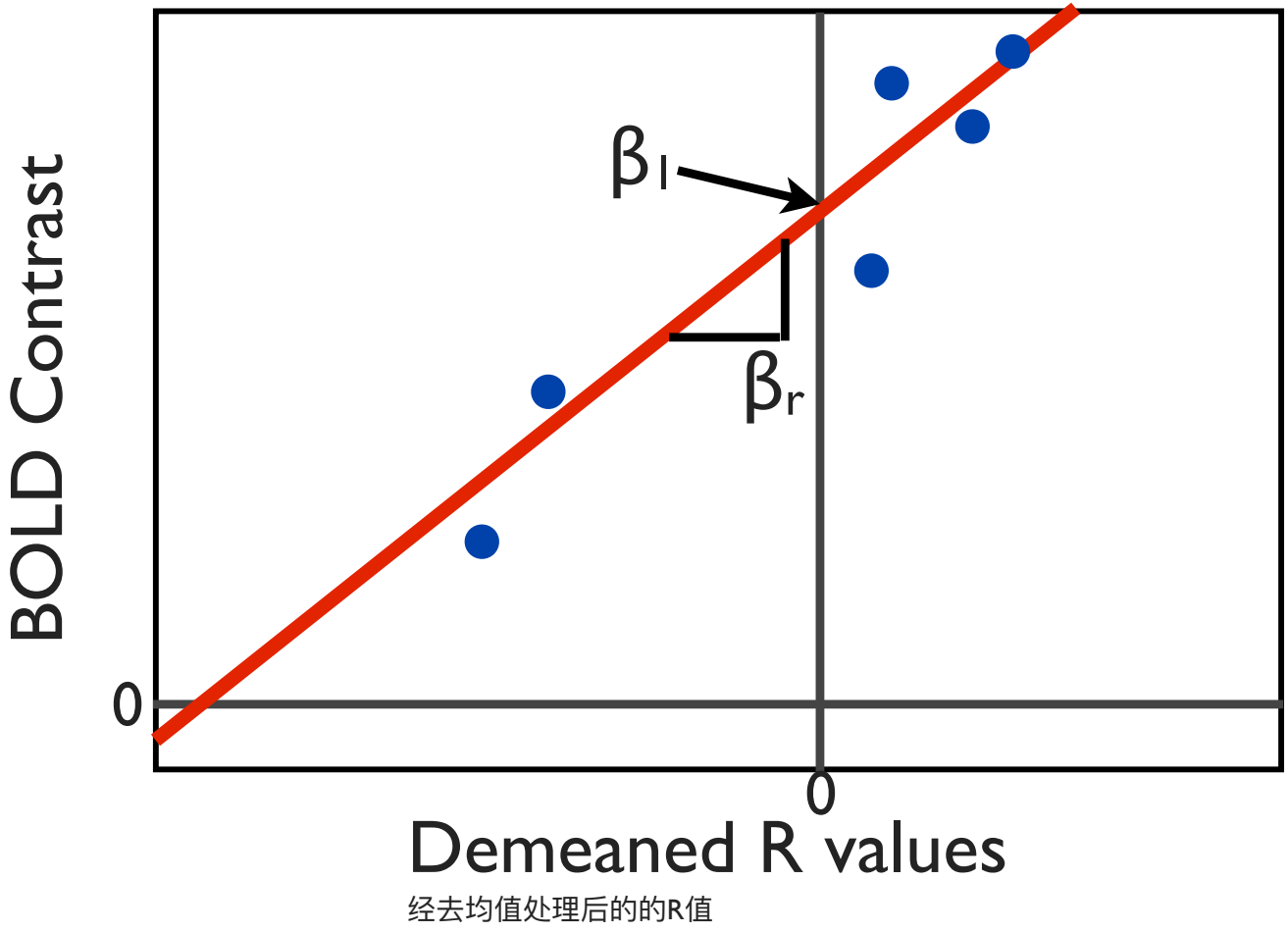
Demeaning

去均值化

mumford.fmripower.org/mean_centering/

β_1 now represents BOLD at group average R

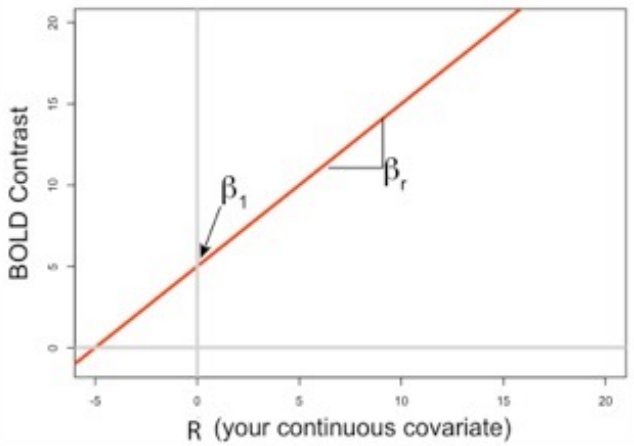
β1现在代表组平均R的BOLD



经去均值处理后的的R值

Demeaning

mumford.fmripower.org/mean_centering/

Design matrix	What does the fitted model look like?	Contrast	Does demeaning change the stats?	Demeaning recommended?
$\begin{pmatrix} 1 & r_1 \\ 1 & r_2 \\ 1 & r_3 \\ 1 & r_4 \\ 1 & r_5 \\ 1 & r_6 \end{pmatrix} \begin{pmatrix} \beta_1 \\ \beta_r \end{pmatrix}$		[1 0]	YES	YES
		[0 1]	NO	YES

Mean centred value = $r_1 - \bar{r}$

where $\bar{r}$ is the mean of r_1 to r_6

Adding or subtracting a mean from EV_2 (i.e. r_1 to r_6) **changes β_1**

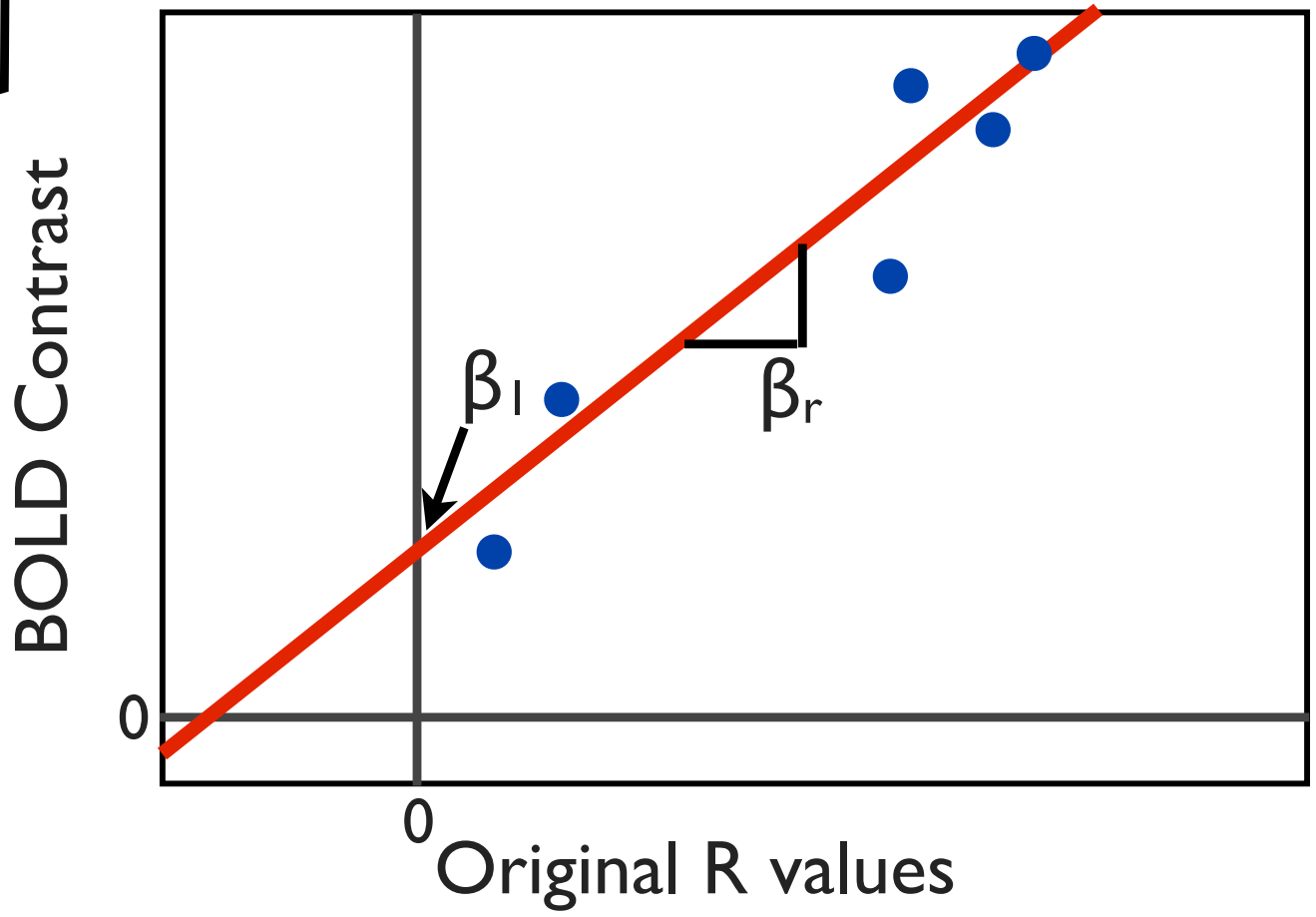
Demeaning

mumford.fmripower.org/
mean_centering/

$$\begin{pmatrix} 1 & r_1 \\ 1 & r_2 \\ 1 & r_3 \\ 1 & r_4 \\ 1 & r_5 \\ 1 & r_6 \end{pmatrix} \begin{bmatrix} \beta_1 \\ \beta_r \end{bmatrix}$$

$$[\,0 \;\; 1\,]$$

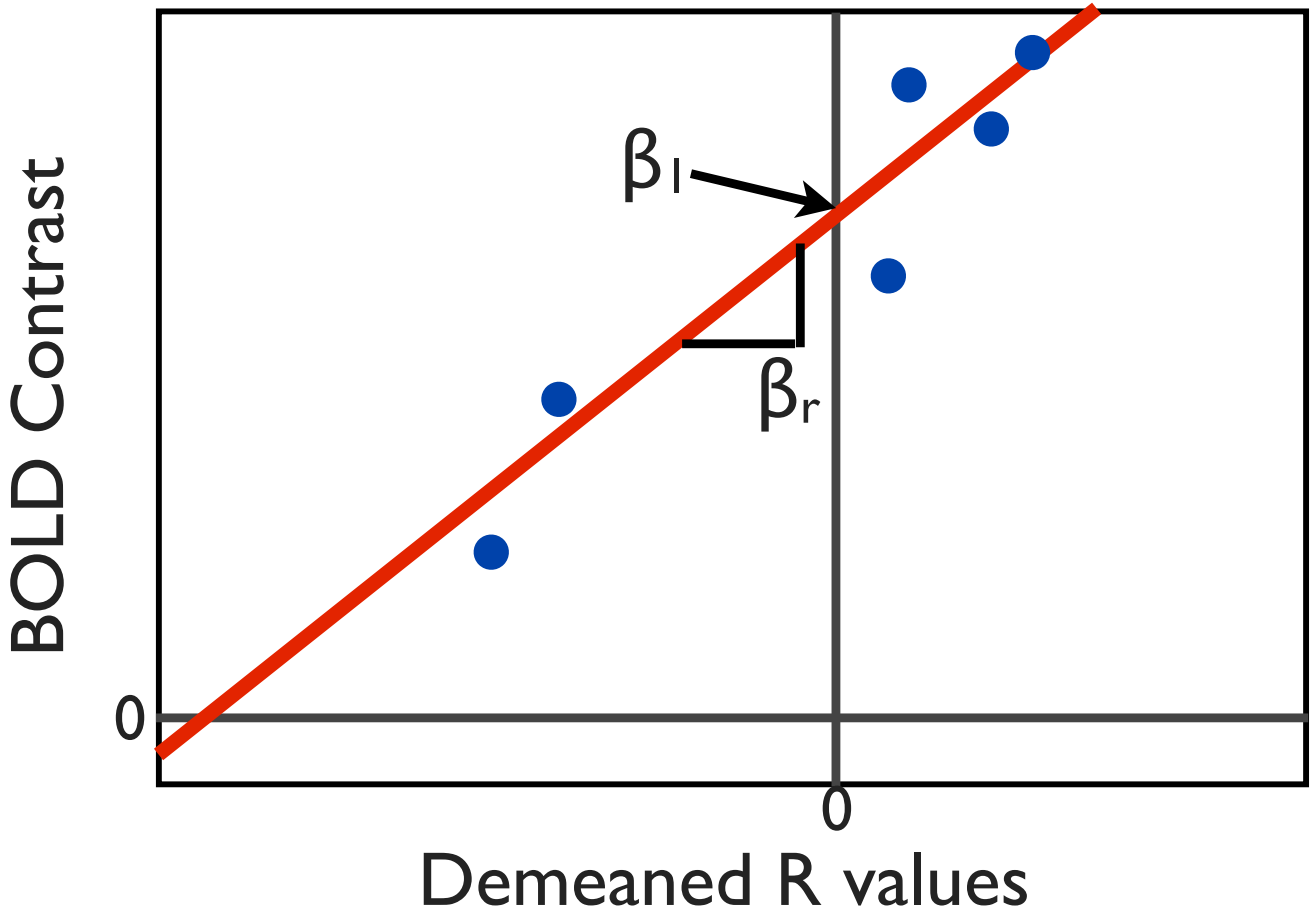
β_1 represents BOLD at R=0



Demeaning

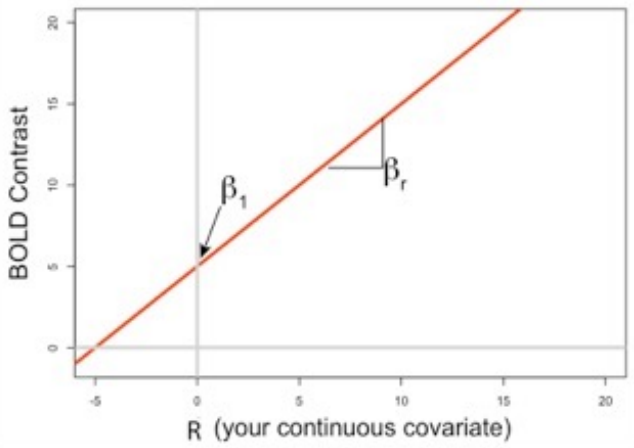
mumford.fmripower.org/mean_centering/

β_1 now represents BOLD at group average R



Demeaning

mumford.fmripower.org/mean_centering/

设计矩阵 **Design matrix**	拟合模型长这样 **What does the fitted model look like?**	对比设置 **Contrast**	去均值改变统计结果了吗? **Does demeaning change the stats?**	**Demeaning recommended?** 推荐去均值操作?
$\begin{pmatrix} 1 & r_1 \\ 1 & r_2 \\ 1 & r_3 \\ 1 & r_4 \\ 1 & r_5 \\ 1 & r_6 \end{pmatrix} \begin{bmatrix} \beta_1 \\ \beta_r \end{bmatrix}$		[1 0]	YES	YES
		[0 1]	NO	YES

Mean centred value = $r_1 - \bar{r}$ 去均值的数据

where $\bar{r}$ is the mean of r_1 to r_6 $\bar{r}$ 是均值

Adding or subtracting a mean from EV_2 (i.e. r_1 to r_6) **changes β_1**

从EV2加入或者去除均值会改变B1的估值

Advanced designs

设计进阶

Case Study: Parametric Designs

案例学习：参数设计

Contact Heat-Evoked Potential Stimulator
接触性热痛刺激器

Scenario:

Interested in specific responses to multiple levels of a painful
刺激对多层次疼痛刺激的具体反应感兴趣

Specific questions:

Are there regions showing significant responses to painful stimuli?
有没有对疼痛刺激有显著反应的区域?

Are there regions where higher intensity stimuli produce larger responses?
有没有高强度刺激产生更大反应的区域?

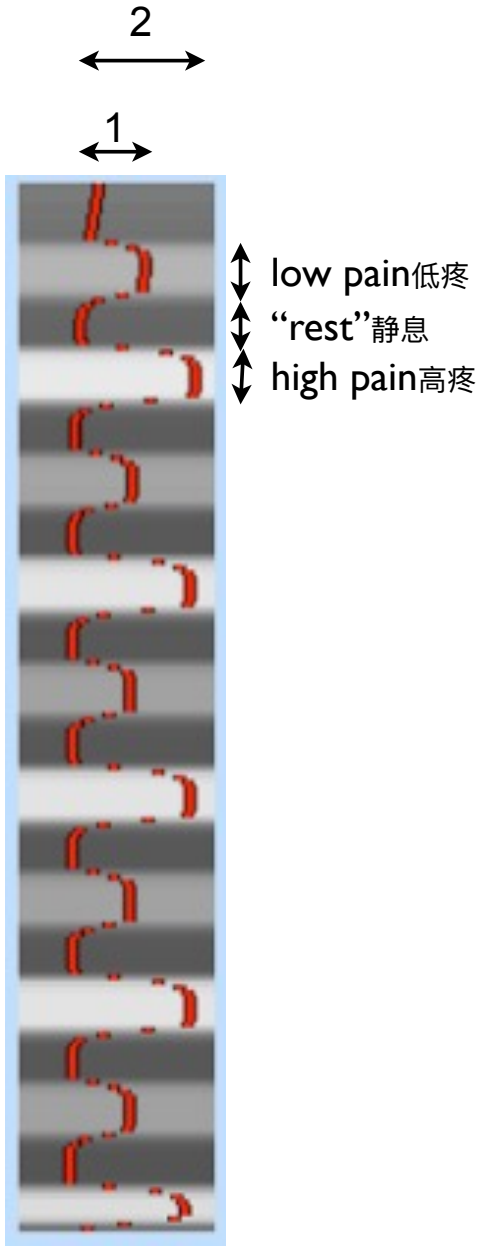
Are there regions with a linear response across multiple levels of stimuli?
是否存在在多个刺激水平上具有线性反应的区域?

Solution:

Multiple regressors 多重回归

Contrasts and F-tests 对比和F检验

Analysis of responses to multiple levels of painful stimuli: modelling 分析多水平疼痛刺激反应：建模



- Possible approach: model a specific hypothesis - high produces twice the response as low

  可能的方法：建立一个特定的假设-高疼产生的反应是低疼的两倍

- Pre-supposes relationship between stimulation strength and response

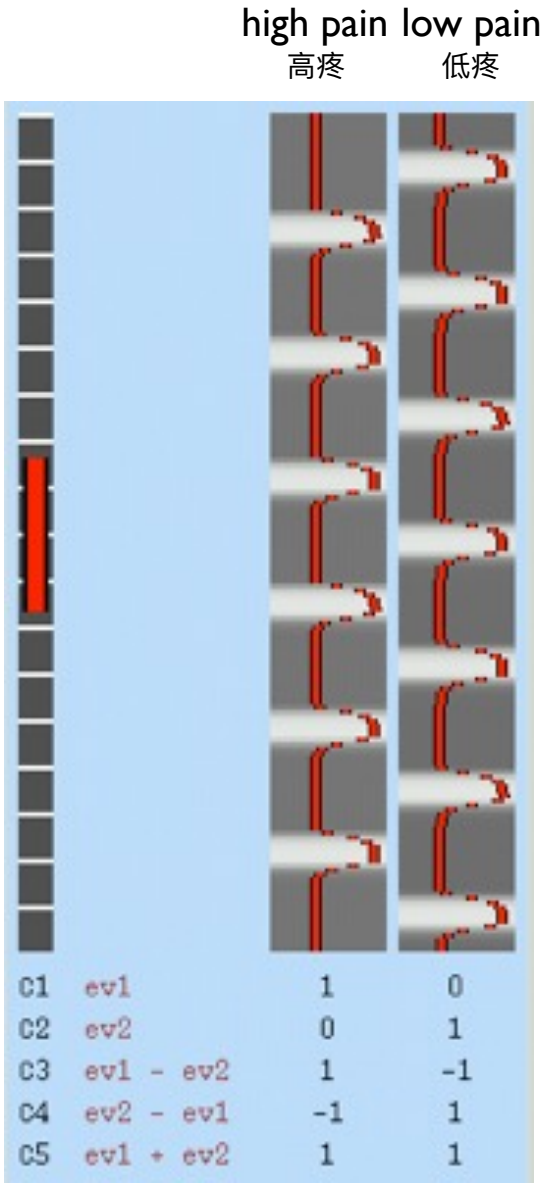
  假设刺激强度与反应的关系

- Can only ask the question about the pre-supposed relationship

  只能问一个关于预先假定的关系的问题

Analysis of responses to multiple levels of painful stimuli: modelling

分析多水平疼痛刺激反应：建模

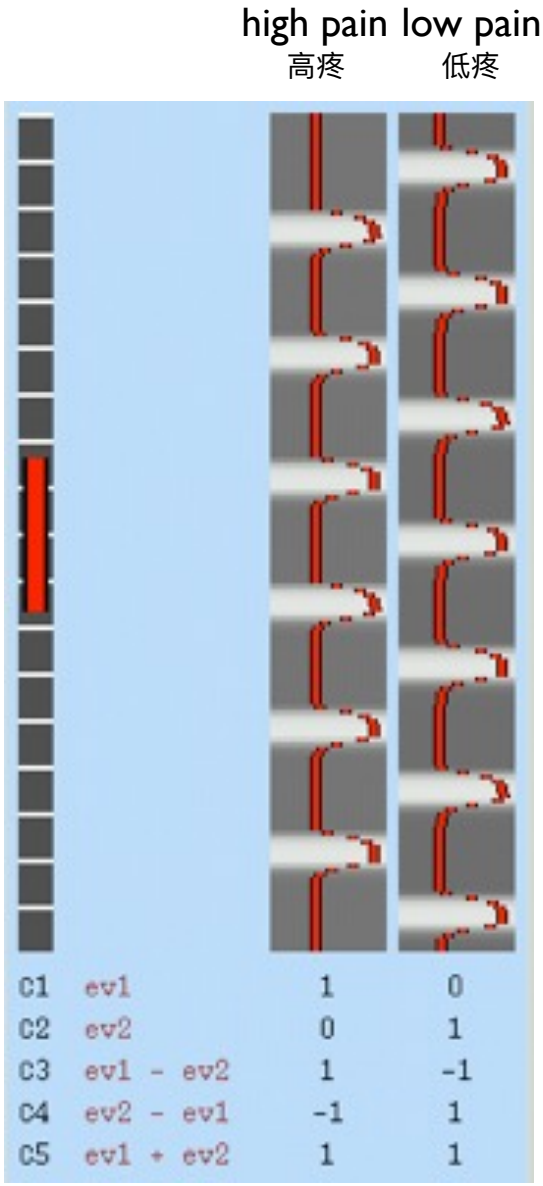


- Better approach: model as if two completely different stimuli
  更好的方法：像两个完全不同的刺激一样建模
- Now, no pre-supposition about relationship between stimulation strength and response
  现在，还没有关于刺激强度和反应之间关系的预先假设

- Can assess responses to individual stimuli
  能评估对个体刺激的反应
  - t-contrast [0 1]:“ response to low pain” 表示低疼

Analysis of responses to multiple levels of painful stimuli: modelling

分析多水平疼痛刺激反应：建模



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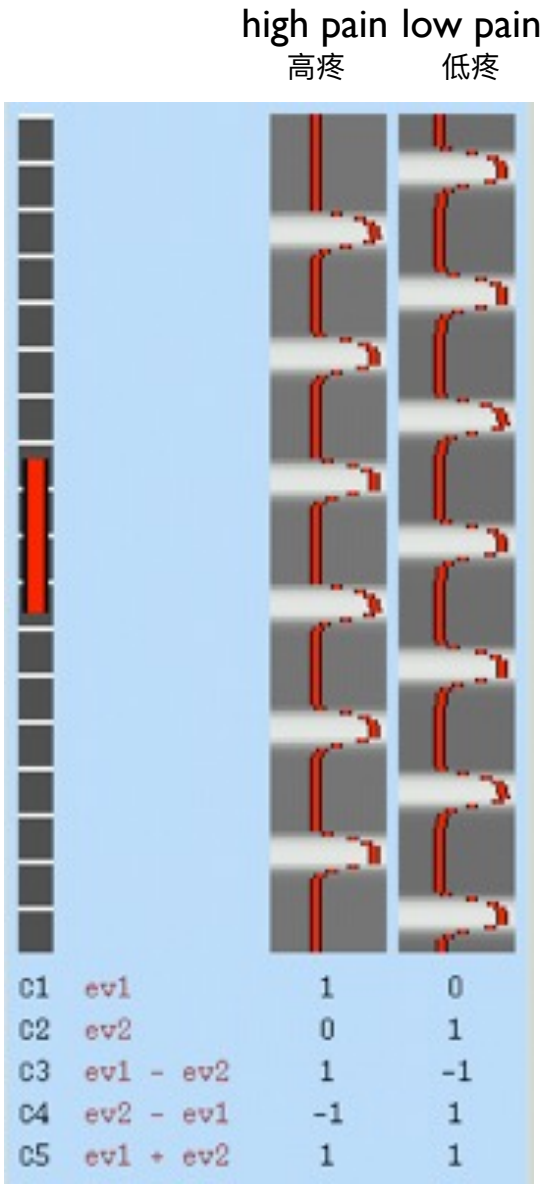
- Can compare the size of the fits of the two regressors 可以比较两个回归函数的拟合大小
  - t-contrast [1 -1] : "is the response to high pain greater than that to low pain ?"
    对高程度疼痛的反应比对低程度疼痛的反应大吗?
  - t-contrast [-1 1] : "is the response to low pain greater than that to high pain ?"
    对低程度疼痛的反应比对高程度疼痛的反应大吗?

Analysis of responses to multiple levels of painful stimuli: modelling

分析多水平疼痛刺激反应：建模



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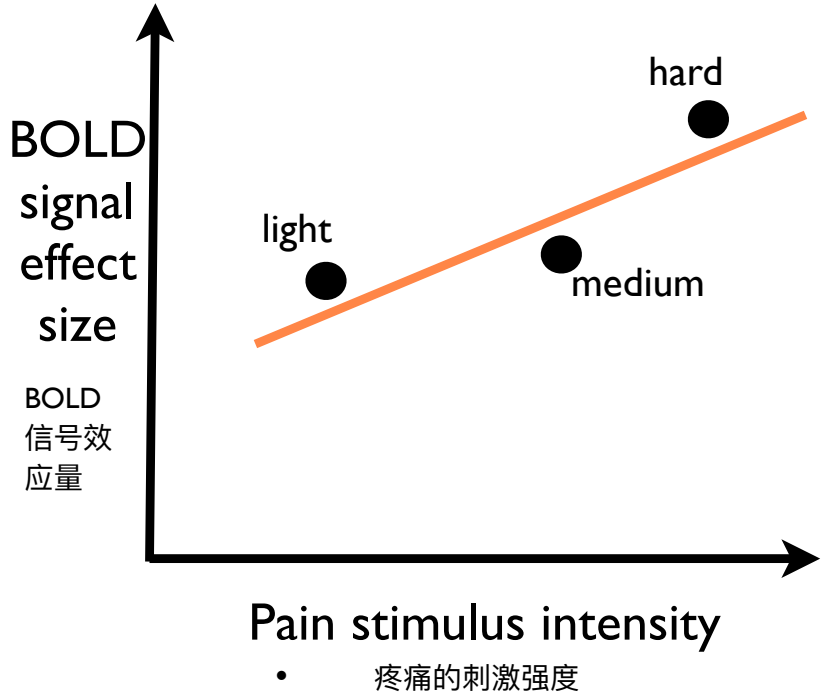
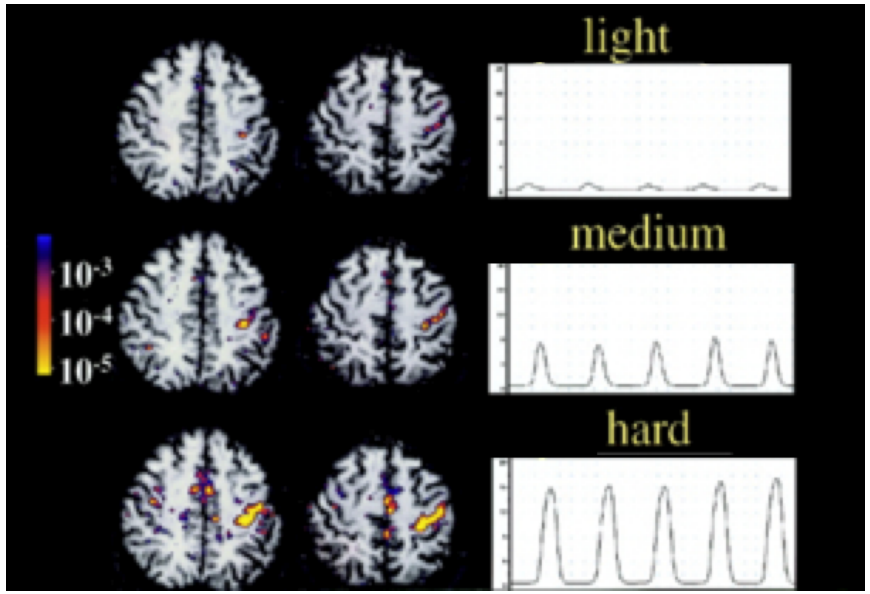
- Average response? 平均响应?
  - t-contrast [1 1] : "is the average response to pain greater than zero?"
    对疼痛的平均反应是否大于零?

Parametric Variation - Linear Trends 参数变化-线性趋势

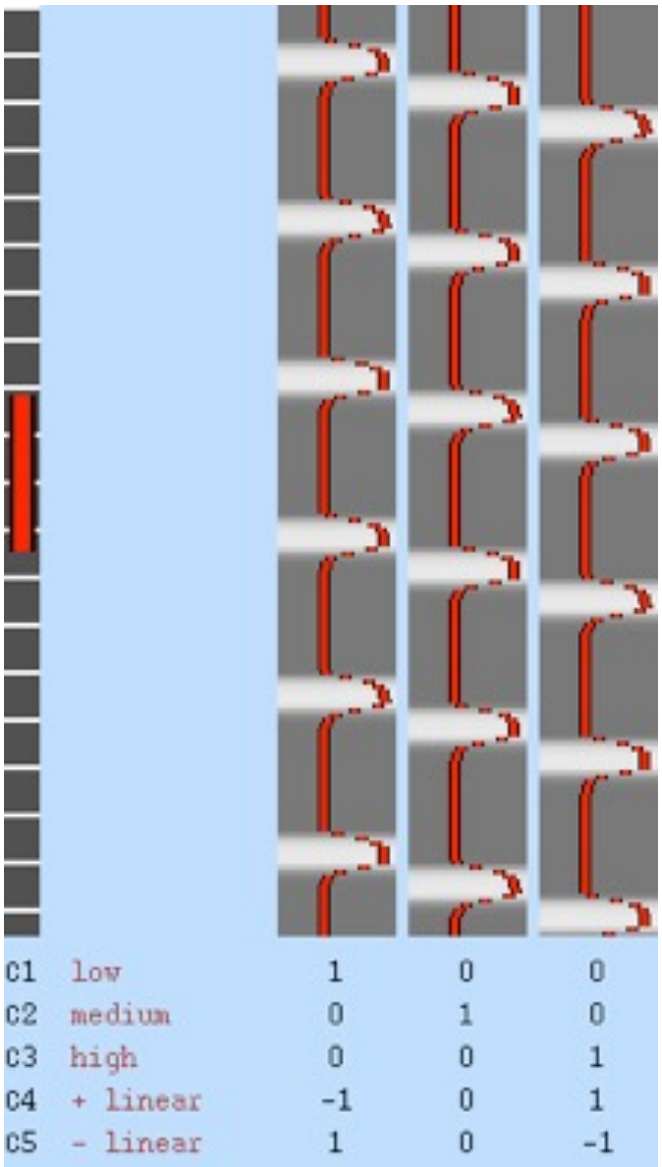
- Is there a linear trend between the BOLD response and the painful stimulus intensity?
  BOLD信号和疼痛的刺激强度之间有线性趋势吗?



- BOLD 信号效应量
- 疼痛的刺激强度

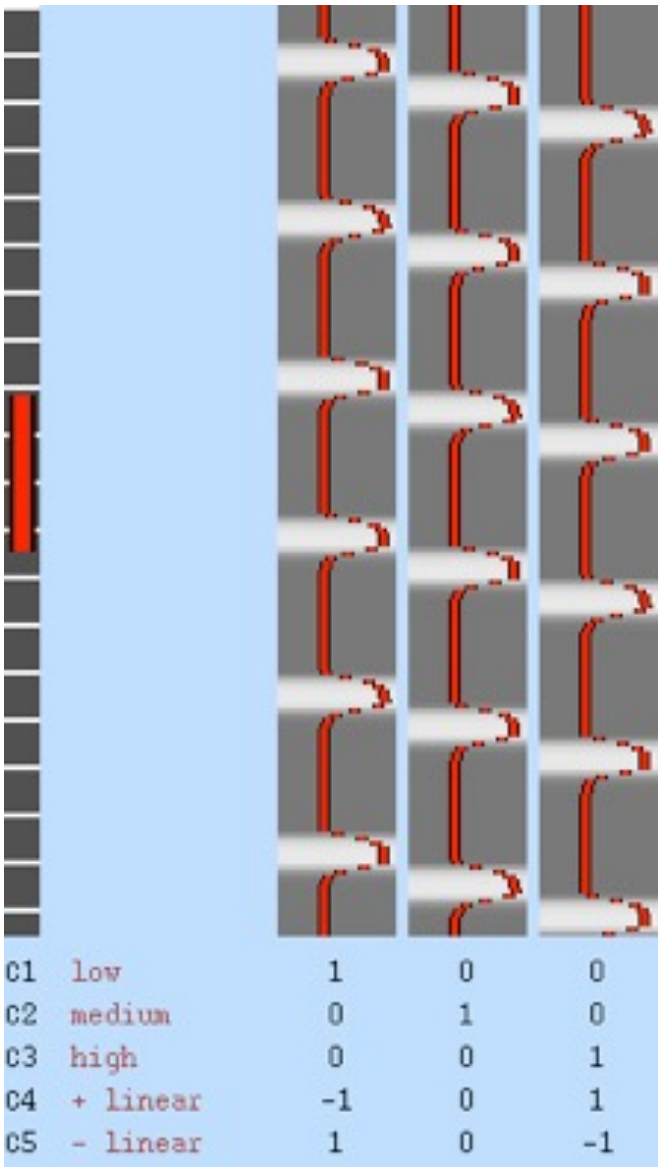


Parametric Variation - Linear Trends 参数变化-线性趋势



- A three-strength experiment 三强度实验
- Is there a linear trend between the BOLD response and some task variable?
  BOLD信号和一些任务变量之间是否存在线性趋势?
- t-contrast [-1 0 1] : Linear trend线性趋势

Parametric Variation - Linear Trends 参数变化-线性趋势



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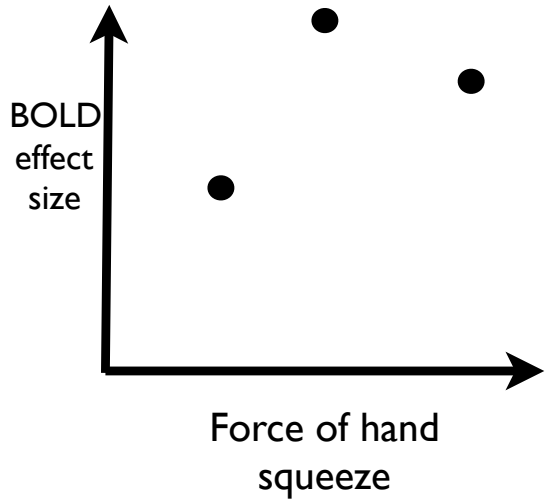
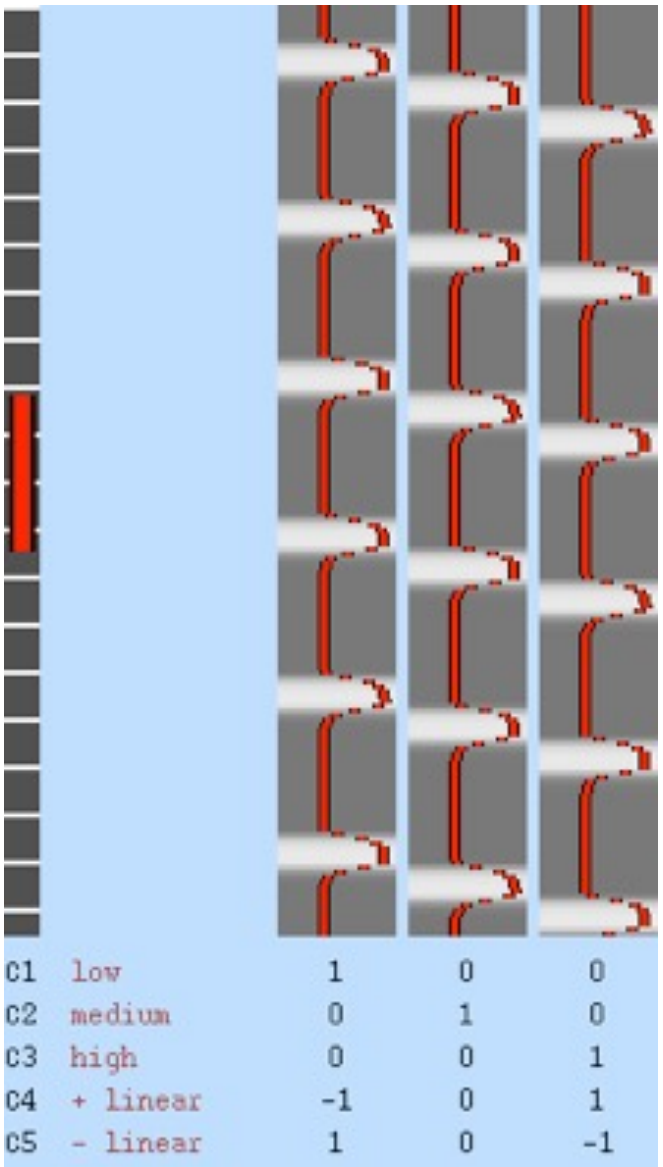


Parametric Variation - Linear Trends 参数变化-线性趋势



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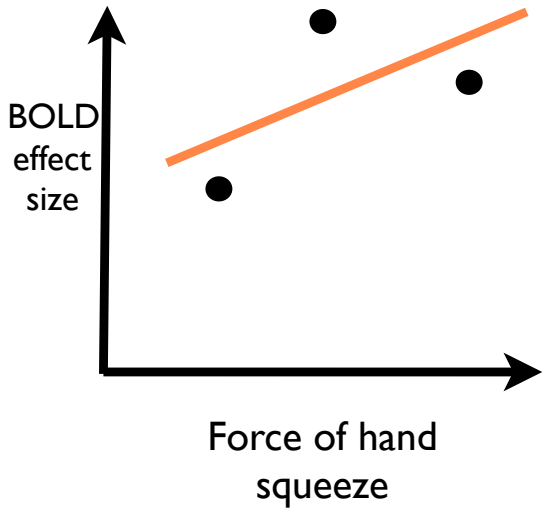

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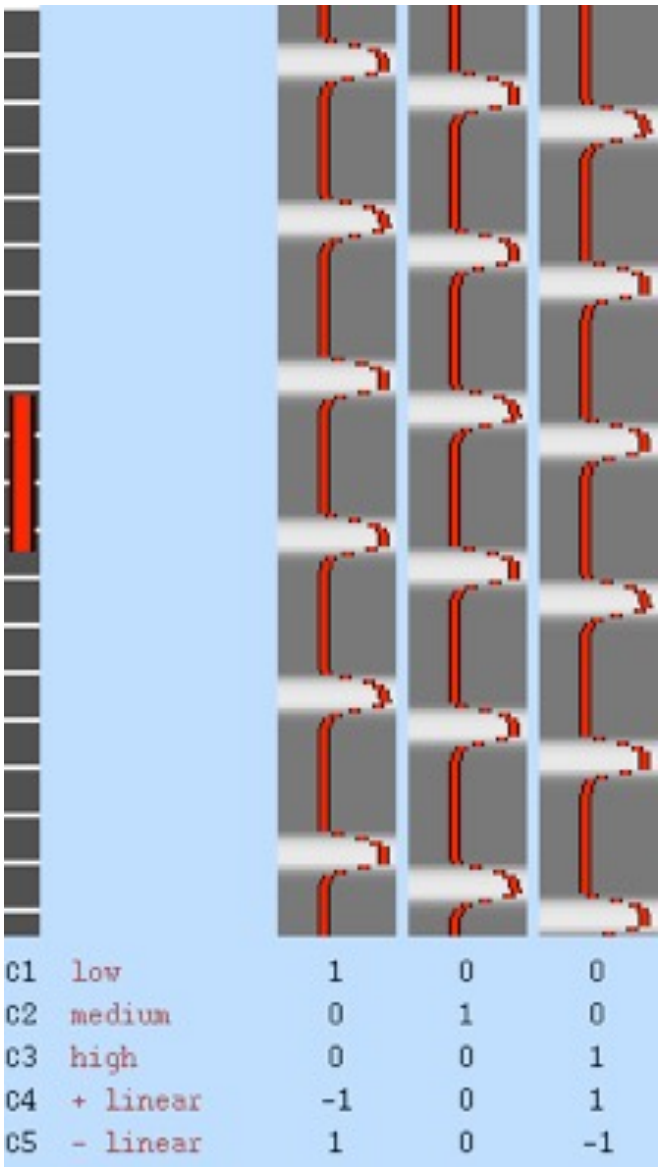

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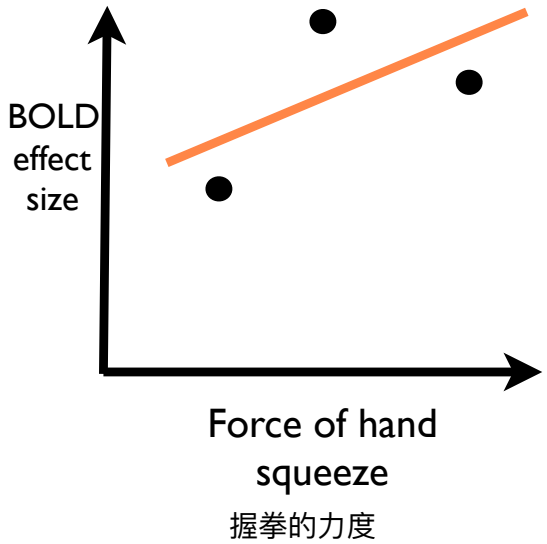

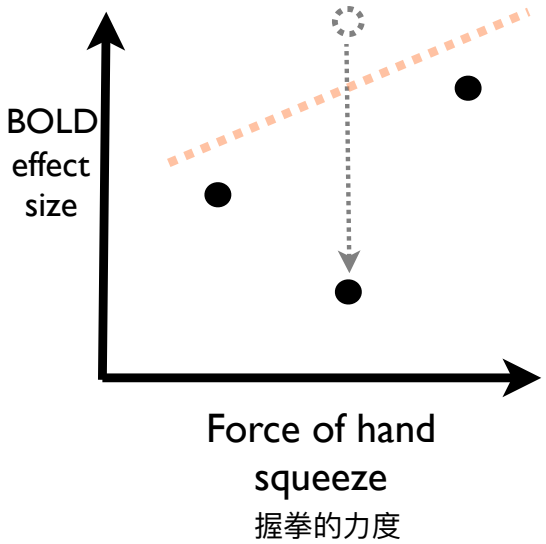

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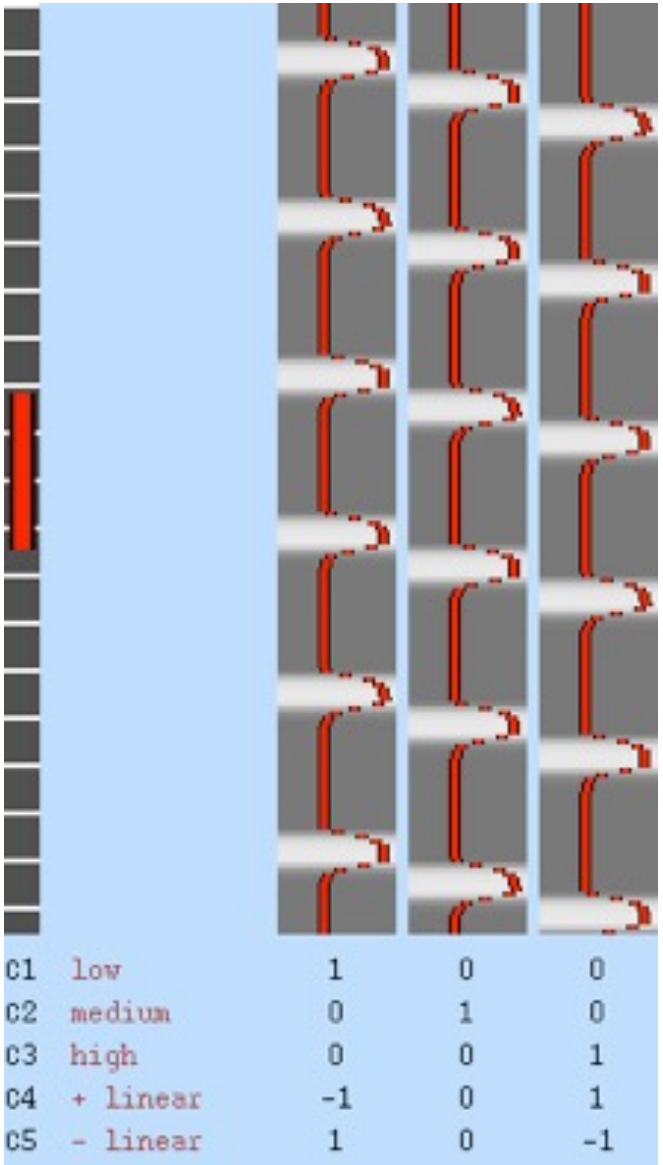

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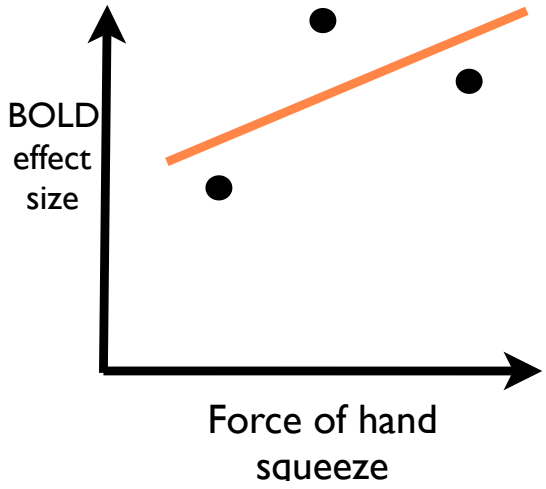
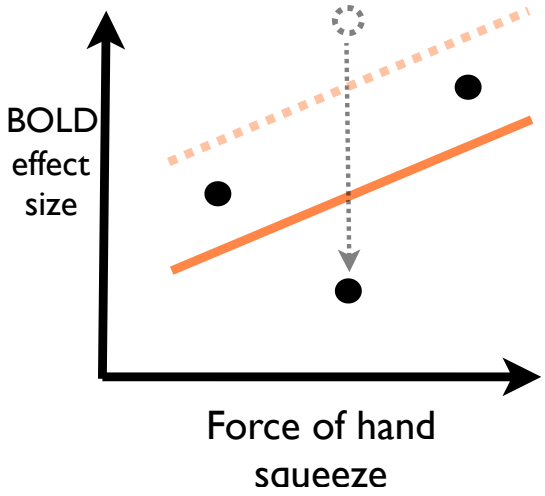
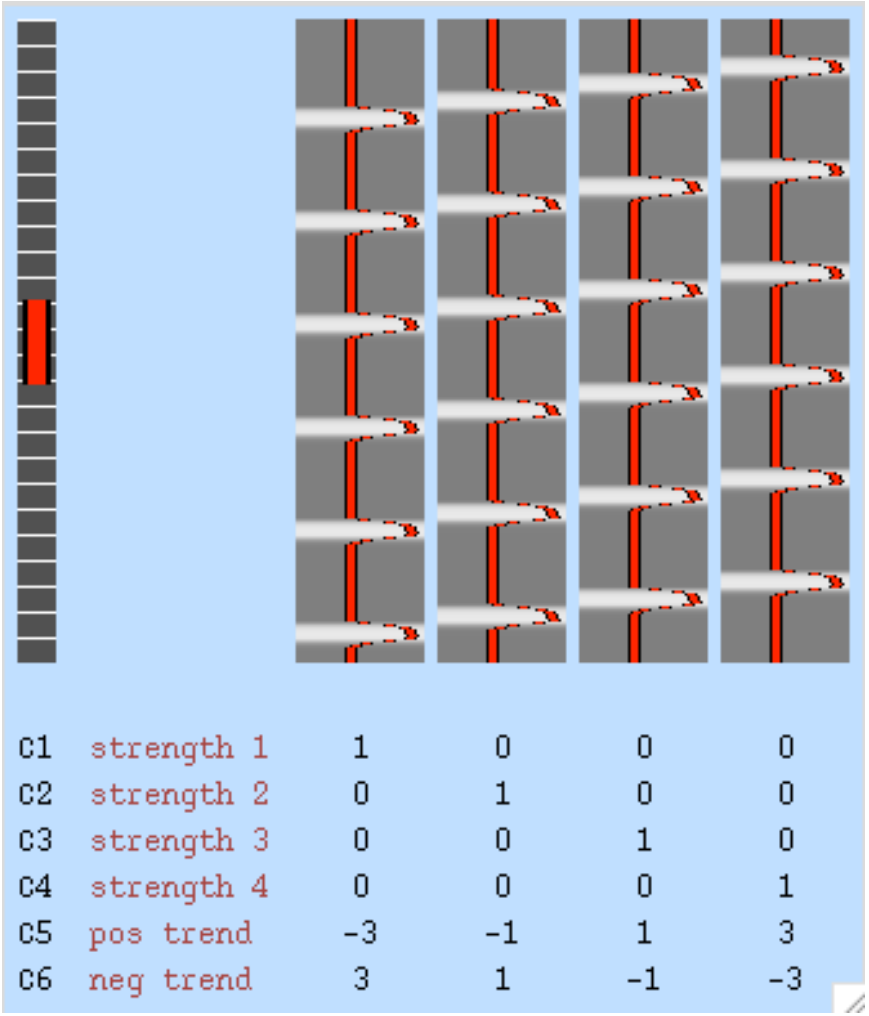




Slope (β_3-β_1) is the same for both 两者斜率相同

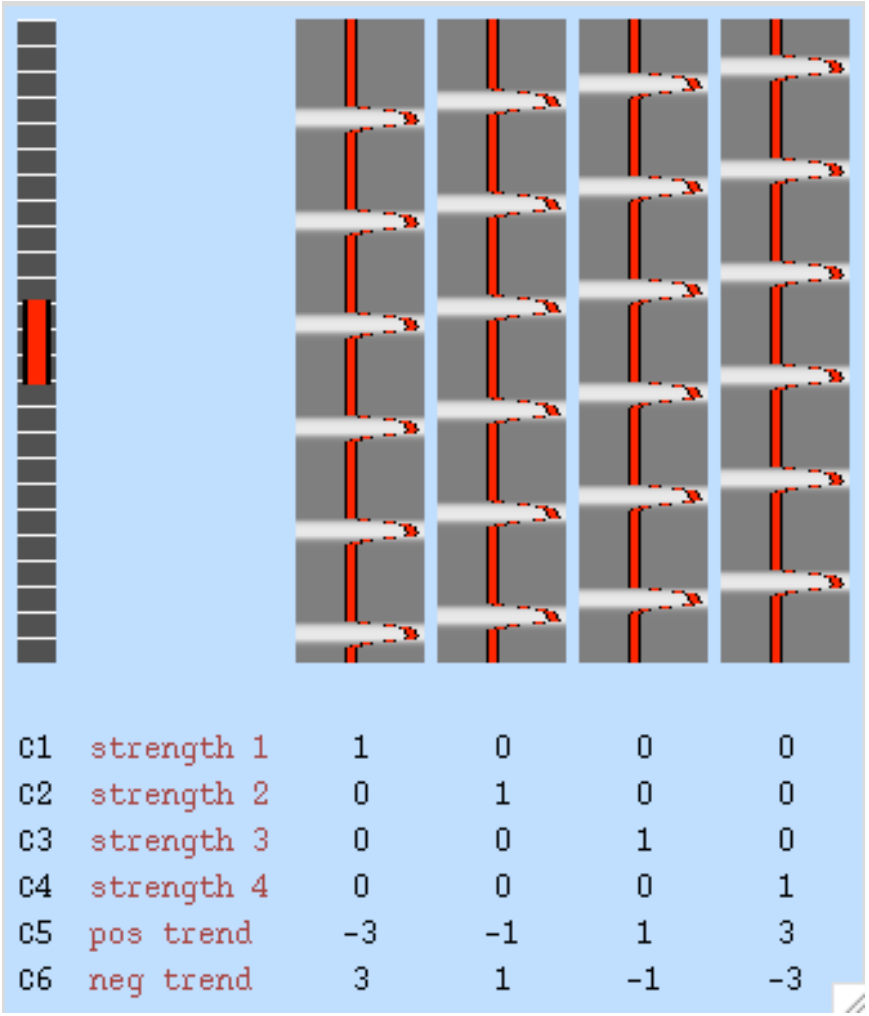
Parametric Variation - Linear Trends 参数变化-线性趋势



C1	strength 1	1	0	0	0
C2	strength 2	0	1	0	0
C3	strength 3	0	0	1	0
C4	strength 4	0	0	0	1
C5	pos trend	-3	-1	1	3
C6	neg trend	3	1	-1	-3

- A four-strength experiment 四强度实验
- t-contrast [-3 -1 1 3] : Positive linear trend
  正向线性趋势

Parametric Variation - Linear Trends 参数变化-线性趋势



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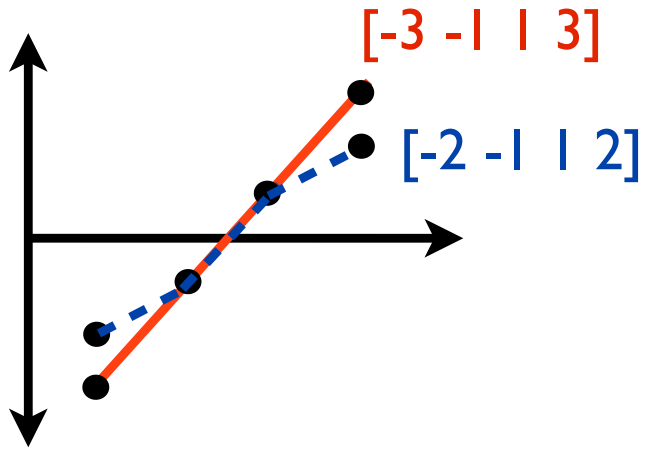
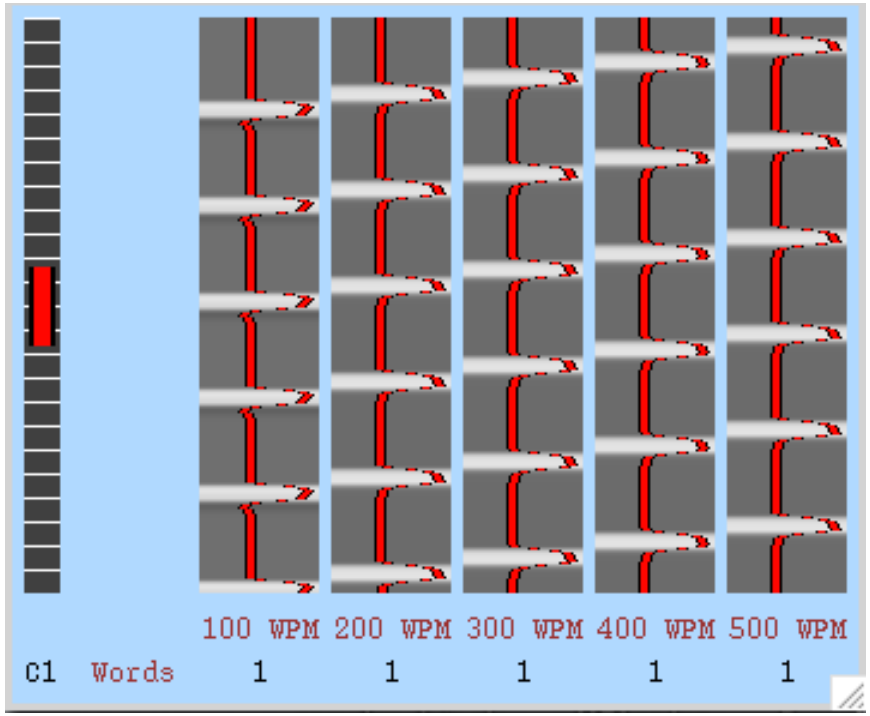


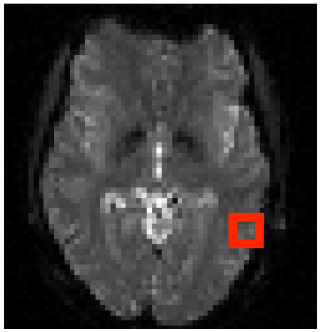
But what if it isn't that predictable?

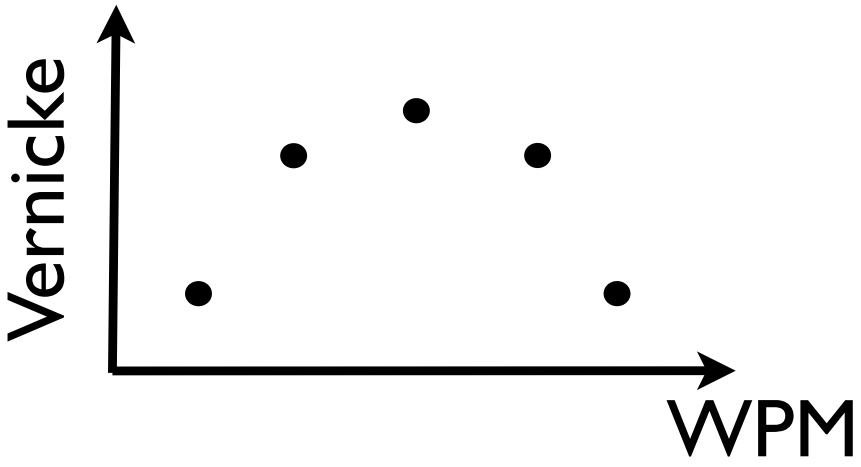
如果不能预测怎么办?

Auditory word presentation at different rates

听觉词汇以不同的频率呈现







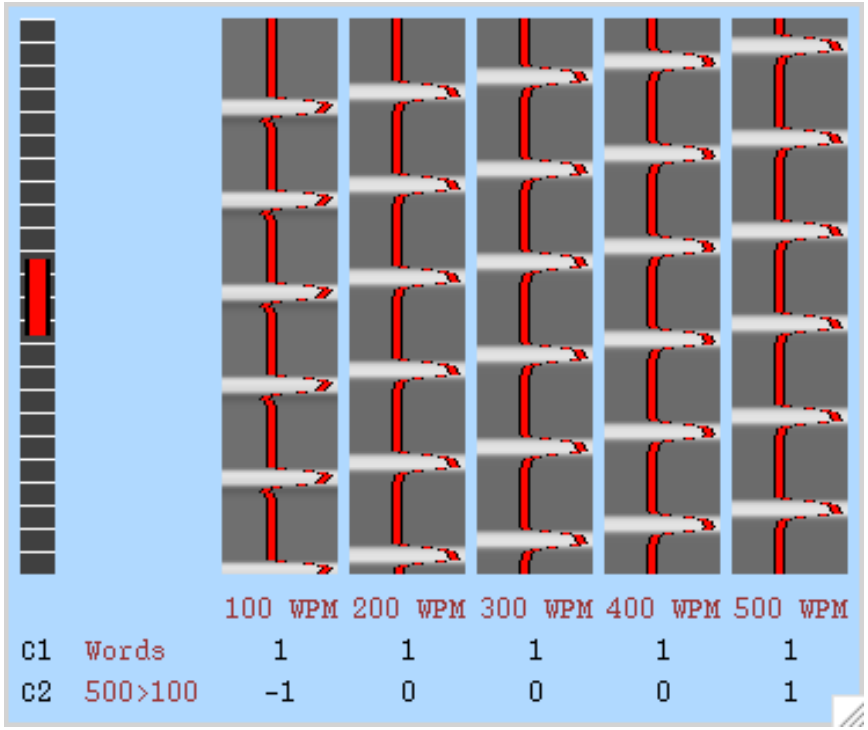
True story

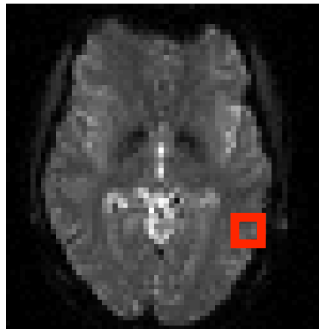
But what if it isn't that predictable?

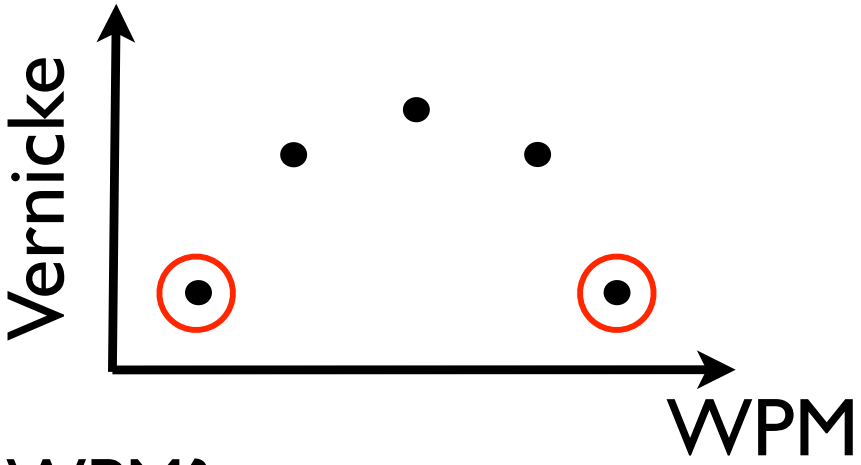
如果不能预测怎么办?

Given this design what would be "reasonable" questions to ask?

对这种设计，有什么"合理"的问题要问?







More activation to 500 than to 100 WPM?

500WPM的激活更强

But no...

True story

But what if it isn't that predictable?

如果不能预测怎么办?

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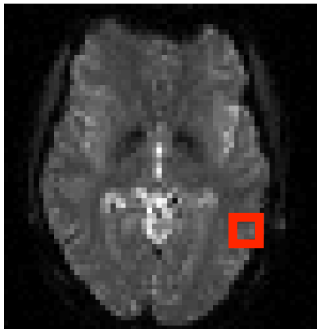
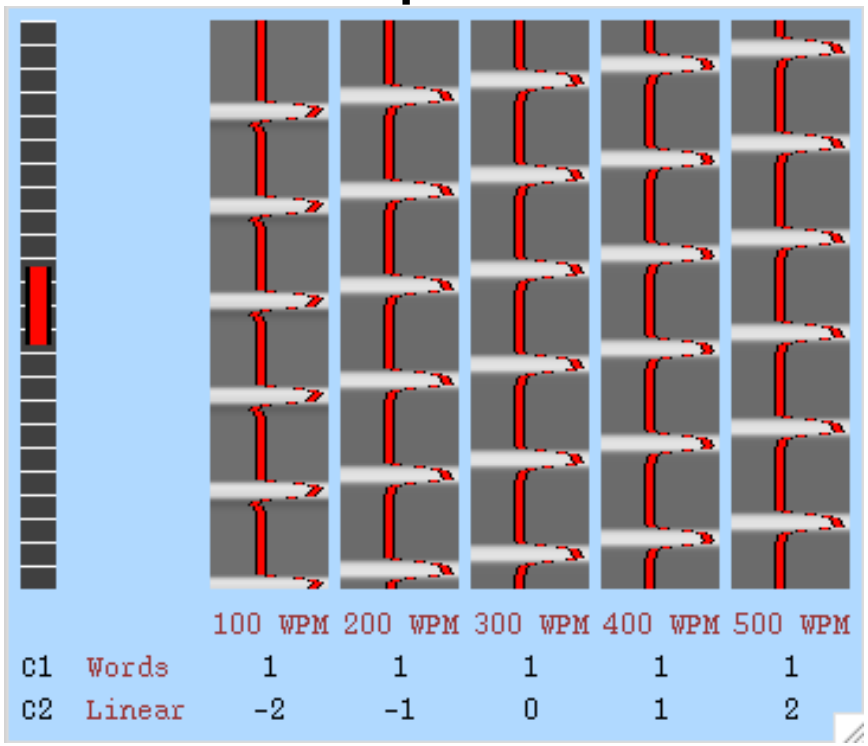
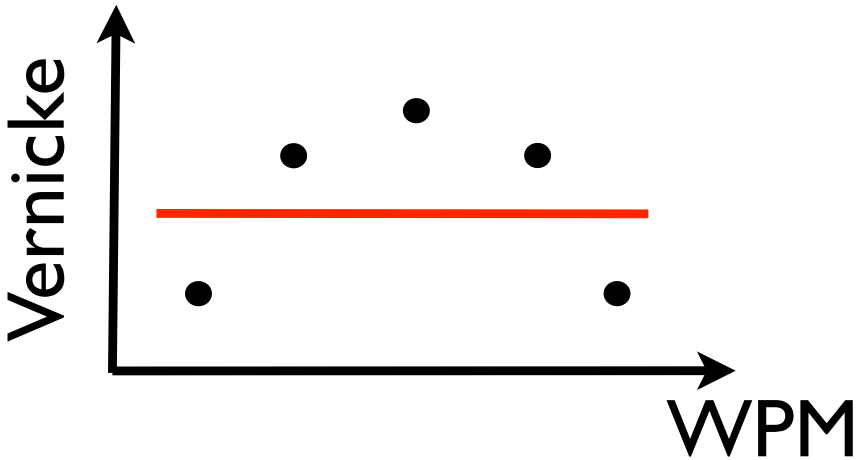
对这种设计，有什么"合理"的问题要问?







Activation proportional to WPM?

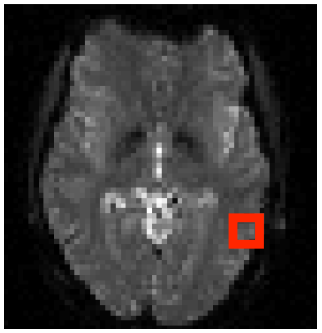
激活与WPM成比例?

Still no...

True story

But what if it isn't that predictable?

如果不能预测怎么办?



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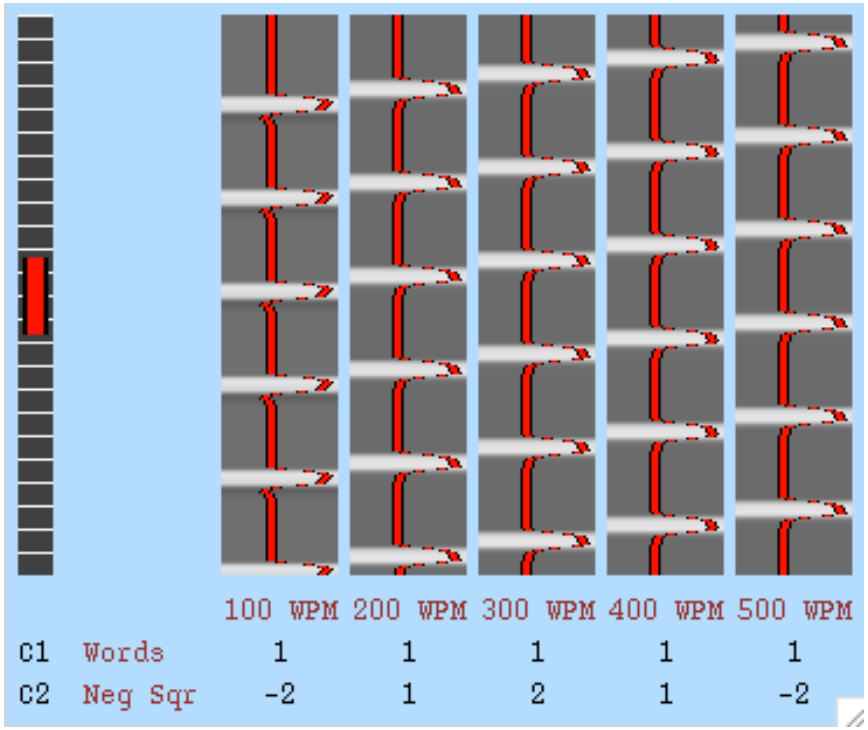
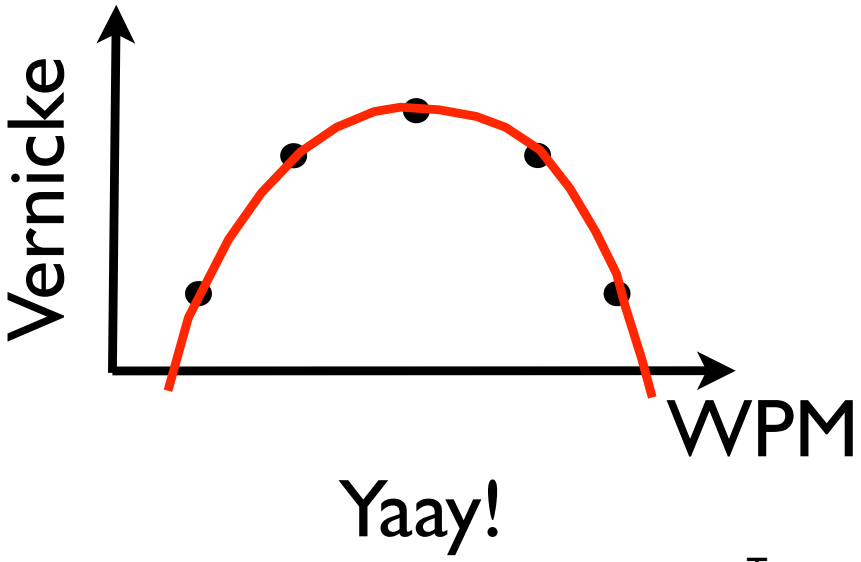


Inversely proportional to WPM squared?

强度与WPM成比例?

But seriously ... would you have asked that question?

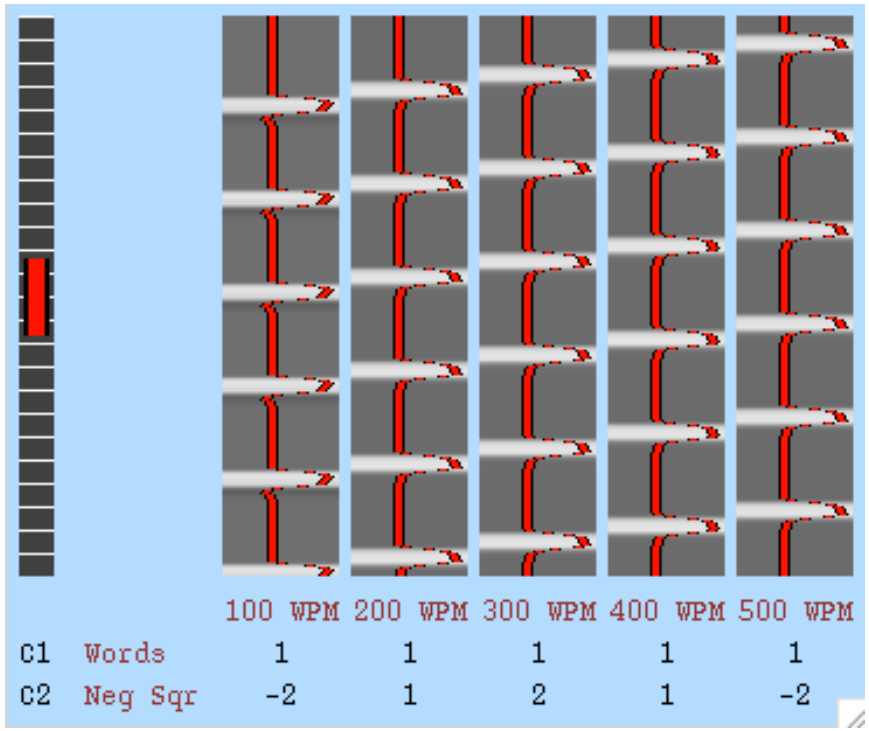
你已经问过那个合理的问题了么



True story

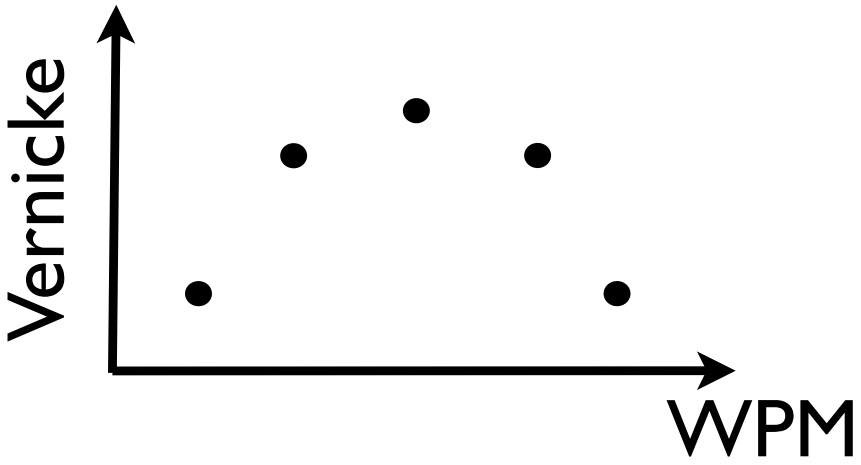
But what if it isn't that predictable?

如果不能预测怎么办?



There is a (very real) risk of missing interesting but unpredicted responses

失去感兴趣的但不可预知的信号有风险



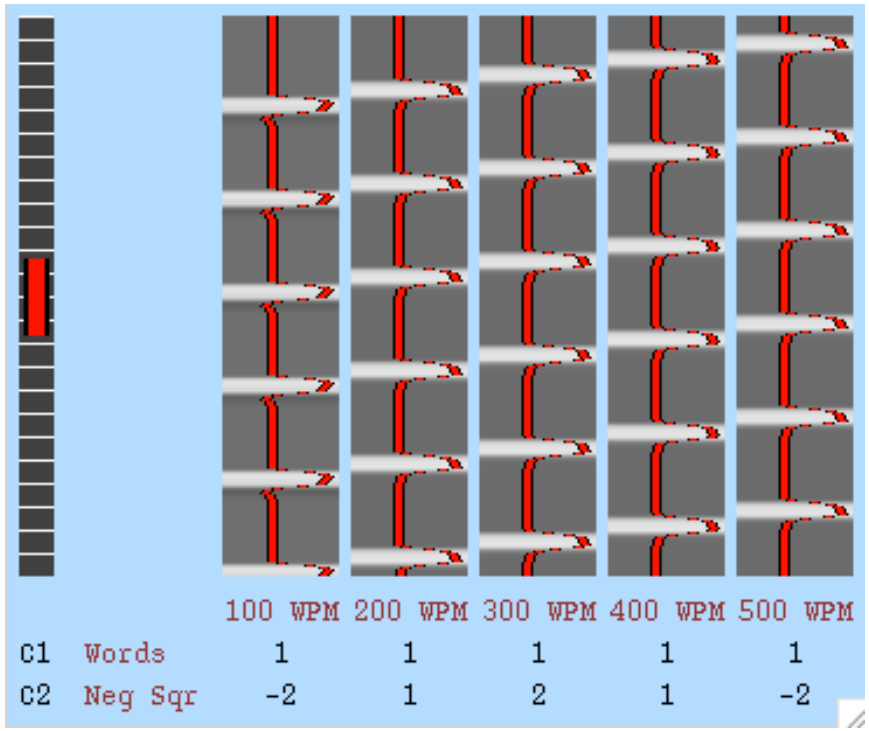
What can we do about that?

我们能怎么做

True story

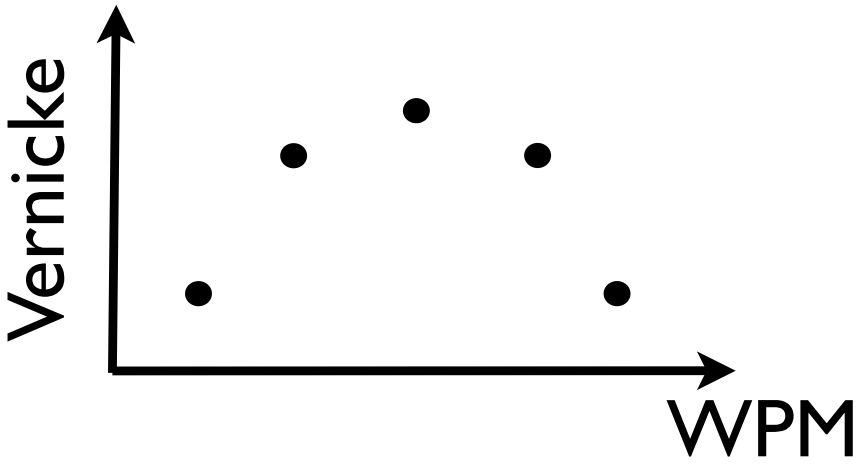
F-contrasts to the rescue

F对比进行补救



We can define an F-contrast that spans "the range of possible responses"

可以定义一个跨越"可能反应范围"的F对比图



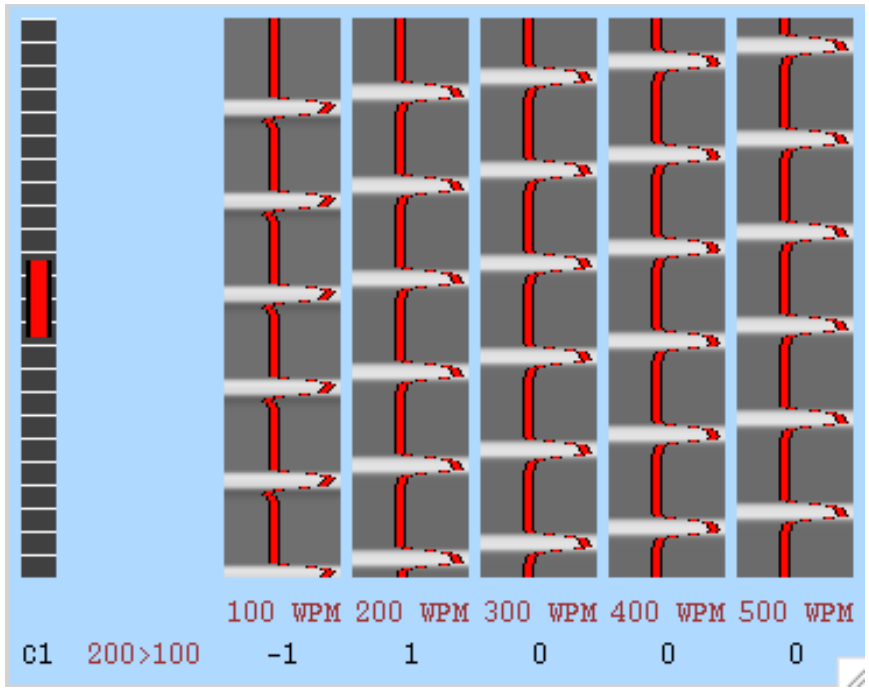
An F-contrast is a series of questions (*t*-contrasts) with an OR between them

f-对比是一系列的问题内部或之间的对比（t-对比）

True story

F-contrasts to the rescue

F对比进行补救



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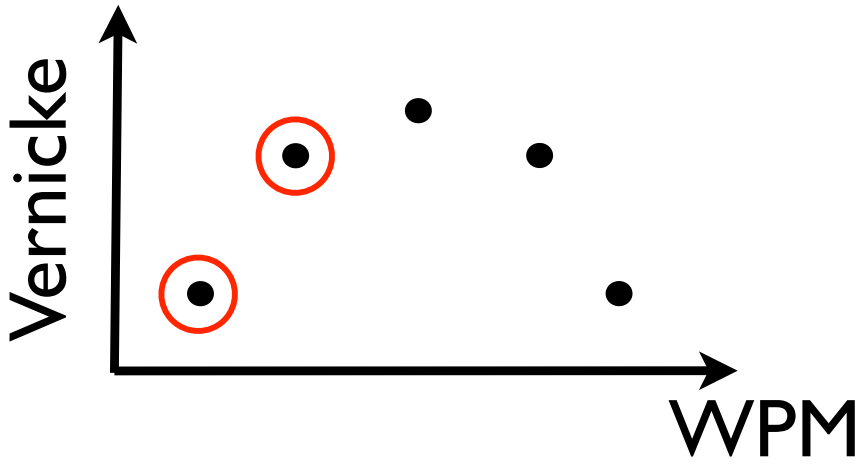


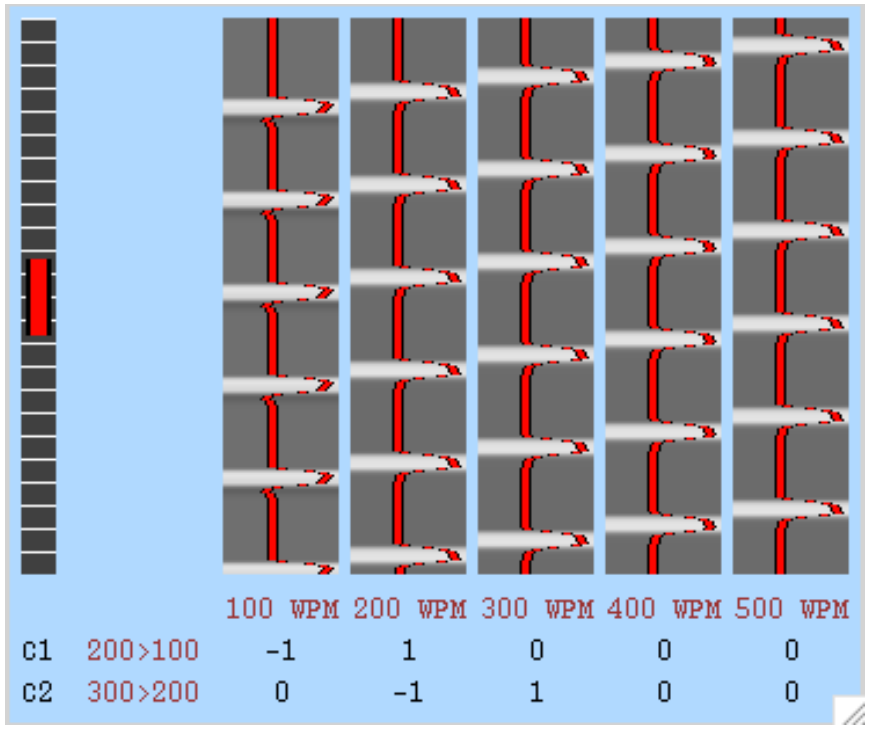
Let's start with "Greater activation to 200 than 100 WPM

从"200比100 wpm有更大的激活"开始

True story

F-contrasts to the rescue

F对比进行补救

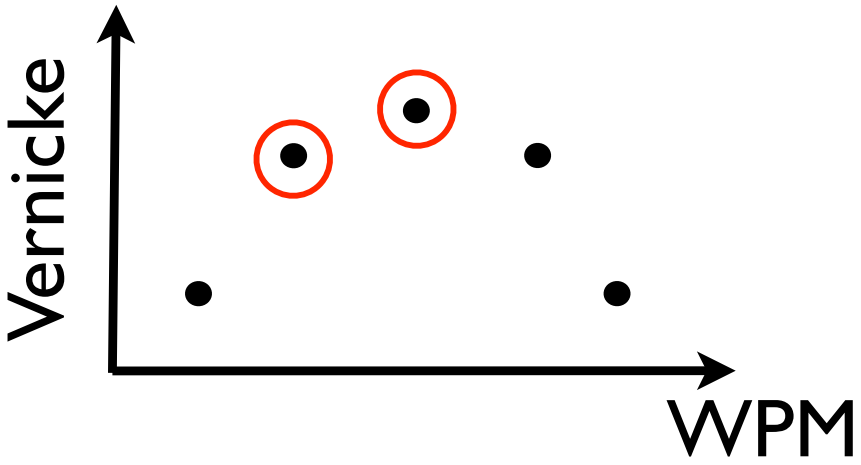


OR

300WPM > 200WPM

We can define an F-contrast that spans "the range of possible responses"

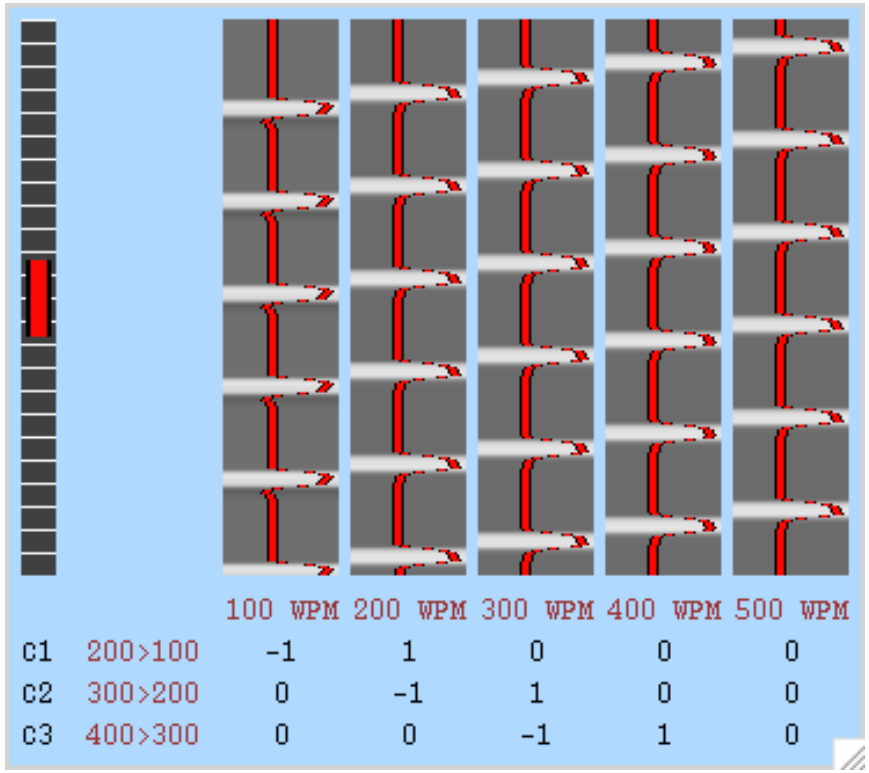
可以定义一个跨越"可能反应范围"的F对比图



True story

F-contrasts to the rescue

F对比进行补救

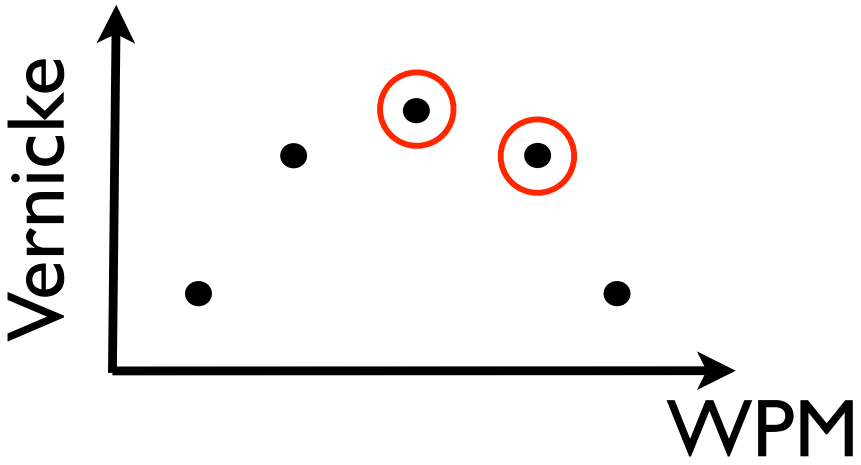


OR

400WPM > 300WPM

We can define an F-contrast that spans "the range of possible responses"

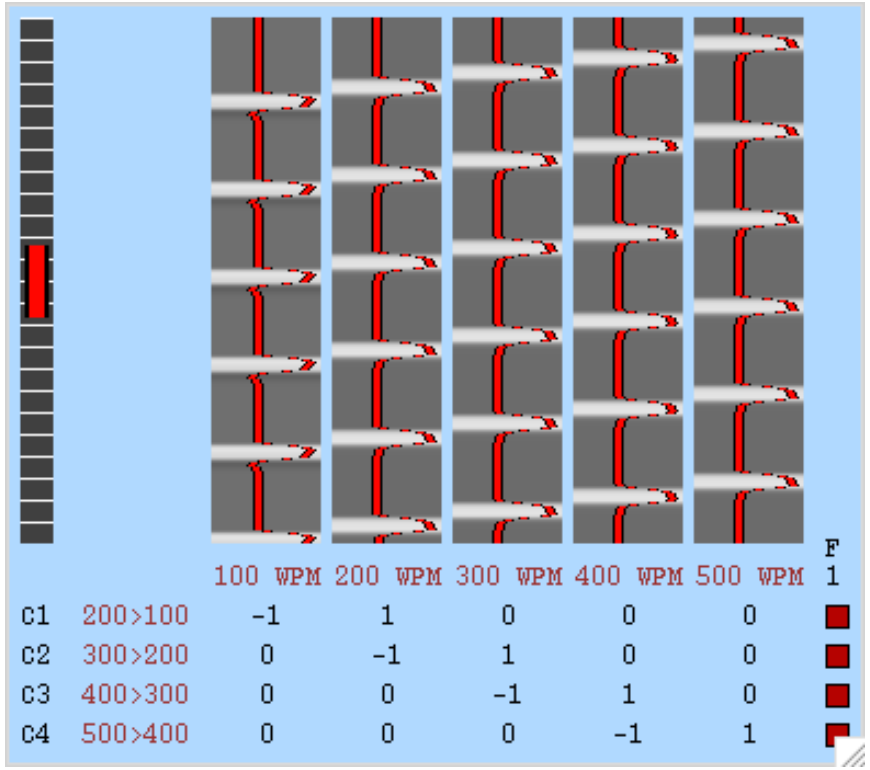
可以定义一个跨越"可能反应范围"的F对比图

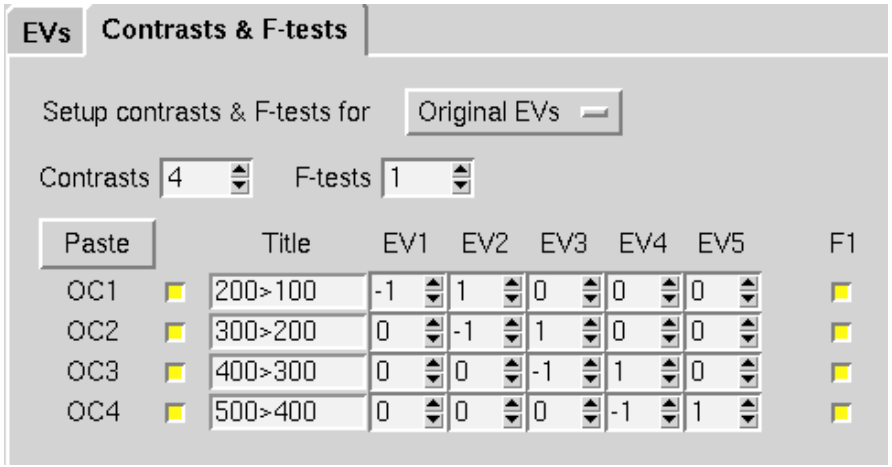


True story

F-contrasts to the rescue

F对比进行补救

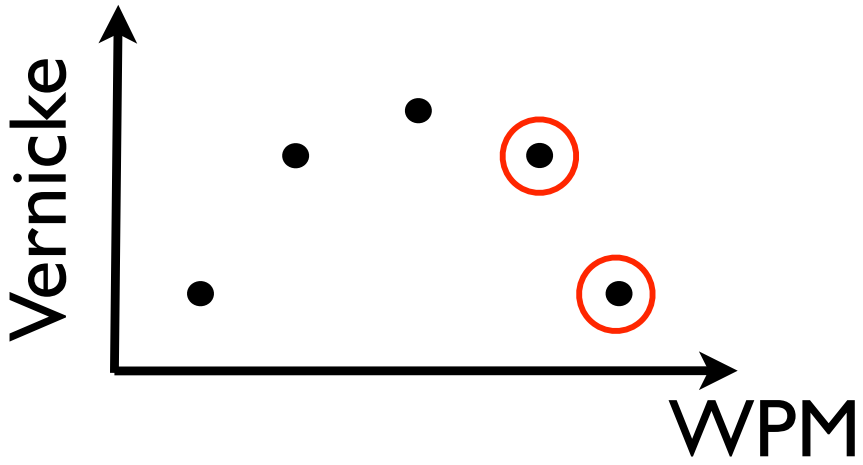




N.B.

OR

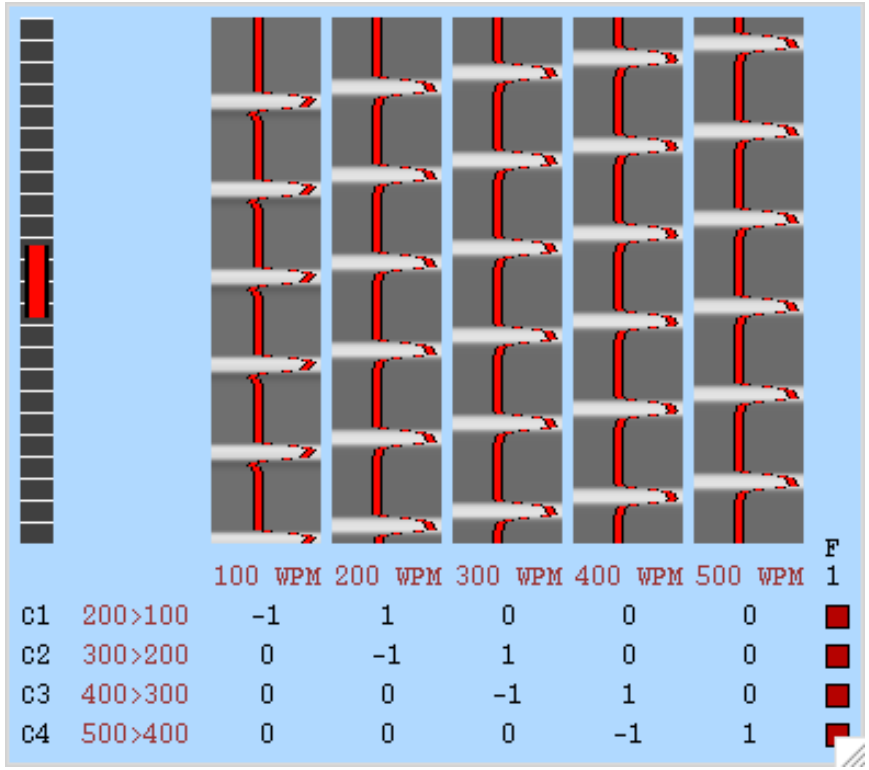
500WPM > 400WPM



True story

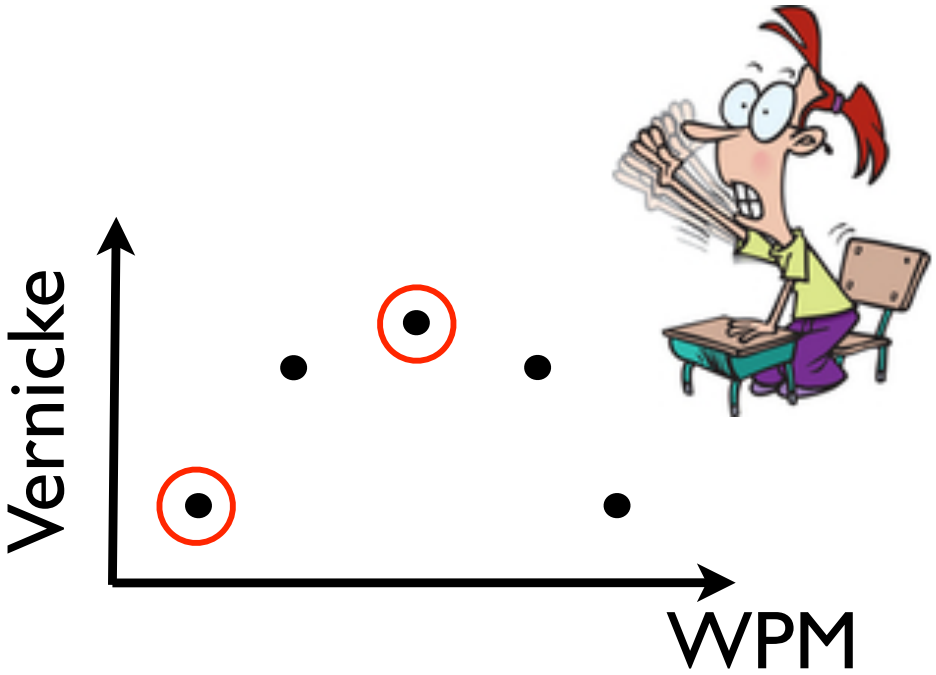
F-contrasts to the rescue

F对比进行补救



But ... that doesn't span all possible response, what about for example 300>100?

但是…这并没有涵盖所有可能的响应，比如300>100?



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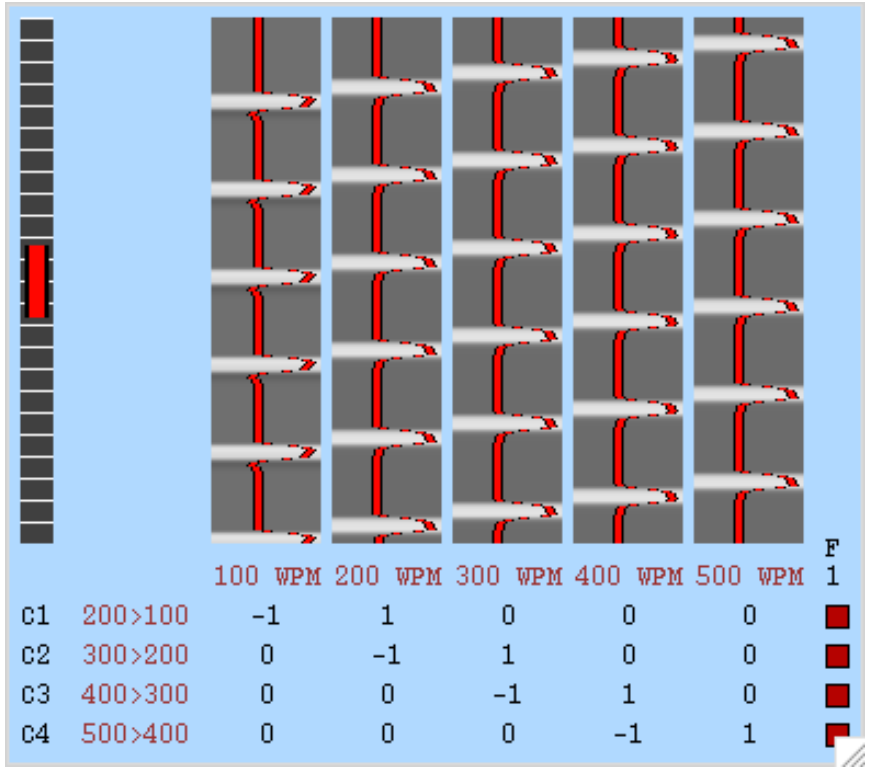
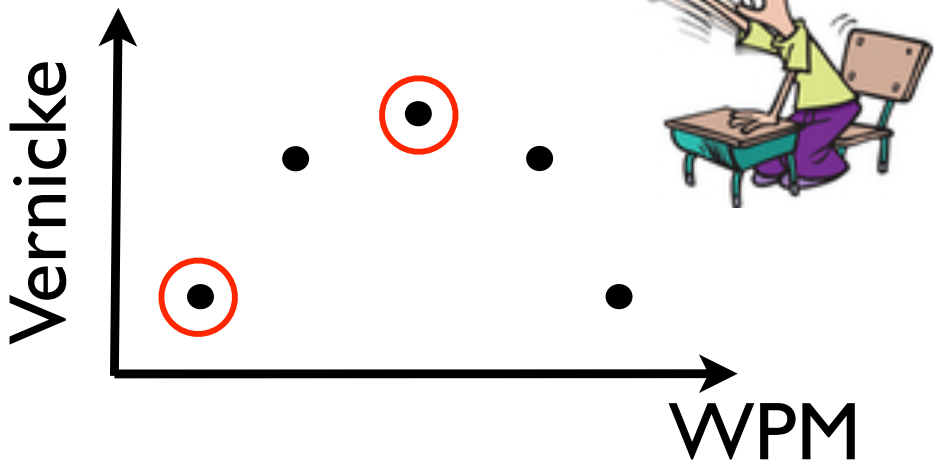


		100 WPM	200 WPM	300 WPM	400 WPM	500 WPM	F 1
c1	200>100	-1	1	0	0	0	
c2	300>200	0	-1	1	0	0	
c3	400>300	0	0	-1	1	0	
c4	500>400	0	0	0	-1	1	

But ... that doesn't span all possible response, what about for example 300>100?

但是…这并没有涵盖所有可能的响应，比如300>100?



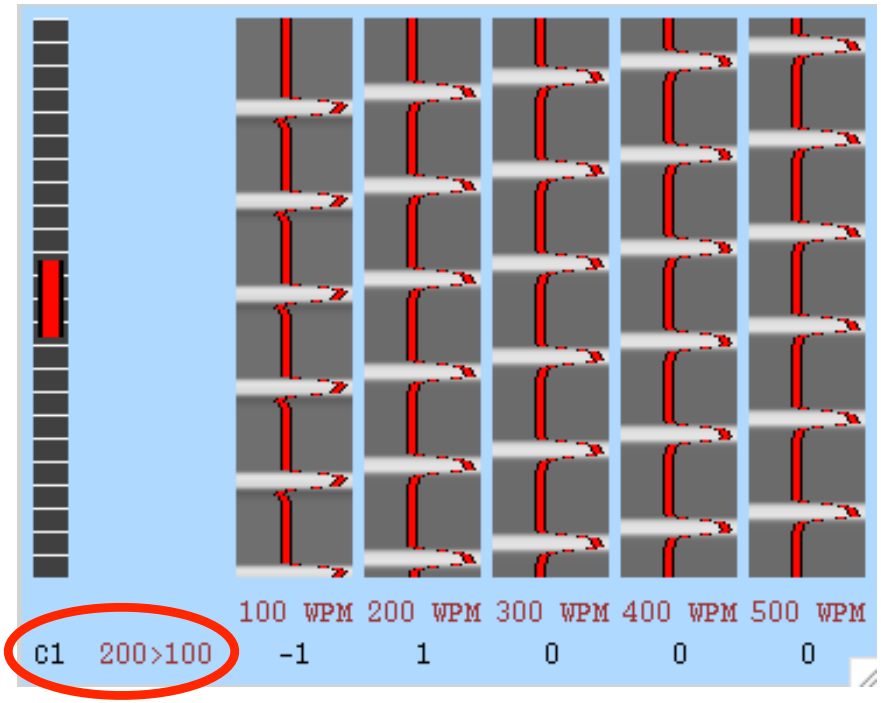
300>100 implies
200>100 AND/OR 300>200
which we have covered

300>100 意味着200>100和/或300>200

True story

F-contrasts to the rescue

F对比进行补救



This *t*-contrast asks "where is 200>100?"

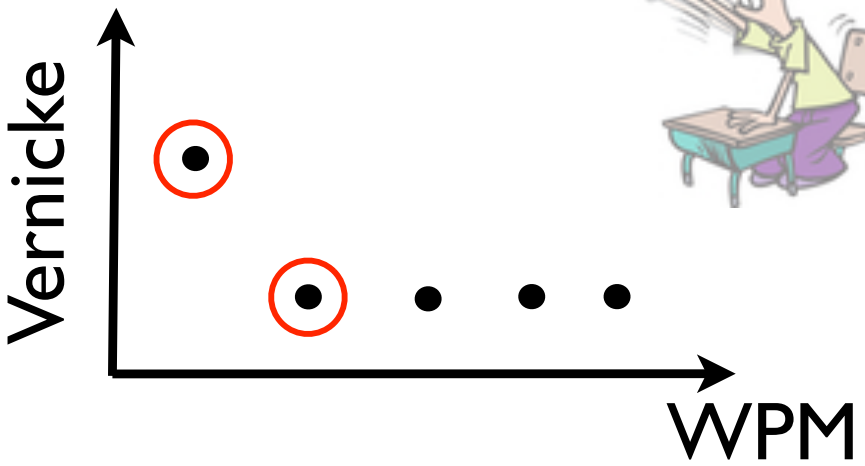
这个T对比表示的是"200>100"的结果

F-contrasts are bi-directional

F对比是双向的

But ... what about for example 100>200, you haven't covered that?

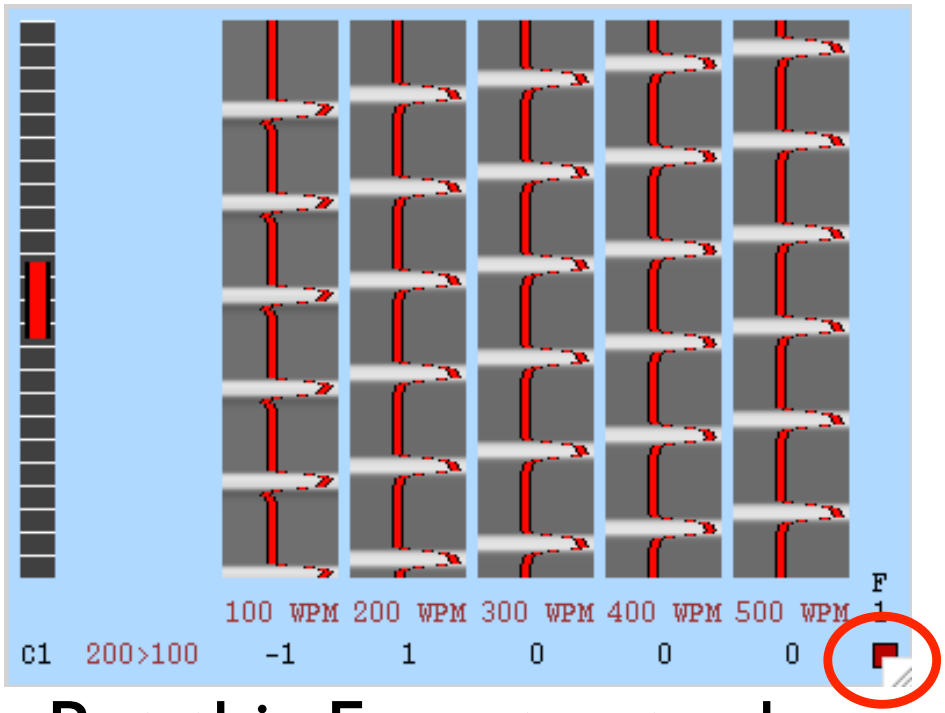
但是像100>200，结果中涉及到了么?



True story

F-contrasts to the rescue

F对比进行补救



But this F-contrast asks "where is 200≠100?"

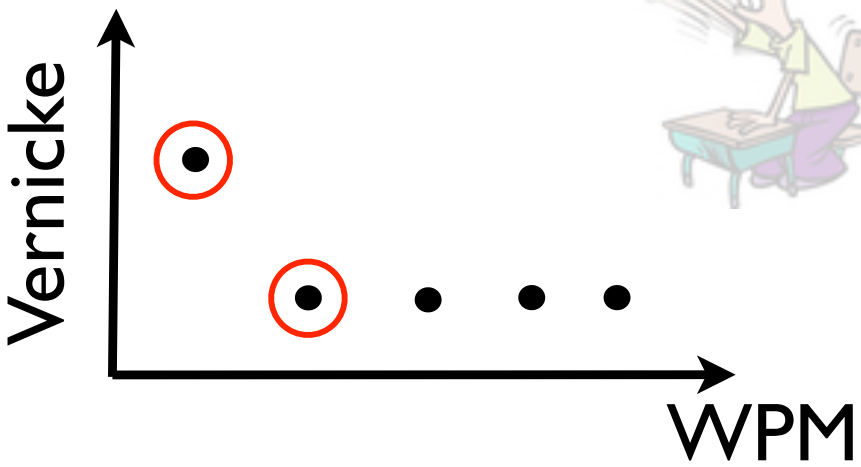
这个F检验表示的是200≠100的结果

F-contrasts are bi-directional

F对比是双向的

But ... what about for example 100>200, you haven't covered that?

但是像100>200，结果中涉及到了么?



True story

Case Study: Factorial Designs and Interactions

案例研究：因子设计和相互作用

Scenario:

- Investigating in multi-sensory regions 多重感觉脑区研究

Specific questions:

- What regions show responses to vision, touch
  哪些区域对视觉、触觉有反应
- What regions respond significantly to both?
  哪些脑区对两者都有显著的反应?
- Are responses additive where there is both visual and touch stimulation, or is there an interaction?
  在有视觉和触觉刺激的情况下，反应是加性的，还是有交互作用?

Solution:

- Specific regressors 特定的回归因子
- Contrast masking 设定对比范围

Multisensory study 多感觉研究

- EV1 models vision on/off EV1表示视觉
- EV2 models touch on/off EV2表示触觉

- Can generate simple contrasts for:

可以创建简单的对比

- vision activation/deactivation [1 0]

视觉激活/抑制

- touch activation/deactivation [0 1]

触觉激活/抑制

- differences in responses [1 -1]

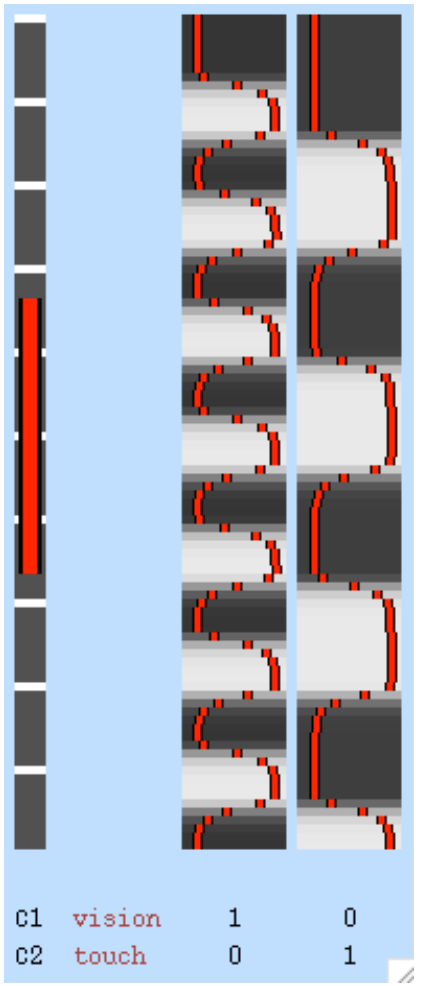
反应的差异

- Regions showing both visual and tactile response??

显示视觉和触觉反应的区域？？

- Not [1 1]: this only assesses the average

不是[1 1]：这只是评估平均值



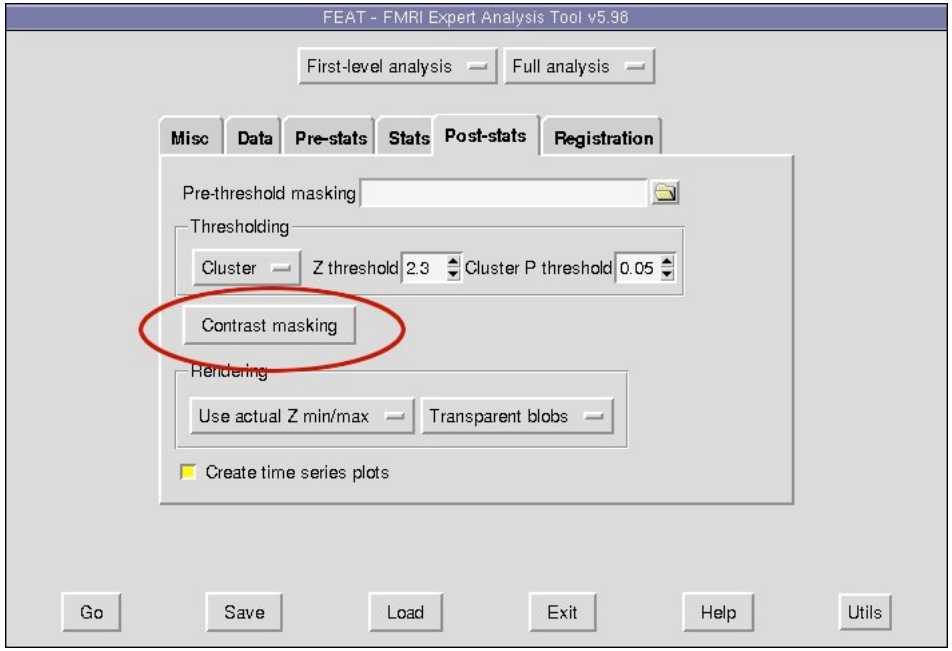
Contrast Masking 对比掩板

- Often it is of interest to identify regions showing significant effects in multiple contrasts (e.g. responds to visual AND tactile stimulations)

通常，人们感兴趣的是确定在多重对比中显示显著效果的区域（例如，对视觉和触觉刺激的反应）

- This can be achieved by masking a thresholded z image for a chosen contrast using the thresholded z image from one or more other contrasts.

这可以通过使用来自一个或多个其他对比度的阈值z图像来掩蔽所选对比度的阈值z图像来实现。



Contrast Masking 对比掩板

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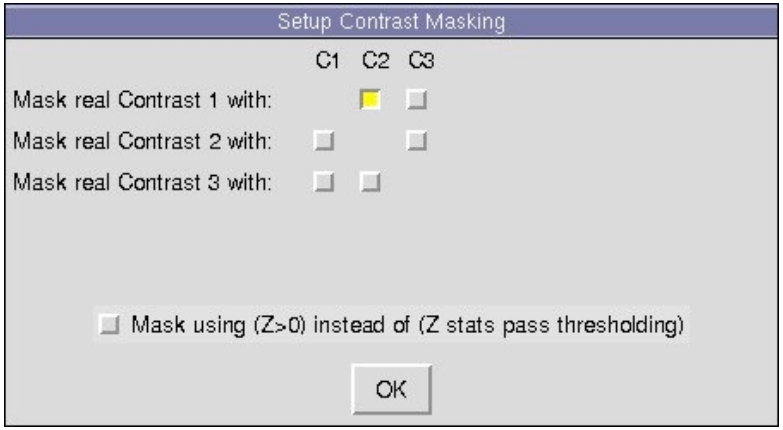
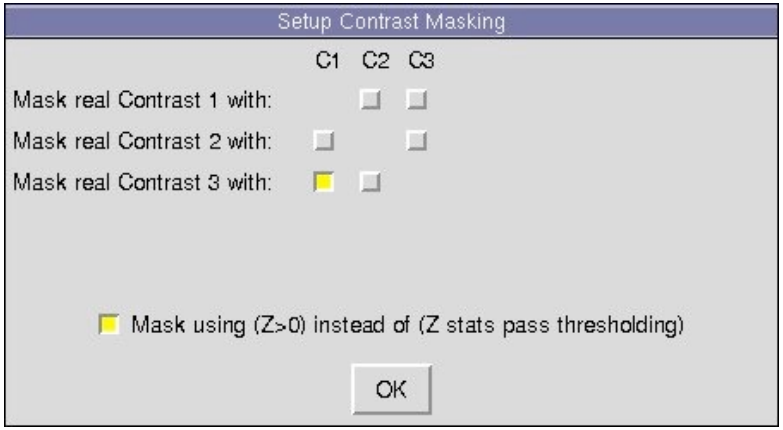


For example, say we had two t contrasts C1 (1 0) and C2 (0 1). We may be interested in only those voxels which are significantly "active" for both contrasts

例如，假设我们有两个t对比c1（1 0）和c2（0 1）
我们可能只对那些对两种对比都有显著激活的体素感兴趣。

Contrast Masking 对比掩板

- Rather than masking with voxels which survive thresholding, it may be desirable to mask using positive z statistic voxels instead 与其使用阈值后仍存在的体素，不如使用Z检验后正向显著的体素。



For example, say that we have two t contrasts C3 (1 -1) and C1 (1 0). It may be desirable to see those voxels for which EV1 is bigger than EV2, only when EV1 is positive

例如，假设我们有两个t对比c3（1,-1）和c1（1,0）
只有当EV1为正时，才希望看到EV1大于EV2的体素。

Factorial design 因子设计

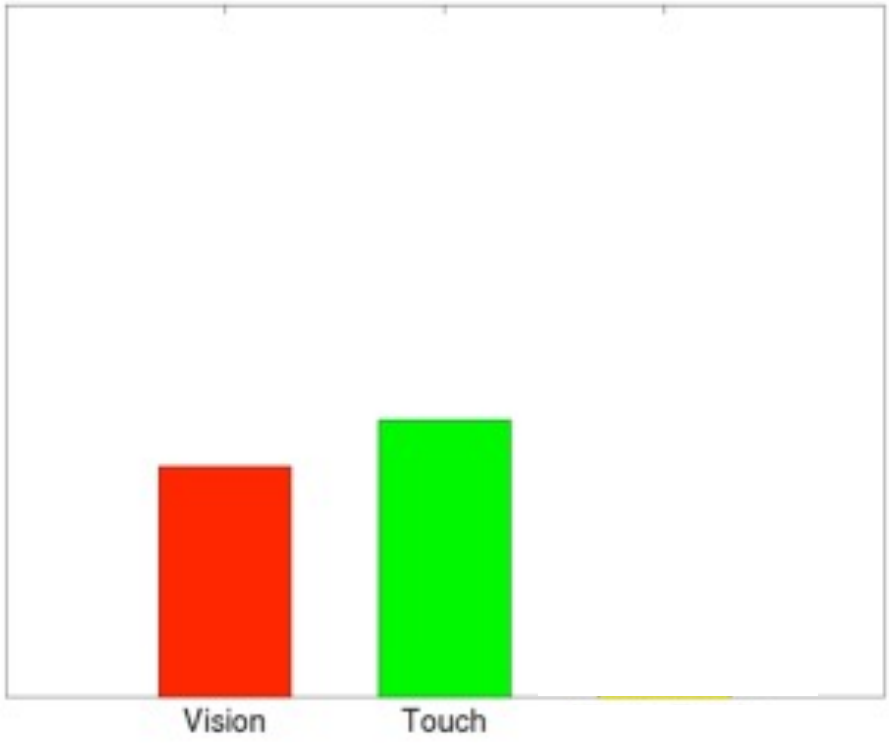
	No Vision	Vision
No Touch		
Touch		

- Allows you to characterise interactions between component processes
  允许您描述成分加工之间的交互
  - i.e. effect that one component has on another
    一种成分对另一种成分的影响

No Interaction Effect

没有交互作用

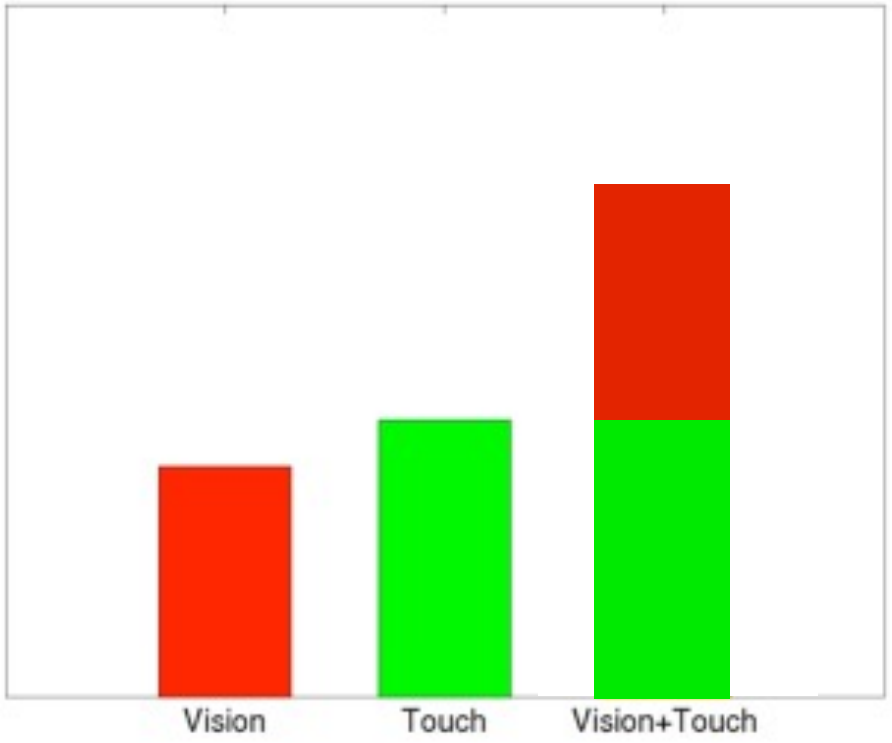
	No Vision	Vision
No Touch		
Touch		



No Interaction Effect

没有交互作用

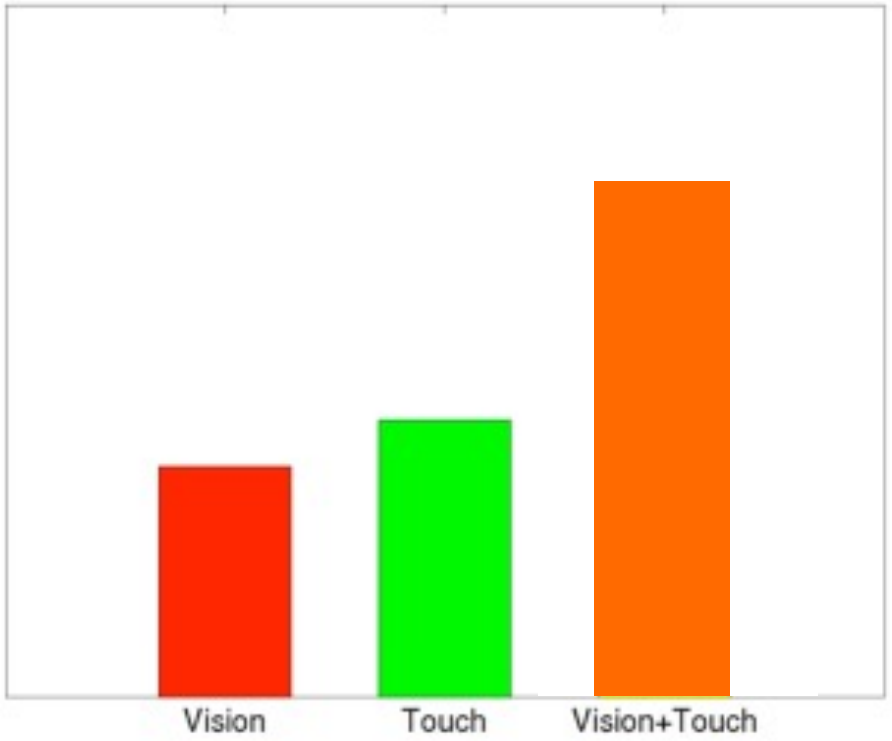
	No Vision	Vision
No Touch		
Touch		



No Interaction Effect

没有交互作用

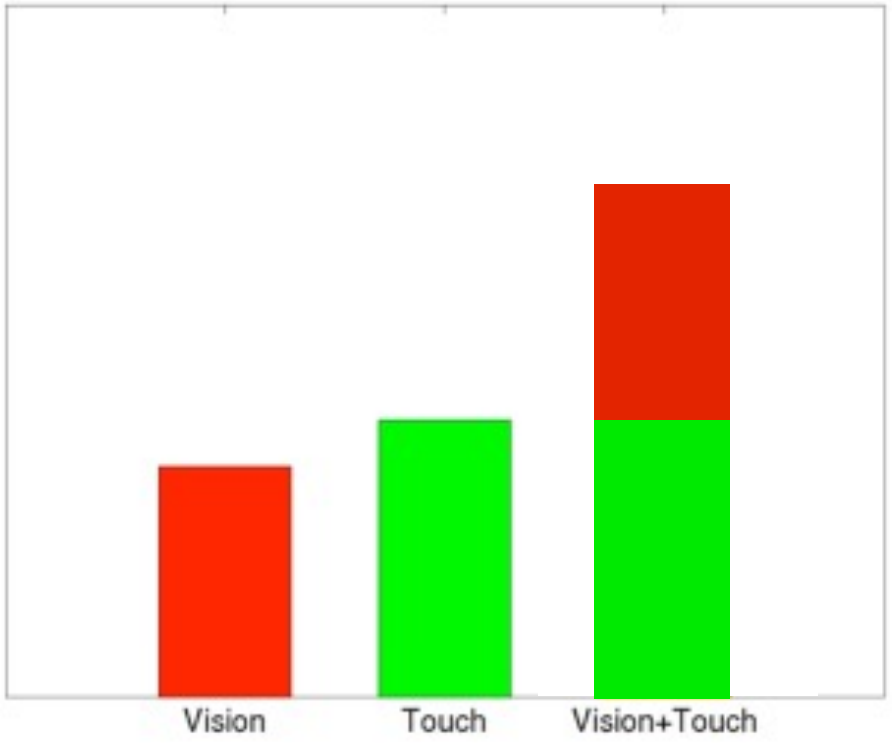
	No Vision	Vision
No Touch		
Touch		



No interaction -
effects add linearly

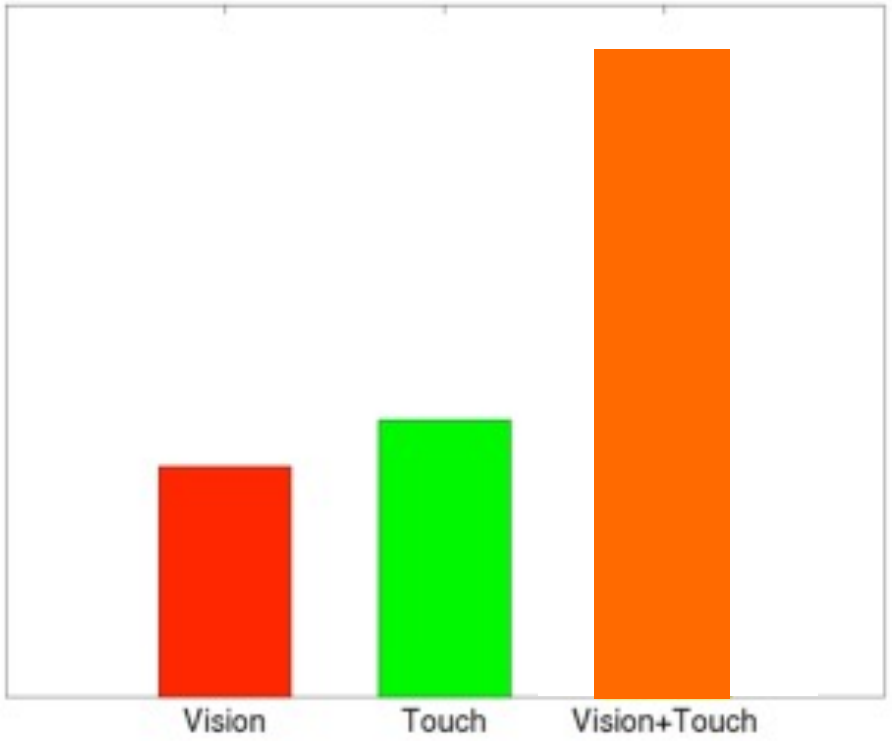
Positive Interaction Effect 正向交互作用

	No Vision	Vision
No Touch		
Touch		



Positive Interaction Effect 正向交互作用

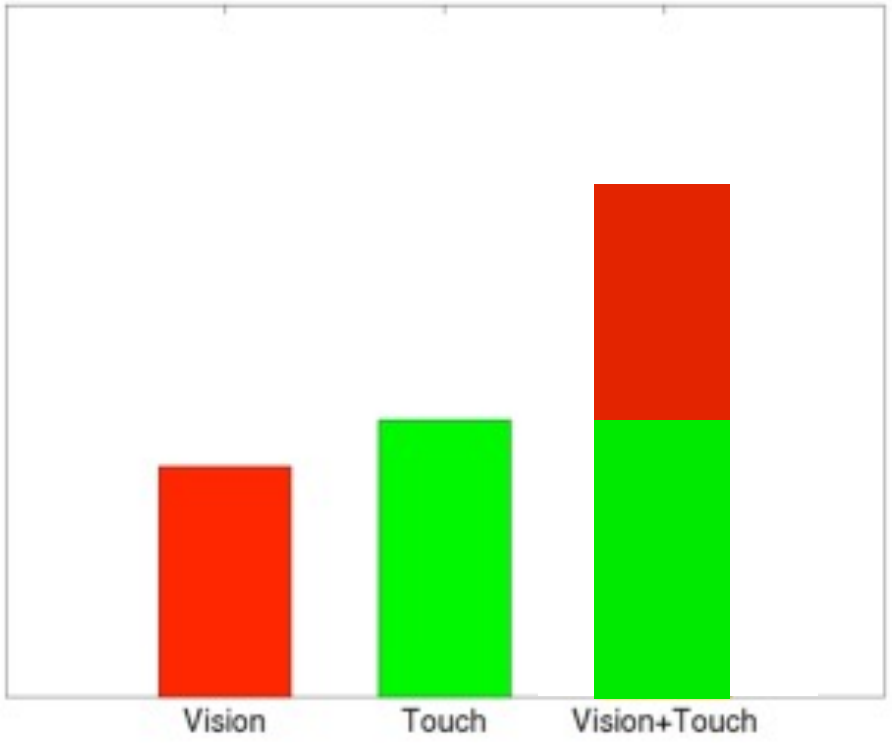
	No Vision	Vision
No Touch		
Touch		



Positive interaction - “superadditive”

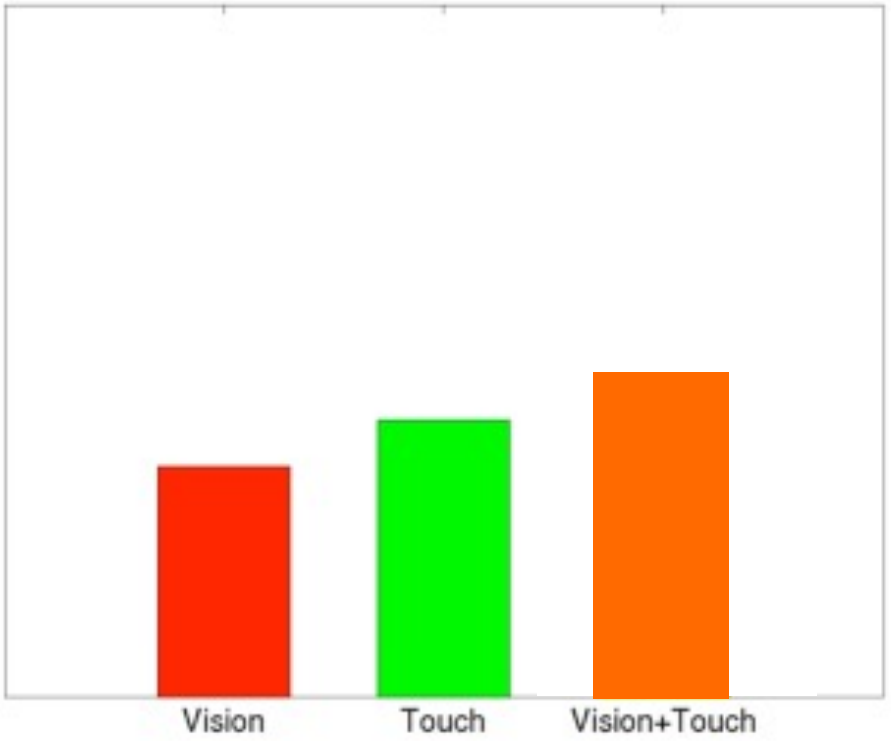
Negative Interaction Effect 负向交互作用

	No Vision	Vision
No Touch		
Touch		



Negative Interaction Effect 负向交互作用

	No Vision	Vision
No Touch		
Touch		



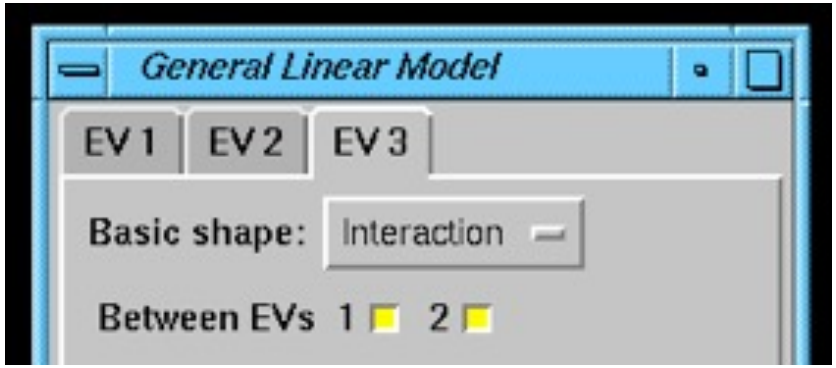
Negative interaction
- "subadditive"

负交互作用-"次加法"

Modelling Interactions Between EVs

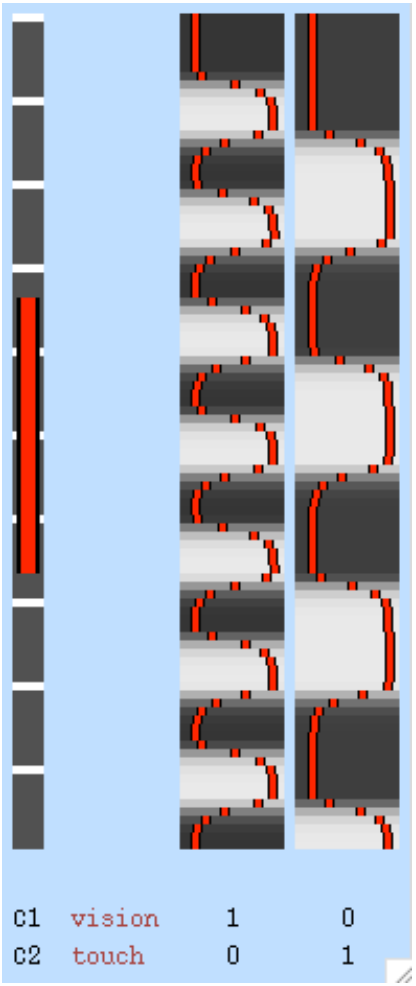
对EV间的交互作用建模

	No Vision	Vision
No Touch		
Touch		



- EV1 models vision on/off
- EV2 models touch on/off

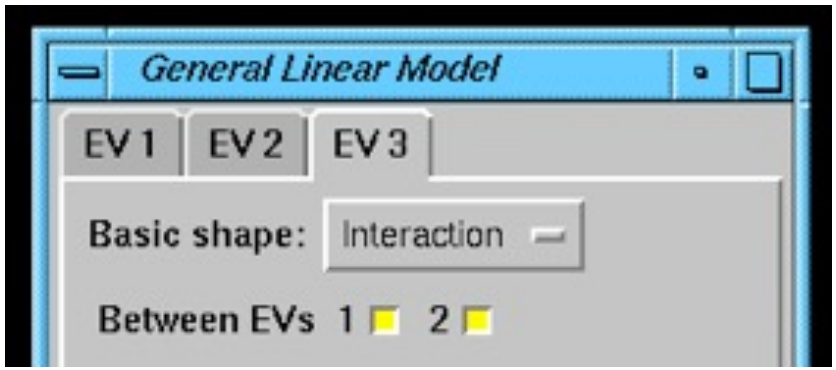
EV1 表示视觉建模
EV2 表示触觉建模



Modelling Interactions Between EVs

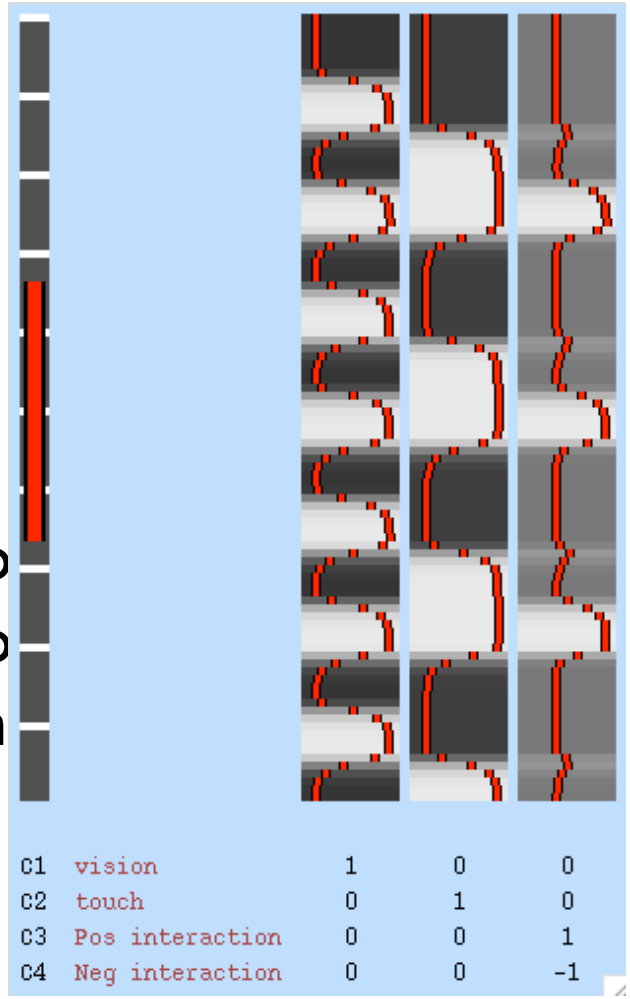
对EV间的交互作用建模

	No Vision	Vision
No Touch		
Touch		



- EV1 models vision on/o
- EV2 models touch on/o
- EV3 Models interaction

EV1 表示视觉
EV2 表示触觉
EV3 表示交互作用



Correlation of EVs

EV的相关

Correlation of EVs

EV的相关

- Correlated EVs are relatively common, but **strong correlation is a problem** in either first-level or group-level designs.

  相关EV相对来说比较常见，但在个体水平或组水平设计中，强相关是一个问题。

- When EVs are correlated, it is the ***unique contribution*** from each EV that determines the model's fit to the data and the statistics.

  当EVs是相关的，它唯一的贡献是决定了模型的拟合数据和统计。

- Start by looking at first-level examples:
  - correlation and rank deficiency
  - design efficiency tool

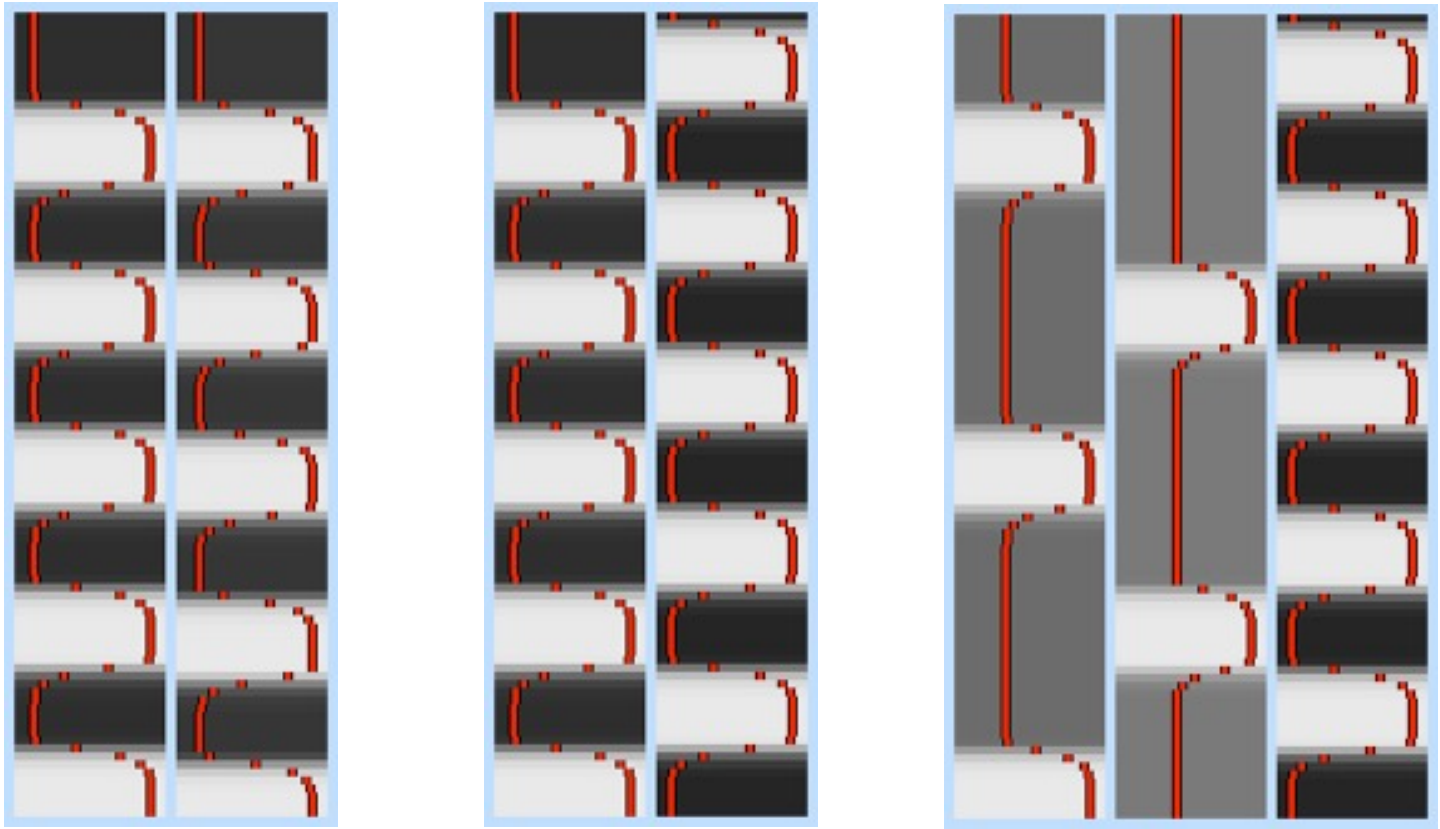
首先看个体水平

相关性与秩

设计的有效性

Correlation of EVs: First-level designs

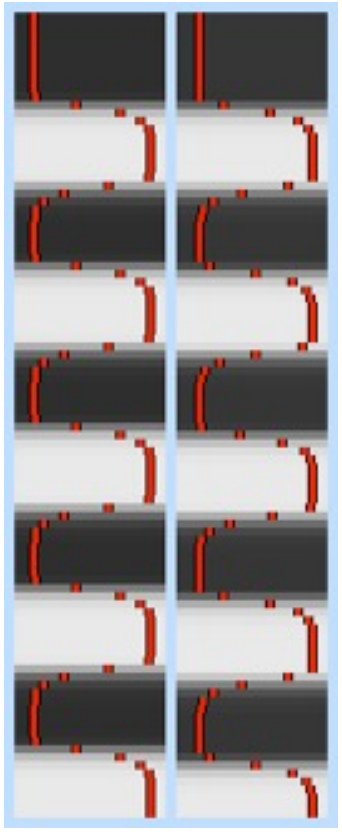
EVs的相关: 个体水平



Design Matrix Rank Deficiency

设计矩阵的秩

- A design matrix is rank deficient when a linear combination of EVs is exactly zero
  - Model can fit exactly the same signal in multiple ways!
- e.g. visual and tactile stimulation occurs at very similar times, so it is not possible to separate the responses!

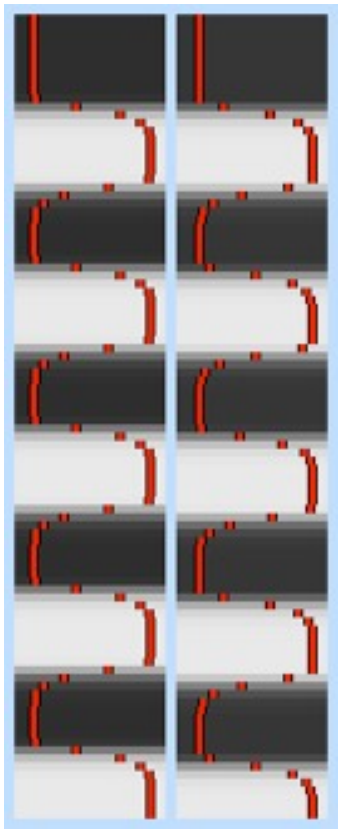


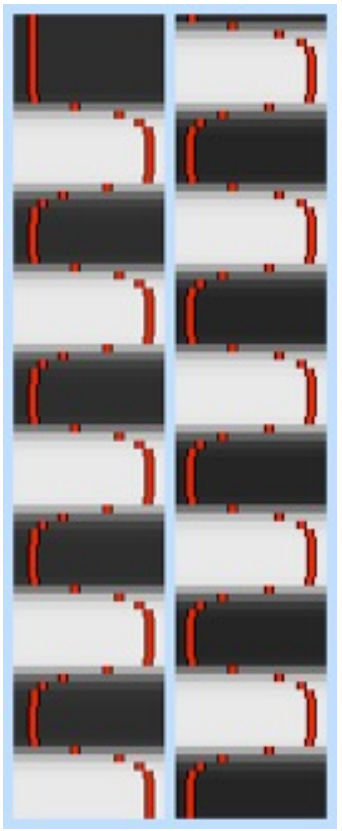
当evs的线性组合为零时，设计矩阵是秩亏的
模型能以多种方式精确地拟合同一信号！
例如，视觉和触觉刺激发生在非常相似的时间
因此不可能分离反应！

Design Matrix Rank Deficiency

设计矩阵的秩

- A design matrix is rank deficient when a linear combination of EVs is exactly zero
  - Model can fit exactly the same signal in multiple ways!
- e.g. visual and tactile stimulations are exactly opposed (so no baseline)

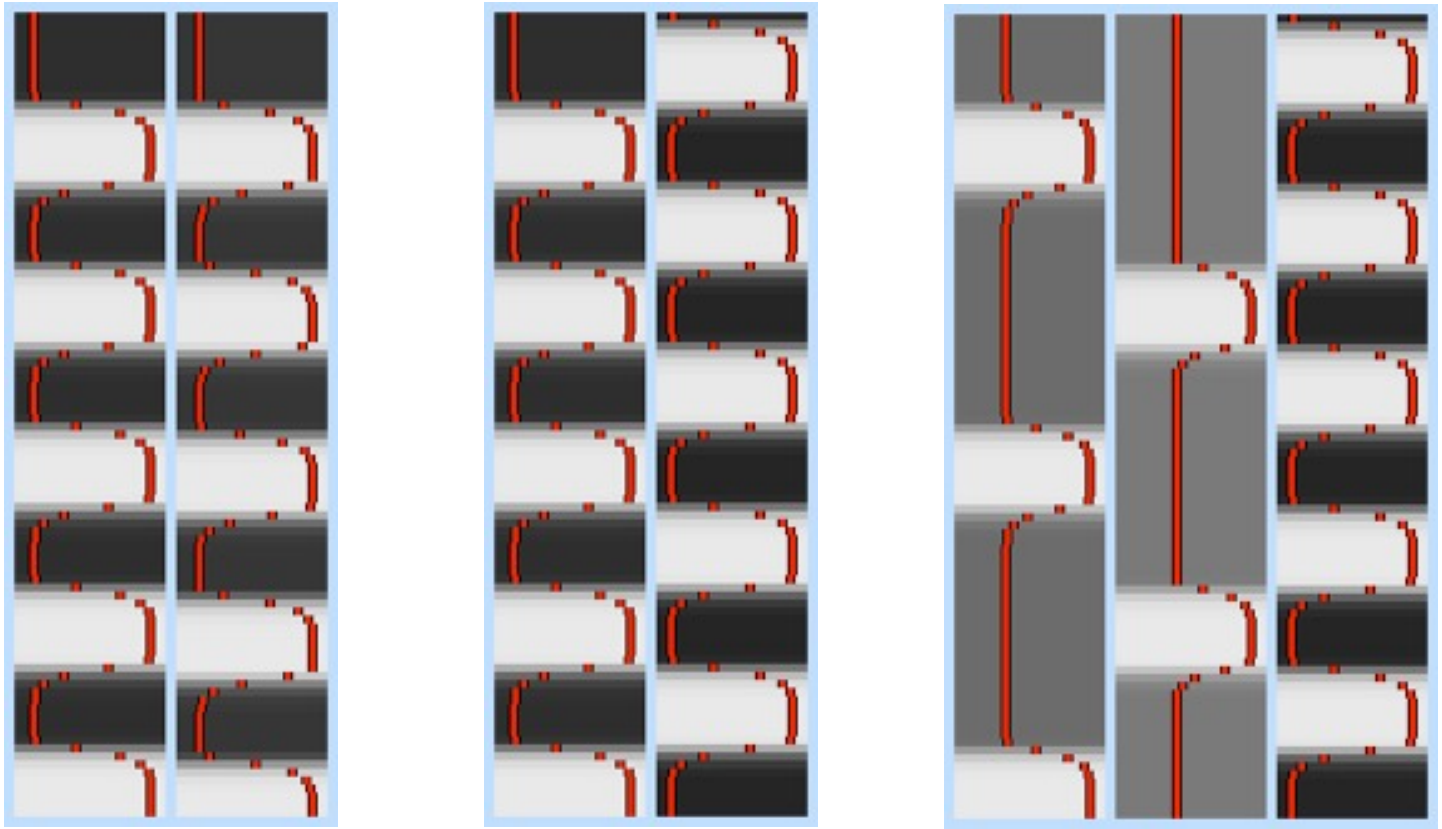




当evs的线性组合为零时，设计矩阵是秩亏的
模型能以多种方式精确地拟合同一信号
例如，视觉和触觉刺激完全相反（因此没有基线）

Design Matrix Rank Deficiency

- A design matrix is rank deficient when a linear combination of EVs is exactly zero
  - Model can fit exactly the same signal in multiple ways!
- e.g. modelling visual, tactile, and rest (the last one is effectively baseline and shouldn't be modelled in FSL)



对视觉、触觉和静息条件建模（最后一个是有效的基线，不应该在FSL中建模）

Close to Rank Deficient Design Matrices

接近秩亏的设计矩阵

- **Good News:** The statistics always take care of being close to rank deficient

  好消息：统计数据总是很接近秩亏的

Close to Rank Deficient Design Matrices

接近秩亏的设计矩阵

- **Good News:** The statistics always take care of being close to rank deficient

  好消息：统计数据总是很接近秩亏的

- **Bad News:** the ignorant experimenter may have found no significant effect, because:

  坏消息：有些实验者可能没有发现明显的效果，因为

  a) Effect size was too small.

  a）效应量太小。

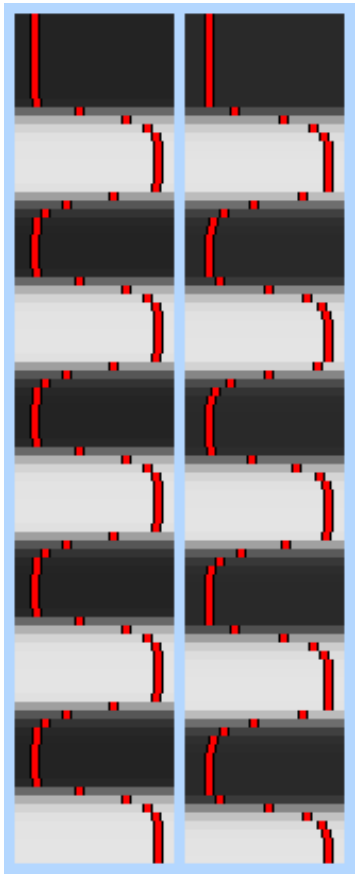
  b) Being close to rank deficient meant finding an effect would have required a HUGE effect size

  e.g. may need a lot of data to determine how two EVs with very similar timings best combine to explain the data.

b）接近秩亏意味着要找到一个效应需要巨大的效应量，例如，可能需要大量数据来确定两个时间非常相似的 EVs 如何最好地结合起来解释数据。

When do we have a problem?

存在的问题



- Depends on SNR, and **crucially** the contrasts we are interested in:

  取决于信噪比，关键是我们感兴趣的对比度：

- [1 -1] e.g. vis-tact??

  [1, -1] 例如视觉-触觉

- [1 1] e.g. average response??

  [1, 1] 例如，平均反应

- [1 0] or [0 1] ?? e.g. visual? or tactile?

  [1, 0] 或 [0, 1] 例如视觉还是触觉

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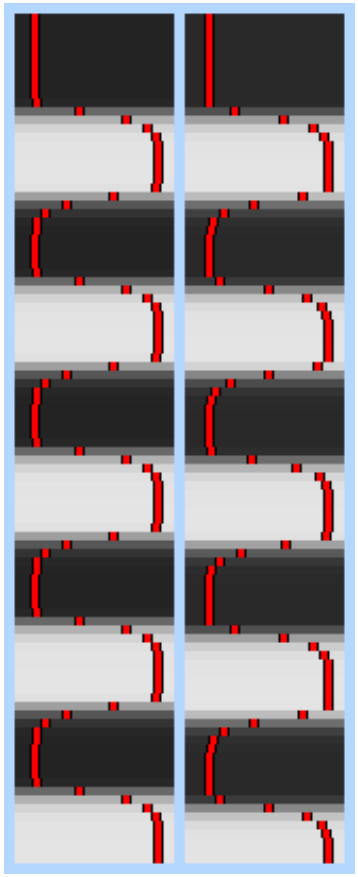


- Depends on SNR, and **crucially** the contrasts we are interested in:

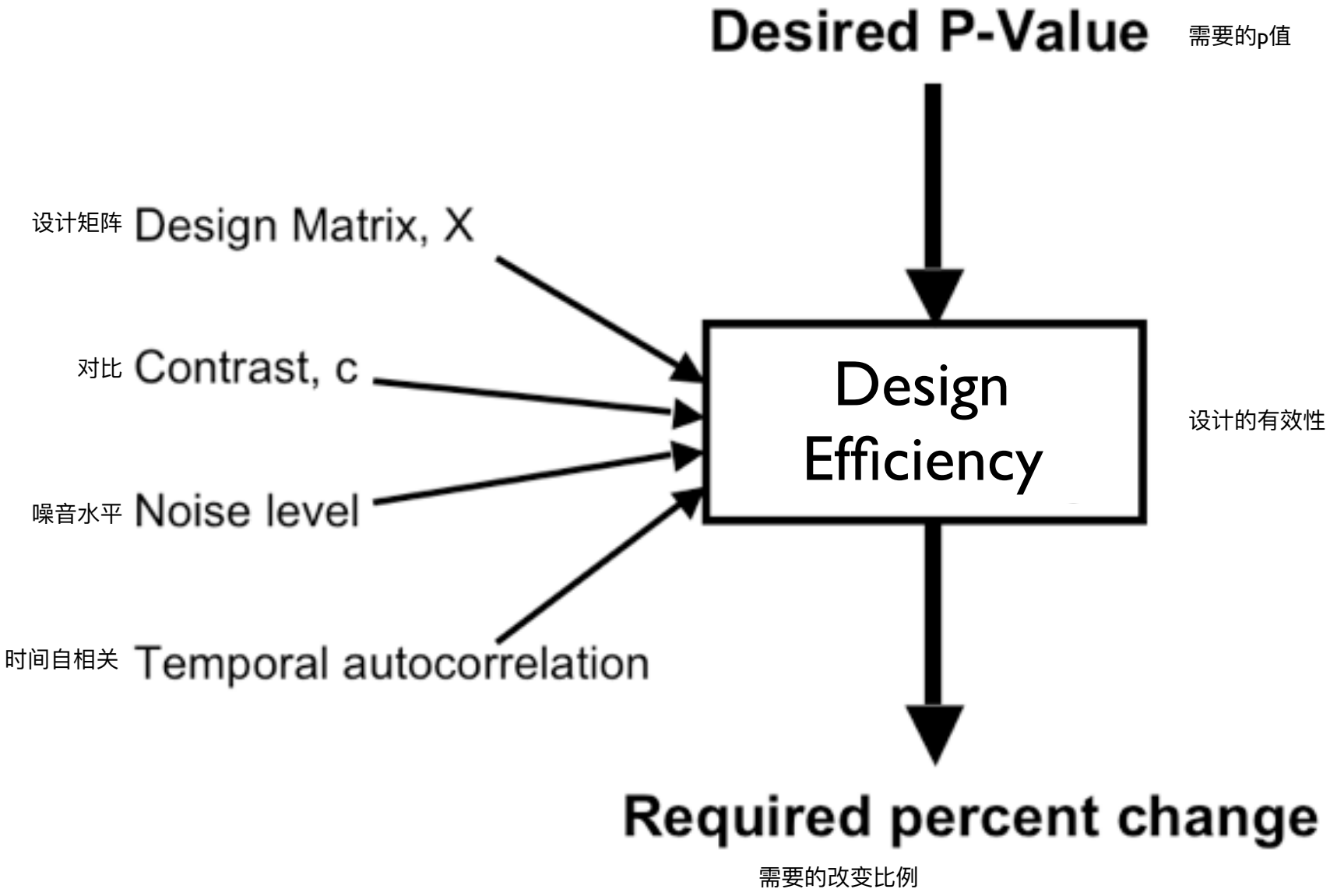
  取决于信噪比，关键是我们感兴趣的对比度：

- [1 -1] e.g. vis-tact??
  - no chance: [1, -1] 例如视觉-触觉 —— 不可能
- [1 1] e.g. average response??
  - no problems: [1, 1] 例如，平均反应 —— 没问题
- [1 0] or [0 1] ?? e.g. visual? or tactile?
  - no chance:

[1, 0] 或 [0, 1] 例如视觉还是触觉 —— 不可能

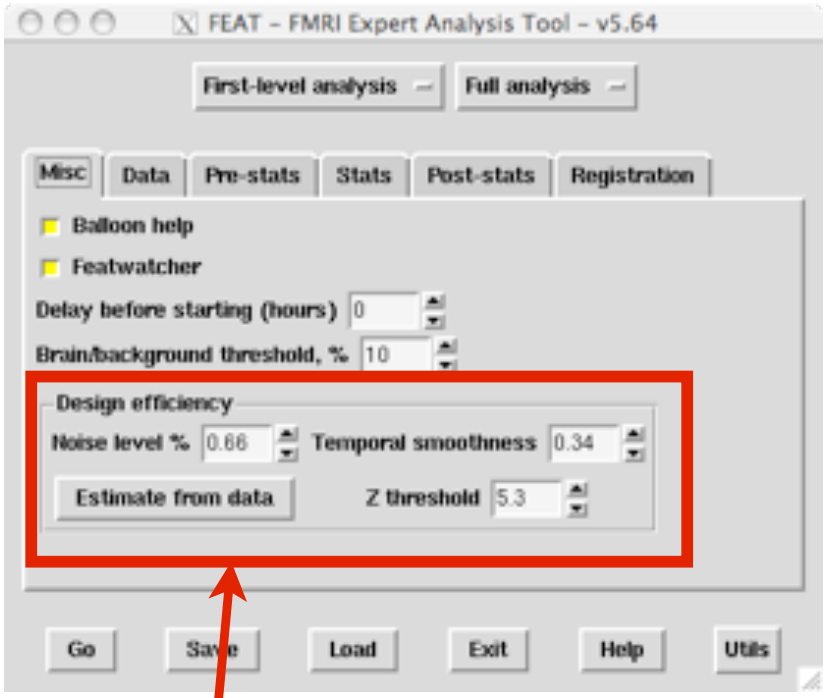
Design Efficiency

设计的有效性



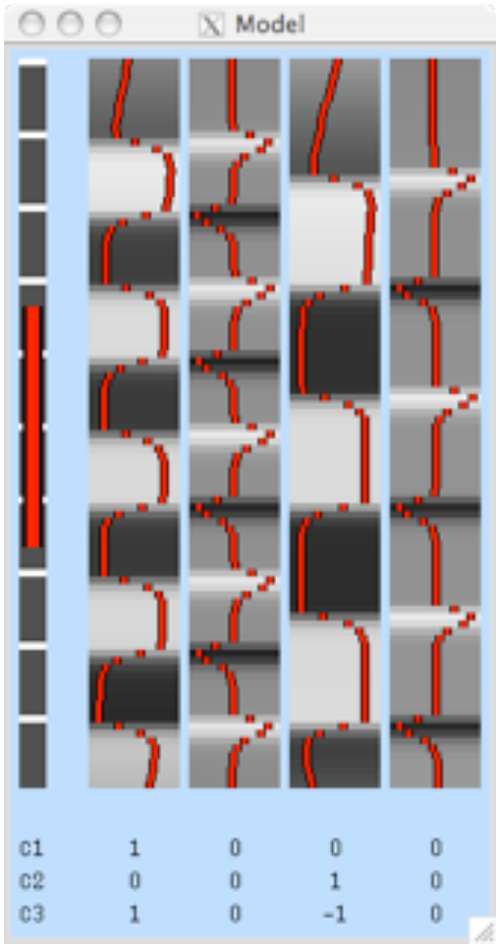
Design Efficiency

设计的有效性



Settings for design efficiency calculations

设计效率计算的设置

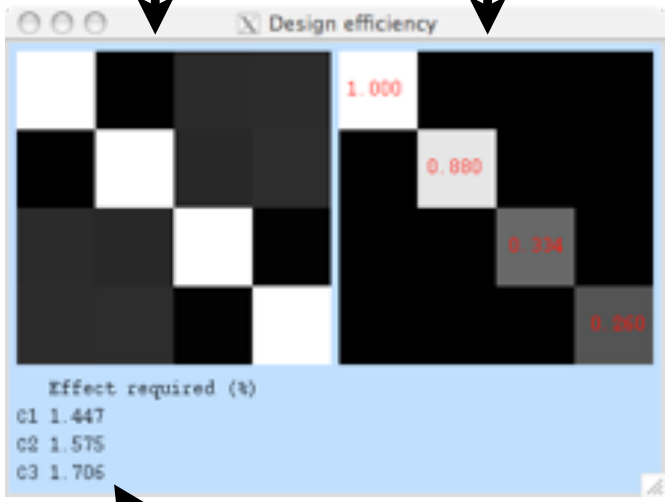


These are the most useful!

这是最有用的

Correlation matrix

Eigenvalues

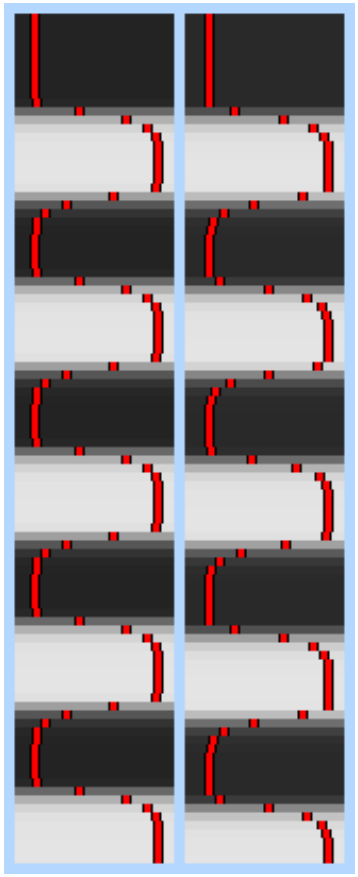


% change required for each contrast to pass specified z-threshold

每个对比度通过指定所需的z阈值更改

When do we have a problem?

什么时候会出现问题呢?



- Depends on SNR, and **crucially** the contrasts we are interested in:

  取决于信噪比，关键是我们感兴趣的对比度：

- [1 -1] e.g. vis-tact??

  Effect size required

  - no chance: **5.3%**

  [1, -1] 例如视觉-触觉 —— 不可能 —— 效应量需要5.3%

- [1 1] e.g. average response??

  - no problems: **0.84%**

  [1, 1] 例如，平均反应 —— 没问题 —— 效应量需要0.84%

- [1 0] or [0 1] ?? e.g. visual? or tactile?

  - no chance: **5.3%**

  [1, 0] 或 [0, 1] 例如视觉还是触觉 —— 不可能 —— 效应量需要5.3%

Case Study: Correlated EVs

案例研究：EVs的相关

Scenario:

Investigating whether there is a relationship between a patient's disease/behavioural scores and their BOLD responses

调查患者的疾病/行为评分与其BOLD信号之间是否存在关系

Problem:

Different scores are likely to be strongly correlated.

Which regions' responses correlate with disease scores but not age?

不同的分数可能有很强的相关性。

哪些区域的反应与疾病评分相关而与年龄无关?

Solutions:

Combination of F-tests and t-tests

f检验和t检验的结合

Correlations, Covariates & Corrections

相关性、协变量和校正

- Consider a case example:

  举个例子：

  - Disease Duration (DD) + age (demeaned)

    疾病持续时间（DD）+年龄 （中心化）

    - where we want to ‘correct’ for age

      我们想“矫正”年龄

Correlations, Covariates & Corrections

相关性、协变量和校正

- Consider a case example: • 举个例子：
- Disease Duration (DD) + age (demeaned) 疾病持续时间（DD）+年龄
  - where we want to 'correct' for age 我们想"矫正"年龄
  - If there is correlation between DD and age then it becomes tricky 如果DD和年龄之间存在相关性，那么就变得棘手了
  - One option is orthogonalisation of DD and age …

一种选择是DD和年龄的正交化…

A better alternative to orthogonalisation

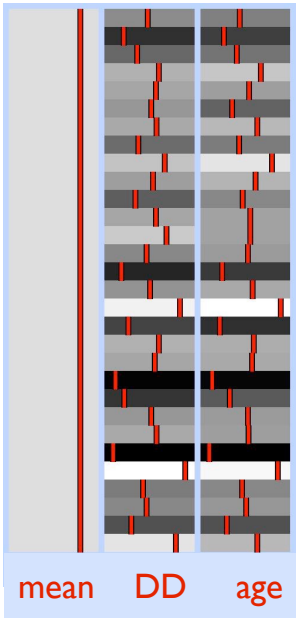
正交化的更好选择

- Consider a case example: • 举个例子：
  - Disease Duration (DD) + age (demeaned) 疾病持续时间（DD）+年龄
    - where we want to 'correct' for age 我们想"矫正"年龄

A better alternative to orthogonalisation

- Consider a case example: 举个例子：
  - Disease Duration (DD) + age (demeaned) 疾病持续时间（DD）+年龄
    - where we want to 'correct' for age 我们想"矫正"年龄

t-test



[0 1 0]

A t-test for a single EV is determined only by variability in BOLD signal that *cannot* be accounted for by other EVs.

单个EVs的t检验仅由BOLD的可变性来确定，其他EVs无法解释这种可变性。

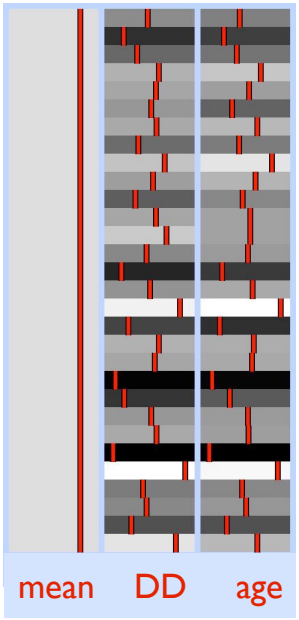
This is a ***conservative*** result: only when DD can *uniquely* explain the measurements will there be a significant result.

这是一个保守的结果：只有当DD能够唯一地解释测量结果时，才会有显著的结果。

A better alternative to orthogonalisation

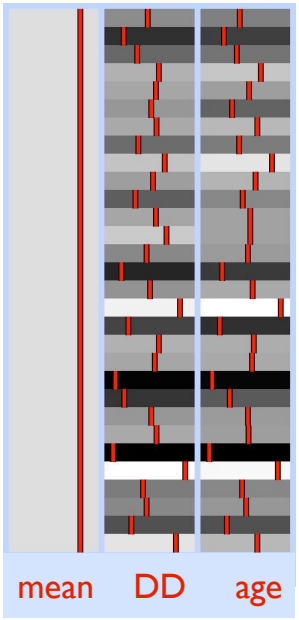
- Consider a case example: • 举个例子：
  - Disease Duration (DD) + age (demeaned) 疾病持续时间（DD）+年龄
    - where we want to 'correct' for age 我们想"矫正"年龄

t-test



[0 1 0]

F-test



[1 0 0]

[0 1 0]

[0 0 1]

A better alternative to orthogonalisation

- Consider a case example: • 举个例子：
  - Disease Duration (DD) + age (demeaned) 疾病持续时间（DD）+年龄
    - where we want to 'correct' for age 我们想"矫正"年龄

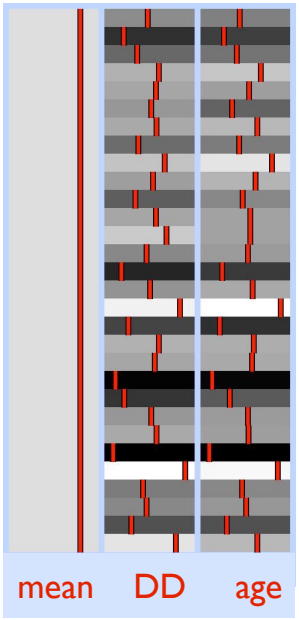
An F-test finds regions where signal can be explained by *any combination* of EVs.

F检验发现信号可以由EVs的任何组合来解释的区域。

Will show significant results where either DD or age or both can explain the measurements.

将显示出重要的结果，其中DD或年龄或两者都可以解释测量结果。

F-test



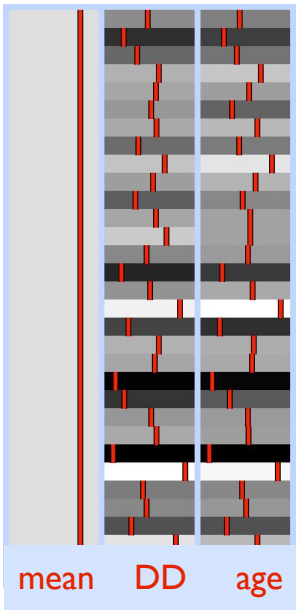
[1 0 0]

[0 1 0]

[0 0 1]

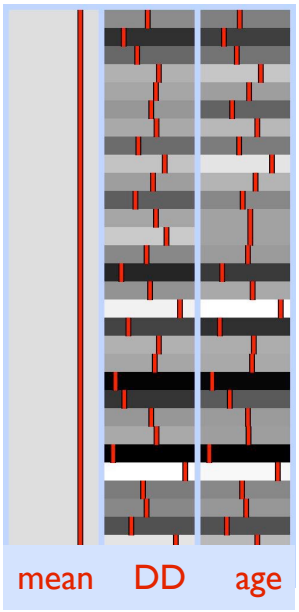
A better alternative to orthogonalisation

t-test



[0 1 0]

F-test



[1 0 0]

[0 1 0]

[0 0 1]

Results (a fairly typical example with strong correlation):

Not significant (t-test)

Significant (F-test)

结果（具有很强相关性的相当典型的示例）：t检验不显著，F检验显著

Interpretation: Significant correlation with *both* DD and age, but cannot separate the effects as they are too highly correlated and the response to unique portions (if any) are too weak.

解释：与DD和年龄都有显著的相关性，但不能分离效果，因为它们相关性太高，对独特部分（如果有的话）的反应太弱。

Follow on: one way to (potentially) separate the effects would be to recruit new subjects such that DD and age were less correlated (need more data to go beyond the above interpretation).

一种（潜在的）分离效应的方法是招募新的受试者，这样DD和年龄的相关性较小（需要更多的数据来超越上述解释）。

That's All Folks

Appendix

附录

Case Studies:

- HRF Variability HRF 变异性
- Perfusion FMRI 灌注fMRI
- Orthogonalisation & more on demeaning

正交 & 中心化

Case Study
案例研究

Scenario: 情景

- Patient vs Control study 病人VS 控制群体
- Patients on a drug treatment 药物治疗的病人
- FMRI cognitive task fMRI 认知任务

Problem: 问题

- Drugs affect cerebral vascularity 药物影响脑血管
- Haemodynamic Response Function (HRF) is altered HRF函数会改变
- Want to separate changes in HRF & neuronal activity
  - otherwise poor HRF model leads to bias in activation strength and increased residual noise

想分离HRF和神经元活动的变化

-否则，较差的HRF模型会导致激活强度的偏差和残余噪声的增加。

Solution: 解决方法

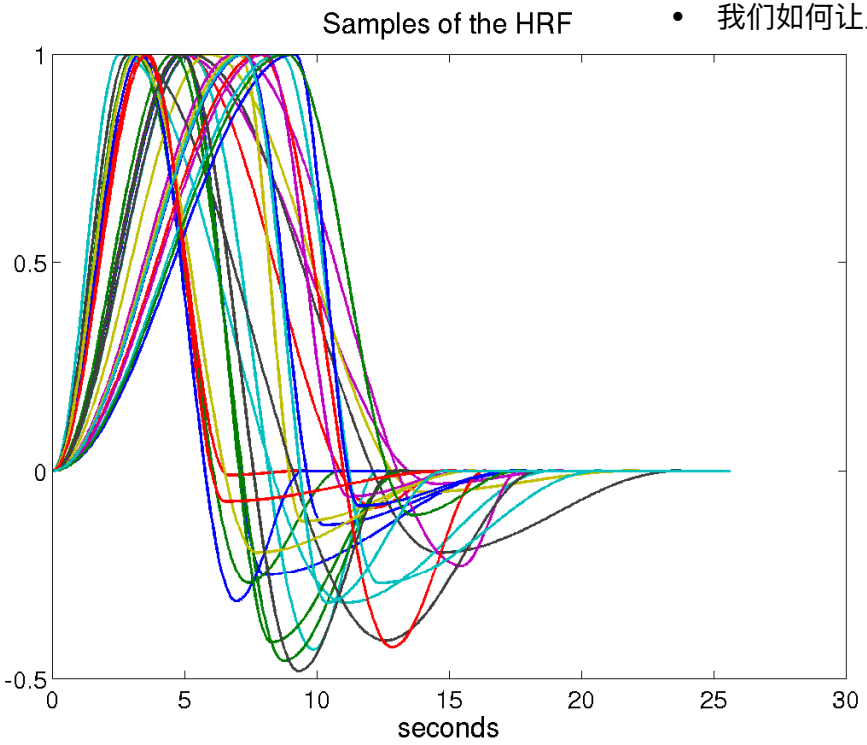
- Basis functions to model HRF variability

建立HRF变异性模型的基函数

Dealing with Variations in Haemodynamics

处理血流动力学变化

- The haemodynamic responses vary between subjects and areas of the brain
  - 被试间及大脑不同区域的血流动力学反应不同
- How do we allow haemodynamics to be flexible but remain plausible?
  - 我们如何让血流动力学变得灵活，但仍然合理?



Reminder: the haemodynamic response function (HRF) describes the BOLD response to a short burst of neural activity

提醒：HRF描述了对短暂神经活动的BOLD反应。

Using Parameterised HRFs

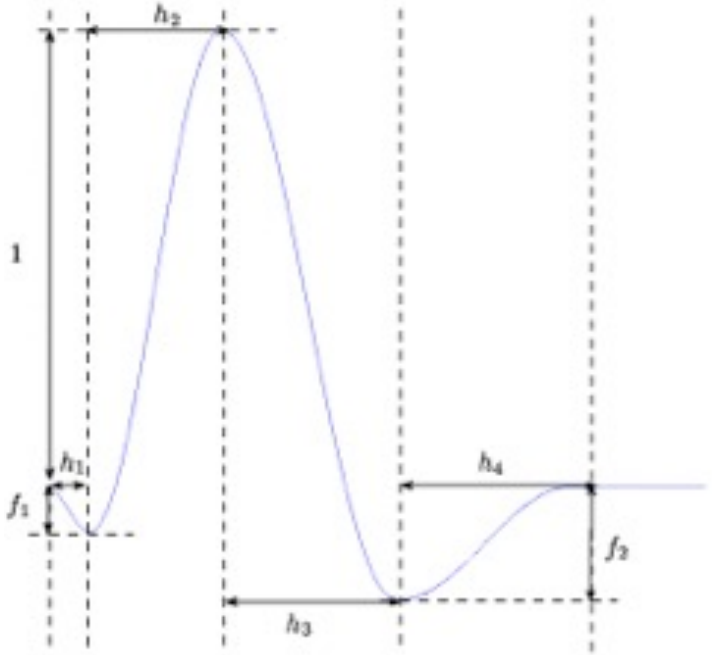
使用参数化的HRFs

- We need to allow flexibility in the shape of the fitted HRF

  允许在拟合的HRF形状上变异性

Ideally, parameterise HRF shape and fit shape parameters to the data

理想情况下，参数化HRF形状，并将形状参数与数据拟合



Needs nonlinear fitting - HARD

需要非线性拟合-困难

Using Basis Sets
使用基础设置

- We need to allow flexibility in the shape of the fitted HRF

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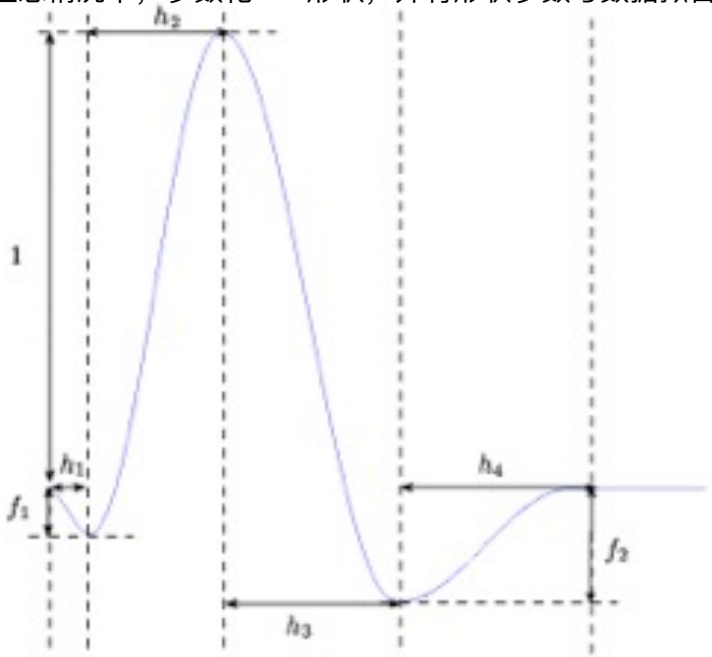
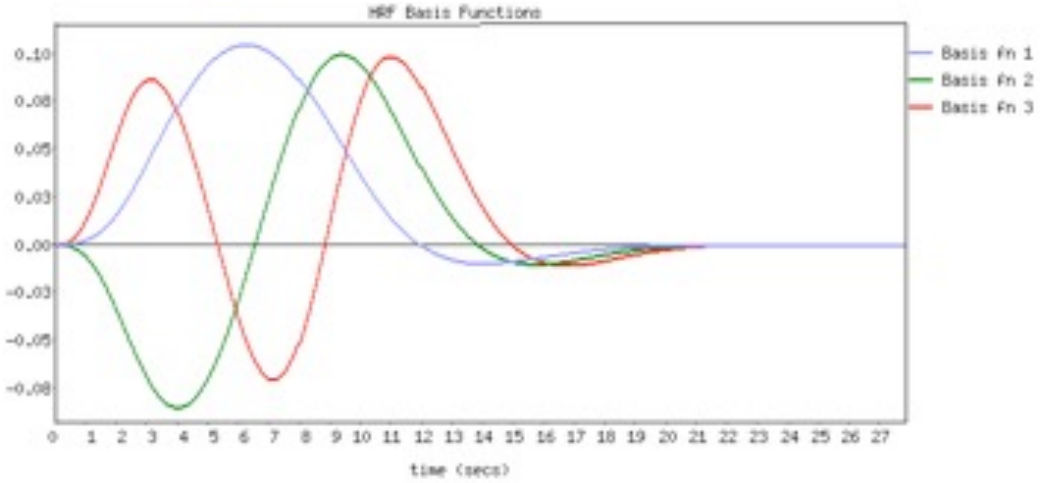


Needs nonlinear fitting - HARD

Or, we can use **linear basis sets** to span the space of expected HRF shapes

或者，我们可以使用线性基集来跨越预期HRF形状的空间。



Linear fitting (use GLM) - EASY

线性拟合（使用gGLM）-简单

Temporal Derivatives 时间导数

- Can model some HRF variability using the temporal derivative
- The temporal derivative of an EV allows for a small shift in time of that EV (it is a small basis set)
- Based upon 1st-order Taylor series expansion:

可以用时间导数模拟一些心率变异性

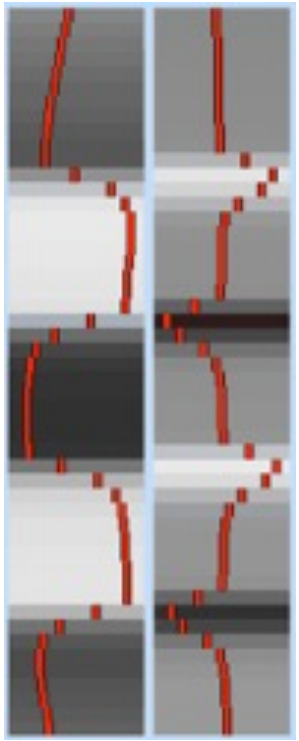
EV的时间导数允许EV的时间发生小的变化（它是一个小的基集）

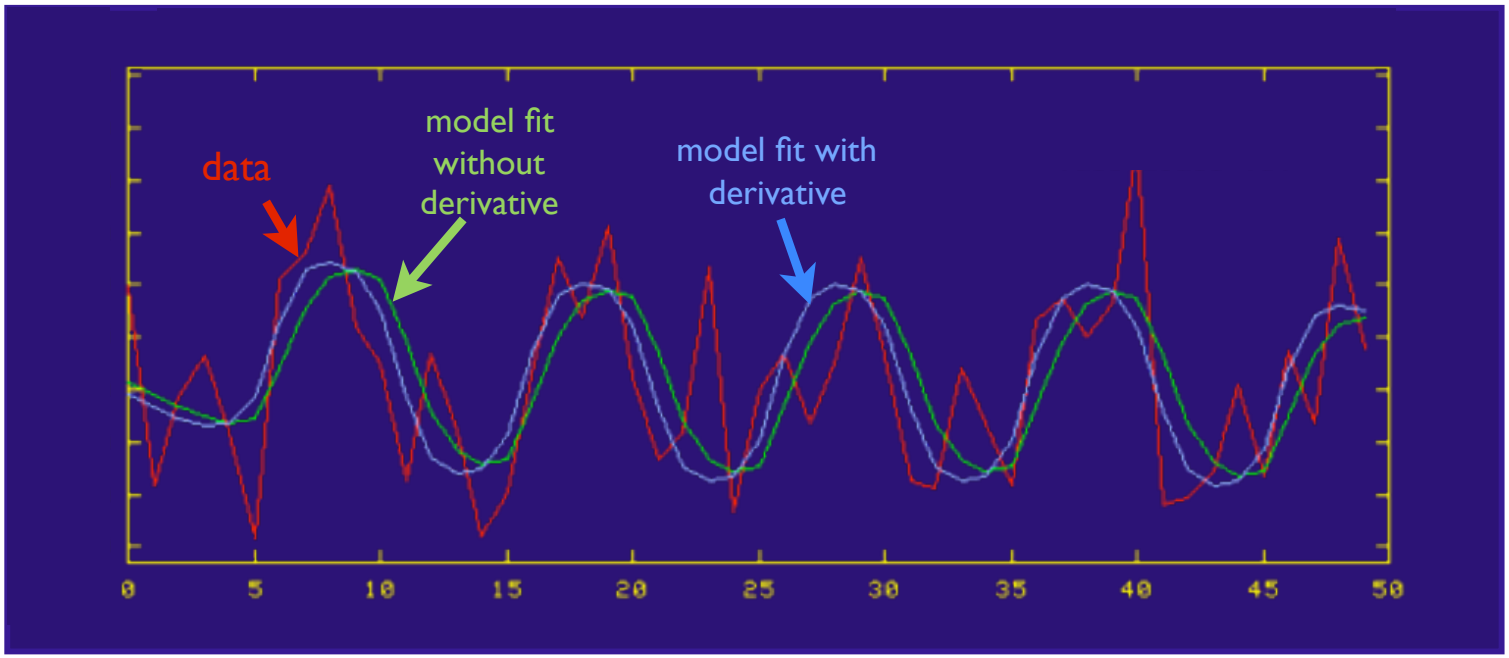
基于一阶泰勒级数展开：

$$f(t+a) \approx f(t) + a.f'(t)$$

Shifted EV　　EV　　Temporal derivative

EV　Temporal derivative





How do HRF Basis Sets Work?

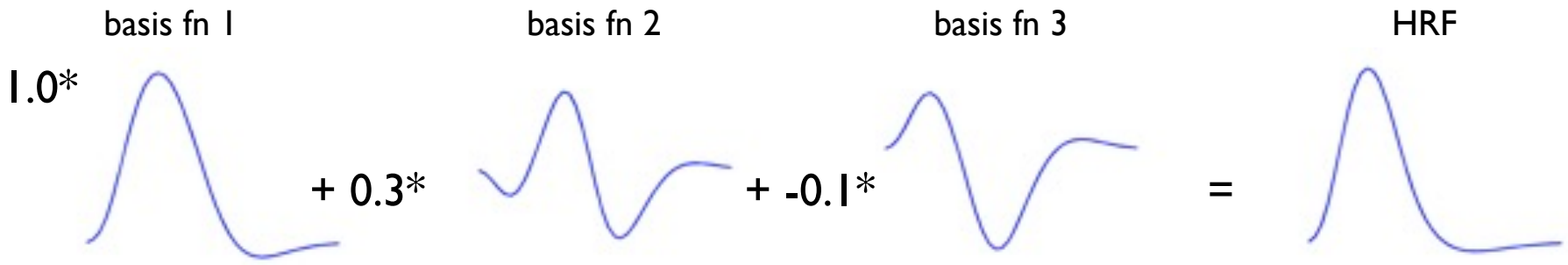
HRF的基本设置是如何工作的?

Temporal derivative is a simple example of a basis function - need more basis functions to allow for shape changes

时间导数是基本函数的一个简单例子-需要更多的基本函数改变形状

Different linear combinations of several basis functions can be used to create different HRF shapes

多个基本函数的不同线性组合可用于创建不同的HRF形状



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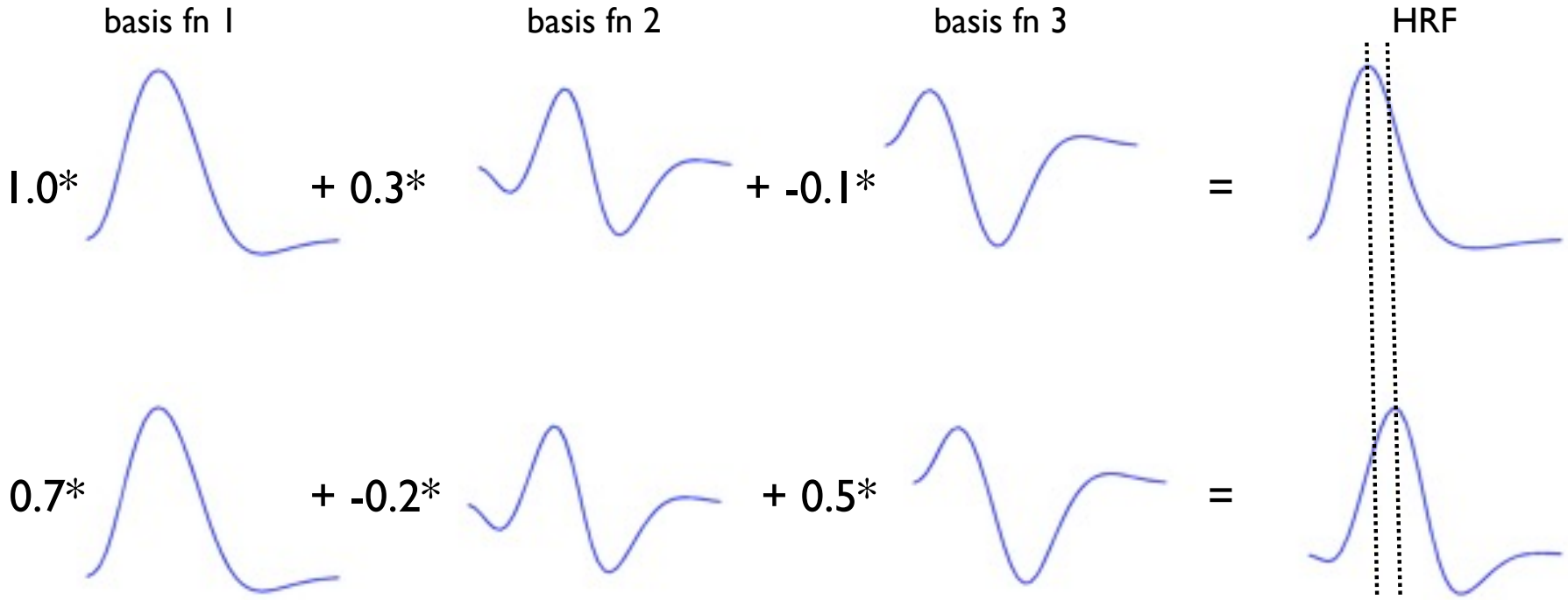


But how do we choose the basis functions?

但是我们如何选择基函数呢?

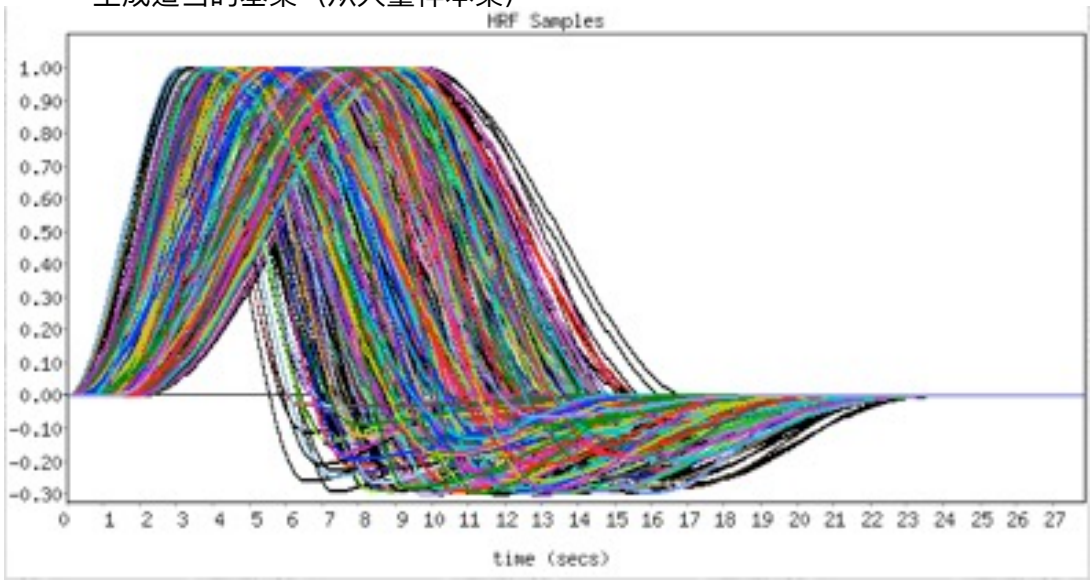
FMRIB's Linear Optimal Basis Set (FLOBS)

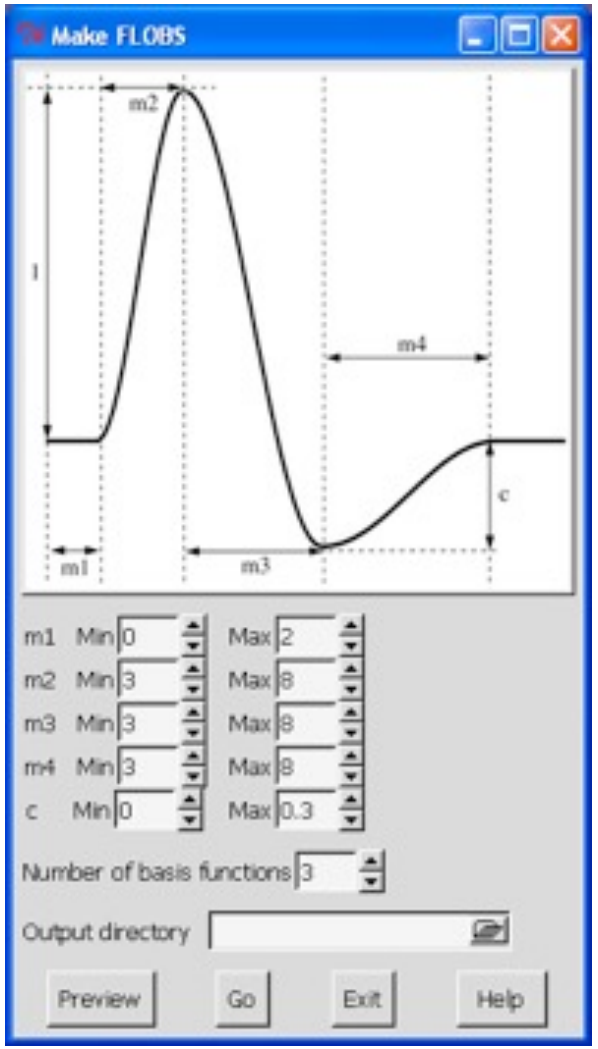
FMRIB的线性最佳基集

Using FLOBS we can:

使用FLOBS我们可以：

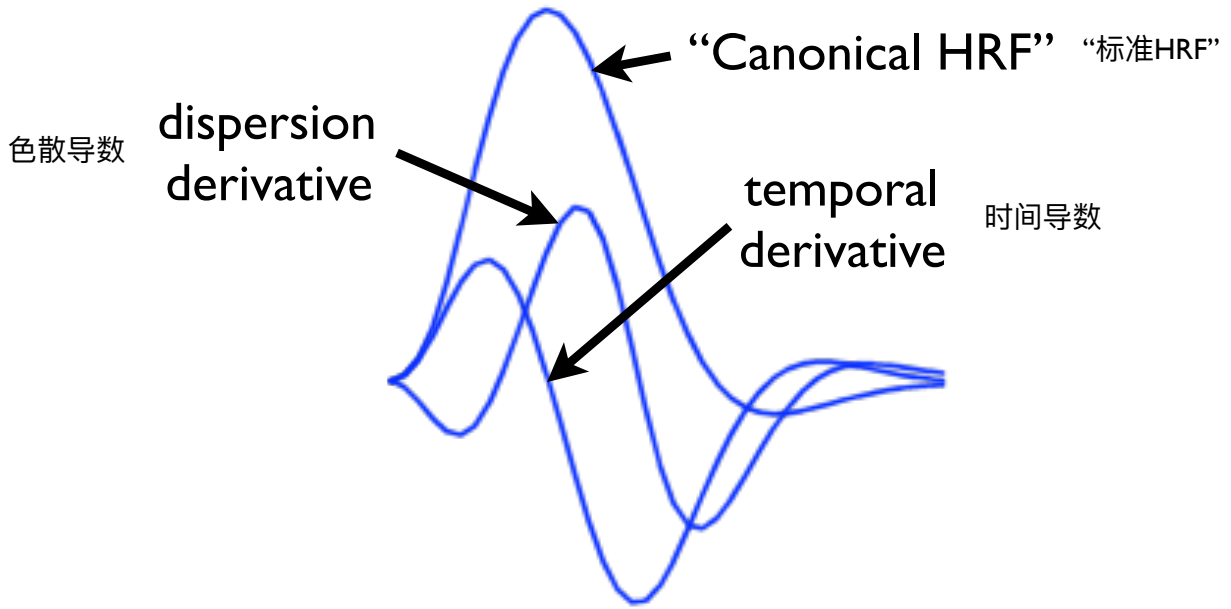
- Specify a priori expectations of parameterised HRF shapes
  指定参数化HRF形状的先验期望值
- Generate an appropriate basis set (from a large set of samples)
  生成适当的基集（从大量样本集）





FMRIB's Linear Optimal Basis Set (FLOBS)

Select the main modes of variation as the optimal basis set 选择主要变化模式作为最优基集

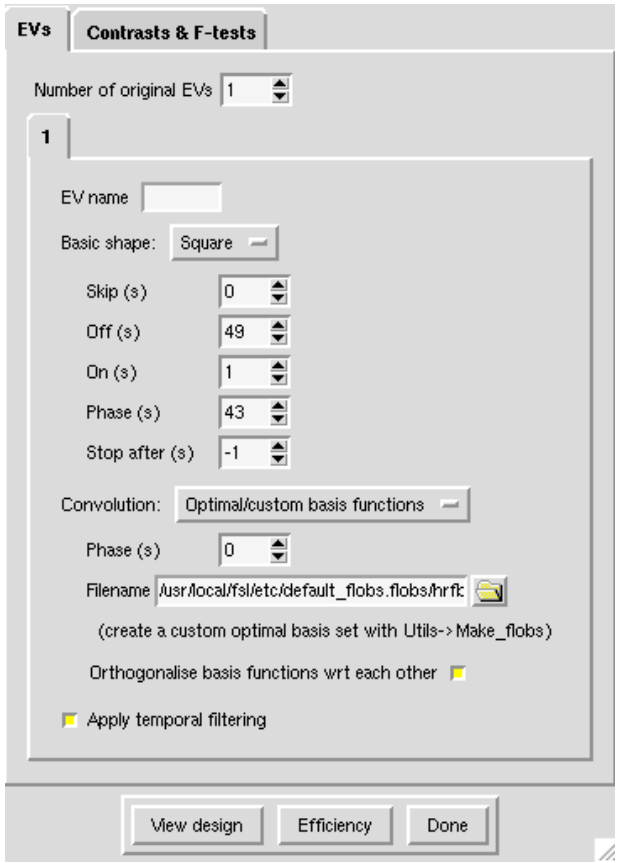


HRF Basis Functions in FEAT

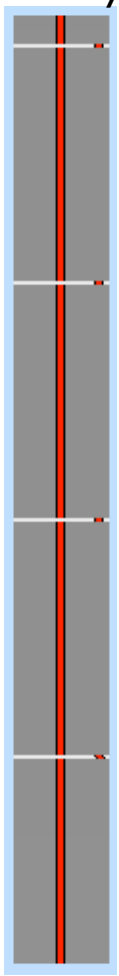
FEAT中的HRF基本功能

The FEAT GUI allows a range of different basis functions to choose from

FEAT 界面允许从一系列不同的基本功能中进行选择

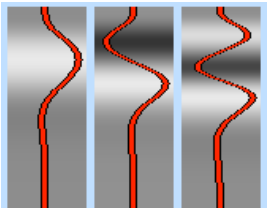


Stimulus/Neural Activity 刺激/神经活动



convolved with

HRF Basis functions HRF基本功能



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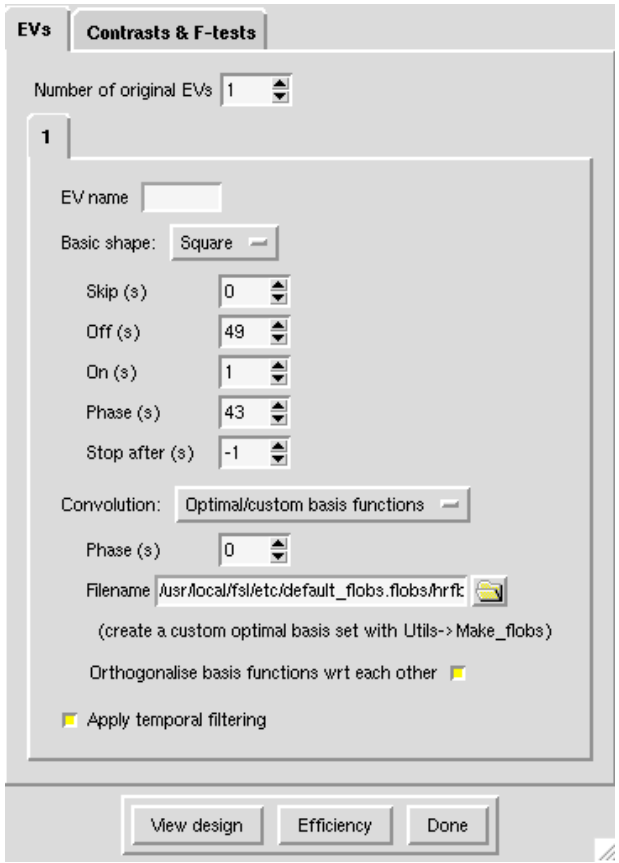
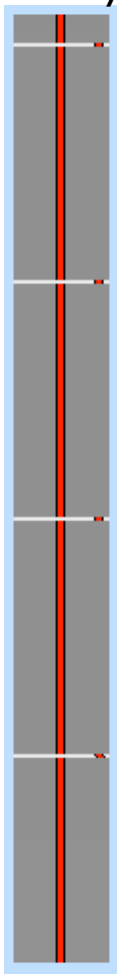


Stimulus/Neural Activity

刺激/神经活动



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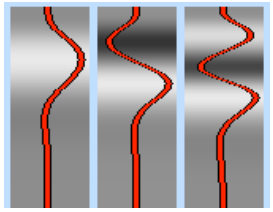
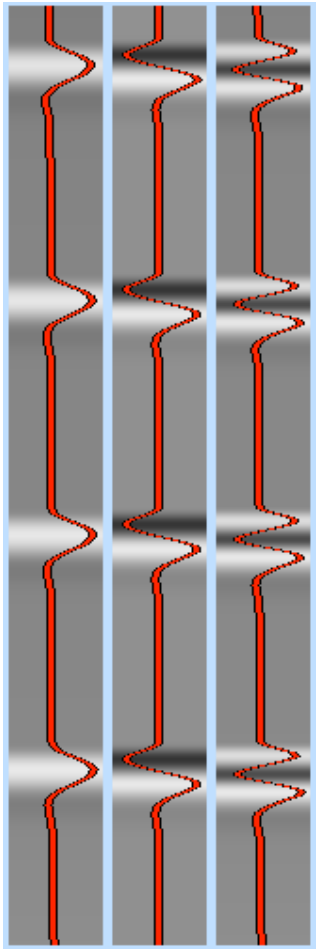
HRF基本功能

HRF Basis functions



Basis function stimulus responses

基本功能刺激反应



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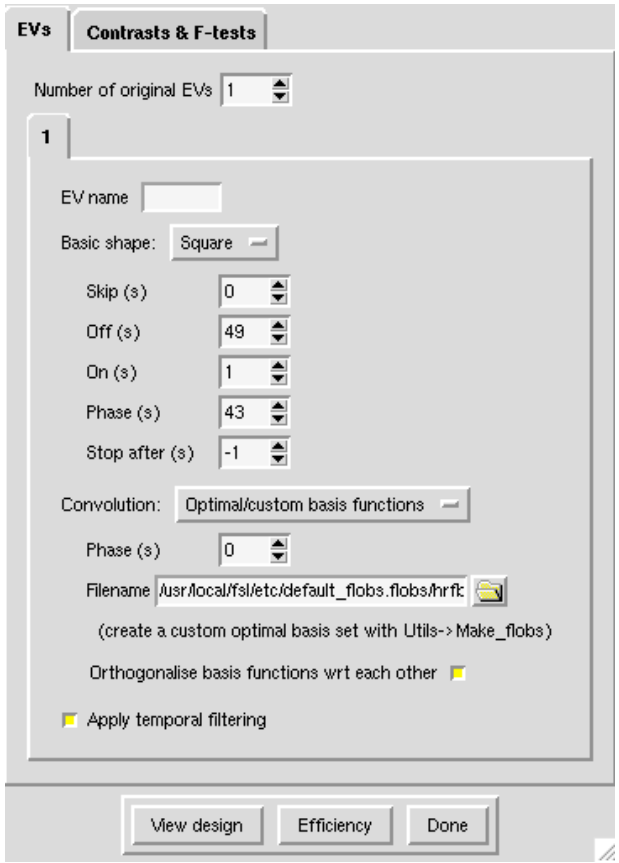

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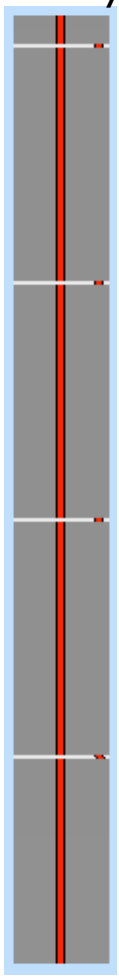

convolved with

HRF基本功能

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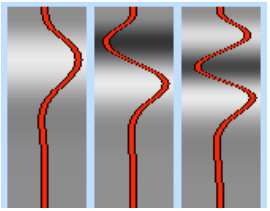
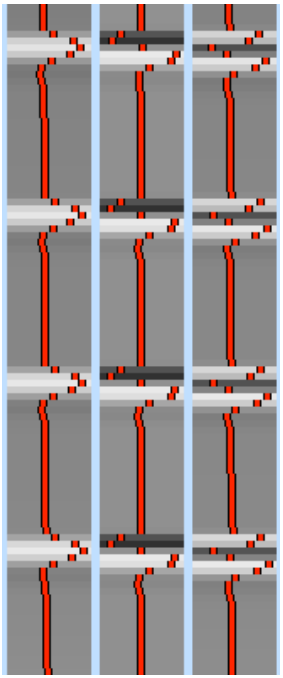


subsample to FMRI resolution

fmri分辨率的子样本

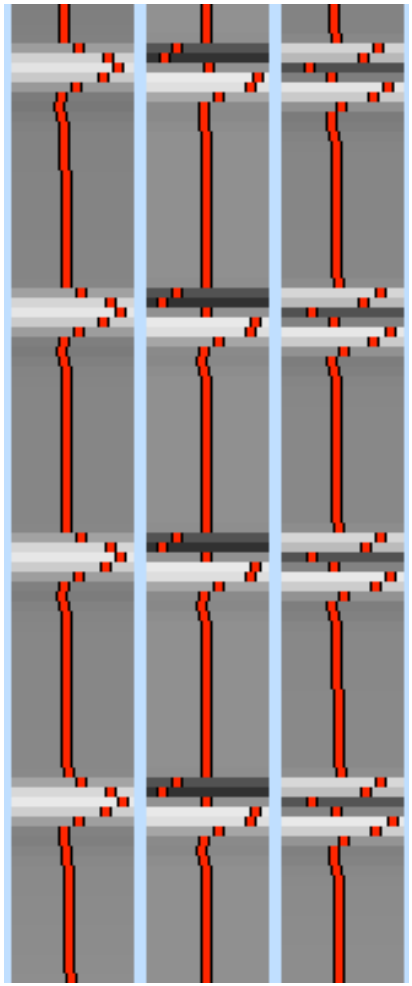
基本功能EVs

Basis function EVs



How do we Test for Significance?

如何考察显著性



Recall that F-tests allow us to test if there is significant amounts of power explained by linear combinations of contrasts

回想一下，F检验允许我们检验是否存在由不同对比的线性组合所解释的变异

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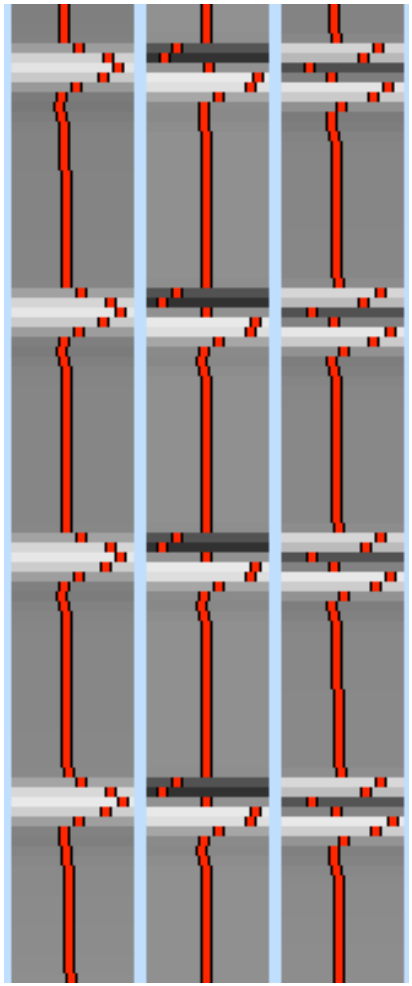

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回想一下，F检验允许我们检验是否存在由不同对比的线性组合所解释的变异

f-contrast matrix:

$$\begin{pmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{pmatrix}$$

But note: the F-test cannot distinguish between a positive or negative activation

但是注意：F检验不能区分阳性激活和阴性激活

HRF Basis Functions in FEAT

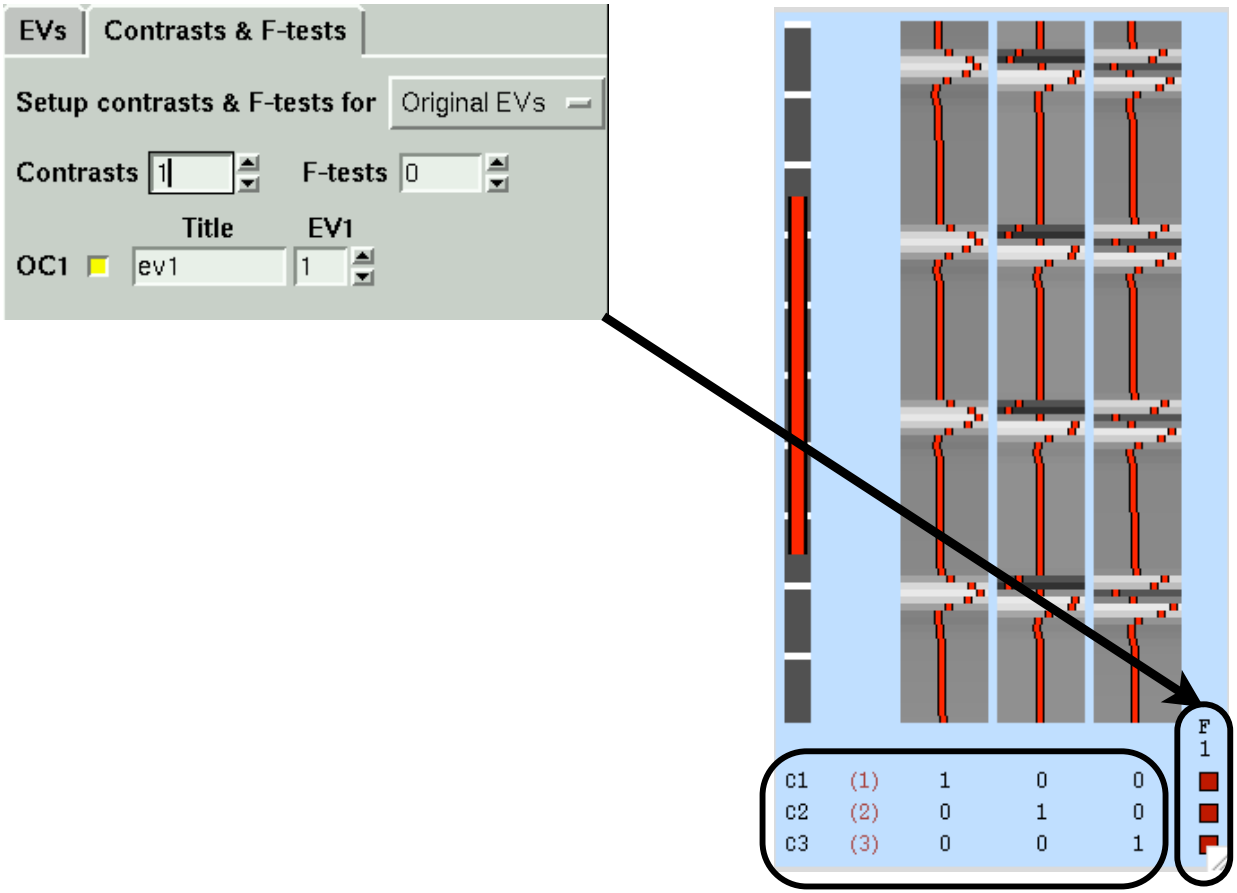
Feat 的基础HRF函数

In FEAT the GUI allows contrasts to be setup on “Original EVs” or “Real EVs”

FEAT中允许在“原始evs”或“真实evs”上设置对比度

“Original EVs” represent the underlying experimental conditions

“原始EVs”代表了基本的实验条件



HRF Basis Functions in FEAT

Feat 的基础HRF函数

In FEAT the GUI allows contrasts to be setup on "Original EVs" or "Real EVs"

FEAT中允许在"原始evs"或"真实evs"上设置对比度

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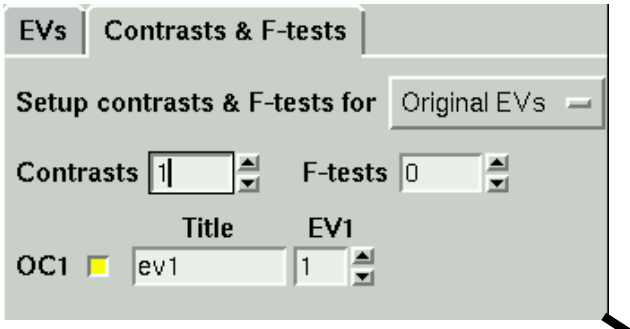
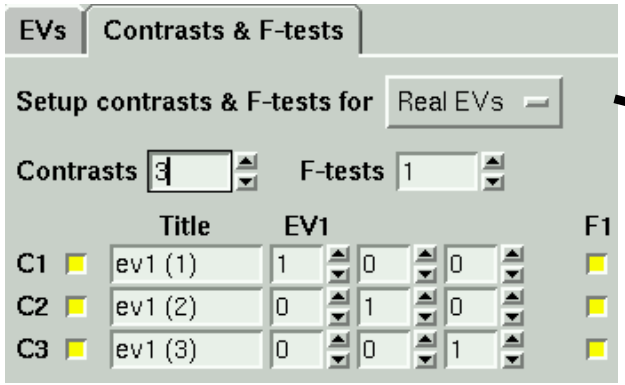
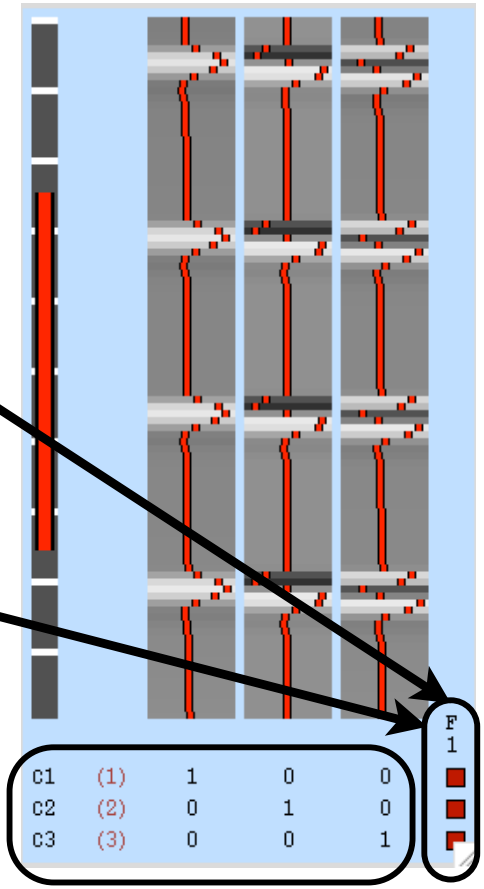


"Real EVs" represent the actual basis function EVs in the design matrix

真实的EVs代表当前设计矩阵中的基本函数EVs



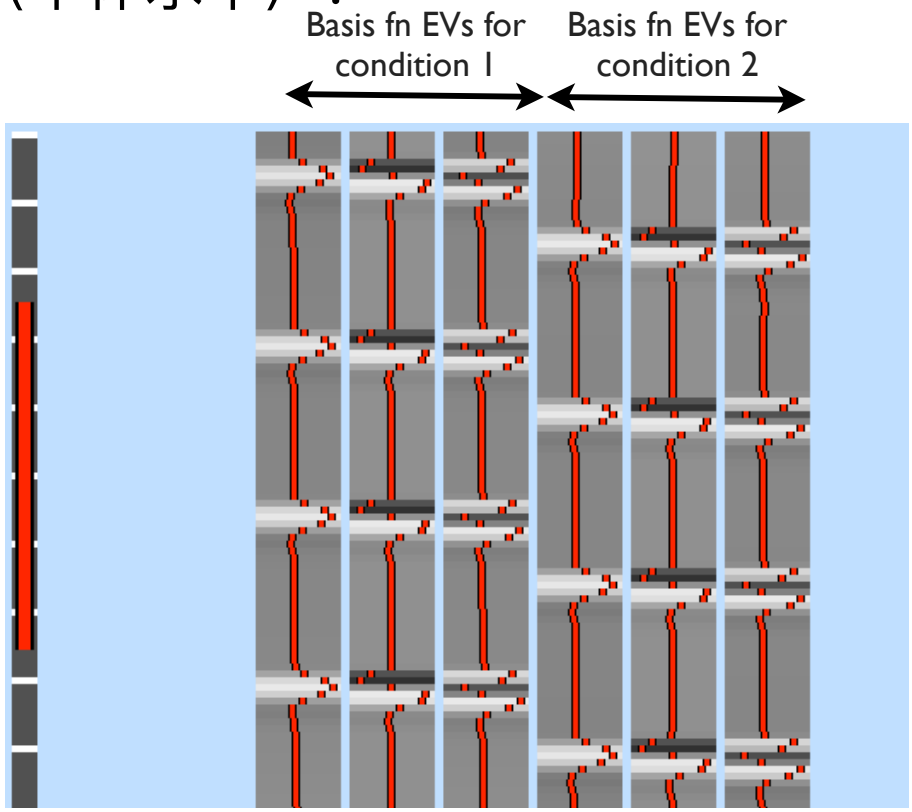


How do we Test for Significant Differences (at first level)?

如何测试显著性差异（个体水平）？

We want to test for a significant difference between two underlying experimental conditions (e.g. two cognitive tasks)

我们想测试两个基本实验条件之间的显著差异（例如两个认知任务）



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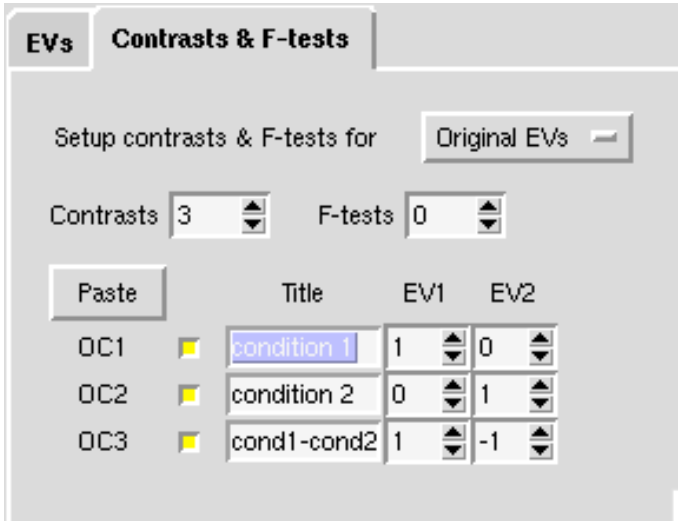

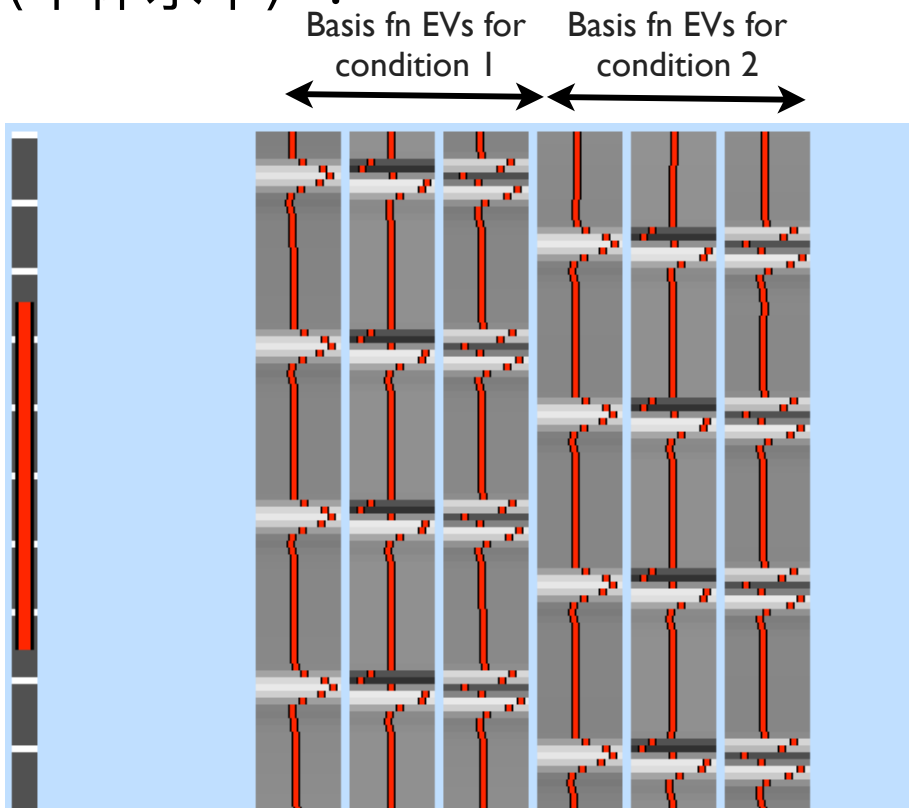

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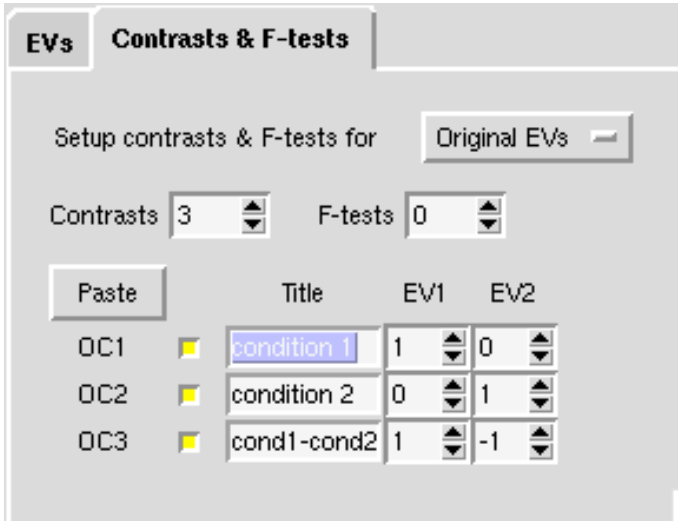

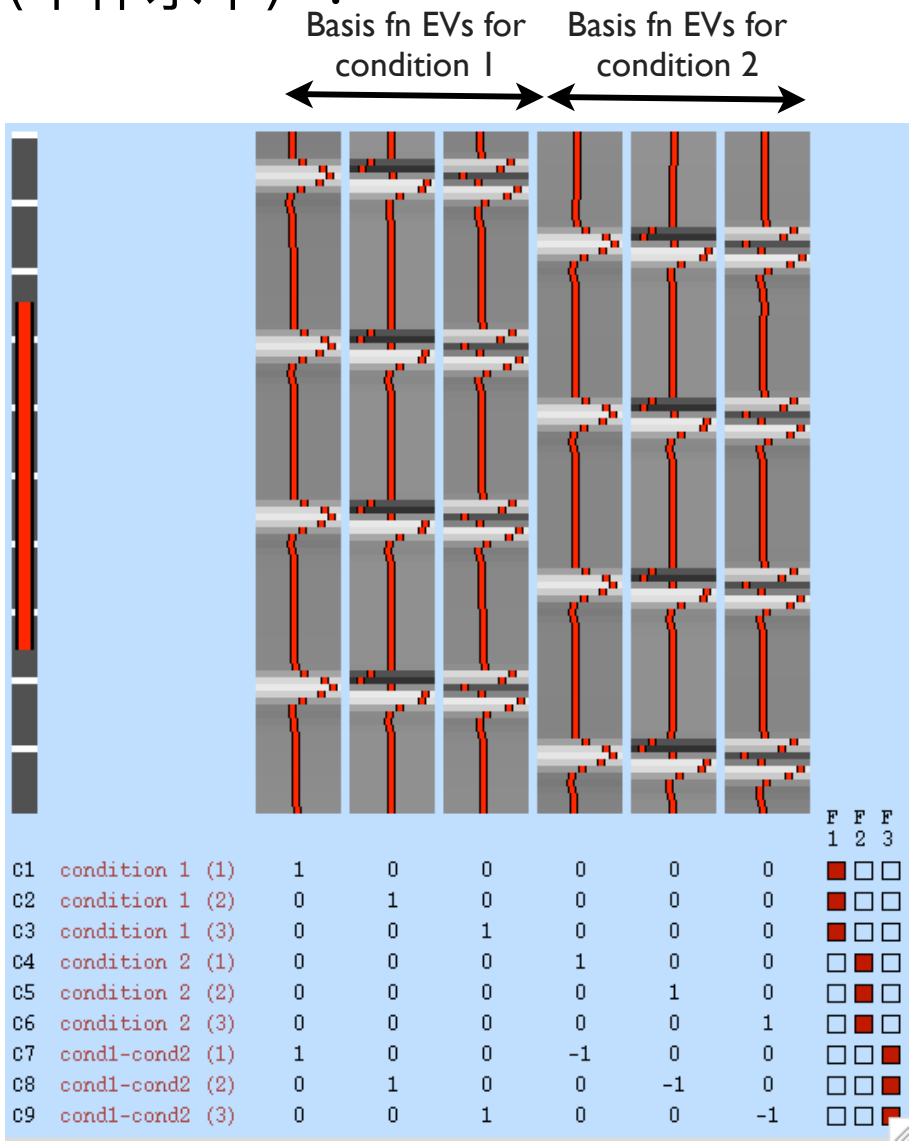

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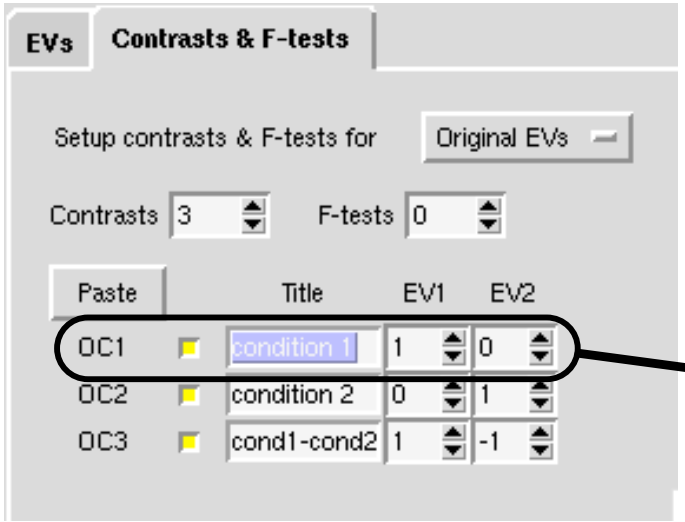

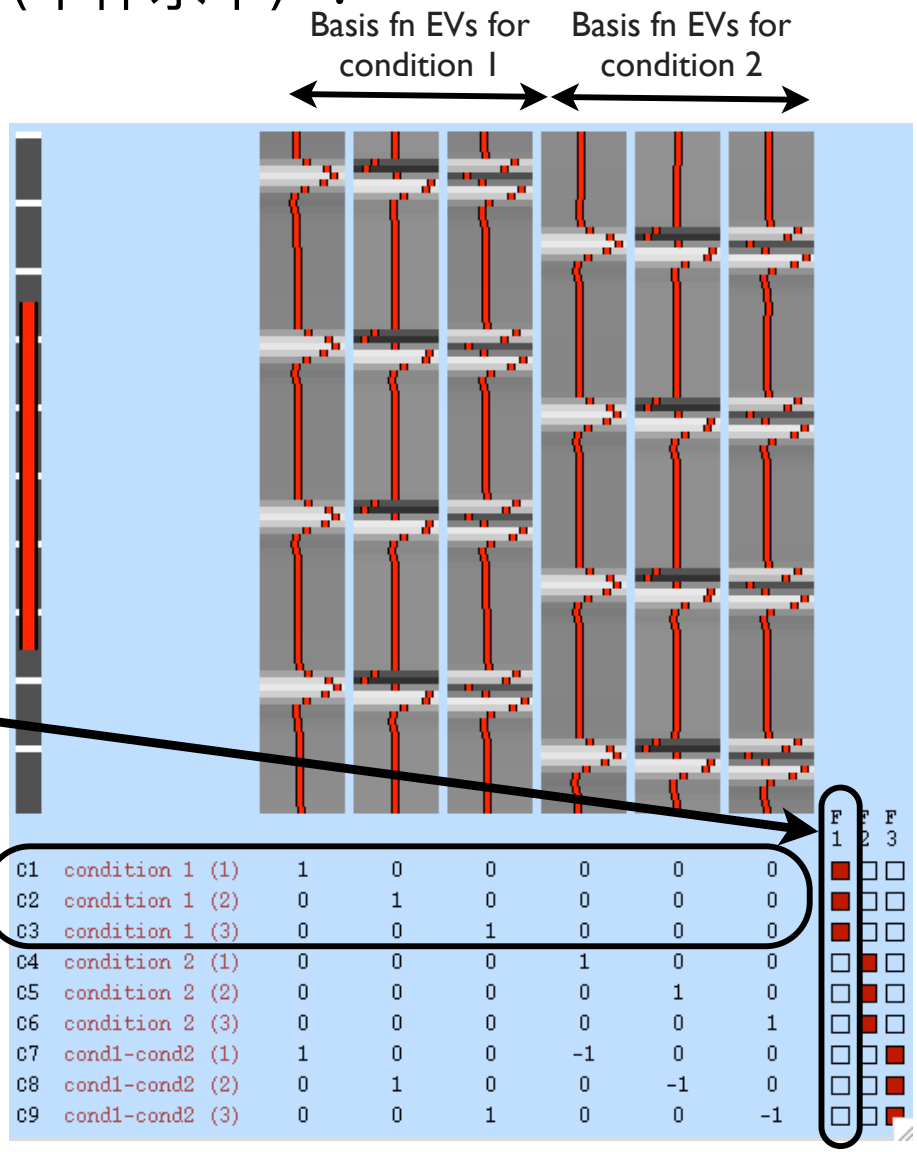

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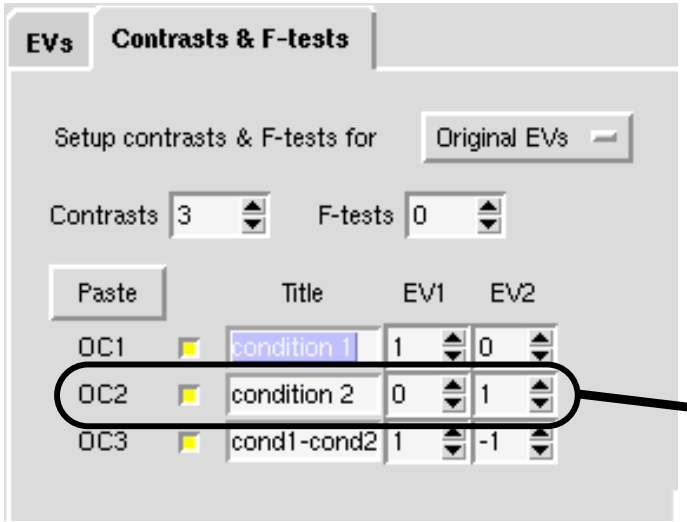

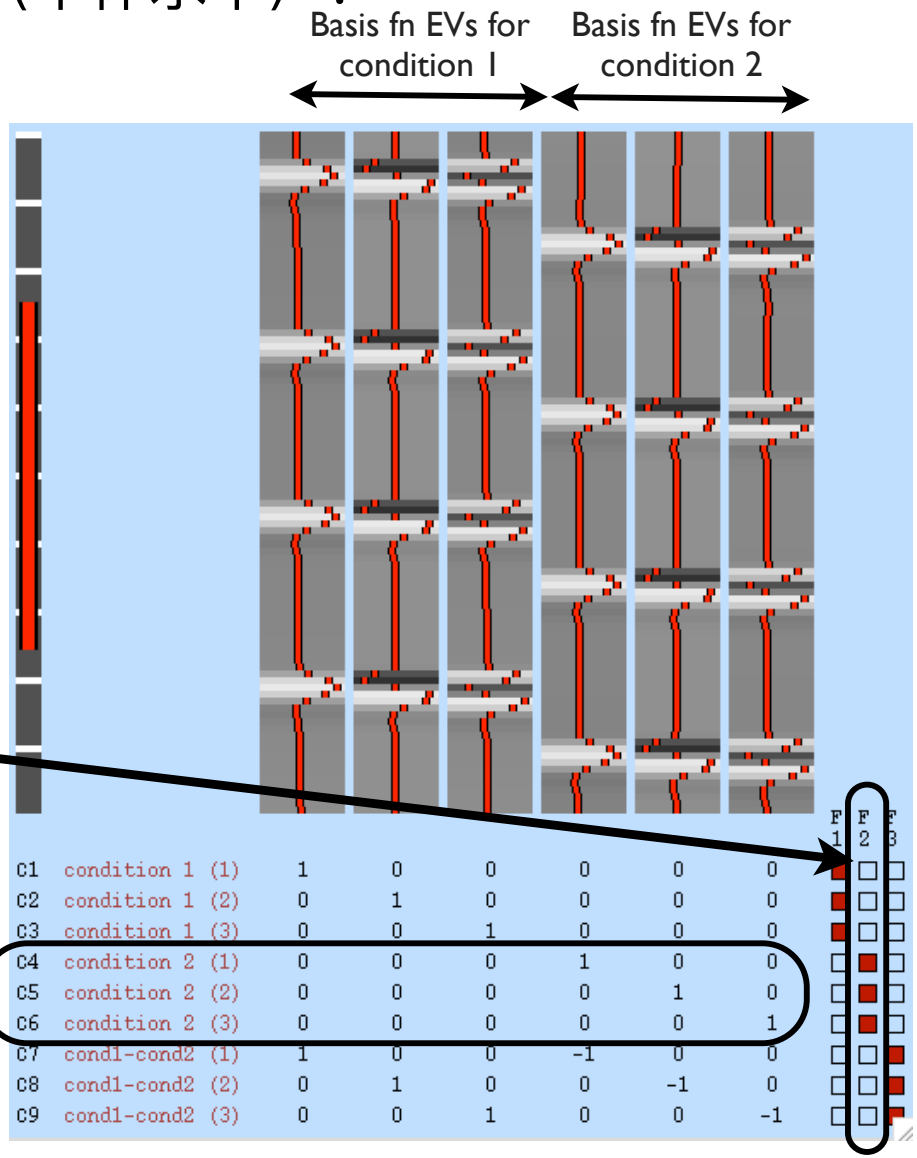

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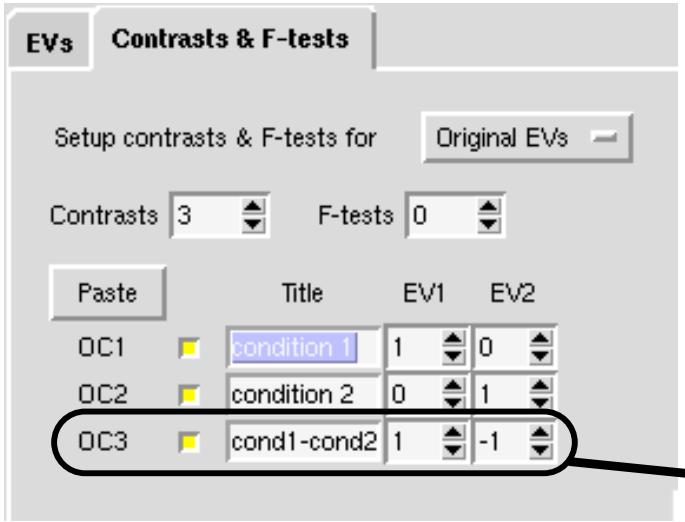
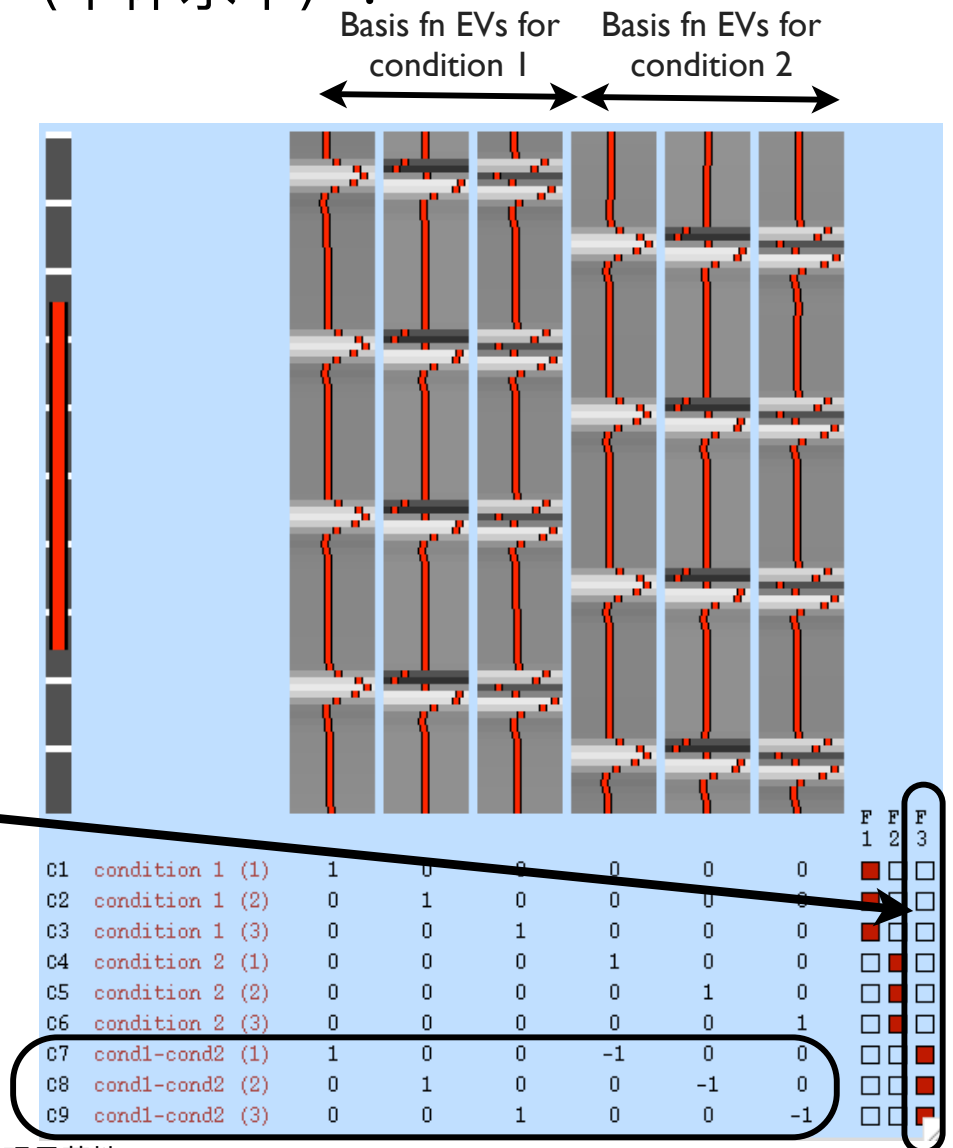




- F-test combines [1 -1] t-contrasts for corresponding basis fn EVs
- this will find significance if there are size **or** shape differences

F检验结合[1-1]t-对比度作为相应的基础函数EVs，如果存在大小或形状差异，会发现显著性

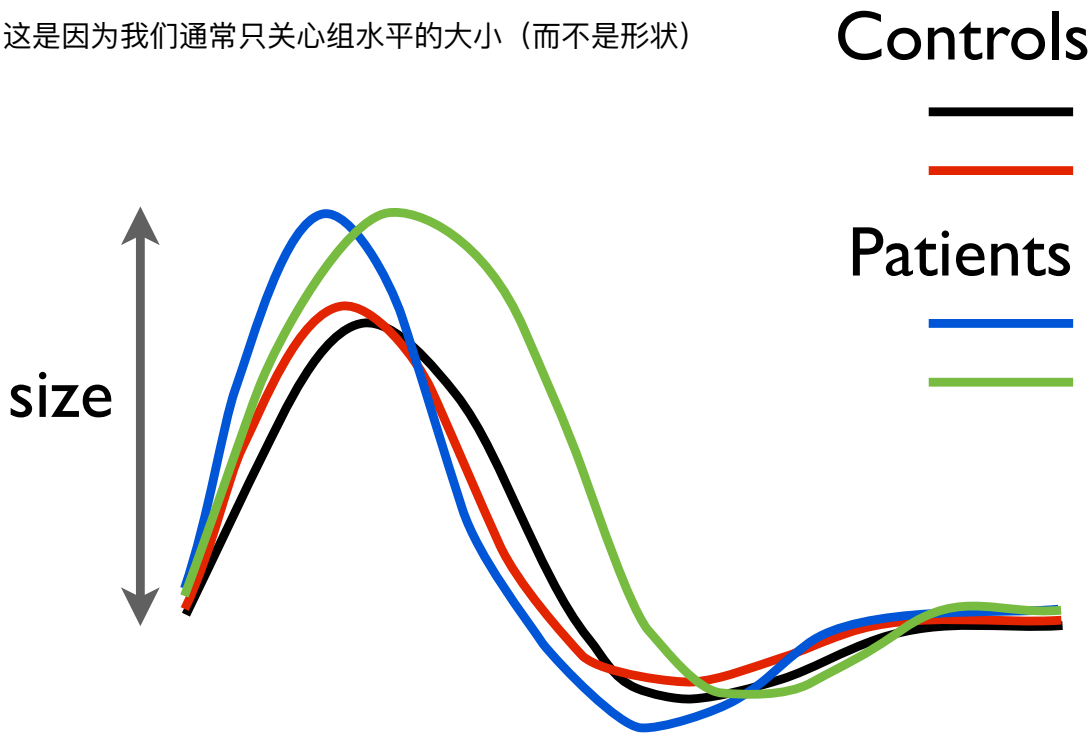
How do we Test for Significant Differences (at higher levels)? 如何测试显著性差异（更高水平）？

- Using basis fns and F-tests is problematic when it comes to doing inference on groups of subjects

  在对一组被试进行推理时，使用基础函数和F检验是有问题的。

- This is because we are typically interested in only size (not shape) at the group level

  这是因为我们通常只关心组水平的大小（而不是形状）



Between group differences in size and shape.

组间大小和形状的差异。

At the group level look at size differences.

组水平上看大小差异。

How do we Test for Significant Differences (at higher levels)?

如何测试显著性差异（更高水平）？

- Using basis fns and F-tests is problematic when it comes to doing inference on groups of subjects 在对一组被试进行推理时，使用基础函数和F检验是有问题的。
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- Options:

1) Only use the "canonical HRF" EV PE in the group inference
   - e.g. when EVs with temporal derivatives, only use the main EV's PE in the group inference

仅在组水平分析中使用标准HRF EV
-例如，当EVs具有时间导数时，仅使用组分析中主要的EV

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     -例如，当EVs具有时间导数时，仅使用组分析中主要的EV
2) Calculate a "size" statistic from the basis function EVs PEs and use in the group inference
   - must use ***randomise*** for this, not standard FEAT/FLAME

根据基本函数EVs pes计算一个"效应量"的统计值，并用于组分析
-必须使用randomise工具，而不是标准FEAT/FLAME

Case Study 案例研究

Scenario: 情景

Pain study of tonic, ongoing pain and involving infusion of drugs during scanning
(or any other slow-acting physiological stimuli e.g. thirst)

长时间持续性疼痛的疼痛研究，包括扫描期间的药物输注（或任何其他慢效生理刺激，如口渴）

Problem: 问题

Very slow changes in BOLD activity (> several minutes)
- slow drifts in noise cannot be separated from neuronally-induced BOLD activity by normal temporal filtering

BOLD信号变化很慢（>几分钟）
-噪声中的慢漂移不能用正常的时间滤波从神经元诱导的BOLD信号中分离出来

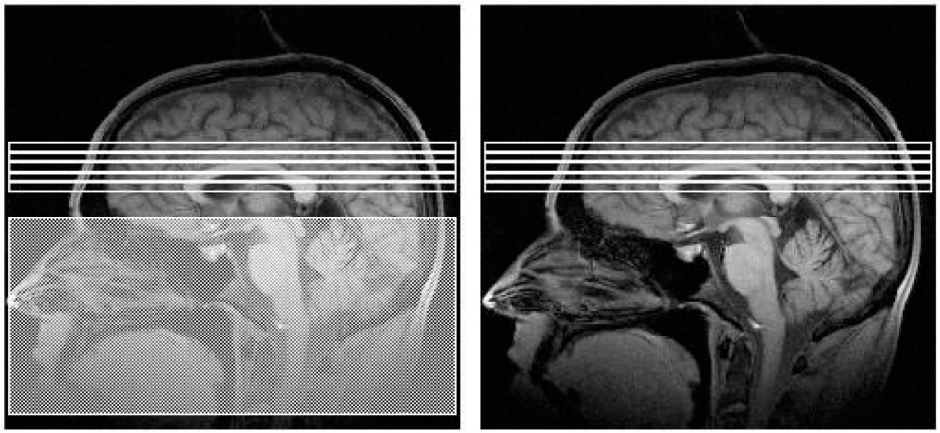
Solution: 解决方法

Alternative to BOLD = Arterial Spin Labelling (ASL)

ASL的替代方法

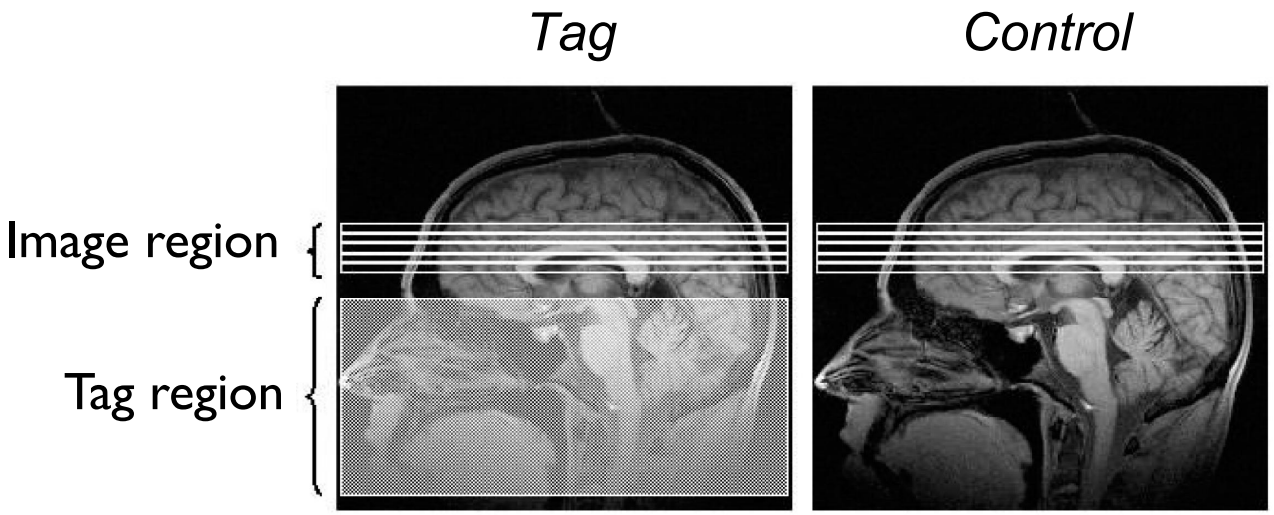
Perfusion FMRI using Arterial Spin Labelling (ASL)

使用ASL的灌注fMRI



- Alternative to BOLD BOLD的替代品
- Noisier than BOLD for high frequency designs 对高频设计，比BOLD噪音更大
- Potentially less noisy than BOLD for low frequency designs 对于低频设计，噪音可能比BOLD低
- More quantitative 更量化
- Only a few slices 只有几个slice

Perfusion FMRI using Arterial Spin Labelling (ASL)



- Blood is **tagged** in the arteries (e.g. in the neck) using an RF pulse
- After a delay to allow tagged blood to flow into the imaging region, the image is read out
- A **control** image is also collected without the tag. The subtraction of the two images gives a **perfusion-weighted image**

- 使用射频脉冲在动脉（如颈部）标记血液
- 一段延迟后，使标记的血液流入成像区域后，读取图像
- 控制图像也在没有标签的情况下被收集。两幅图像相减，得到灌注加权图像

Perfusion FMRI Modelling

灌注fMRI 建模

- Timeseries alternates between "control" (up) and "tag" (down)
- Activation seen as modulation of control-tag difference
- There are two GLM approaches available in FEAT:

- 时间序列在“control”（向上）和“tag”（向下）之间切换
- 激活被看做成控制tag差异的调节
- 在FEAT中有两种GLM方法可用：

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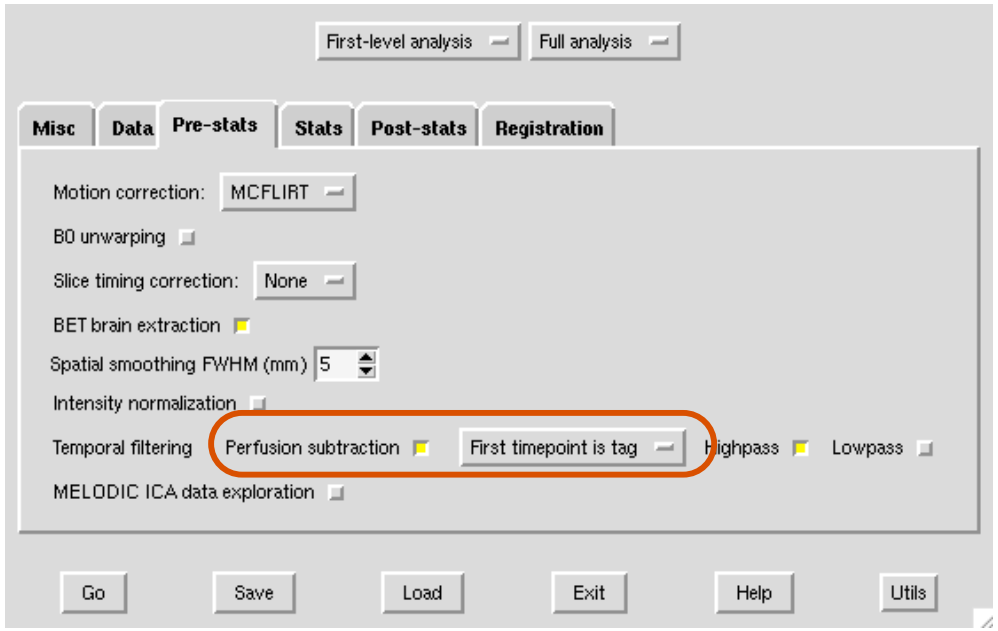
1) Pre-subtract data (using sinc interpolation) 事先减去数据（使用sinc插值）



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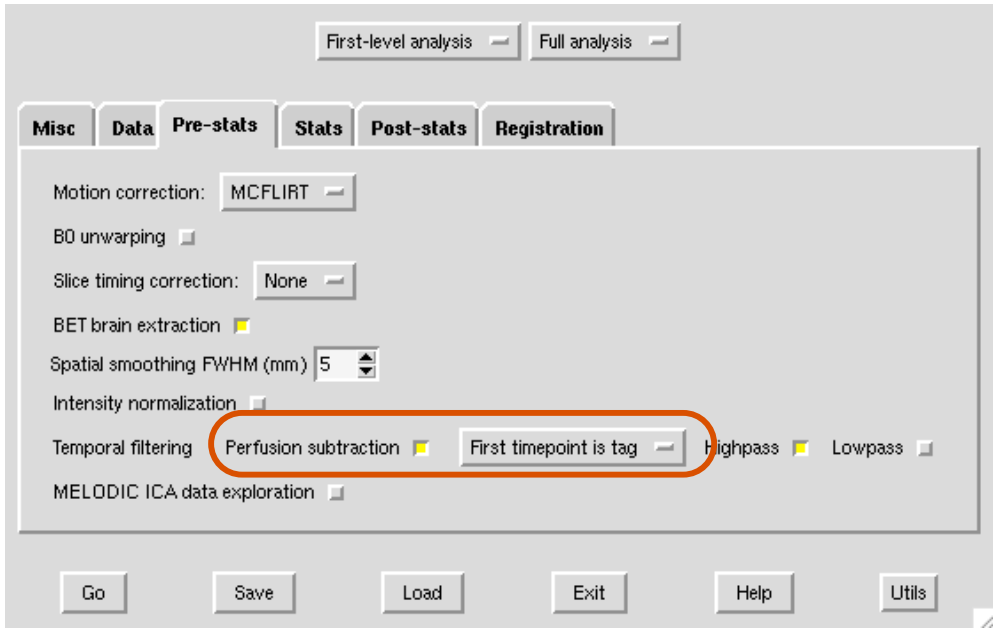
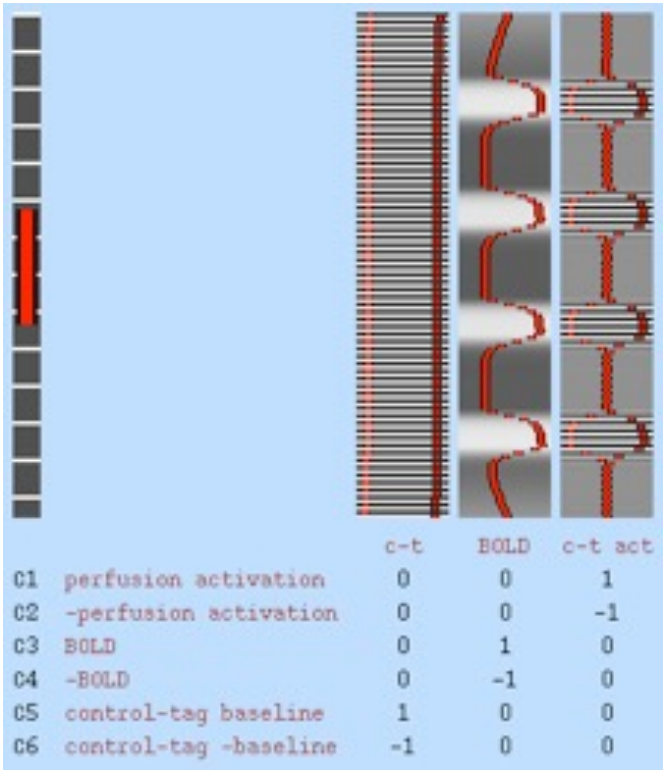


2) Use full model of unsubtracted data

使用未提取数据的完整模型



Simultaneous BOLD and Perfusion FMRI Modelling

BOLD 和 灌注fMRI 同时建模

- Dual-echo sequences commonly used to extract BOLD and perfusion changes simultaneously
- Traditionally, separate analysis of low TE (for perfusion) and high TE (for BOLD) results in biased results

- 双回波序列通常用于同时提取BOLD和灌注变化
- 传统上，对低TE（灌注）和高TE（BOLD）的单独分析会导致有偏差的结果

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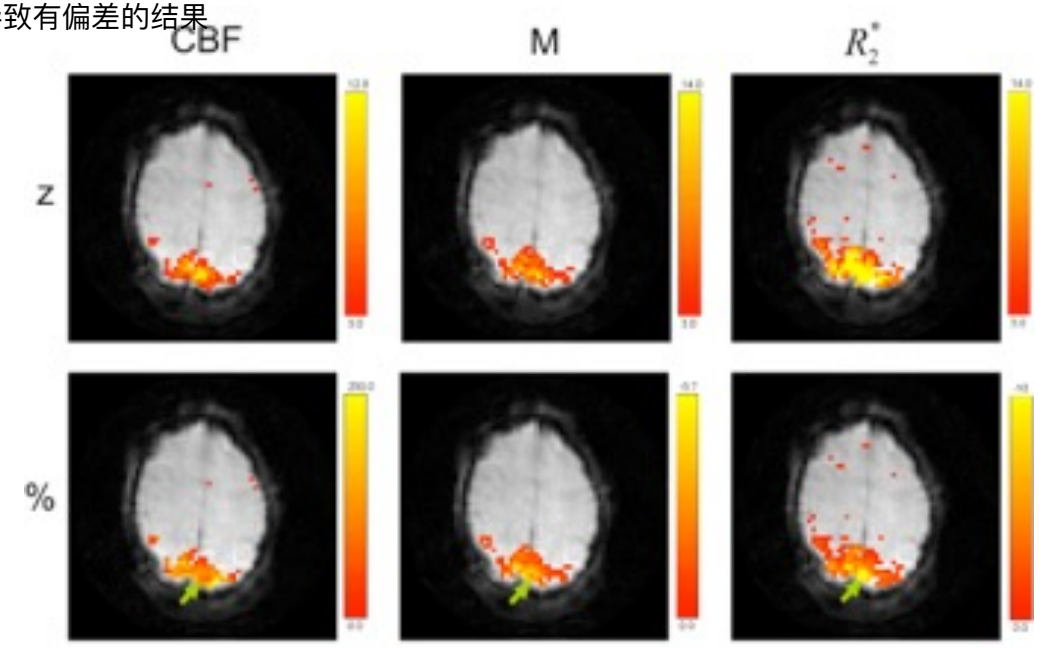
- **FABBER** uses nonlinear simultaneous modelling of both TEs to give uncontaminated, more sensitive information

FABBER使用两个TE的非线性同时建模来提供未污染的、更敏感的信息

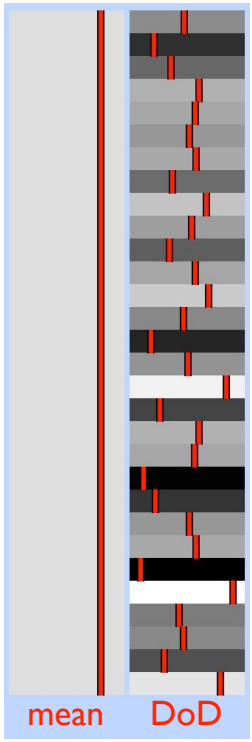


Orthogonalisation - A cautionary tale

正交——一个警示

- You are running a study to see what parts of the brain are less active when performing a task in patients with the neurodegenerative disease “Syndrome X”
  - 你想看看在患有“X综合征”的神经退行性疾病患者执行任务时，大脑的哪些部分不太活跃。
- In particular you want to know in what areas the activity is proportional to the duration of the disease (DoD)

特别是你想知道在哪些脑区的活动与疾病的持续时间（DoD）成正比



So you set up a design where you model the activation as a linear function of DoD (and a mean)

所以你建立了一个设计，把激活作为DoD的线性函数（以及一个平均值）建模

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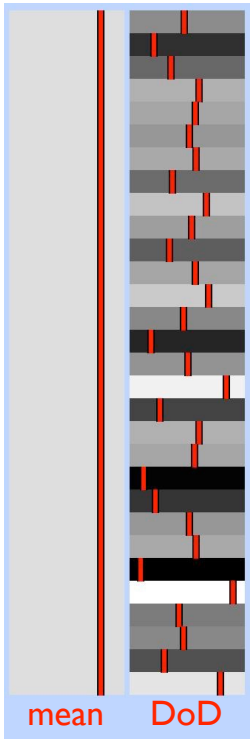

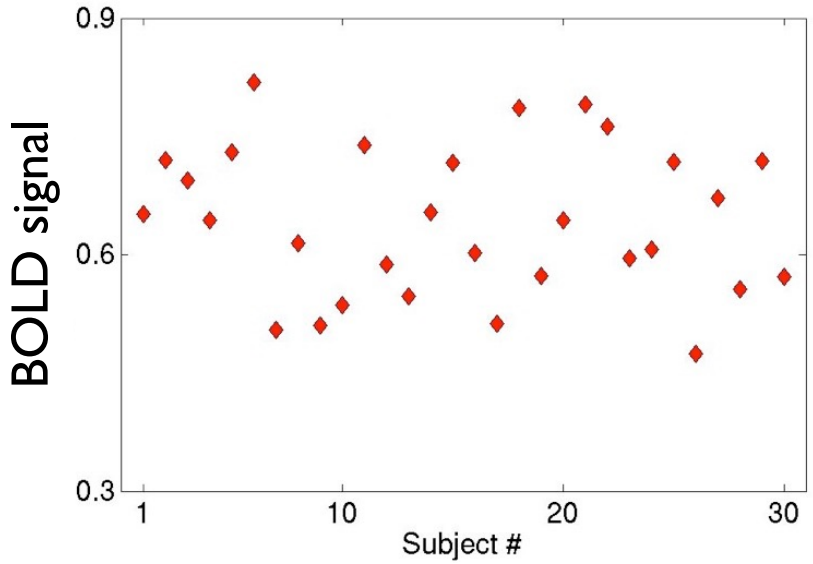

And in one voxel the data happens to look like this 一个体素的数据是这样的

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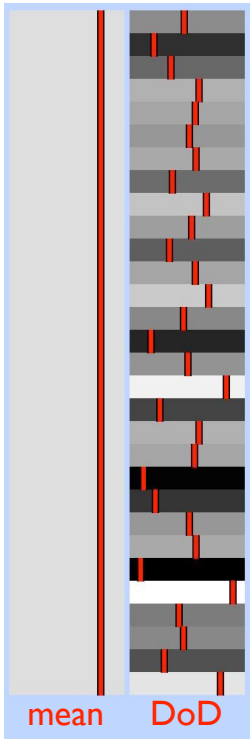
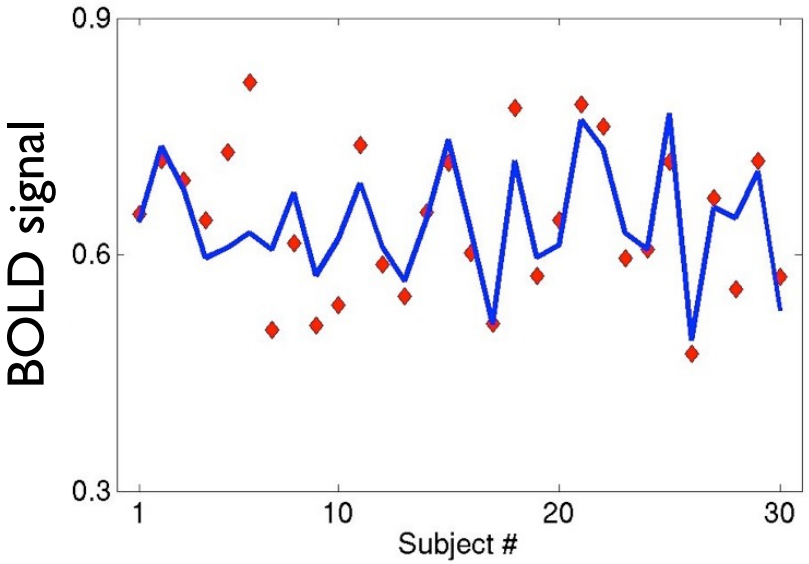


$$\begin{bmatrix} 0.808 \\ -0.005 \end{bmatrix}$$



$t = -6.33$

And this is the model fit to the data. You are very pleased with yourself.

这是符合数据的模型。你很满意。

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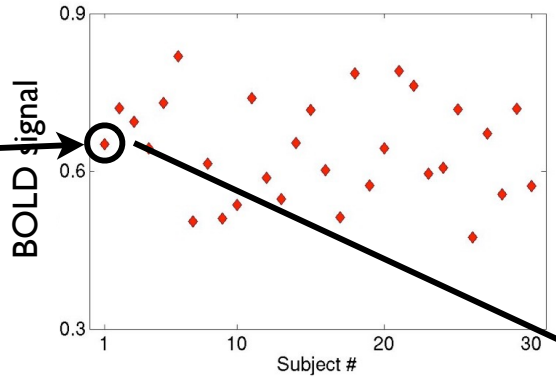
use as y-value



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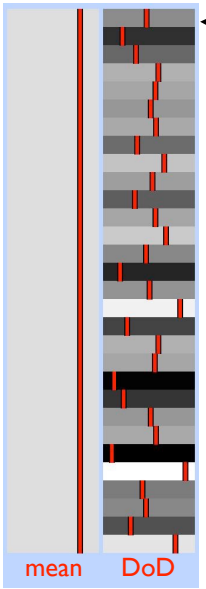

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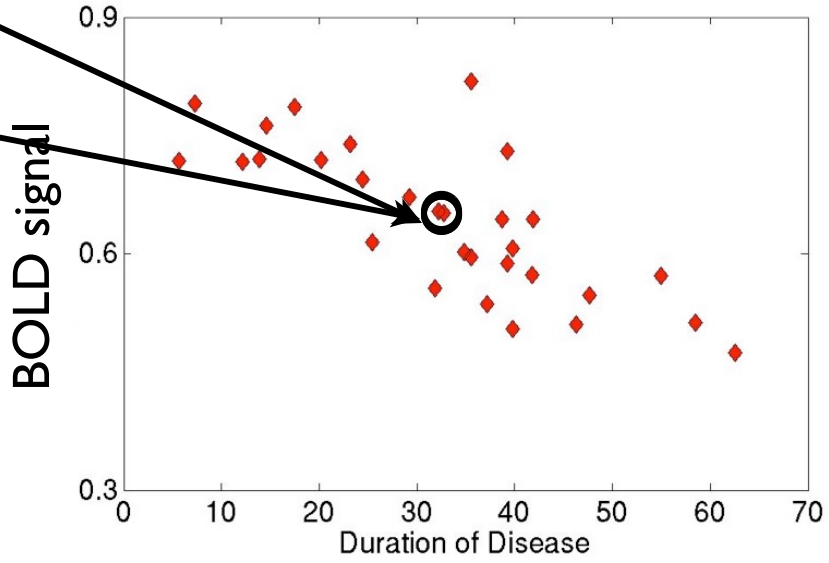
A different way of looking at your data

换一个角度看你的数据



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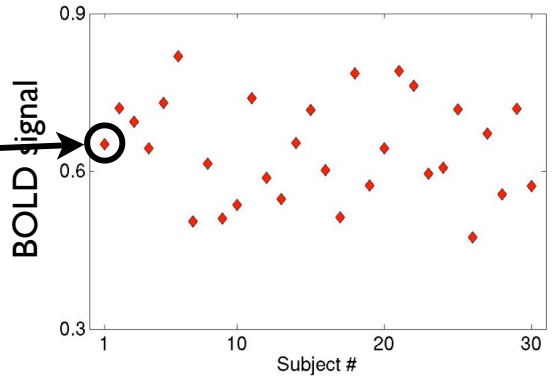
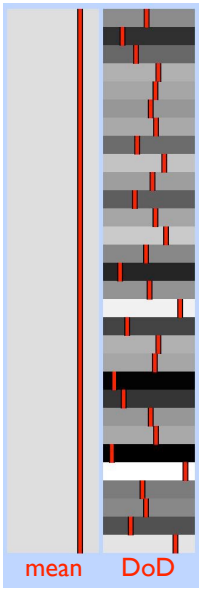
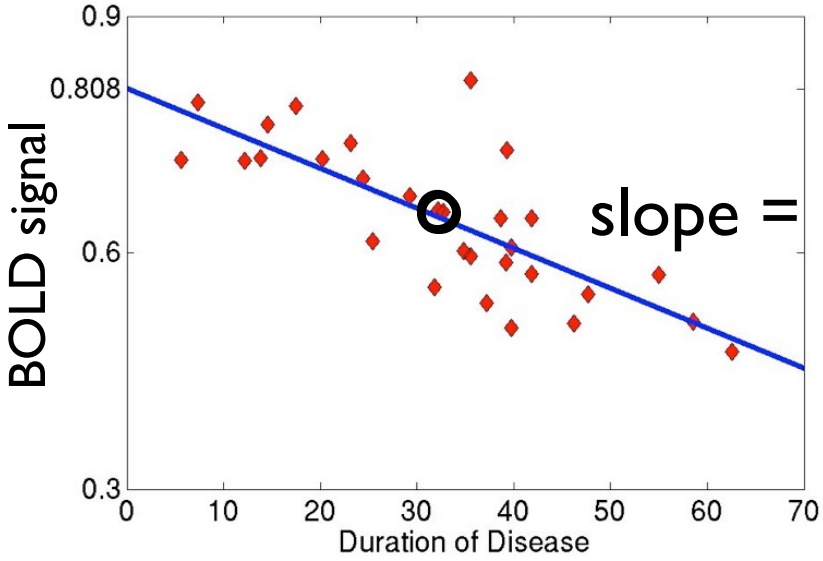




use as x-value

$$\begin{bmatrix} 0.808 \\ -0.005 \end{bmatrix}$$

A different way of looking at your data



slope = -0.005

And at your model fit

以及你的模型拟合程度

Orthogonalisation - A cautionary tale

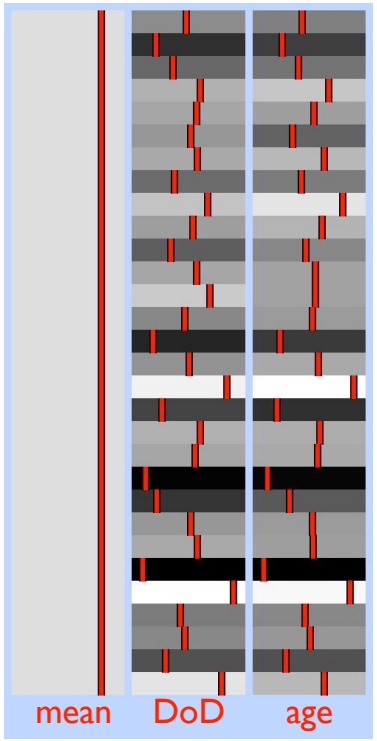
正交——一个警示

- In particular you want to know in what areas the activity is proportional to the duration of the disease (DoD)

特别是你想知道在哪些脑区的活动与疾病的持续时间（DoD）成正比

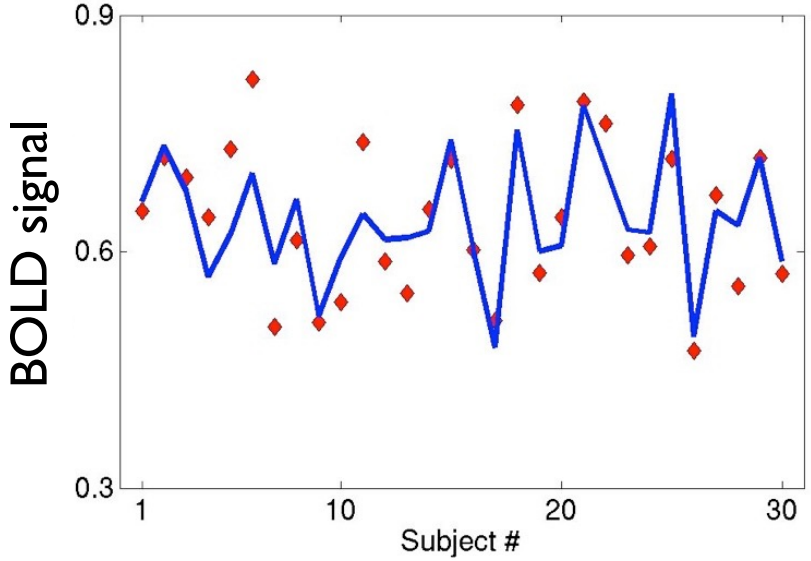
- Then someone points out that we all suffer from a neurodegenerative disease called "life"

有人指出我们都患有一种叫做"生命"的神经退行性疾病



So you complement your design with an (uninteresting) **age** regressor

所以你用（不感兴趣的）年龄作为回归因子来补充你的设计



And the model fit still looks good

(maybe even a little better) 模型看起来依然很好（甚至比之前还好）

Orthogonalisation - A cautionary tale

正交——一个警示

- In particular you want to know in what areas the activity is proportional to the duration of the disease (DoD)

特别是你想知道在哪些脑区的活动与疾病的持续时间（DoD）成正比

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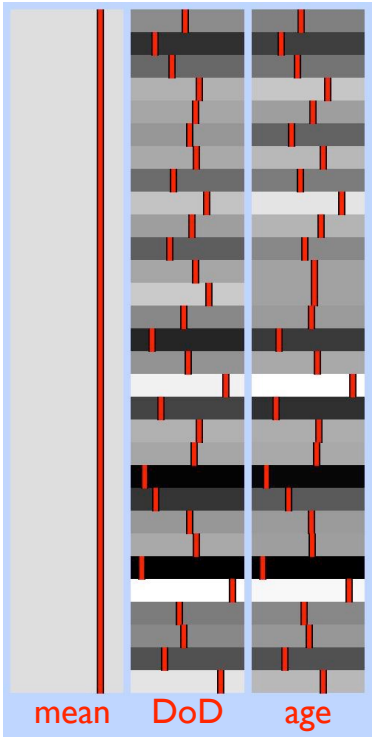
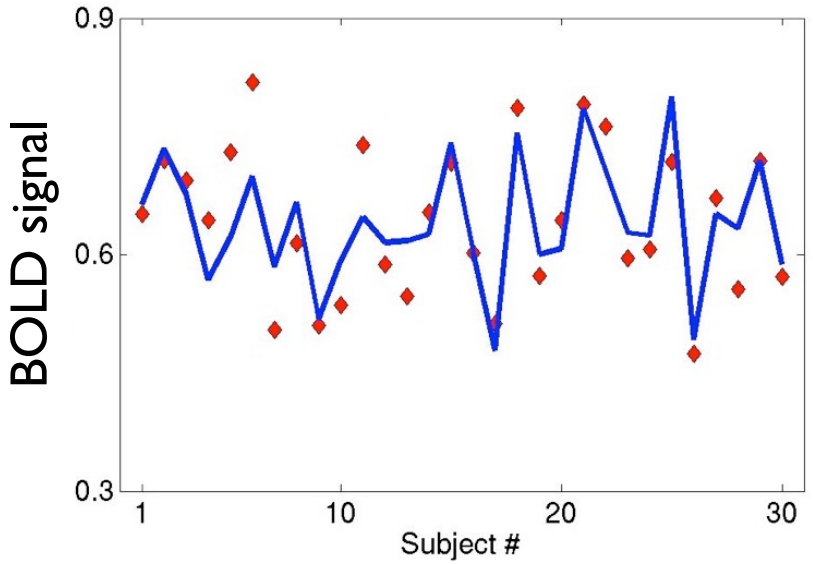
有人指出我们都患有一种叫做"生命"的神经退行性疾病

[0 1 0]



And you test your DoD for significance

测试DoD的显著性



$t = 0.11$

What on earth just happened?

发生了什么?

Orthogonalisation - A cautionary tale

正交——一个警示

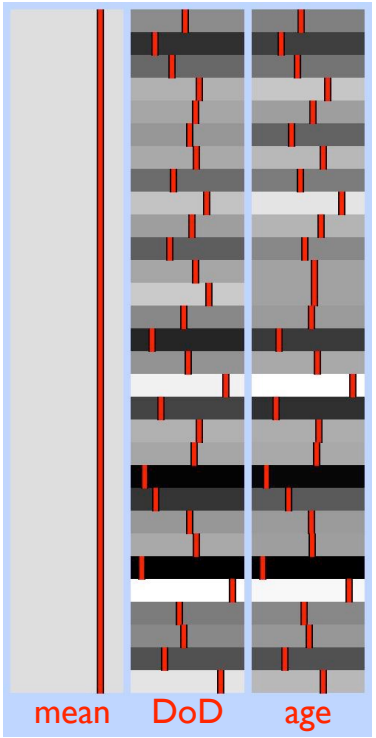
- In particular you want to know in what areas the activity is proportional to the duration of the disease (DoD)

特别是你想知道在哪些脑区的活动与疾病的持续时间（DoD）成正比

- Then someone points out that we all suffer from a neurodegenerative disease called "life"

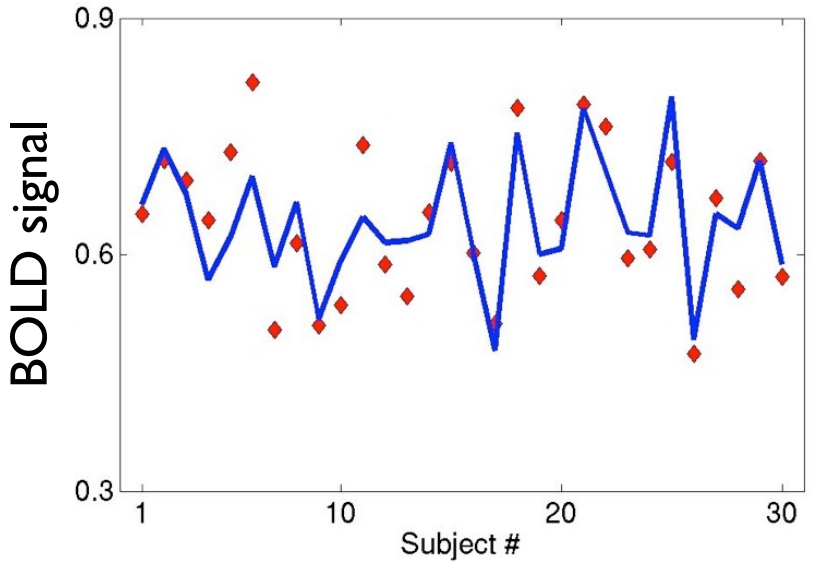
有人指出我们都患有一种叫做"生命"的神经退行性疾病

[0 0 1]



Is it that age explains everything?

年龄解释了一切吗?



$t = -2.84$

No, not all of it. So what happened?

当然不是全部，那是怎么回事

Orthogonalisation - A cautionary tale

正交——一个警示

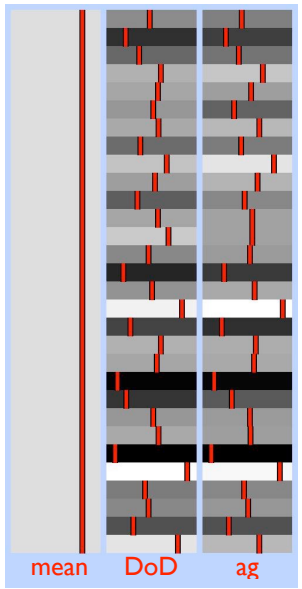
- Remember how we have been saying "GLM tests for a regressor after it has explained as much as it possibly can using the other regressors"?

  刚才提到过"在使用其他回归器解释了尽可能多的变异之后，再对一个回归因子进行GLM检验"

- But what does that really mean?

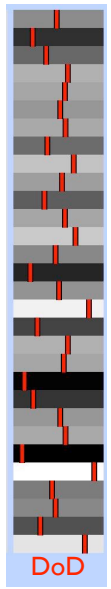
这到底是什么意思

[0 1 0]



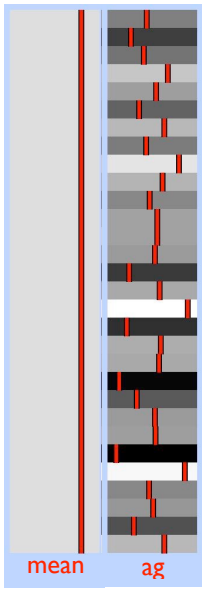
Full model

全模型



The regressor we want to test

想考察的回归因子



"The other regressors"

其他回归因子

Orthogonalisation - A cautionary tale

正交——一个警示

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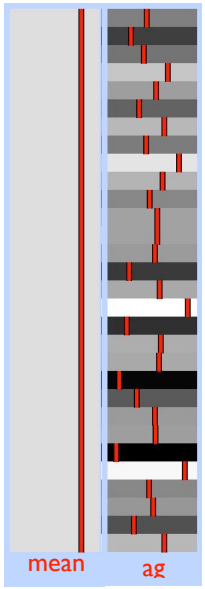
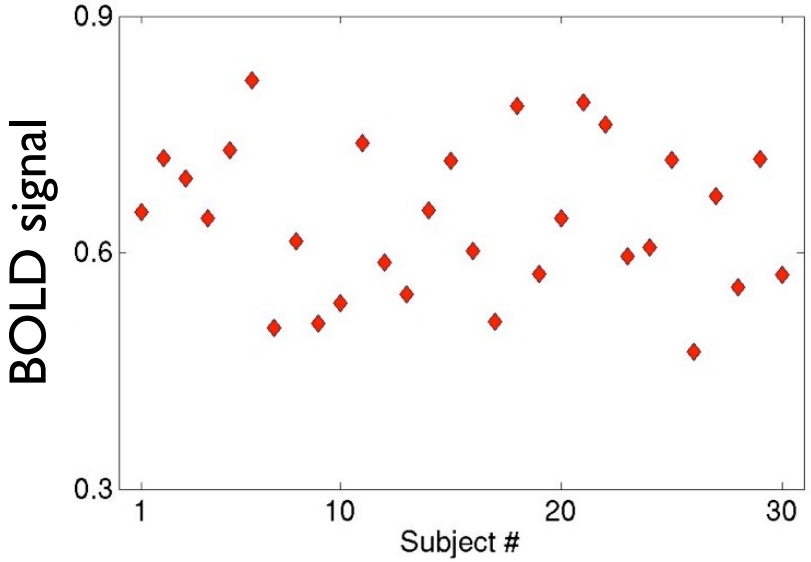
- So, lets use "the other regressors" to explain these data

所以，让我们用"其他回归因子"来解释这些数据



"The other regressors"

其他回归因子



Orthogonalisation - A cautionary tale

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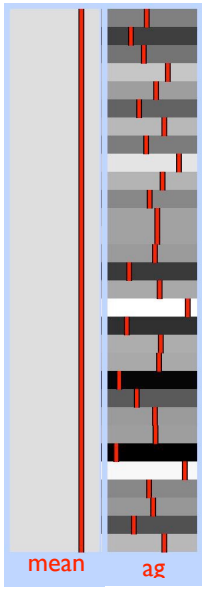
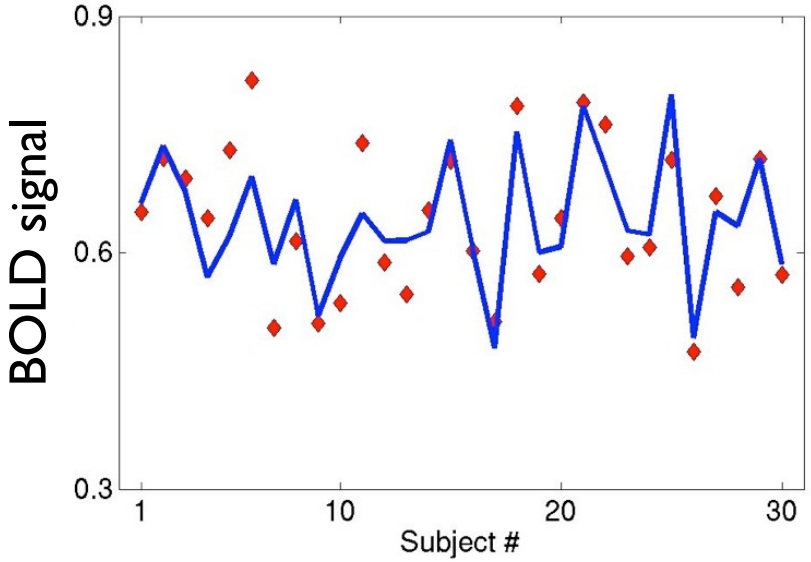


"The other regressors"

其他回归因子



By fitting them to the data

用其拟合数据

Orthogonalisation - A cautionary tale

正交——一个警示

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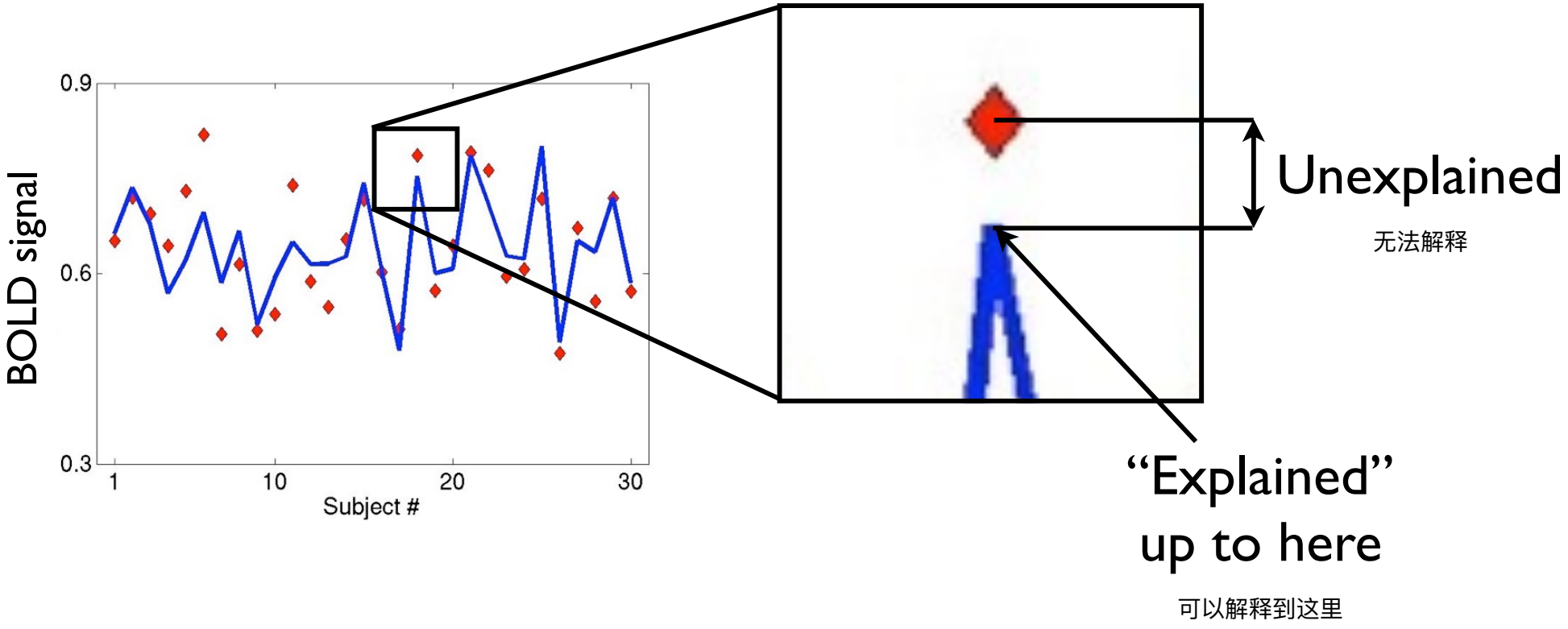
刚才提到过"在使用其他回归器解释了尽可能多的变异之后，再对一个回归因子进行GLM检验"

- And what is left is the "unexplained" part

剩下的"无法解释"的部分是什么



Orthogonalisation - A cautionary tale

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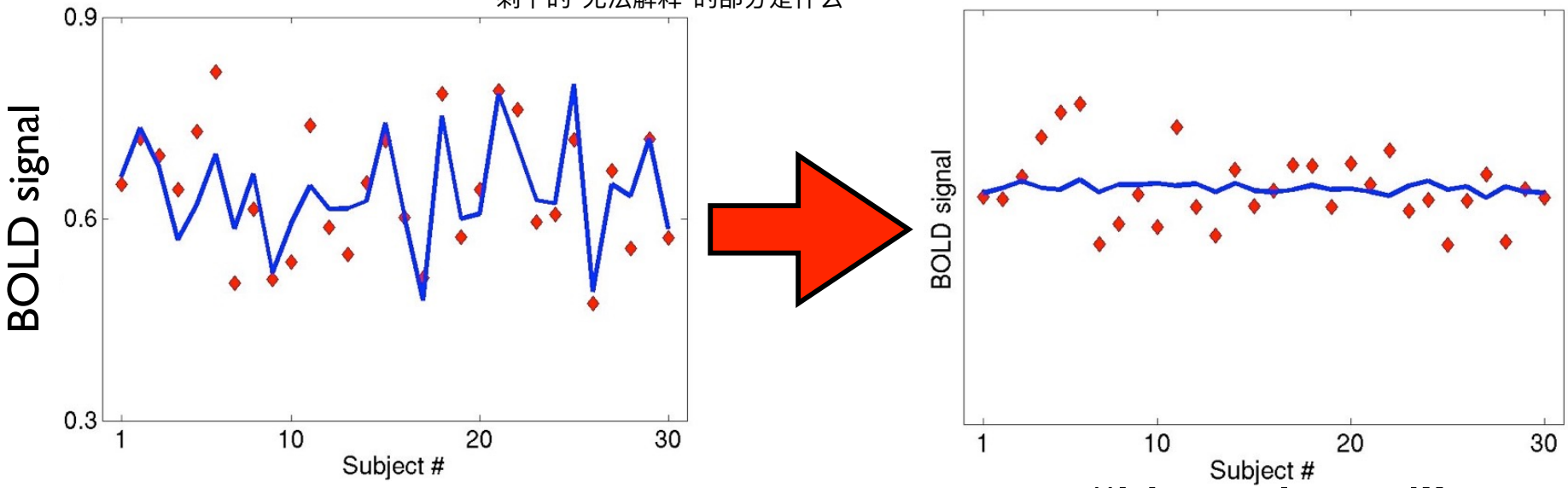


Original and "Explanation"

原始的和"被解释的"

"Unexplained"
(not well represented by DoD)

"未解释的"（不能被DoD很好代表）

Orthogonalisation - A cautionary tale

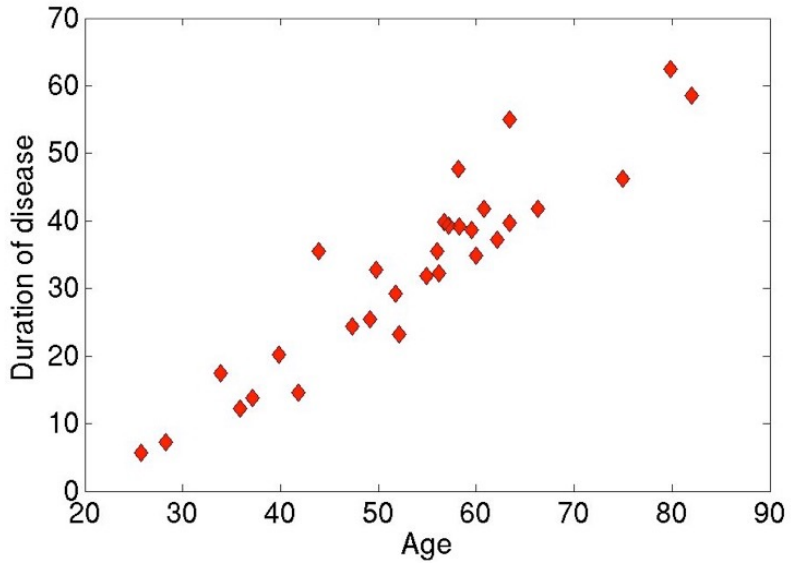
正交——一个警示

- Remember how we have been saying "GLM tests for a regressor after it has explained as much as it possibly can using the other regressors"?

刚才提到过"在使用其他回归器解释了尽可能多的变异之后，再对一个回归因子进行GLM检验"

- And the reason for all of this is that Age and DoD are correlated

这一切的原因是年龄和DoD是相关的



- GLM says "I cannot be sure if this explanatory power belongs to you or to you. So neither can have it."
- Much like a parent would.

GLM说："我不确定这种解释力是属于你还是属于你。所以两人都不能拥有它。"（像极了夫妻的世界）

Orthogonalisation - A cautionary tale

正交——一个警示

- So what about orthogonalisation then. What does that do?

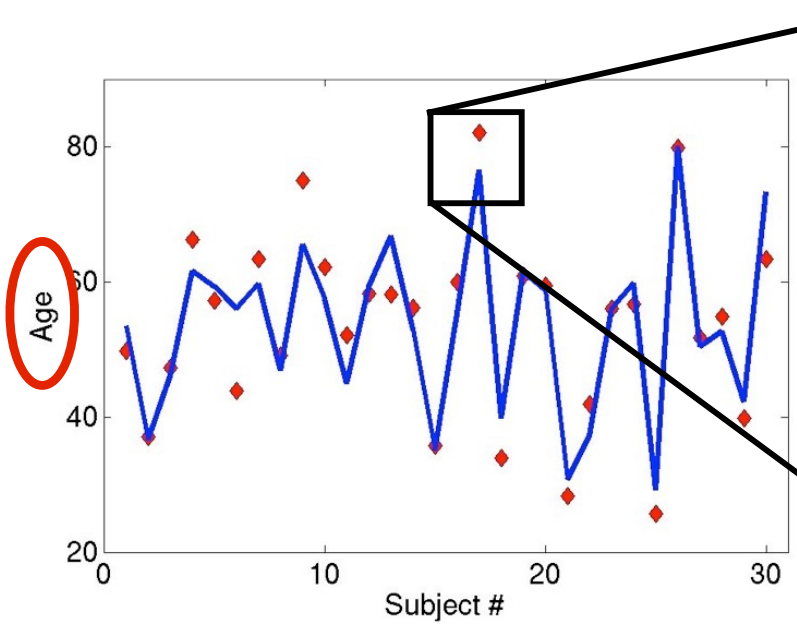
那么正交化有什么用?

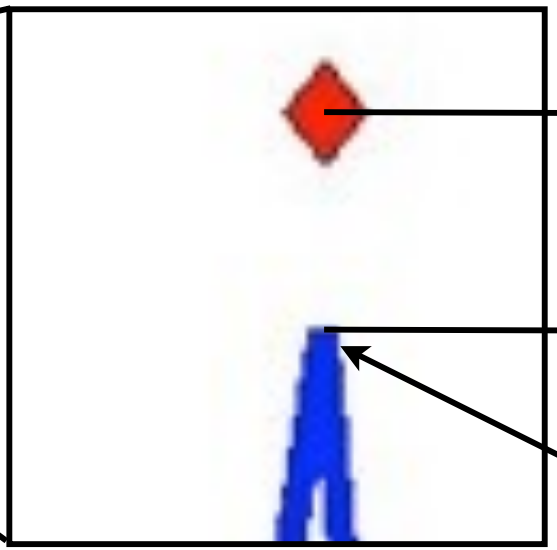
- To orthogonalise A with B is to say to B "You, B, can have all the explanatory power. A doesn't get any".

把A和B正交就是对B说"B，可以拥有所有的解释力"。A一点也没有。

- Let us see how we would orthogonalise Age w.r.t. DoD

让我们看看如何将DoD和年龄正交化





"Unexplained" – Unique to Age

"未解释的"
相当于年龄

DoD "explains" up to here

DoD可以解释到这

Orthogonalisation - A cautionary tale

正交——一个警示

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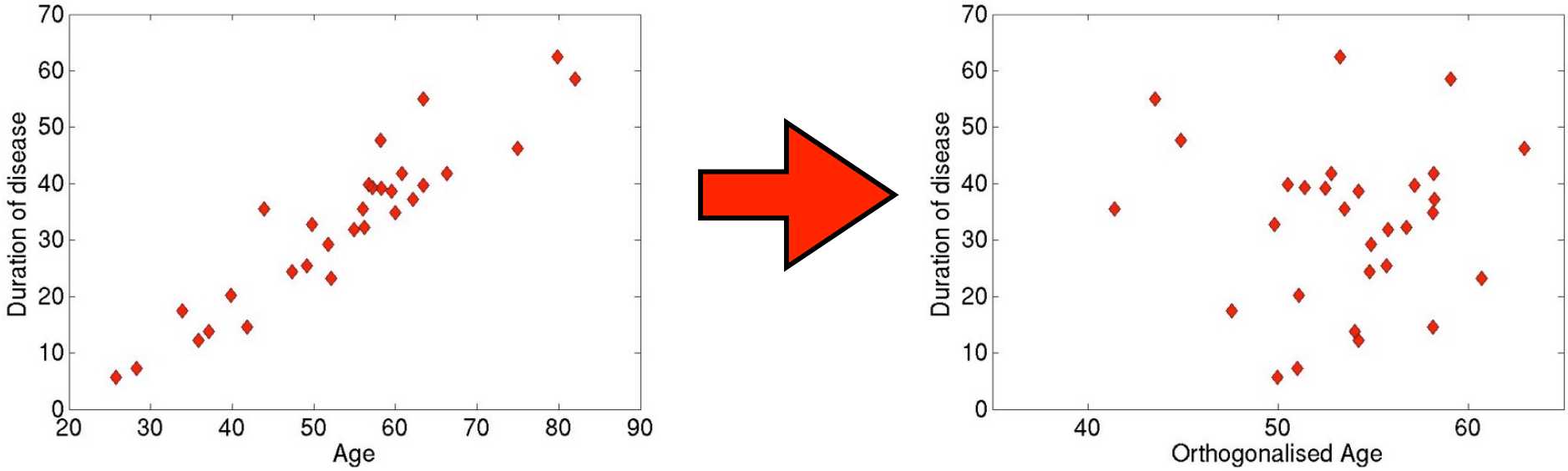
  把A和B正交就是对B说"B，可以拥有所有的解释力"。A一点也没有。

- And this "unique" part is "Age orthogonalised w.r.t. DoD"

  其中非常特殊的部分是年龄和DoD正交的部分



Orthogonalisation - A cautionary tale

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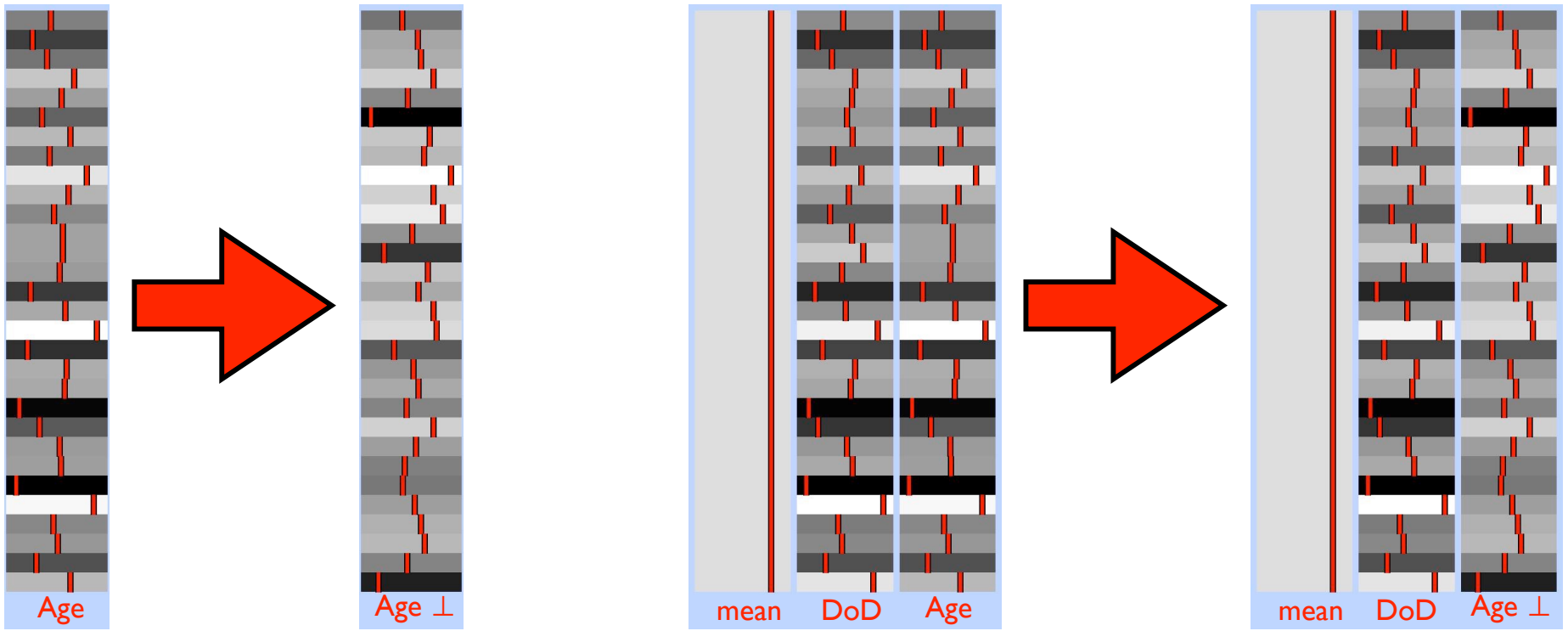

Orthogonalisation - A cautionary tale

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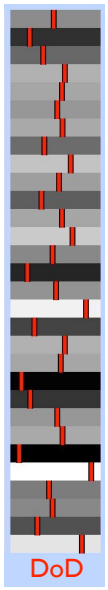
- And then fit DoD to the unexplained part

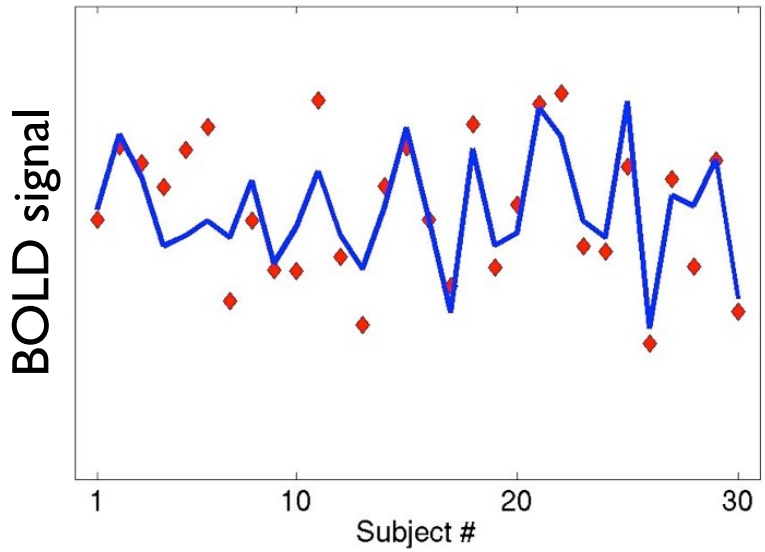
把DoD拟合到未解释的部分



The regressor we want to test

要考察的回归因子

$t = -7.08$



Fitted to the unexplained part

拟合到未解释的部分

Orthogonalisation - A cautionary tale

正交——一个警示

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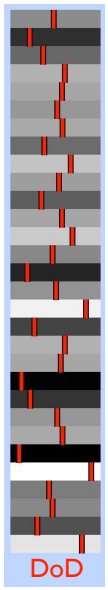
把DoD拟合到未解释的部分



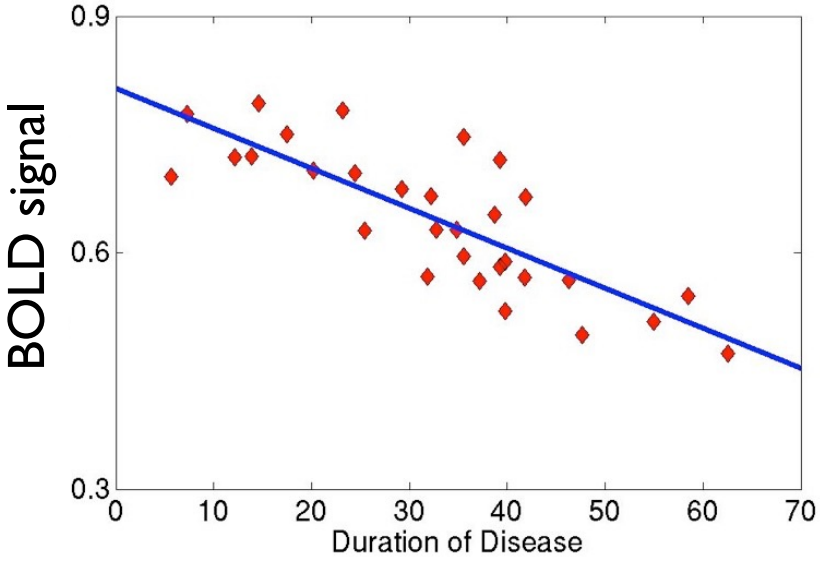
The regressor we want to test

要考察的回归因子

Or viewed in the other way

或者用另一种方式去看

$t = -7.08$



Fitted to the unexplained part

拟合到未解释的部分

A better alternative to orthogonalisation

代替正交的更好的方法

- Look at the results of F-tests on the combined effects:

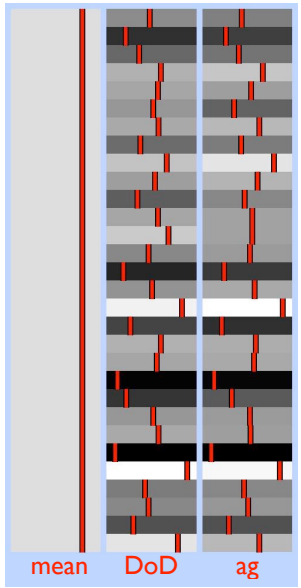
  看一下关于这些效应的F检验的结果

  - mean + DoD + age 均值+DoD+年龄
  - DoD + age (as DoD and age are demeaned)

    DoD+年龄（因为两者已经去均值化）
- Plus the t-test on the desired effect: DoD 把对DoD进行T检验

t-test

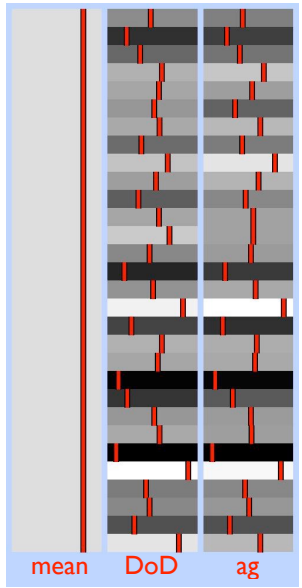
T检验



[0 1 0]

F-tests

F检验



[1 0 0]

[0 1 0]

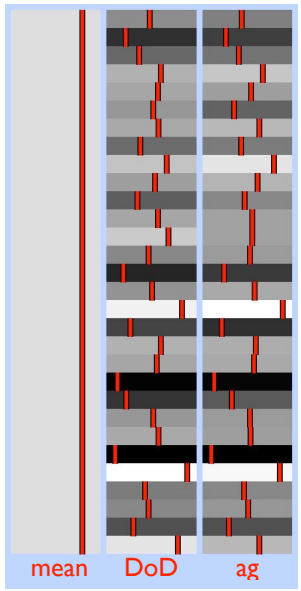
[0 0 1]

A better alternative to orthogonalisation

代替正交的更好的方法

t-test

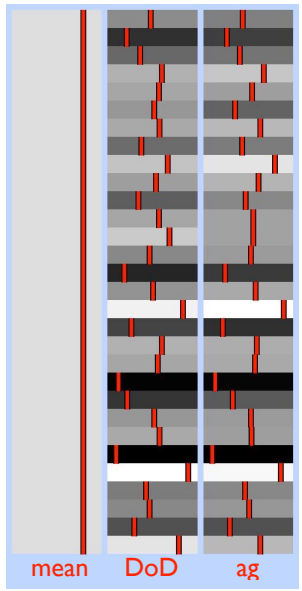
T检验



[0 1 0]

F-tests

F检验



[1 0 0]

[0 1 0]

[0 0 1]

Results: 结果

Not significant 不显著

Both significant 都显著

Interpretation: Significant correlation with *both* DoD and age, but cannot separate the effects as they are too highly correlated and the response to unique portions (if any) are too weak.

解释：与DoD和年龄都有显著的相关性，但不能将影响分开，因为它们的相关性太高，对独特部分（如果有的话）的反应太弱。

Follow on: to separate effects could potentially recruit new subjects such that DoD and age were less correlated.

为了分离效果，可能会招募新的被试，这样DoD和年龄的相关性就更小。

Orthogonalisation - A cautionary tale

- So what has orthogonalisation done for us?

  那么正交化能为我们做什么?

- When we orthogonalised DoD with Age we took all the explanatory power that was shared/common to Age and DoD and put **all of it** with DoD.

  当将DoD与年龄正交时，将所有与年龄和DoD共享/共同的解释能力，全部交给DoD。

- This gave a highly significant effect of DoD

  这使DoD产生了非常显著的影响

- But was this a good thing to do?

  但这是件好事吗?

- No! There is nothing in our data that allows us to say if the effect came from Age or Disease Duration. We have just made an arbitrary decision to attribute it to Disease Duration.

  不！在数据中，没有任何东西能说这种影响是来自年龄还是DoD。我们做了一个武断的决定，认为它是DoD

- GLM did the right thing by saying: "I don't know who this belongs to, so I can't give it to either"

  glm说得对："我不知道这是谁的，所以我也不能给他。"

Orthogonalisation - A cautionary tale

正交——一个警示

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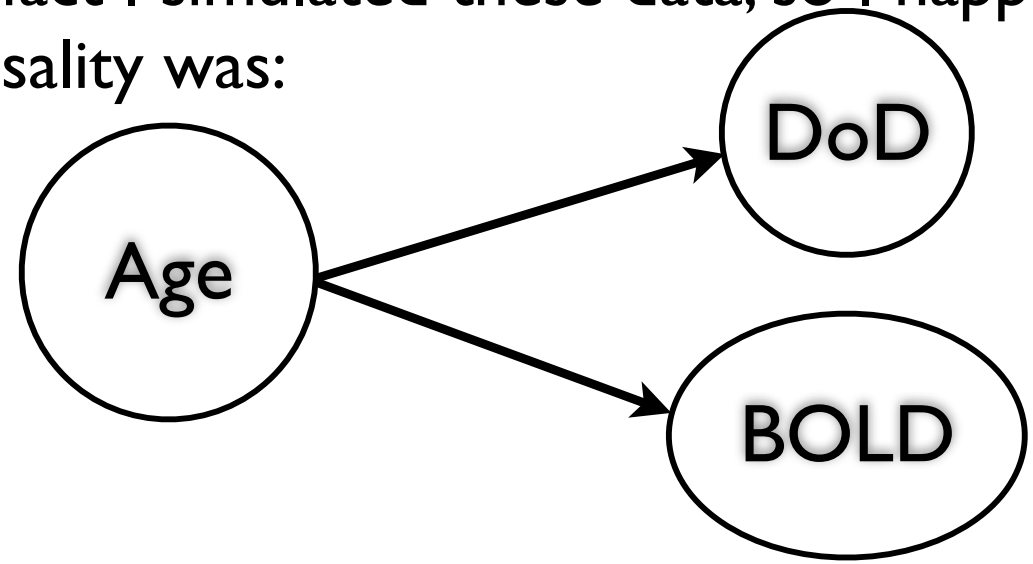
glm说得对："我不知道这是谁的，所以我也不能给他。"

- And in fact I simulated these data, so I happen to know that the causality was:

事实上，我模拟了这些数据，所以我碰巧知道它们的因果关系是：



When to orthogonalise?

何时才能用正交?

- ESSENTIALLY NEVER: The GLM automatically deals with correlations between regressors in a conservative manner.

  本质上从来不能：glm以一种保守的方式自动处理回归者之间的相关性。

  - We generally cannot be certain which of two correlated regressors contributes to BOLD signal effects. e.g. head motion or task?

    通常无法确定两个相关回归函数中的哪一个会导致BOLD效应。例如，头部运动或任务?

- Orthogonalisation may make sense in certain models where causality is unambiguous.

  在某些因果关系明确的模型中，正交可能是有意义的。

  - I challenge someone to give me an unambiguous example.

    我质疑了之前给我的一个明确的例子。

  - However, it is usually still clearer to conduct the appropriate F-tests and t-tests and interpret these results since all the information is there. It generally isn't necessary or safe to arbitrarily force explanatory power with orthogonalisation.

    然而，由于所有的信息都在那里，所以通常很清楚要进行适当的f-检验和t-检验并解释这些结果。通常情况下，用正交来强行解释是不必要或不安全的。

Demeaning

去均值

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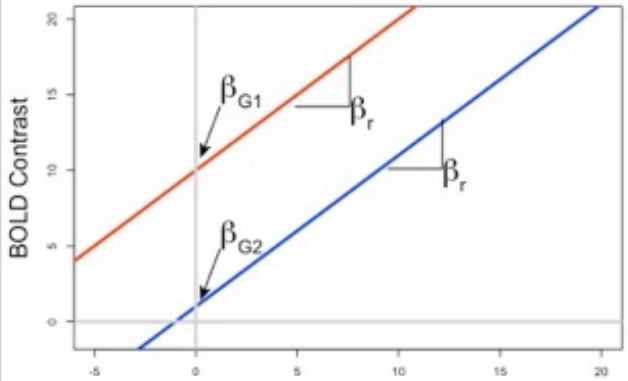
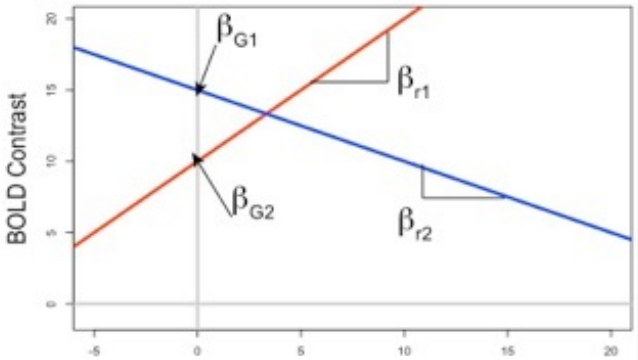
Design matrix 设计矩阵	What does the fitted model look like? 拟合模型的样子	Contrast 对比	Does demeaning change the stats? 去均值改变了统计结果么	Demeaning recommended? 是否推荐去均值?
$\begin{pmatrix} 1 & 0 & r_1 \\ 1 & 0 & r_2 \\ 1 & 0 & r_3 \\ 0 & 1 & r_4 \\ 0 & 1 & r_5 \\ 0 & 1 & r_6 \end{pmatrix} \begin{pmatrix} \beta_{G1} \\ \beta_{G2} \\ \beta_r \end{pmatrix}$	 **Same slope in both groups** 两组中斜率相同	[1 -1 0]	NO	YES
		[0 0 1]	NO	YES
		[1 0 0] or [0 1 0]	YES	YES

Demeaning

mumford.fmripower.org/mean_centering/

Design matrix	What does the fitted model look like?	Contrast	Does demeaning change the stats?	Demeaning recommended?
$\begin{pmatrix} 1 & 0 & r_1 & 0 \\ 1 & 0 & r_2 & 0 \\ 1 & 0 & r_3 & 0 \\ 0 & 1 & 0 & r_4 \\ 0 & 1 & 0 & r_5 \\ 0 & 1 & 0 & r_6 \end{pmatrix}$ $\begin{pmatrix} \beta_{G1} \\ \beta_{G2} \\ \beta_{r1} \\ \beta_{r2} \end{pmatrix}$	 **Different slopes in the two groups** 两组中斜率不同	[1 -1 0 0]	YES	YES*
		[1 0 0 0] or [0 1 0 0]	YES	YES*
		[0 0 1 -1] or [0 0 1 0] or [0 0 0 1]	NO	YES

Do not demean *within* groups
组内未去均值

Demean all values *and then* split into groups
将所有数值去均值，再分组

YES* = it is probably better to do it, although these contrasts are *VERY* hard to interpret either way
最好进行去中心化，虽然这些比较可能很难解释