



# Resting state fMRI and ICA

## 静息态fMRI和ICA

- Resting state fMRI (静息态fMRI)
- Independent Component Analysis (ICA)  
(独立成分分析)
- Single-subject ICA clean-up (单样本ICA去噪)
- Multi-subject ICA and dual regression  
(多样本ICA和双回归)



# Resting state methods

## ICA

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- Multivariate voxel-based approach  
基于体素的多变量方法
- Finds interesting structure in the data  
寻找数据中的感兴趣结构
- Exploratory “model-free” method  
探索性的“无模型”方法
- Spatial approach  
空间维度

## Network modelling (网络建模)

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- Node-based approach (first need to parcellate the brain into functional regions)  
基于节点的方法（首先需要将大脑分为不同的功能区域）
- Map connections between specific brain regions (connectomics)  
特定脑区之间的连接图谱（连接组学）
- Temporal approach  
时间维度



# Resting state fMRI

静息态fMRI



# Model-based (GLM) analysis

## 基于模型 (GLM的) 分析

$$\text{Measured Signal} = \text{Signal Component} + \text{Noise}$$

The diagram illustrates the decomposition of a measured signal into its components. On the left, a vertical wavy line represents the 'Measured Signal'. An equals sign follows it. To the right of the equals sign is another vertical wavy line representing the 'Signal Component'. To the right of the signal component is a plus sign. To the right of the plus sign is a third vertical wavy line representing the 'Noise'.

- Model each measured time-series as a linear combination of signal and noise 将每个时间序列建模为信号和噪声的线性组合
- If the design matrix does not capture every signal, we typically get wrong inferences! 如果设计矩阵没有捕获每个信号, 我们通常会得到错误的推论



# Data Analysis

## Confirmatory 确定性的

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- “How well does my model fit to the data?”  
(我的模型与数据的匹配程度如何?)

Problem → Data →

Model → Analysis

→ Results

- results depend on the model  
结果取决于模型

## Exploratory 探索性的

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- “Is there anything interesting in the data?”  
(数据中有什么有趣的东西吗?)

Problem → Data →

Analysis → Model

→ Results

- can give unexpected results  
可以有预料之外的结果



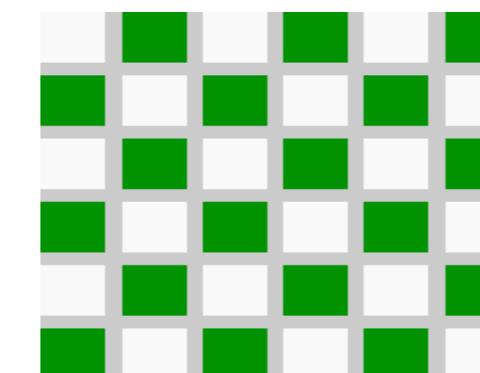
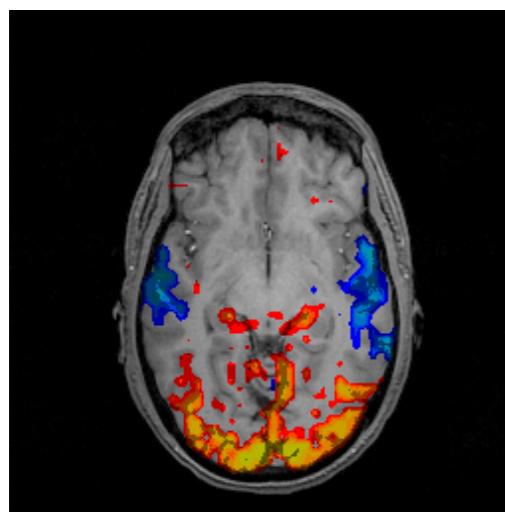
# FMRI inferential path

fMRI推论路径

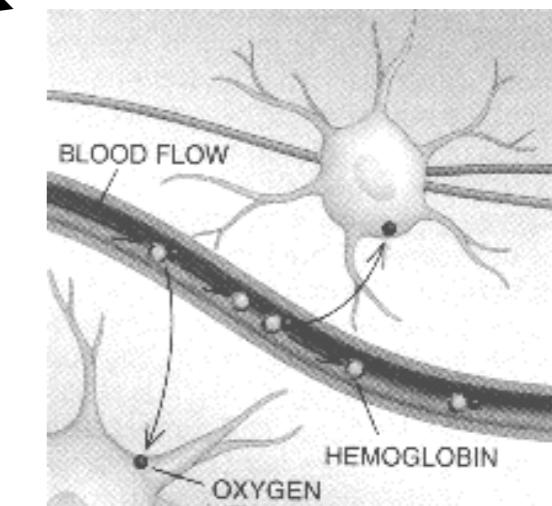
Experiment 实验

Interpretation  
of final results

解释最终结果



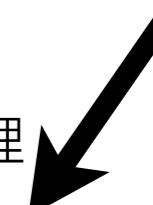
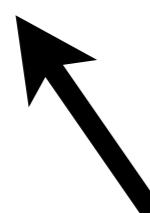
Physiology 生理



MR Physics MR物理



Analysis 分析

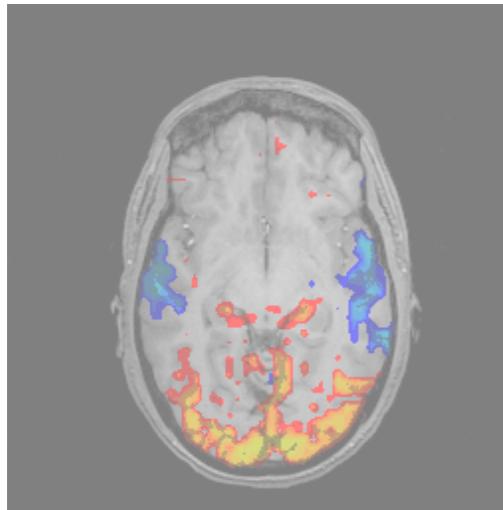


# Variability in fMRI

## fMRI的变异性 Experiment

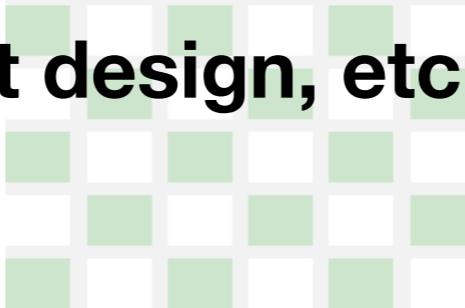
**suboptimal event timing,** 不适合的事件发生时间

Interpretation  
of final results



**filtering & sampling artefacts,  
design misspecification, stats &  
thresholding issues etc.**

滤波、采样伪影，design错误设定，统计和阈值问题等



**secondary activation, ill-defined baseline, resting-fluctuations etc.**

次级激活，基线不明确，静息波动等

MR Physics

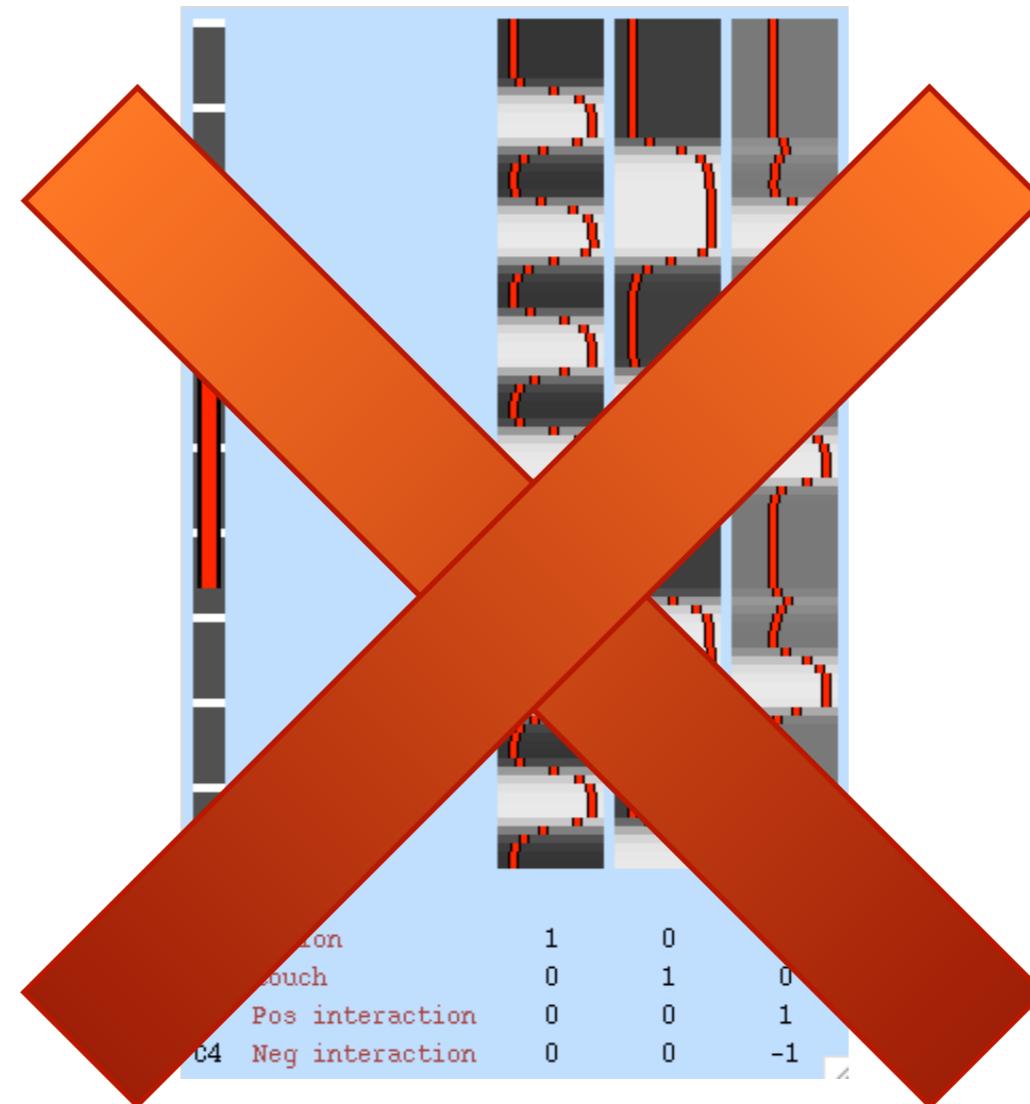
**MR noise, MR 噪声**

**field inhomogeneity, 磁场不均匀  
MR artefacts etc. MR 伪影等**

# Independent Component Analysis

独立成分分析

# Model-free? 无模型?



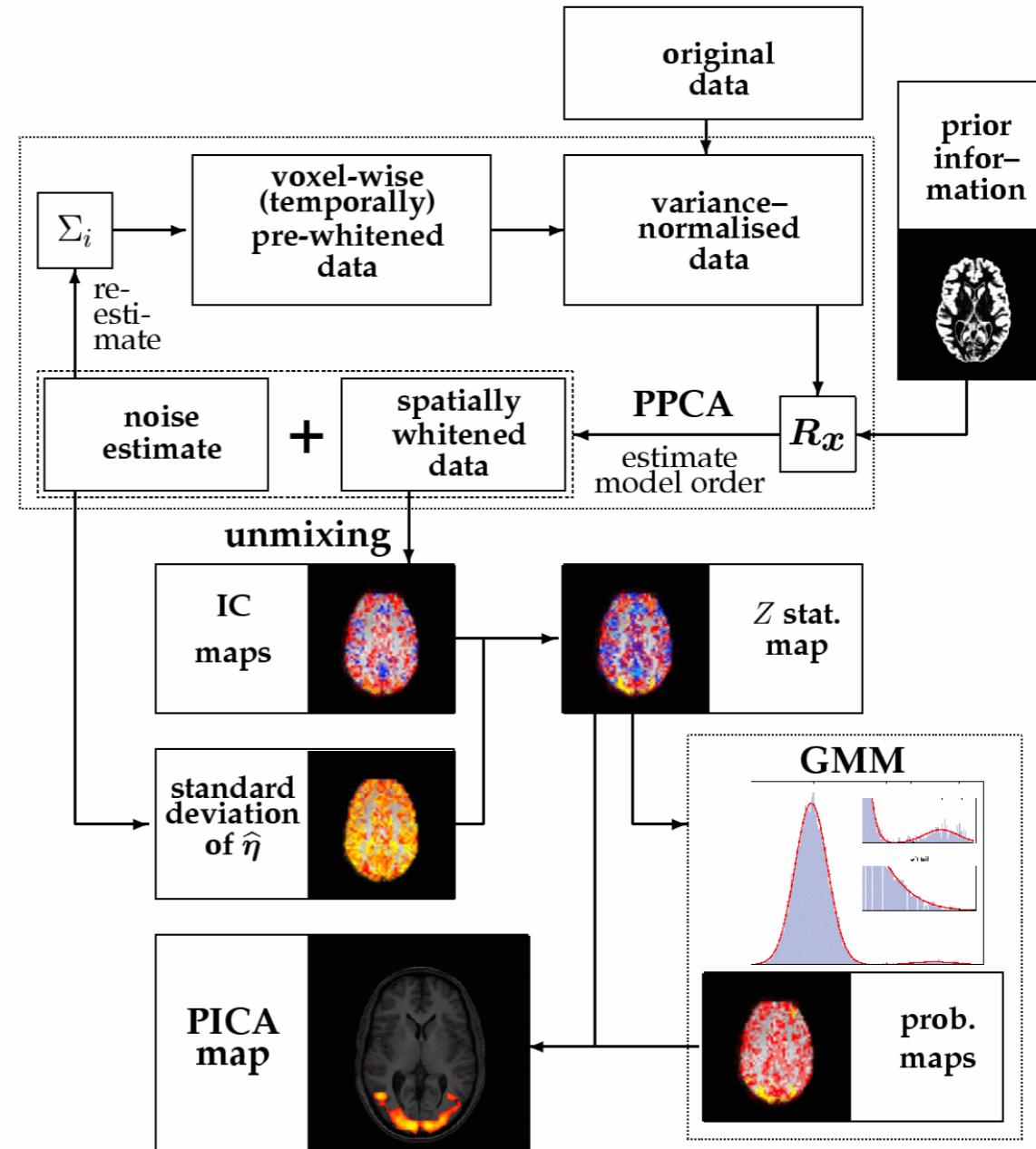
There is no explicit time-series model of assumed ‘activity’  
没有明确的假设“激活”的时间序列模型



# Model-free? 无模型?



$$Y^i = S^i A^i + E^i, \quad \text{where} \quad E_{j,j}^i \sim \mathcal{N}(0, \sigma_Y^2 I)$$



There is an underlying mathematical  
(generative) model  
潜在的数学 (生成) 模型

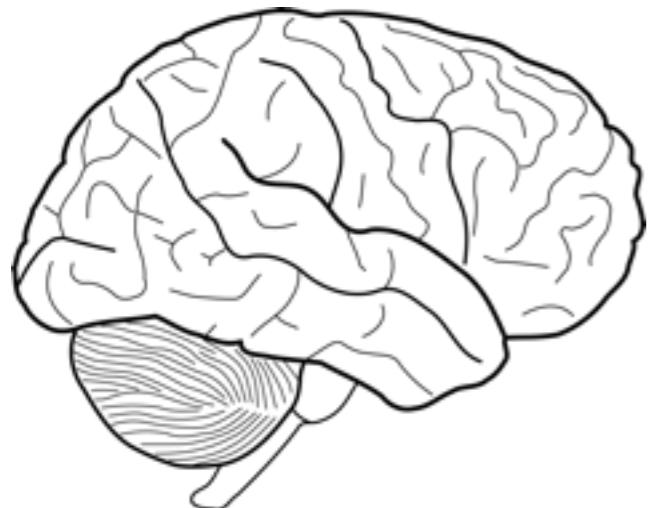


# Decomposition techniques 分解技术

- try to ‘explain’ / represent the data (试着解释或表示数据)
- by calculating quantities that summarise the data  
通过计算汇总数据的数量
- by extracting underlying ‘hidden’ features that are ‘interesting’ 通过提取“有趣”的潜在“隐藏”特征
- differ in what is considered ‘interesting’ “有趣”的定义不同
- are localised in time and/or space (Clustering)  
聚焦于时间和/或空间 (聚类分析)
- explain observed data variance (PCA, FDA, FA)  
解释观察到的数据差异
- are maximally independent (ICA)最大程度的独立成分

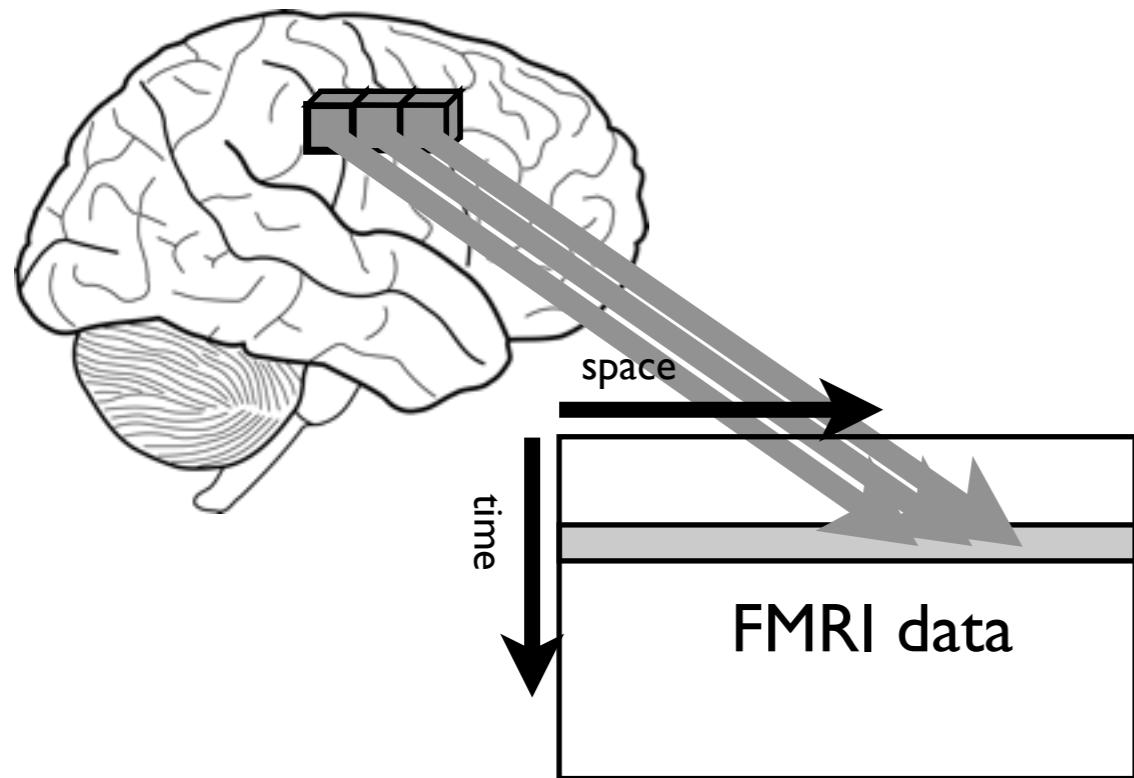
# Melodic

multivariate linear decomposition: 多元线性分解



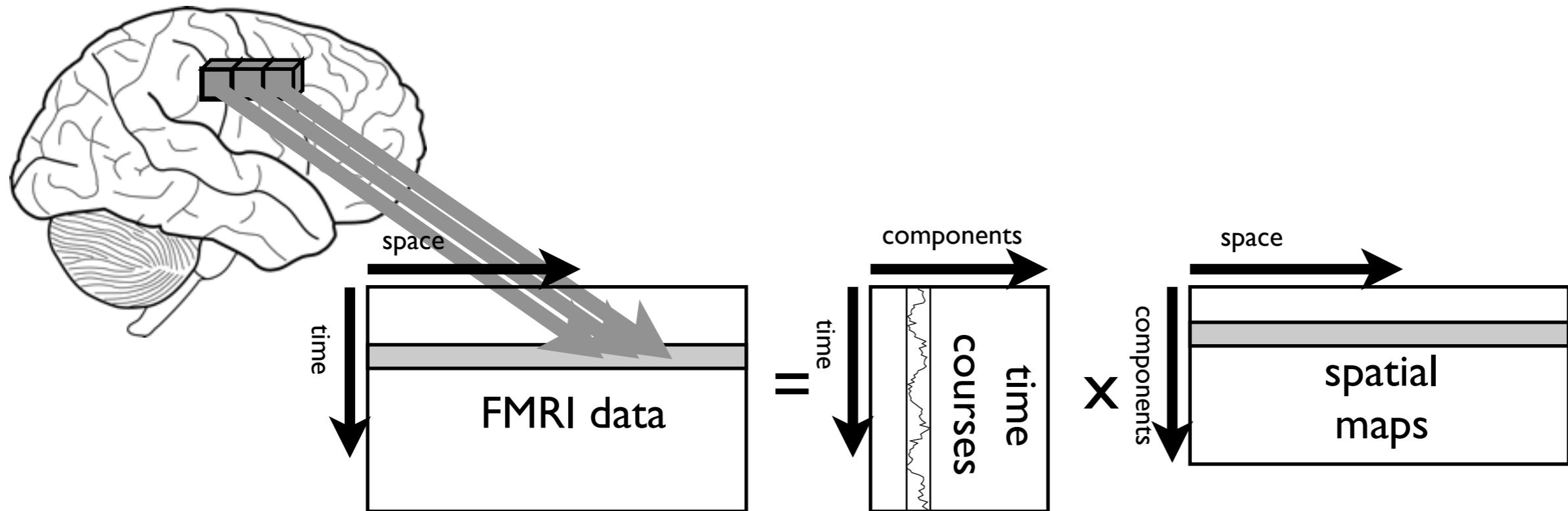
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multivariate linear decomposition: 多元线性分解



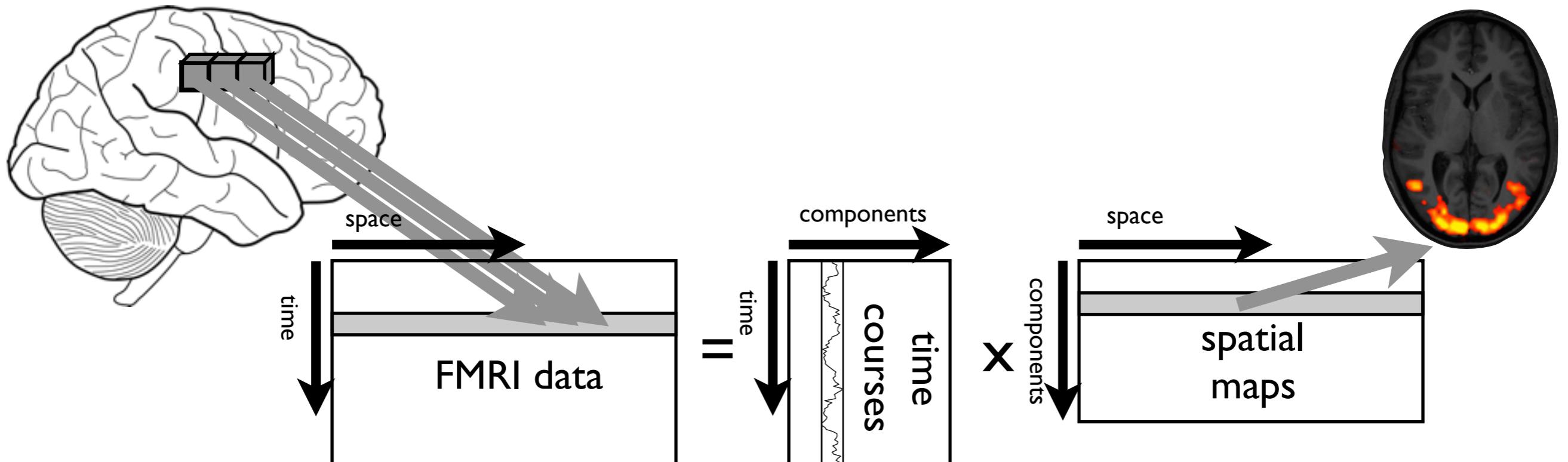
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multivariate linear decomposition: 多元线性分解



# Melodic

multivariate linear decomposition: 多元线性分解



Data is represented as a 2D matrix and  
decomposed into components

数据被转化为2维矩阵并分解成不同成分

# Melodic

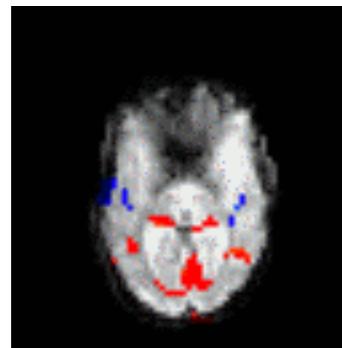
multivariate linear decomposition: 多元线性分解



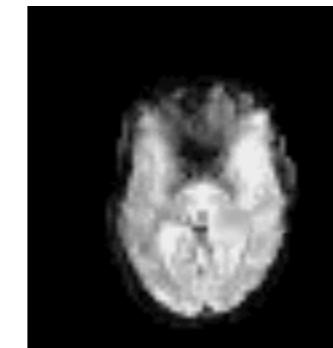
Data is represented as a 2D matrix and  
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数据被转化为2维矩阵并分解成不同成分

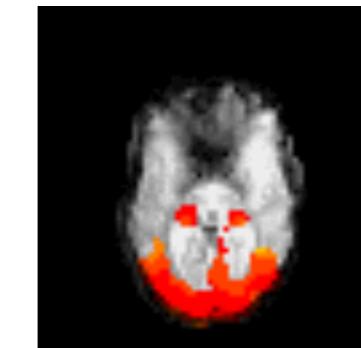
# What are components? 什么是成分?



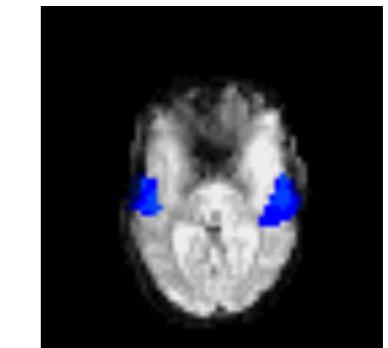
$\approx$



+



+



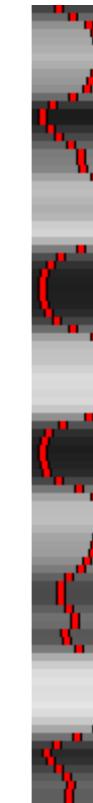
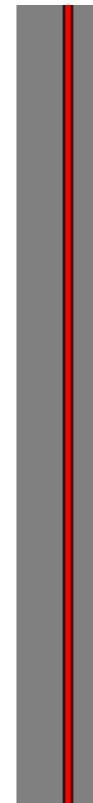
$\times$

$\times$

$\times$

- express observed data as linear combination of spatio-temporal processes

通过线性组合时-空加工过程表达观察到的数据



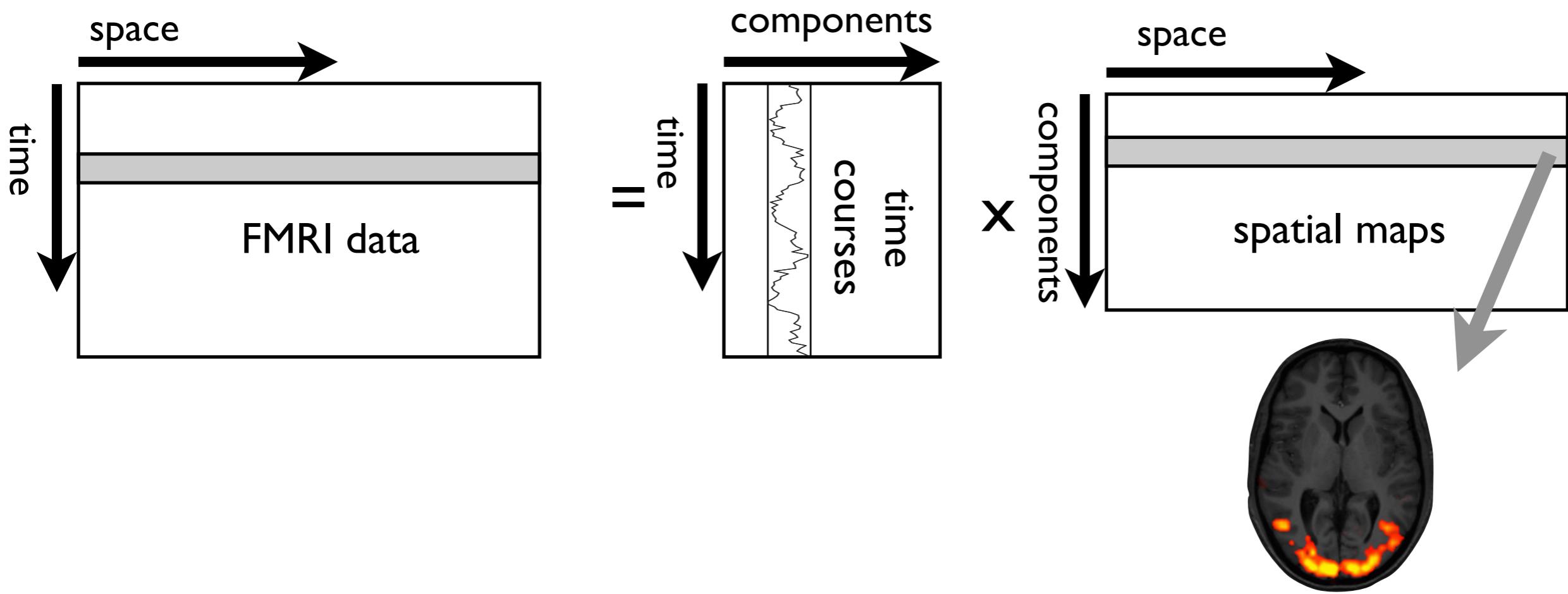
- techniques differ in the way data is represented by components

技术差异阻碍了通过成分代表数



# Spatial ICA for fMRI

fMRI的空间ICA



- data is decomposed into a set of **spatially independent** maps and a set of time-courses

数据被分解成一组空间独立的图像和一组时间序列



McKeown et al.  
HBM 1998

# Independence

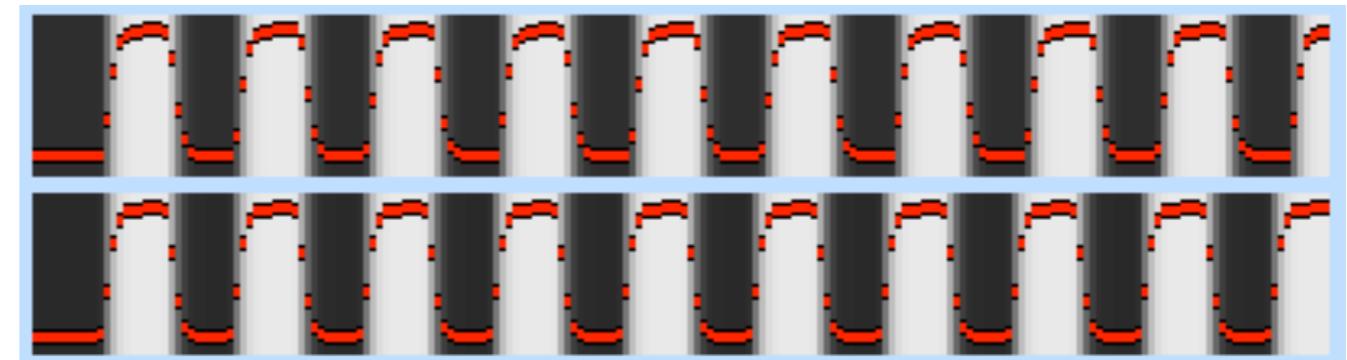
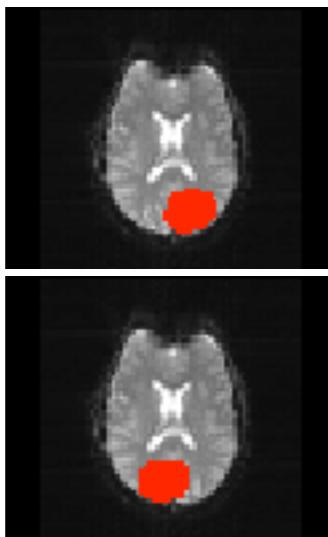
独立成分



# PCA vs. ICA ?

Simulated  
Data  
模拟数据

(2 components, slightly  
different time courses)  
2个成分，时间序列略有不同



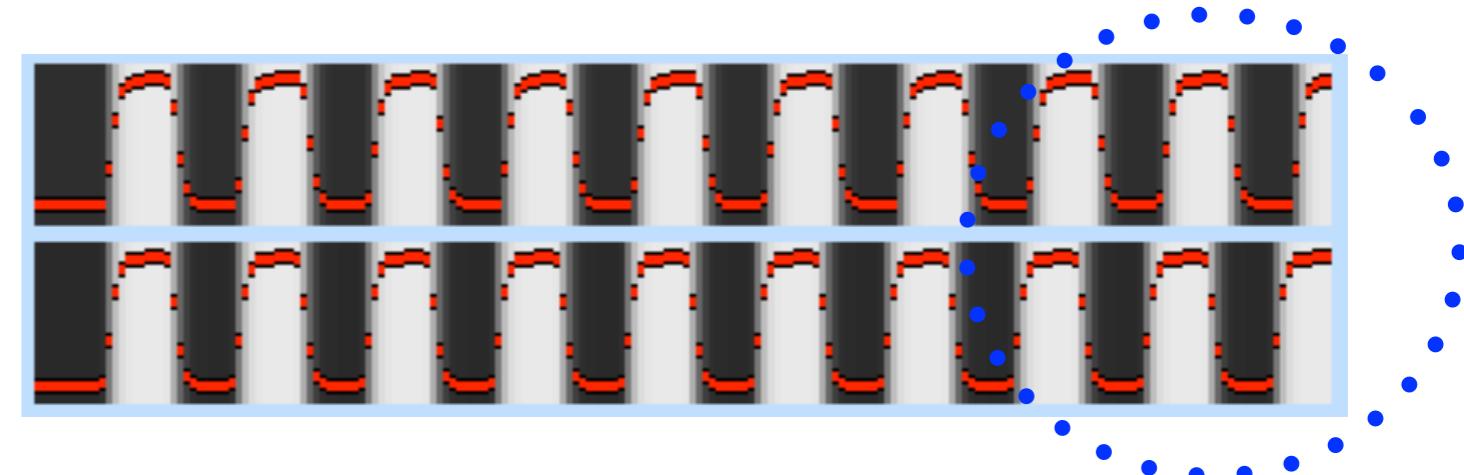
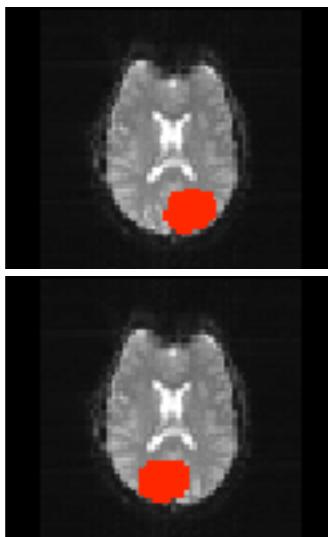


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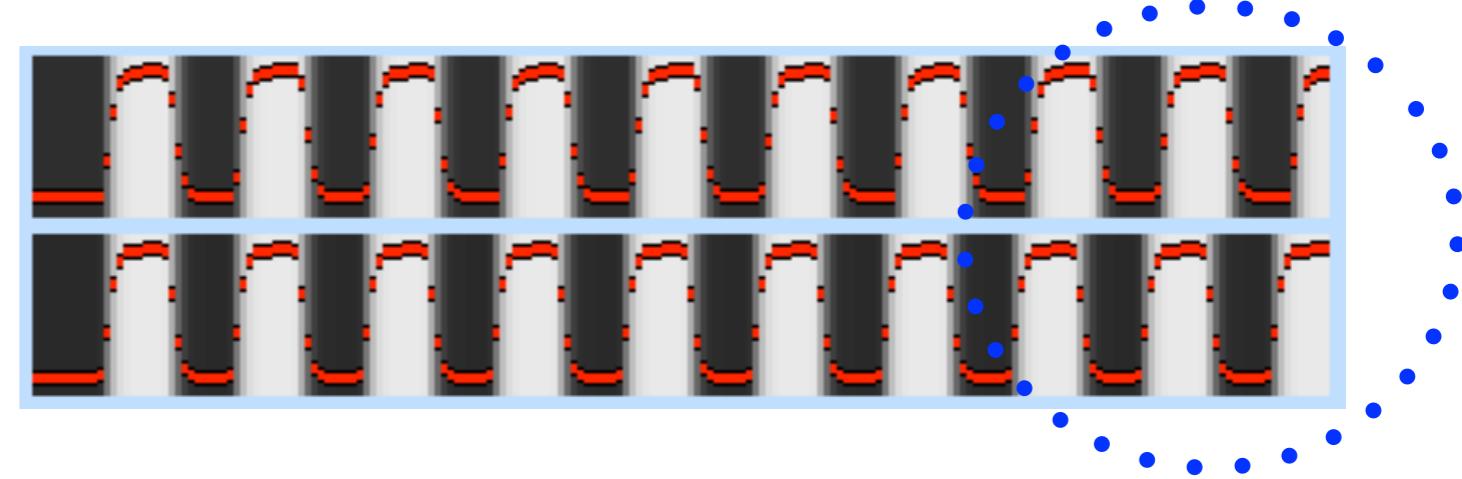
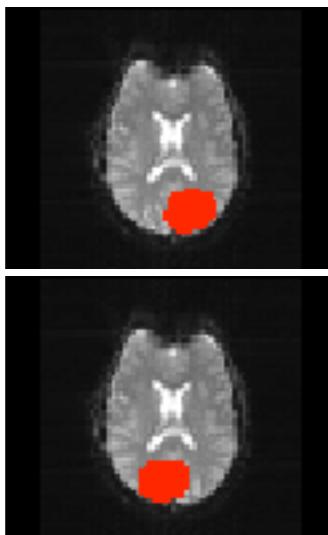




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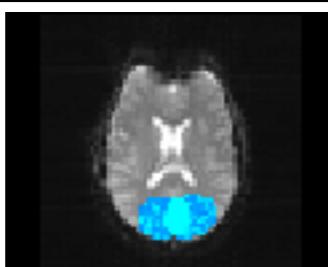


PCA

- Timecourses

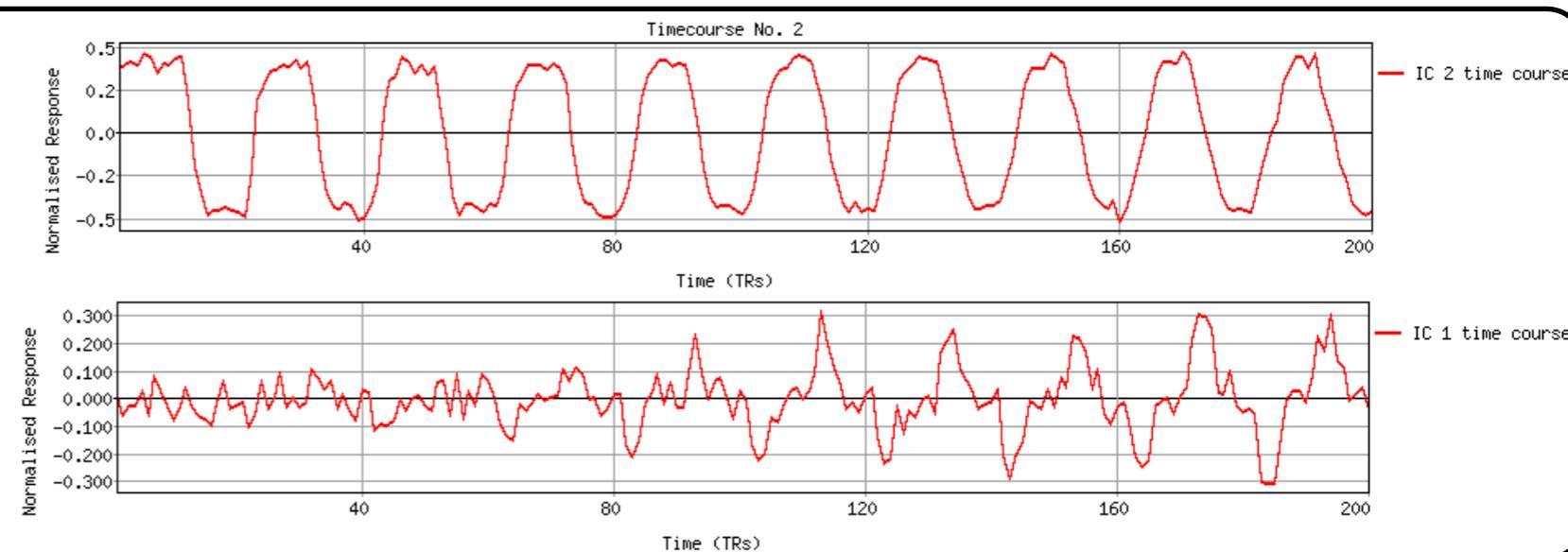
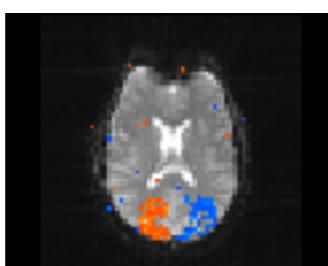
orthogonal

时间序列正交



- Spatial maps and  
timecourses

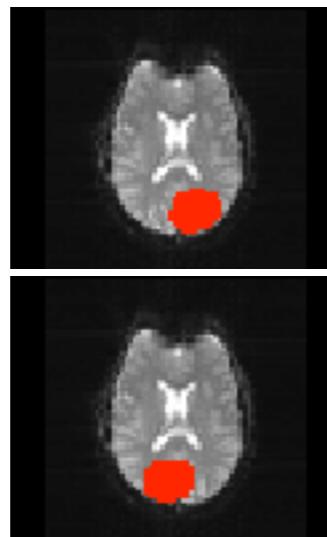
“wrong” 空间图像和时  
间序列有差



# PCA vs. ICA ?

## Simulated Data 模拟数据

(2 components, slightly different time courses)  
2个成分，时间序列略有不同



## PCA

- Timecourses

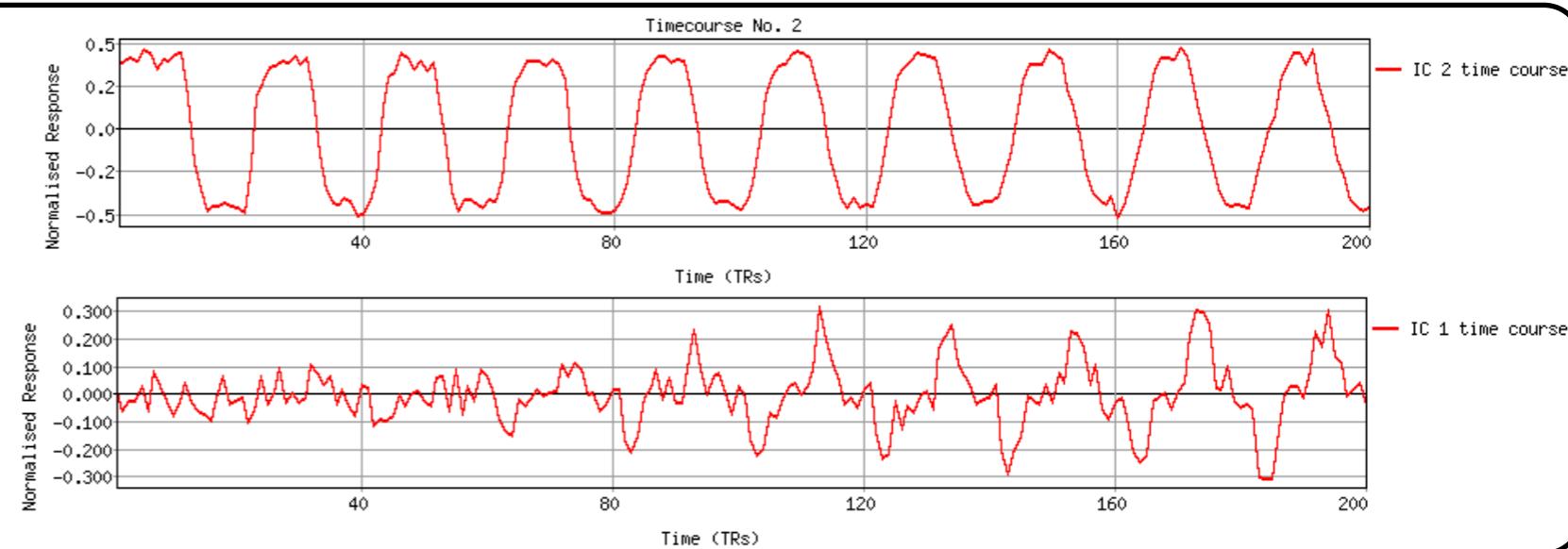
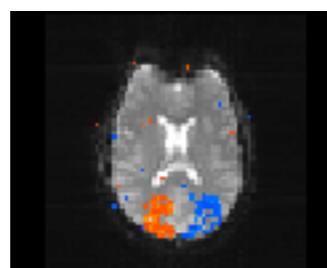
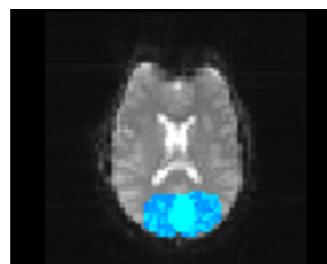
orthogonal

时间序列正交

- Spatial maps and timecourses

“wrong” 空间图像和时

间序列有差



## ICA

- Timecourses

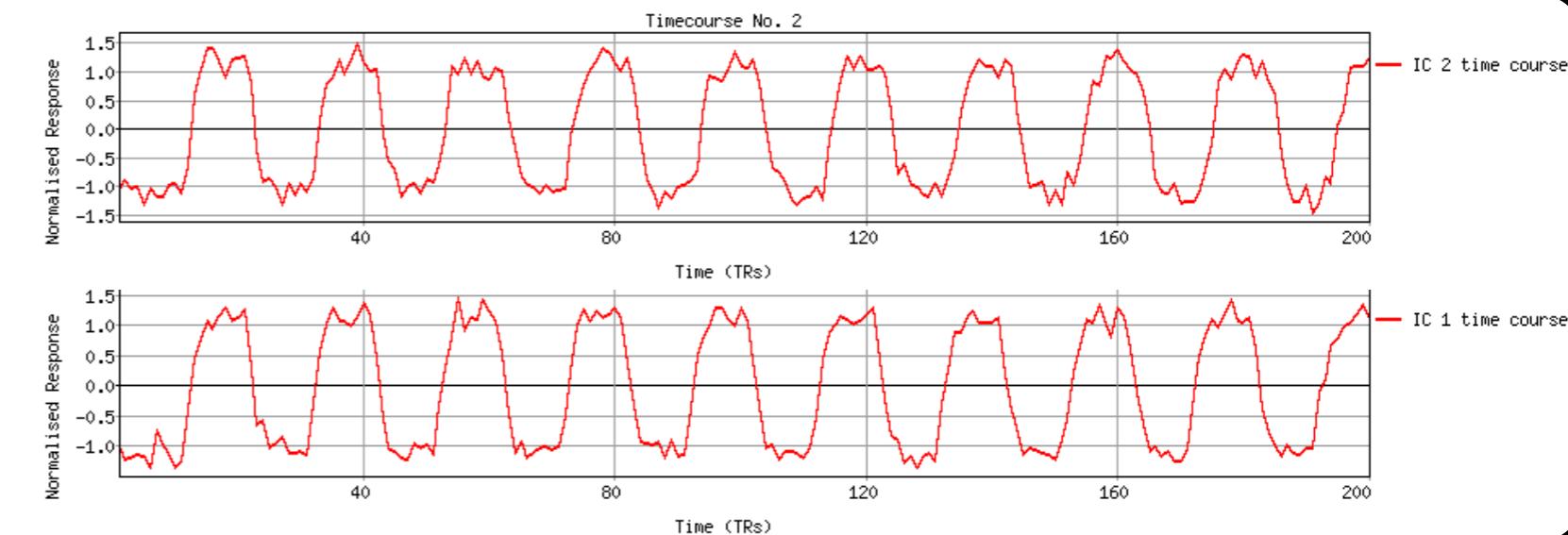
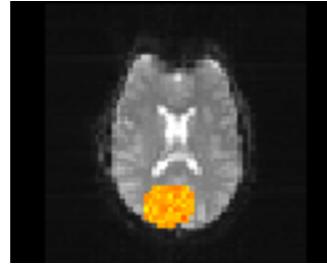
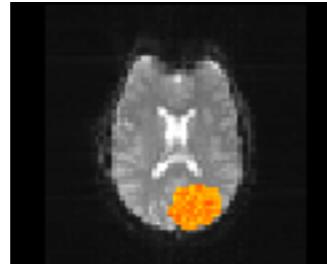
non-co-linear

时间序列非线性

- Spatial maps and timecourses

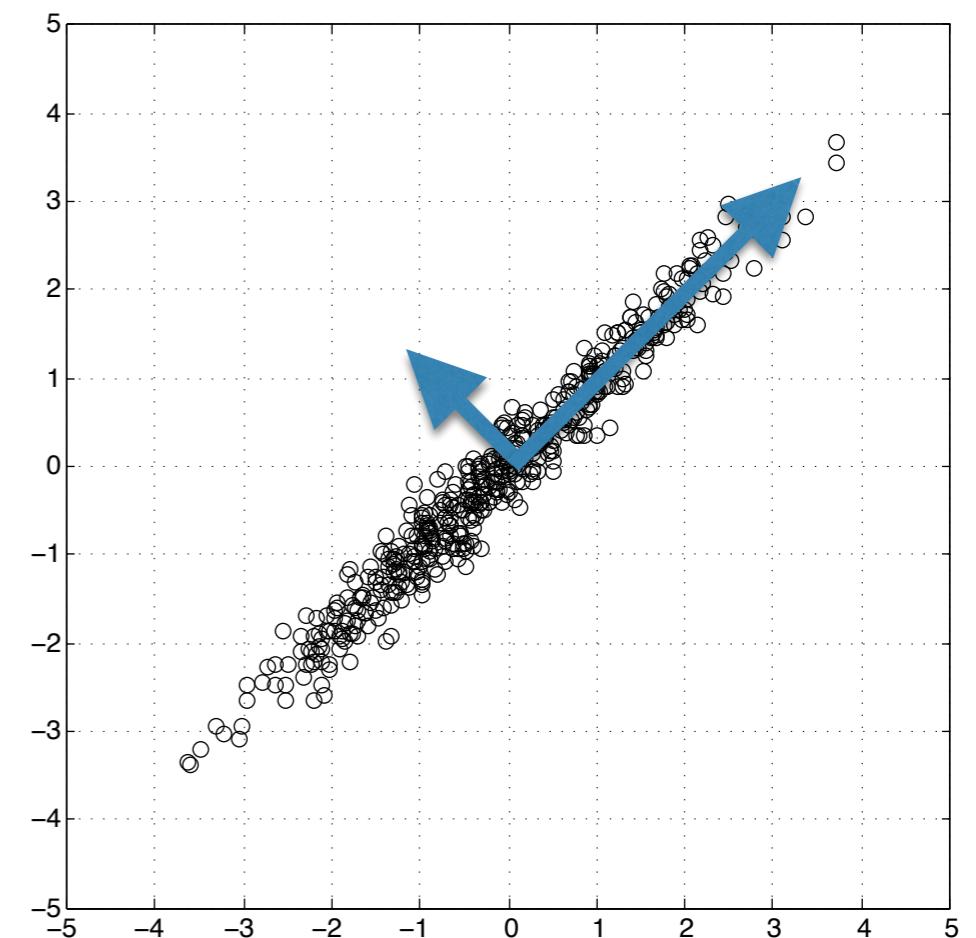
“right” 空间图像和时间

序列相对应



# PCA vs. ICA

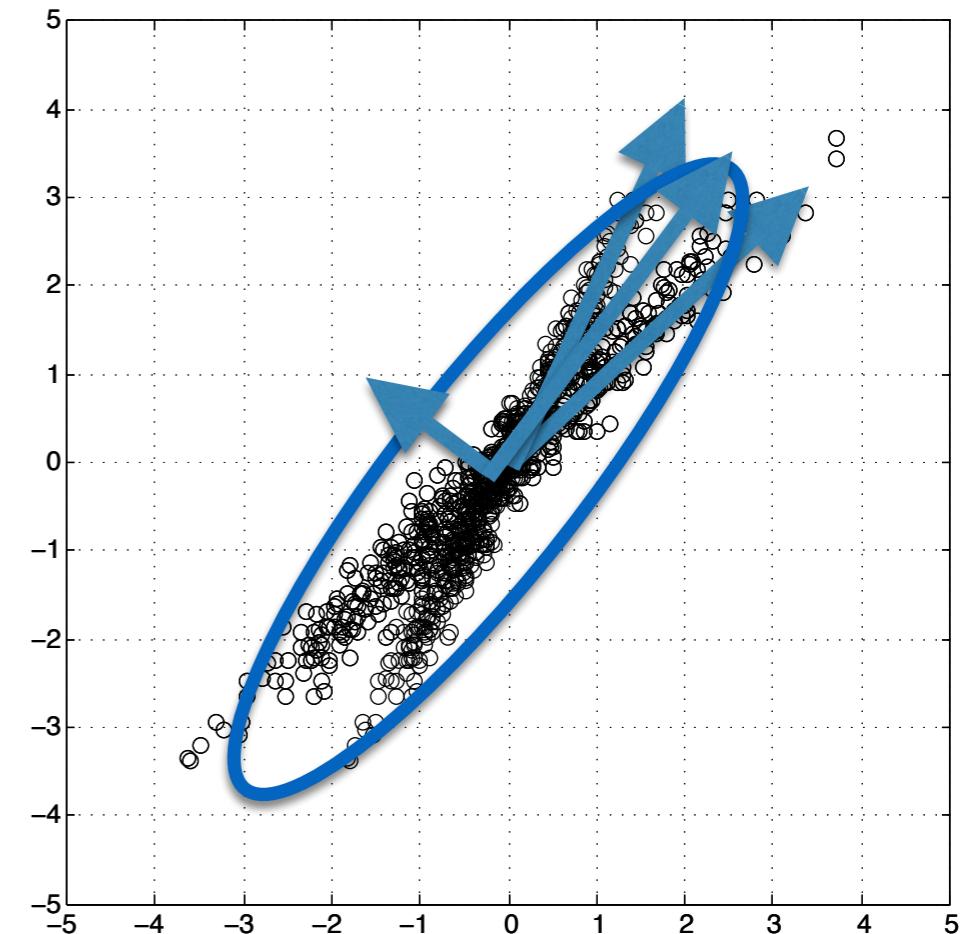
- PCA finds projections of maximum amount of variance in Gaussian data (uses 2nd order statistics only)  
PCA 在高斯数据中寻找最多方差值的投射 (仅使用二阶统计)



Gaussian data

# PCA vs. ICA

- PCA finds projections of maximum amount of variance in Gaussian data (uses 2nd order statistics only)
- Independent Component Analysis (ICA) finds projections of maximal independence in non-Gaussian data (using higher-order statistics)  
独立成分分析 (ICA) 在非正态数据中寻找最大程度独立的投射 (使用高阶统计数据)



non-Gaussian  
data

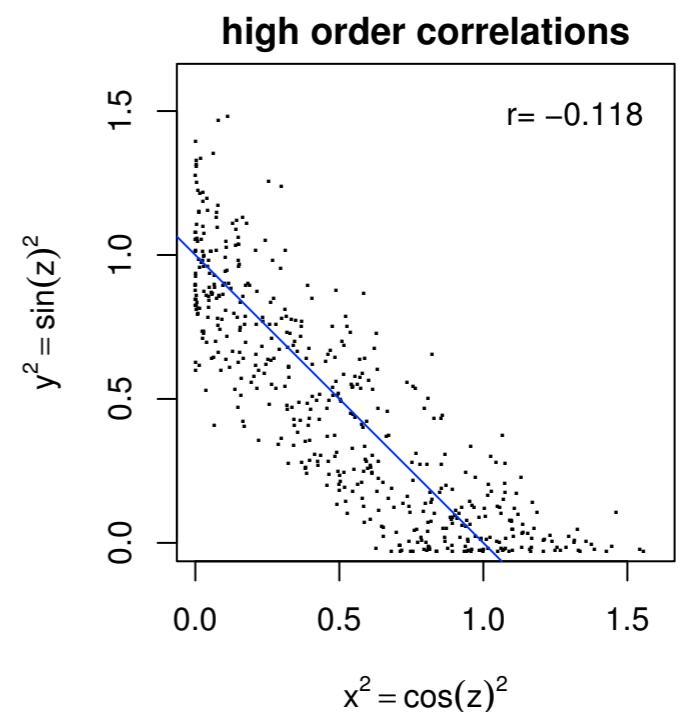
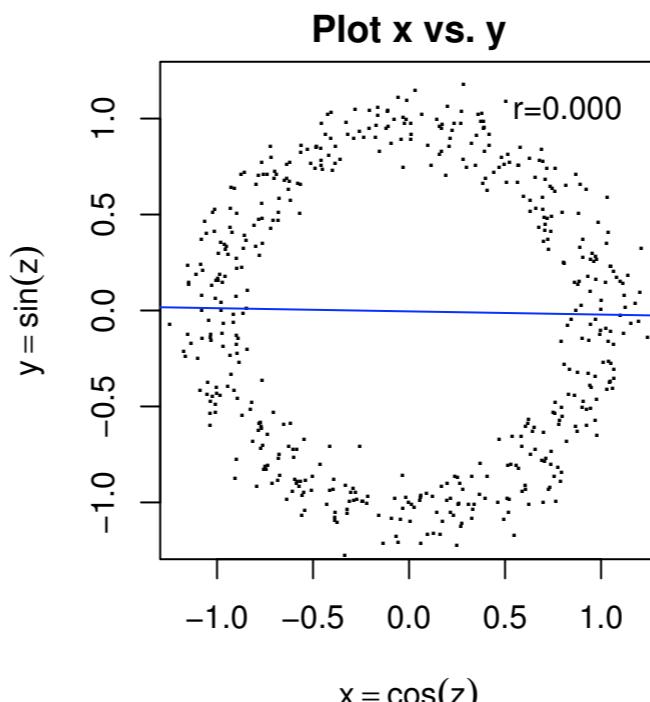
# Correlation vs. independence

相关与独立性

- de-correlated signals can still be dependent  
不相关的成分也可能是非独立的
- higher-order statistics (beyond mean and variance) can reveal these dependencies  
高阶统计信息（超出平均值和方差）可以揭示这些依赖关系



- Stone et al. 2002





# Non-Gaussianity 非正态的



sources

源

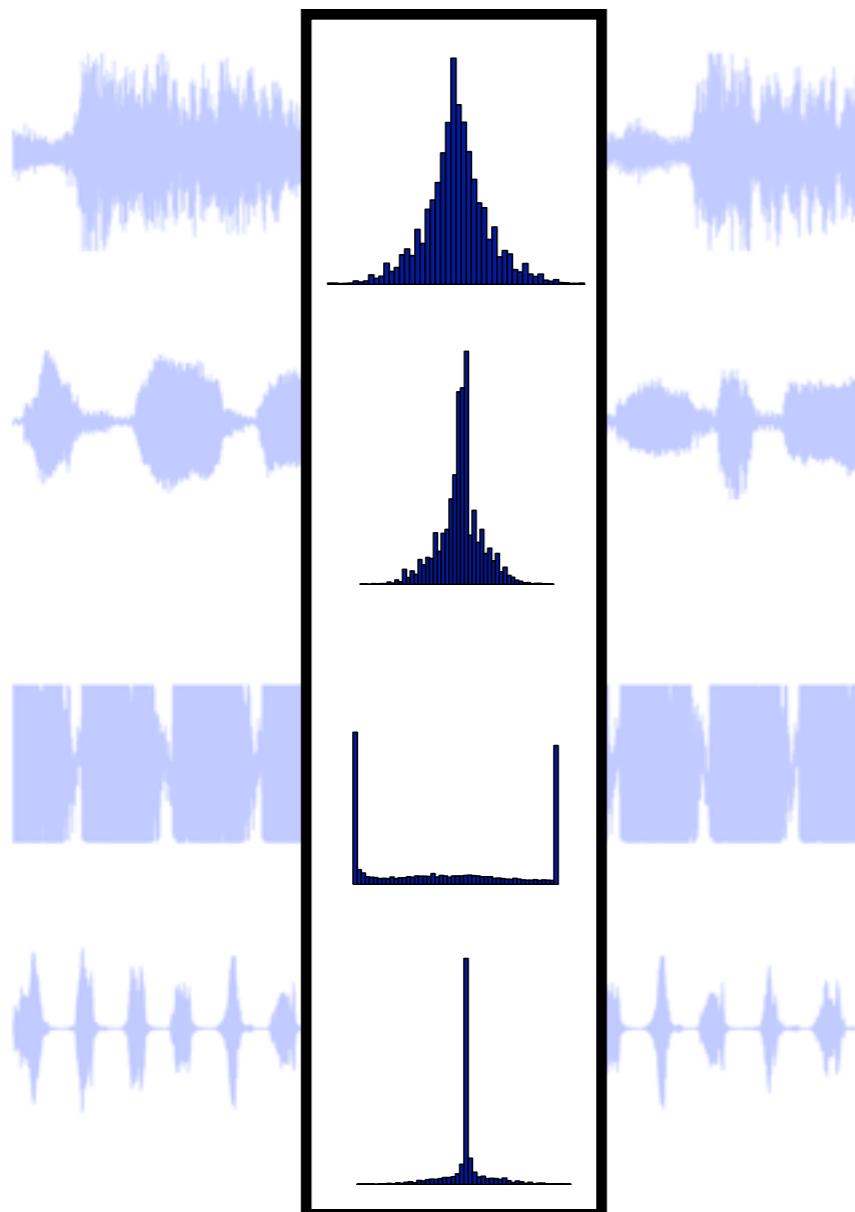


mixtures

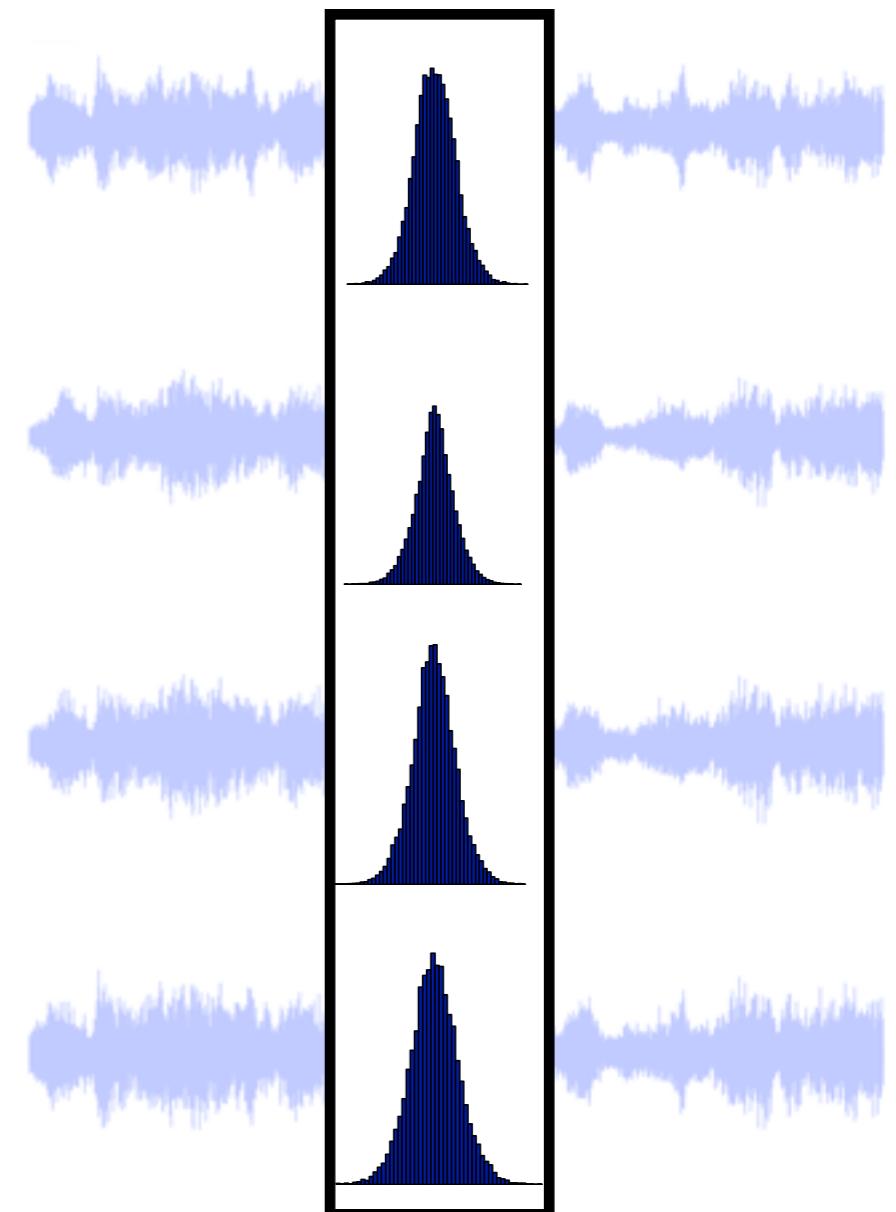
混合后



# Non-Gaussianity



non-Gaussian  
非正态



Gaussian  
正态



# ICA estimation

- Random mixing results in more Gaussian-shaped PDFs (Central Limit Theorem)  
随机混合产生更多高斯形状的概率密度方程分布 (中央极限定理)
- conversely: 相反  
if mixing matrix produces less Gaussian-shaped PDFs this is unlikely to be a random result  
如果混合矩阵产生的高斯形概率密度较少, 那这不太可能是随机的结果  
→ measure non-Gaussianity 测量非正态性
- can use neg-entropy as a measure of non-Gaussianity 可以用负熵作为非正态性的度量指标





# ICA estimation

- need to find an **unmixing matrix** such that the dependency between estimated sources is minimised  
需要找到一个与估计来源依赖关系最低的无混合矩阵
- need (i) a **contrast (objective/cost) function** to drive the unmixing which measures statistical independence and (ii) an **optimisation technique**:  
需要： (i) 对比（目标/成本）功能来驱动测量统计独立性的解码过程 (ii) 优化的技术
- kurtosis or cumulants & gradient descent (**Jade**)  
峰度或累积量&梯度下降
- maximum entropy & gradient descent (**Infomax**)  
最大熵 &梯度下降
- neg-entropy & fixed point iteration (**FastICA**)  
负熵 &定点迭代

# Overfitting & thresholding

过度拟合 & 阈值



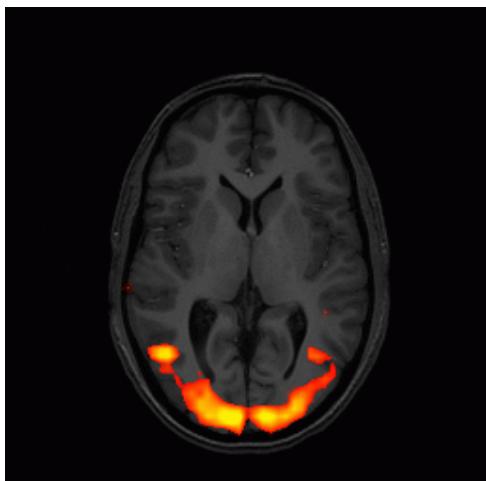
# The ‘overfitting’ problem

过度拟合问题

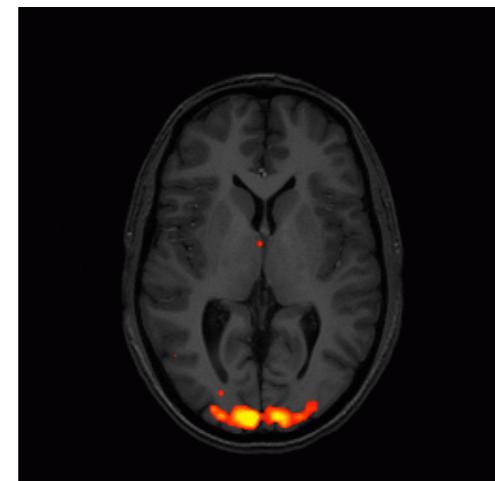
fitting a noise-free model to noisy observations:

将无噪声模型拟合到噪声观测结果：

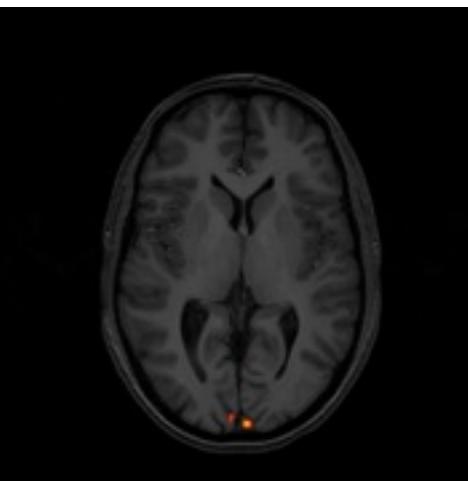
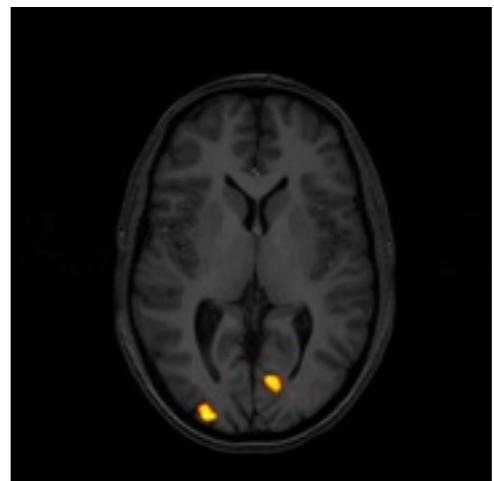
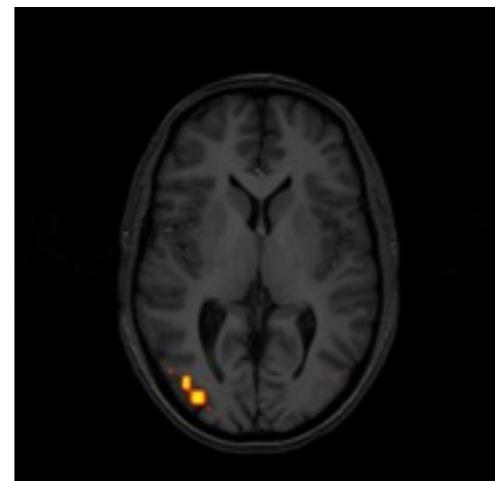
- no control over signal vs. noise (non-interpretable results)  
对信号与噪声没有控制 (不可解释的结果)
- statistical significance testing not possible  
无法进行统计显著性测试



GLM analysis



standard ICA (unconstrained)

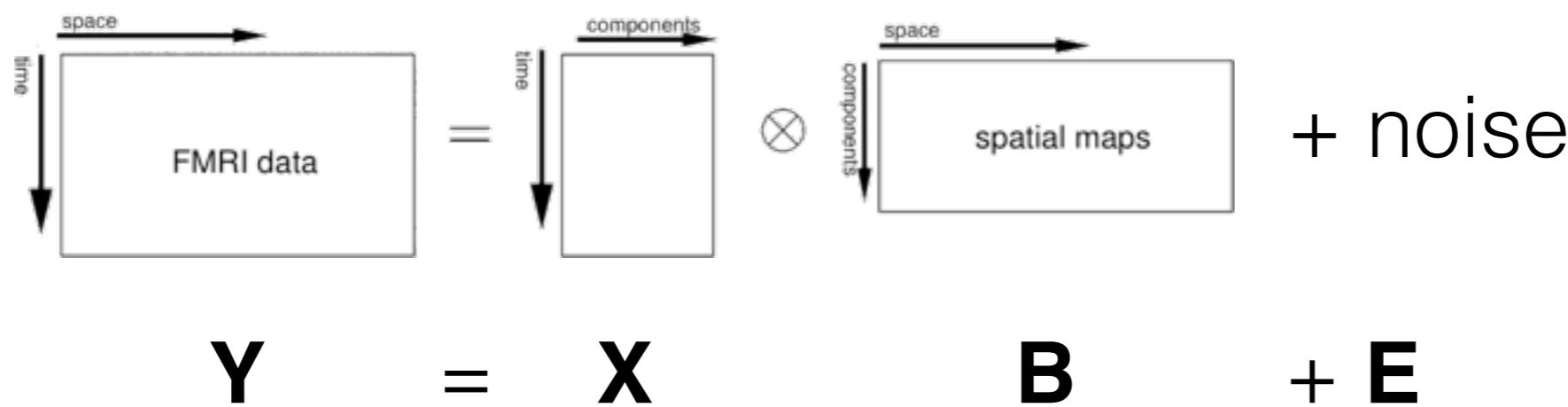




# Probabilistic ICA model

概率 ICA 模型

statistical “latent variables” model: we observe linear mixtures of hidden sources in the presence of Gaussian noise  
统计“潜变量”模型：在高斯噪声存在的情况下，我们观察到隐藏源的线性混合物

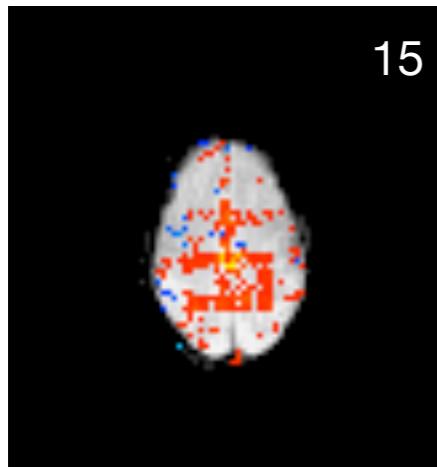


Issues:

- Model Order Selection: how many components?  
模型选择：多少个成分合适?
- Inference: how to threshold ICs? 如何为独立成分设置阈值?

# Model Order Selection

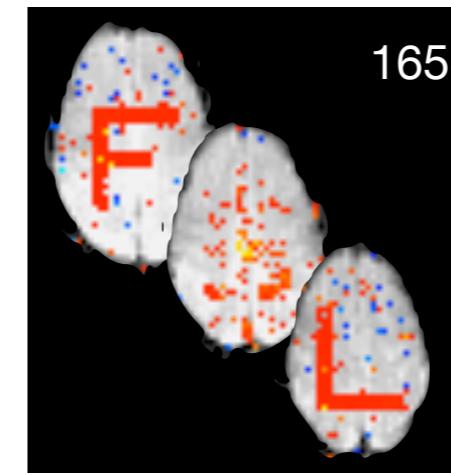
‘How many components’?



15

*under-fitting:* the amount of explained data variance is insufficient to obtain good estimates of the signals

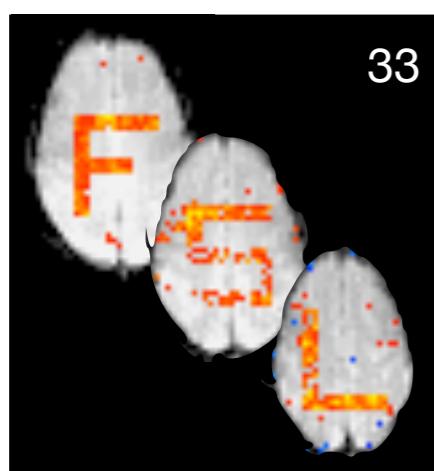
拟合不足：解释的数据方差量不足以获得信号的良好估计值



165

*over-fitting:* the inclusion of too many components leads to fragmentation of signal across multiple component maps, reducing the ability to identify the signals of interest

过度拟合：包含太多成分会导致多个成分对应信号碎片化，降低识别感兴趣信号的能力

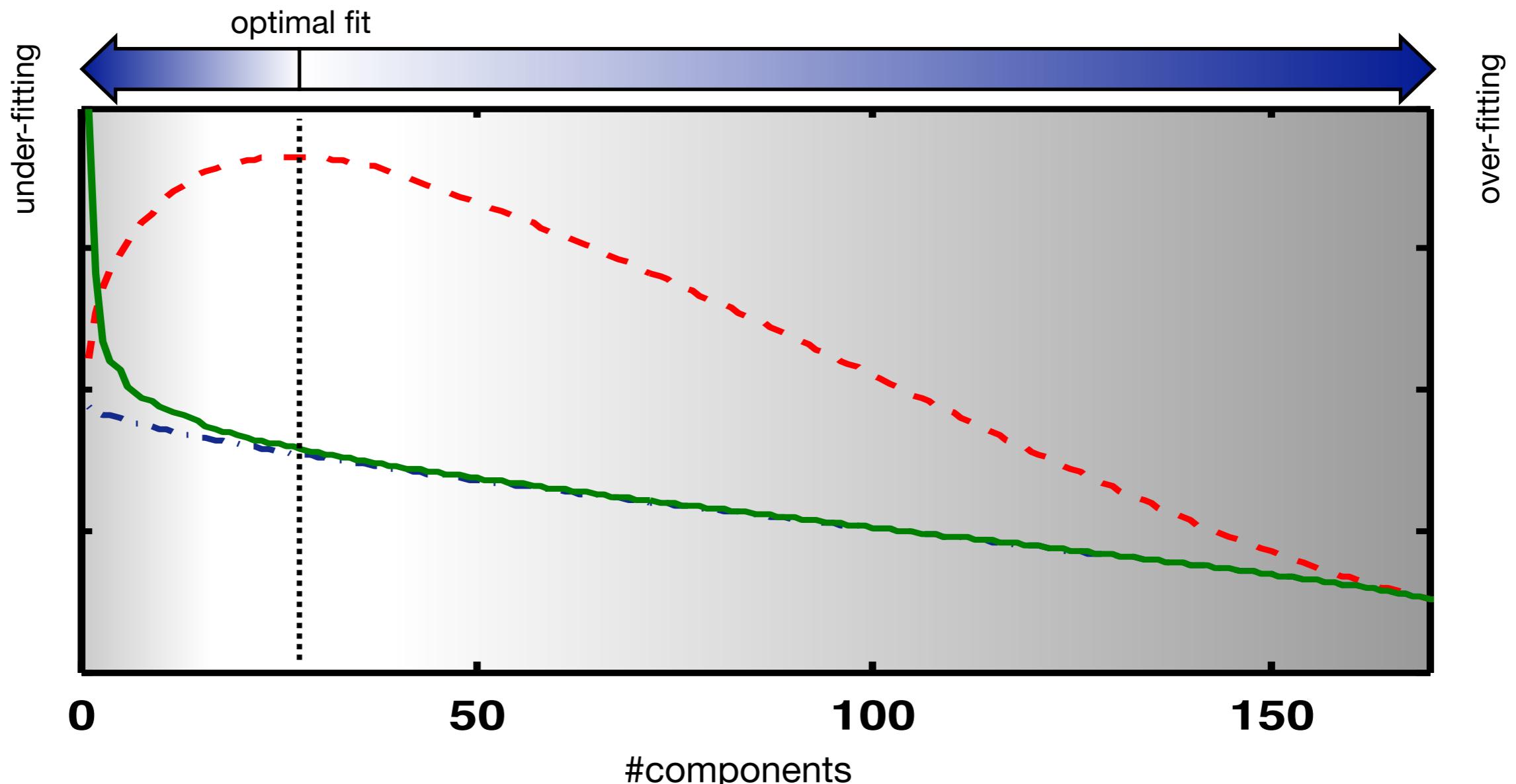


33

*optimal fitting:* the amount of explained data variance is sufficient to obtain good estimates of the signals while preventing further splits into spurious components

最佳拟合：解释的数据方差数量足以获得信号的良好估计值，同时防止进一步拆分无用成分

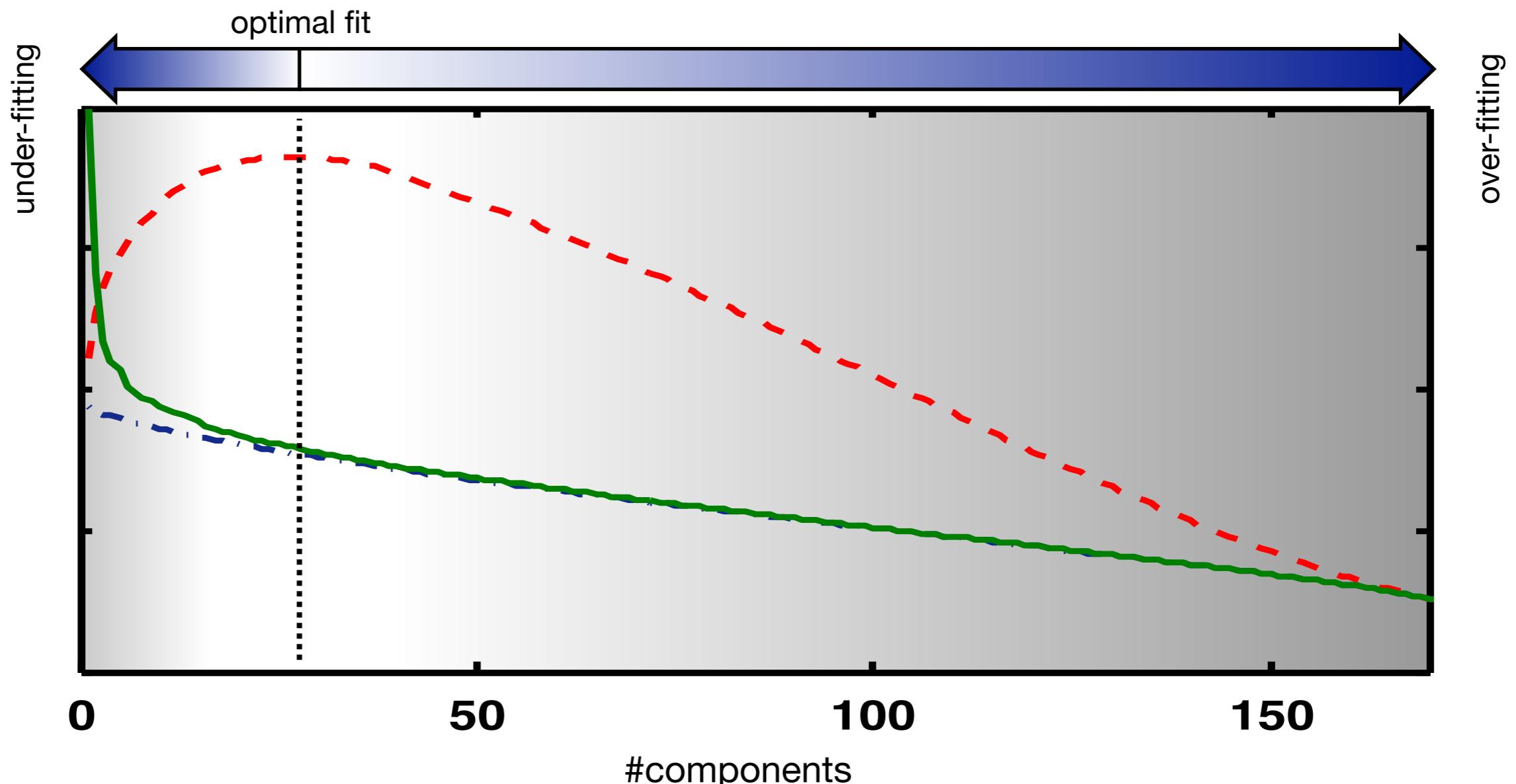
# Model Order Selection



- observed Eigenspectrum of the data covariance matrix
- - - Laplace approximation of the posterior probability of the model order
- · - theoretical Eigenspectrum from Gaussian noise

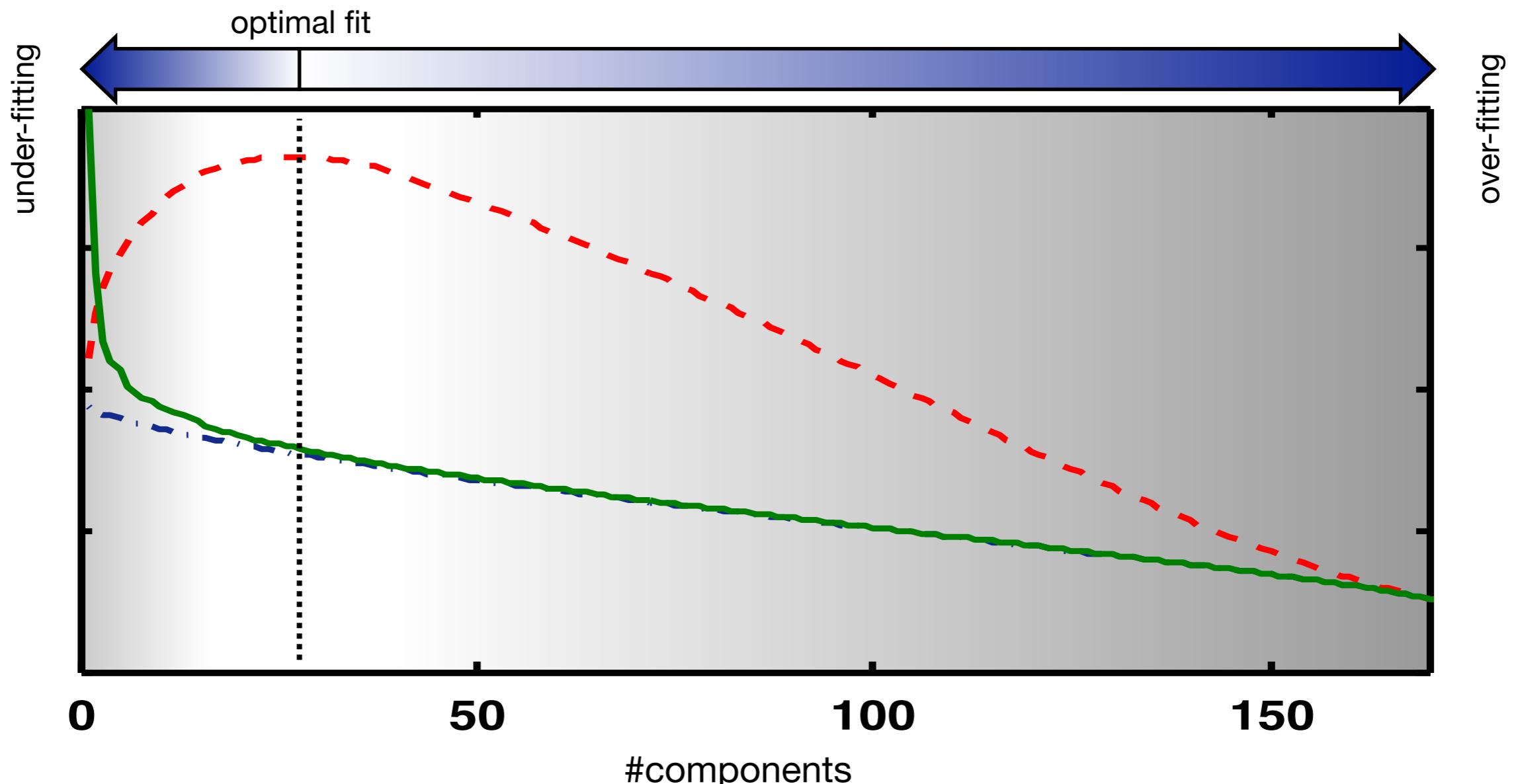


# Model Order Selection



- observed Eigenspectrum of the data covariance matrix
- - - Laplace approximation of the posterior probability of the model order
- · - theoretical Eigenspectrum from Gaussian noise

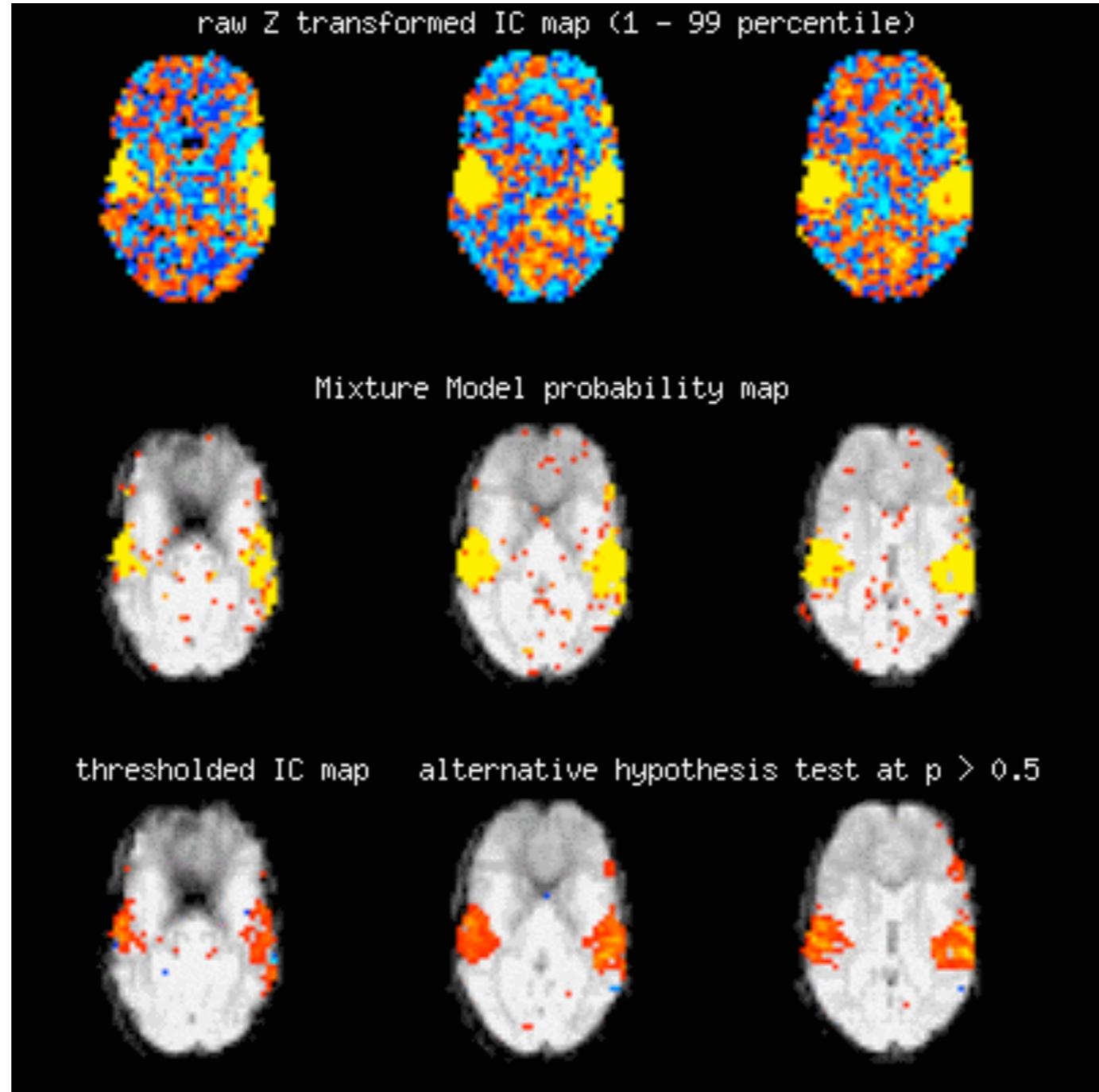
# Model Order Selection



- observed Eigenspectrum of the data covariance matrix
- - - Laplace approximation of the posterior probability of the model order
- · - theoretical Eigenspectrum from Gaussian noise

# Thresholding

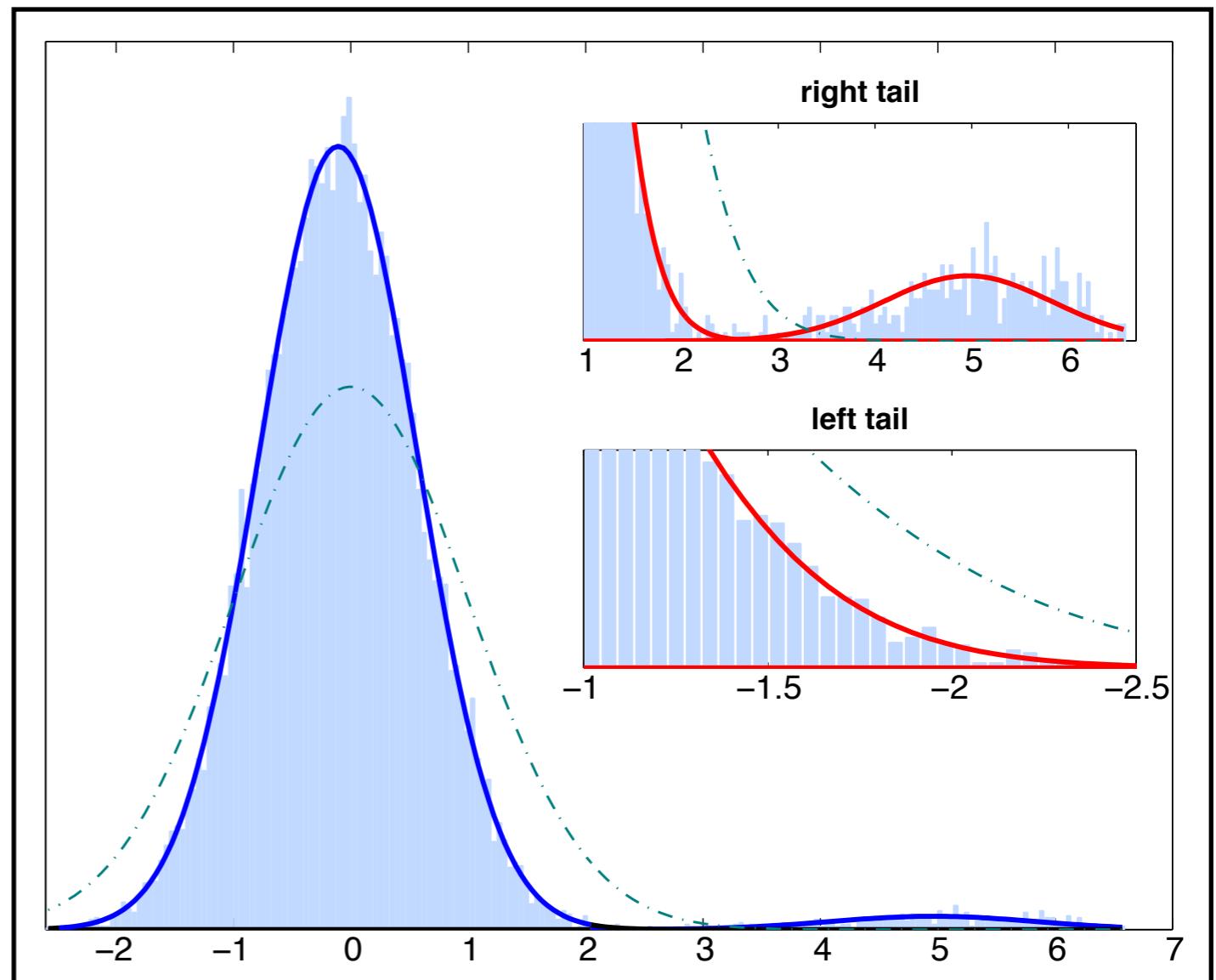
## 设阈值



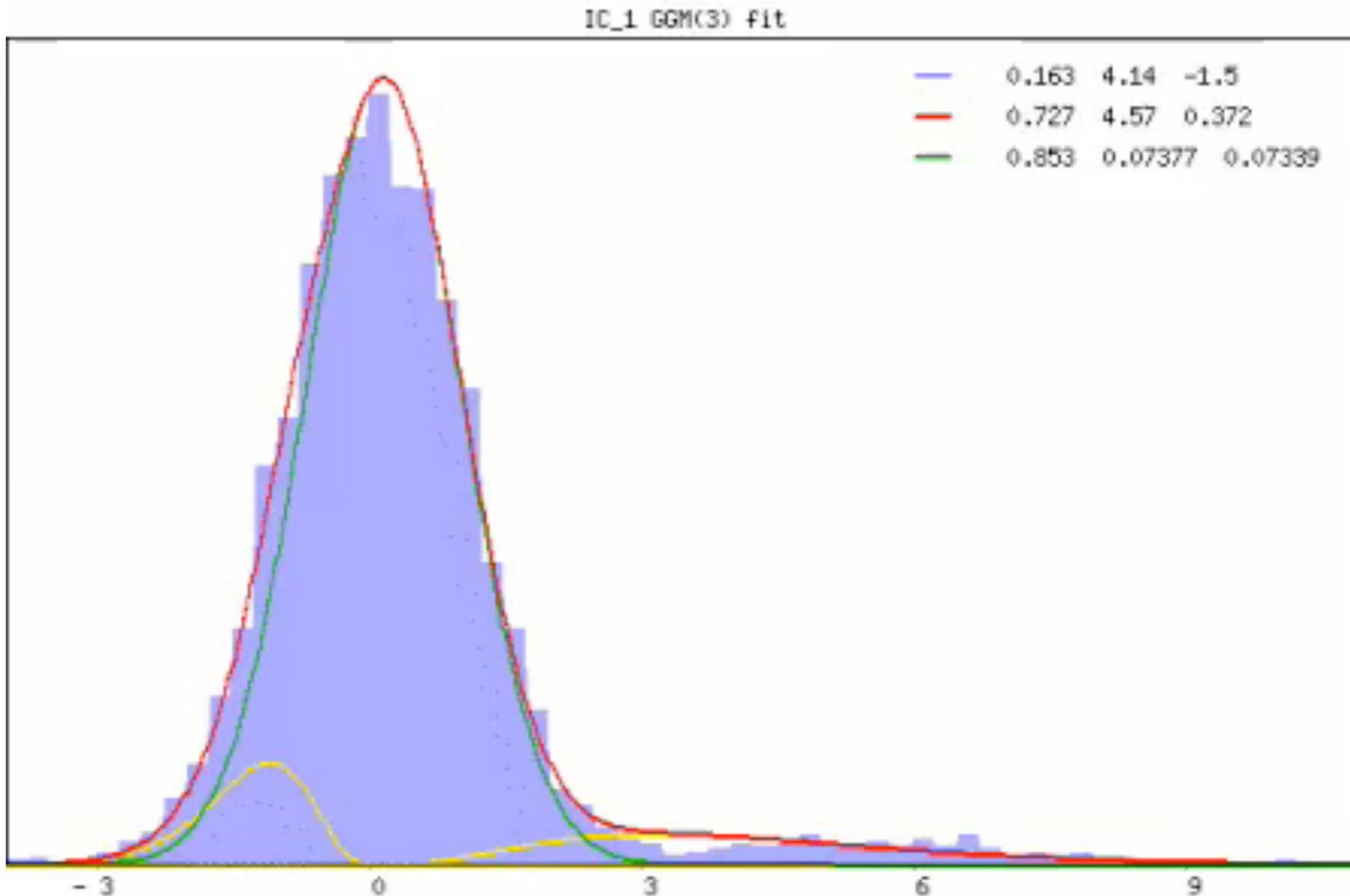
# Thresholding

设阈值

- classical null-hypothesis testing is invalid  
经典的零假设检验无效
- data is assumed to be a linear combination of signals and noise  
数据被假定为信号和噪声的线性组合
- the distribution of the estimated spatial maps is a mixture distribution!  
估计空间图像的分布是混合分布



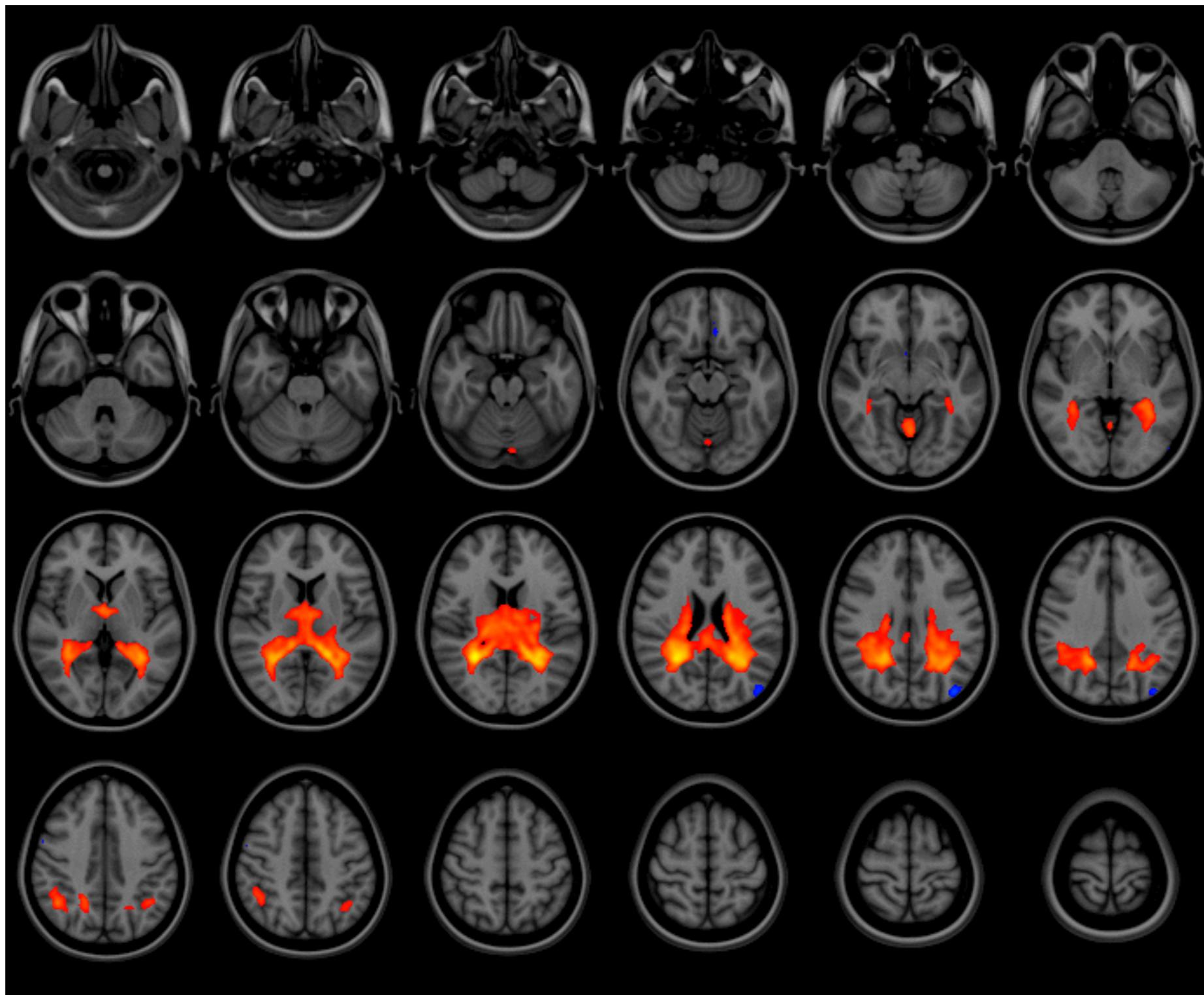
# Alternative Hypothesis Test



- use Gaussian/Gamma mixture model fitted to the histogram of intensity values (using EM) 使用高斯/伽玛混合模型拟合的强度值直方图

# What about overlap?

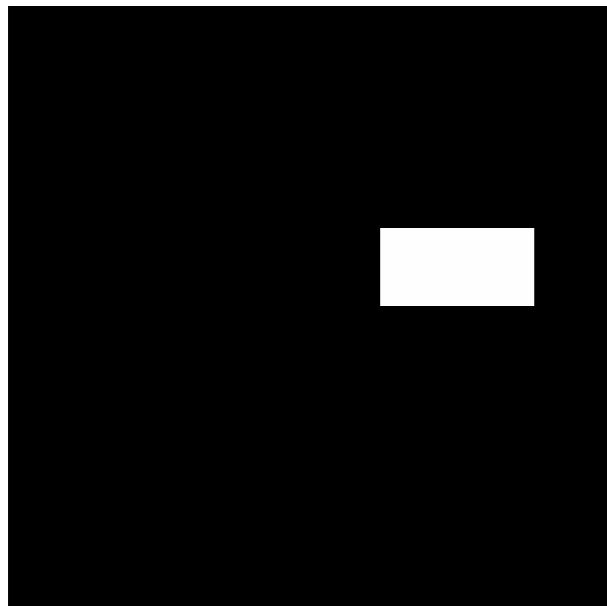
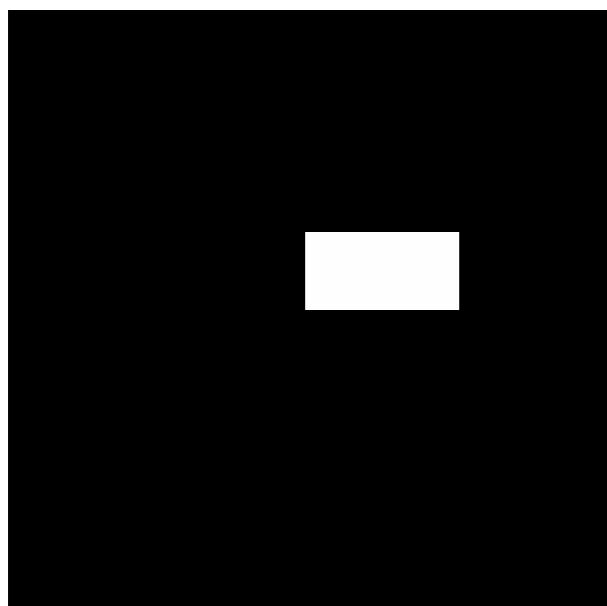
重叠怎么办？





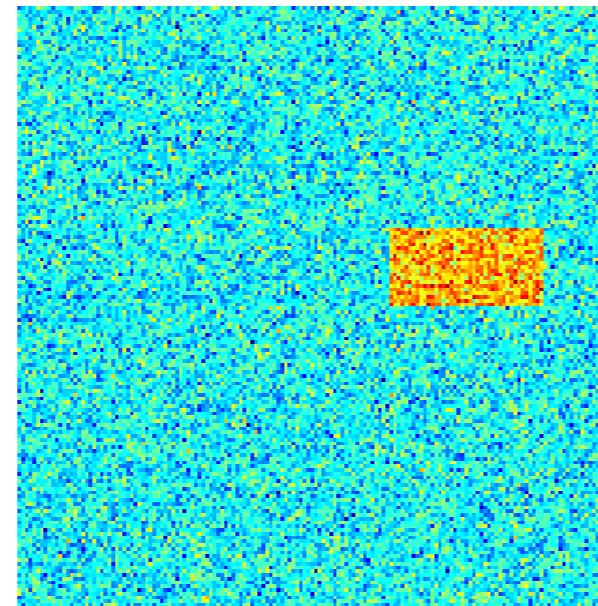
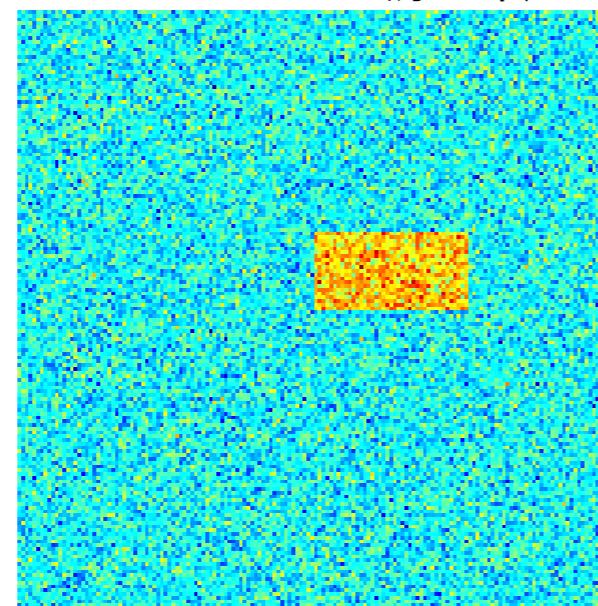
# What about overlap?

Sources 源



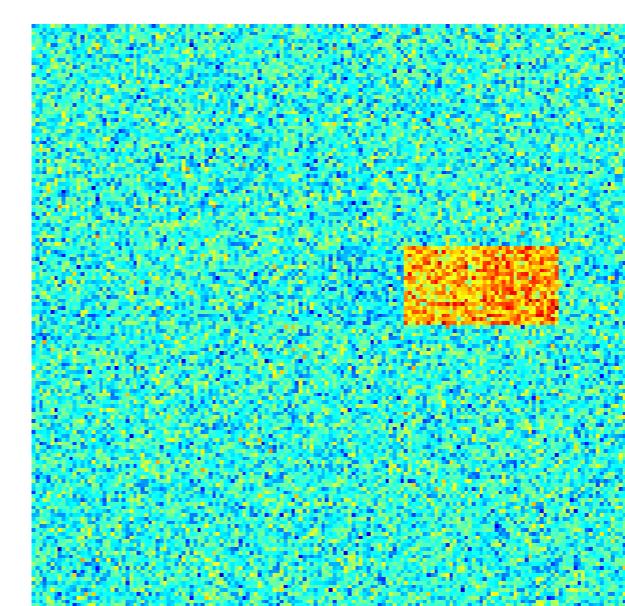
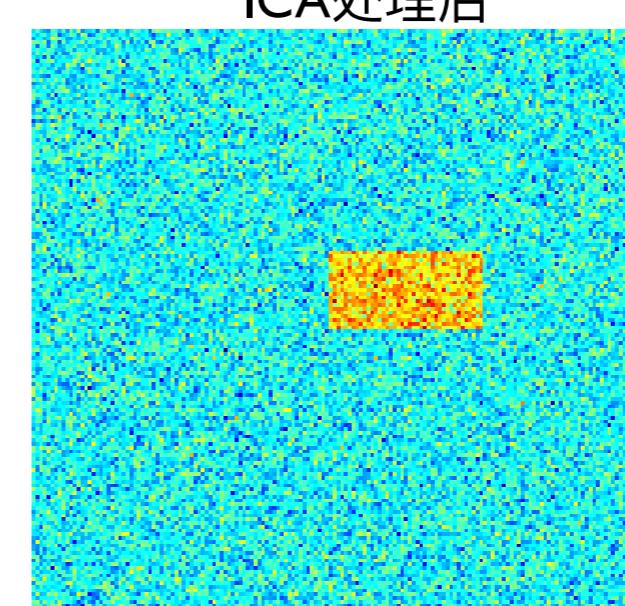
重叠怎么办?

Sources +  
noise 源+噪声



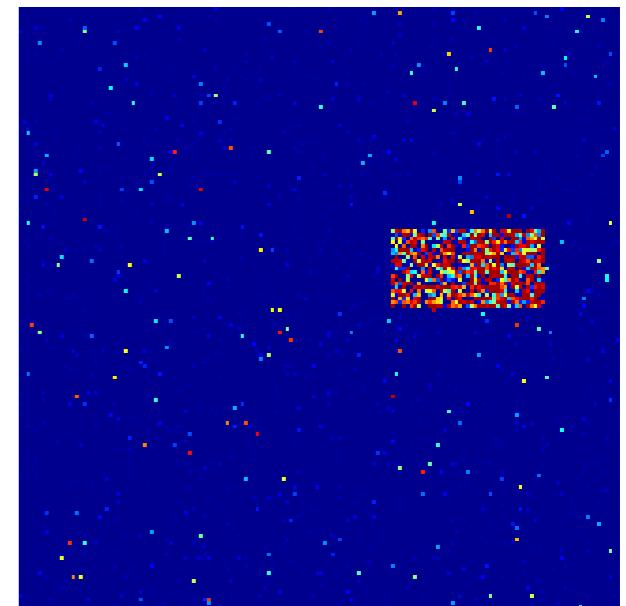
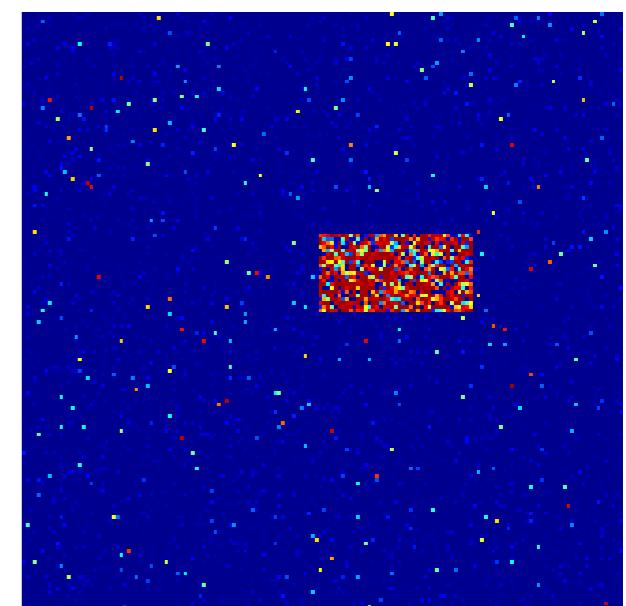
ICA

solution  
ICA处理后



after

thresholding  
设阈值以后



$\rho = 0.5$

$\rho < 0.1$

$\rho = 0$

$\rho \approx 0.5$

# ICA cleanup

ICA 数据清理

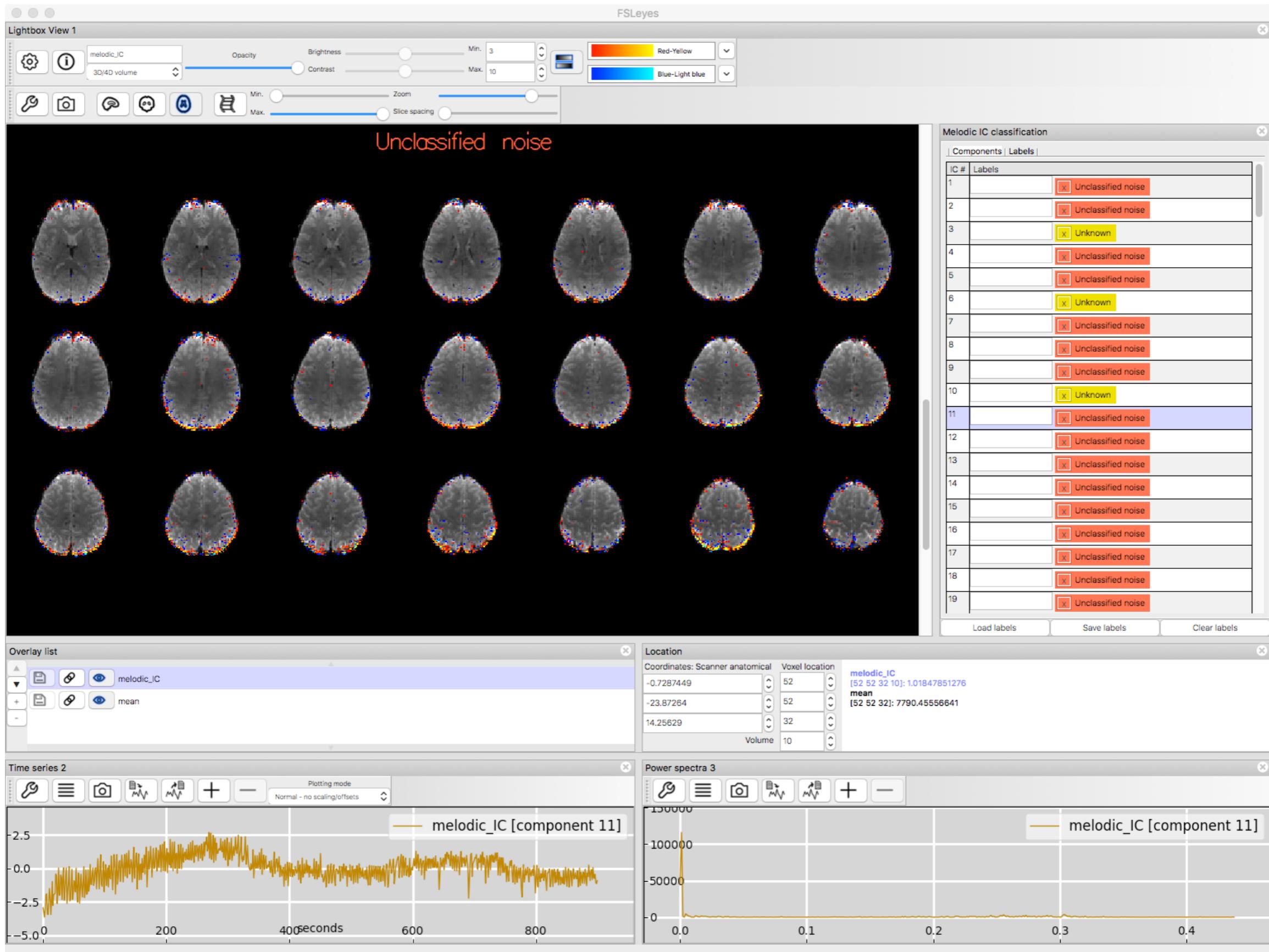


# Artefact detection

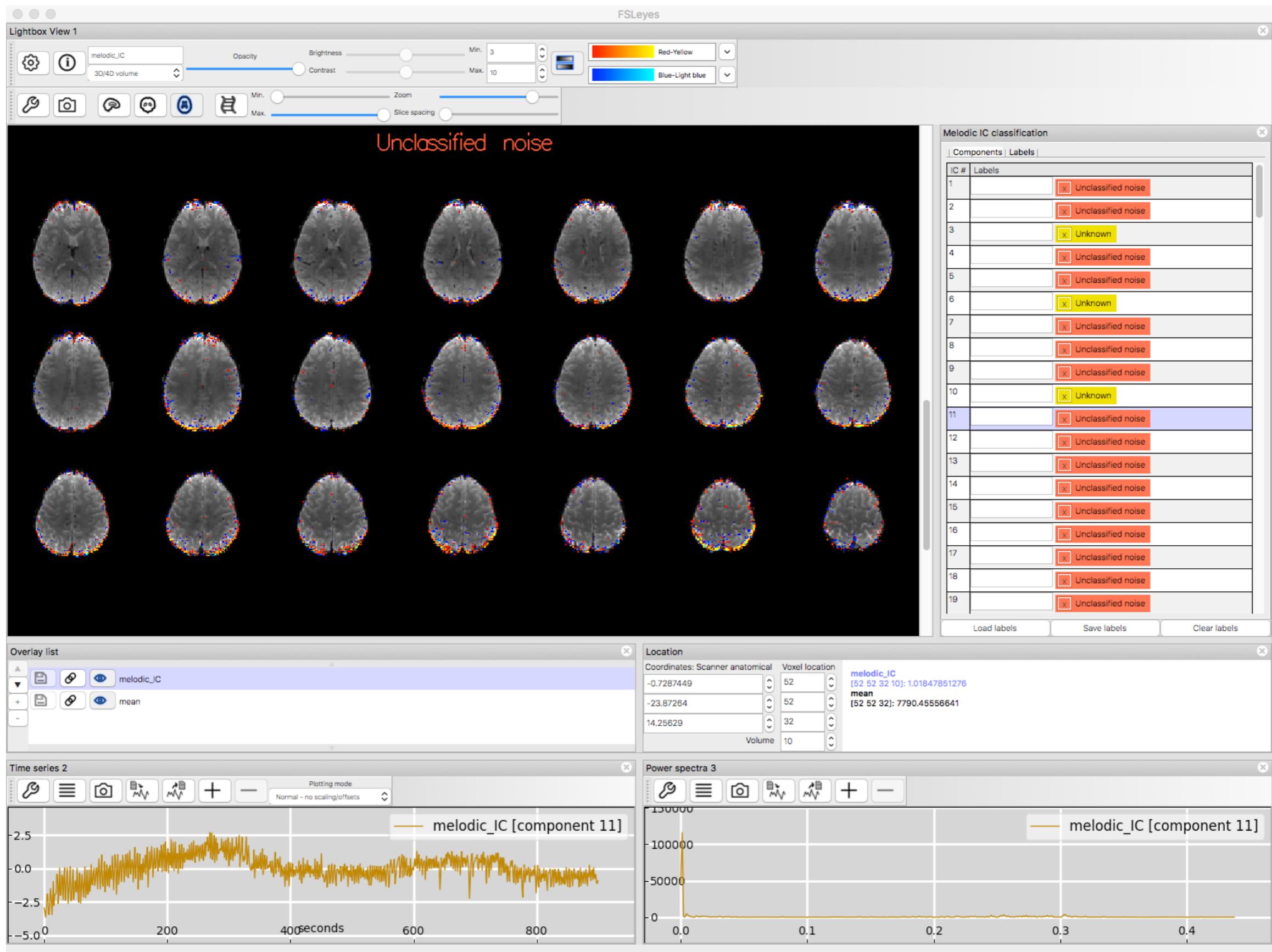
伪迹检测

- FMRI data contain a variety of source processes  
FMRI 数据包含各种来源的加工过程
- Artifactual sources typically have unknown spatial and temporal extent and cannot easily be modelled accurately  
伪迹源通常具有未知的空间和时间范围，并且不容易准确建模
- Exploratory techniques do not require a priori knowledge of time-courses and spatial maps  
探索性技术不需要事先了解时间序列和空间图像

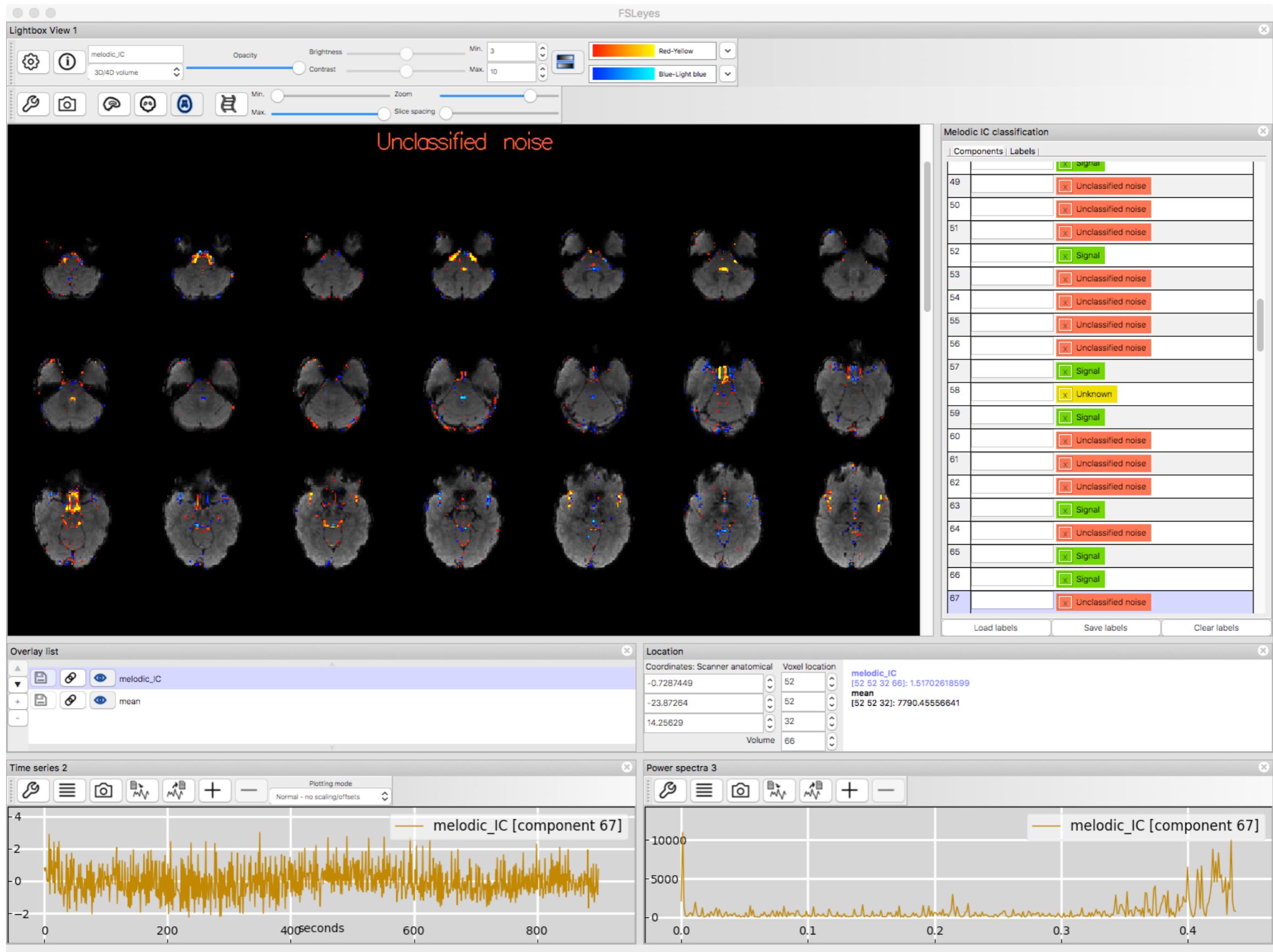
# FSLeyes Melodic Mode



# motion 头动

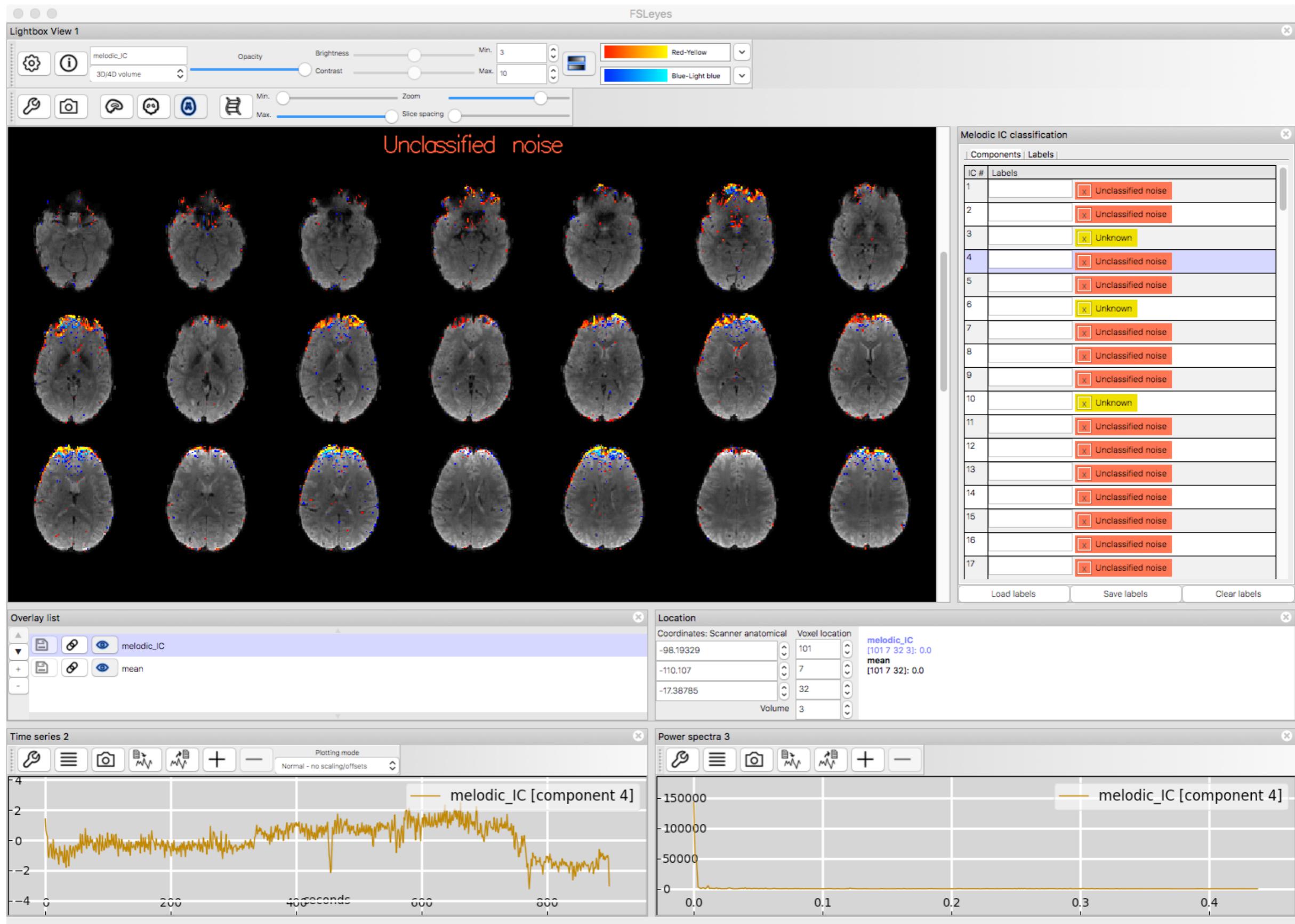


# cardiac 心脏



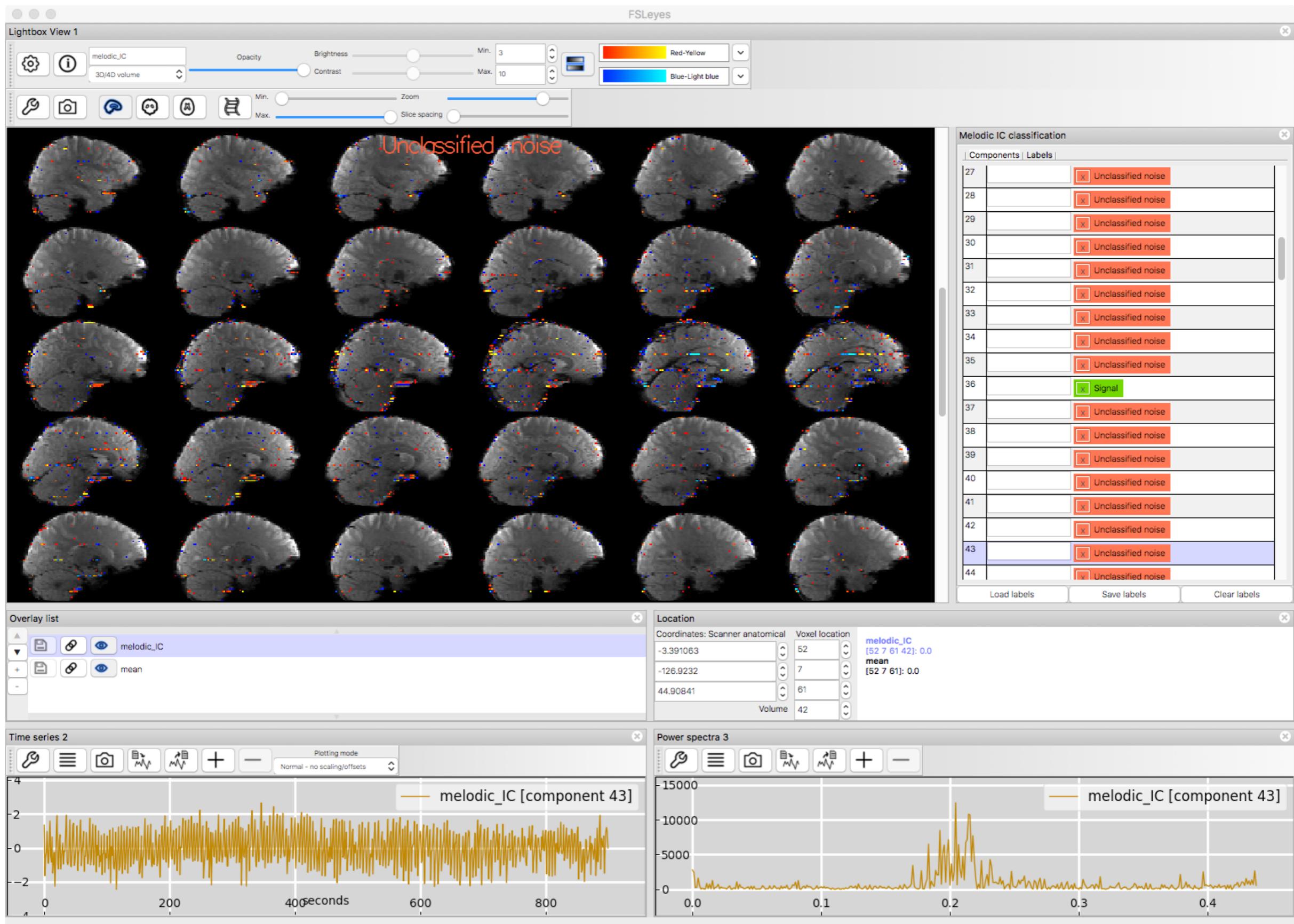


# susceptibility motion 磁化率敏感头动



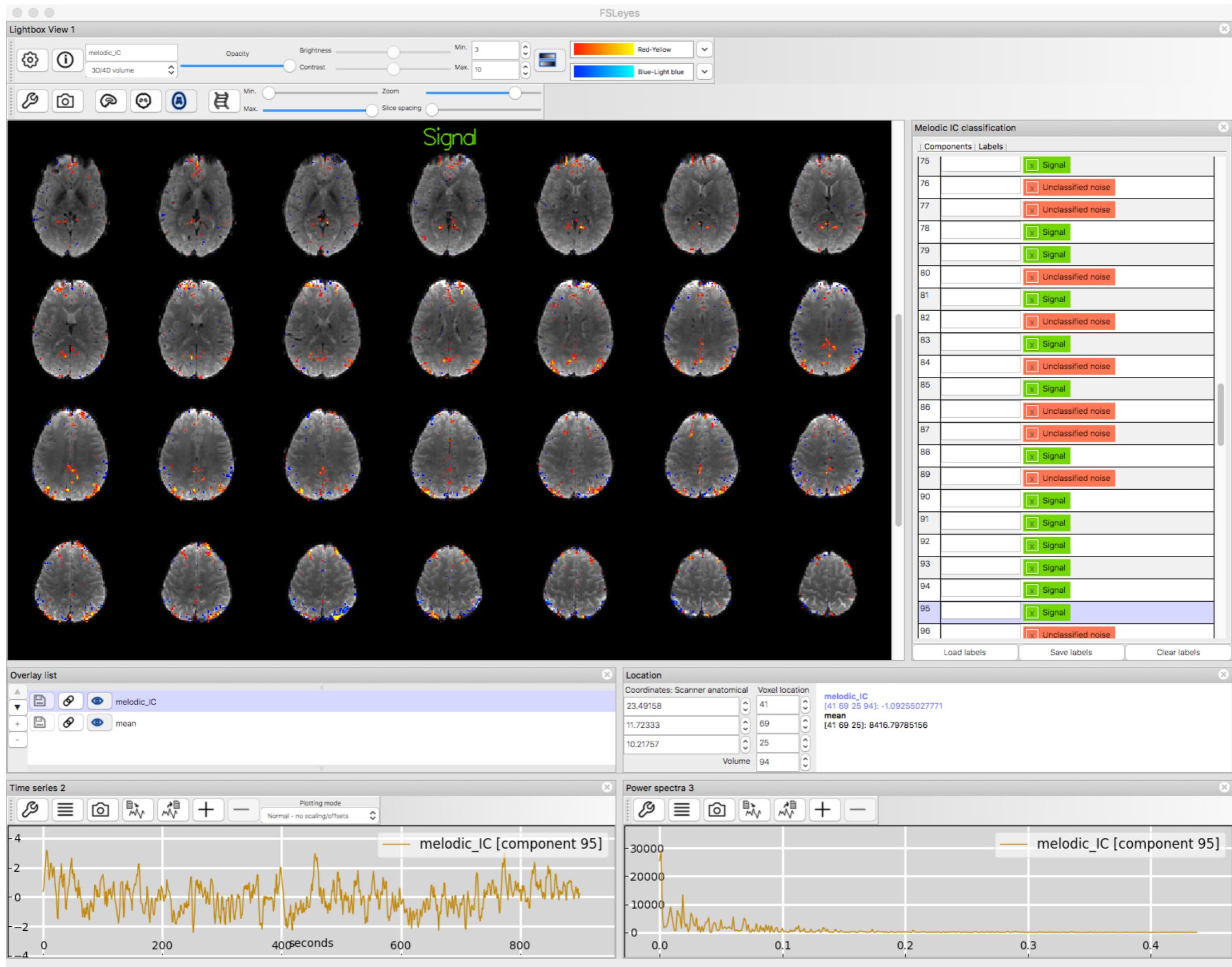


# multiband 多频带

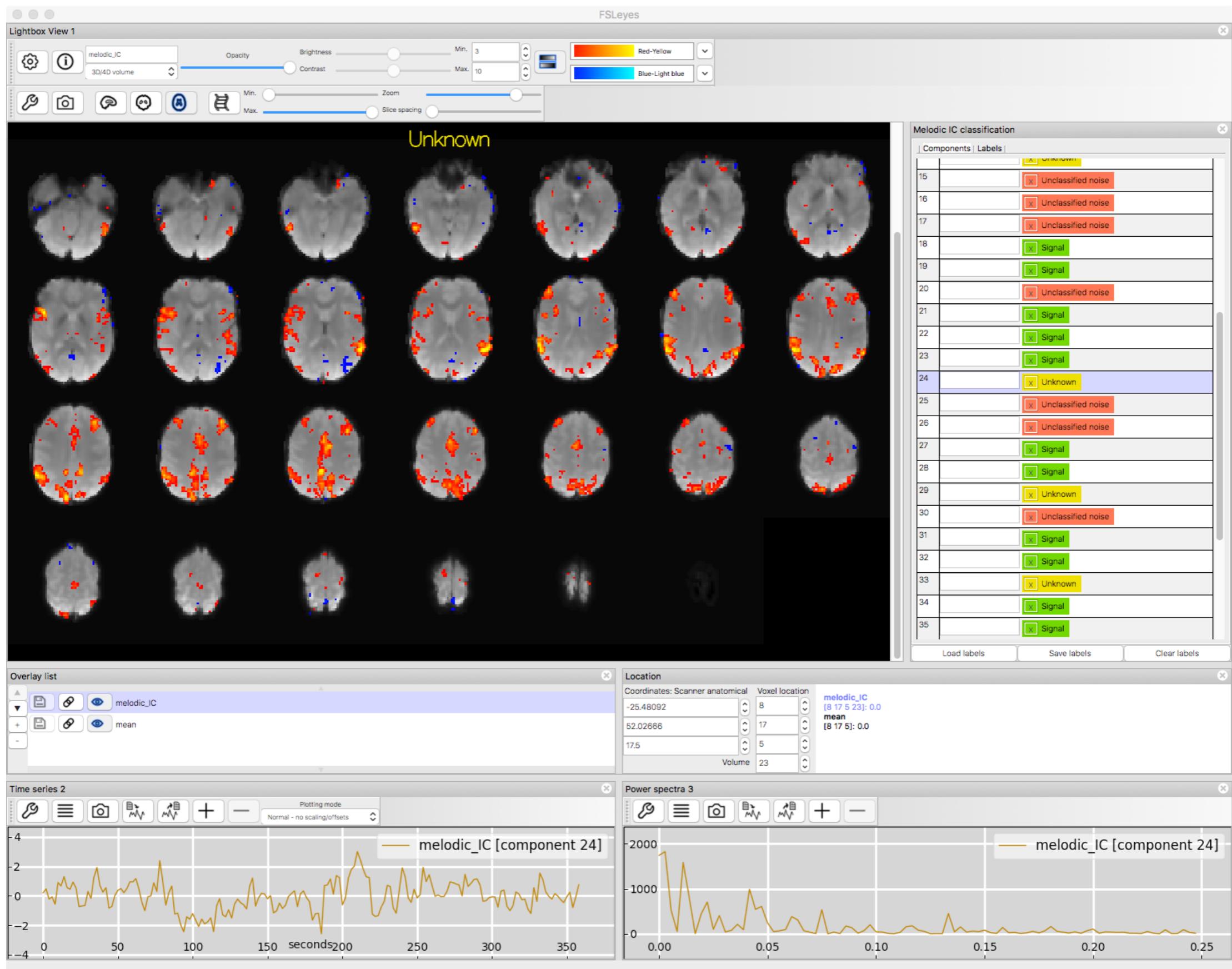




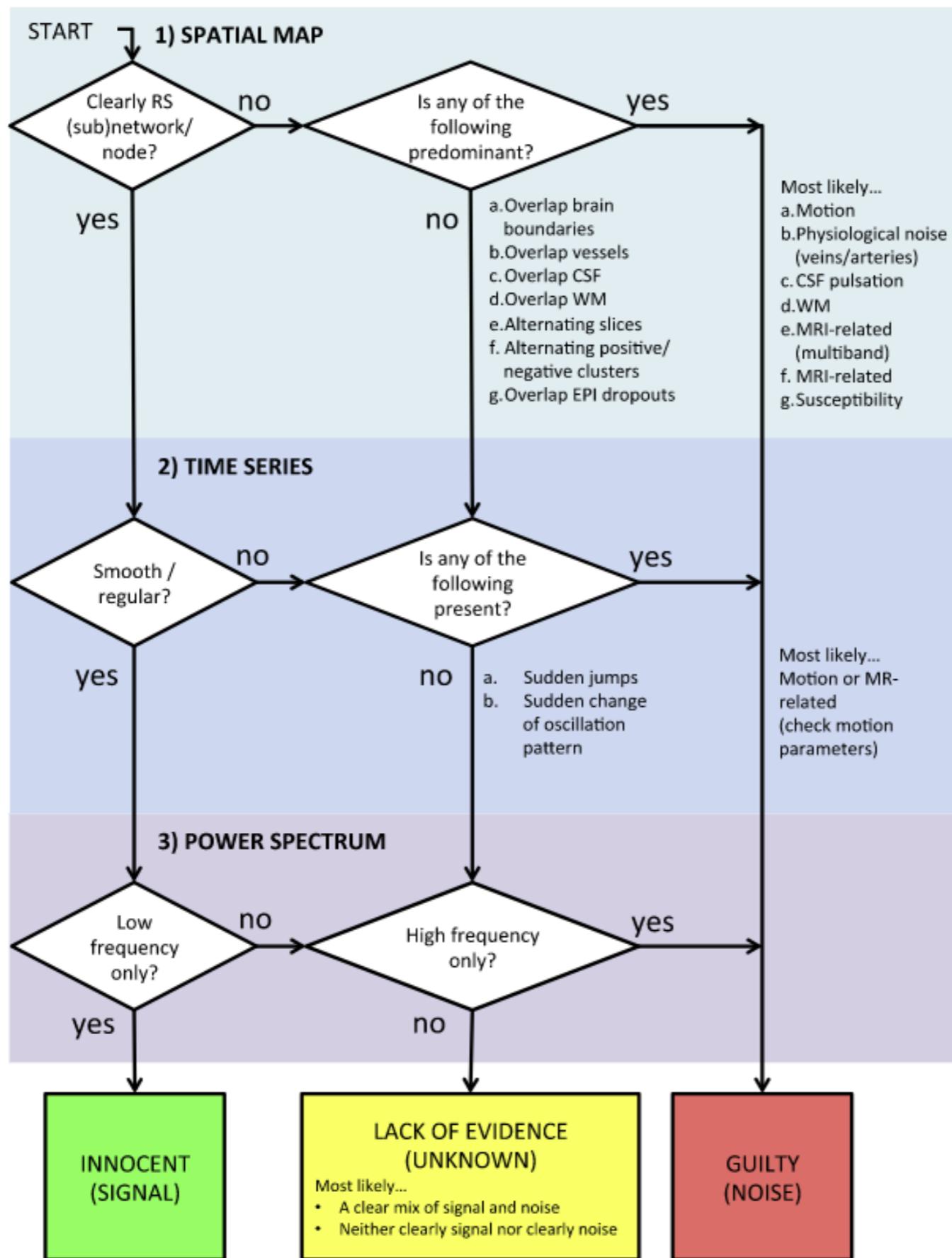
# signal 信号



# FSI effects of scan parameters 扫描参数效应



# manual classification 手动分类



Griffanti et al (2016).

<https://doi.org/10.1016/j.neuroimage.2016.12.036>



# semi-automatic classification

半自动分类



# semi-automatic classification

半自动分类

- FIX ([fsl.fmrib.ox.ac.uk/fsl/fslwiki/FIX](http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FIX))
  - Classifier with many features 具有许多功能的分类器
  - Requires manually labelled training data 需要手动标记训练数据
  - 99% accuracy on high-quality data 高质量数据 99% 的准确率



# semi-automatic classification

半自动分类

- FIX ([fsl.fmrib.ox.ac.uk/fsl/fslwiki/FIX](http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FIX))
  - Classifier with many features 具有许多功能的分类器
  - Requires manually labelled training data 需要手动标记训练数据
  - 99% accuracy on high-quality data 高质量数据 99% 的准确率
- ICA-AROMA ([github.com/rhr-pruim/ICA-AROMA](https://github.com/rhr-pruim/ICA-AROMA))
  - Simple classifier with only 4 features  
仅具有 4 个功能的简单分类器
  - No training data required 无需训练数据
  - Mainly designed for motion artefacts 主要用于头动伪迹

# Multi-subject ICA

多被试ICA



# Different ICA models 不同的ICA模型

## Single-Session ICA

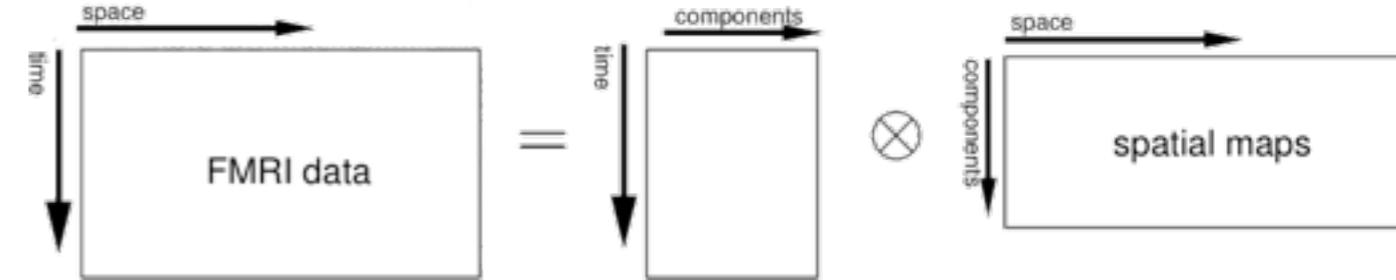
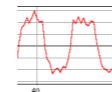
单阶段ICA

each ICA component comprises:



**spatial map & timecourse**

每个ICA成分包括空间图和时间序列



## Multi-Session or Multi-Subject ICA: **Concatenation approach**

多阶段/多被试ICA 串联方法

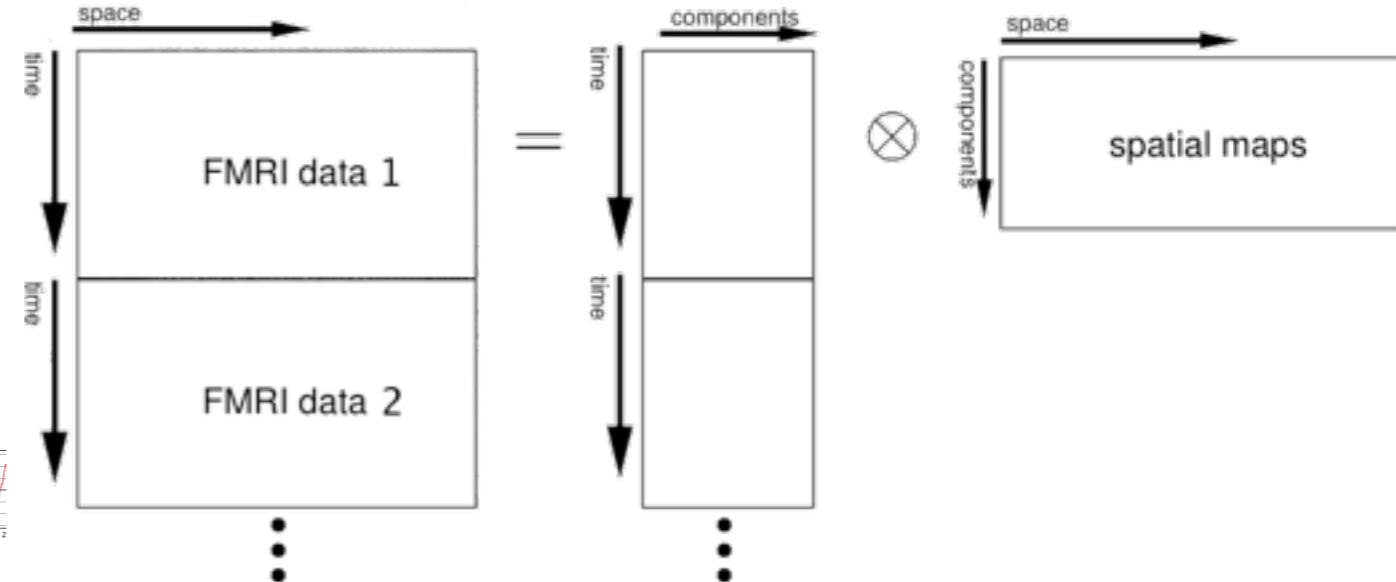
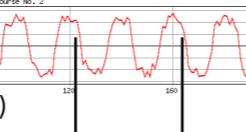
each ICA component comprises:



**spatial map & timecourse**

(that can be split up into subject-specific  
chunks)

每个ICA成分包括空间图和时间序列 (可以被分为被试特定的模块)



## Multi-Session or Multi-Subject ICA: **Tensor-ICA approach**

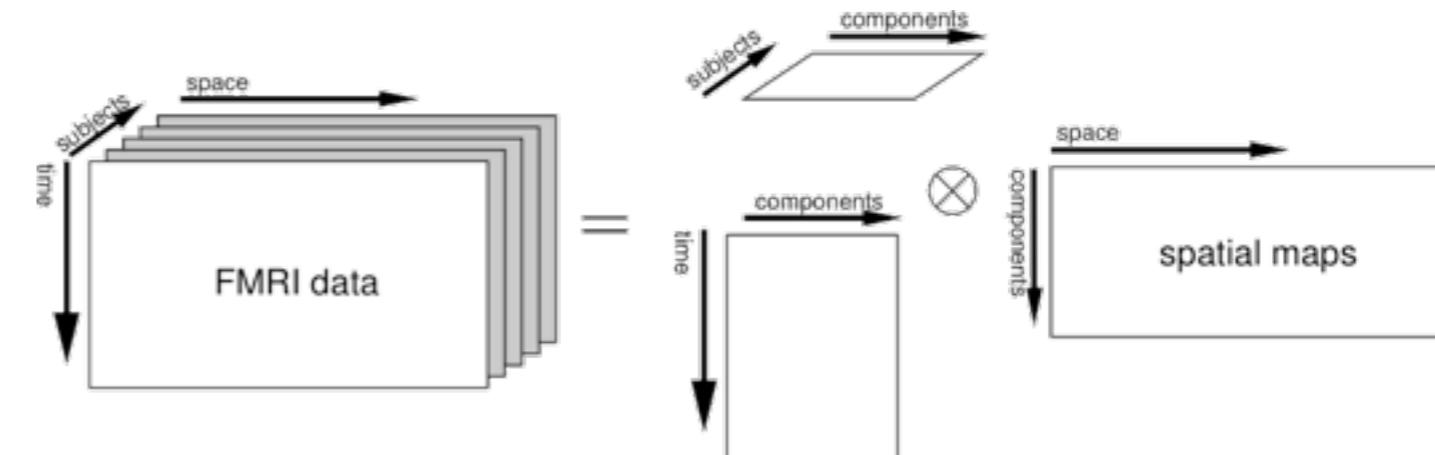
多阶段/多被试ICA 张量-ICA方法

each ICA component comprises:



**spatial map, session-long-timecourse  
& subject-strength plot**

每个ICA成分包括空间图和时间序列以及被试强度图



# Different ICA models 不同的ICA模型

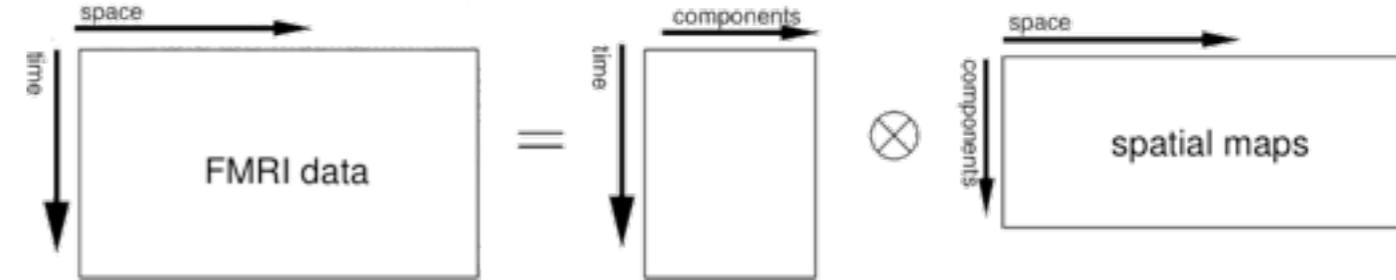
## Single-Session ICA

单阶段ICA

each ICA component comprises:

**spatial map & timecourse**

每个ICA成分包括空间图和时间序列



## Multi-Session or Multi-Subject ICA: **Concatenation approach**

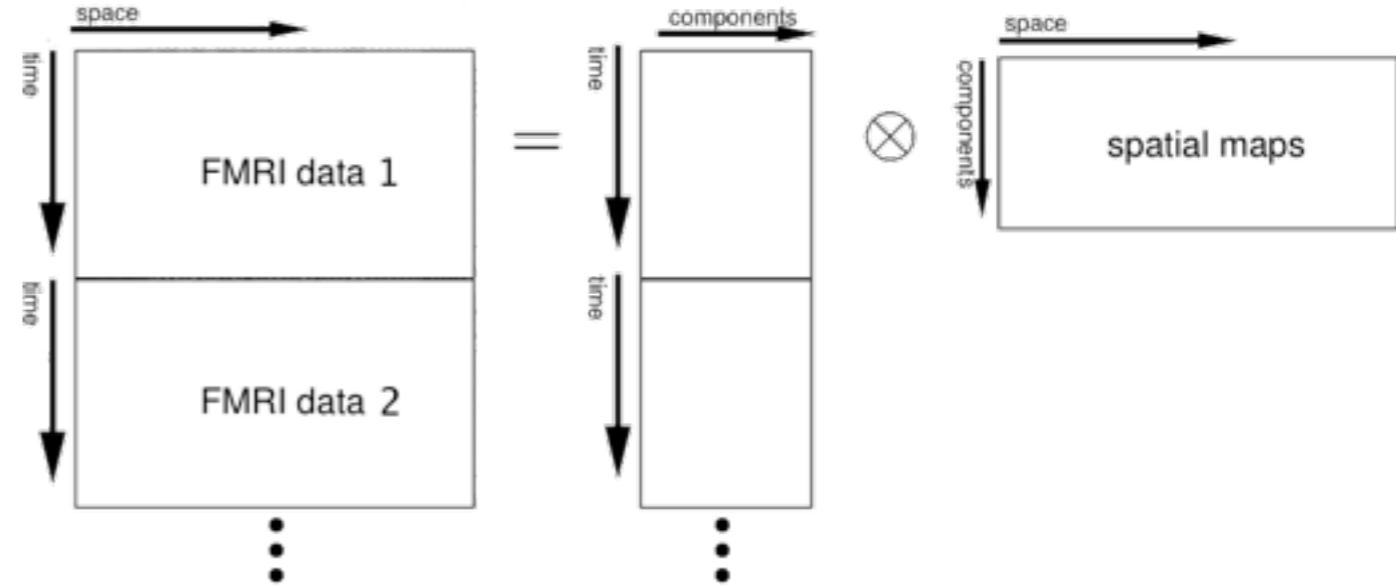
多阶段/多被试ICA 串联方法

good when:

each subject has DIFFERENT timeseries

e.g. resting-state fMRI

适用于每个被试有不同的时间序列时，如静息态fMRI



## Multi-Session or Multi-Subject ICA: **Tensor-ICA approach**

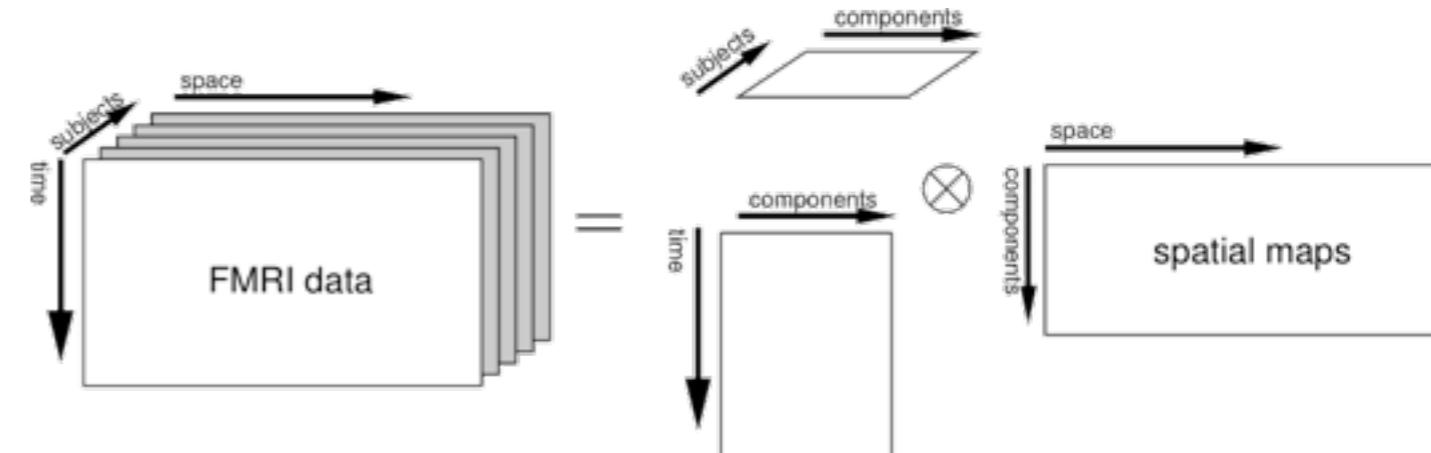
多阶段/多被试ICA 张量-ICA方法

good when:

each subject has SAME timeseries

e.g. activation fMRI

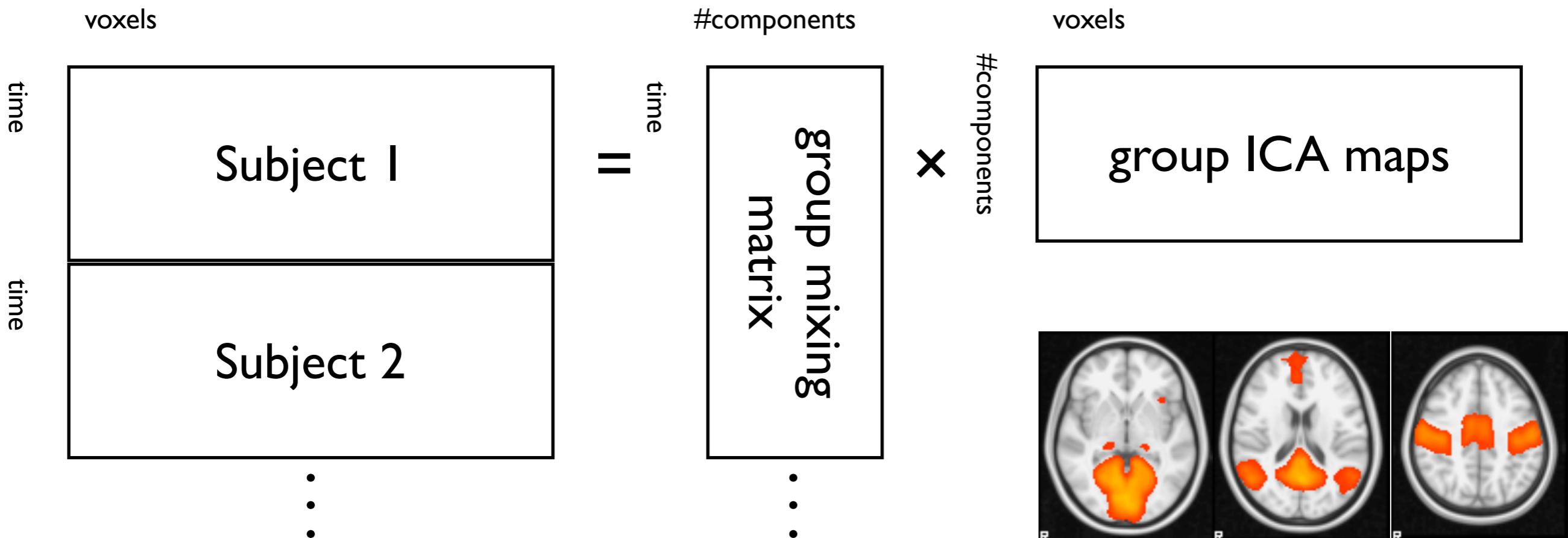
适用于每个被试有相同的时间序列时，如激活fMRI





# Concatenated ICA 串联ICA

- Concatenate all subjects' data temporally 在时间上串联所有被试的数据
- Then run ICA 然后运行ICA
- More appropriate than tensor ICA (for RSNs) 比张量ICA (对于RSN) 更合适





# Resting state multi-subject ICA

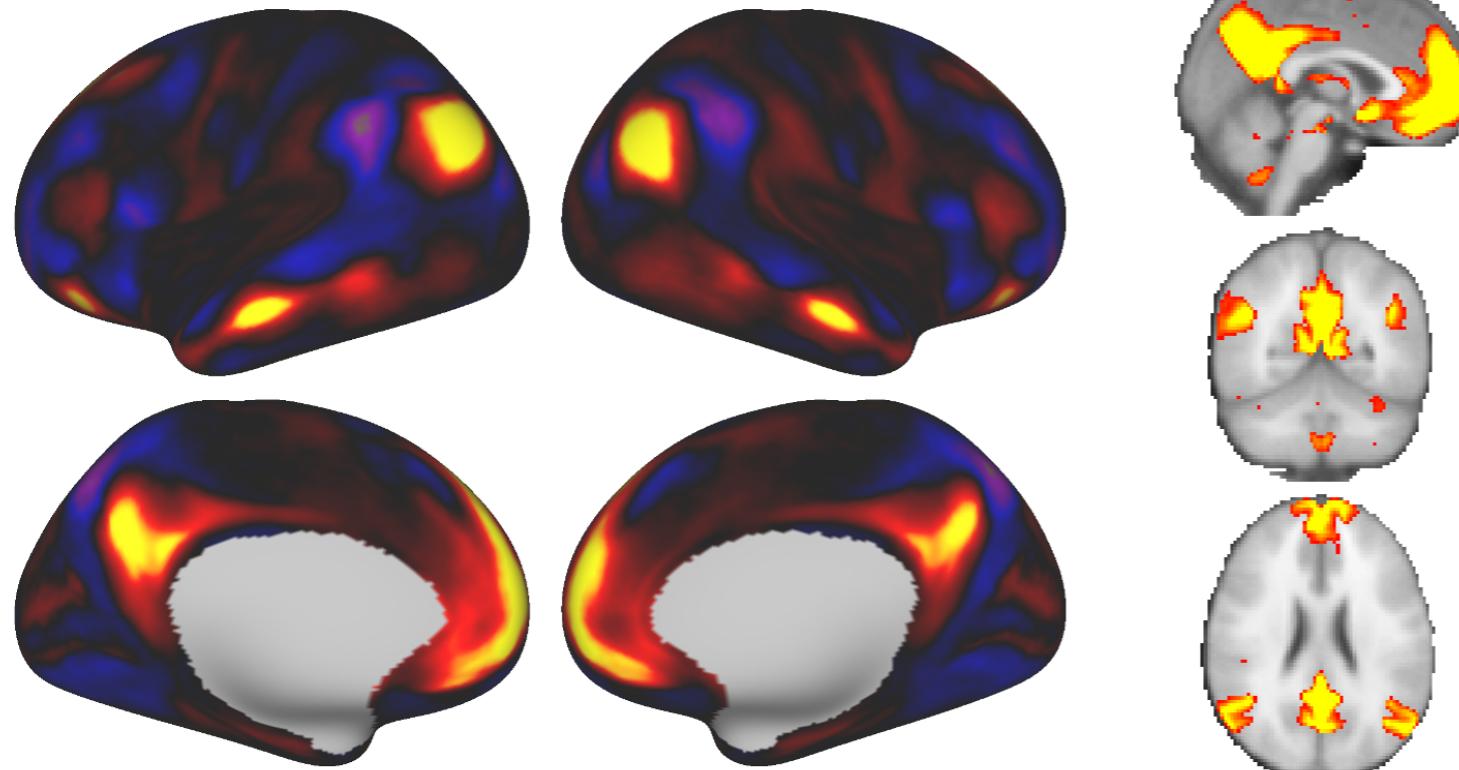
静息态多被试ICA

- Why not just run ICA on each subject separately?  
为什么不只对每个被试分别运行ICA?
  - Correspondence problem (eg RSNs across subjects)  
对应问题 (例如跨被试的RSN)
  - Different splittings sometimes caused by small changes in the data (naughty ICA!)  
有时由于数据的微小变化而导致不同的分裂形式 (调皮的ICA! )
- Instead - start with a “group-average” ICA
  - But then need to relate group maps back to the individual subjects  
相反-从“组平均” ICA开始  
但随后需要将组水平图映射回单被试水平

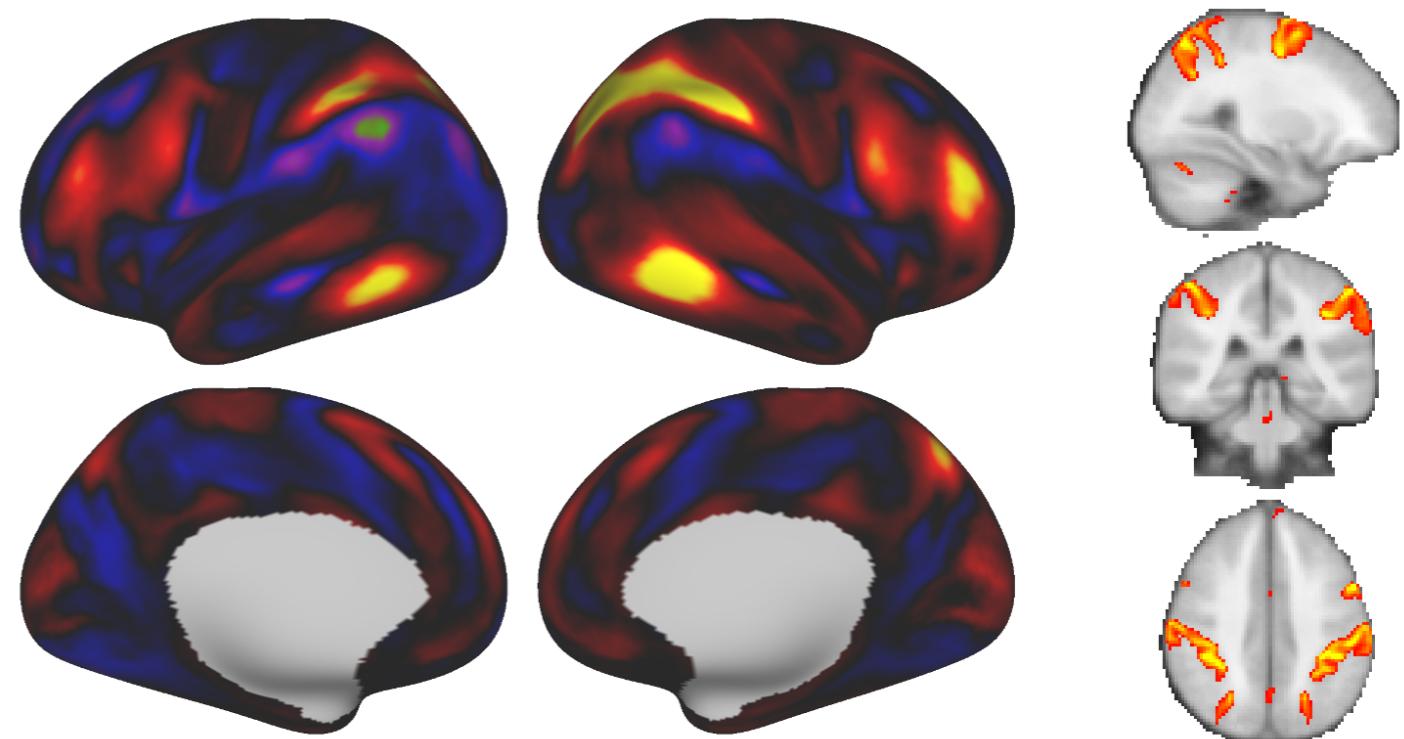


# Resting state networks 静息态网络

**Default Mode Network**



**Dorsal Attention Network**





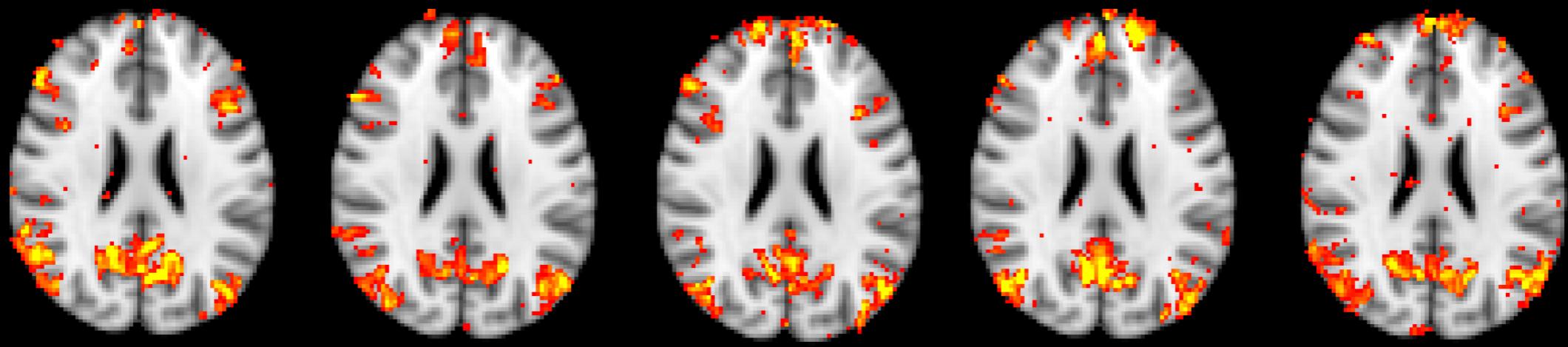
# Resting state multi-subject ICA

静息态多被试ICA

Group ICA map



Example subject maps derived from dual regression





# Dual Regression 双回归

Two steps that both involve multiple regression:

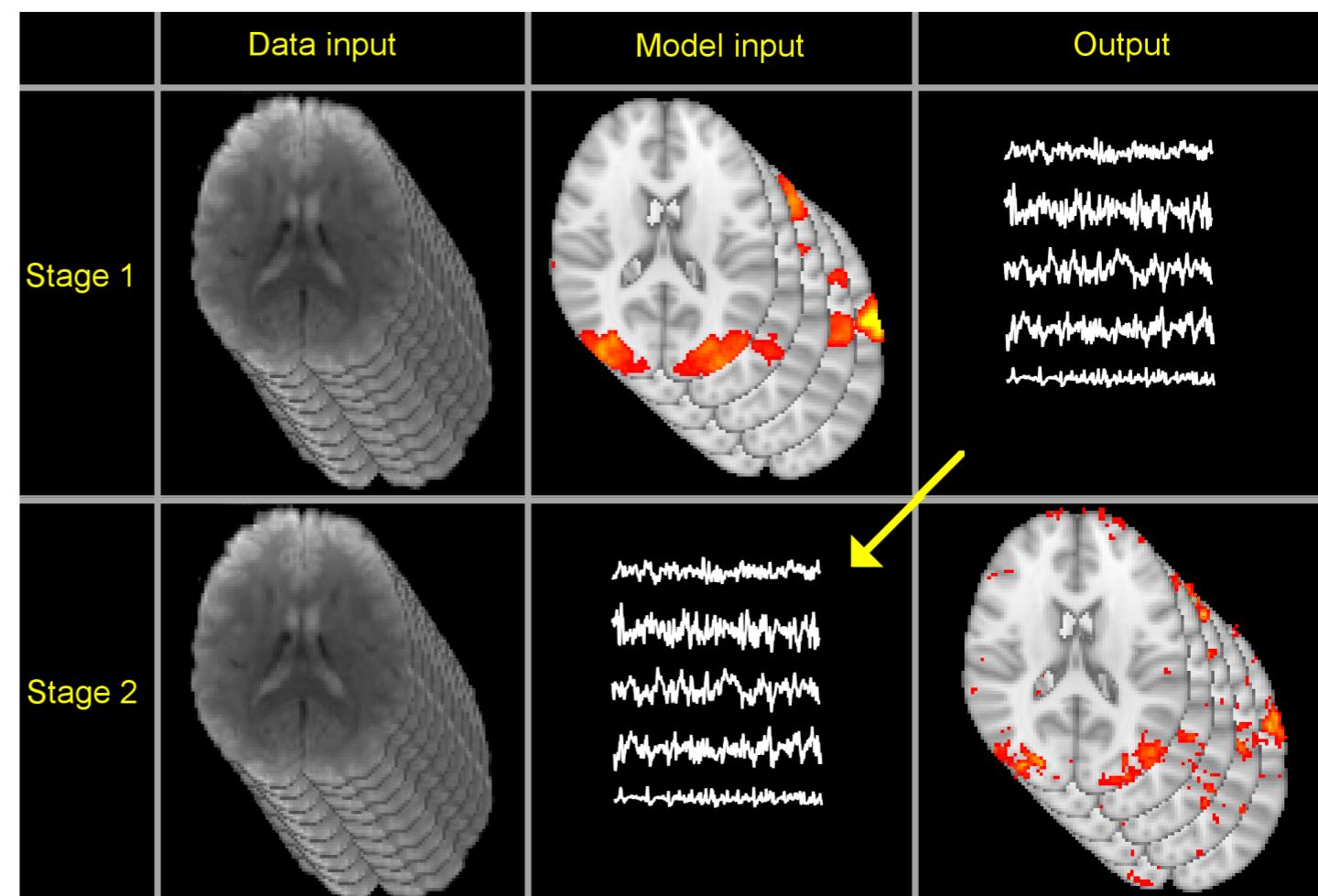
两个步骤都涉及多元回归：

1. Extract subject timeseries

提取被试时间序列

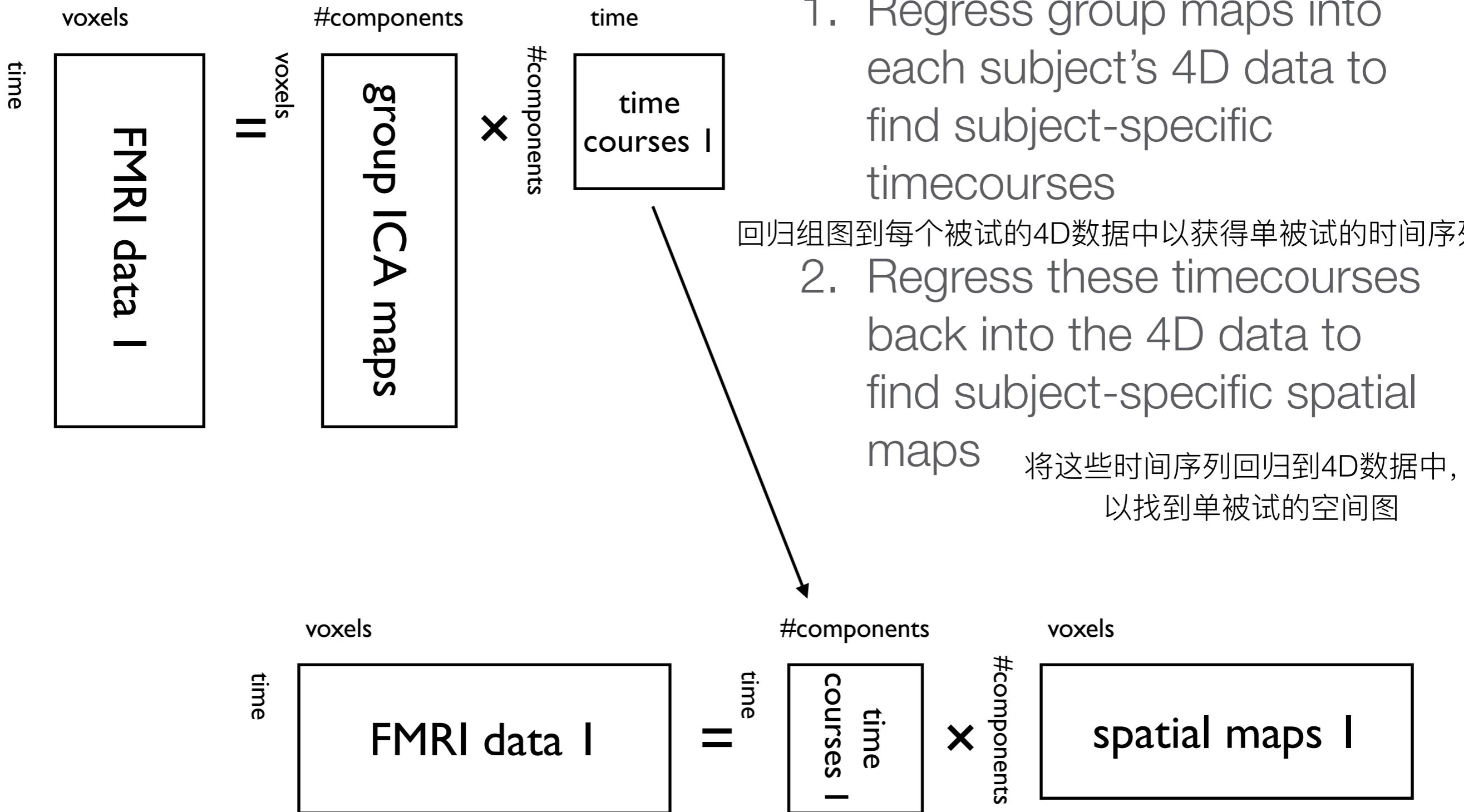
2. Extract subject maps

提取被试空间图



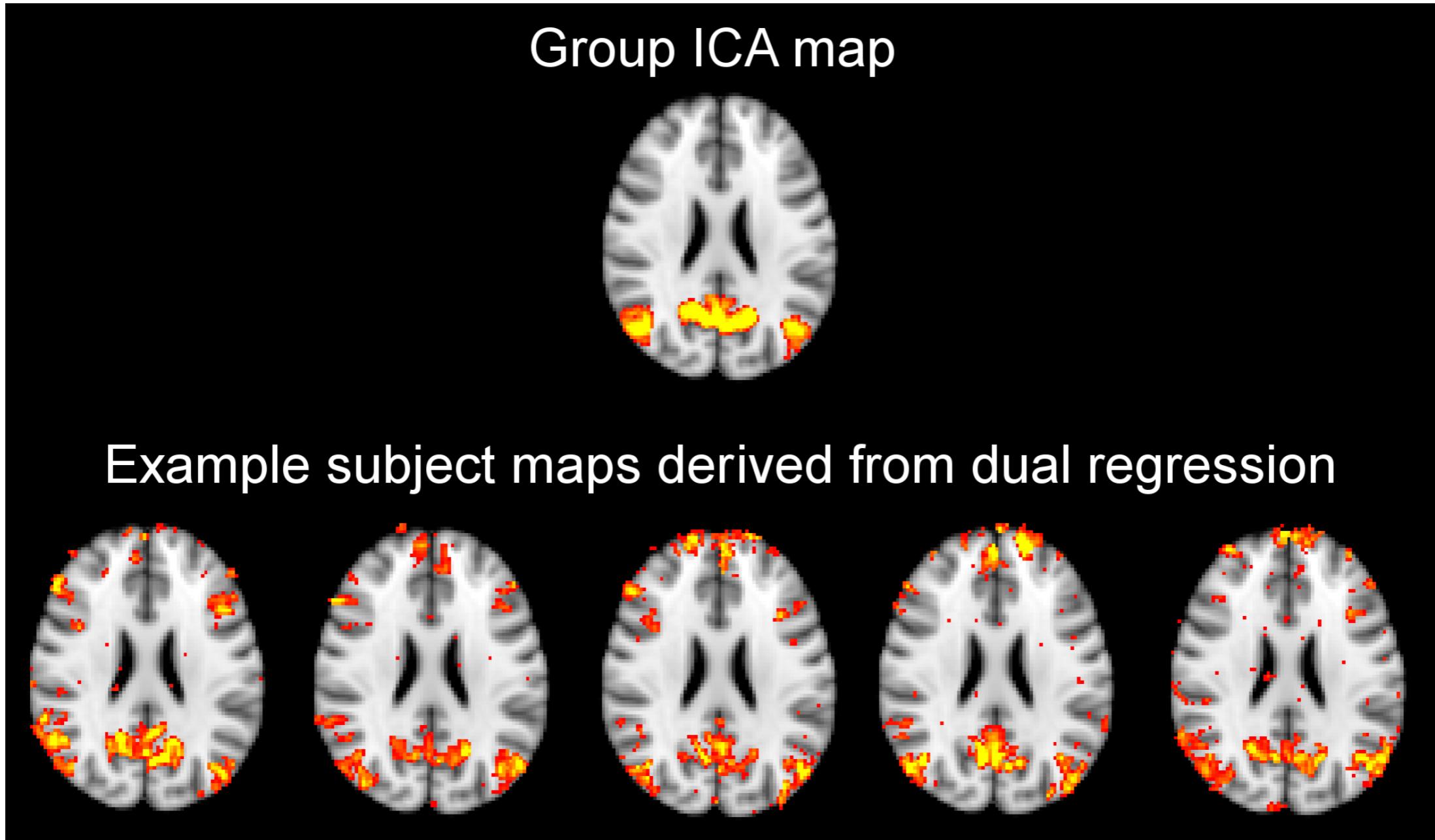


# Dual Regression 双回归





# Dual Regression 双回归





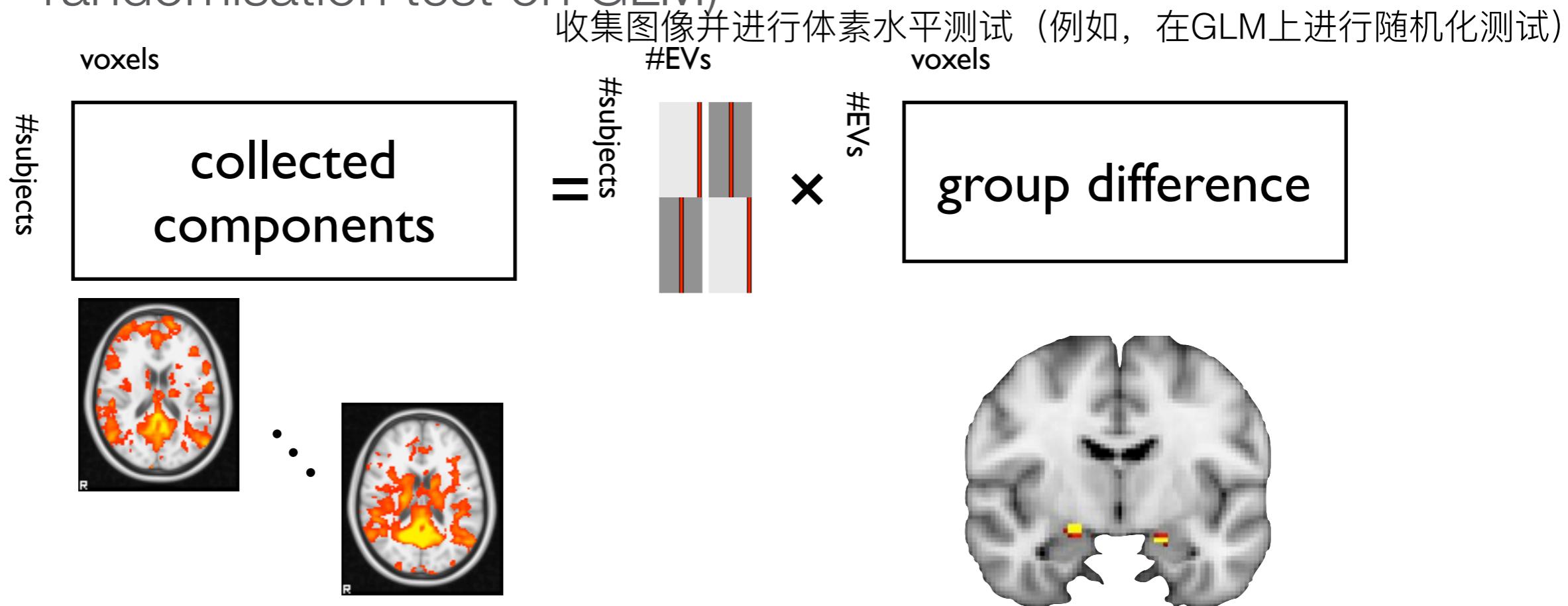
# Running dual\_regression 运行双回归

```
[i$lay:~] dual_regression.sh  
dual_regression v0.5 (beta)  
  
***NOTE*** ORDER OF COMMAND-LINE ARGUMENTS IS DIFFERENT FROM PREVIOUS VERSION  
  
Usage: dual_regression <group_IC_maps> <des_norm> <design.mat> <design.con> <n_perm> <output_directory> <input1> <input2> <input3> .....  
e.g. dual_regression groupICA.gica/groupmelodic.ica/melodic_IC 1 design.mat design.con 500 grot `cat groupICA.gica/.filelist`  
  
<group_IC_maps> 4D image containing spatial IC maps (melodic_IC) from the whole-group ICA analysis  
<des_norm> 0 or 1 (1 is recommended). Whether to variance-normalise the timecourses used as the stage-2 regressors  
<design.mat> Design matrix for final cross-subject modelling with randomise  
<design.con> Design contrasts for final cross-subject modelling with randomise  
<n_perm> Number of permutations for randomise; set to 1 for just raw tstat output, set to 0 to not run randomise at all.  
<output_directory> This directory will be created to hold all output and logfiles  
<input1> <input2> ... List all subjects' preprocessed, standard-space 4D datasets  
  
<design.mat> <design.con> can be replaced with just  
-1 for group-mean (one-group t-test) modelling.  
If you need to add other randomise option then just edit the line after "EDIT HERE" below  
  
[i$lay:~]
```

- FSL command line tool, combining: FSL命令行工具，包含：
  - DR to create subject-wise estimates (stage 1 + stage 2)  
双回归创建个体水平的估计值（阶段1 + 阶段2）
  - Group comparison using randomise (stage 3)
    - randomise进行组水平比较

# Group comparison 组水平比较

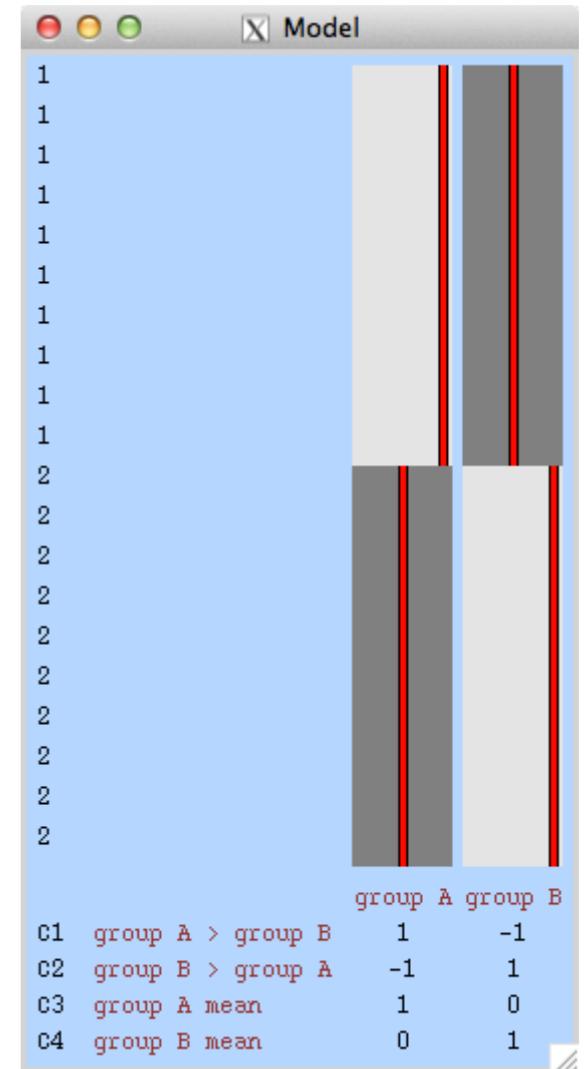
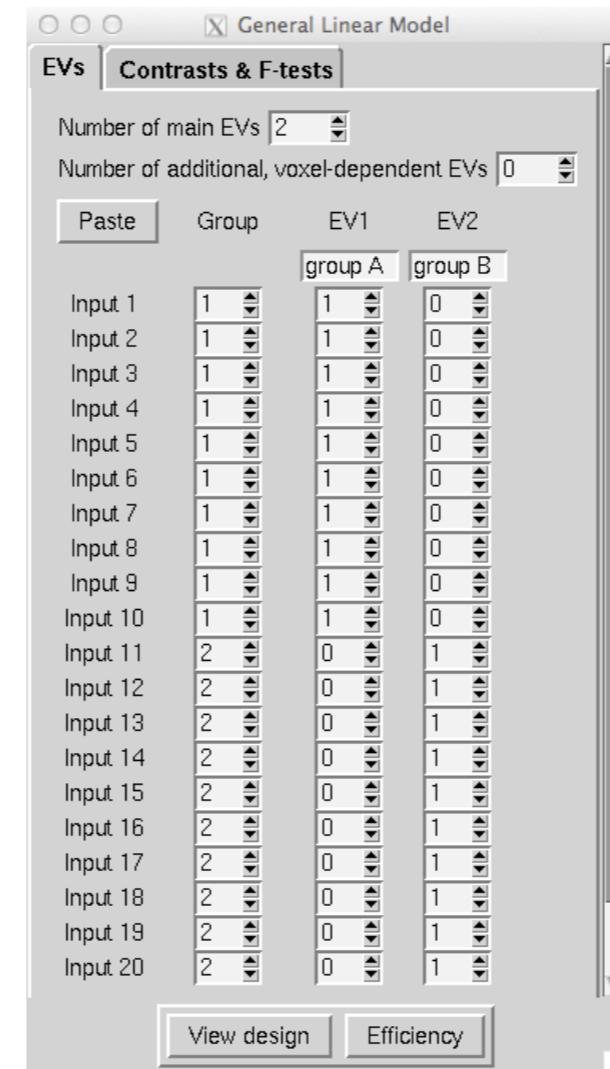
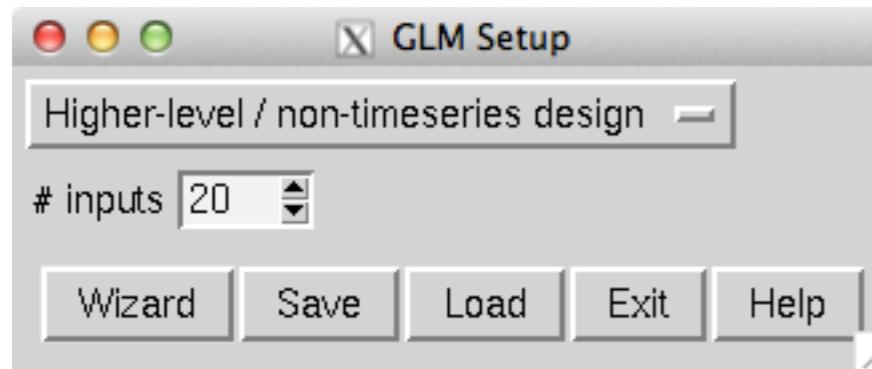
- Collect maps and perform voxel-wise test (e.g. randomisation test on GLM)



- Can now do voxelwise testing across subjects, separately for each original group ICA map
  - Can choose to look at strength-and-shape differences
- 现在可以对每个原始组水平ICA图  
进行被试间的体素水平检验
- 可以选择查看差异的强度和形状



# Group analysis on maps 空间图像组分析



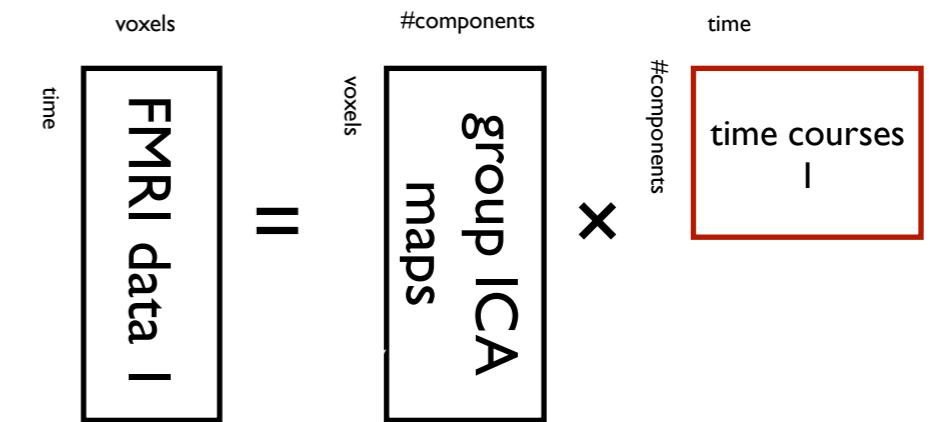
- can use the Glm tool (Glm\_gui on mac) to create GLM design and contrast matrices

可以使用GlM工具（在Mac上为GlM\_gui）来创建GLM设计和对比矩阵



# Dual regression outputs 双回归的输出

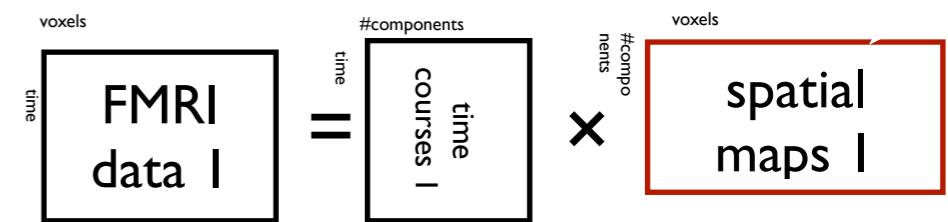
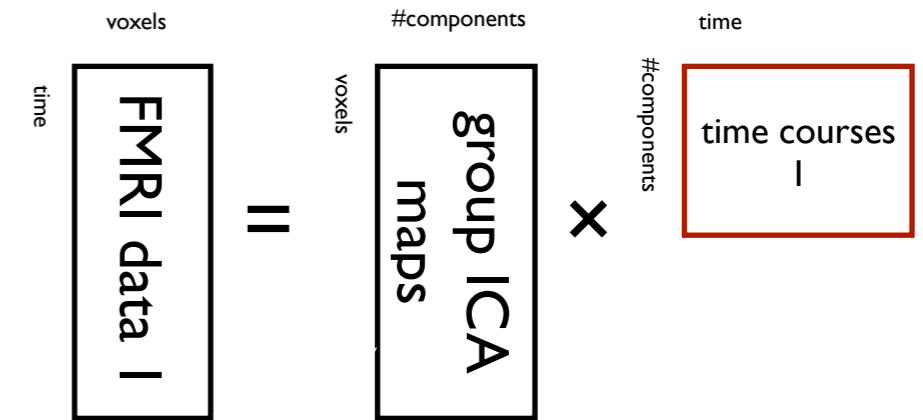
- dr\_stage1\_subject[#SUB].txt - the timeseries outputs of stage 1 of the dual-regression.  
双回归第一阶段的时间序列输出值





# Dual regression outputs 双回归的输出

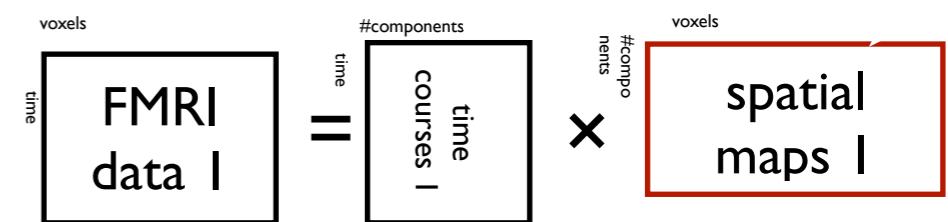
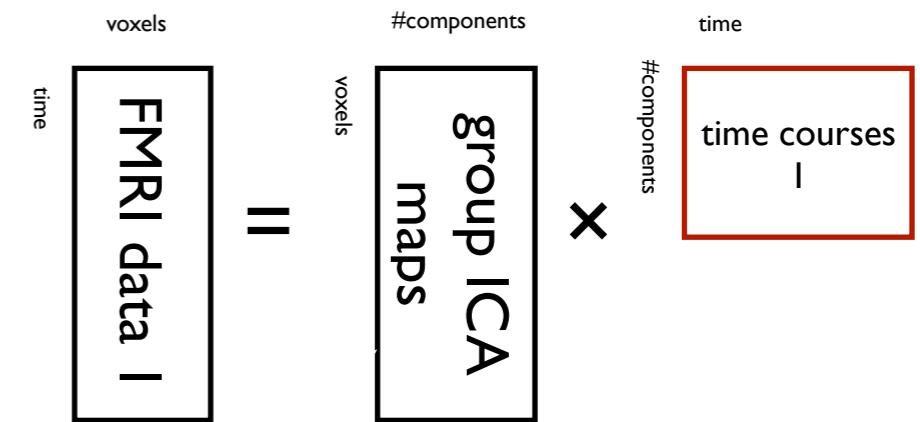
- dr\_stage1\_subject[#SUB].txt - the timeseries outputs of stage 1 of the dual-regression.  
双回归第一阶段的时间序列输出值
- dr\_stage2\_subject[#SUB].nii.gz - the spatial maps outputs of stage 2 of the dual-regression.  
双回归第二阶段的空间图输出





# Dual regression outputs 双回归的输出

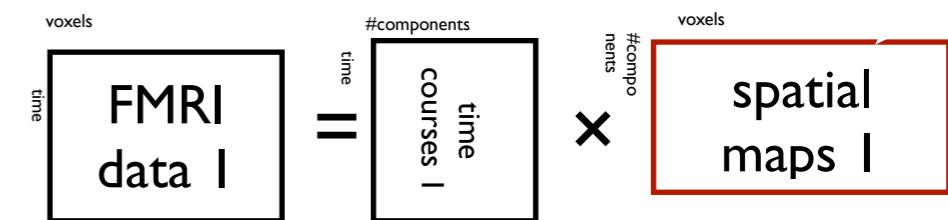
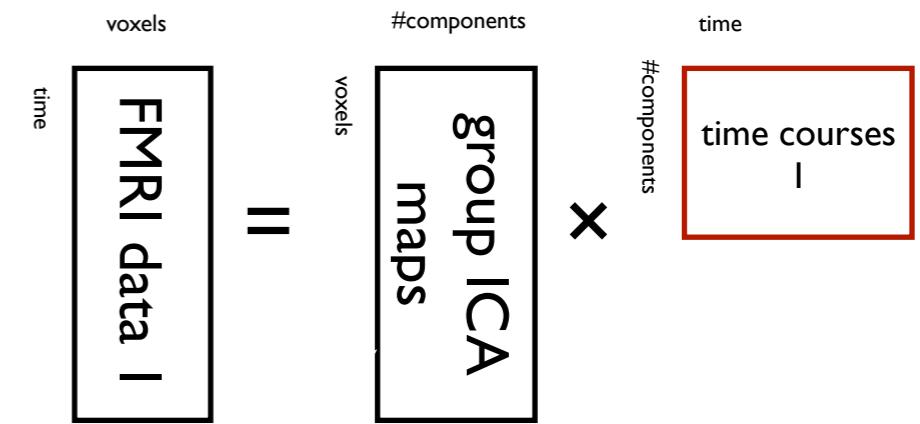
- dr\_stage1\_subject[#SUB].txt - the timeseries outputs of stage 1 of the dual-regression.  
双回归第一阶段的时间序列输出值
- dr\_stage2\_subject[#SUB].nii.gz - the spatial maps outputs of stage 2 of the dual-regression.  
双回归第二阶段的空间图输出
- dr\_stage2\_ic[#ICA].nii.gz - the re-organised parameter estimate images  
估计图像的重建参数





# Dual regression outputs 双回归的输出

- dr\_stage1\_subject[#SUB].txt - the timeseries outputs of stage 1 of the dual-regression.  
双回归第一阶段的时间序列输出值
- dr\_stage2\_subject[#SUB].nii.gz - the spatial maps outputs of stage 2 of the dual-regression.  
双回归第二阶段的空间图输出
- dr\_stage2\_ic[#ICA].nii.gz - the re-organised parameter estimate images  
估计图像的重建参数
- dr\_stage3\_ic[#ICA]\_tstat[#CON].nii.gz - the output from randomise  
非参置换检验randomise的输出值

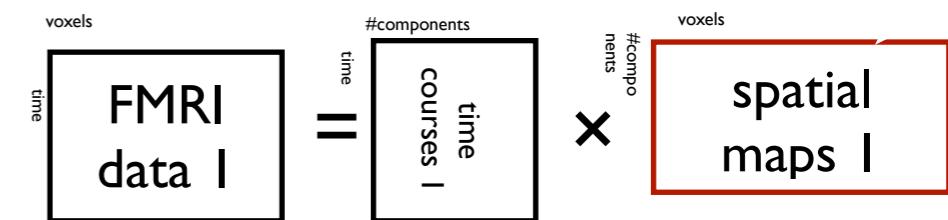
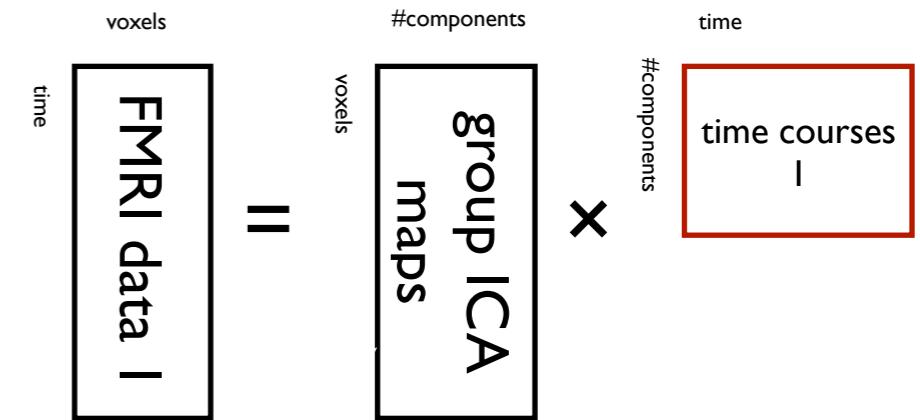




# Dual regression outputs 双回归的输出

- dr\_stage1\_subject[#SUB].txt - the timeseries outputs of stage 1 of the dual-regression.  
双回归第一阶段的时间序列输出值
- dr\_stage2\_subject[#SUB].nii.gz - the spatial maps outputs of stage 2 of the dual-regression.  
双回归第二阶段的空间图输出
- dr\_stage2\_ic[#ICA].nii.gz - the re-organised parameter estimate images  
估计图像的重建参数
- dr\_stage3\_ic[#ICA]\_tstat[#CON].nii.gz - the output from randomise  
非参置换检验randomise的输出值

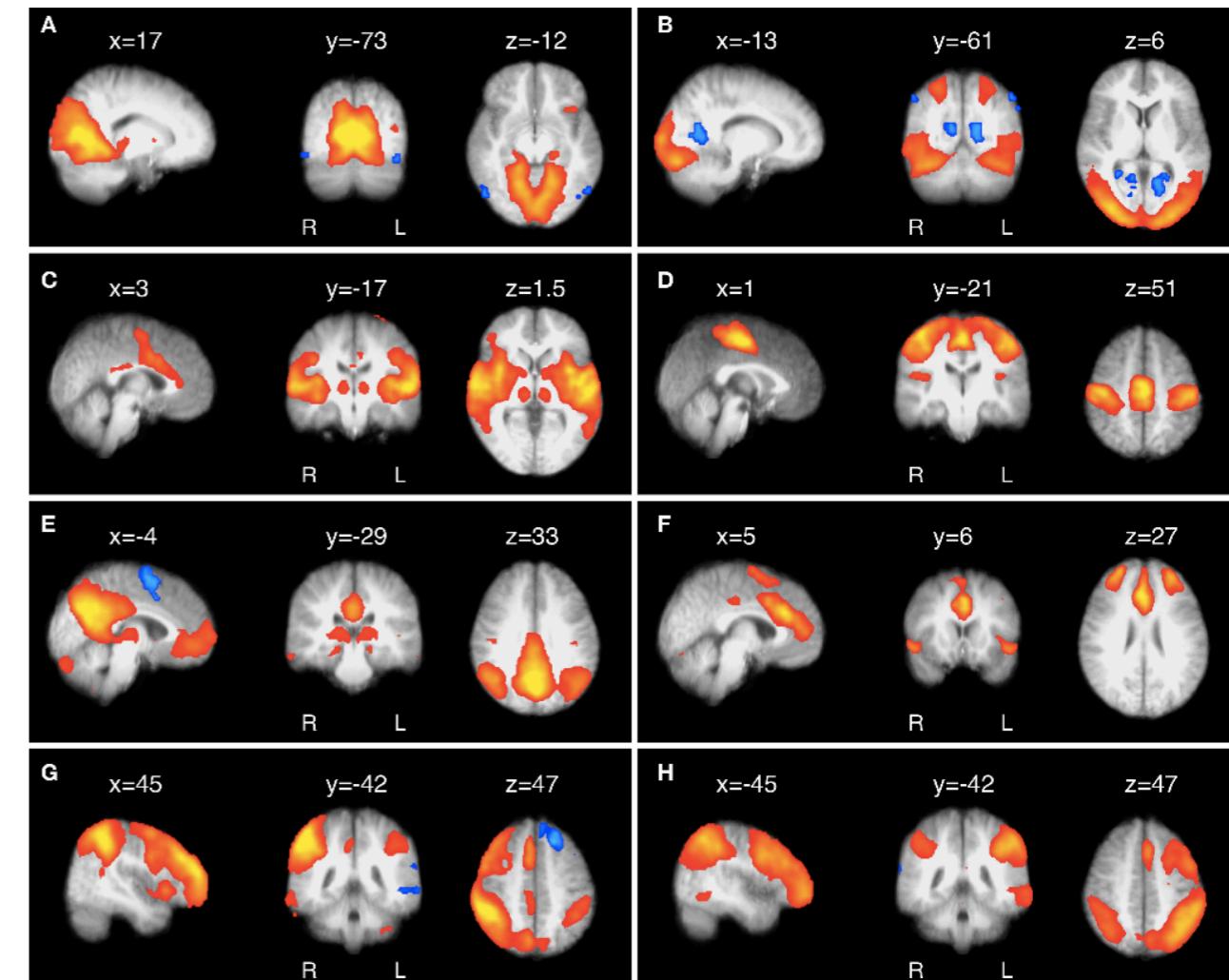
(corrected for multiple comparisons across voxels  
but not across #components!!)  
进行体素水平的多重比较校正而不是成分水平





# Group template maps 组模板图

- Generate from the data using ICA 使用ICA从数据生成
  - use all data to get unbiased templates 使用所有数据获取无偏的模板

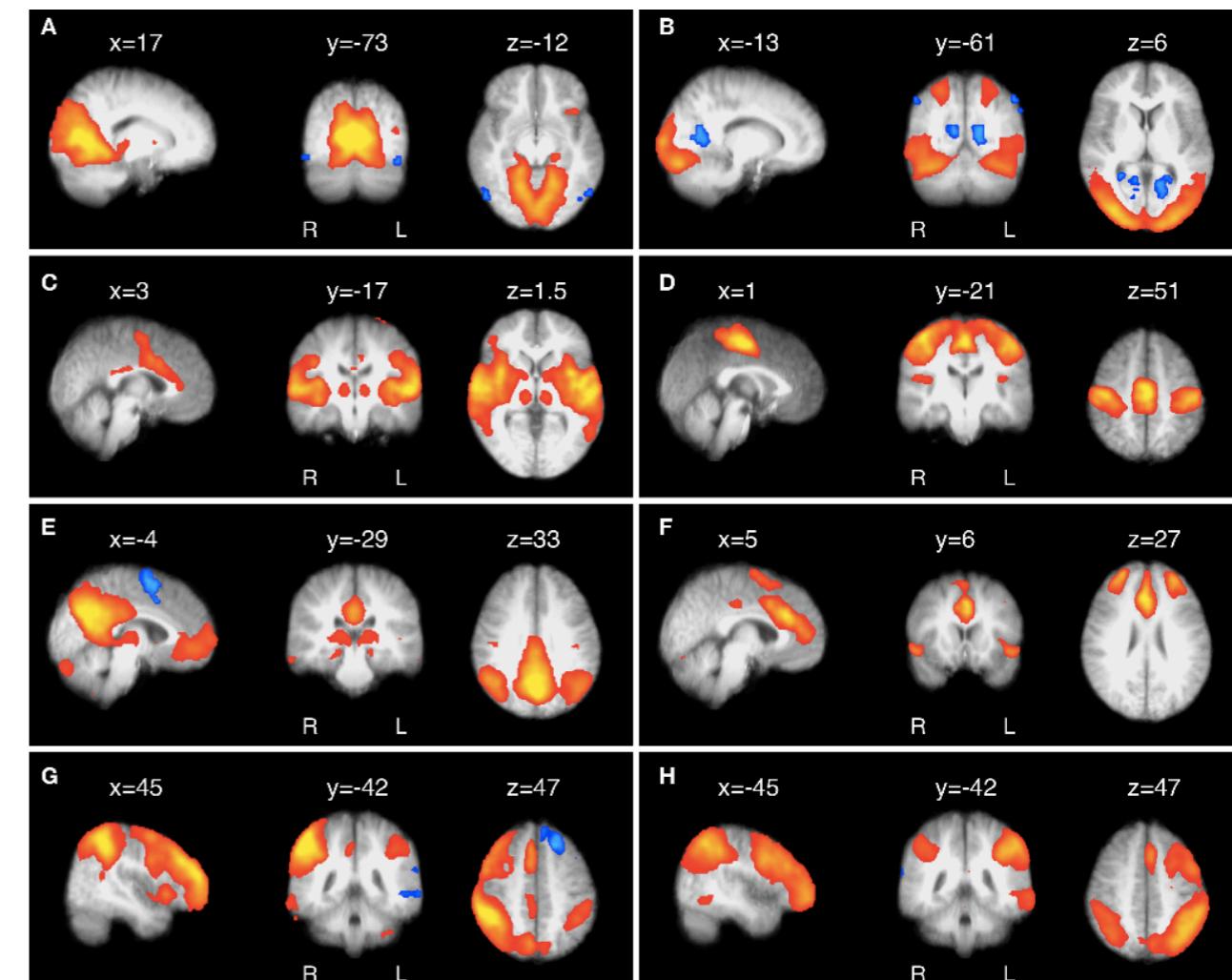


template RSNs

<http://www.fmrib.ox.ac.uk/analysis/research>

# Group template maps 组模板图

- Generate from the data using ICA 使用ICA从数据生成
  - use all data to get unbiased templates 使用所有数据获取无偏的模板
  - use independent control group 使用独立的对照组
  - will model signals and artefacts 为信号和伪影建模

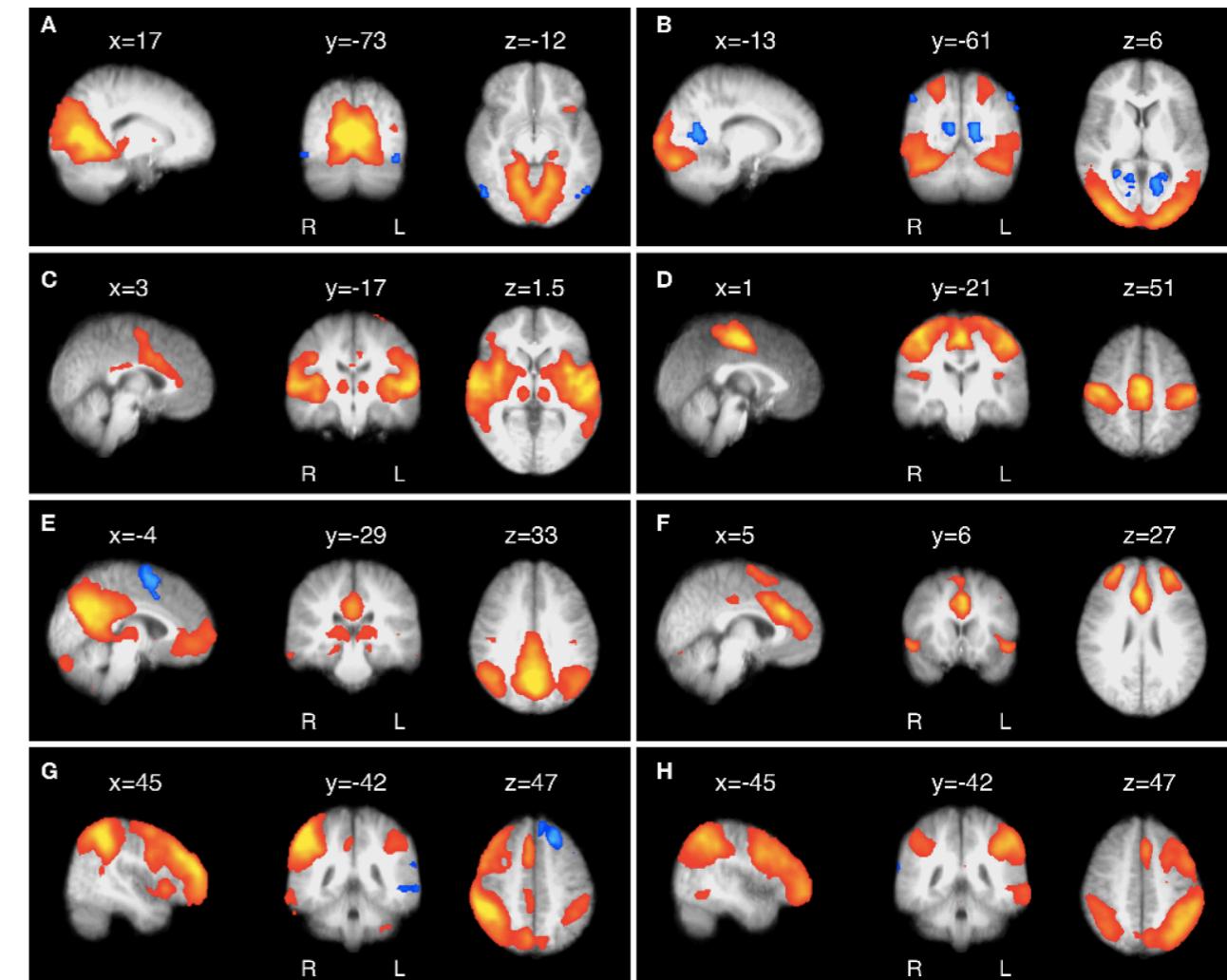


template RSNs

<http://www.fmrib.ox.ac.uk/analysis/research>

# Group template maps 组模板图

- Generate from the data using ICA 使用ICA从数据生成
  - use all data to get unbiased templates 使用所有数据获取无偏的模板
  - use independent control group 使用独立的对照组
  - will model signals and artefacts 为信号和伪影建模
- use existing template 使用现有模板



template RSNs  
<http://www.fmrib.ox.ac.uk/analysis/research>

# The book:





That's all folks

