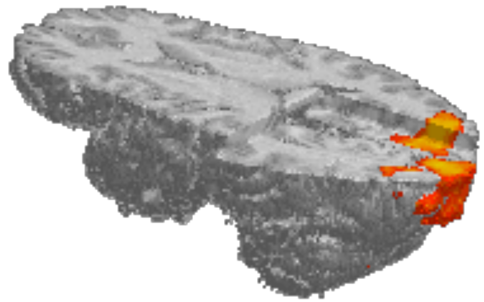
FMRI Pre-Processing and Model-Based Statistics

fMRI预处理及基于模型的统计

- Brief intro to FMRI experiments and analysis (实验和分析简介)
- FMRI pre-stats image processing (统计前图像处理)
- Simple Single-Subject Statistics (单被试的统计)
- Multi-Level FMRI Analysis (多水平fMRI分析)
- Advanced FMRI Analysis (高级分析)



中文翻译：王继源 孔亚卓

FMRI Pre-Statistics

FMRI在统计之前

- Brief intro to FMRI analysis (fMRI分析简介)

FMRI pre-statistical image processing (统计前图像处理)

- Reconstruction from k-space data (k空间数据重建)
- Motion correction (运动校正)
- Slice timing correction (时间层校正)
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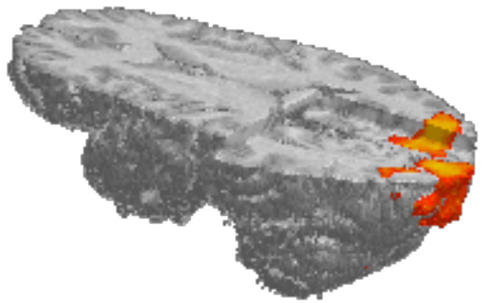
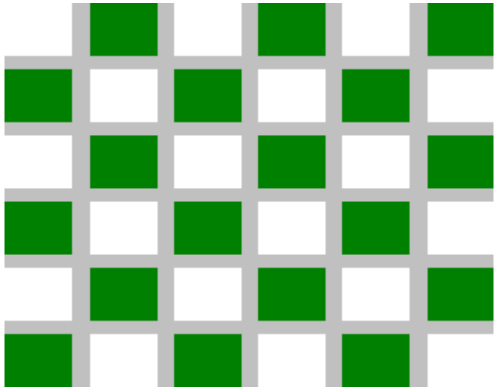
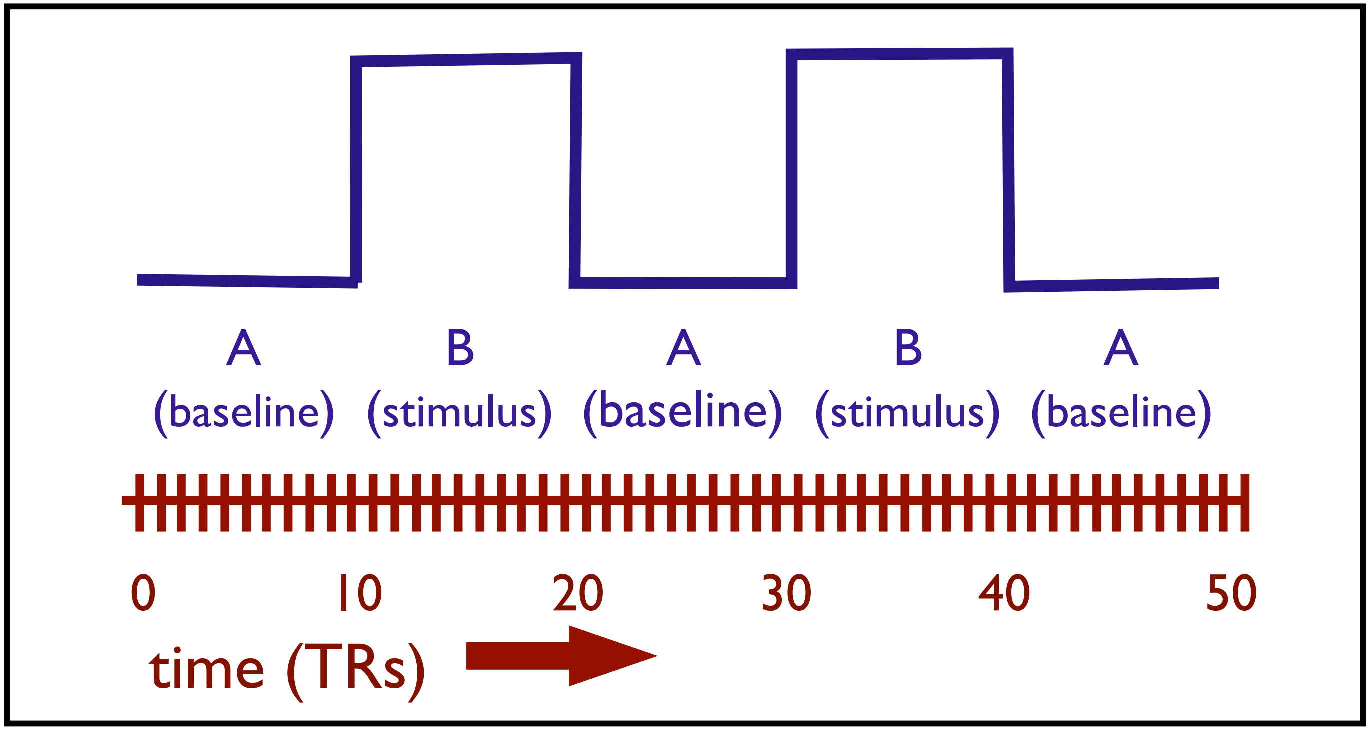


FMRI Experiments 实验

Stimulus刺激



e.g. flashing chequerboard
闪烁的棋盘

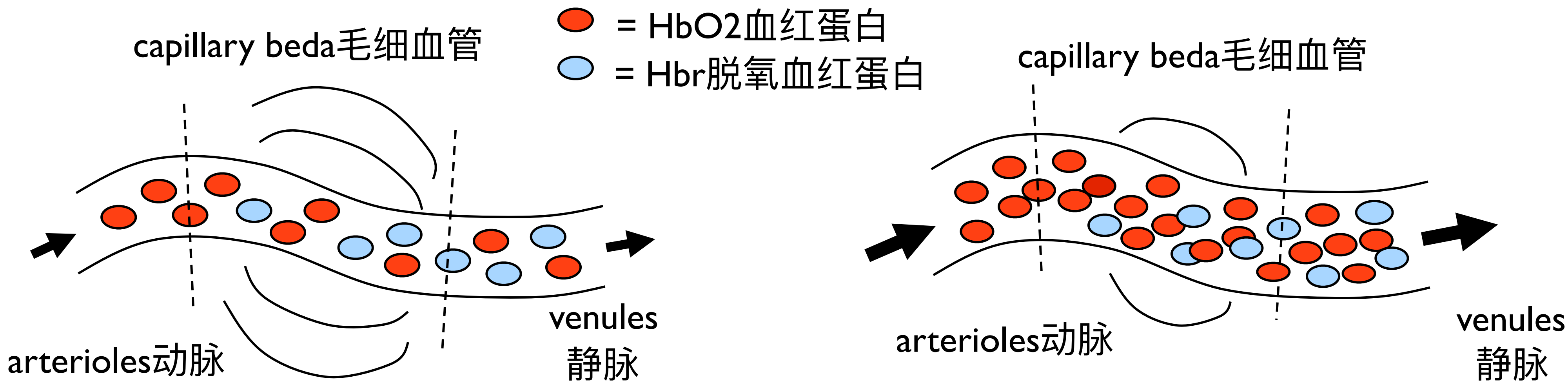


- Simple paradigm design 简单范式设计:
  - stimulus vs baseline 刺激vs基线
  - constant stimulus "intensity" 恒定刺激强度
  - constant block lengths 恒定block长度
  - many repetitions: ABABA 重复很多次的ABABA模式
- Need baseline (rest) condition to measure *change*
  需要基线（静息）来测量改变

The Haemodynamic Response
血液动力学响应

Basal State基线态

Activated State激活态



Activation leads to激活导致: CBF 脑血流 ↑ CBV 脑血容 ↑ $CMRO_2$ 耗氧率 ↑ [Hbr] 脱氧蛋白 ↓ Field change 场变化 ↓ MRI signal 信号 ↑

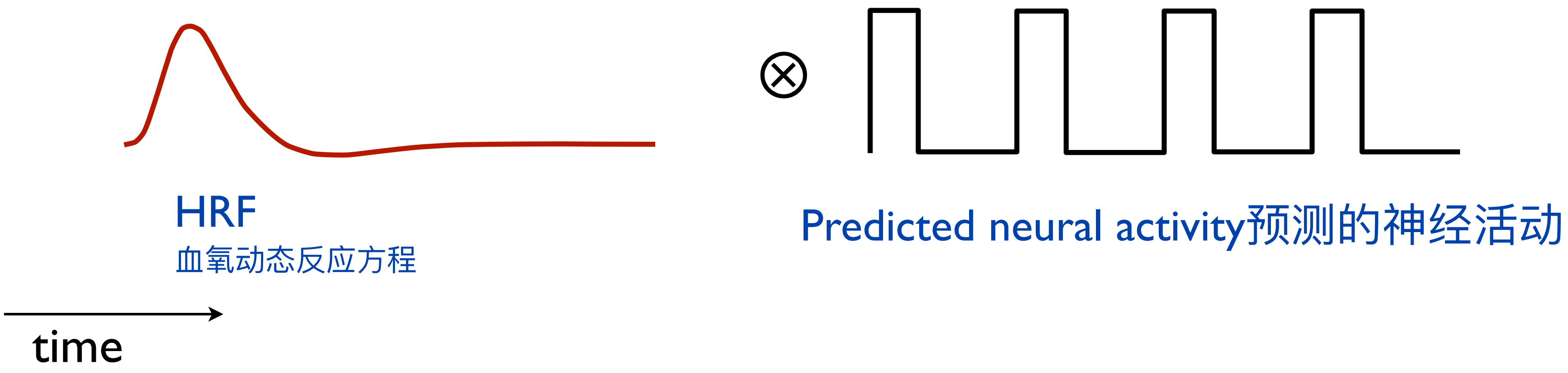
- Field changes (perturbations) --> dephasing --> T_2* effect
- BOLD-tuned MRI (T_2*-weighted) is sensitive to this effect

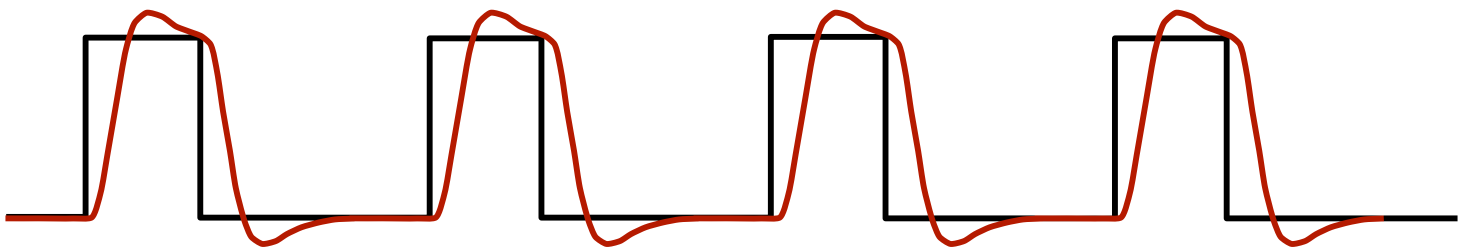
场变化 (扰动) --> 失相位 --> T_2* 效应

BOLD-调制过的MRI(T_2*-加权) 对这个效应很敏感

Predicted Response 预测响应

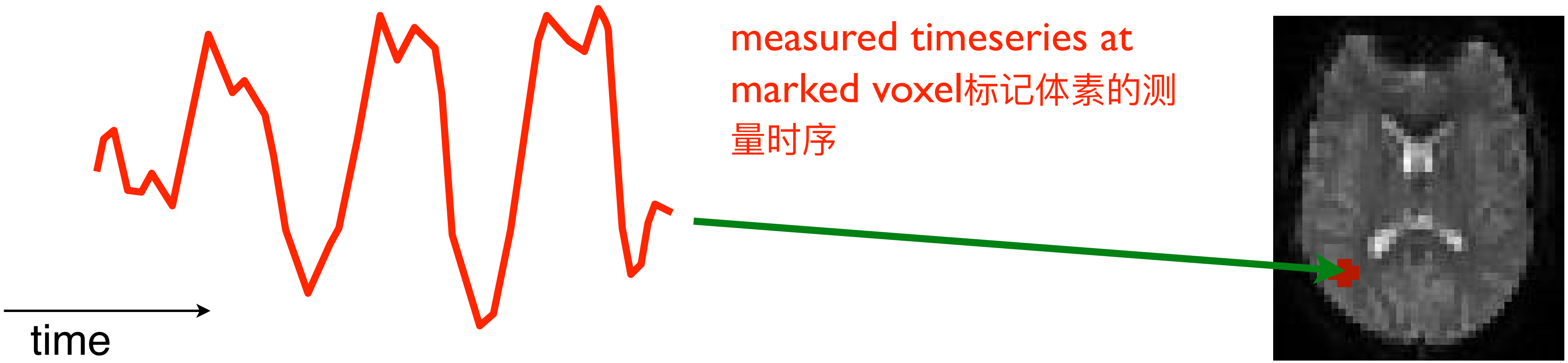
- The process can be modelled by convolving the activity curve with a "haemodynamic response function" or HRF. 这个过程可以用活动曲线和HRF的卷积来建模





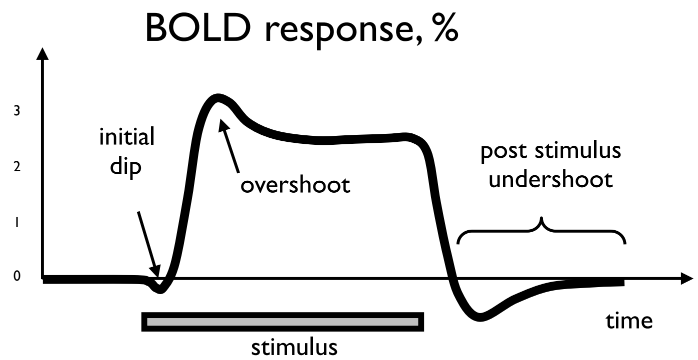
FMRI Experiments: Analysis 分析

- Each voxel contains a time-varying signal(BOLD signal)
  每体素含随时间变化的信号（血氧水平依赖信号）

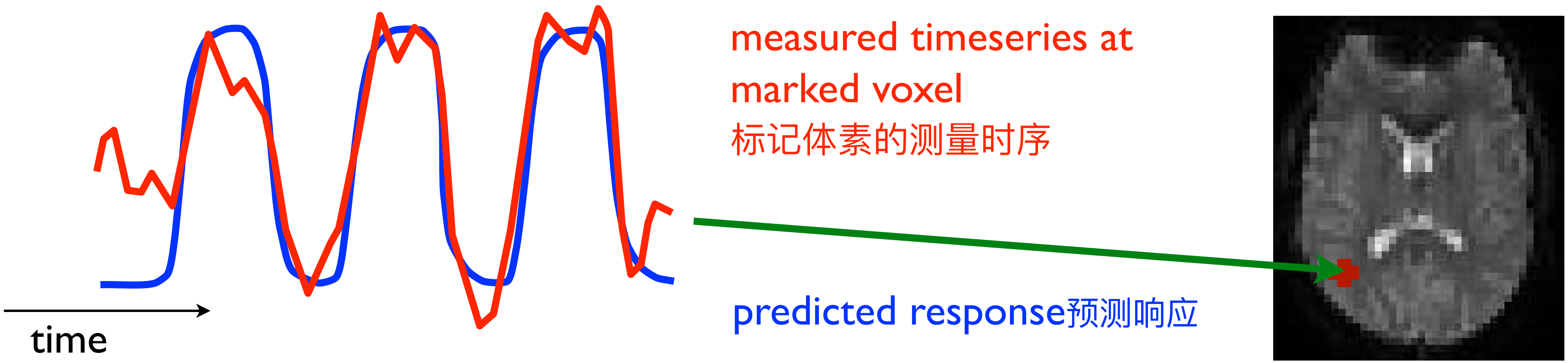


FMRI Experiments: Analysis 分析

- Each voxel contains a time-varying signal(BOLD signal)
  每体素含随时间变化的信号（BOLD信号）
- Model the stimulus-induced change in BOLD signal(predicted response)
  因刺激导致的BOLD信号改变建模（预测响应）

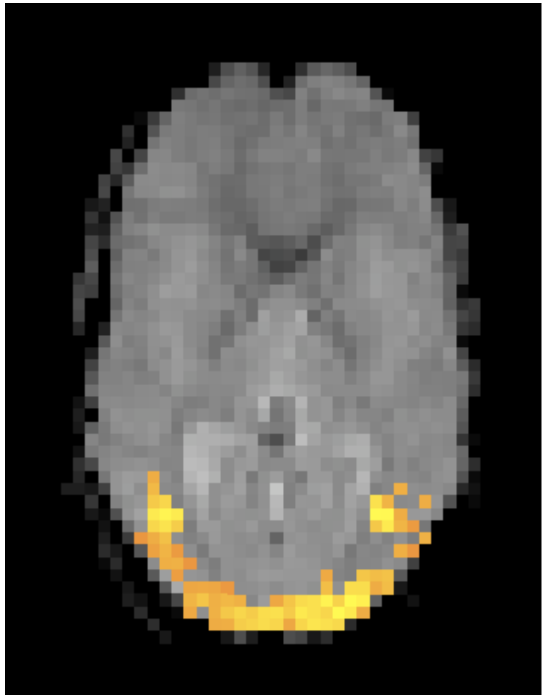


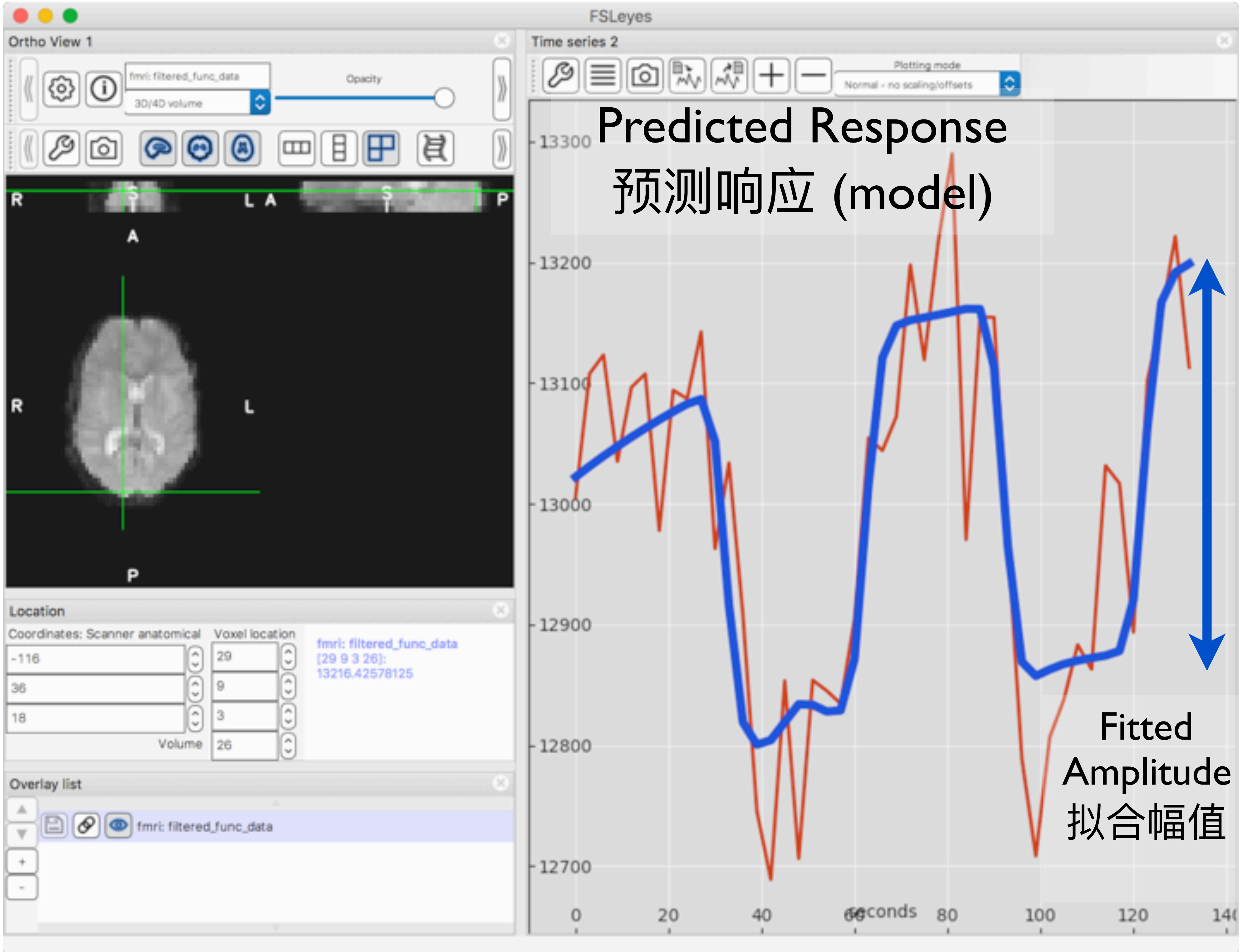
- Find which voxels have signals that match the model
  找哪些体素的信号和模型匹配
- Good match implies activation related to stimulus
  匹配度高代表和刺激相关的激活

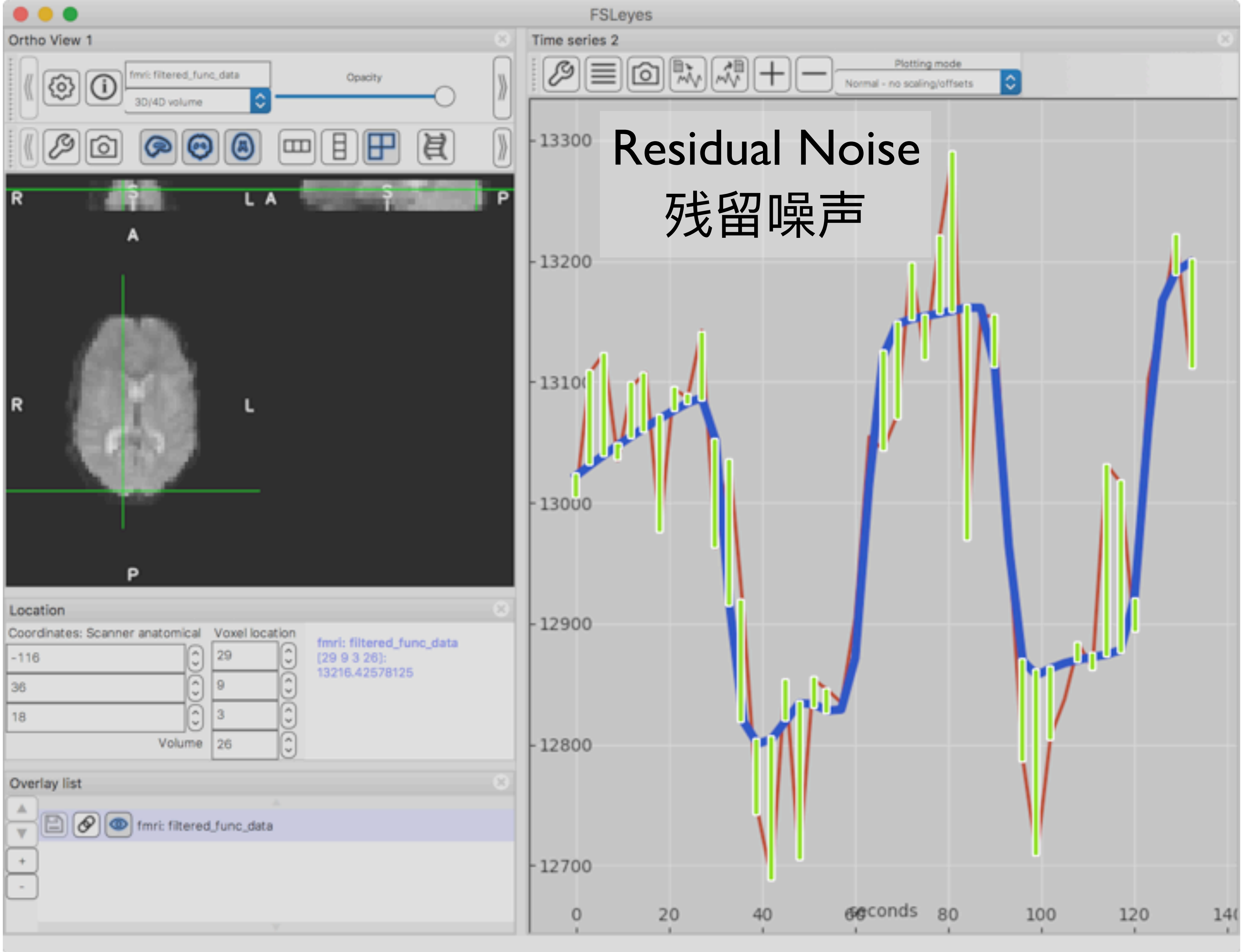


Standard GLM Analysis 标准一般线性模型分析

- Correlate model at each voxel separately 每个体素独立相关的模型
  - Measure residual noise variance
    测量残余噪音方差
  - *t*-statistic = model fit / noise amplitude
    t检验=模型拟合/噪音幅值
  - Threshold *t*-stats and display map
    t检验阈值和显示图




FSLeyes
Ortho View 1
Time series 2
Predicted Response
预测响应 (model)
Fitted
Amplitude
拟合幅值
Location
Coordinates: Scanner anatomical
Voxel location
fmri: filtered_func_data
[29 9 3 26]:
13216.42578125
Volume
Overlay list
fmri: filtered_func_data
seconds
13300
13200
13100
13000
12900
12800
12700
0
20
40
60
80
100
120


FSLeyes
Ortho View 1
Time series 2
Residual Noise
残留噪声
Location
Coordinates: Scanner anatomical
Voxel location
Volume
Overlay list
fmri: filtered_func_data
seconds

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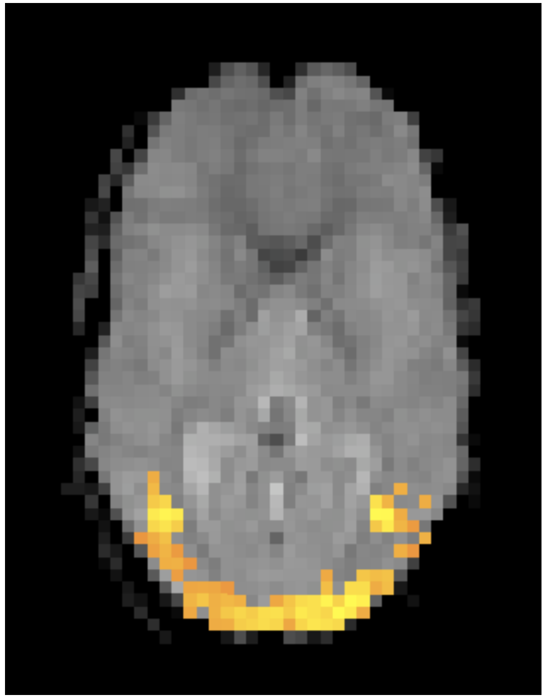

Signals of no interest (e.g. artifacts) can affect both activation strength and residual noise variance

无关信号（如伪影）会同时影响激活强度和噪音残差

Use pre-processing to reduce/eliminate some of these effects
使用预处理可以减少或者消除这些效应

FMRI Pre-Statistics 统计之前

FMRI pre-statistical image processing统计前图像处理:

- Reconstruction from k-space data(k空间数据重建)
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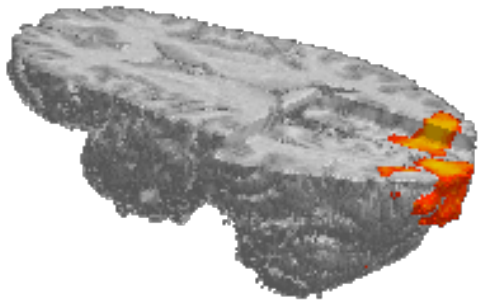
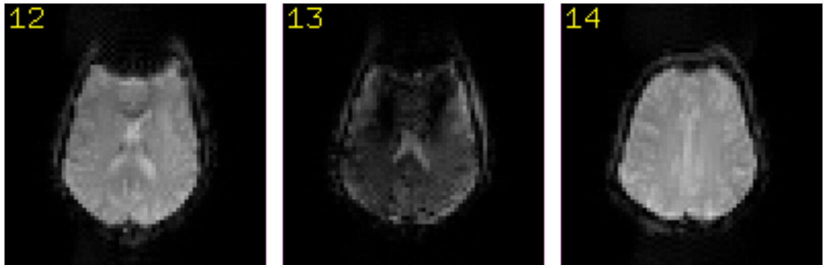
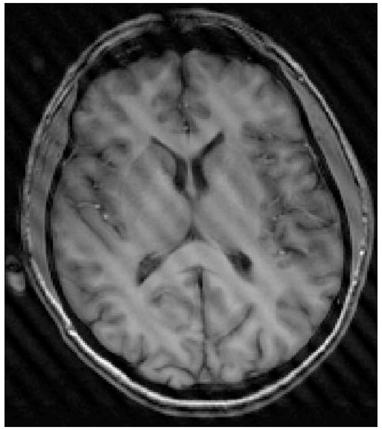


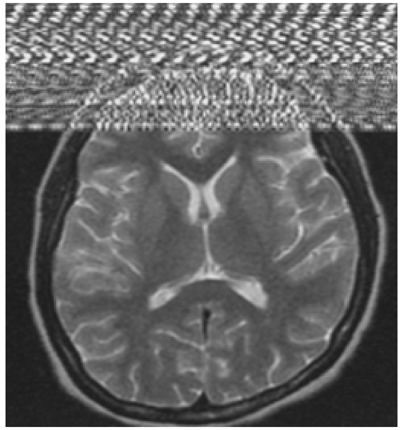
Image Reconstruction 图像重建

- Convert k-space data to images将k空间数据转换为图像:
  - reconstruction algorithms重建算法
- Occasionally get problematic data偶尔会收到有问题的数据
  - e.g. slice timing errors, RF spikes, RF interference

时间层错误，射频尖脉冲，射频干扰







- Correct using custom-built initial analysis stages

使用定制的初始分析阶段进行校正

- Scanner artefacts can be found by 检查伪影的方式:

looking at data exploratory analysis 探索性分析(ICA),

FMRI Pre-Statistics 统计之前

FMRI pre-statistical image processing统计前图像处理:

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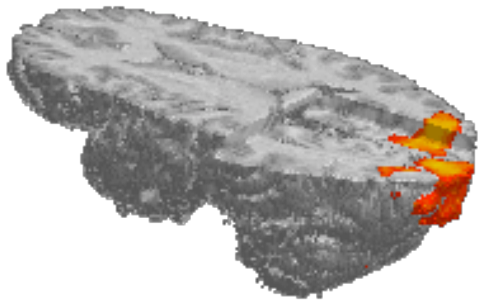
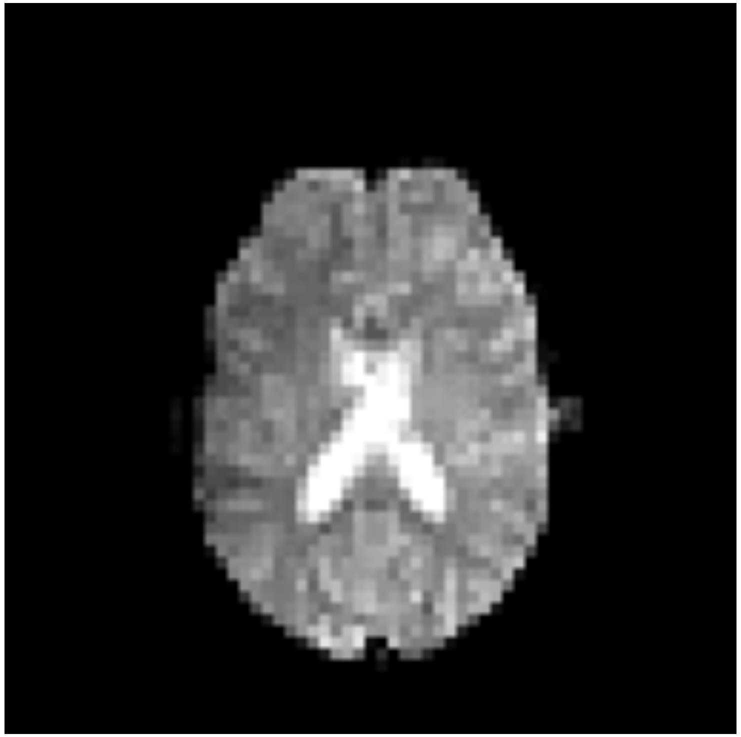


Motion Correction: Why? 为什么要运动校正

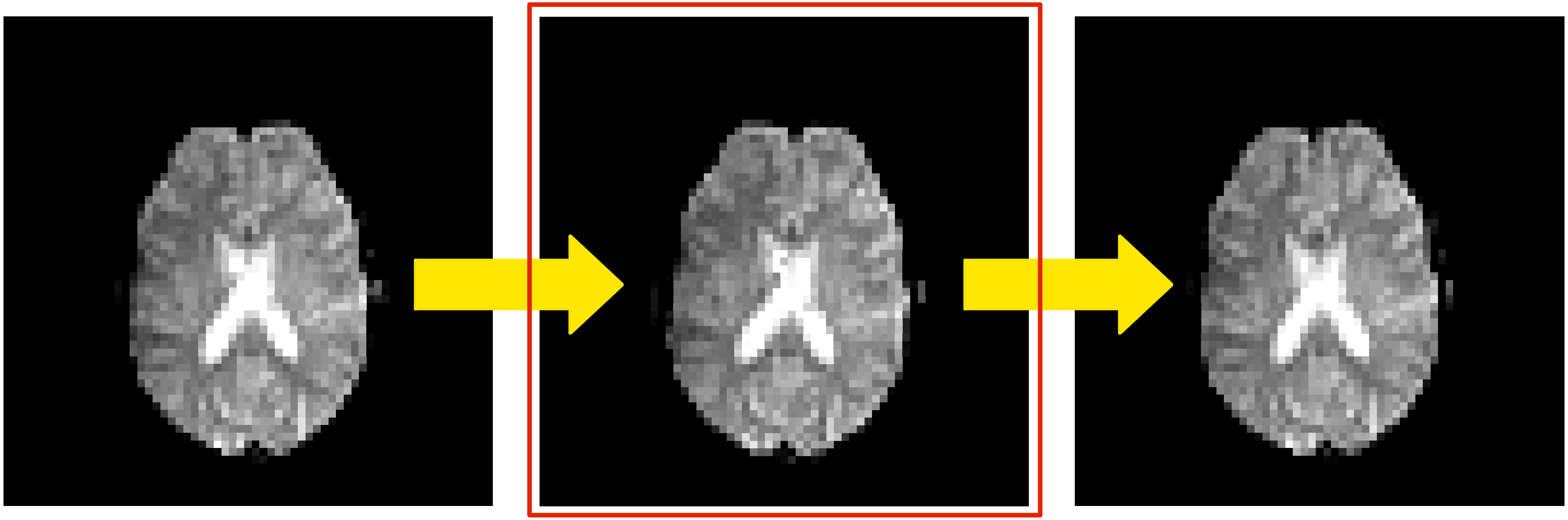
- People always move in the scanner
  人在磁共振扫描仪里总会移动
- Even with padding around the head there is still some motion
  即使带了头垫还是会有移动
- Need each voxel to correspond to a consistent anatomical point for each point in time
  需要保证每个时间点上的每个体素都与解剖点一致
- Motion correction realigns to a common reference
  头动校正调整到共同参考位置



- Very important correction as small motions (e.g. 1% of voxel size) near strong intensity boundaries may induce a 1% signal change > BOLD
  有高强边界的小幅运动会导致至少1%BOLD信号改变，所以头动校正很重要

Motion Correction 头动校正

= multiple registration多重配准



Select a MC target (reference) for all FMRI volumes.在所有图像帧里选一个校正参考目标

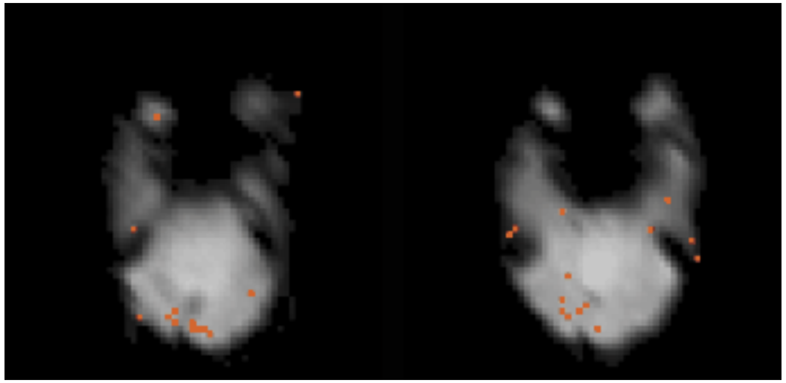
Can use either one original volume, mean of several, standard space image etc.
可使用一个原始帧，几个帧图像的平均，或者标准空间图像

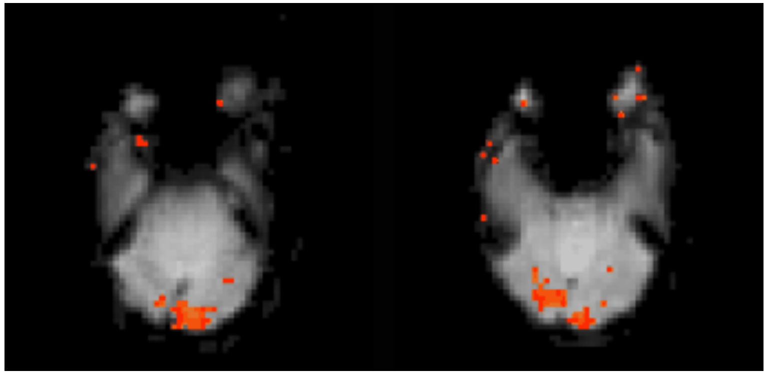
Register each FMRI volume to target separately
把每个图像帧单独配准到目标图像

Use rigid body (6 DOF)
用刚体(6自由度)

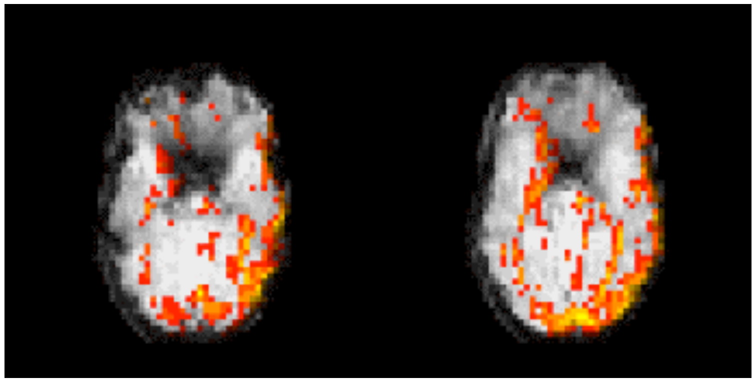
Effect of Motion Correction 校正效果

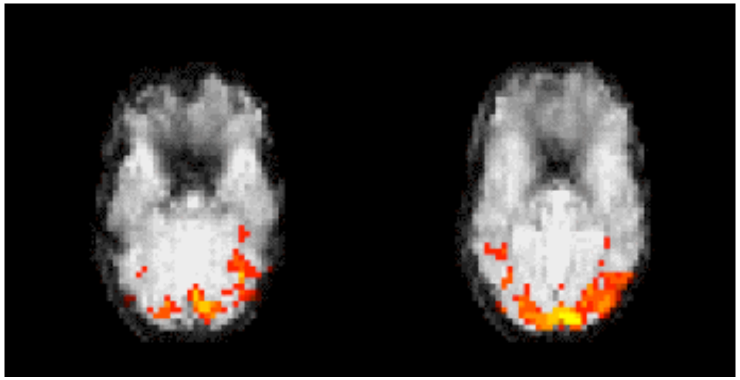
Uncorrelated Motion 未校正





Stimulus Correlated Motion 刺激相关运动



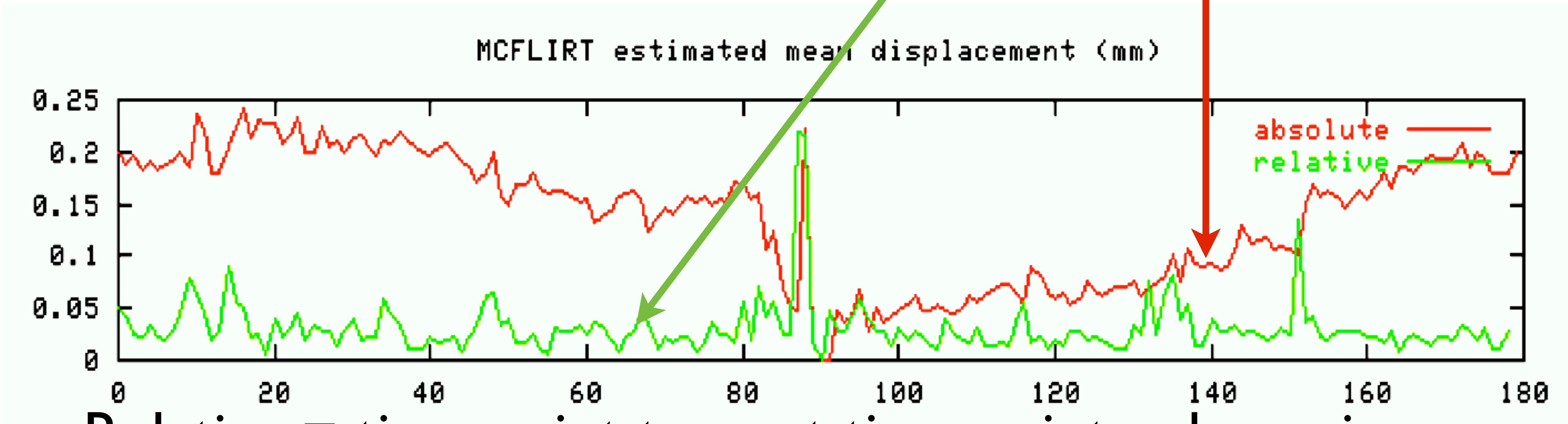


Without MC 未校正 With MC 校正

Motion Parameter Output 运动参数输出

Summary of total motion (relative and absolute)

相对和绝对运动总结



Relative = time point to next time point - shows jumps

相对=一个时间点到下一个时间点-显示跳动

Absolute = time point to reference - shows jumps & drifts

绝对=时间到参考-显示跳动&漂移

Note that large jumps are more serious than slower drifts, especially in the relative motion plot

请注意，较大的跳跃比较慢的漂移更严重，尤其是在相对运动图中

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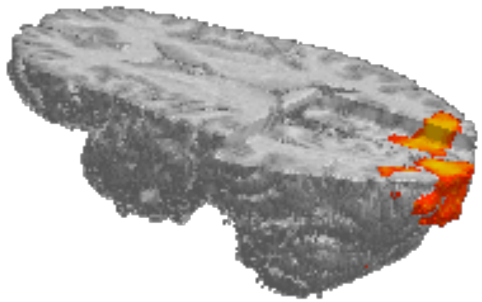
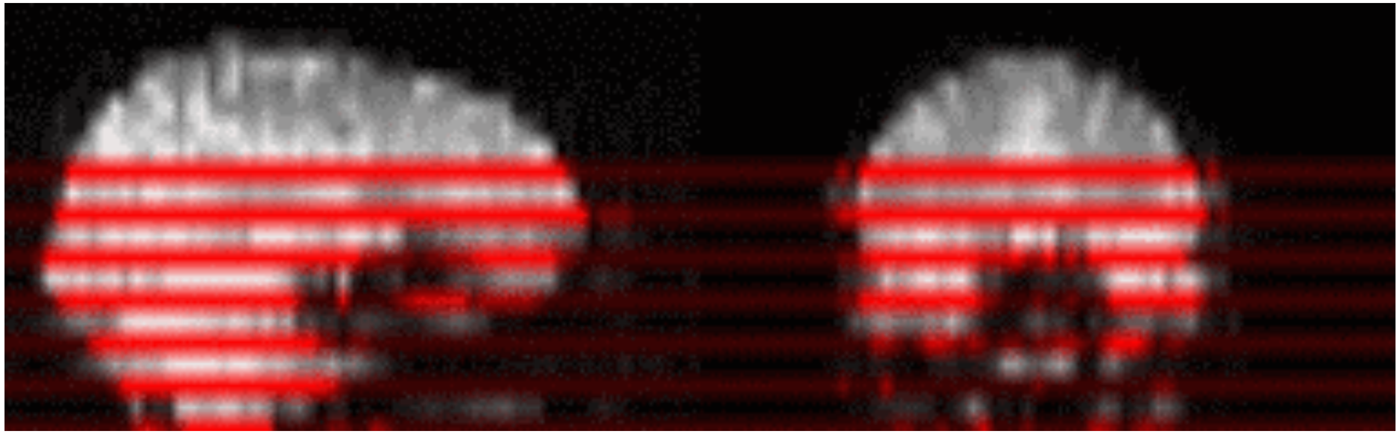


Slice Timing Correction 时间层校正



Almost all FMRI scanning takes each slice separately
几乎所有的fMRI扫描都是独立获得每个切片。

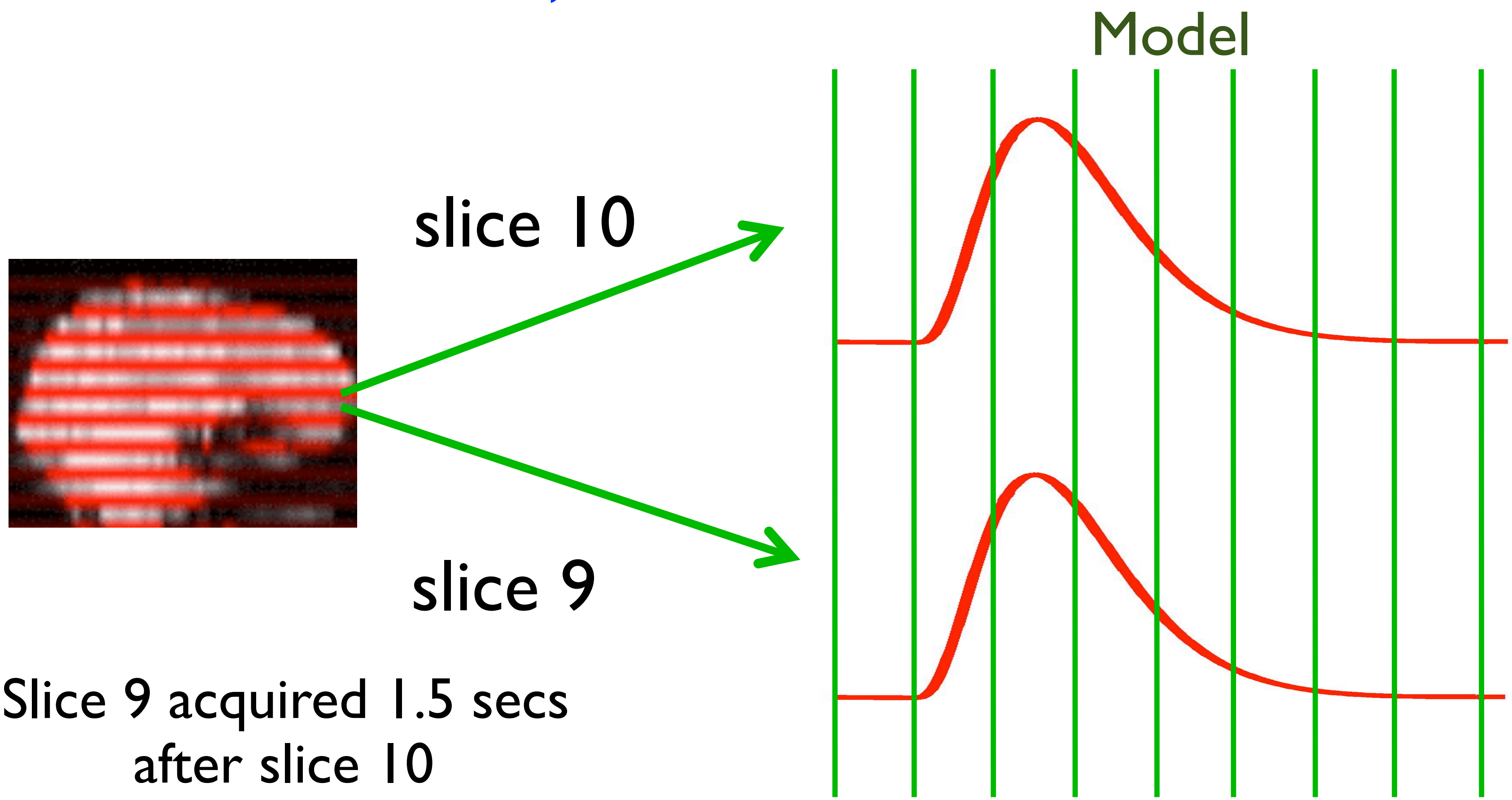
Each slice is scanned at a slightly different time
每个切片的扫描时间都会有轻微不同。

Slice order can be interleaved (as shown) or sequential (up or down)
切片顺序可以交错（如图所示）或顺序（向上或向下）

Slice Timing 时间层

Without any adjustment, the model timing is always the same

不做调整时，模型时间总是相同的



Slice 9 acquired 1.5 secs after slice 10

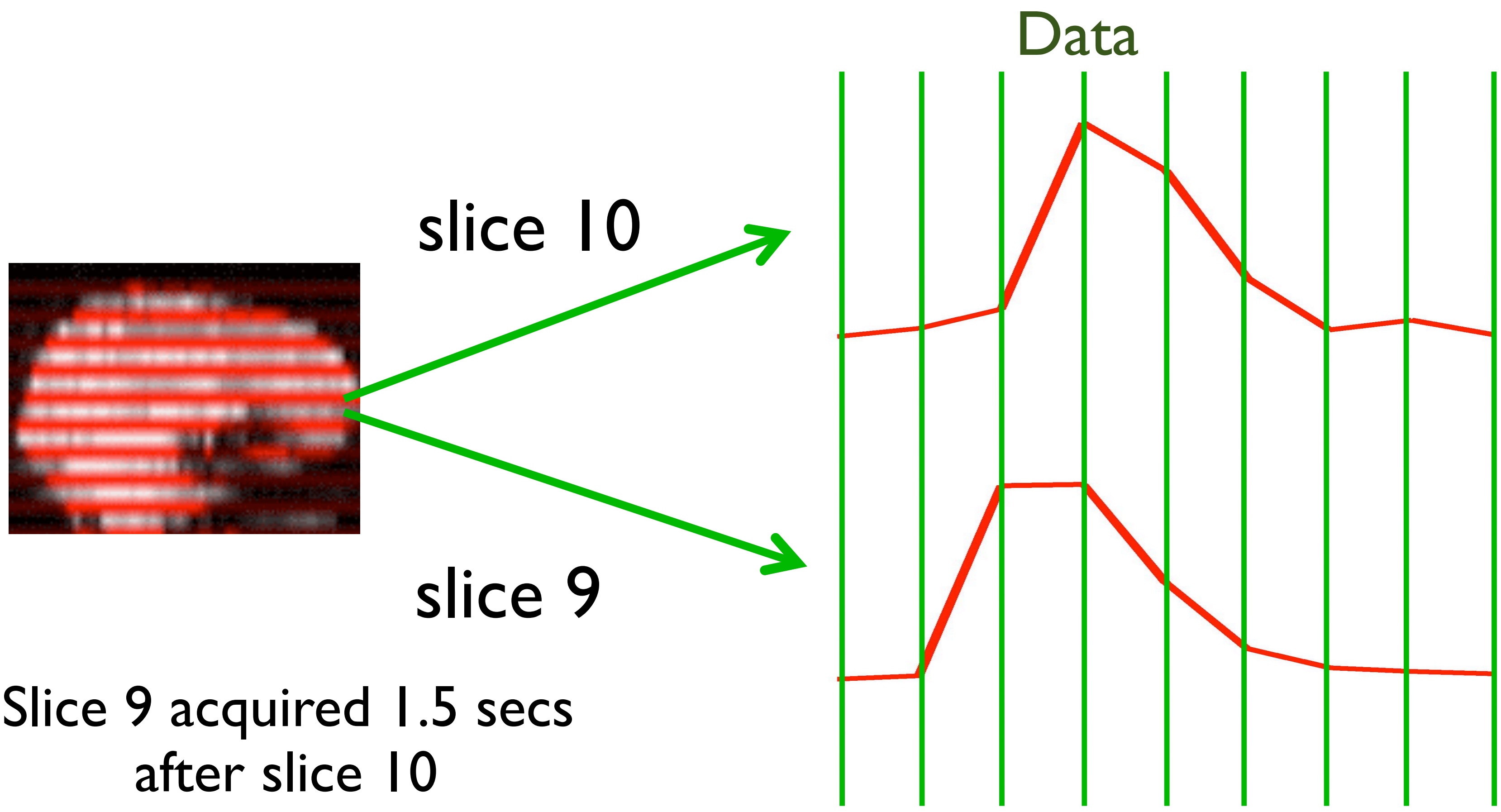
切片10在切片9后1.5s采集

acquisition timing (TRs)

采集时间(TRs)

Slice Timing 时间层

... but the timing of each slice's data is *different*
但是实际数据的时间层是不同的

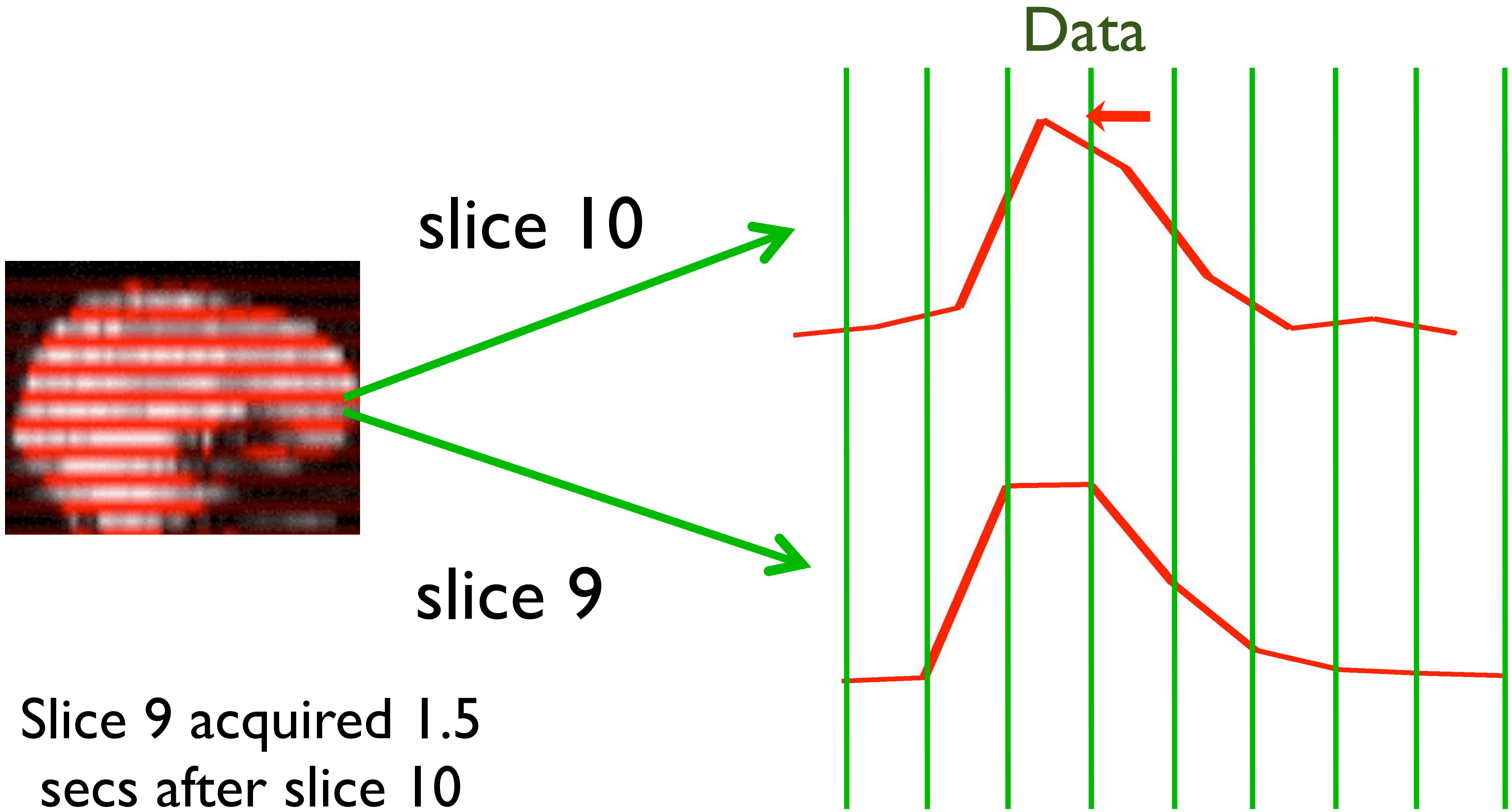


Slice 9 acquired 1.5 secs
after slice 10
切片10在切片9后1.5s采集

acquisition timing (TRs)
采集时间(TRs)

Slice Timing 时间层

Can get consistency by shifting the ***data***
可以通过移位数据来保持一致



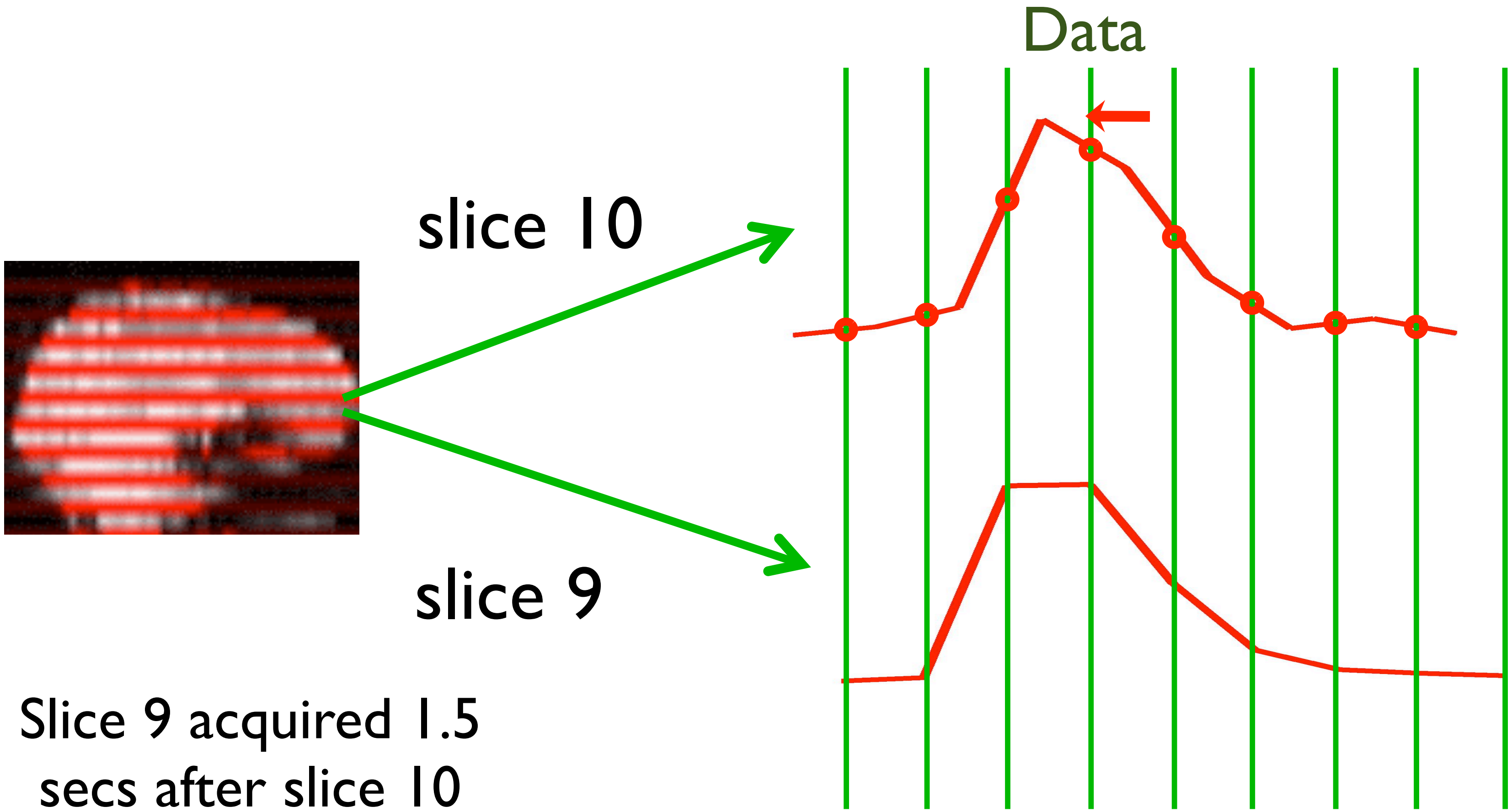
Slice 9 acquired 1.5 secs after slice 10
切片10在切片9后1.5s采集

acquisition timing (TRs)
采集时间

Slice Timing 时间层

... and then interpolating the data = ***slice timing correction***

之后插值数据，这就是时间层校正



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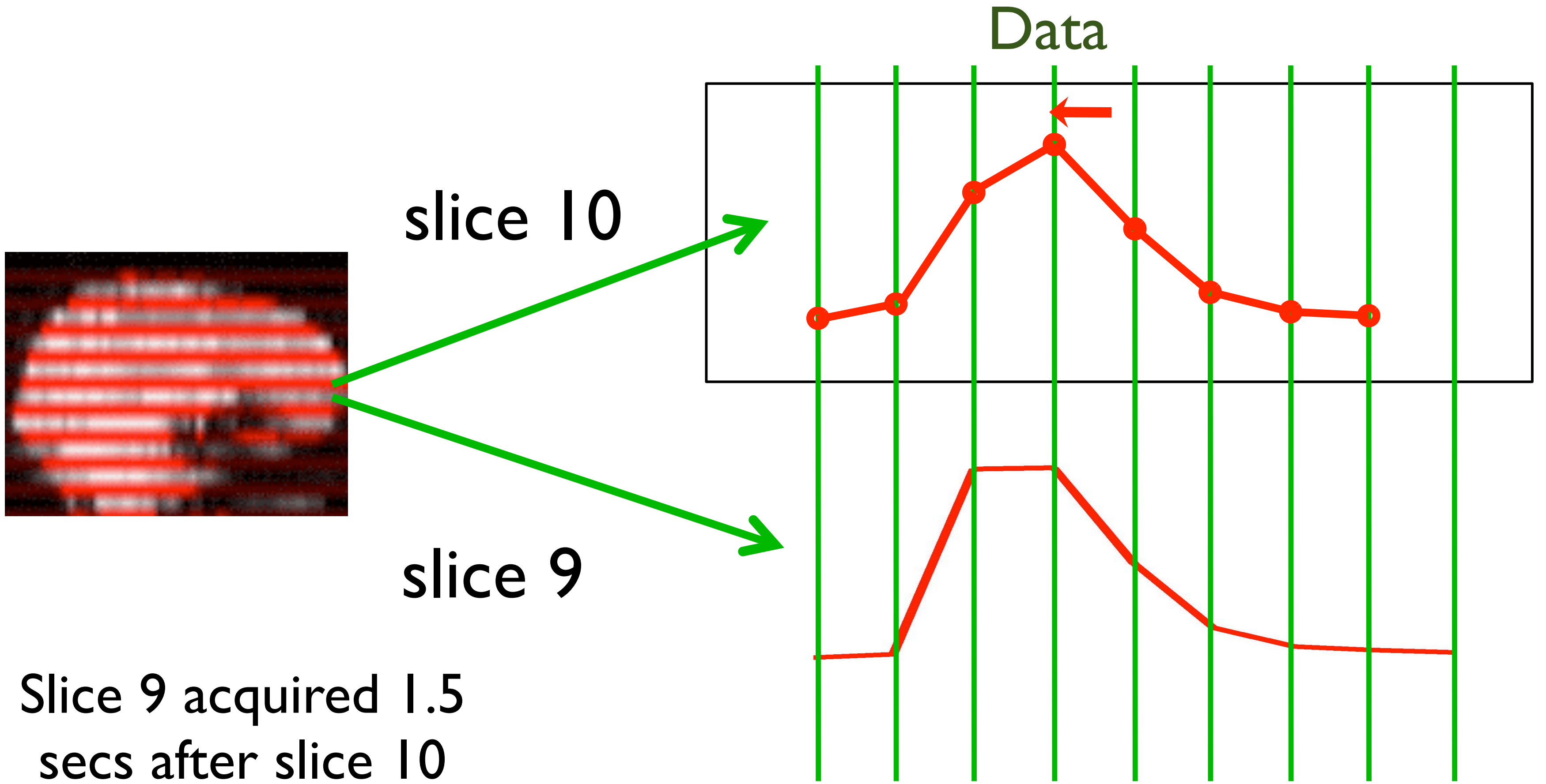


Slice 9 acquired 1.5 secs after slice 10

切片10在切片9后1.5s采集

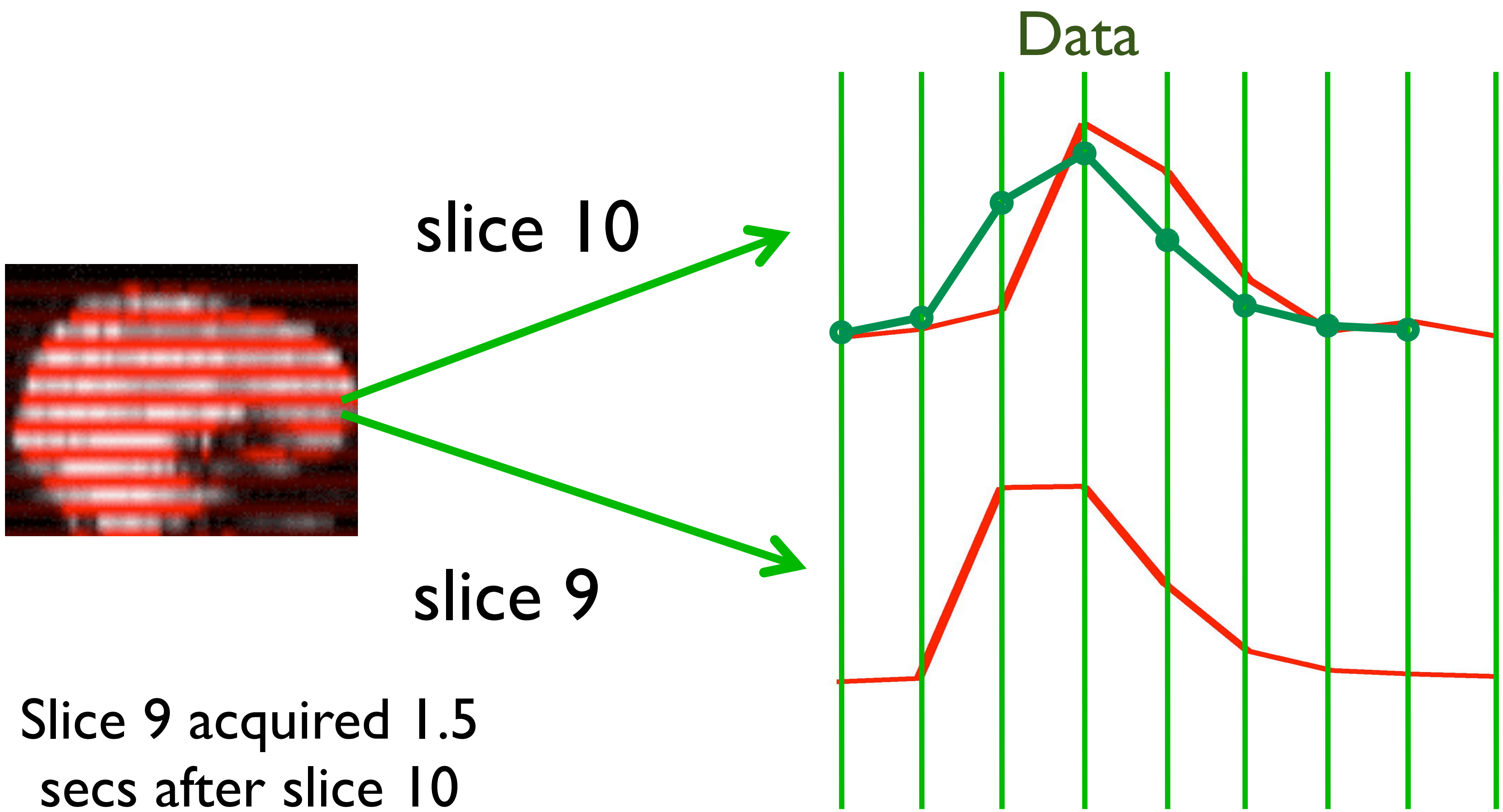
acquisition timing (TRs)

采集时间

Slice Timing 时间层

The result of slice timing correction is that the data is changed (degraded) by interpolation

时间层校正的结果是数据通过插值被改变（降低）了



Slice 9 acquired 1.5 secs after slice 10

切片10在切片9后1.5s采集

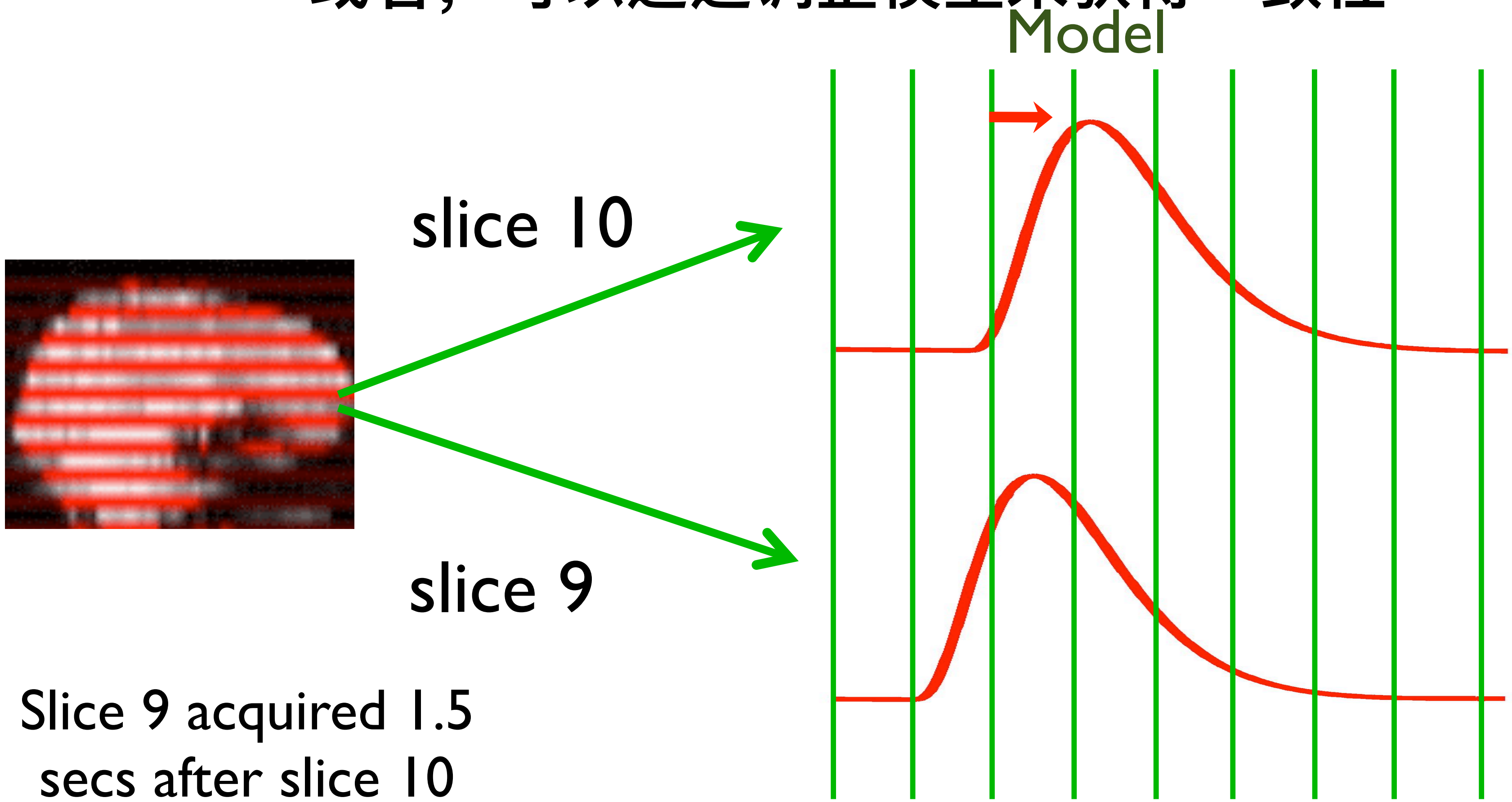
acquisition timing (TRs)

采集时间

Slice Timing 时间层

Alternatively, can get consistency by shifting the ***model***

或者，可以通过调整模型来获得一致性



Slice 9 acquired 1.5 secs after slice 10
切片10在切片9后1.5s采集

acquisition timing (TRs)
采集时间

Slice Timing 时间层

One way to shift the model is to use the ***temporal derivative in the GLM***
一种调整模型的办法是利用*GLM*里的时间导数

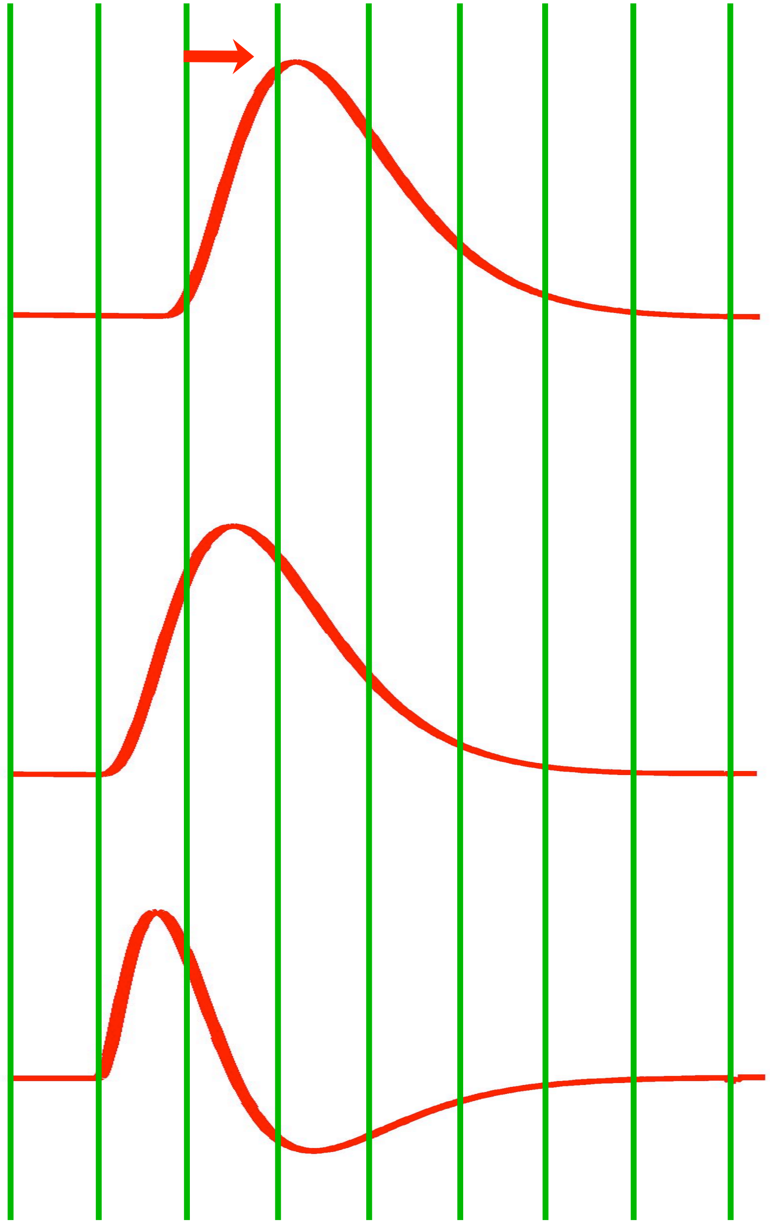
Shifted Model
改变后模型

=

Original Model
原始模型

-

Temporal Derivative
时间导数



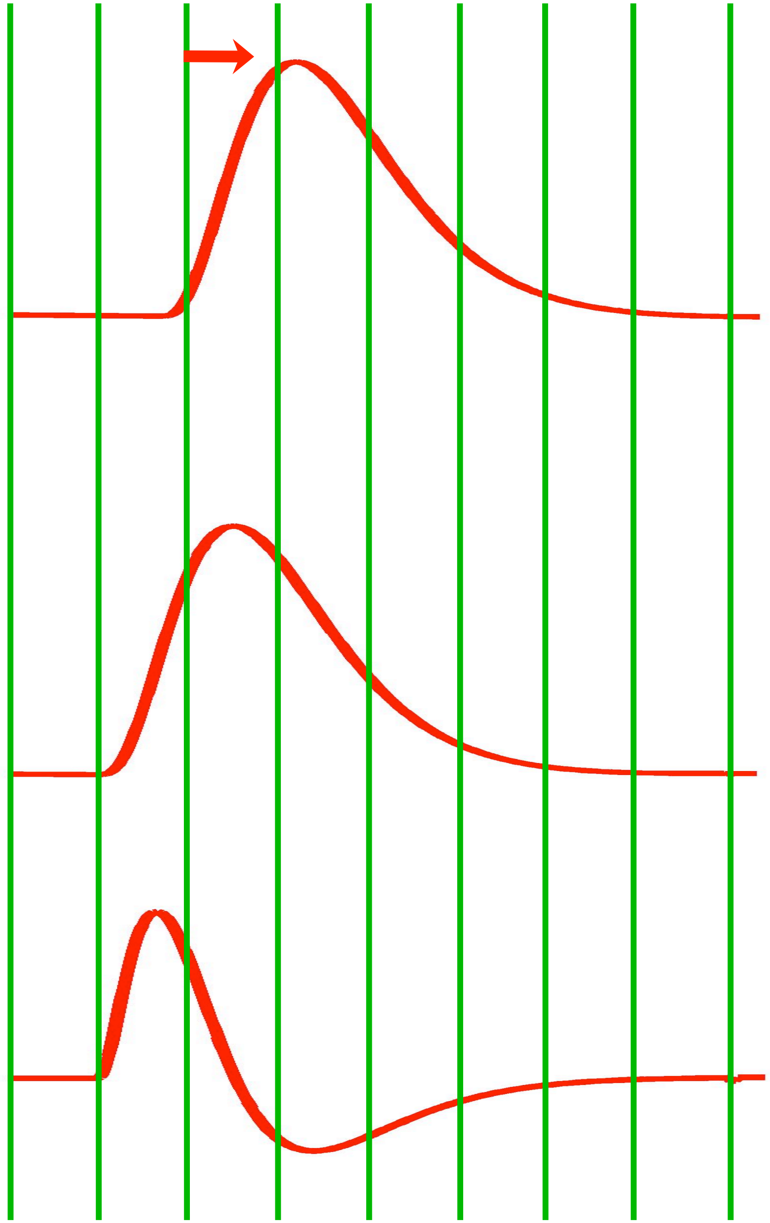
Based on Taylor approx:
$m(t+a) = m(t) + a.m'(t)$
基于泰勒近似公式

Slice Timing 时间层

Shifting the model also accounts for variations in the HRF delay
调整模型同时解释了HRF延迟的变异

- as the HRF is known to vary between subjects, sessions, etc.
  因为HRF随被试，session等变化

This is the recommended solution for slice timing
这是解决时间层问题的推荐办法



Motion Problems 头动问题

Motion correction eliminates gross motion changes but assumes *rigid-body motion* - not true if slices acquired at different times

运动校正可消除总体运动变化，但采用刚体运动 - 如果在不同时间获取切片，则不正确

Other motion artefacts persist including:

Spin-history changes, B_0 (susceptibility) interactions & Interpolation effects

其他运动伪影仍然存在，包括：自旋历史变化，B0（磁化率）相互作用和插值效应

Such artefacts can severely degrade functional results

Severity usually worse for *stimulus-correlated* motion

此类伪像会严重降低功能结果的强度，与刺激相关的运动通常会变得更糟

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Some *potential* analysis remedies for motion artefacts include:
运动伪影的一些潜在分析补救措施包括：

- including motion parameter regressors in GLM
在GLM中包括运动参数回归
- removing artefacts with ICA denoising通过ICA去噪去除伪影
- outlier timepoint detection and exclusion (via GLM)
离群时间点检测和排除（通过GLM）
- rejection of subjects displaying “excessive” motion
拒绝显示“过度”运动的被试

No simple rule of thumb defining "too much" motion
没有简单的经验法则来定义“太多”的运动

FMRI Pre-Statistics 统计之前

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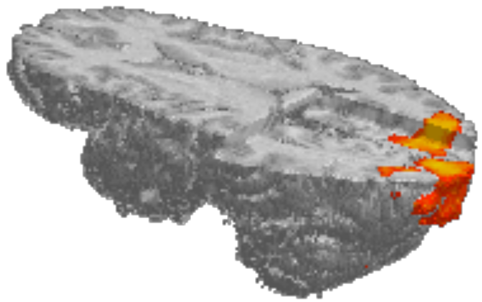
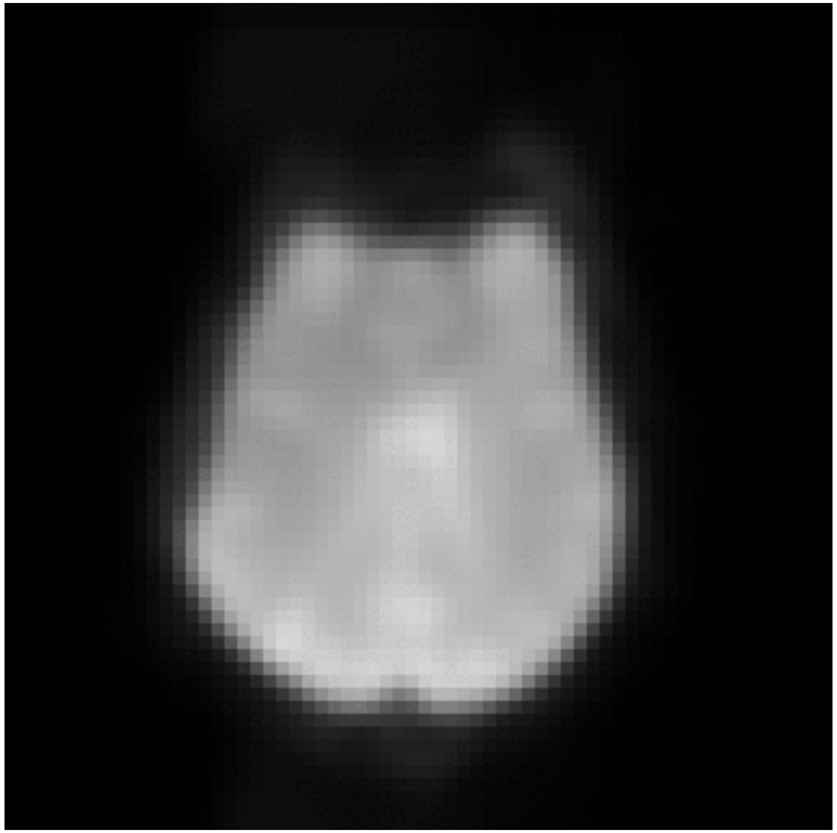


Spatial Filtering 空间滤波



Why do it?为什么做呢?

1. Increases signal to noise ratio if size of the blurring is less than size of activation
   如果模糊大小小于激活大小，则增加信噪比

2. Need minimum "smoothness" to use *Gaussian random field theory* for thresholding
   需要最小的“平滑度”以使用高斯随机场理论进行阈值化

However: 然而会

- Reduces small activation areas 减少小激活区域
- Safest option is to do a small amount of smoothing
  最安全的选择是做少量的平滑处理
- Alternative thresholding/stats eliminates the need for smoothing (e.g. randomise, TFCE)
  替代阈值/统计信息消除了对平滑处理的需求（例如随机化，TFCE）

Spatial Filtering: How? 如何操作?

Spatial filtering done by a 3D convolution with a Gaussian (cf. 1D convolution with HRF for model)
通过高斯3D卷积进行空间滤波（参见模型，使用HRF进行一维卷积）

Each voxel intensity is replaced by a *weighted* average of neighbouring intensities
每个体素强度被相邻强度的加权平均值代替

A Gaussian function in 3D specifies weightings and neighbourhood size
3D中的高斯函数指定权重和邻域大小

Weights

0.1	0.3	0.4	0.3	0.1
0.3	0.6	0.8	0.6	0.3
0.4	0.8	1.0	0.8	0.4
0.3	0.6	0.8	0.6	0.3
0.1	0.3	0.4	0.3	0.1

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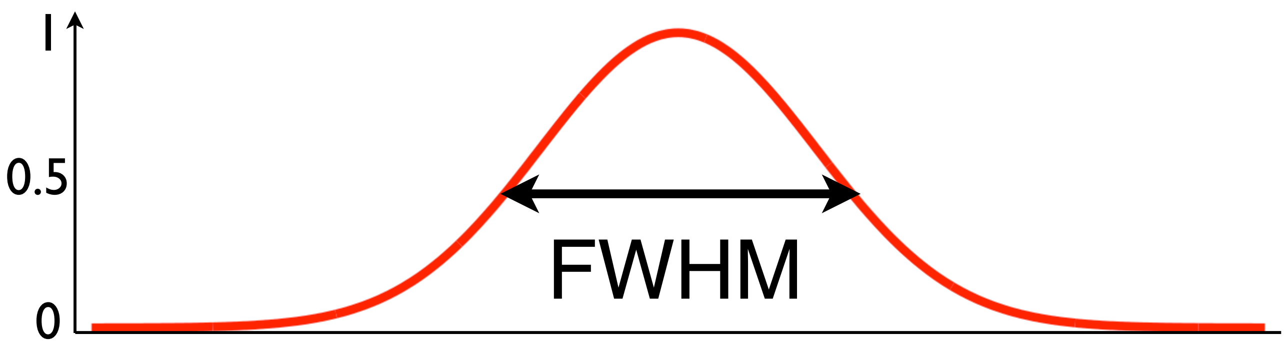


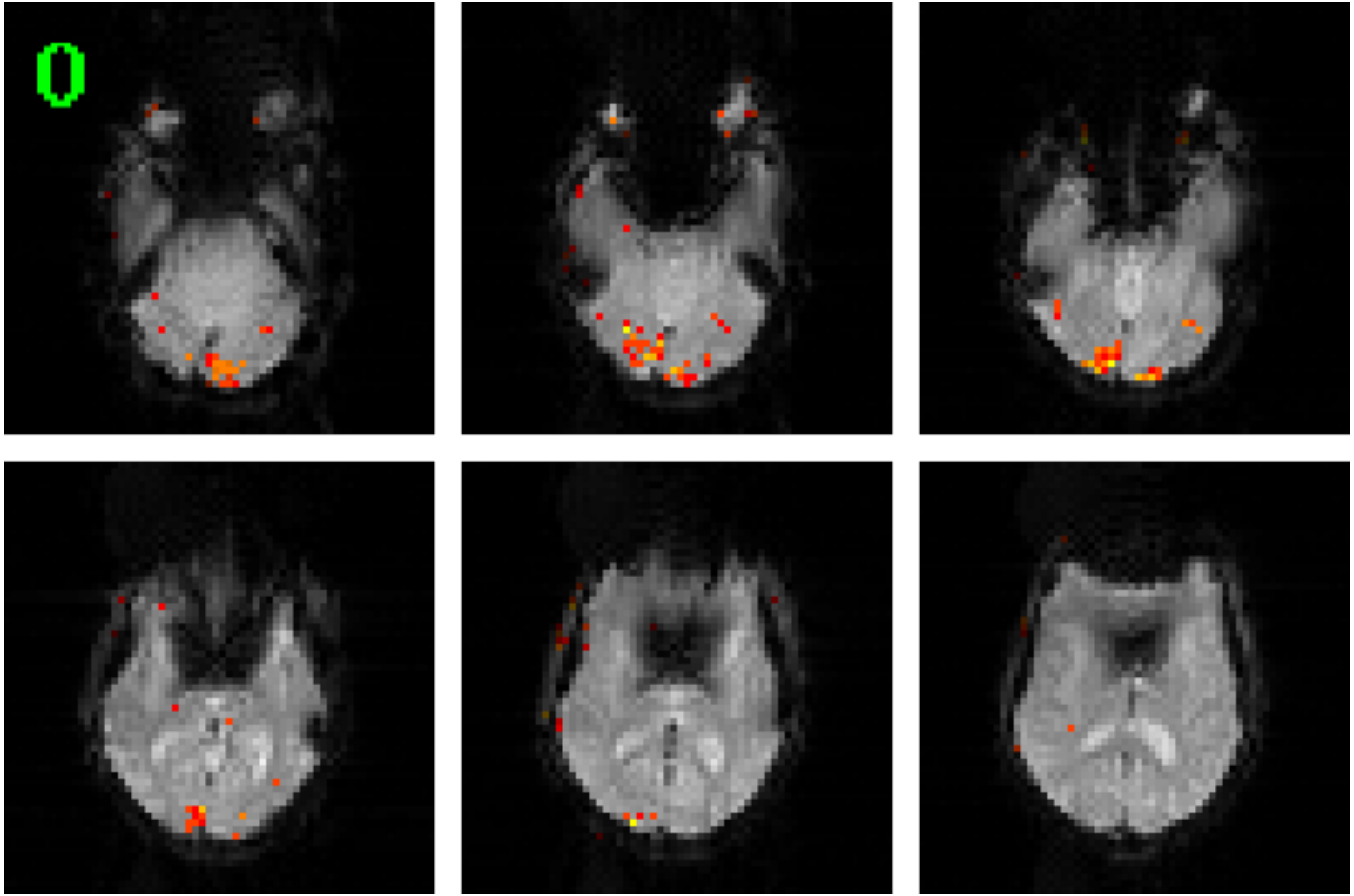
Weights

0.1	0.3	0.4	0.3	0.1
0.3	0.6	0.8	0.6	0.3
0.4	0.8	1.0	0.8	0.4
0.3	0.6	0.8	0.6	0.3
0.1	0.3	0.4	0.3	0.1

FWHM

Specify amount by Full Width Half Maximum (FWHM)
= distance between 0.5 values
通过全宽半高指定数值=0.5倍值之间的距离

Spatial Filtering: Results at Different FWHM 空间滤波：不同全宽半高的结果



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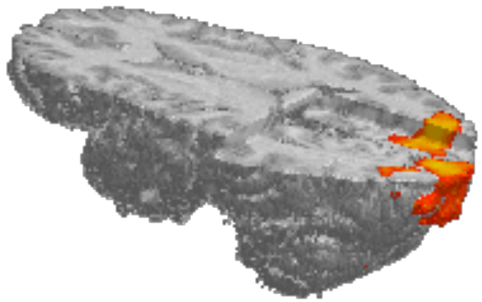


Temporal Filtering: Why? 为何时域滤波

- Time series from each voxel contain scanner-related and physiological signals + high frequency noise

每个体素的时间序列包含与扫描仪相关的信号和生理信号以及高频噪声

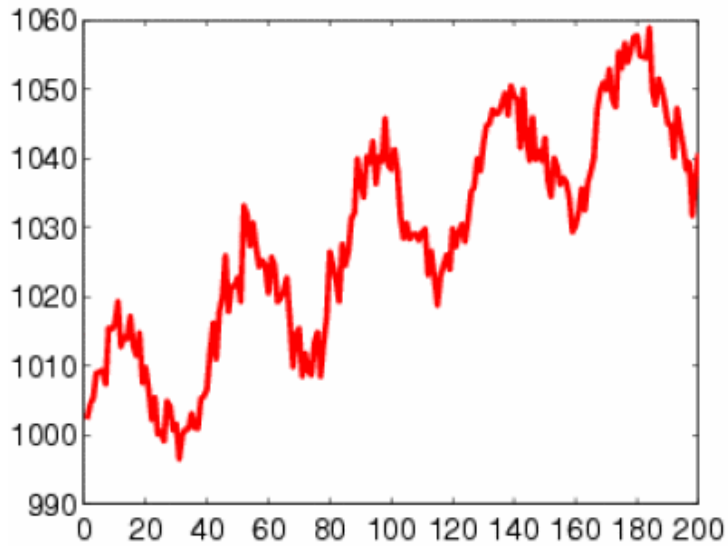
- Scanner-related and physiological signals (cardiac cycle, breathing etc) can have both high and low frequency components

扫描仪相关的和生理信号（心脏周期，呼吸等）可能同时具有高频和低频成分

- These signals + noise hide activation

这些信号+噪音隐藏激活

Raw Signal原始数据



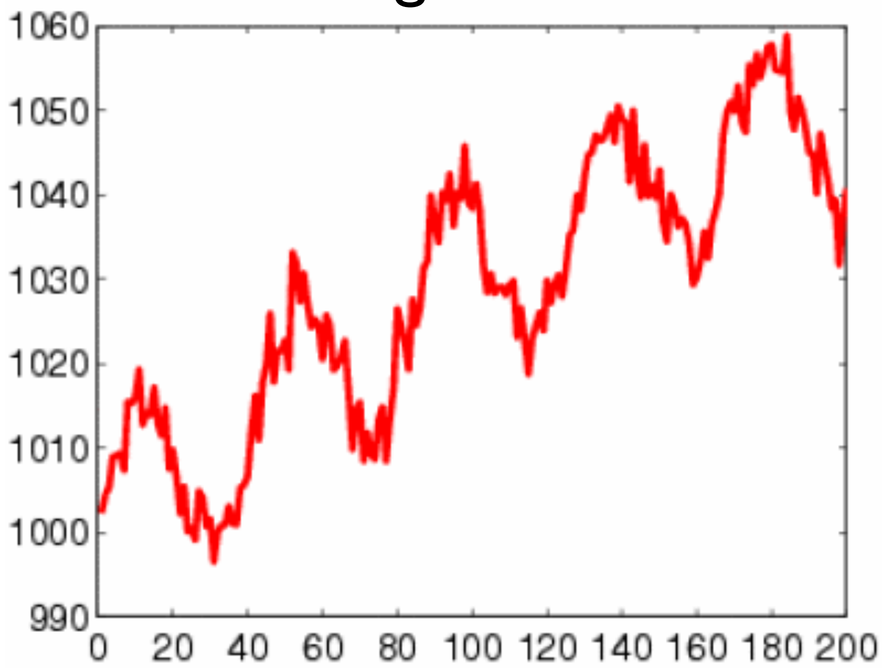
What is temporal filtering? 什么是时域滤波?

- Removal of high frequencies, low frequencies or both, *without removing signals of interest*

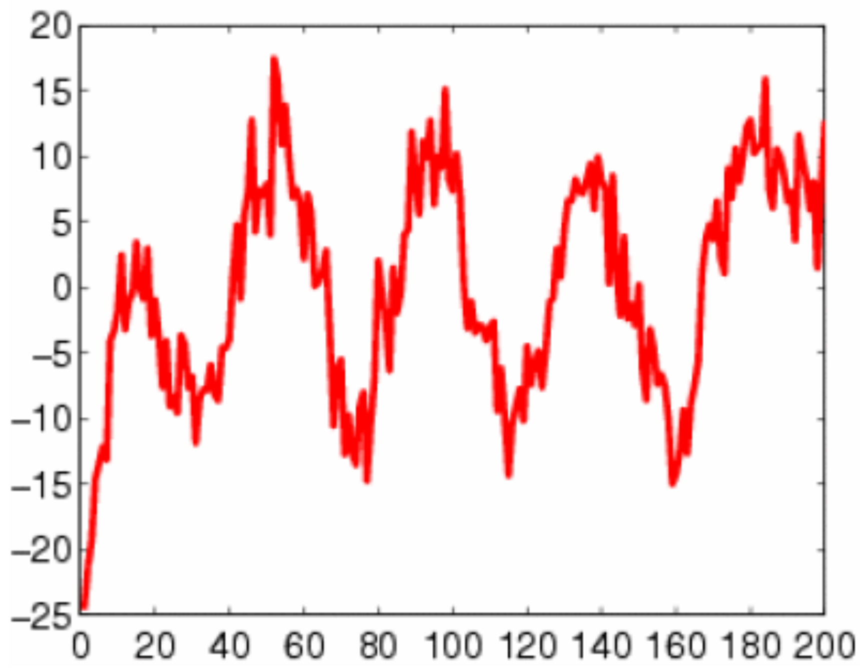
去除高低频噪音，不去掉感兴趣信号

Temporal Filtering: Highpass 时域滤波：高通

Raw Signal原始数据



Highpass Filtered高通滤波



- Removes low frequency signals, including linear trend

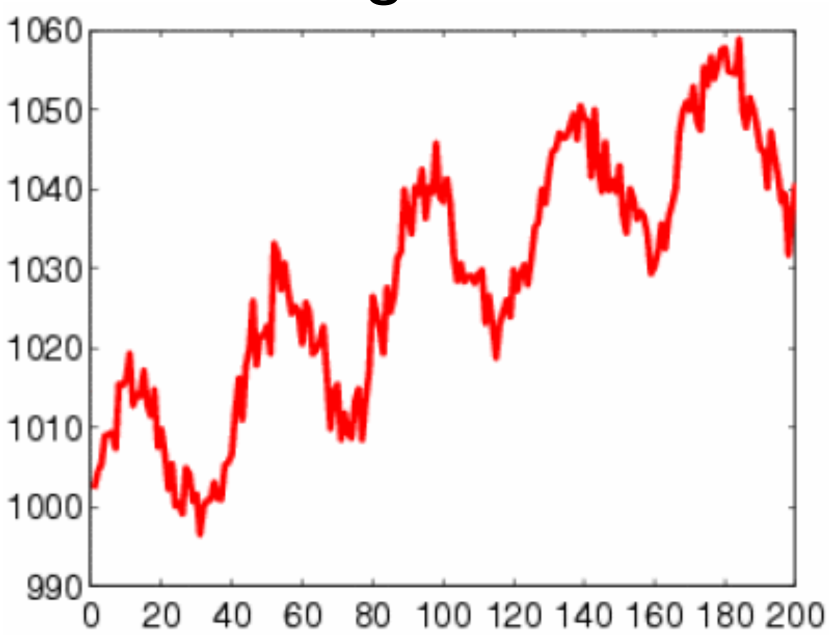
去掉低频信号，包括线性趋势

- Must choose cutoff frequency carefully (lower than frequencies of interest = longer period)

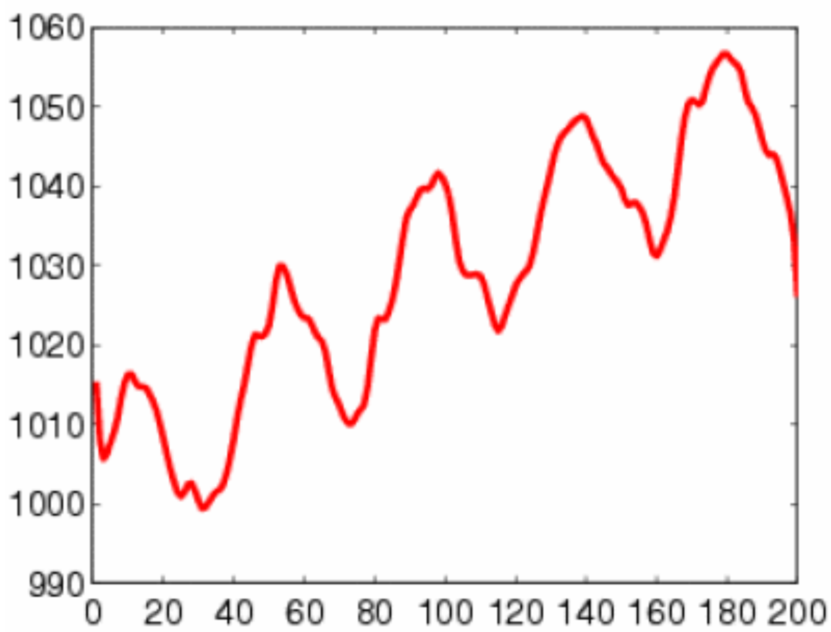
必须仔细选择截止频率（低于感兴趣的频率=更长的时间）

Temporal Filtering: Lowpass 时域滤波：低通

Raw Signal原始数据



Lowpass Filtered低通滤波

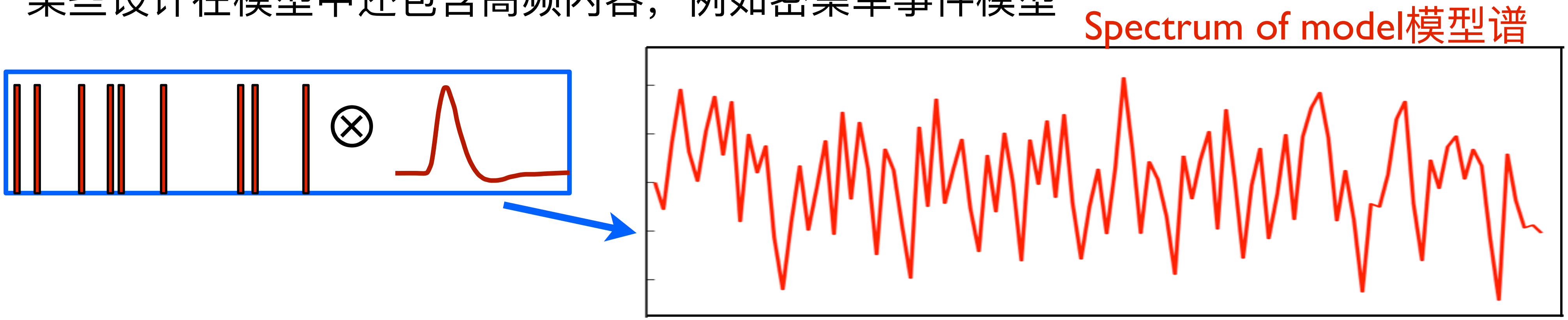


Removes high frequency noise 去掉高频噪音

Only useful if the predicted model does not also contain high frequencies…
仅当预测的模型也不包含高频时才有用...

Filtering & Temporal Autocorrelation 滤波&时域自相关

Some designs also contain high frequency content *in the model* e.g. Dense Single-Event Model:
某些设计在模型中还包含高频内容，例如密集单事件模型



- In these cases, lowpass filtering removes too much signal
  这些例子里，低通去掉了太多信号

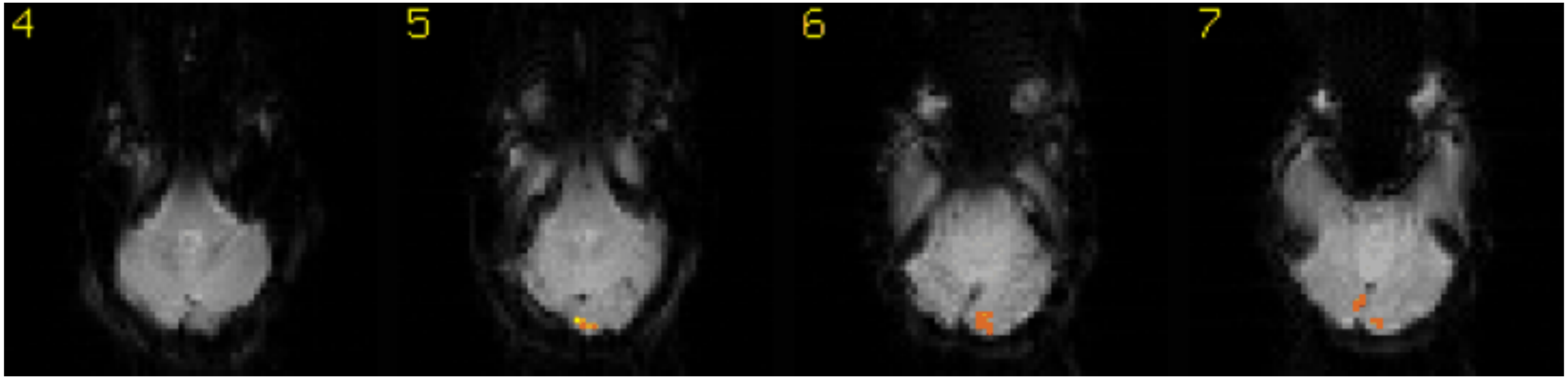
- Also, need noise data to correctly estimate autocorrelation (to make statistics valid - see later)
  ➜ avoid lowpass filtering
  另外，需要噪声数据来正确估计自相关（以使统计数据有效-请参阅下文）➜避免低通滤波

Recommendations建议:

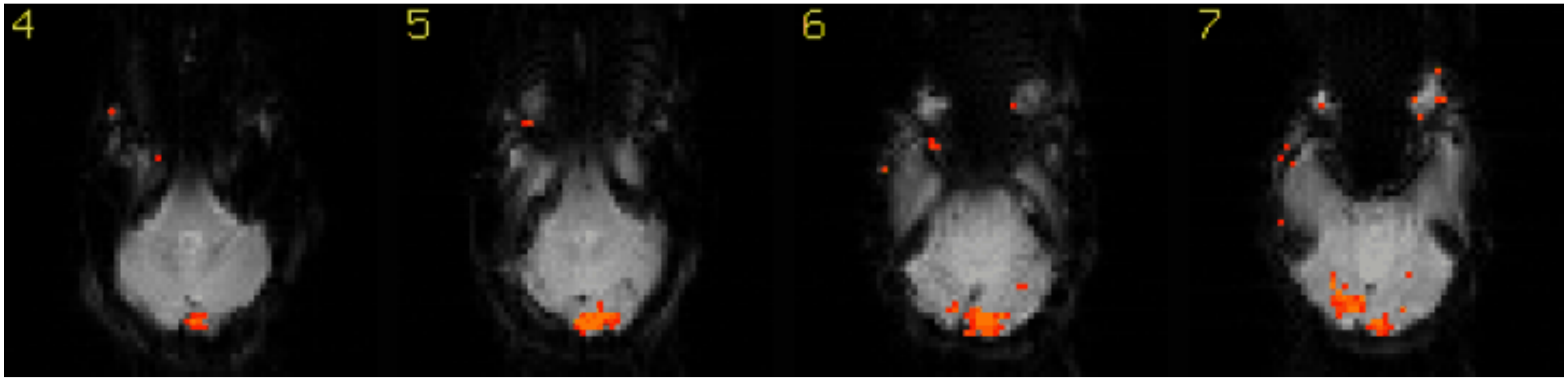
- Use ***Highpass only*** 仅使用高通
- Ensure cutoff frequency higher than model frequencies (can use the Estimate button in the GUI - see practical)
  确保截止频率高于模型频率 （可以使用GUI中的“估计”按钮-参看练习）
- Lower limit on cutoff frequency for good autocorrelation estimation(e.g. for TR=3s, cutoff period > 90s)
  较低的截止频率限制可实现良好的自相关估算（例如，对于TR = 3s，截止时间> 90s）

Effect of Temporal Filtering 时域滤波的影响

No Temporal Filtering无时域滤波



Highpass Temporal Filtering高通滤波



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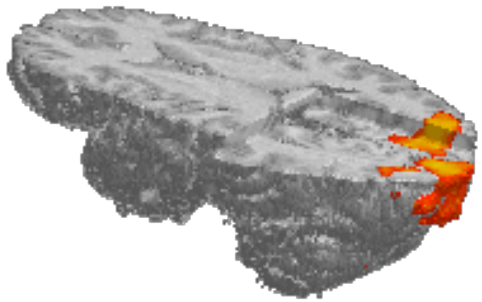
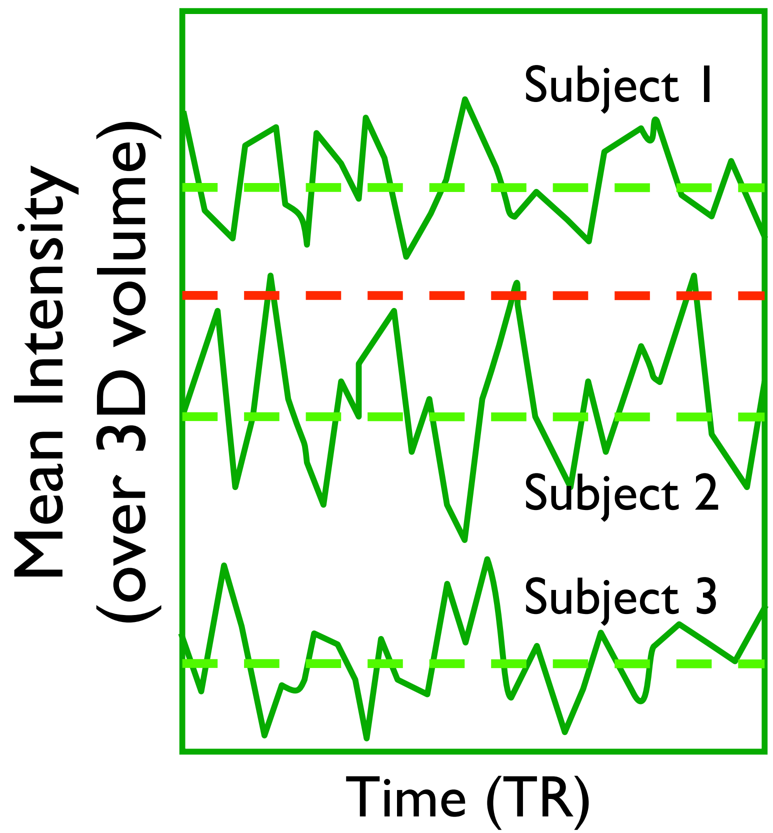


Global Intensity Normalisation 全局强度标准

- Mean intensity of the whole dataset changes between subjects and sessions
  整个数据集的平均强度会在被试和实验阶段之间变化
  - due to various uninteresting factors (e.g. caffeine levels) 因为一些不相关的因素（如咖啡因水平）
- Want the same mean signal level for each subject (taken over all voxels and all timepoints: i.e. 4D)
  希望每个受试者具有相同的平均信号水平（在所有体素和所有时间点上都如此：即4D）
- Scale each 4D dataset by a *single value* to get the overall 4D mean (dotted line) to be the same
  通过单个值来缩放每个4D数据集来使得总体4D平均值（虚线）相同
- Automatically done within FEAT
  在FEAT里会自动完成



Summary 总结

Reconstruction 重建	Create image and remove gross artefacts 创建图像并删除严重伪影
Motion Correction 运动矫正	Get consistent anatomical coordinates (always do this) 获取一致的解剖坐标（总是这样做）
Slice Timing 时间层校正	Get consistent acquisition timing (use temporal derivative instead) 获取一致的采集时间（改为使用时间导数）
Spatial Smoothing 空间滤波	Improve SNR & validate GRF 改善SNR并验证GRF
Temporal Filtering 时域滤波	Highpass: Remove *slow* drifts高通：去掉低频扰动 Lowpass: Avoid for autocorr est.低通：避免自相关
Intensity Normalisation 强度标准化	4D: Keeps overall signal mean constant across sessions 4D：所有session期间保持整体信号平均值不变