

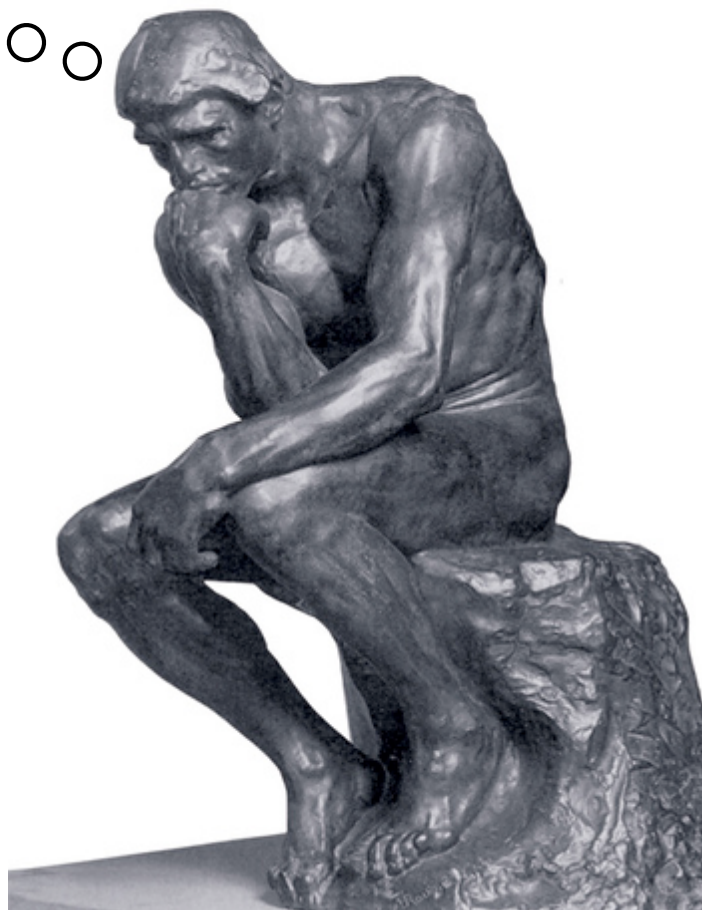
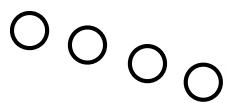


Inference 推断

how surprising is your statistic? (thresholding)

你的统计有多惊喜? (阈限)

But ... can I
trust it?





Outline大纲

- Null-hypothesis and Null-distribution 零假设和零分布
- Multiple comparisons and Family-wise error 多重比较和族错误率
- Different ways of being surprised 惊奇的不同方式
 - Voxel-wise inference (Maximum z) 体素推断 (最大z)
 - Cluster-wise inference (Maximum size) 簇水平推断 (最大尺寸)
- Parametric vs non-parametric tests 参数vs非参检验
- Enhanced clusters 增强的簇
- FDR - False Discovery Rate FDR-错误发现率



Outline大纲

- Null-hypothesis and Null-distribution 零假设和零分布
- Multiple comparisons and Family-wise error 多重比较和族错误率
- Different ways of being surprised 惊奇的不同方式
 - Voxel-wise inference (Maximum z) 体素推断 (最大z)
 - Cluster-wise inference (Maximum size) 簇水平推断 (最大尺寸)
- Parametric vs non-parametric tests 参数vs非参检验
- Enhanced clusters 增强的簇
- FDR - False Discovery Rate FDR-错误发现率

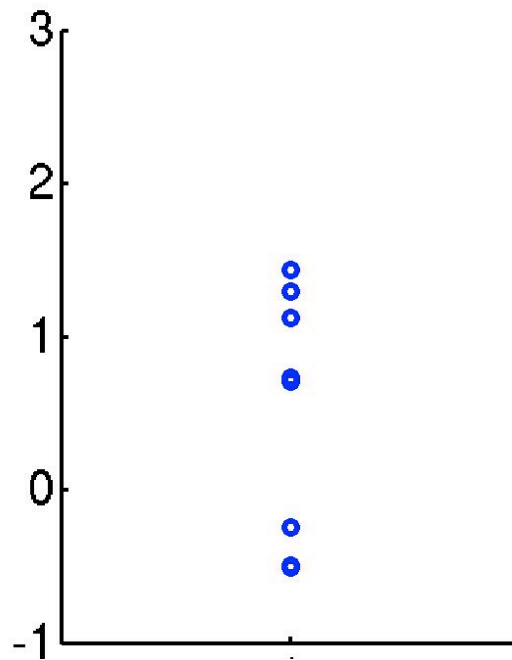


The task of classical inference

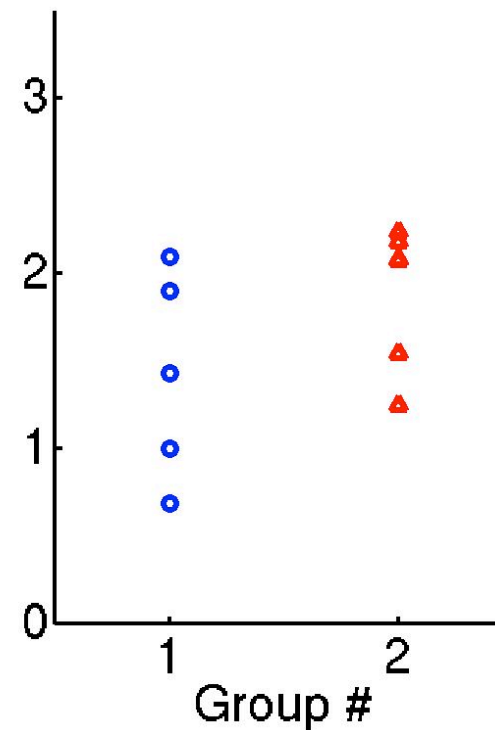
经典推断的任务

- Given some data we want to know if (e.g.) a mean is different from zero or if two means are different

给一些数据我们想知道平均值是否不同于0，或者两个平均值是否不同



$> 0 ?$



Different? 不同?

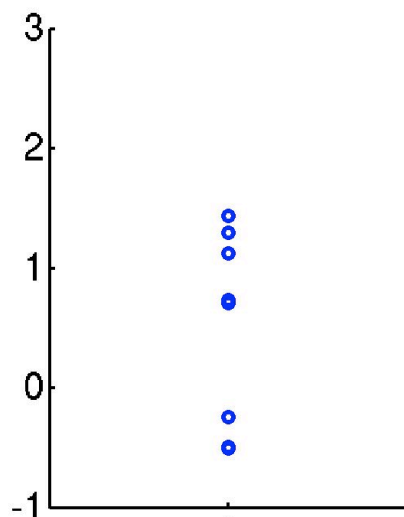


Tools of classical inference 经典推断的工具

I. A null-hypothesis 零假设

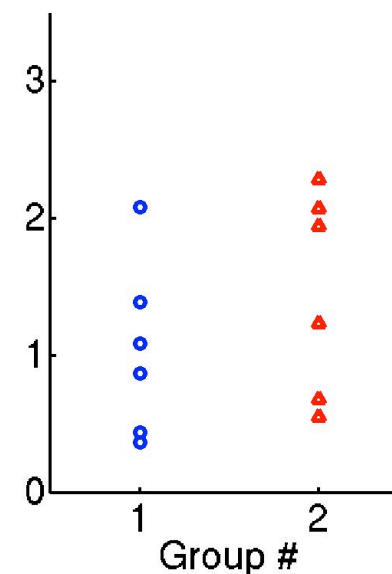
Typically the opposite of what we actually “hope”, e.g.
通常是我们所“期望”的反面

There is **no** effect of
treatment: $\mu = 0$
治疗无效 $\mu = 0$



There is **no** difference
between groups: $\mu_1 = \mu_2$

组之间无差 $\mu_1 = \mu_2$





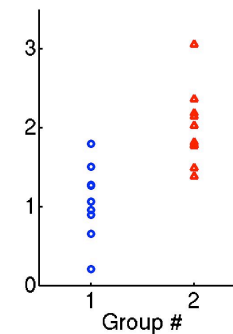
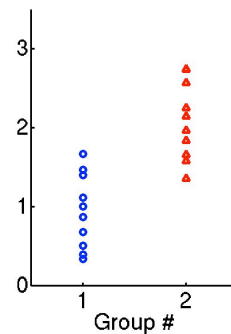
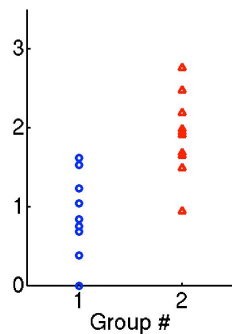
Tools of classical inference 经典推断的工具

1. A null-hypothesis 零假设

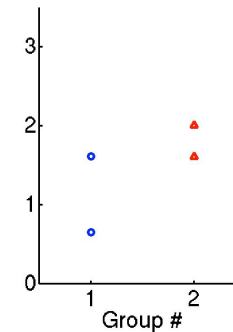
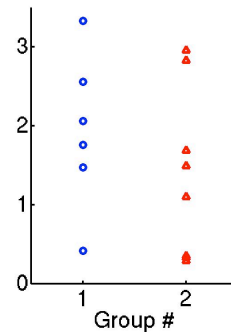
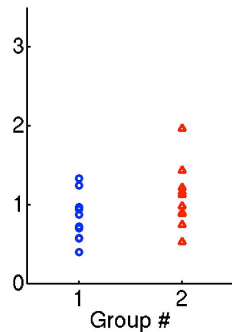
2. A test-statistic 检验统计

Assesses “trustworthiness”
评估可信度

Trustworthy
可信的



Dodgy
不可靠的





Tools of classical inference 经典推断的工具

1. A null-hypothesis 零假设

2. A test-statistic 检验统计

Assesses “trustworthiness” 评估可信度

A t -statistic reflects precisely this

t 统计正好反映了这点

$$t = \sqrt{n} \frac{\bar{x}_1 - \bar{x}_2}{\sqrt{\sigma^2}}$$

Many measurements:
Trustworthy
多次测量：可信

Large difference:
Trustworthy
较大差异：可信

Small variability:
Trustworthy
较小的变异：可信

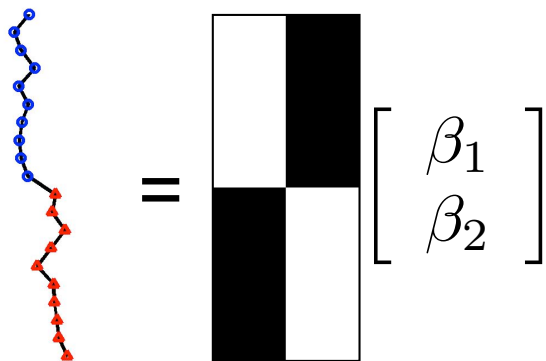


Tools of classical inference 经典推断的工具

1. A null-hypothesis 零假设

2. A test-statistic 检验统计

Or expressed in GLM lingo
或者以GLM术语表示



Large difference: Trustworthy
较大差异: 可信

$\bar{x}_1 - \bar{x}_2$

$$t = \frac{\mathbf{c}^T \hat{\boldsymbol{\beta}}}{\sqrt{\sigma^2} \sqrt{\mathbf{c}^T (\mathbf{X}^T \mathbf{X})^{-1} \mathbf{c}}}$$

$$\begin{bmatrix} \hat{\beta}_1 \\ \hat{\beta}_2 \end{bmatrix} = \begin{bmatrix} \bar{x}_1 \\ \bar{x}_2 \end{bmatrix}$$

Small variability: Trustworthy 小变异: 可信
Many measurements: Trustworthy 很多测量: 可信



Tools of classical inference 经典推断的工具

1. A null-hypothesis 零假设
2. A test-statistic 检验统计
3. A null-distribution 零分布

Let us assume there is no difference, i.e. the null-hypothesis is true.
假设没区别，零假设正确

We might then get these data
我们可能得到这些数据

$$= \begin{bmatrix} \text{white} & \text{black} \\ \text{black} & \text{white} \end{bmatrix} \begin{bmatrix} \beta_1 \\ \beta_2 \end{bmatrix} + \mathbf{e}$$

$$t = 2.19$$

$$t = \frac{\mathbf{c}^T \hat{\boldsymbol{\beta}}}{\sqrt{\sigma^2 \mathbf{c}^T (\mathbf{X}^T \mathbf{X})^{-1} \mathbf{c}}}$$

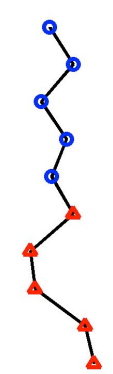
$\mathbf{c}^T \hat{\boldsymbol{\beta}} = 1.17$
 $\sigma^2 = 0.71$
 Constant 常量



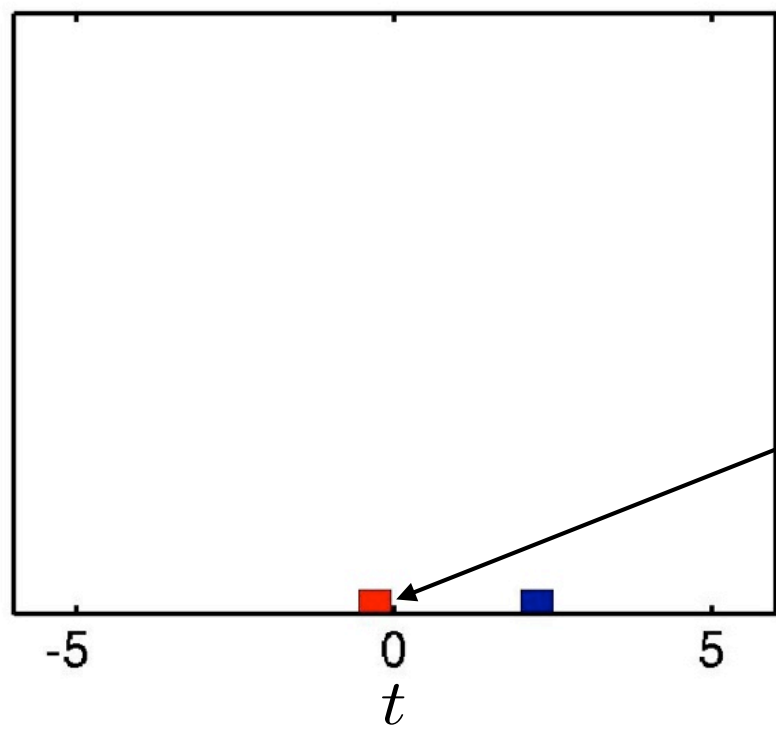
Tools of classical inference 经典推断的工具

- 1. A null-hypothesis 零假设
- 2. A test-statistic 检验统计
- 3. A null-distribution 零分布

or we could have gotten these
我们也可能获得这些数据



$$= \begin{bmatrix} \blacksquare & \blacksquare \\ \blacksquare & \square \end{bmatrix} \begin{bmatrix} \beta_1 \\ \beta_2 \end{bmatrix} + \mathbf{e}$$



$$t = -0.51$$

$$t = \frac{\mathbf{c}^T \hat{\boldsymbol{\beta}}}{\sqrt{\sigma^2 \mathbf{c}^T (\mathbf{X}^T \mathbf{X})^{-1} \mathbf{c}}}$$

$\mathbf{c}^T \hat{\boldsymbol{\beta}} = -0.37$

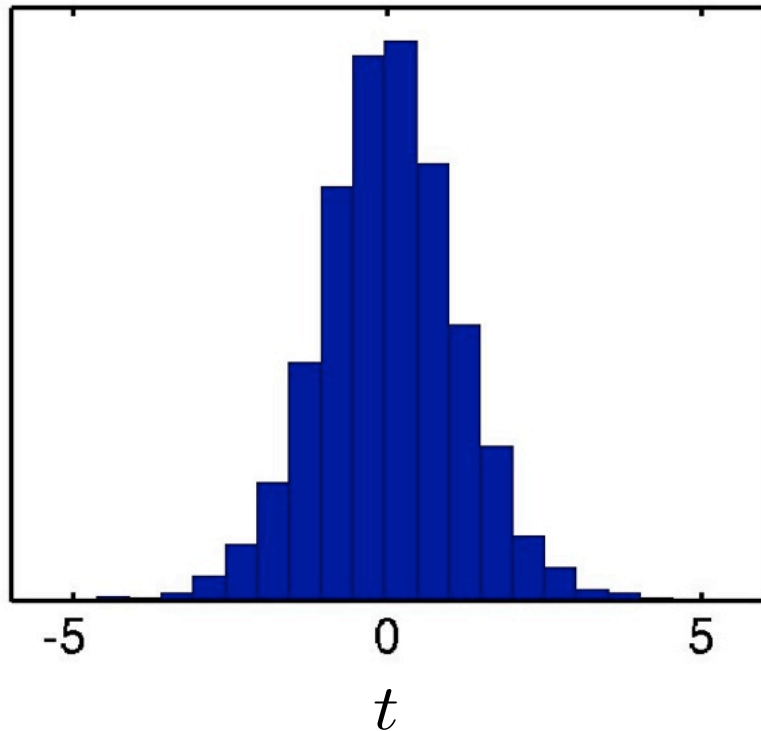
$\sigma^2 = 1.28$

Constant 常量



Tools of classical inference 经典推断的工具

1. A null-hypothesis 零假设
2. A test-statistic 检验统计
3. A null-distribution 零分布

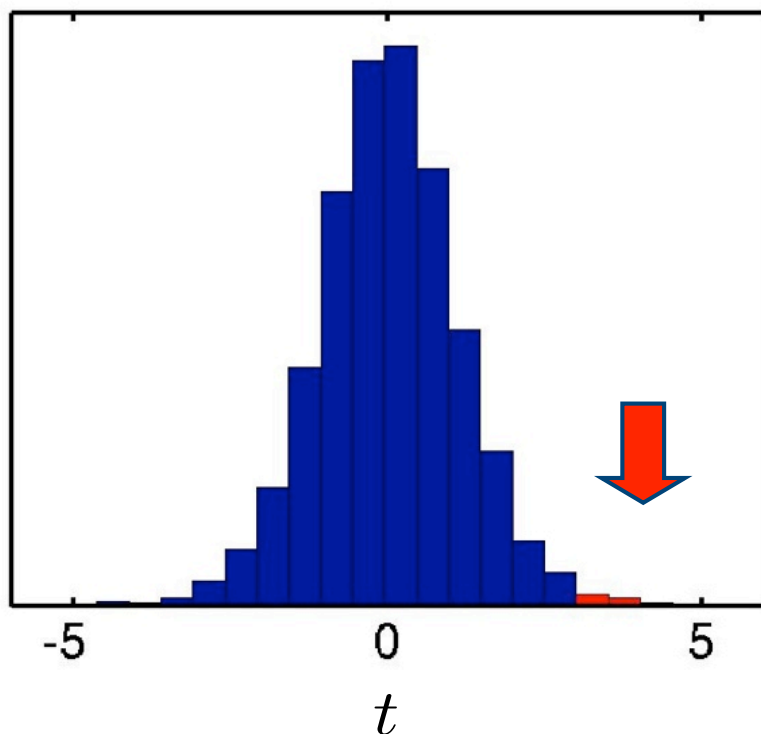


So, why is this helpful?
那么，为什么这样有帮助呢？



Tools of classical inference 经典推断的工具

1. A null-hypothesis 零假设
2. A test-statistic 检验统计
3. A null-distribution 零分布



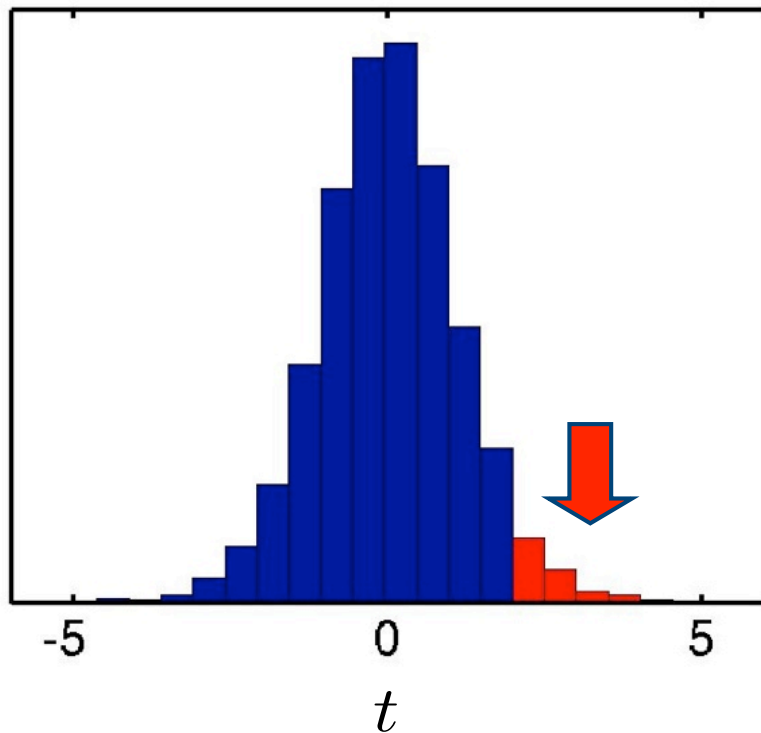
Well, it for example tells us that in $\sim 1\%$ of the cases $t > 3.00$, even when the null-hypothesis is true.

好吧，他告诉我们大约1%的可能是 $t > 3.00$ ，即零假设为真。



Tools of classical inference 经典推断的工具

1. A null-hypothesis 零假设
2. A test-statistic 检验统计
3. A null-distribution 零分布



Or that in $\sim 5\%$ of the cases $t > 1.99$.

When the null-hypothesis is true.

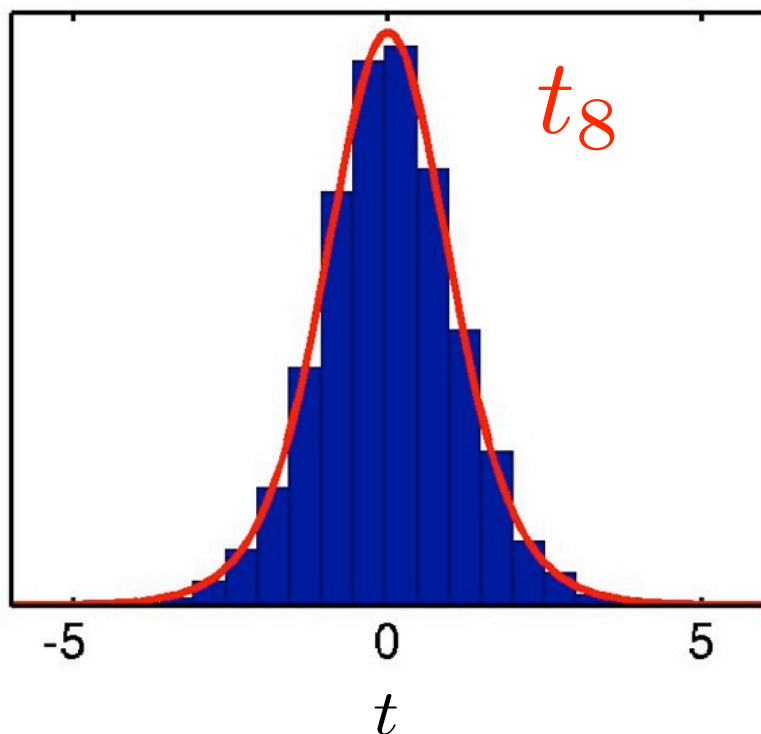
或者在5%的情况下 $t > 1.99$

当零假设为真



Tools of classical inference 经典推断的工具

1. A null-hypothesis 零假设
2. A test-statistic 检验统计
3. A null-distribution 零分布

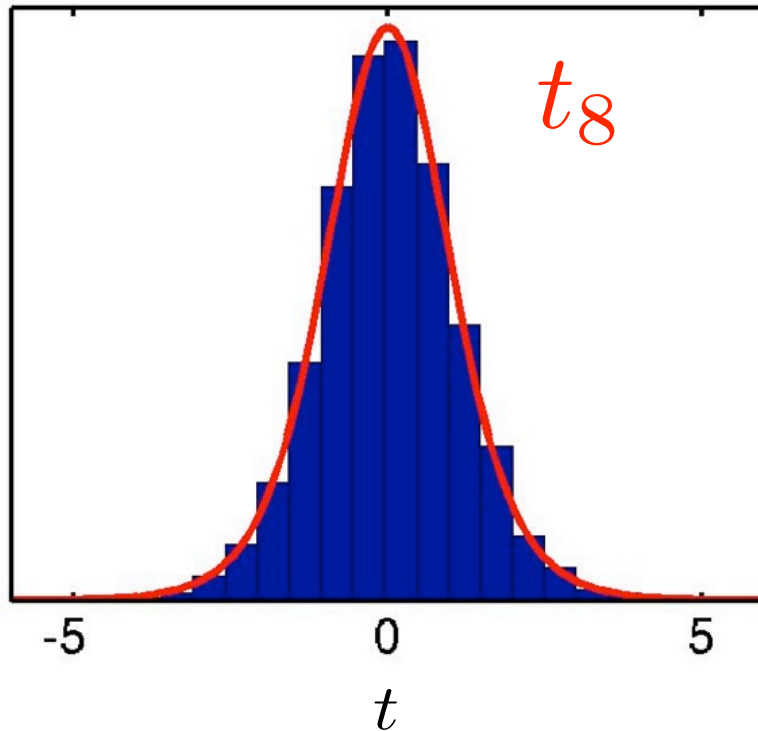


And best of all: This distribution is known *i.e.* one can calculate it.
Much as one can calculate sine or cosine
最重要的是：这种分布是已知的，即可以计算它。
就像每一个人可以计算正弦或余弦



Tools of classical inference 经典推断的工具

1. A null-hypothesis 零假设
2. A test-statistic 检验统计
3. A null-distribution 零分布



And best of all: This distribution is known *i.e.* one can calculate it.
Much as one can calculate sine or cosine
最重要的是：这种分布是已知的，即可以计算它。
就像每一个人可以计算正弦或余弦

Provided that $\mathbf{e} \sim N(0, \sigma^2)$
规定 $\mathbf{e} \sim N(0, \sigma^2)$



An example experiment 举例实验

1. A null-hypothesis 零假设

$$H_0: \bar{x}_1 = \bar{x}_2, H_1: \bar{x}_1 > \bar{x}_2$$

2. A test-statistic 检验统计

3. A null-distribution 零分布

So, with these tools let us do an experiment

利用这些工具，我们来做个实验



An example experiment 举例实验

1. A null-hypothesis 零假设

$$H_0: \bar{x}_1 = \bar{x}_2, H_1: \bar{x}_1 > \bar{x}_2$$

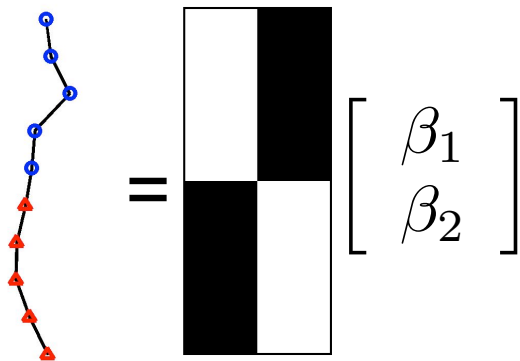
2. A test-statistic 检验统计

$$t_8 = 2.64$$

3. A null-distribution 零分布

So, with these tools let us do an experiment

利用这些工具，我们来做个实验



$$t = \frac{\mathbf{c}^T \hat{\boldsymbol{\beta}}}{\sqrt{\sigma^2} \sqrt{\mathbf{c}^T (\mathbf{X}^T \mathbf{X})^{-1} \mathbf{c}}} = \frac{1.53}{\sqrt{0.85} \sqrt{0.4}} = 2.64$$



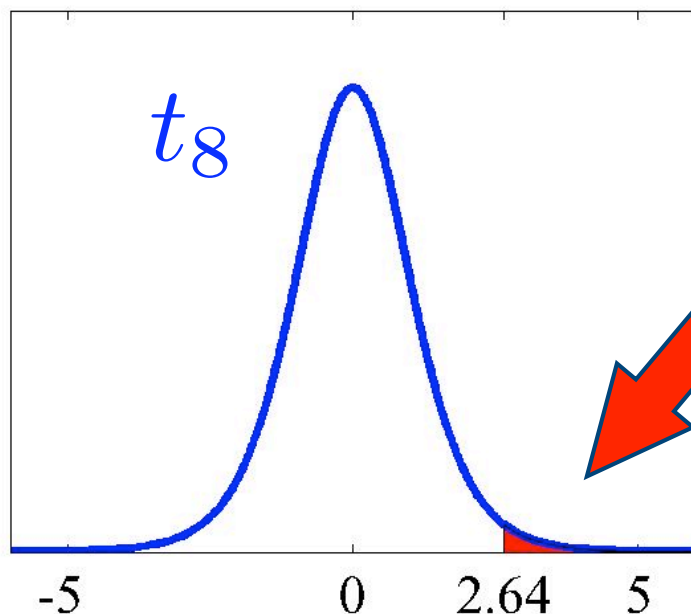
An example experiment 举例实验

1. A null-hypothesis 零假设
2. A test-statistic 检验统计
3. A null-distribution 零分布

$$H_0: \bar{x}_1 = \bar{x}_2, H_1: \bar{x}_1 > \bar{x}_2$$

$$t_8 = 2.64$$

So, with these tools let us do an experiment
利用这些工具，我们来做个实验



If the null-hypothesis is true,
we would expect to have a
~1.46% chance of
finding a t-value this large or
larger

如果原假设为真，则我们期望有1.46%的机会
找到如此大或更大的t值



An example experiment 举例实验

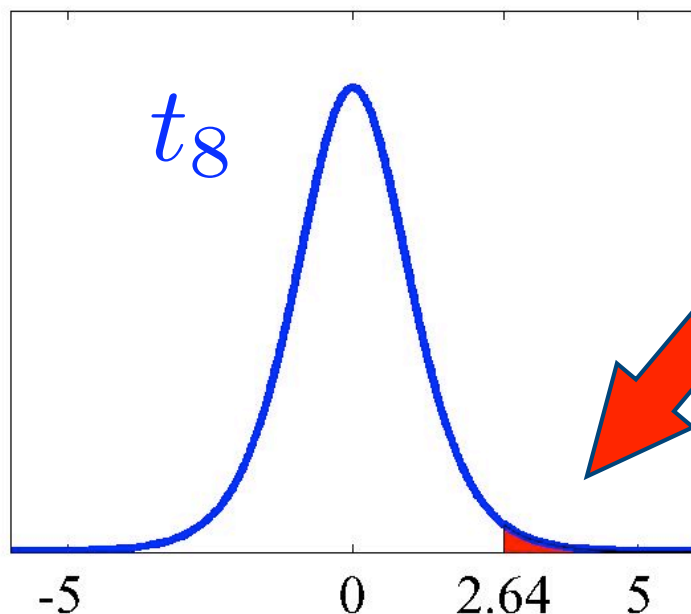
1. A null-hypothesis 零假设
2. A test-statistic 检验统计
3. A null-distribution 零分布

$$H_0: \bar{x}_1 = \bar{x}_2, H_1: \bar{x}_1 > \bar{x}_2$$

$$t_8 = 2.64$$

$$t_8 = 2.64^*$$

So, with these tools let us do an experiment
利用这些工具，我们来做个实验



There is ~1.46% risk that we reject the null-hypothesis (i.e. claim we found something) when the null is actually true. We can live with that (well, I can).
当零假设确实为真时，我们有1.46%的风险会拒绝零假设（即声称我们发现了某些东西）我们可以接受这种情况（嗯，至少我可以）



False positives/negatives 假阳性/阴性

- I am sure you have all heard about “**false positives**” and “**false negatives**”. 我相信大家都听说过“假阳性”和“假阴性”。
- **But what does that actually mean?** 但这实际上是什么意思？



False positives/negatives 假阳性/阴性

- I am sure you have all heard about “**false positives**” and “**false negatives**”. 我相信大家都听说过“假阳性”和“假阴性”。
- **But what does that actually mean?** 但这实际上是什么意思?
- We want to perform an experiment and as part of that we define a null-hypothesis, e.g. $H_0 : \mu = 0$
我们想进行一个实验，并在其中定义一个零假设
- **Now what can happen?** 现在会发生什么?



False positives/negatives 假阳性/阴性

- I am sure you have all heard about “**false positives**” and “**false negatives**”. 我相信大家都听说过“假阳性”和“假阴性”。
- But what does that actually mean? 但这实际上是什么意思?
- We want to perform an experiment and as part of that we define a null-hypothesis, e.g. $H_0 : \mu = 0$
我们想进行一个实验，并在其中定义一个零假设
- Now what can happen? 现在会发生什么?

H_0 is true真 } True state of affairs 真实情况
 H_0 is false假 }



False positives/negatives 假阳性/阴性

- I am sure you have all heard about “**false positives**” and “**false negatives**”. 我相信大家都听说过“假阳性”和“假阴性”。
- But what does that actually mean? 但这实际上是什么意思?
- We want to perform an experiment and as part of that we define a null-hypothesis, e.g. $H_0 : \mu = 0$
我们想进行一个实验，并在其中定义一个零假设
- Now what can happen? 现在会发生什么?

H_0 is true真 } True state of affairs 真实情况
 H_0 is false假 }

We don't reject H_0 不拒绝 H_0 } Our decision 我们的决定
We reject H_0 拒绝 H_0 }



False positives/negatives 假阳性/阴性

H_0 is true真 } True state of affairs真实情况
 H_0 is false假 }

We don't reject H_0 不拒绝 H_0 } Our decision我们的决定
We reject H_0 拒绝 H_0 }

We don't reject H_0 不拒绝 We reject H_0 拒绝

H_0 is true为真

H_0 is false为假



False positives/negatives 假阳性/阴性

H_0 is true真 } True state of affairs真实情况
 H_0 is false假 }

We don't reject H_0 不拒绝 H_0 } Our decision我们的决定
We reject H_0 拒绝 H_0 }

We don't reject H_0 不拒绝 We reject H_0 拒绝

H_0 is true为真



H_0 is false为假






False positives/negatives 假阳性/阴性

H_0 is true真 } True state of affairs真实情况
 H_0 is false假 }

We don't reject H_0 不拒绝 H_0 } Our decision我们的决定
We reject H_0 拒绝 H_0 }

We don't reject H_0 不拒绝 We reject H_0 拒绝

H_0 is true为真		False positive假阳性
H_0 is false为假	False negative假阴性	



False positives/negatives 假阳性/阴性

H_0 is true真 } True state of affairs真实情况
 H_0 is false假 }

We don't reject H_0 不拒绝 H_0 } Our decision我们的决定
We reject H_0 拒绝 H_0 }

We don't reject H_0 不拒绝 We reject H_0 拒绝

H_0 is true为真



False positive
Type I error
假阳性, I类误差

H_0 is false为假

False negative
Type II error
假阴性, II类误差





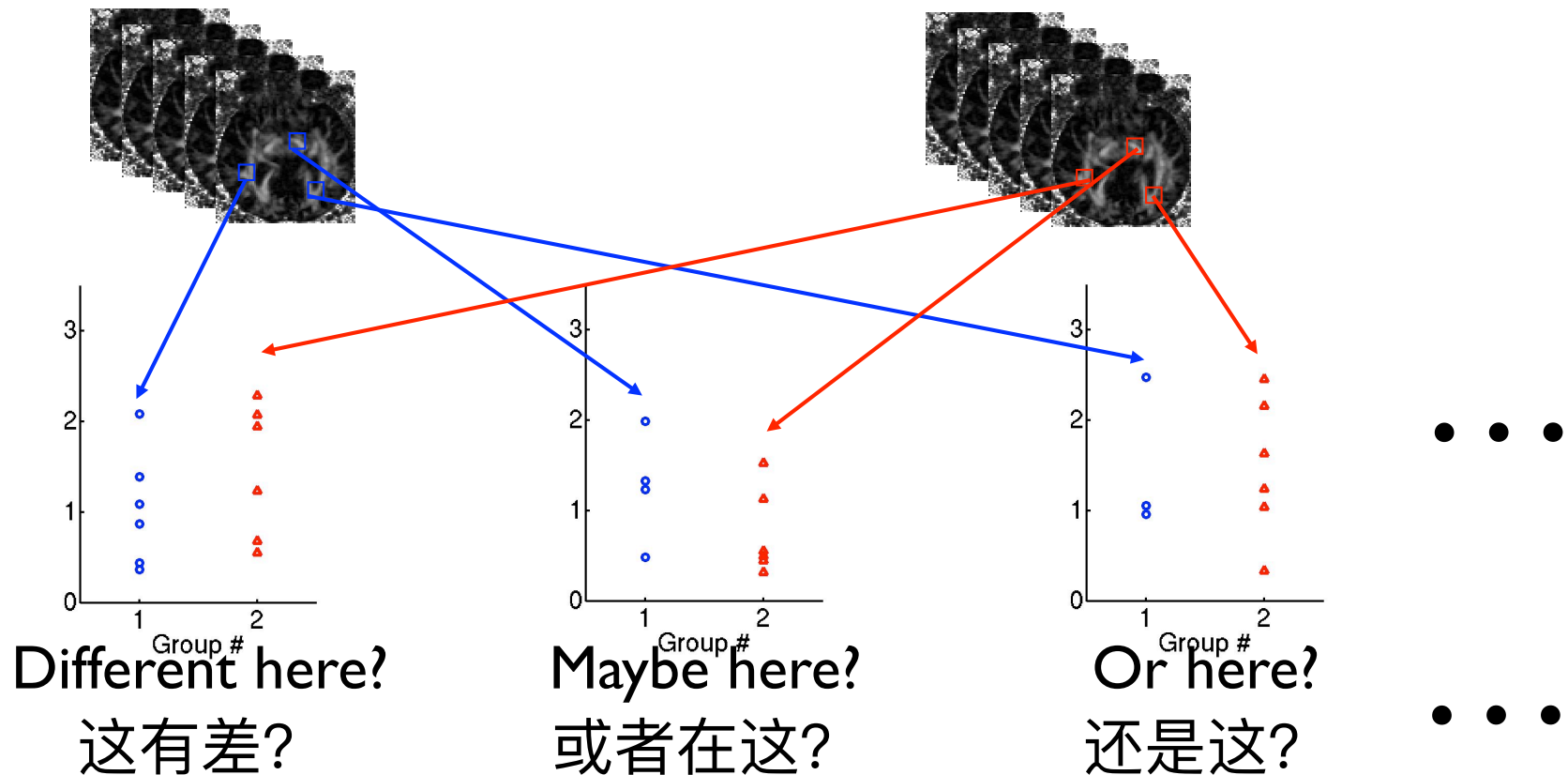
Outline大纲

- Null-hypothesis and Null-distribution 零假设和零分布
- Multiple comparisons and Family-wise error 多重比较和族错误率
- Different ways of being surprised 惊奇的不同方式
 - Voxel-wise inference (Maximum z) 体素推断 (最大z)
 - Cluster-wise inference (Maximum size) 簇水平推断 (最大尺寸)
- Parametric vs non-parametric tests 参数vs非参检验
- Enhanced clusters 增强的簇
- FDR - False Discovery Rate FDR-错误发现率



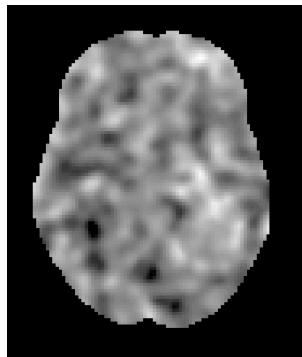
Multiple Comparisons 多重比较

- In neuroimaging we typically perform **many** tests as part of a study 在神经影像学中，我们通常会执行许多检验，作为研究的一部分



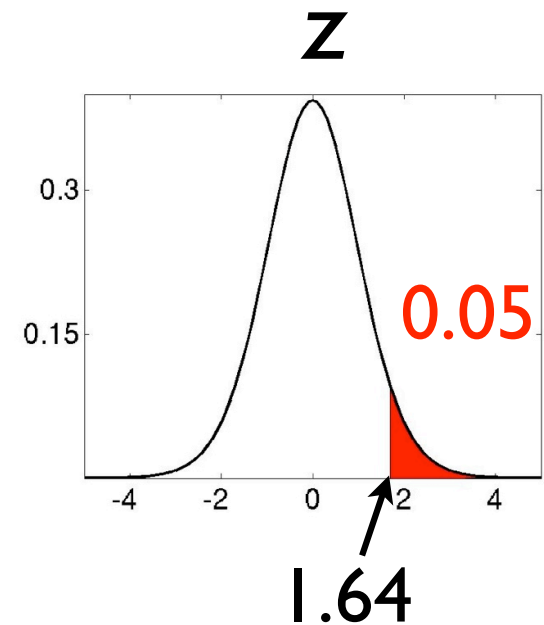


What happens when we apply this to imaging data? 我们把这个运用到图像数据会发生啥?



z-map where each voxel $\sim N$.
Null-hypothesis true everywhere, i.e. **NO ACTIVATIONS**

每个体素正态分布的z图。
零假设在所有位置都对，也就是没激活



z-map
thresholded at
1.64
阈值在1.64



16 clusters
288 voxels
~5.5% of the voxels
差不多有16个簇，288个体素，
约占这些体素的5.5%

That's a **LOT** of false positives
有很多误报（假阳性）

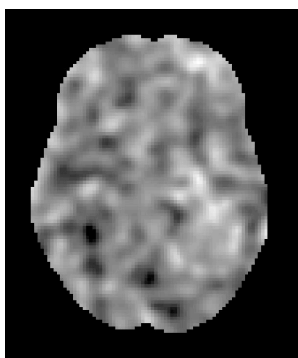


Italians doing maths: The Bonferroni correction

意大利人的数学：Bonferroni校正

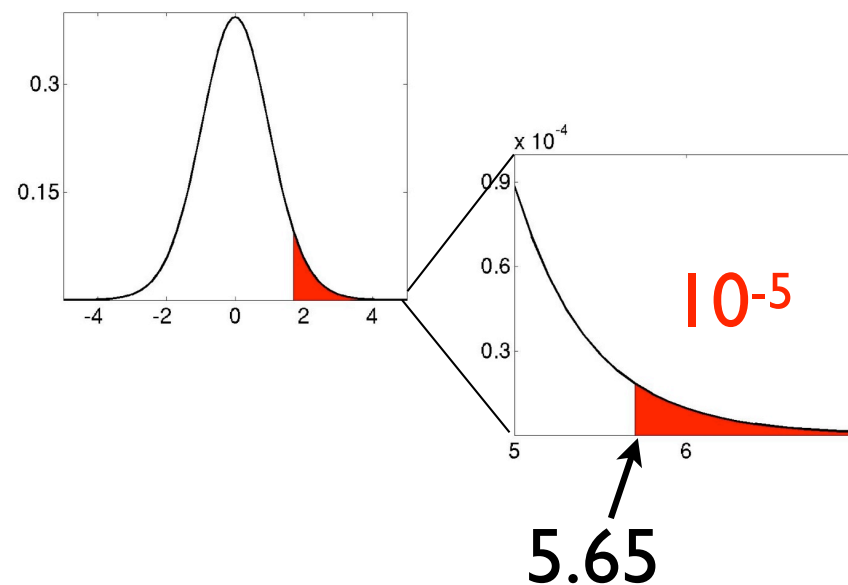
Bonferroni says threshold at α divided by # of tests

阈值应该是 α 除以测试次数



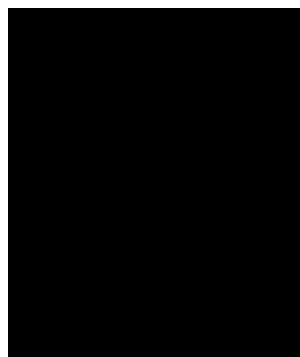
5255 voxels

$$0.05/5255 \approx 10^{-5}$$



z-map
thresholded at
5.65

阈值在5.65



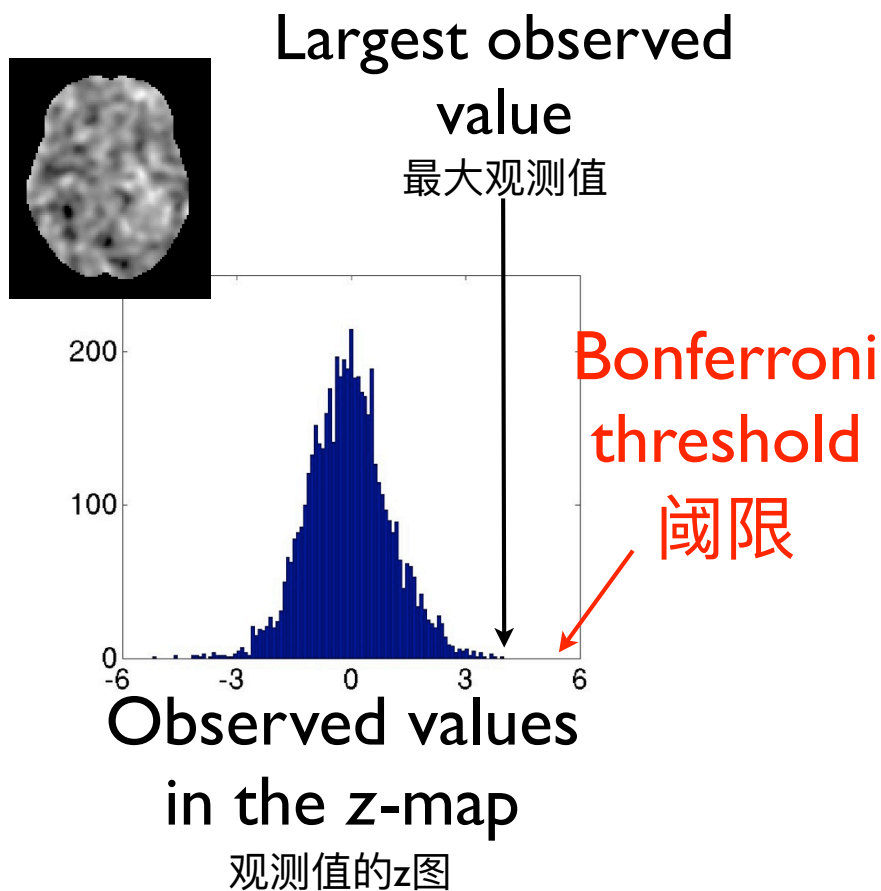
No false positives.
Hurrah for Italy!

无误报。意大利万岁!

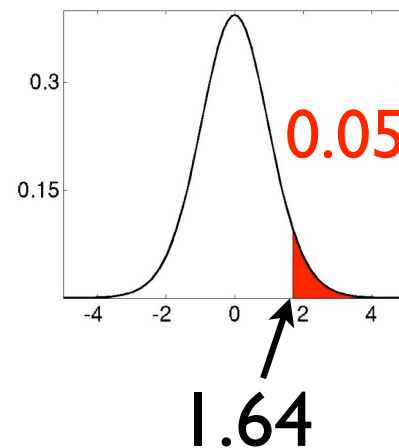


But ... doesn't 5.65 sound very high?

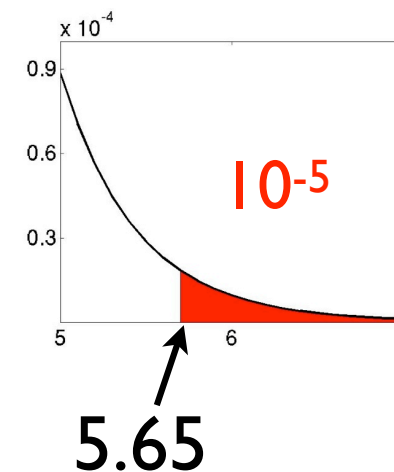
但是5.65听起来不是很高么



Too lenient
太宽容



Too harsh
太苛刻



So what do we want then?

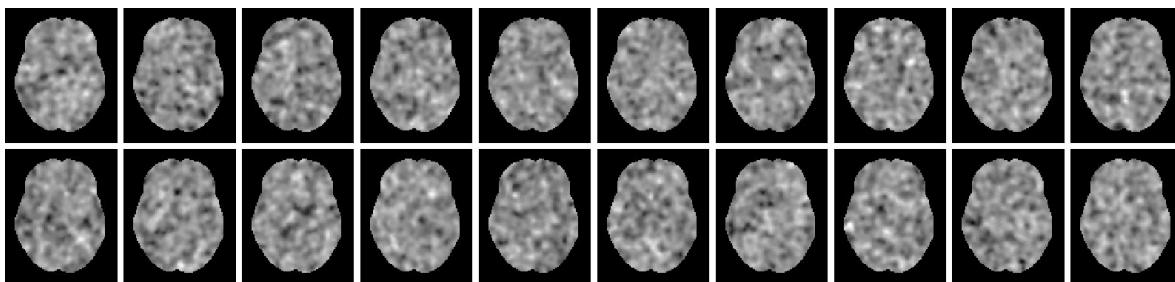
我们到底想要什么?



Family-wise error 族错误率

Let's say we perform a series of identical studies

假设我们进行了一系列完全相同的研究



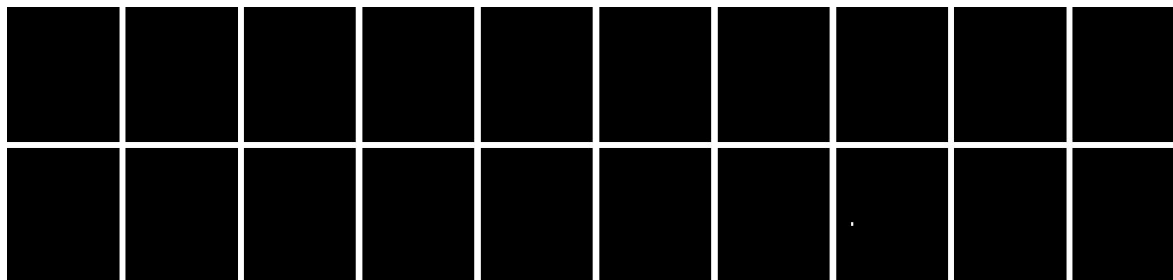
Each z-map is the end result of a study 每个z图都是研究的最终结果

Let us further say that the null-hypothesis is true.

我们进一步说零假设正确。

We want to threshold the data so that only once in 20 studies do we find a voxel above this threshold.

我们想对数据进行阈值处理，以便20个研究中只有一次发现体素高于此阈值。



But how do we find such a threshold?

但我们怎么找到这个阈值呢



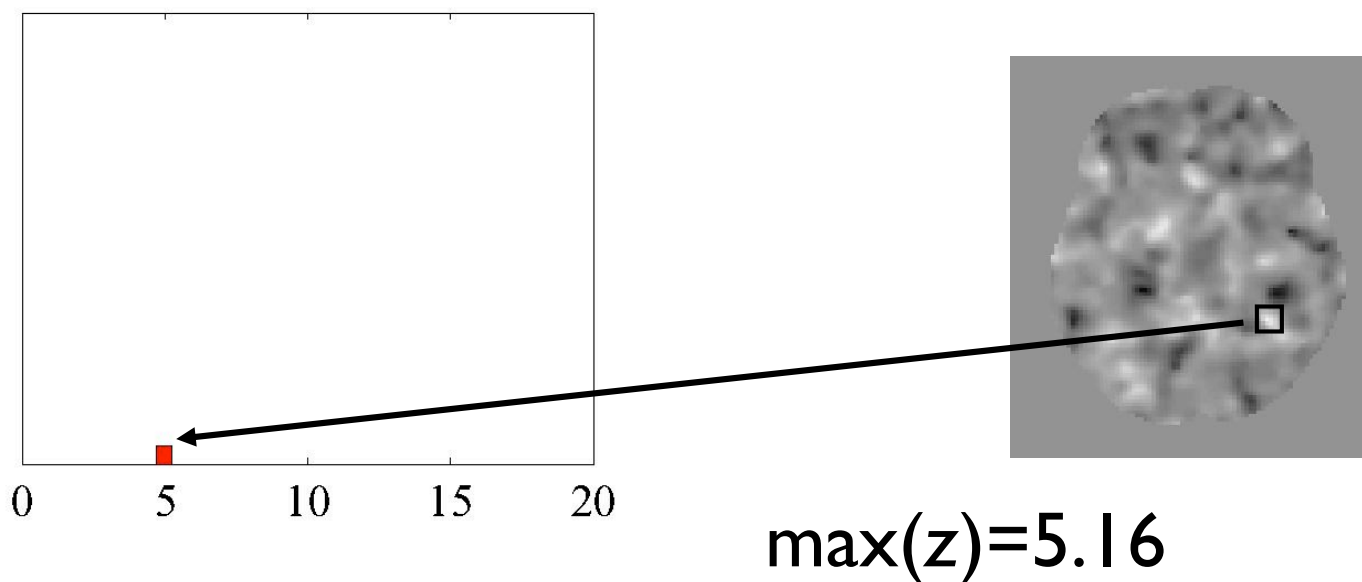
Outline大纲

- Null-hypothesis and Null-distribution 零假设和零分布
- Multiple comparisons and Family-wise error 多重比较和族错误率
- Different ways of being surprised 惊奇的不同方式
 - Voxel-wise inference (Maximum z) 体素推断 (最大z)
 - Cluster-wise inference (Maximum size) 簇水平推断 (最大尺寸)
- Parametric vs non-parametric tests 参数vs非参检验
- Enhanced clusters 增强的簇
- FDR - False Discovery Rate FDR-错误发现率



Maximum z 最大z值

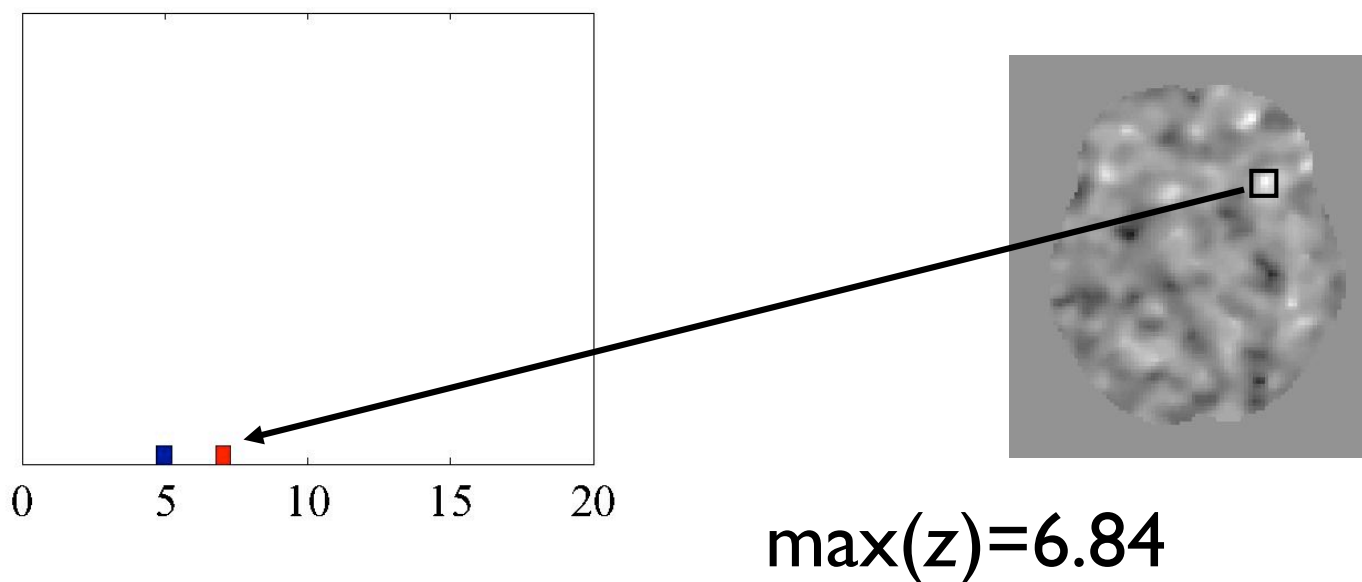
- When we want to control “family-wise error”, what do we in practice want?
我们什么时候想控制族错误率，我们实际想要什么呢？
- If the null-hypothesis is true (no activation) we want to reject it no more than 5% of the time. 如果零假设为真（无激活），我们想要不大于5%的时候拒绝他。
- And if we reject anything, we will definitely reject the most “extreme” value ($\max(z)$) in the brain. 如果我们拒绝了所有，我们肯定会拒绝大脑中的最极端的值($\max(z)$)





Maximum z 最大z值

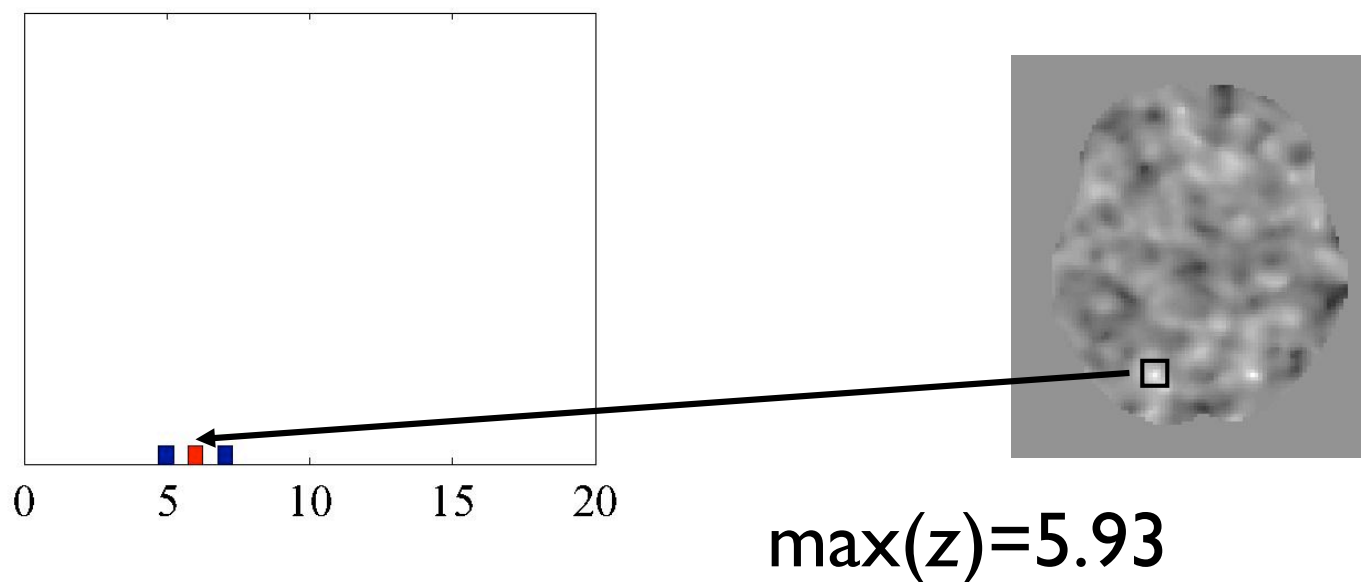
- When we want to control “family-wise error”, what do we in practice want?
我们什么时候想控制族错误率，我们实际想要什么呢？
- If the null-hypothesis is true (no activation) we want to reject it no more than 5% of the time. 如果零假设为真（无激活），我们想要不大于5%的时候拒绝他。
- And if we reject anything, we will definitely reject the most “extreme” value ($\max(z)$) in the brain. 如果我们拒绝了所有，我们肯定会拒绝大脑中的最极端的值($\max(z)$)





Maximum z 最大z值

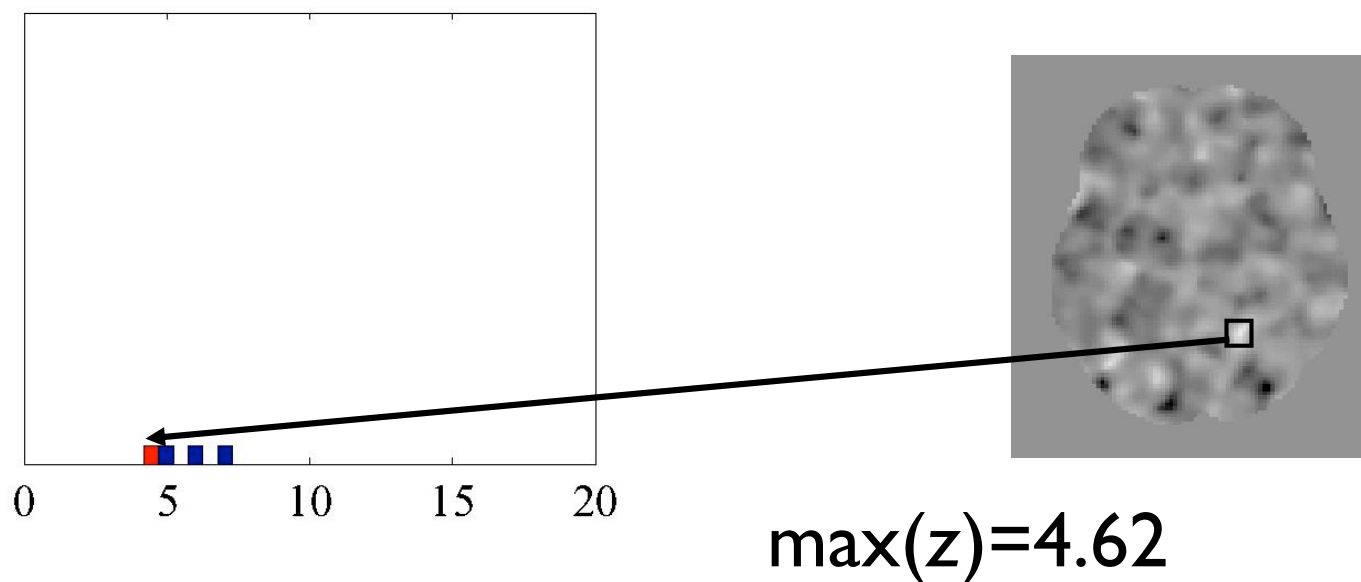
- When we want to control “family-wise error”, what do we in practice want?
我们什么时候想控制族错误率，我们实际想要什么呢？
- If the null-hypothesis is true (no activation) we want to reject it no more than 5% of the time. 如果零假设为真（无激活），我们想要不大于5%的时候拒绝他。
- And if we reject anything, we will definitely reject the most “extreme” value ($\max(z)$) in the brain. 如果我们拒绝了所有，我们肯定会拒绝大脑中的最极端的值($\max(z)$)





Maximum z 最大z值

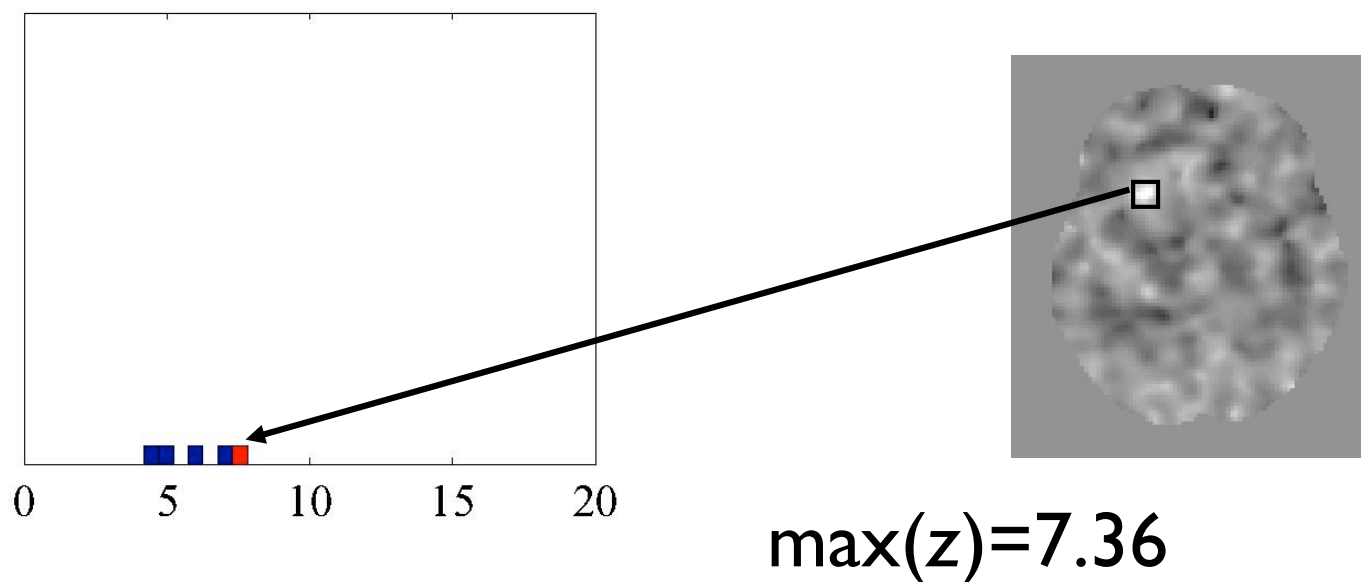
- When we want to control “family-wise error”, what do we in practice want?
我们什么时候想控制族错误率，我们实际想要什么呢？
- If the null-hypothesis is true (no activation) we want to reject it no more than 5% of the time. 如果零假设为真（无激活），我们想要不大于5%的时候拒绝他。
- And if we reject anything, we will definitely reject the most “extreme” value ($\max(z)$) in the brain. 如果我们拒绝了所有，我们肯定会拒绝大脑中的最极端的值($\max(z)$)





Maximum z 最大z值

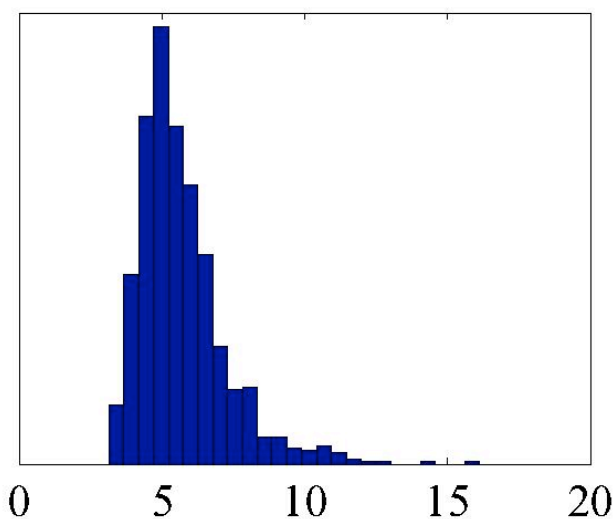
- When we want to control “family-wise error”, what do we in practice want?
我们什么时候想控制族错误率，我们实际想要什么呢？
- If the null-hypothesis is true (no activation) we want to reject it no more than 5% of the time. 如果零假设为真（无激活），我们想要不大于5%的时候拒绝他。
- And if we reject anything, we will definitely reject the most “extreme” value ($\max(z)$) in the brain. 如果我们拒绝了所有，我们肯定会拒绝大脑中的最极端的值($\max(z)$)





Maximum z 最大 z 值

- When we want to control “family-wise error”, what do we in practice want?
我们什么时候想控制族错误率，我们实际想要什么呢？
- If the null-hypothesis is true (no activation) we want to reject it no more than 5% of the time. 如果零假设为真（无激活），我们想要不大于5%的时候拒绝他.
- And if we reject anything, we will definitely reject the most “extreme” value ($\max(z)$) in the brain. 如果我们拒绝了所有，我们肯定会拒绝大脑中的最极端的值($\max(z)$)

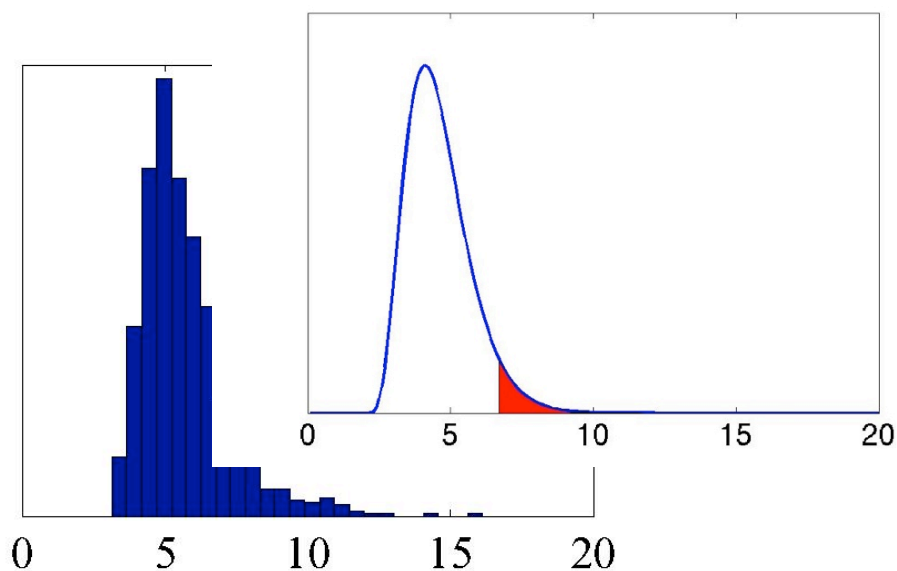


Etc...



Maximum z 最大z值

- When we want to control “family-wise error”, what do we in practice want?
我们什么时候想控制族错误率，我们实际想要什么呢？
- If the null-hypothesis is true (no activation) we want to reject it no more than 5% of the time. 如果零假设为真（无激活），我们想要不大于5%的时候拒绝他。
- And if we reject anything, we will definitely reject the most “extreme” value ($\max(z)$) in the brain. 如果我们拒绝了所有，我们肯定会拒绝大脑中的最极端的值($\max(z)$)

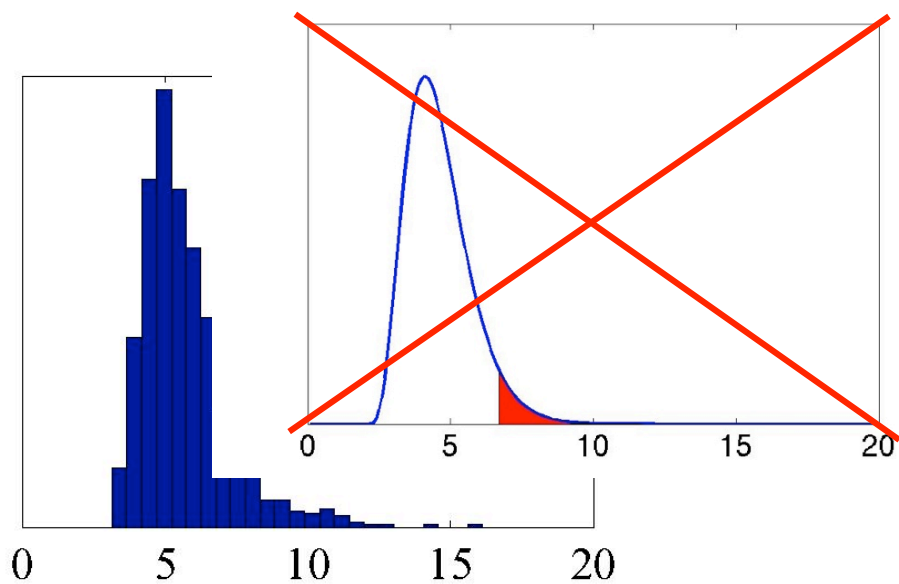


This is the distribution we want to use for our FWE control.
这是我们要用于FWE控制的分布。



Maximum z 最大z值

- When we want to control “family-wise error”, what do we in practice want?
我们什么时候想控制族错误率，我们实际想要什么呢？
- If the null-hypothesis is true (no activation) we want to reject it no more than 5% of the time. 如果零假设为真（无激活），我们想要不大于5%的时候拒绝他。
- And if we reject anything, we will definitely reject the most “extreme” value ($\max(z)$) in the brain. 如果我们拒绝了所有，我们肯定会拒绝大脑中的最极端的值($\max(z)$)



This is the distribution we want to use
for our FWE control.
But there is no known expression for
it! ☹️

这是我们要用于FWE控制的分布。但
是没有已知的表达方式! ☹️



Outline大纲

- Null-hypothesis and Null-distribution 零假设和零分布
- Multiple comparisons and Family-wise error 多重比较和族错误率
- Different ways of being surprised 惊奇的不同方式
 - Voxel-wise inference (Maximum z) 体素推断 (最大z)
 - Cluster-wise inference (Maximum size) 簇水平推断 (最大尺寸)
- Parametric vs non-parametric tests 参数vs非参检验
- Enhanced clusters 增强的簇
- FDR - False Discovery Rate FDR-错误发现率

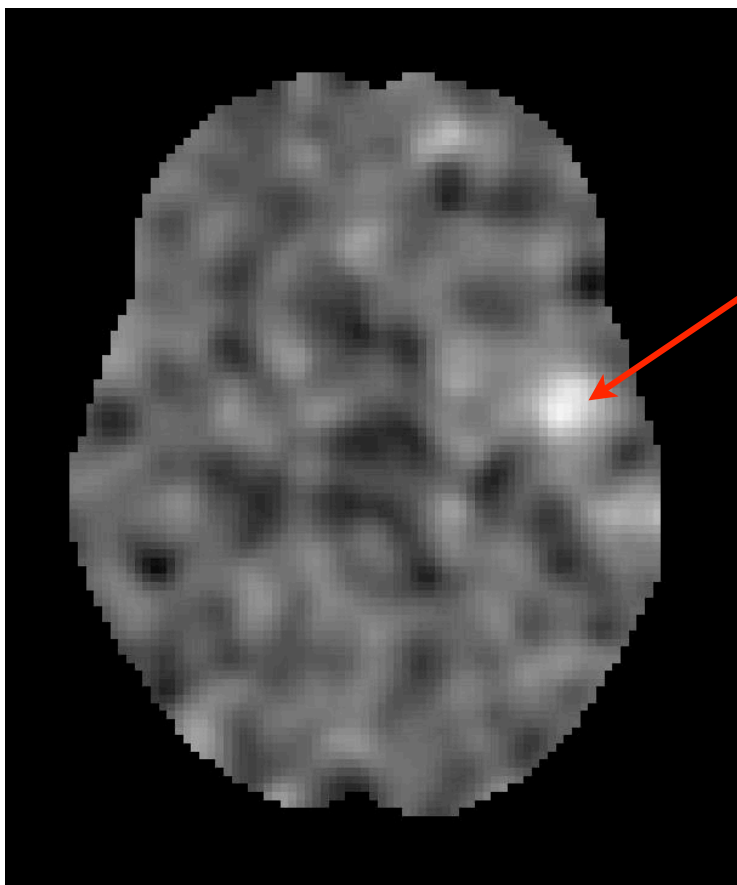


Spatial extent: another way to be surprised

空间范围：另一个让人惊奇的方式

This far we have talked about voxel-based tests

目前为止我们讨论了基于体素的检验。



We say: Look! A z-value of 7. That is so surprising (under the null-hypothesis) that I will have to reject it. (Though we are of course secretly delighted to do so)

看z值等于7，太令人意外了（在零假设下），我不得不拒绝他。（虽然我们当然很乐意这么做。）

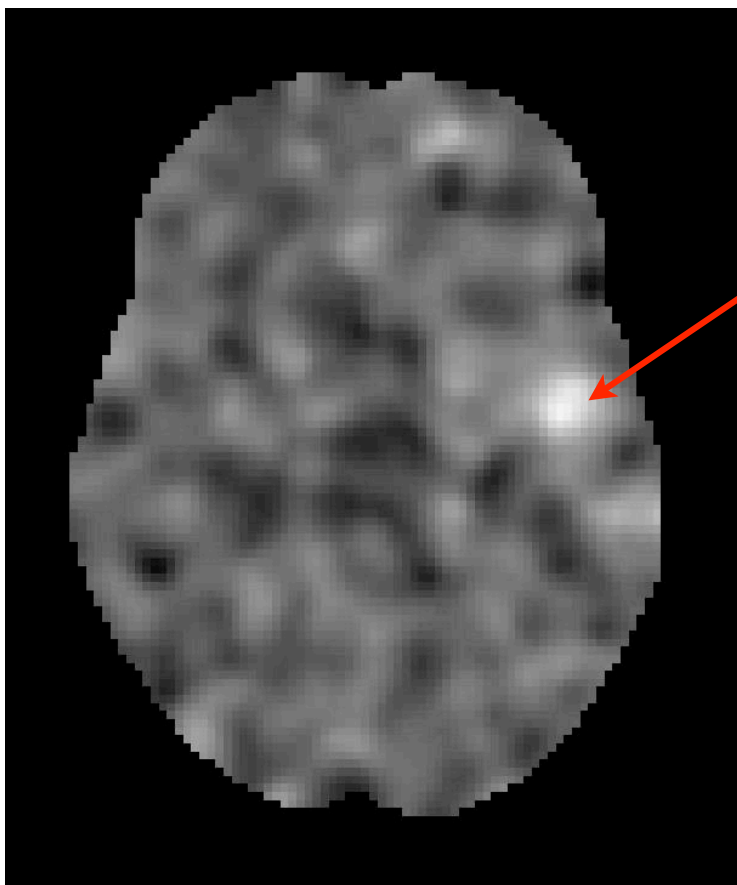


Spatial extent: another way to be surprised

空间范围：另一个让人惊奇的方式

This far we have talked about voxel-based tests

目前为止我们讨论了基于体素的检验。



We say: Look! A z-value of 7. That is so surprising (under the null-hypothesis) that I will have to reject it. (Though we are of course secretly delighted to do so)

看z值等于7，太令人意外了（在零假设下），我不得不拒绝他。（虽然我们当然很乐意这么做。）

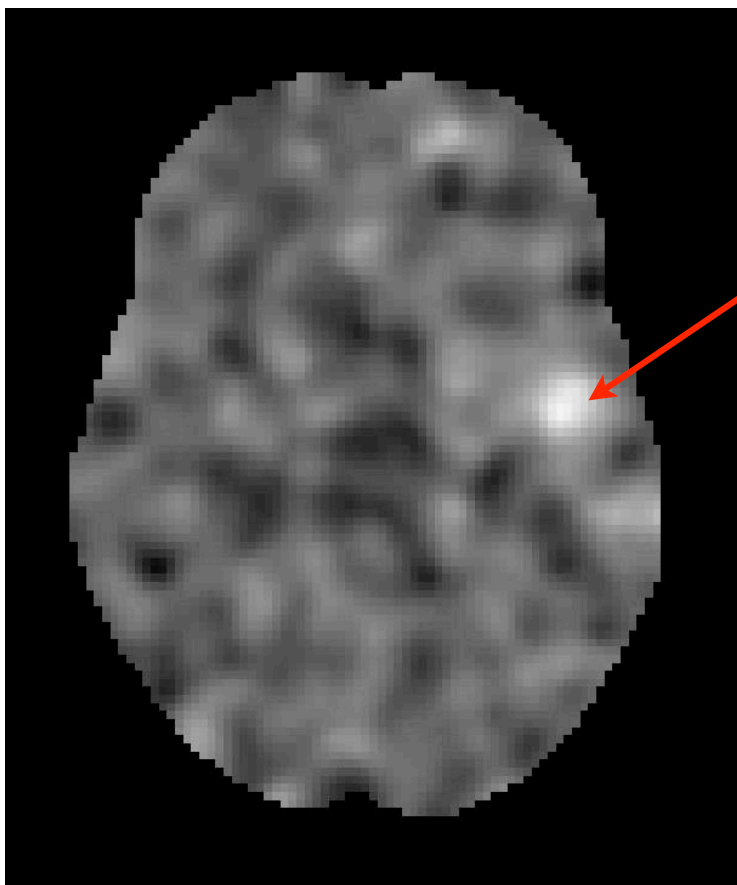


Spatial extent: another way to be surprised

空间范围：另一个让人惊奇的方式

This far we have talked about voxel-based tests

目前为止我们讨论了基于体素的检验。



We say: Look! A z-value of 7. That is so surprising (under the null-hypothesis) that I will have to reject it. (Though we are of course secretly delighted to do so)

看z值等于7，太令人意外了（在零假设下），我不得不拒绝他。（虽然我们当然很乐意这么做。）

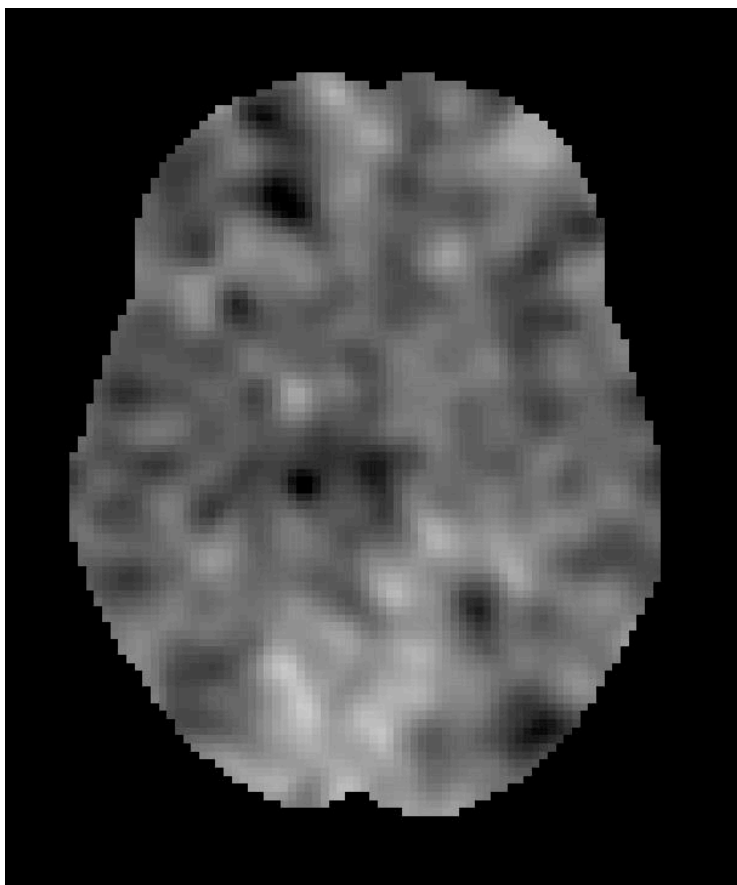


Spatial extent: another way to be surprised

空间范围：另一个让人惊奇的方式

But sometimes our data just aren't that surprising.

但有时候我们的数据就没这么意外了。



Nothing surprising here! The largest z-value is ~ 4 . We cannot reject the null-hypothesis, and we are **devastated**.

这里不足为奇！最大的z值为 ~ 4 。我们不能拒绝零假设，我们为此感到伤心绝望。



Spatial extent: another way to be surprised

空间范围：另一个让人惊奇的方式

So we threshold the z-map at 2.3 (arbitrary threshold) and look at the spatial extent of clusters

因此，我们将z-map的阈值定为2.3（任意阈值），然后查看簇的空间范围



We say: Look at that **whopper!** **301** connected voxels all with z-values > 2.3 . That is really surprising (under the null-hypothesis). I will have to reject it.

看看那个弥天大谎！301个连接的体素均具有z值 > 2.3 。这确实令人惊讶（在原假设下）。我将不得不拒绝它。

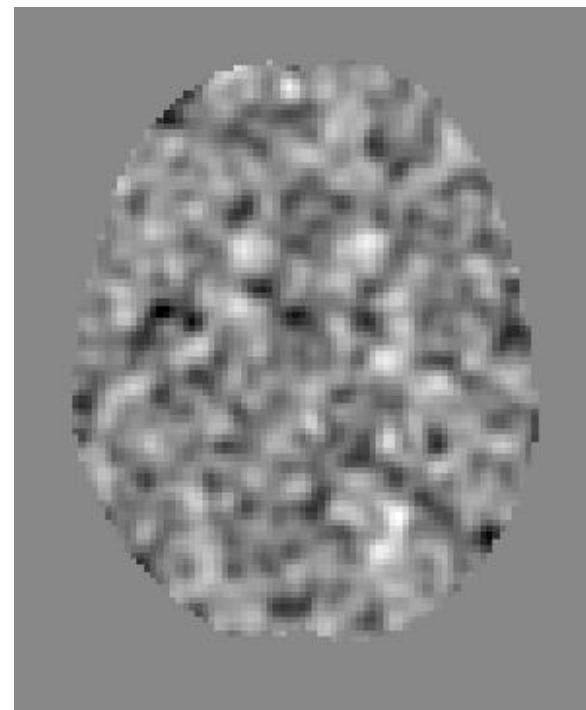


Distribution of Max Cluster Size

最大簇大小分布

As with the z-values we need a “null-distribution”. What would that look like in this case?

与z值一样，我们要零分布。这种情况下，看起来是啥样？



Let's say we have acquired some data

我们采集了一堆数据

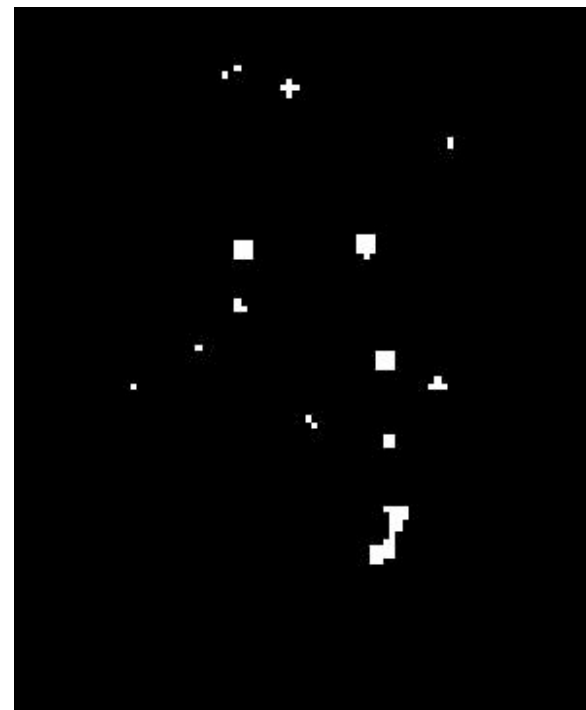


Distribution of Max Cluster Size

最大簇大小分布

If we reject any cluster we will reject the largest. So what we want is the distribution of the largest cluster, under the null-hypothesis.

如果我们拒绝任何集群，我们将拒绝最大的集群。所以我们想要的是零假设下最大簇的分布。



Threshold the
z-map at 2.3
(arbitrary)

武断地把阈值设在2.3



Distribution of Max Cluster Size

最大簇大小分布

If we reject any cluster we will reject the largest. So what we want is the distribution of the largest cluster, under the null-hypothesis.

如果我们拒绝任何集群，我们将拒绝最大的集群。所以我们想要的是零假设下最大簇的分布。



Locate the largest cluster anywhere in the brain.

找到大脑中任何位置的最大簇

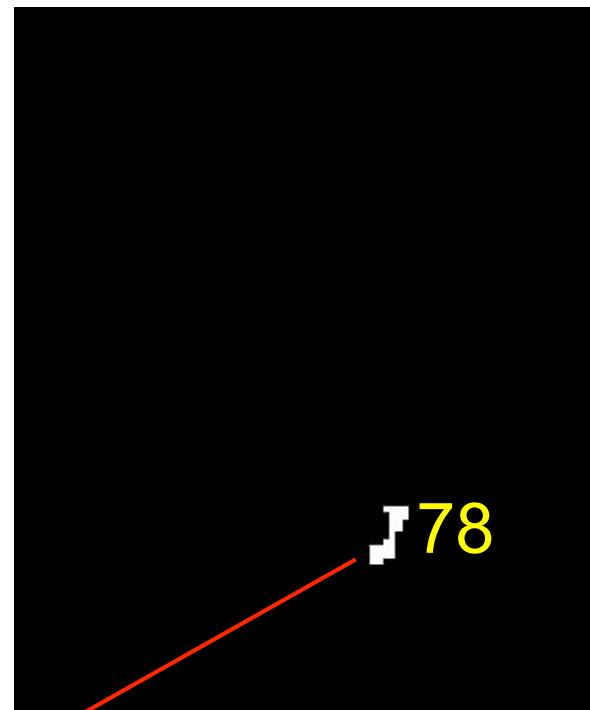
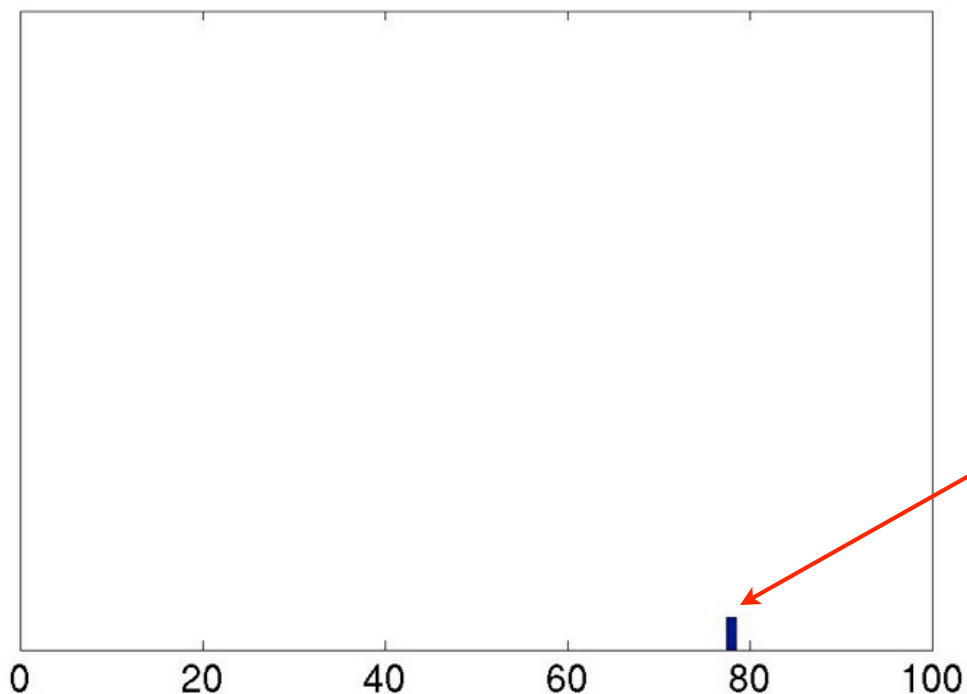


Distribution of Max Cluster Size

最大簇大小分布

If we reject any cluster we will reject the largest. So what we want is the distribution of the largest cluster, under the null-hypothesis.

如果我们拒绝任何集群，我们将拒绝最大的集群。所以我们想要的是零假设下最大簇的分布。



And record how large it is.

记录下有多大。

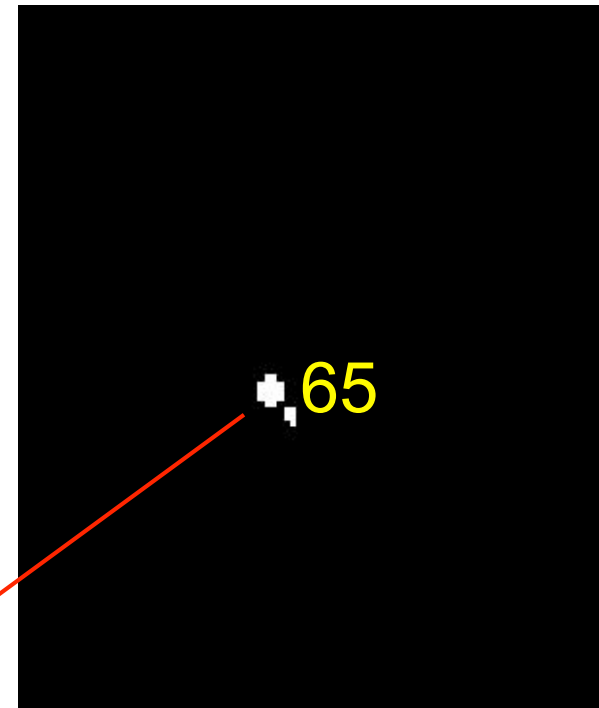
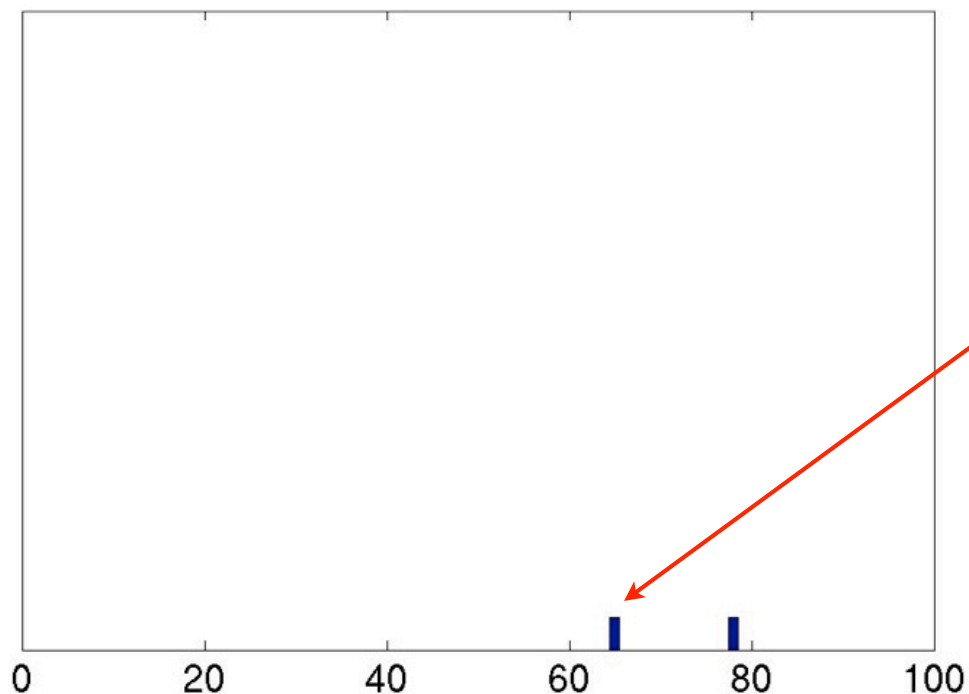


Distribution of Max Cluster Size

最大簇大小分布

If we reject any cluster we will reject the largest. So what we want is the distribution of the largest cluster, under the null-hypothesis.

如果我们拒绝任何集群，我们将拒绝最大的集群。所以我们想要的是零假设下最大簇的分布。



And do the same for another experiment...
对另一个实验也如此...

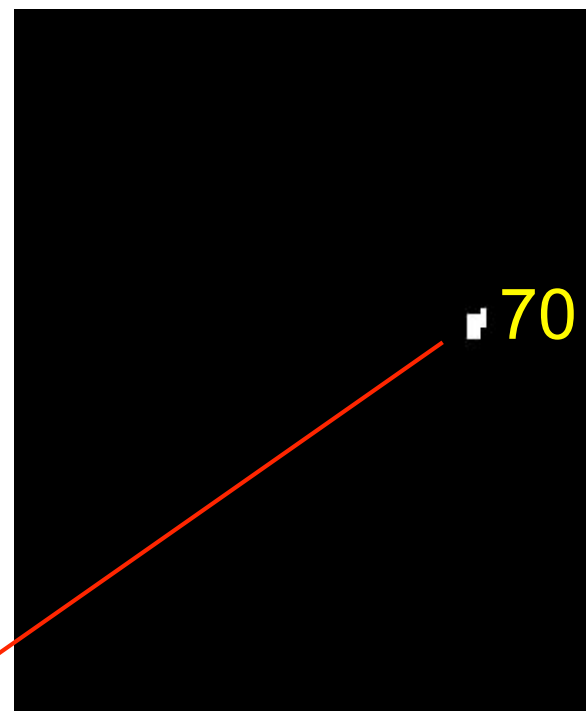
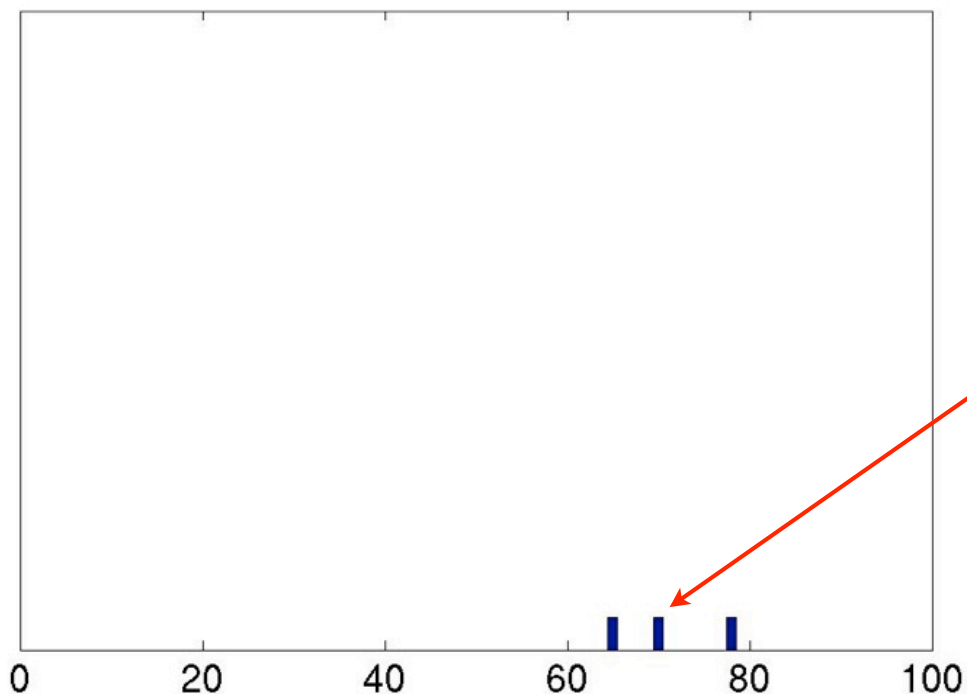


Distribution of Max Cluster Size

最大簇大小分布

If we reject any cluster we will reject the largest. So what we want is the distribution of the largest cluster, under the null-hypothesis.

如果我们拒绝任何集群，我们将拒绝最大的集群。所以我们想要的是零假设下最大簇的分布。



Etc ...

继续。。。。

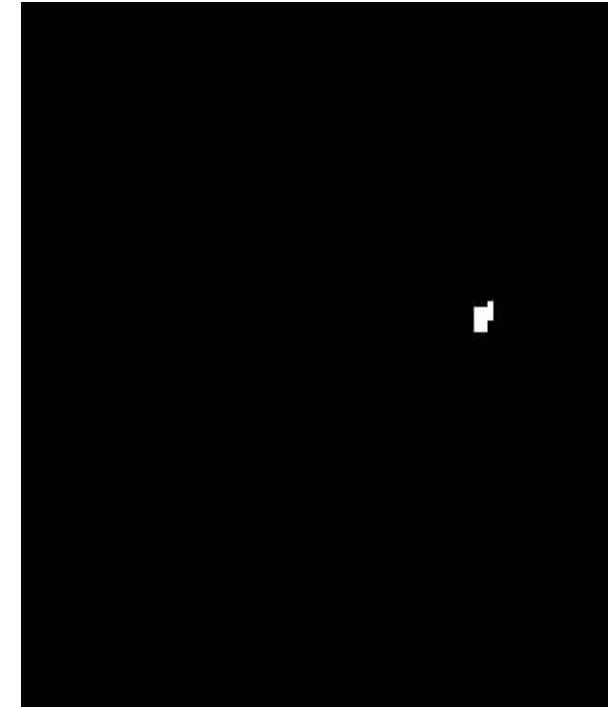
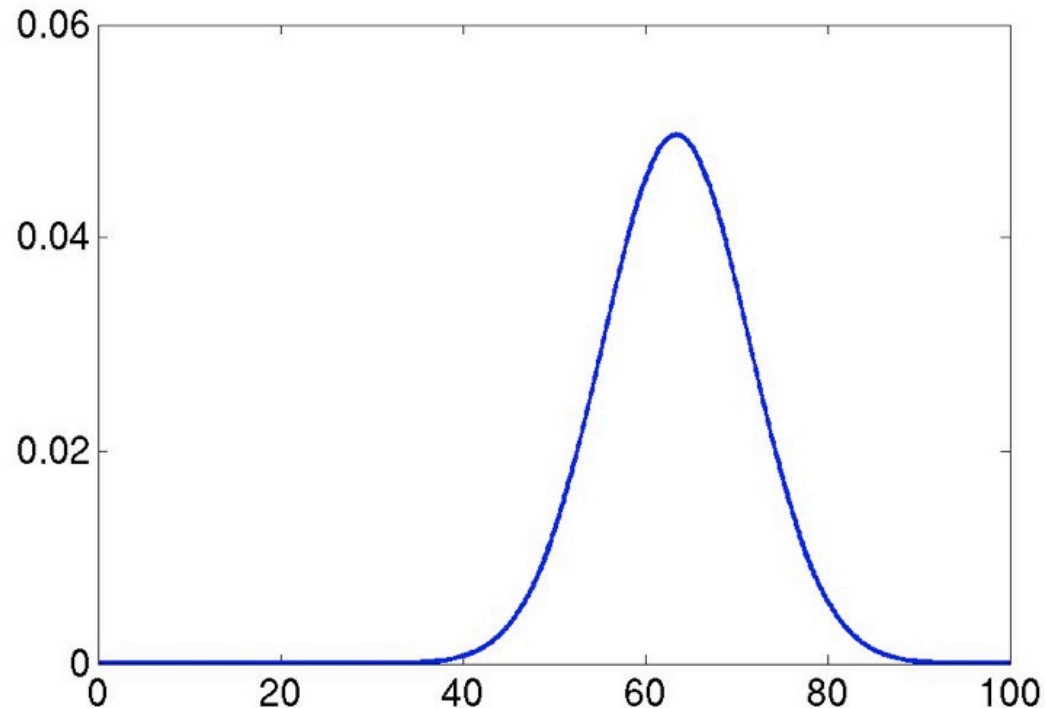


Distribution of Max Cluster Size

最大簇大小分布

If we reject any cluster we will reject the largest. So what we want is the distribution of the largest cluster, under the null-hypothesis.

如果我们拒绝任何集群，我们将拒绝最大的集群。所以我们想要的是零假设下最大簇的分布。



Until we have ...

直到我们...



Distribution of Max Cluster Size

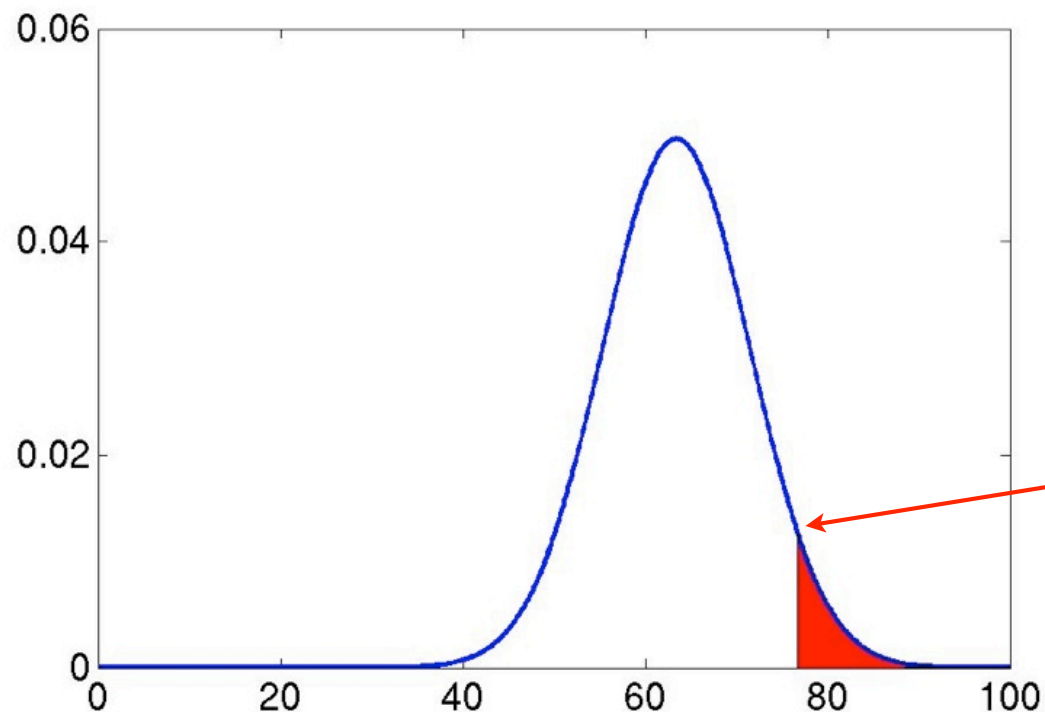
最大簇大小分布

If we reject any cluster we will reject the largest. So what we want is the distribution of the largest cluster, under the null-hypothesis.

如果我们拒绝任何集群，我们将拒绝最大的集群。所以我们想要的是零假设下最大簇的分布。

If we find a cluster larger than 76 voxels we reject the null-hypothesis.

如果我们找到一个簇比76个体素多，我们拒绝零假设。



And this (76) is the level we want to threshold at

这个数就是我们想要的阈限。



Distribution of Max Cluster Size

最大簇大小分布

So, just as was the case for the t-values, we now have a distribution f that allows us to calculate a Family Wise threshold u pertaining to cluster size.

因此，就像t值一样，我们现在有一个分布 f 它使我们能够计算与簇大小有关的总体的阈值 u 。

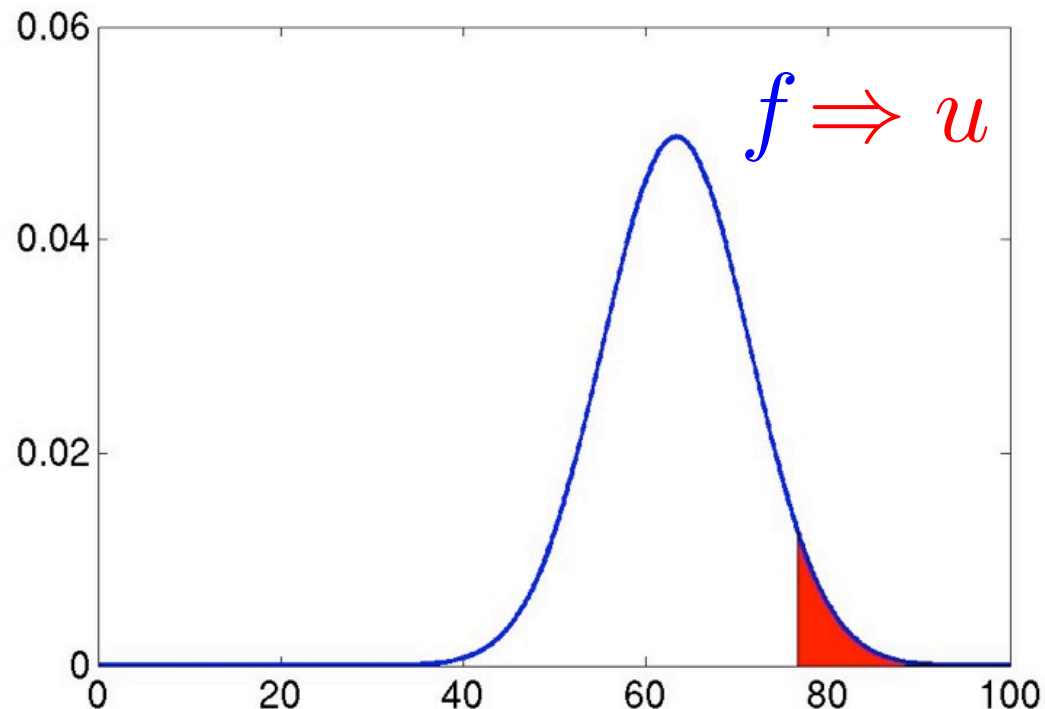
But what does

f and u

crucially

depend on?

但 f 和 u 关键取决于什么?





Distribution of Max Cluster Size

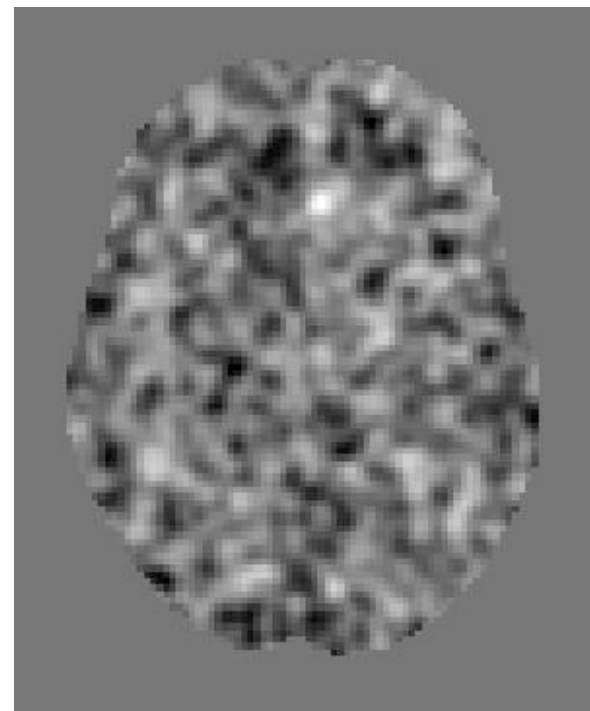
最大簇大小分布

So, just as was the case for the t-values, we now have a distribution f that allows us to calculate a Family Wise threshold u pertaining to cluster size.

因此，就像t值一样，我们现在有一个分布 f 它使我们能够计算与簇大小有关的总体的阈值 u 。

f depends crucially on the initial “cluster-forming” threshold?

f 关键取决于
初始“簇形成”的阈值?



$$z = 2.3$$

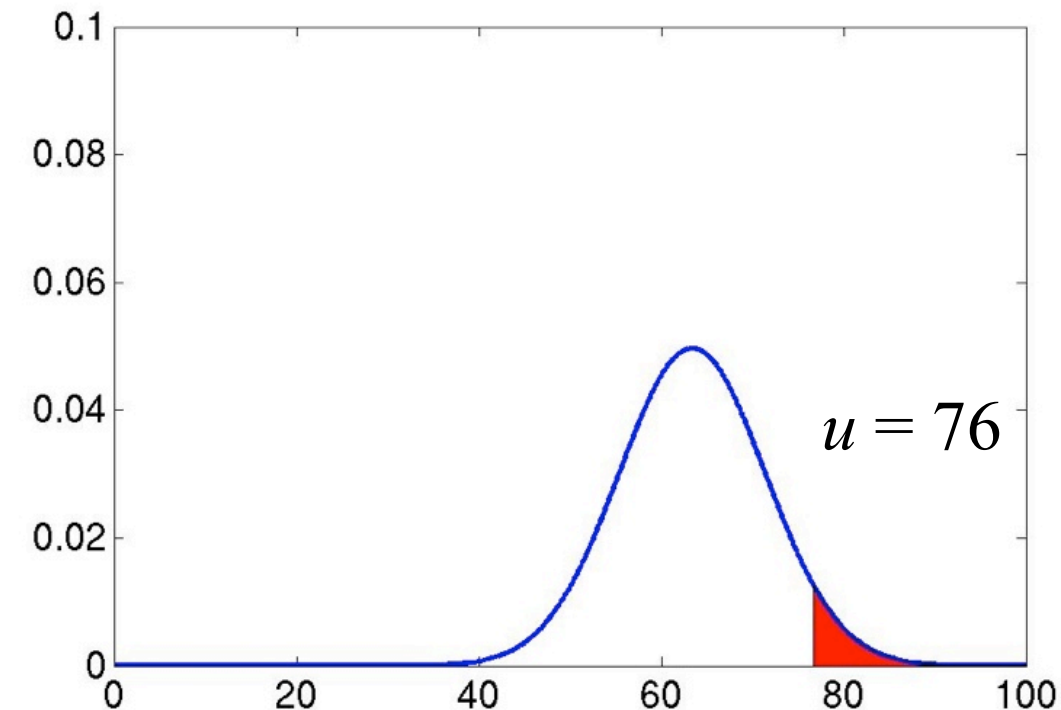


Distribution of Max Cluster Size

最大簇大小分布

So, just as was the case for the t-values, we now have a distribution f that allows us to calculate a Family Wise threshold u pertaining to cluster size.

因此，就像t值一样，我们现在有一个分布 f 它使我们能够计算与簇大小有关的总体的阈值 u 。



f depends crucially on the initial “cluster-forming” threshold?

f 关键取决于
初始“簇形成”的阈值?



$z = 2.3$

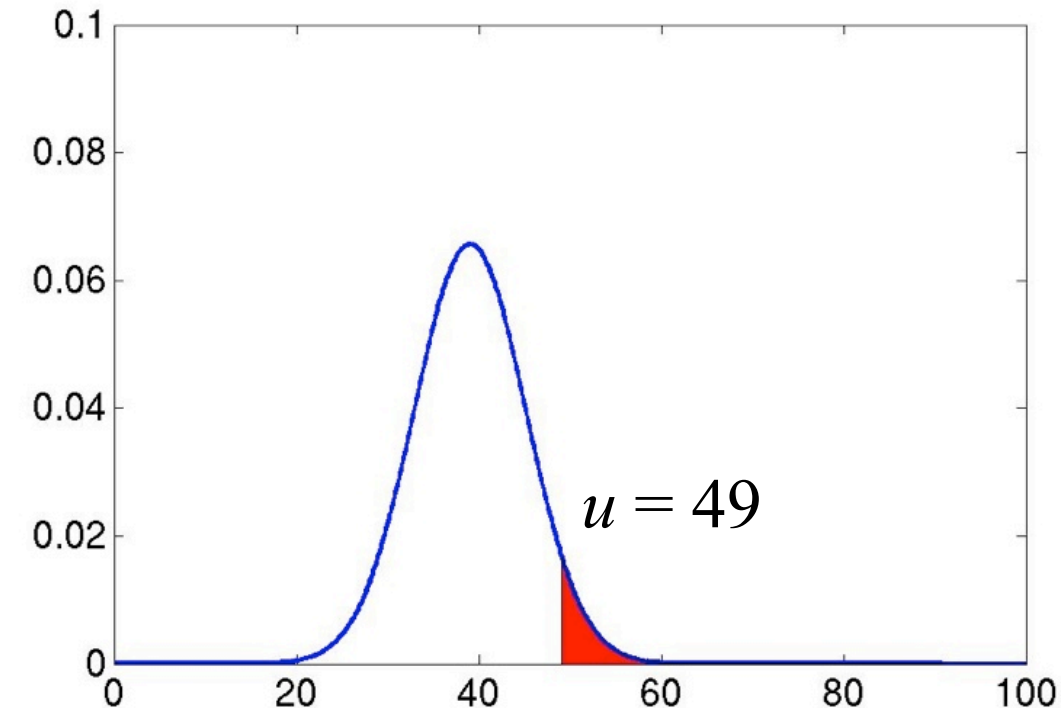


Distribution of Max Cluster Size

最大簇大小分布

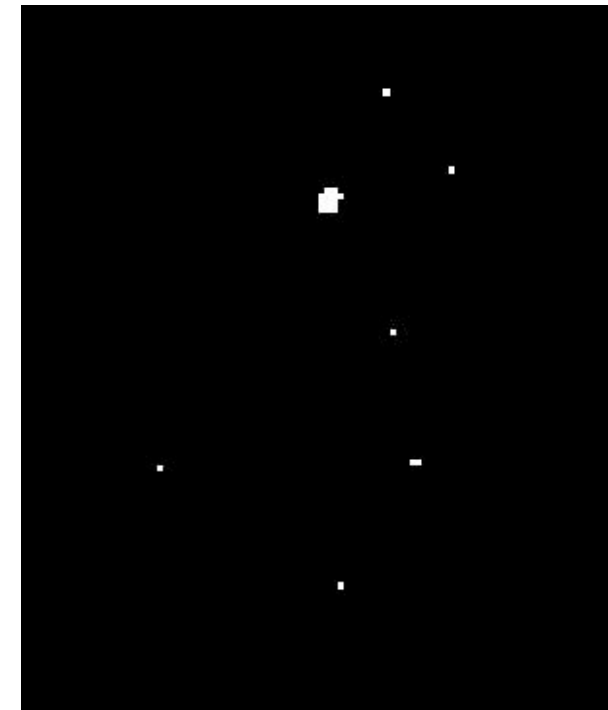
So, just as was the case for the t-values, we now have a distribution f that allows us to calculate a Family Wise threshold u pertaining to cluster size.

因此，就像t值一样，我们现在有一个分布 f 它使我们能够计算与簇大小有关的总体的阈值 u 。



f depends crucially on the initial “cluster-forming” threshold?

f 关键取决于
初始“簇形成”的阈值?



$z = 2.7$



Distribution of Max Cluster Size

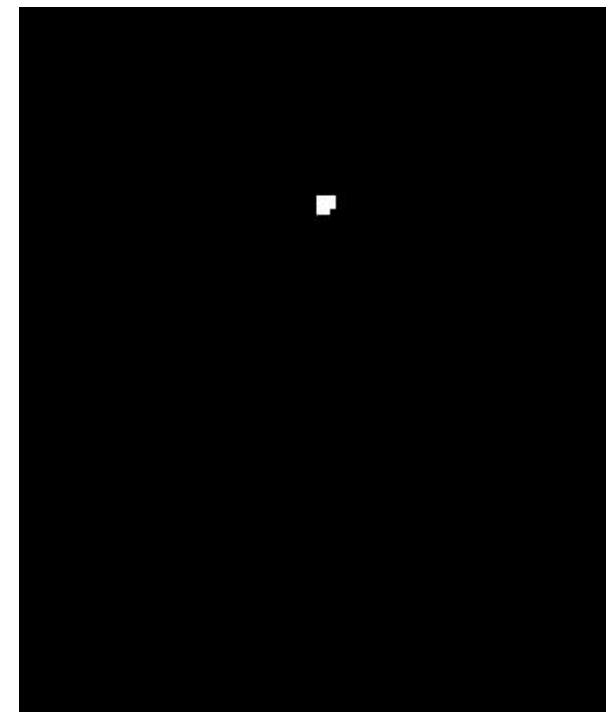
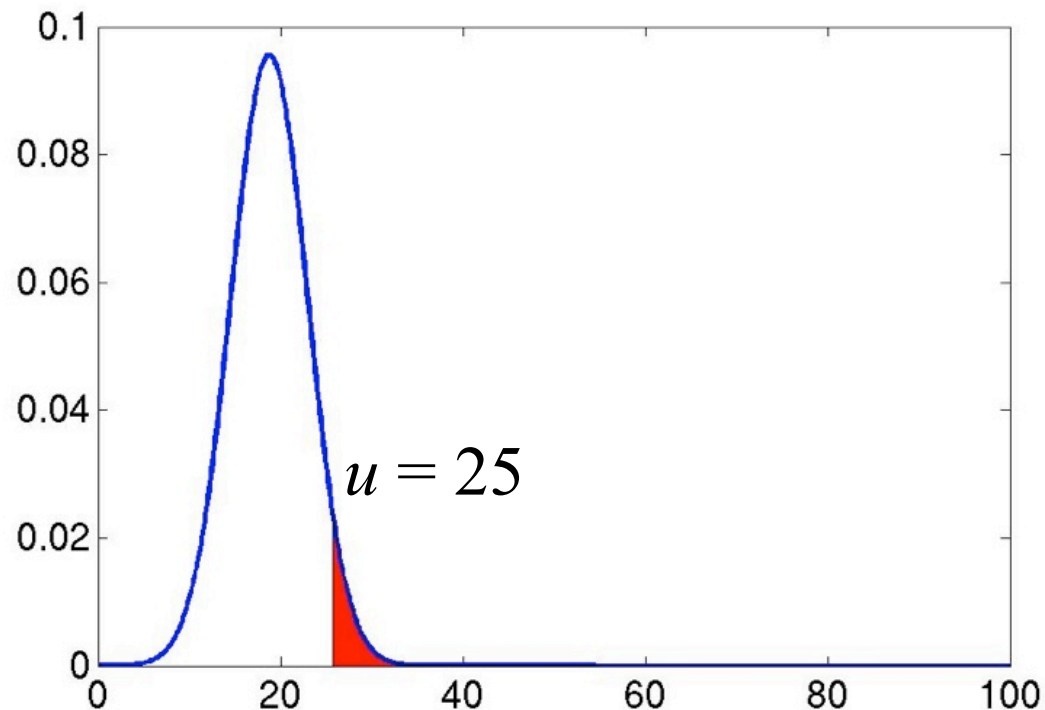
最大簇大小分布

So, just as was the case for the t-values, we now have a distribution f that allows us to calculate a Family Wise threshold u pertaining to cluster size.

因此，就像t值一样，我们现在有一个分布 f 它使我们能够计算与簇大小有关的总体的阈值 u 。

f depends crucially on the initial “cluster-forming” threshold?

f 关键取决于
初始“簇形成”的阈值?



$z = 3.1$



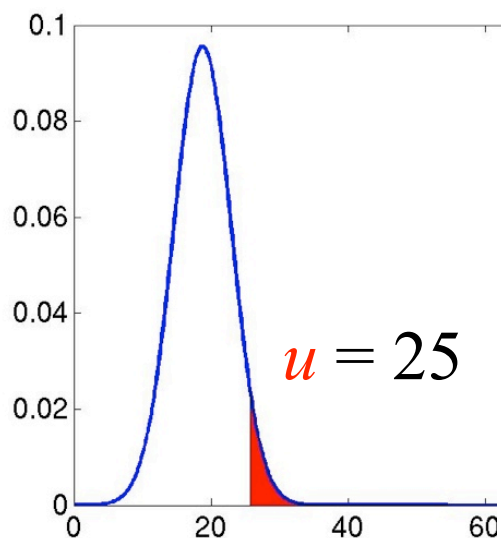
Distribution of Max Cluster Size

最大簇大小分布

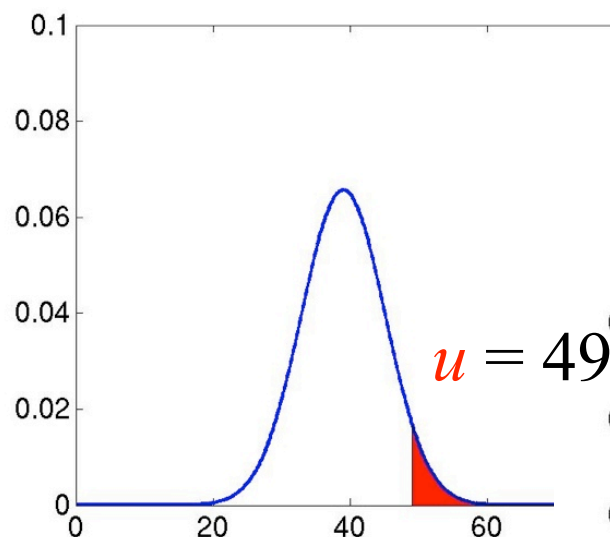
Hence the distribution for the cluster size should really be written $f(z)$ and the same for $u(z)$

因此簇大小的分布应该写成 $f(z)$ ，同样的 $u(z)$ 也是。

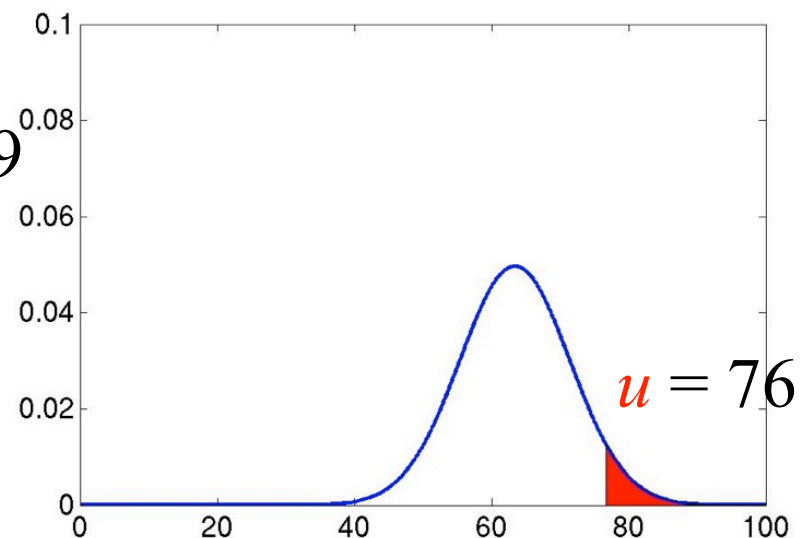
$z = 3.1$



$z = 2.7$



$z = 2.3$



But as before we don't have an expression for these distributions.

就像之前一样，我们不知道这些分布的表达式。



Outline大纲

- Null-hypothesis and Null-distribution 零假设和零分布
- Multiple comparisons and Family-wise error 多重比较和族错误率
- Different ways of being surprised 惊奇的不同方式
- Voxel-wise inference (Maximum z) 体素推断 (最大z)
- Cluster-wise inference (Maximum size) 簇水平推断 (最大尺寸)
- Parametric vs non-parametric tests 参数vs非参检验
- Enhanced clusters 增强的簇
- FDR - False Discovery Rate FDR-错误发现率



Parametric vs non-parametric

参数对非参

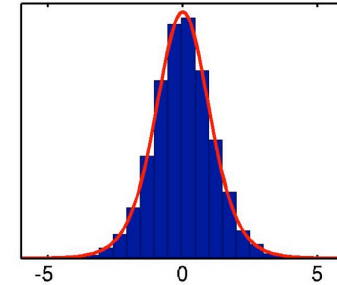
- As we described earlier, one of the great things about for example the t-test is that we know the null-distribution

之前所说，t检验最大的一点优点是我们知道零分布。

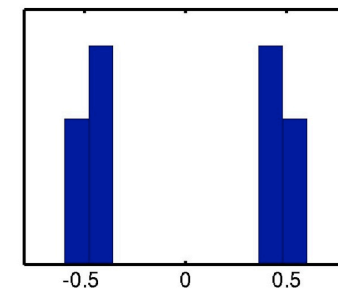
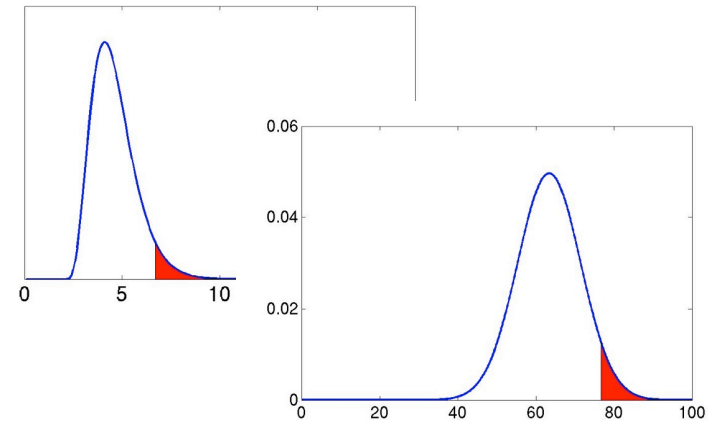
- But most distributions are not that simple
但大多数分布不是如此简单

- And errors are not always normal-distributed

误差并不总是正态分布



Provided that $\mathbf{e} \sim N(0, \sigma^2)$





Example: VBM-style analysis

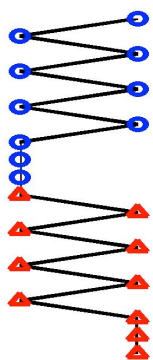
例如VBM类型的分析

- Our data is segmented grey matter maps 数据是分割好的灰质图
- A voxel is either grey matter, or not. 一个体素是或不是灰质

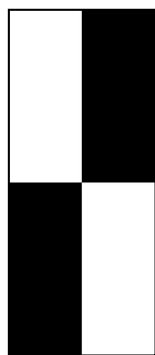
Group #1
(Oxford students)
组1 牛津学生



Group #2
(Train spotters)
组2 训练好的观察者



=

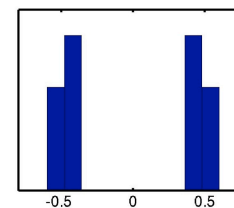


$$\begin{bmatrix} \beta_1 \\ \beta_2 \end{bmatrix}$$



$$\begin{bmatrix} \beta_1 \\ \beta_2 \end{bmatrix} = \begin{bmatrix} 0.4 \\ 0.6 \end{bmatrix} \text{ Ok!}$$

hist(e)



~ N?

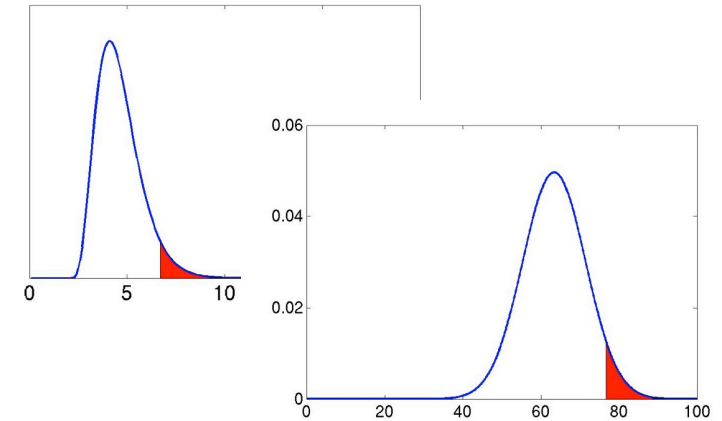




Parametric vs non-parametric

参数对非参

- There are approximations to the Max-z and Max-size statistics
Max-z和Max-size统计信息近似
- These are valid under certain sets of assumptions
这些在某些假设下有效
- But can be a problem when applied outside of that set of assumptions
在另外一些情况下可能会有问题



- Search area “large relative to boundary”
- “High enough” cluster forming threshold
- Normal distributed errors



Cluster failure: Why fMRI inferences for spatial extent have inflated false-positive rates

Anders Eklund^{a,b,c,1}, Thomas E. Nichols^{d,e}, and Hans Knutsson^{b,c}

^aDivision of Medical Informatics, Department of Biomedical Engineering, Linköping University, S-581 85 Linköping, Sweden; ^bDivision of Statistics and Machine Learning, Department of Computer and Information Science, Linköping University, S-581 83 Linköping, Sweden; ^cCenter for Medical Image Science and Visualization, Linköping University, S-581 83 Linköping, Sweden; ^dDepartment of Statistics, University of Warwick, Coventry CV4 7AL, United Kingdom; and ^eWMG, University of Warwick, Coventry CV4 7AL, United Kingdom

Edited by Emery N. Brown, Massachusetts General Hospital, Boston, MA, and approved May 17, 2016 (received for review February 12, 2016)

The most widely used task functional magnetic resonance imaging (fMRI) analyses use parametric statistical methods that depend on a variety of assumptions. In this work, we use real resting-state data and a total of 3 million random task group analyses to compute empirical familywise error rates for the fMRI software packages SPM, FSL, and AFNI. We find that the false-positive rates are inflated (FWE), the chance of one or more false positives, and empirically measure the FWE as the proportion of analyses that give rise to any significant results. Here, we consider both two-sample and one-sample designs. Because two groups of subjects are randomly drawn from a large group of healthy controls, the null hypothesis



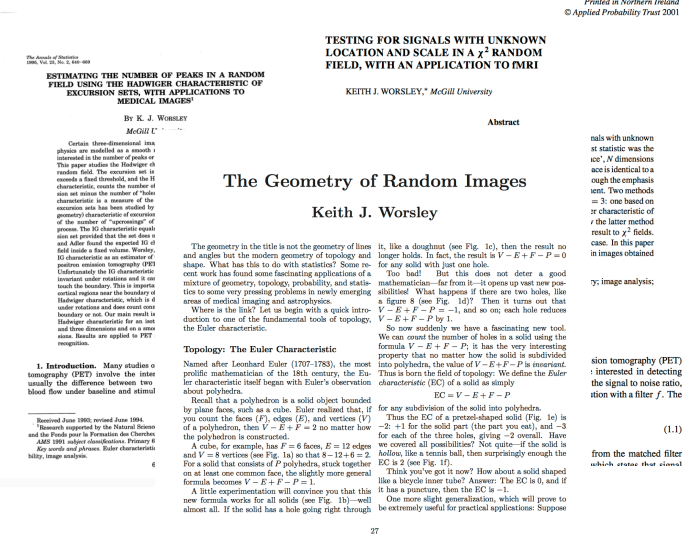
Parametric vs non-parametric

参数对非参

- Those approximations were based on Gaussian Random Field Theory, and was an impressive body of work
近似基于高斯随机场理论，令人印象深刻的工作

- They served us fantastically well at a time when we had little choice
在我们别无选择的时候，他们为我们提供了出色的服务

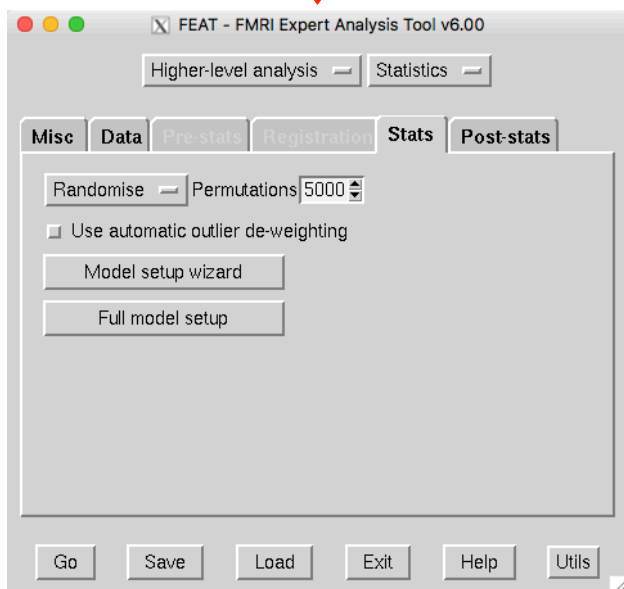
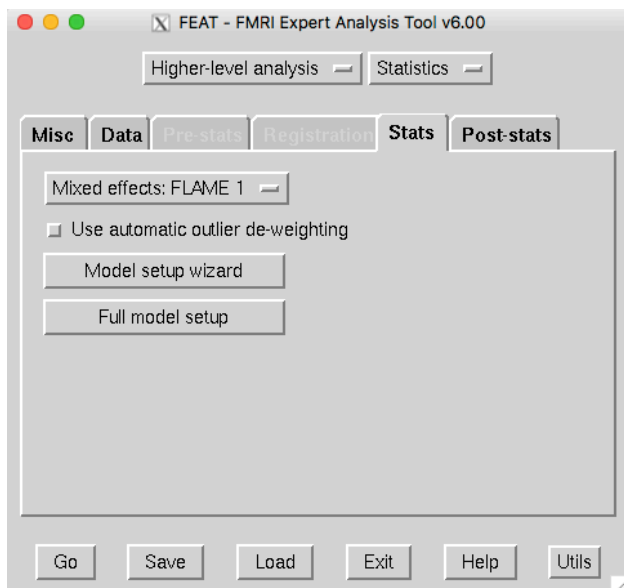
- But the future is non-parametric
但未来属于非参检验！





Parametric vs non-parametric

参数对非参



The Red (randomise)

Baron

红色巨头 (randomise工具)



FLAME going down in flames

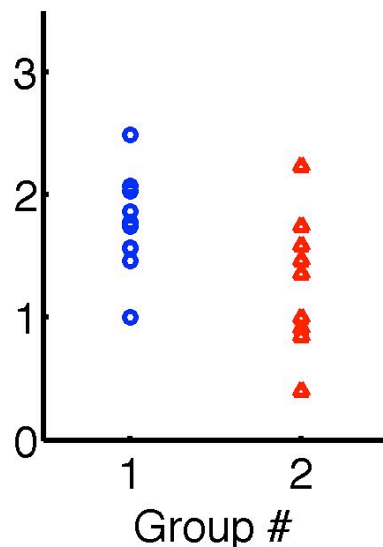
FLAME在硝烟中阵亡



A simple permutation test 简单的置换检验

- We can permute the data itself to create a distribution that we can use to test our statistic.
我们可以对数据本身进行置换，以创建可用于测试统计信息的分布。
- + Makes very few assumptions about the data 对数据做很少的假设
- + Works for any test statistic 适应于任何统计

We have performed an experiment
我们做了个实验



And calculated a statistic,
e.g. a t -value 计算了 t 值

$$t = 2.27$$

If the null-hypothesis is true, there is no difference between the groups. That means we should be able to “re-label” the individual points without changing anything.

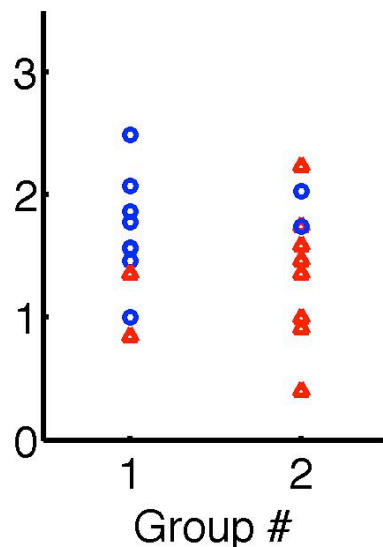
如果零假设为真，则组间没有差异。这意味着我们应该能够“重新标记”各个点，而不会造成任何改变。



A simple permutation test 简单的置换检验

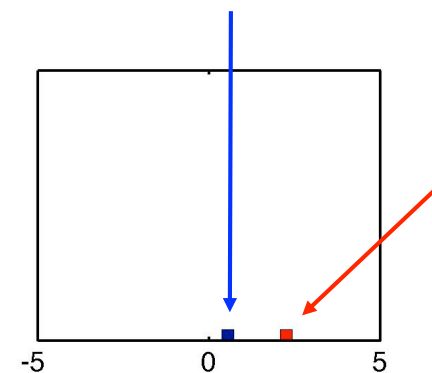
- We can permute the data itself to create a distribution that we can use to test our statistic.
我们可以对数据本身进行置换，以创建可用于测试统计信息的分布。
- + Makes very few assumptions about the data 对数据做很少的假设
- + Works for any test statistic 适应于任何统计

One re-labelling
第一次重标记



t -value after re-labelling
重标记后 t 值

$$t = 0.67$$



Original
labelling
原始标记

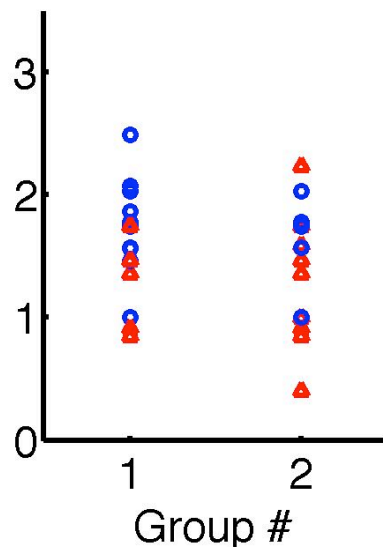
Let's start collecting them 开始收集他们



A simple permutation test 简单的置换检验

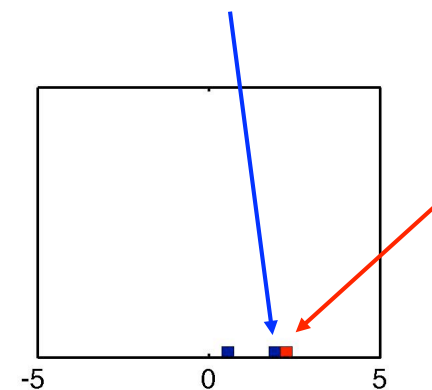
- We can permute the data itself to create a distribution that we can use to test our statistic.
我们可以对数据本身进行置换，以创建可用于测试统计信息的分布。
- + Makes very few assumptions about the data 对数据做很少的假设
- + Works for any test statistic 适应于任何统计

Second re-labelling
第二次重标记



t -value after re-labelling
标记后的 t 值

$$t = 1.97$$



Original labelling
原始标记

And another one 另一个



A simple permutation test 简单的置换检验

- We can permute the data itself to create a distribution that we can use to test our statistic.
我们可以对数据本身进行置换，以创建可用于测试统计信息的分布。
- + Makes very few assumptions about the data 对数据做很少的假设
- + Works for any test statistic 适应于任何统计

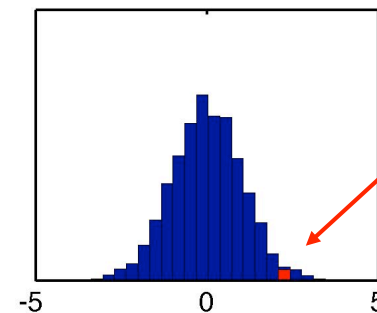
Of the 5000 re-labellings, only 90 had a t-value > 2.27 (the original labelling).

在5000个重新标记中，只有90个的t值> 2.27（原始标记）。

I.e. there is only a ~1.8% (90/5000) chance of obtaining a value > 2.27 if there is no difference between the groups

C.f. $p(x \geq 2.27) = 1.79\%$ for t_{18}

即如果各组之间没有差异，则只有1.8% (90/5000) 的机会获得> 2.27的值。C.F. t_{18} 的 $p(x \geq 2.27) = 1.79\%$



Original labelling
原始标记

5000 re-labellings. Phew!

5000次重标记，啧啧！



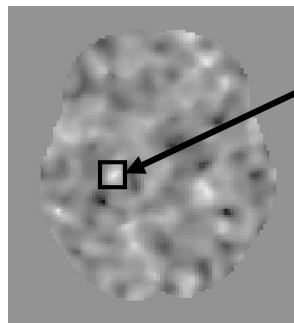
And we can use this for any statistic

我们可以对任何统计使用这个

This is what we got 这是我们得到的

We compared activation by painful stimuli in two groups of 5 subjects each.

我们比较了两组中每组5名受试者的疼痛刺激激活情况。



Very intriguing activation. $t_8 = 4.65$ 非常奇妙的激活

Prof. ran to write to Science.

But, did she jump the gun?

教授跑去给Science投稿了，但是他操之过急了吗？



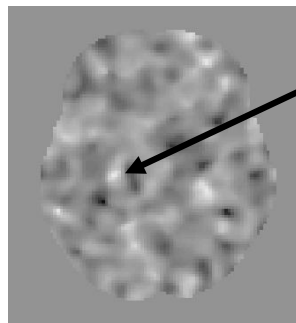
And we can use this for any statistic

我们可以对任何统计使用这个

This is what we got 这是我们得到的

We compared activation by painful stimuli in two groups of 5 subjects each.

我们比较了两组中每组5名受试者的疼痛刺激激活情况。

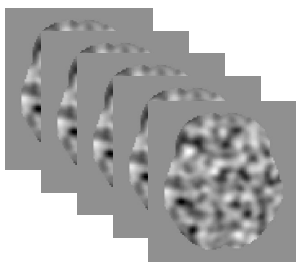


Very intriguing activation. $t_8 = 4.65$ 非常奇妙的激活

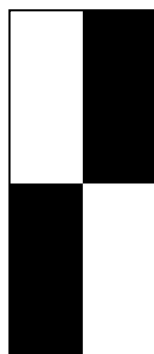
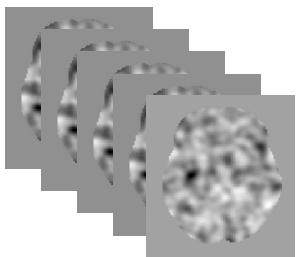
Prof. ran to write to Science.

But, did she jump the gun?
教授跑去给Science投稿了，但是他操之过急了吗？

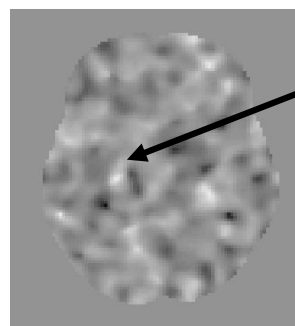
Group 1



Group 2



2nd level model
第二水平模型



$\max(t) = 4.65$

Our group difference map
我们差异图



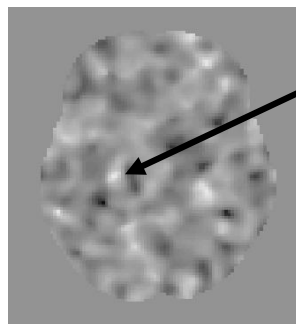
And we can use this for any statistic

我们可以对任何统计使用这个

This is what we got 这是我们得到的

We compared activation by painful stimuli in two groups of 5 subjects each.

我们比较了两组中每组5名受试者的疼痛刺激激活情况。



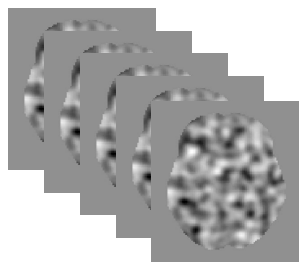
Very intriguing activation. $t_8 = 4.65$ 非常奇妙的激活

Prof. ran to write to Science.

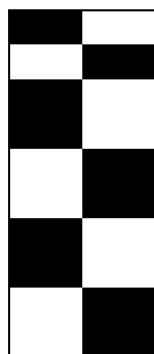
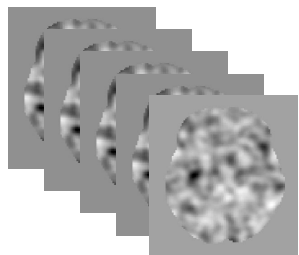
But, did she jump the gun?

教授跑去给Science投稿了，但是他操之过急了吗？

Group 1

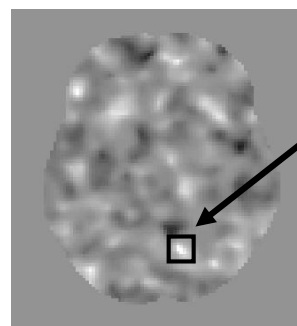


Group 2



Permuted model

置换模型



Permuted group difference map

置换组 差异图

$\max(t) = 8.23$



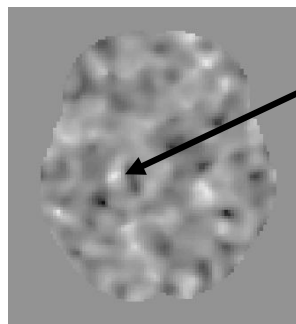
And we can use this for any statistic

我们可以对任何统计使用这个

This is what we got 这是我们得到的

We compared activation by painful stimuli in two groups of 5 subjects each.

我们比较了两组中每组5名受试者的疼痛刺激激活情况。

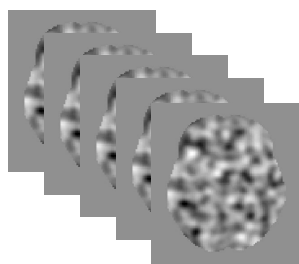


Very intriguing activation. $t_8 = 4.65$ 非常奇妙的激活

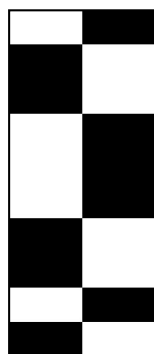
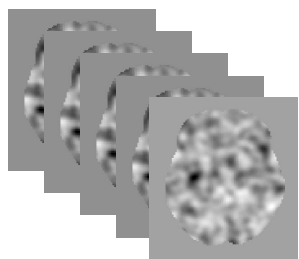
Prof. ran to write to Science.

But, did she jump the gun?
教授跑去给Science投稿了，但是他操之过急了吗？

Group 1



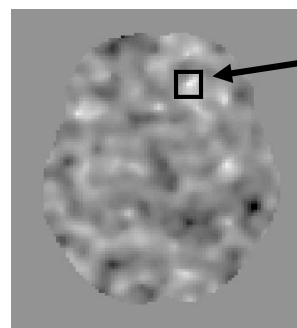
Group 2



2nd

Permutation

第二次置换



$\max(t) = 5.43$

2nd permuted map

第二次置换图



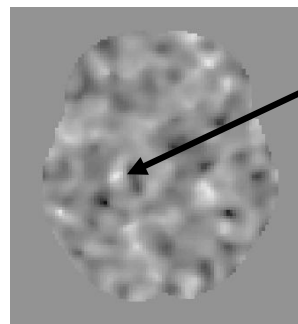
And we can use this for any statistic

我们可以对任何统计使用这个

This is what we got 这是我们得到的

We compared activation by painful stimuli in two groups of 5 subjects each.

我们比较了两组中每组5名受试者的疼痛刺激激活情况。

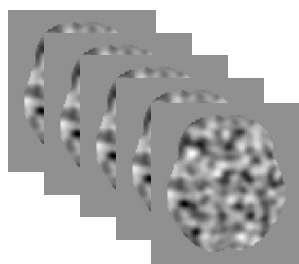


Very intriguing activation. $t_8 = 4.65$ 非常奇妙的激活

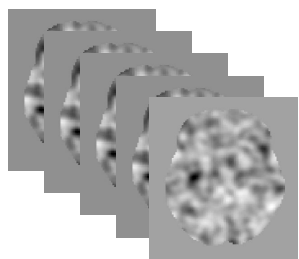
Prof. ran to write to Science.

But, did she jump the gun?
教授跑去给Science投稿了，但是他操之过急了吗？

Group 1



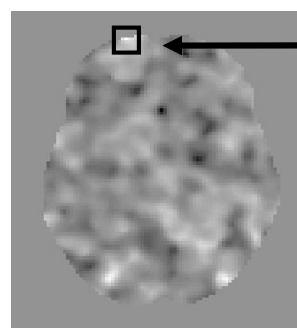
Group 2



2nd

Permutation

第三次置换



$\max(t) = 5.84$

2nd permuted map

第三次置换图



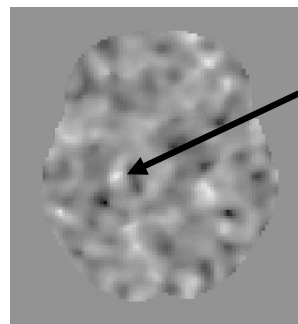
And we can use this for any statistic

我们可以对任何统计使用这个

This is what we got 这是我们得到的

We compared activation by painful stimuli in two groups of 5 subjects each.

我们比较了两组中每组5名受试者的疼痛刺激激活情况。



Very intriguing activation. $t_8 = 4.65$ 非常奇妙的激活

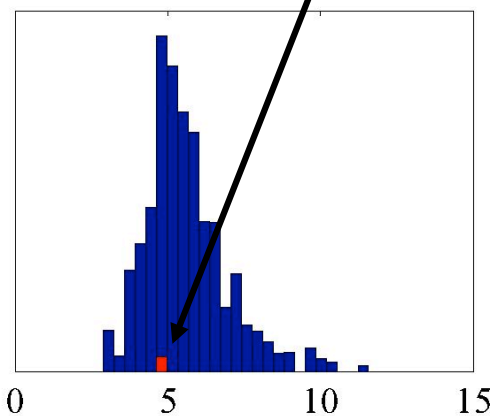
Prof. ran to write to Science.

But, did she jump the gun?

教授跑去给Science投稿了，但是他操之过急了吗？

Original labelling

原始标记



5000 permutations

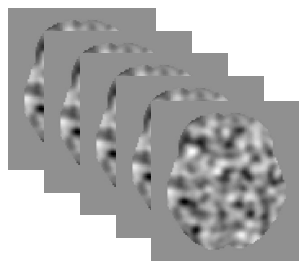
5000次置换

3925 permutations yielded higher max(t)-value than original labelling.

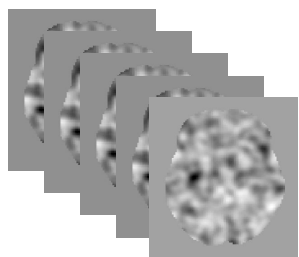
We **cannot** reject the null-hypothesis.

3925次置换导致的最大t值比原始标记高。我不能拒绝零假设

Group 1



Group 2





But beware the “exchangeability”

但要小心“可交换性”

- When we swap the labels of two data-points we need to make sure that they are “exchangeable”

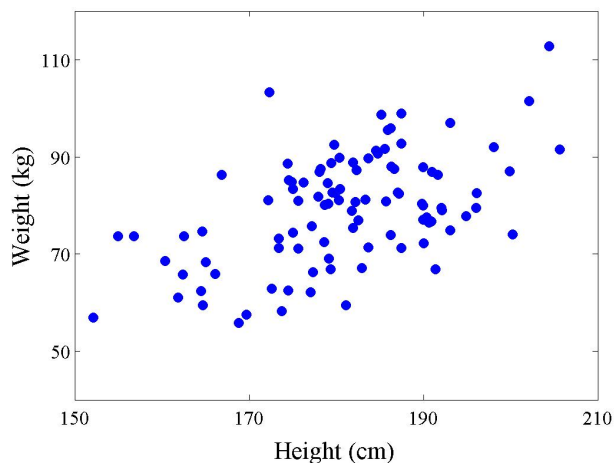
当我们置换两个数据点的标记时，要确保他们可交换

- I will start to explain “exchangeability” through a case that is **not**

我将通过一个不可交换的例子开始解释可交换性

- But first we need to learn about covariance matrices

但首先我们得了解协方差矩阵



Height and weight of a
random sample of
Swedish men

瑞典男子随机样本的身高和体重



Covariance matrices

协方差矩阵

- When we swap the labels of two data-points we need to make sure that they are “exchangeable”

当我们置换两个数据点的标记时，要确保他们可交换

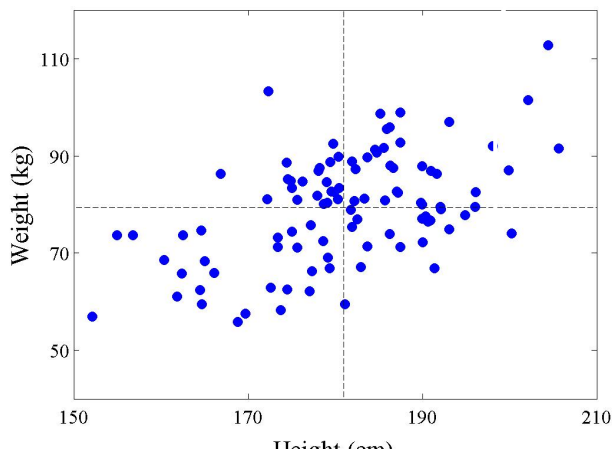
- I will start to explain “exchangeability” through a case that is **not**

我将通过一个不可交换的例子开始解释可交换性

- But first we need to learn about covariance matrices

但首先我们得了解协方差矩阵

Mean height ≈ 181 cm 平均身高181cm



Mean weight ≈ 79.4 kg

平均体重79.4kg

Characterised
by two means

用两个平均值表征



Covariance matrices

协方差矩阵

- When we swap the labels of two data-points we need to make sure that they are “exchangeable”

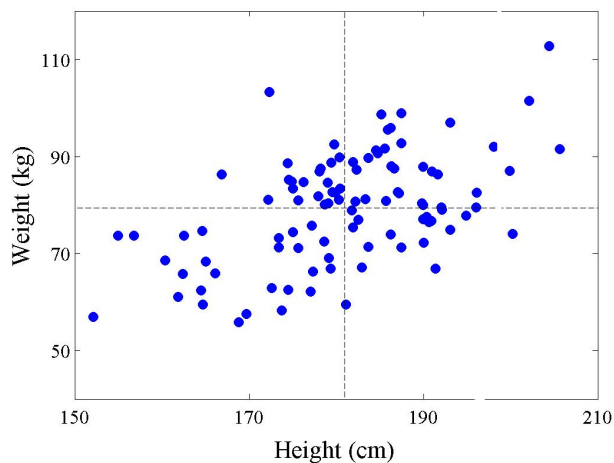
当我们置换两个数据点的标记时，要确保他们可交换

- I will start to explain “exchangeability” through a case that is **not**

我将通过一个不可交换的例子开始解释可交换性

- But first we need to learn about covariance matrices

但首先我们得了解协方差矩阵



$$\Sigma = \begin{bmatrix} 130 & 52 \\ 52 & 165 \end{bmatrix}$$

And a
covariance -
matrix
协方差矩阵



Covariance matrices

协方差矩阵

- When we swap the labels of two data-points we need to make sure that they are “exchangeable”

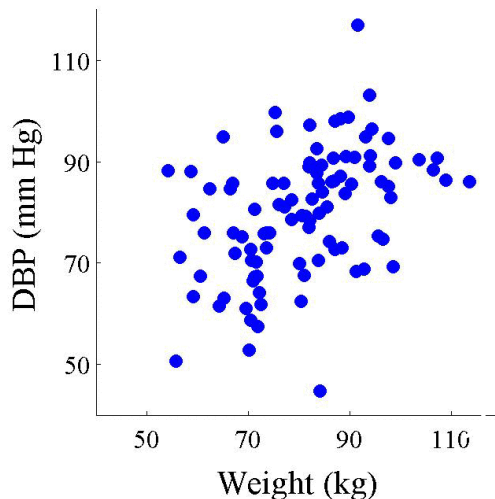
当我们置换两个数据点的标记时，要确保他们可交换

- I will start to explain “exchangeability” through a case that is **not**

我将通过一个不可交换的例子开始解释可交换性

- But first we need to learn about covariance matrices

但首先我们得了解协方差矩阵



$$\Sigma = \begin{bmatrix} 130 & 52 & 4.8 \\ 52 & 165 & 69 \\ 4.8 & 69 & 156 \end{bmatrix}$$



Covariance matrices

协方差矩阵

- When we swap the labels of two data-points we need to make sure that they are “exchangeable”

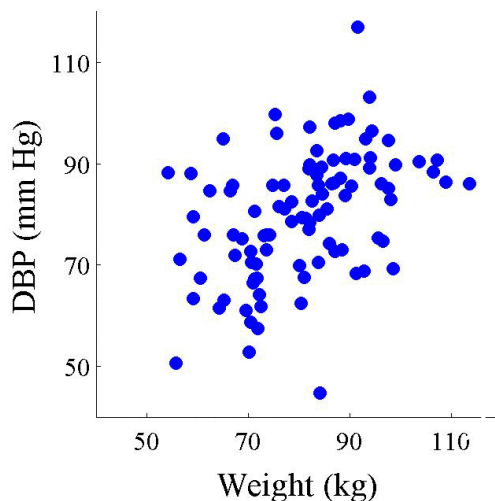
当我们置换两个数据点的标记时，要确保他们可交换

- I will start to explain “exchangeability” through a case that is **not**

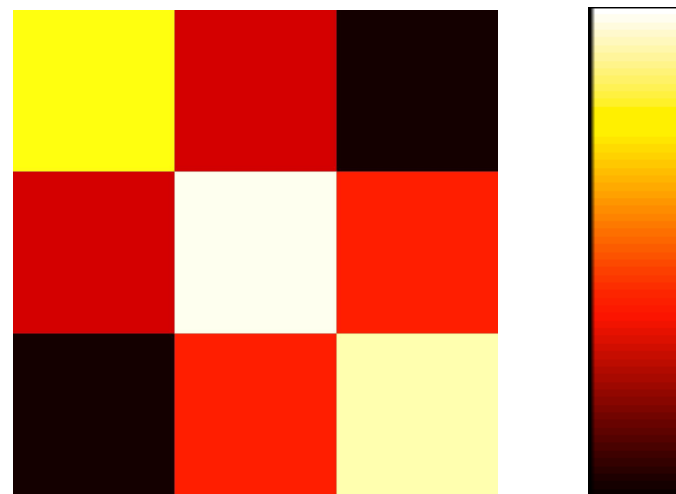
我将通过一个不可交换的例子开始解释可交换性

- But first we need to learn about covariance matrices

但首先我们得了解协方差矩阵



$$\Sigma =$$

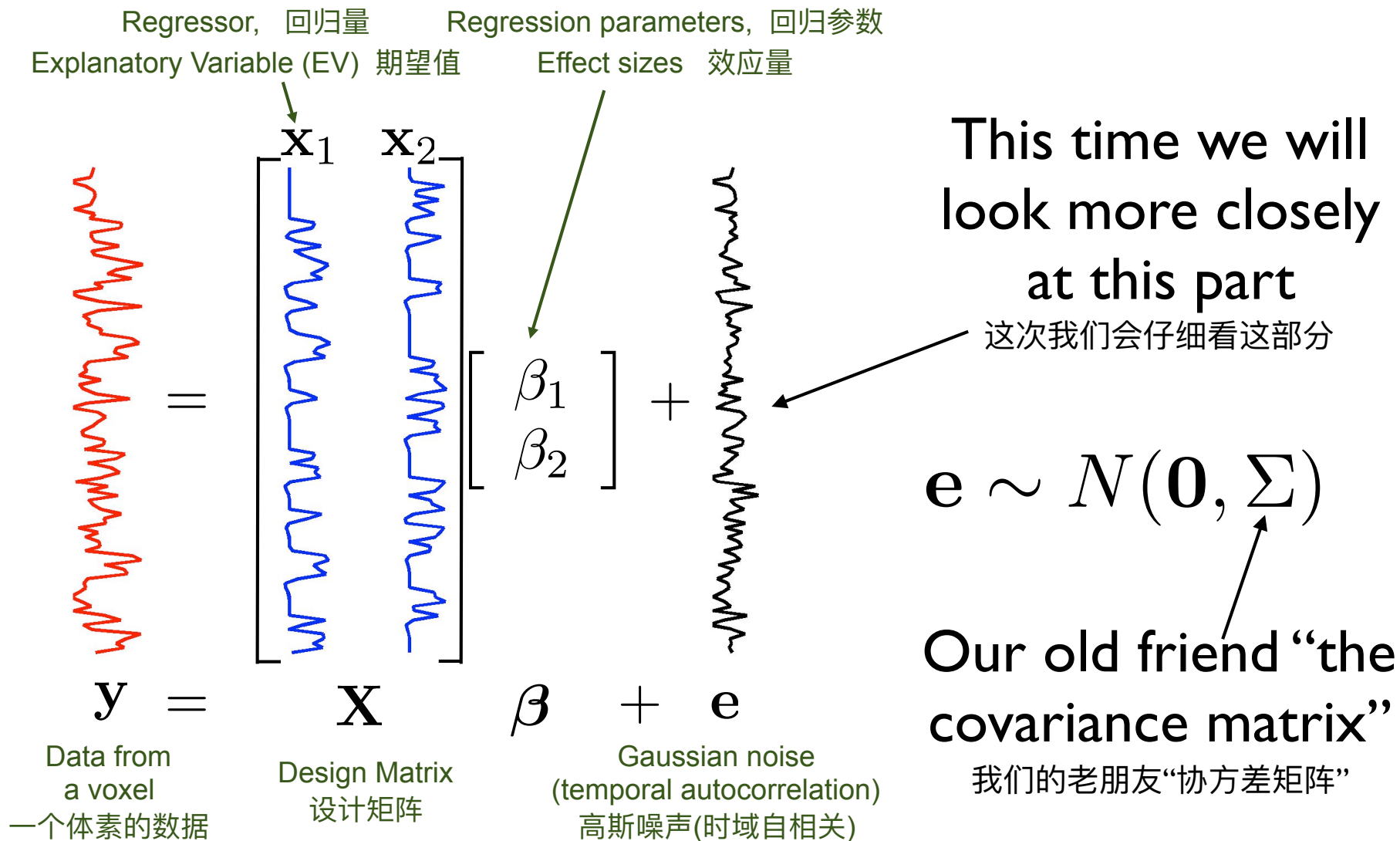




1st level fMRI data is not exchangeable

第一阶的功能磁共振成像数据不可交换

- You may, or may not, have seen this slide in the 1st level GLM talk. 你或许在第一阶的GLM讨论中见过这个幻灯片

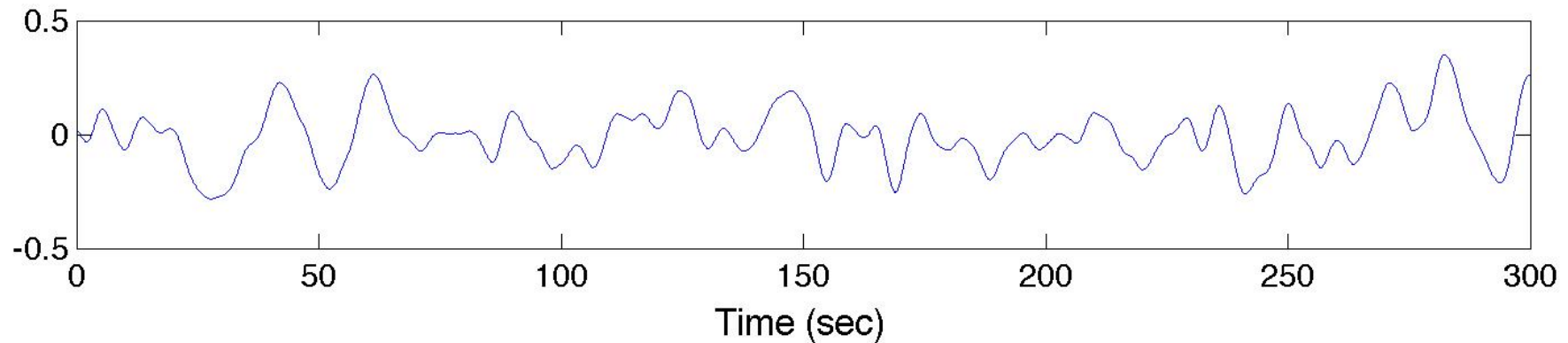




1st level fMRI data is not exchangeable

第一阶的功能磁共振成像数据不可交换

- One important component of noise in fMRI consists of physiological/neuronal events convolved by the HRF
fMRI中一个重要的噪声组分是由生理/神经时间与HRF的卷积造成的。



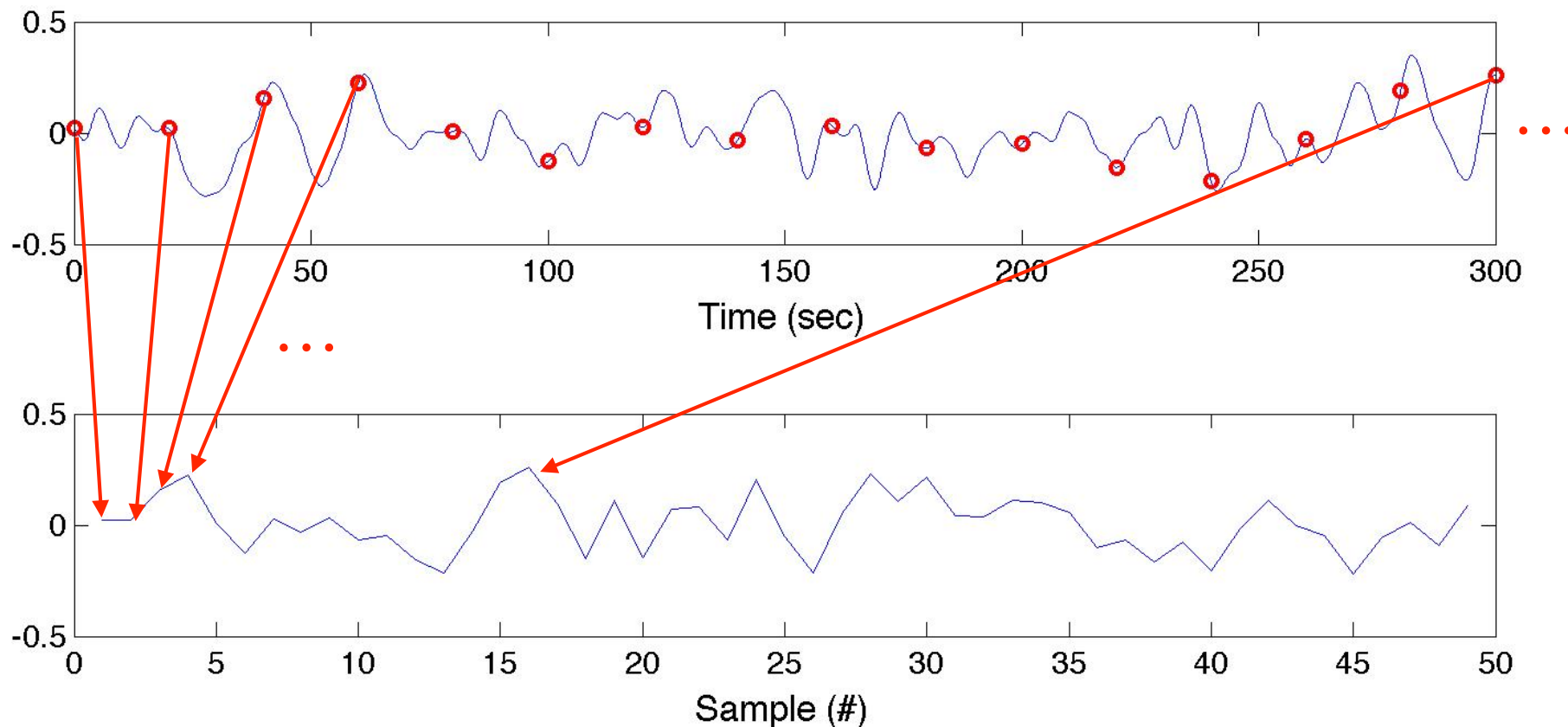


1st level fMRI data is not exchangeable

第一阶的功能磁共振成像数据不可交换

- One important component of noise in fMRI consists of physiological/neuronal events convolved by the HRF

fmri中一个重要的噪声组分是由生理/神经时间与HRF的卷积造成的。



If we sample this every 20 seconds it no longer looks “smooth”

如果我们每个20s采样，他看起来不再“平滑”

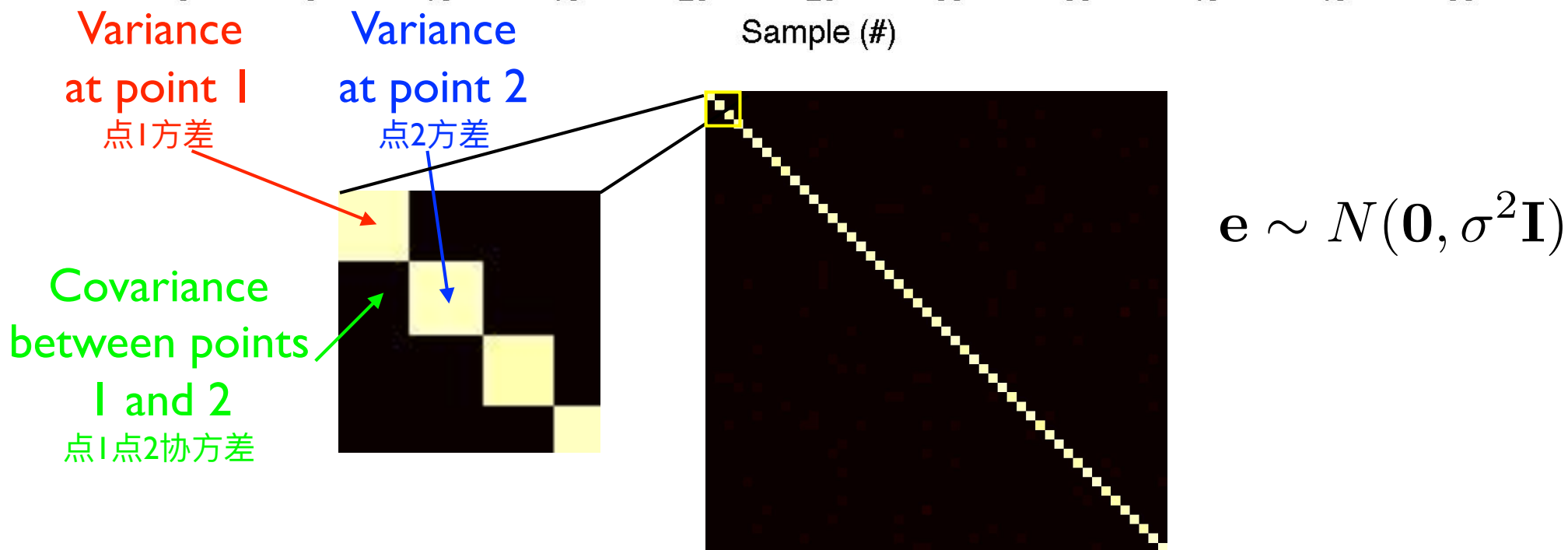
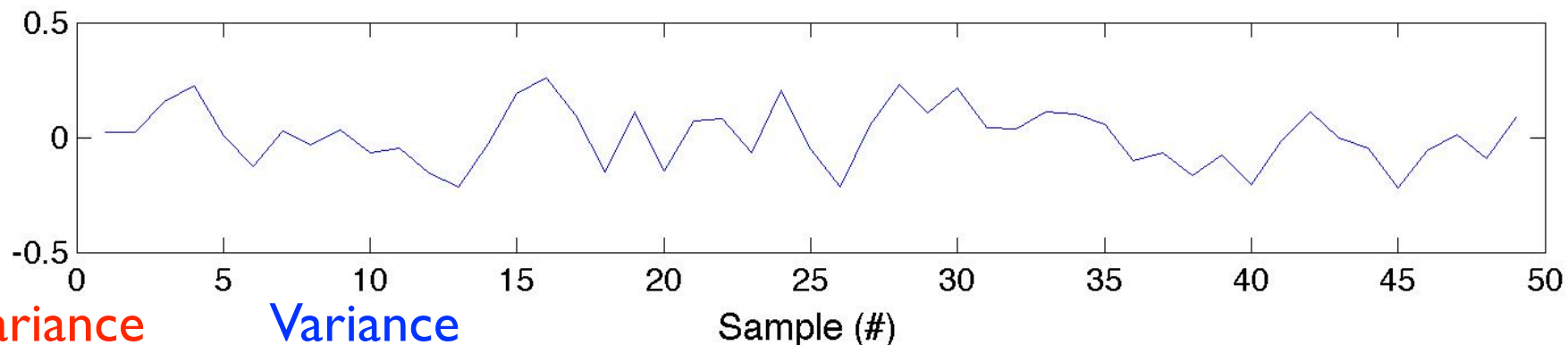


1st level fMRI data is not exchangeable

第一阶的功能磁共振成像数据不可交换

- One important component of noise in fMRI consists of physiological/neuronal events convolved by the HRF

fmri中一个重要的噪声组分是由生理/神经时间与HRF的卷积造成的。



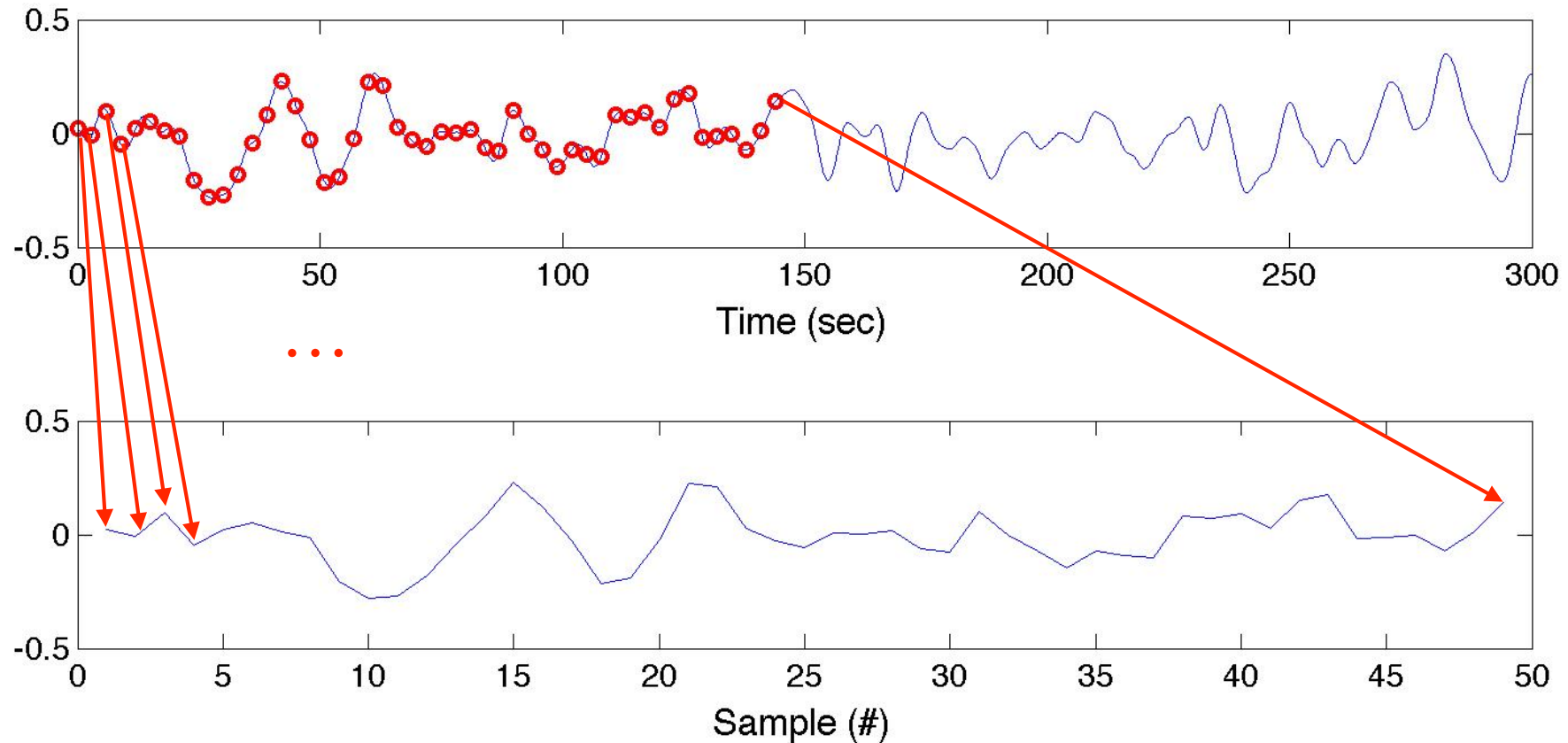


1st level fMRI data is not exchangeable

第一阶的功能磁共振成像数据不可交换

- One important component of noise in fMRI consists of physiological/neuronal events convolved by the HRF

fmri中一个重要的噪声组分是由生理/神经时间与HRF的卷积造成的。



But that is not a realistic TR. What about every 3 seconds?

但这个TR不现实，3s咋样？

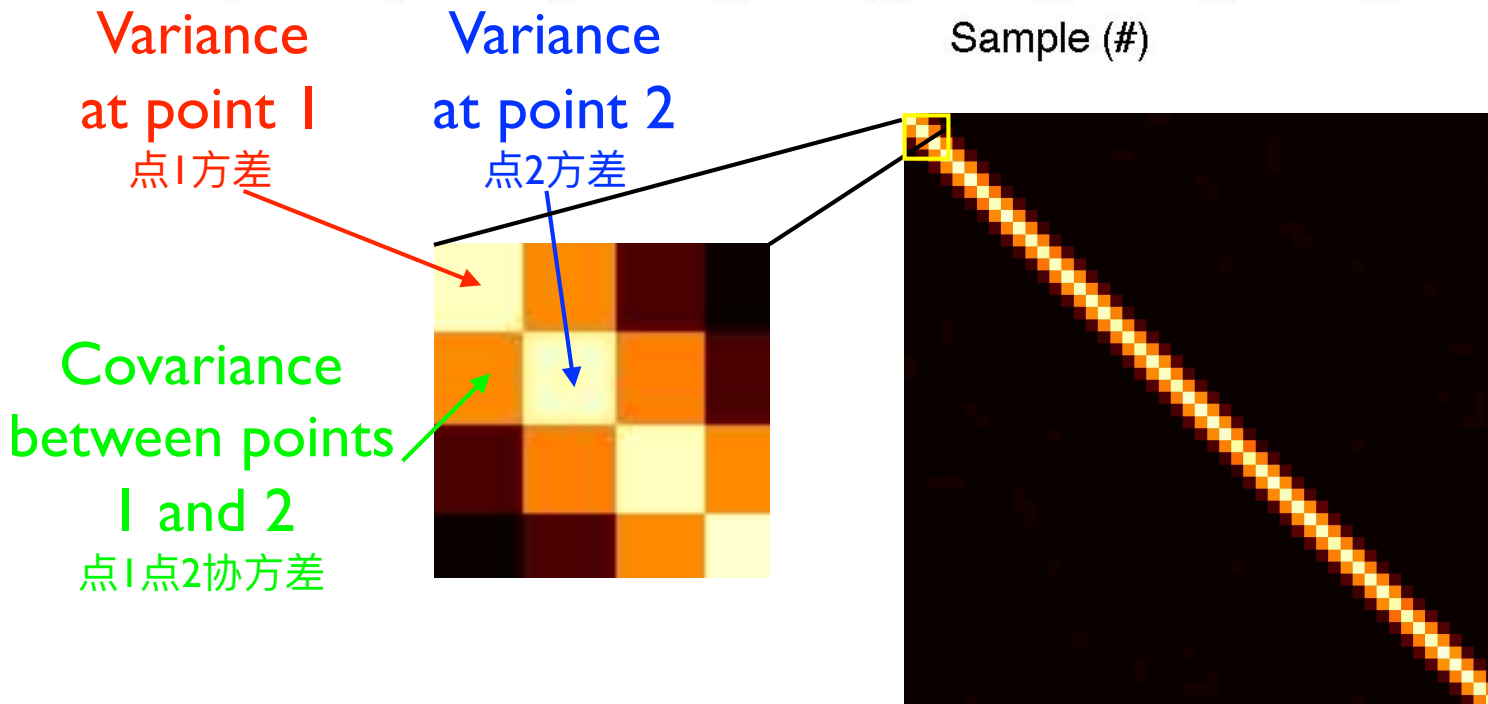
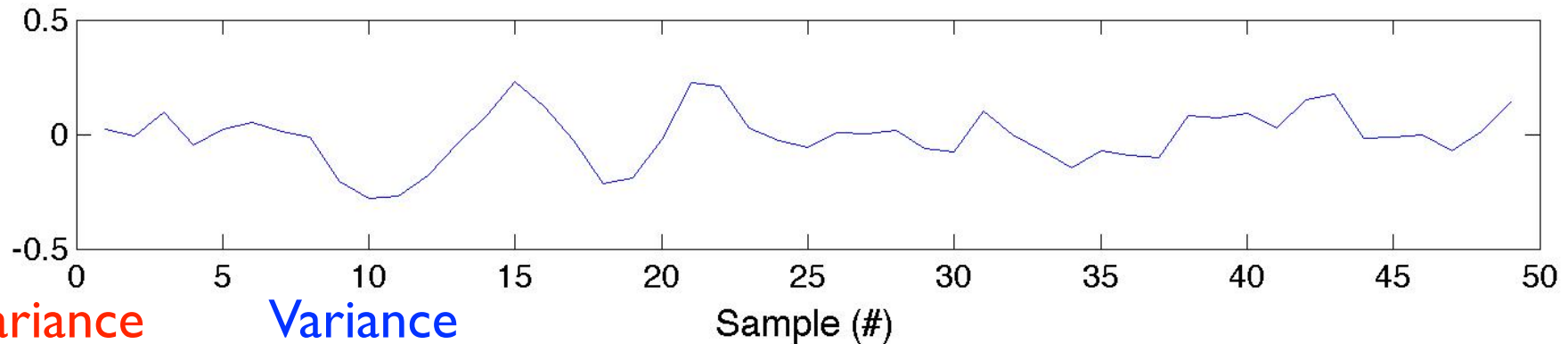


1st level fMRI data is not exchangeable

第一阶的功能磁共振成像数据不可交换

- One important component of noise in fMRI consists of physiological/neuronal events convolved by the HRF

fmri中一个重要的噪声组分是由生理/神经时间与HRF的卷积造成的。

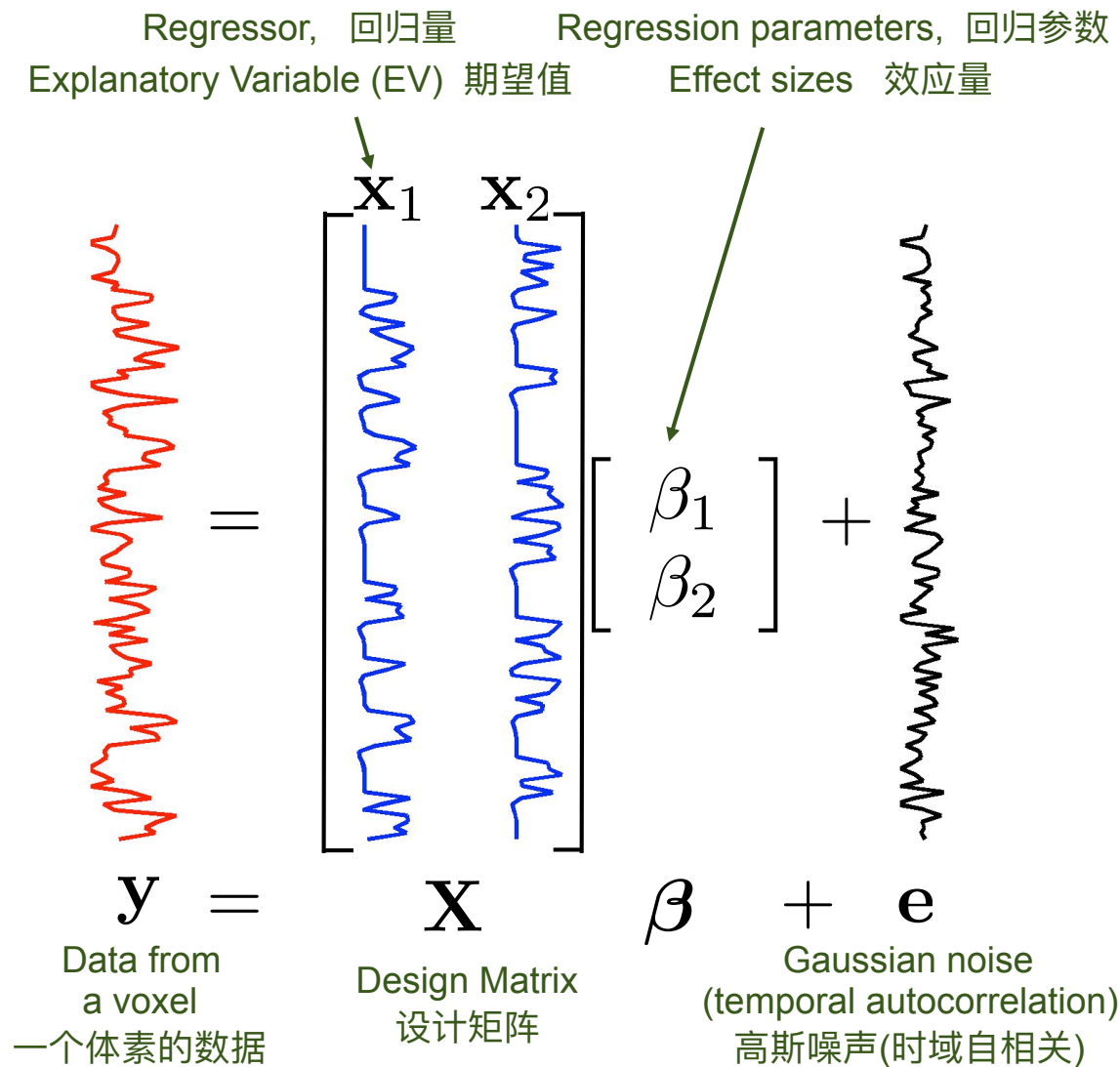




1st level fMRI data is not exchangeable

第一阶的功能磁共振成像数据不可交换

- Let us now return to our model again 我们再返回模型



- The model consists of our regressors X and the noise model
模型由回归量 X 和噪声组成
- All permutations must result in “equivalent models”
所有的置换一定会造成“等效模型”
- Let us now see what happens if we swap two data-points (points 5 and 10)
让我们看看如果交换两个数据点会发生什么。

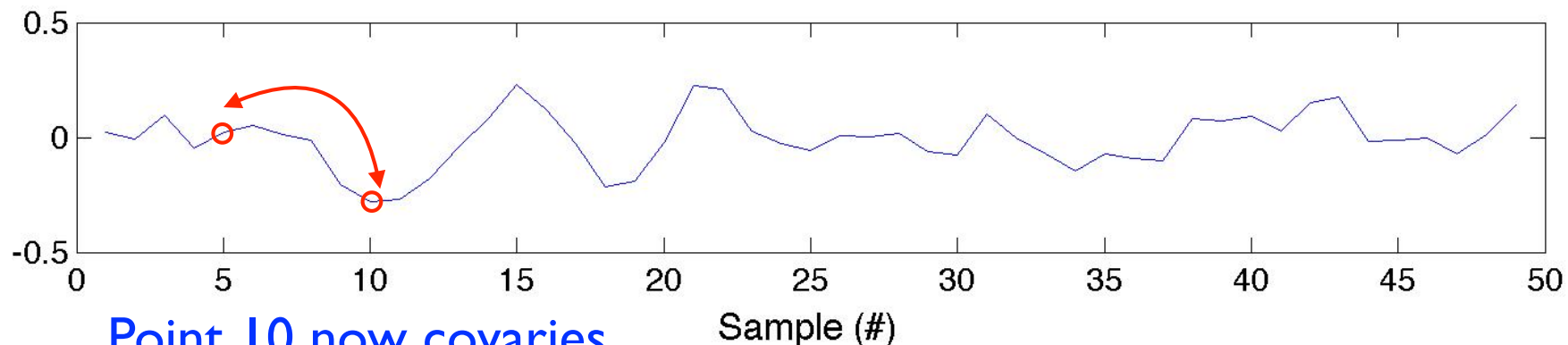


1st level fMRI data is not exchangeable

第一阶的功能磁共振成像数据不可交换

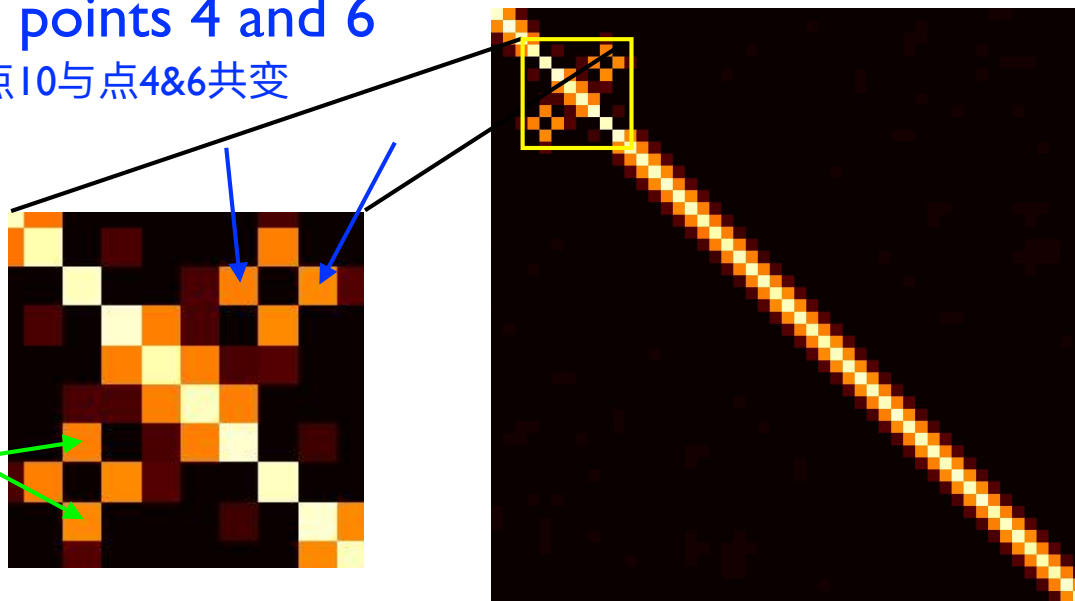
- One important component of noise in fMRI consists of physiological/neuronal events convolved by the HRF

fmri中一个重要的噪声组分是由生理/神经时间与HRF的卷积造成的。



Point 10 now covaries
with points 4 and 6
点10与点4&6共变

“Point 5” now
covaries with
points 9 and 11
点5和点9&11共变



And the models
are no longer
equivalent
模型不再等价

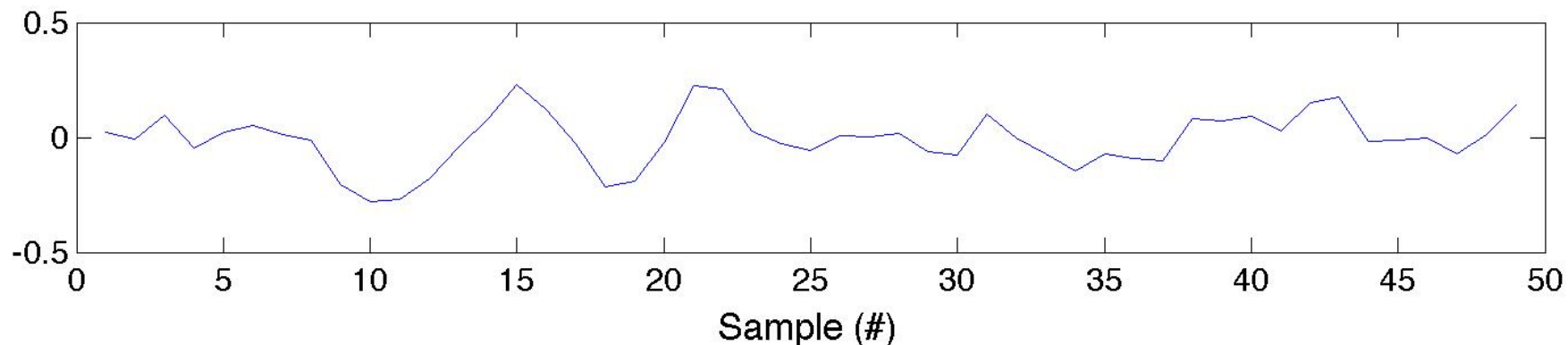


1st level fMRI data is not exchangeable

第一阶的功能磁共振成像数据不可交换

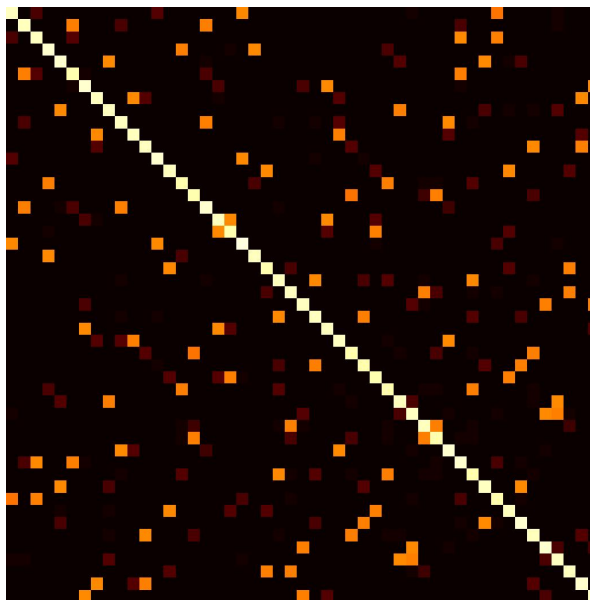
- One important component of noise in fMRI consists of physiological/neuronal events convolved by the HRF

fmri中一个重要的噪声组分是由生理/神经时间与HRF的卷积造成的。



And for a random permutation ...

对于随机的置换...



And the models are no longer equivalent

模型也不再等价



Back to exchangeability

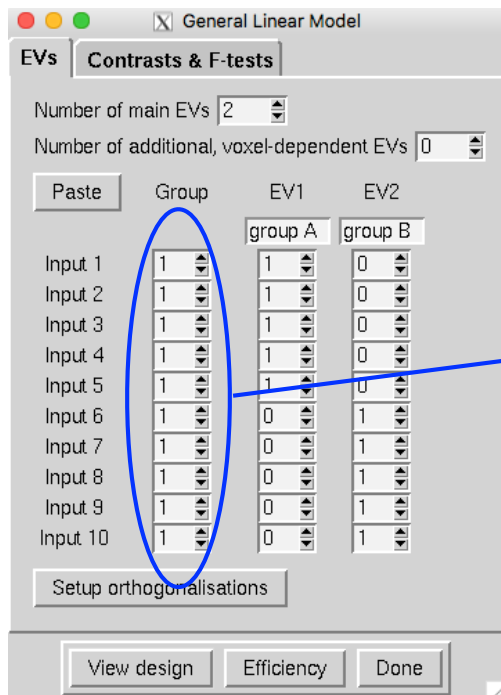
回到可交换性

- Data-points are not “exchangeable” if swapping them means that the noise covariance-matrix ends up looking differently. 如果交换数据点造成了噪声协方差矩阵的差异，他们就不可交换。
- Formally “The joint distribution of the data must be unchanged by the permutations under the null-hypothesis”. 在零假设下进行置换，数据的联合分布一定不变。
- If the noise covariance-matrix has non-zero off-diagonal elements (covariances) you need to beware. 如果噪声协方差矩阵有非零的非对角线元素(协方差)，你要小心。
- You typically never estimate or see the covariance-matrix. You need to “imagine it” and determine from that if there is a problem. 通常你不能估计或看到协方差矩阵，需要你去想象他并判断是否有问题。



Examples of exchangeability: 可交换例子:

Two groups unpaired 两组非配对

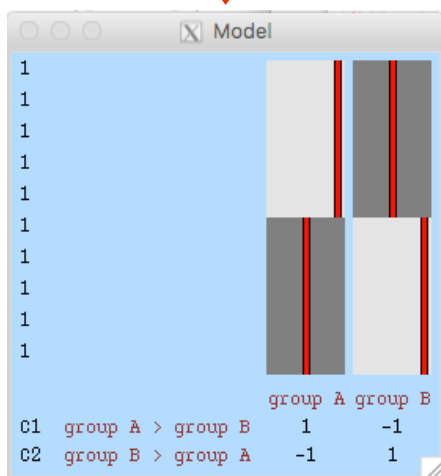


This is the “exchangeability group”. Here all scans are in the same group, which means any scan can be exchanged for any other.

这是可交换组，所有扫描在同一组里，意味着任一扫描可以随意置换

N.B. The “group” labelling is used for completely different purposes when using FLAME/GRFT

注意：进行FLAME/GRFT时，“组”标记用于完全不同的目的。



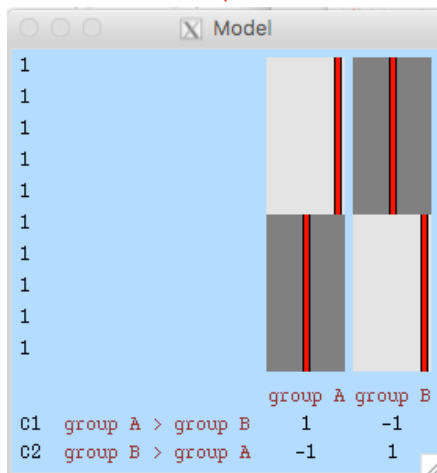
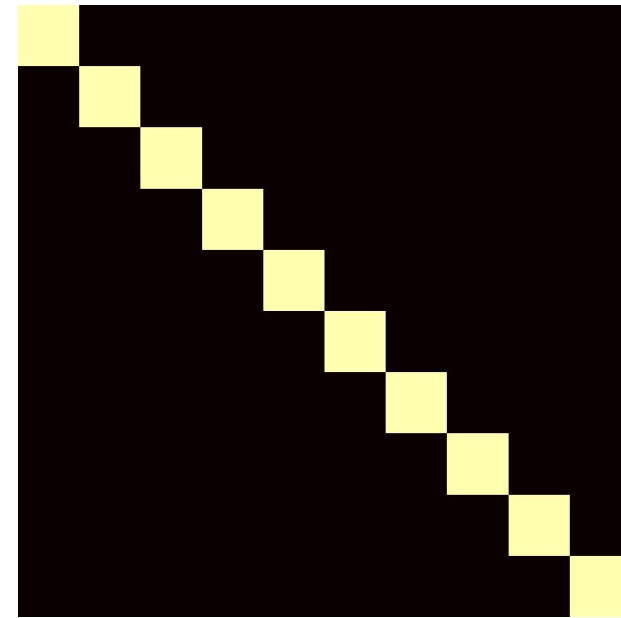
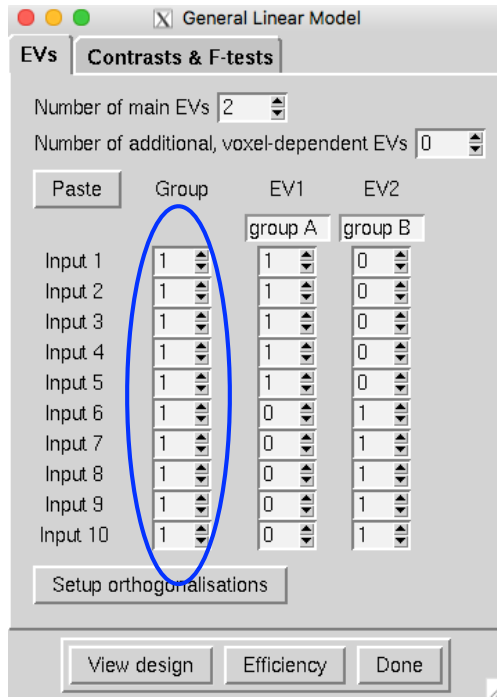


Examples of exchangeability: 可交换例子:

Two groups unpaired 两组非配对

Assumed covariance matrix

假设的协方差矩阵



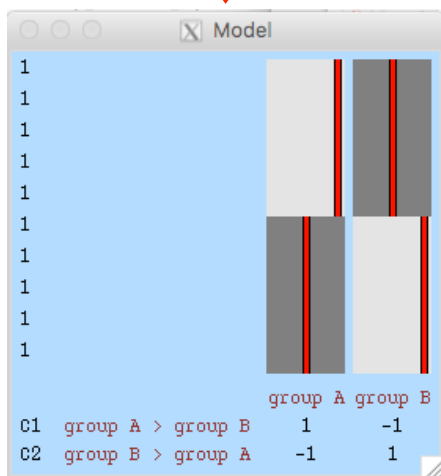
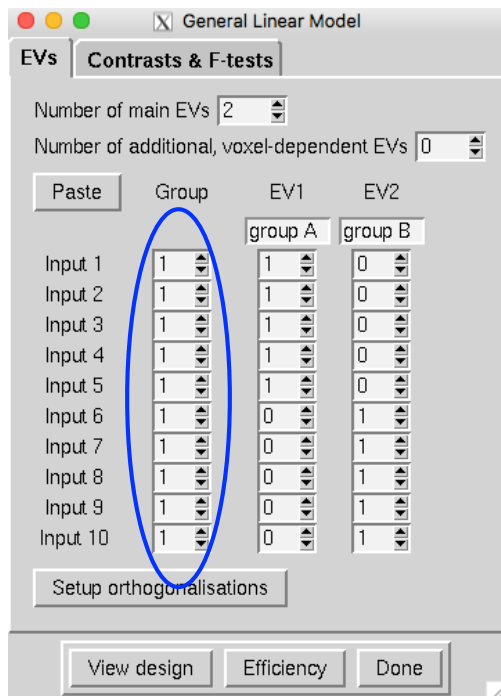
The implicit assumption here is that data from all subjects have the same uncertainty and are all independent
这隐含假设是来自所有被试的数据都具有相同不确定性并且都是独立的。



Examples of exchangeability: 可交换例子:

Two groups unpaired 两组非配对

Original Perm 1 Perm 2 Perm 3

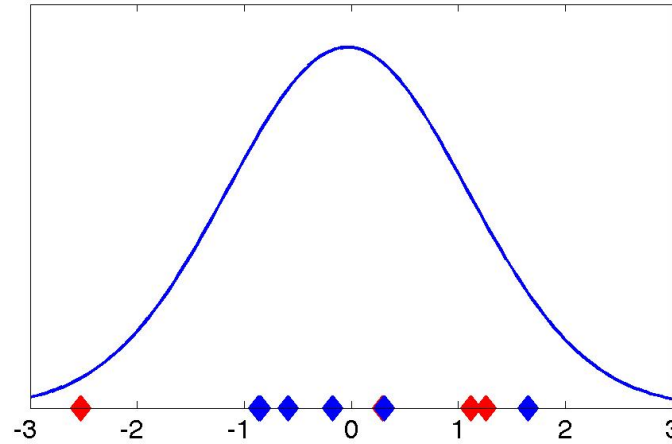
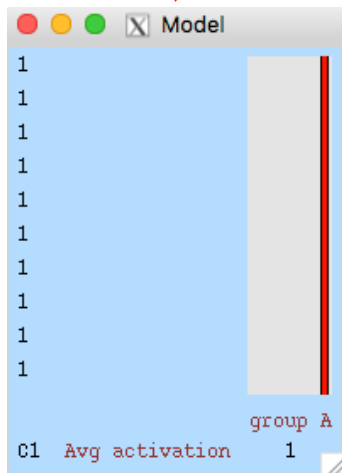
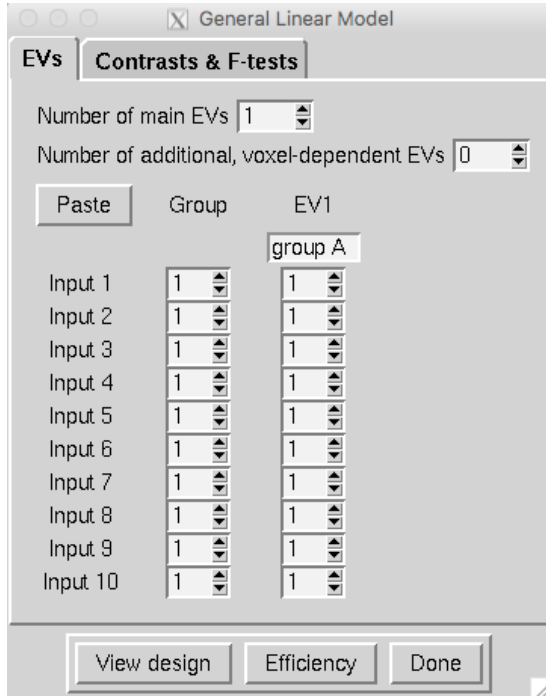


N.B. Equivalent 等效的

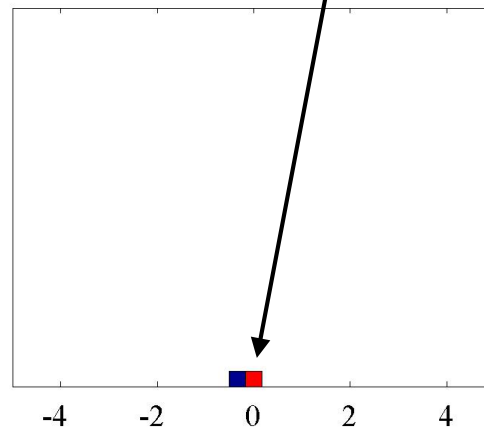


Examples of exchangeability: 可交换例子:

Single group average 单组平均

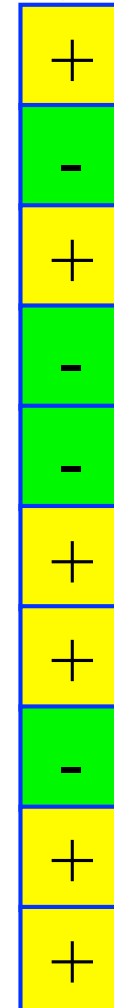


$$t = -0.09$$



First flip

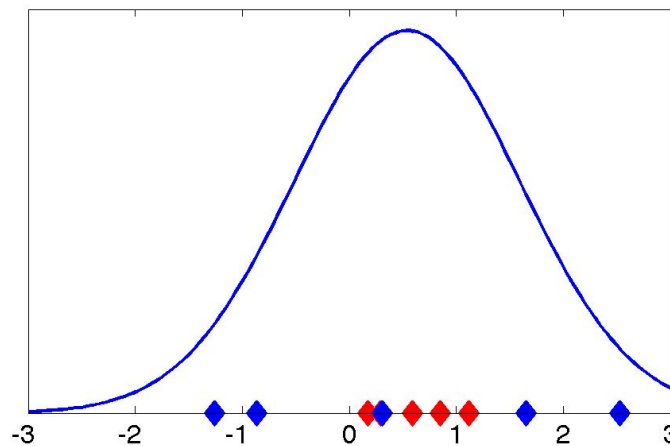
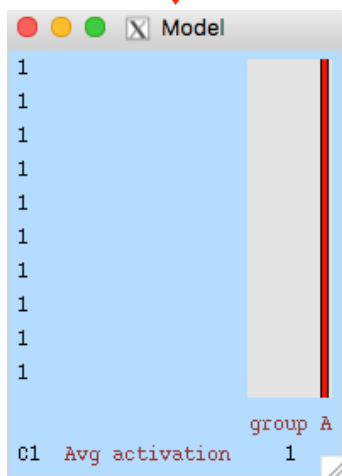
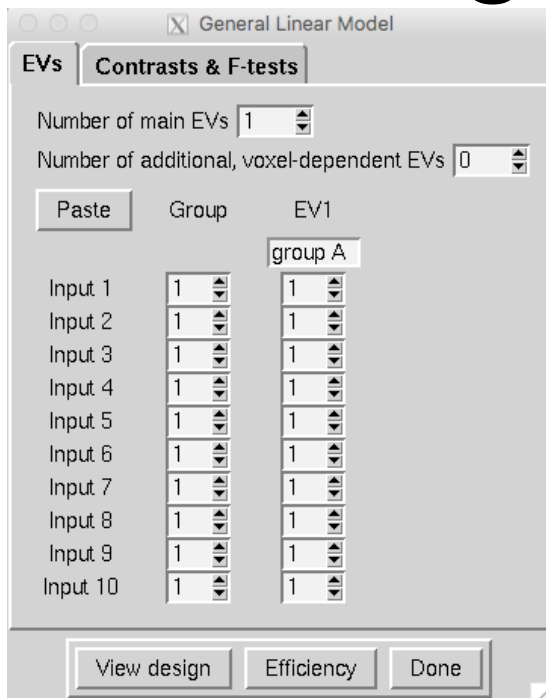
第一次置换



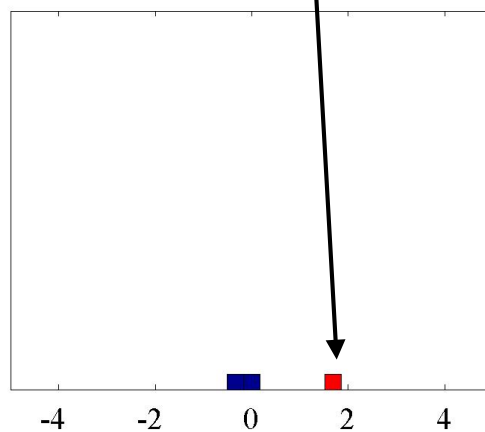


Examples of exchangeability: 可交换例子:

Single group average 单组平均

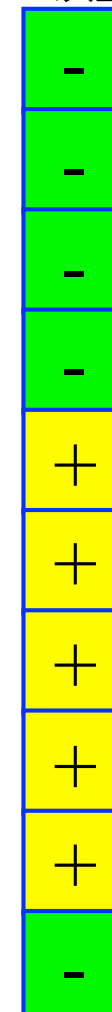


$$t = 1.54$$



Second flip

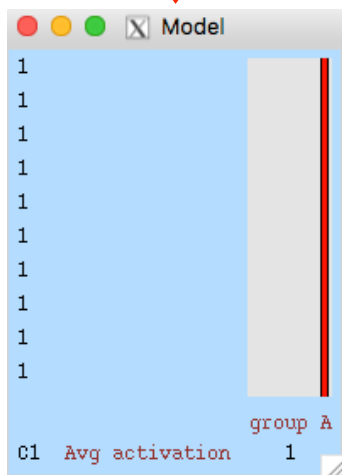
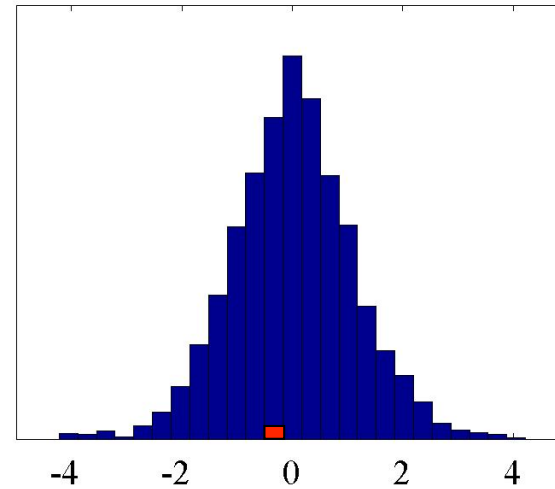
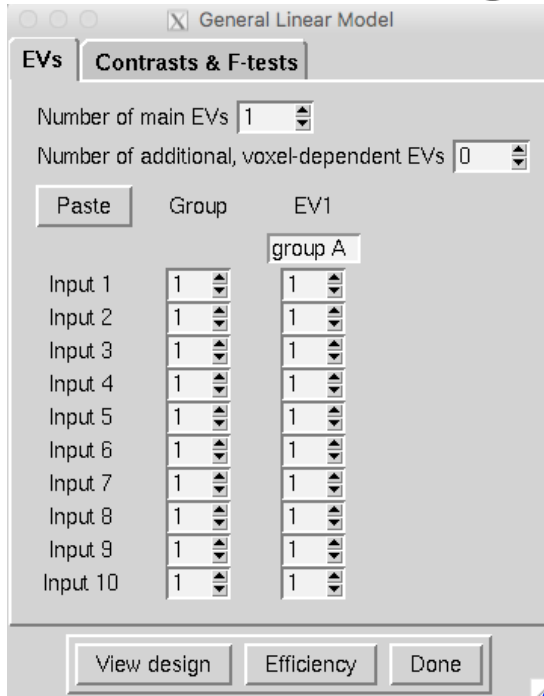
第二次置换





Examples of exchangeability: 可交换例子:

Single group average 单组平均



And the assumptions are: 假设是

- Symmetric errors 对称误差
- Errors independent 误差独立
- Subjects drawn from a single population
来自单一人群的被试



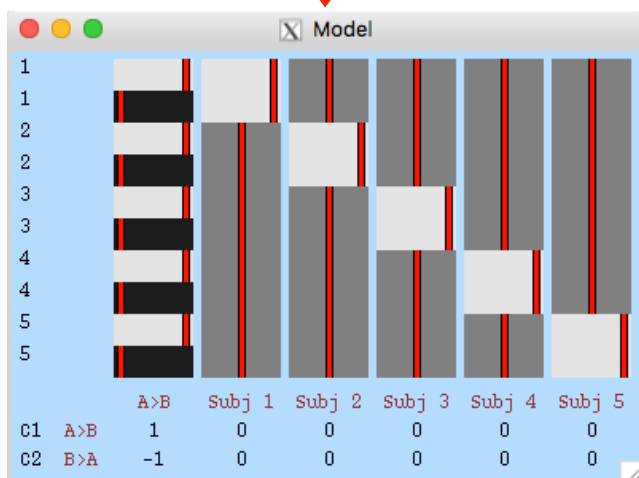
Examples of exchangeability: 可交换例子:

Two groups paired 两组配对

	Group	EV1	EV2	EV3	EV4	EV5	EV6
Input 1	1	1	1	0	0	0	0
Input 2	1	-1	1	0	0	0	0
Input 3	2	1	0	1	0	0	0
Input 4	2	-1	0	1	0	0	0
Input 5	3	1	0	0	1	0	0
Input 6	3	-1	0	0	1	0	0
Input 7	4	1	0	0	0	1	0
Input 8	4	-1	0	0	0	1	0
Input 9	5	1	0	0	0	0	1
Input 10	5	-1	0	0	0	0	1

Here we can only exchange scans within each subject. I.e. Input 1 for Input 2, Input 3 for Input 4 etc

这里我们只能交换被试内的扫描，也就是1对2，3对4





Examples of exchangeability: 可交换例子:

Two groups paired 两组配对

Assumed covariance matrix

假设的协方差矩阵

General Linear Model

EVs Contrasts & F-tests

Number of main EVs 6

Number of additional, voxel-dependent EVs 0

Group	EV1	EV2	EV3	EV4	EV5	EV6
	A>B	Subj 1	Subj 2	Subj 3	Subj 4	Subj 5
Input 1	1	1	0	0	0	0
Input 2	1	-1	1	0	0	0
Input 3	2	1	0	1	0	0
Input 4	2	-1	0	1	0	0
Input 5	3	1	0	0	1	0
Input 6	3	-1	0	0	1	0
Input 7	4	1	0	0	0	1
Input 8	4	-1	0	0	0	1
Input 9	5	1	0	0	0	1
Input 10	5	-1	0	0	0	1

Setup orthogonalisations

View design Efficiency Done



允许互换



Model

	A>B	Subj 1	Subj 2	Subj 3	Subj 4	Subj 5
1	1	0	0	0	0	0
1	-1	1	0	0	0	0
2	1	0	1	0	0	0
2	-1	0	1	0	0	0
3	1	0	0	1	0	0
3	-1	0	0	1	0	0
4	1	0	0	0	1	0
4	-1	0	0	0	1	0
5	1	0	0	0	0	1
5	-1	0	0	0	0	1

C1 A>B 1 0 0 0 0 0

C2 B>A -1 0 0 0 0 0

The implicit assumption here is that data from all subjects have the same uncertainty and that there is no dependence between subjects

隐含假设是所有被试的数据具有相同不确定性，并且被试间没有依赖性。



Examples of exchangeability: 可交换例子:

Two groups paired 两组配对

Assumed covariance matrix

假设的协方差矩阵

General Linear Model

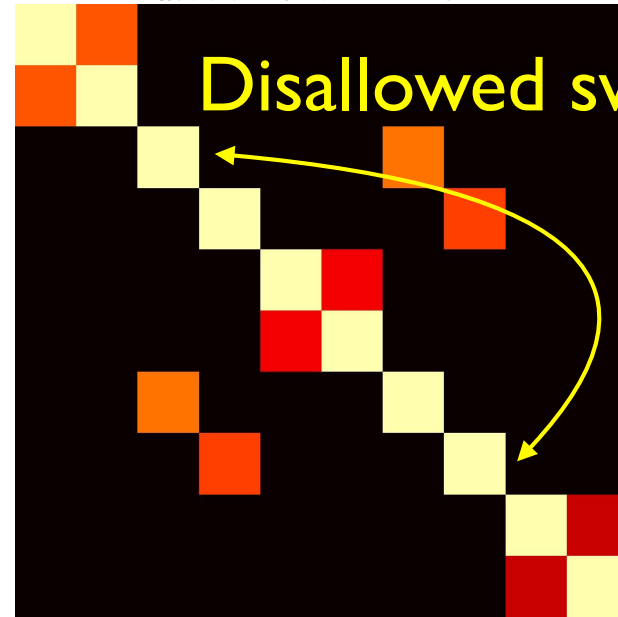
EVs | Contrasts & F-tests

Number of main EVs: 6
Number of additional, voxel-dependent EVs: 0

	Group	EV1	EV2	EV3	EV4	EV5	EV6
		A>B	Subj 1	Subj 2	Subj 3	Subj 4	Subj 5
Input 1	1	1	1	0	0	0	0
Input 2	1	-1	1	0	0	0	0
Input 3	2	1	0	1	0	0	0
Input 4	2	-1	0	1	0	0	0
Input 5	3	1	0	0	1	0	0
Input 6	3	-1	0	0	1	0	0
Input 7	4	1	0	0	0	1	0
Input 8	4	-1	0	0	0	1	0
Input 9	5	1	0	0	0	0	1
Input 10	5	-1	0	0	0	0	1

Setup orthogonalisation

View design | Efficiency | Done



Disallowed swap 不允许互换



Model

1						
1						
2						
2						
3						
3						
4						
4						
5						
5						

	A>B	Subj 1	Subj 2	Subj 3	Subj 4	Subj 5
C1	A>B	1	0	0	0	0
C2	B>A	-1	0	0	0	0

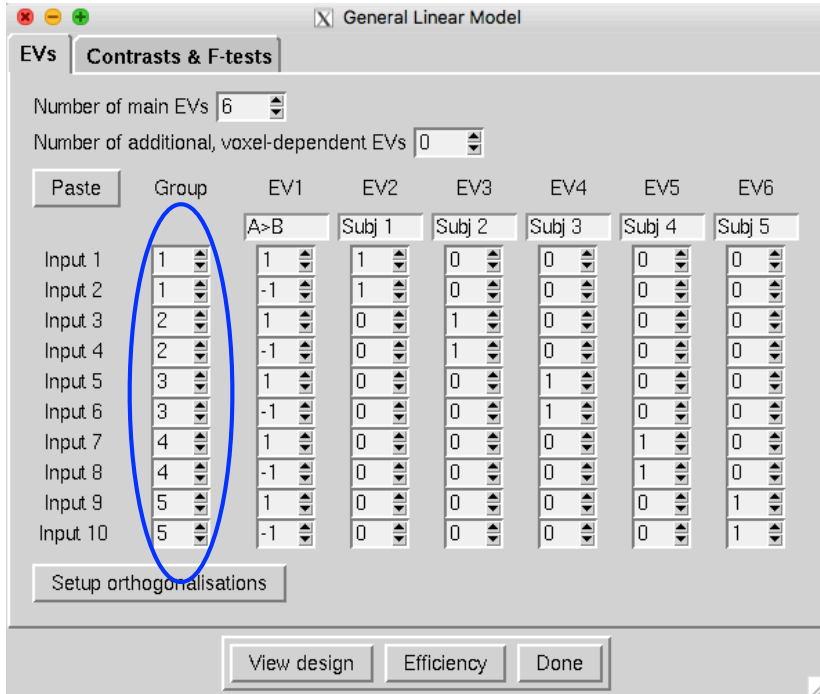
The implicit assumption here is that data from all subjects have the same uncertainty and that there is no dependence between subjects

隐含假设是所有被试的数据具有相同不确定性，并且被试间没有依赖性。

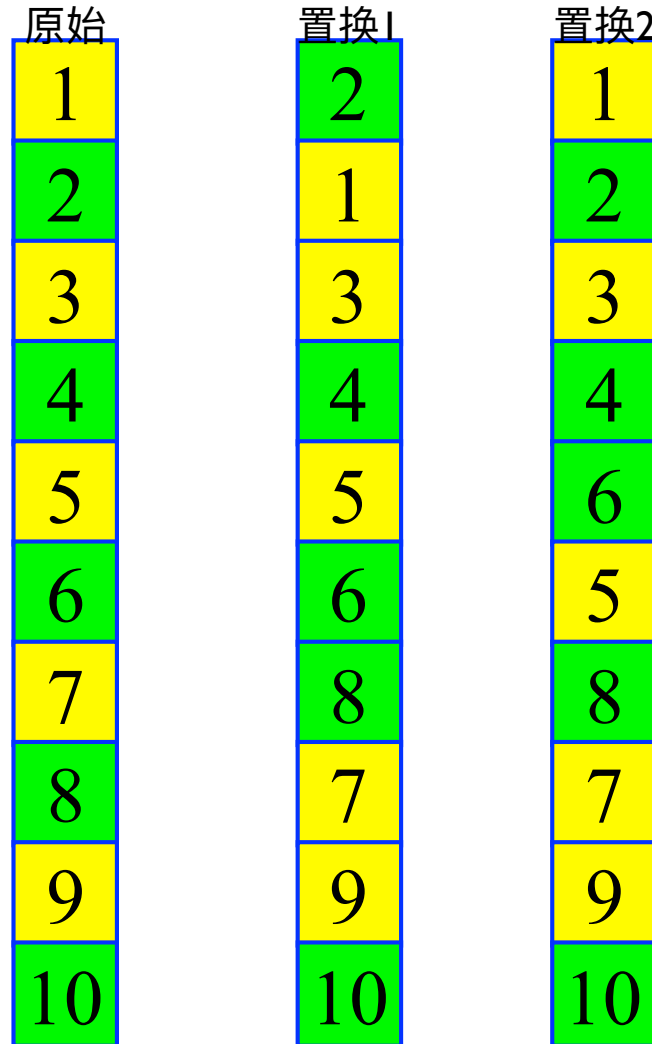


Examples of exchangeability: 可交换例子:

Two groups paired 两组配对



Original Perm 1 Perm 2 ...





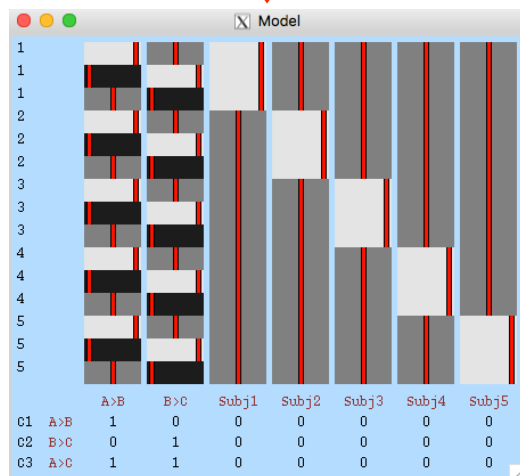
Examples of exchangeability: 可交换例子: blocked ANOVA 组块方差分析

Number of main EVs: 7
Number of additional, voxel-dependent EVs: 0

Paste	Group	EV1	EV2	EV3	EV4	EV5	EV6	EV7
Input 1	1	1	0	1	0	0	0	0
Input 2	1	-1	1	0	0	0	0	0
Input 3	1	0	-1	1	0	0	0	0
Input 4	2	1	0	0	1	0	0	0
Input 5	2	-1	1	0	1	0	0	0
Input 6	2	0	-1	0	1	0	0	0
Input 7	3	1	0	0	0	1	0	0
Input 8	3	-1	1	0	0	1	0	0
Input 9	3	0	-1	0	0	1	0	0
Input 10	4	1	0	0	0	0	1	0
Input 11	4	-1	1	0	0	0	1	0
Input 12	4	0	-1	0	0	0	1	0
Input 13	5	1	0	0	0	0	0	1
Input 14	5	-1	1	0	0	0	0	1
Input 15	5	0	-1	0	0	0	0	1

Same as previous: We can only swap labels within each subject

和之前一样，我们只能在被试内交换标记





Examples of exchangeability: 可交换例子:

blocked ANOVA 组块方差分析

Assumed covariance matrix

假设的协方差矩阵

General Linear Model

EVs **Contrasts & F-tests**

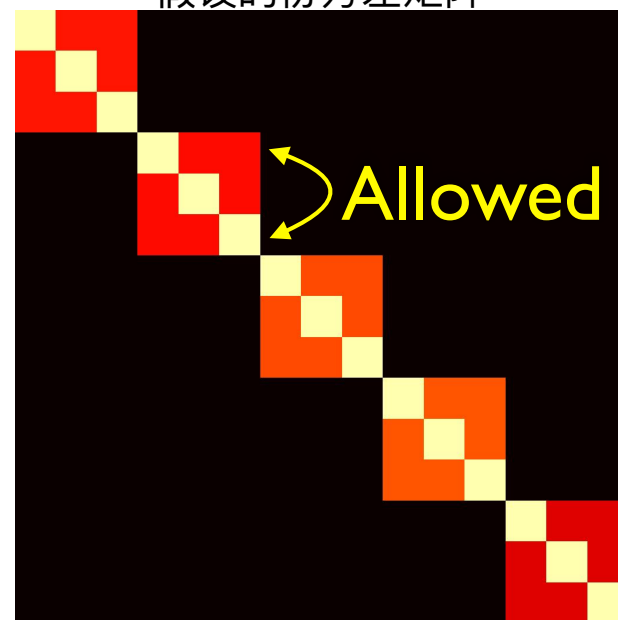
Number of main EVs 7

Number of additional, voxel-dependent EVs 0

Paste	Group	EV1	EV2	EV3	EV4	EV5	EV6	EV7
		A>B	B>C	Subj1	Subj2	Subj3	Subj4	Subj5
Input 1	1	1	0	1	0	0	0	0
Input 2	1	-1	1	0	0	0	0	0
Input 3	1	0	-1	1	0	0	0	0
Input 4	2	1	0	0	1	0	0	0
Input 5	2	-1	1	0	1	0	0	0
Input 6	2	0	-1	0	1	0	0	0
Input 7	3	1	0	0	0	1	0	0
Input 8	3	-1	1	0	0	1	0	0
Input 9	3	0	-1	0	0	1	0	0
Input 10	4	1	0	0	0	0	1	0
Input 11	4	-1	1	0	0	0	1	0
Input 12	4	0	-1	0	0	0	1	0
Input 13	5	1	0	0	0	0	0	1
Input 14	5	-1	1	0	0	0	0	1
Input 15	5	0	-1	0	0	0	0	1

Setup orthogonalisations

View design Efficiency Done



允许交换



Model

1							
1							
1							
2							
2							
2							
3							
3							
3							
4							
4							
4							
5							
5							
5							

	A>B	B>C	Subj1	Subj2	Subj3	Subj4	Subj5
C1	A>B	1	0	0	0	0	0
C2	B>C	0	1	0	0	0	0
C3	A>C	1	1	0	0	0	0

Assumptions: All subjects from the same “population”, no dependence between subjects and “compound symmetry” within subjects

假设：所有被试来自同一人群，被试间无依赖性，并且被试内“复合对称”



Examples of exchangeability: 可交换例子:

blocked ANOVA 组块方差分析

Assumed covariance matrix

假设的协方差矩阵

General Linear Model

EVs **Contrasts & F-tests**

Number of main EVs 7

Number of additional, voxel-dependent EVs 0

Paste	Group	EV1	EV2	EV3	EV4	EV5	EV6	EV7
		A>B	B>C	Subj1	Subj2	Subj3	Subj4	Subj5
Input 1	1	1	0	1	0	0	0	0
Input 2	1	-1	1	0	1	0	0	0
Input 3	1	0	-1	1	0	0	0	0
Input 4	2	1	0	0	1	0	0	0
Input 5	2	-1	1	0	1	0	0	0
Input 6	2	0	-1	0	1	0	0	0
Input 7	3	1	0	0	0	1	0	0
Input 8	3	-1	1	0	0	1	0	0
Input 9	3	0	-1	0	0	1	0	0
Input 10	4	1	0	0	0	0	1	0
Input 11	4	-1	1	0	0	0	1	0
Input 12	4	0	-1	0	0	0	1	0
Input 13	5	1	0	0	0	0	0	1
Input 14	5	-1	1	0	0	0	0	1
Input 15	5	0	-1	0	0	0	0	1

Setup orthogonalisations

View design Efficiency Done



Assumptions: All subjects from the same “population”, no dependence between subjects and “compound symmetry” within subjects

假设：所有被试来自同一人群，被试间无依赖性，并且被试内“复合对称”



Model

1							
1							
1							
2							
2							
2							
3							
3							
3							
4							
4							
4							
5							
5							
5							

	A>B	B>C	Subj1	Subj2	Subj3	Subj4	Subj5
C1	A>B	1	0	0	0	0	0
C2	B>C	0	1	0	0	0	0
C3	A>C	1	1	0	0	0	0



Examples of exchangeability: 可交换例子:

blocked ANOVA 组块方差分析

Assumed covariance matrix

假设的协方差矩阵

General Linear Model

EVs Contrasts & F-tests

Number of main EVs 7

Number of additional, voxel-dependent EVs 0

Paste	Group	EV1	EV2	EV3	EV4	EV5	EV6	EV7
		A>B	B>C	Subj1	Subj2	Subj3	Subj4	Subj5
Input 1	1	1	0	1	0	0	0	0
Input 2	1	-1	1	0	1	0	0	0
Input 3	1	0	-1	1	0	0	0	0
Input 4	2	1	0	0	1	0	0	0
Input 5	2	-1	1	0	1	0	0	0
Input 6	2	0	-1	0	1	0	0	0
Input 7	3	1	0	0	0	1	0	0
Input 8	3	-1	1	0	0	1	0	0
Input 9	3	0	-1	0	0	1	0	0
Input 10	4	1	0	0	0	0	1	0
Input 11	4	-1	1	0	0	0	1	0
Input 12	4	0	-1	0	0	0	1	0
Input 13	5	1	0	0	0	0	0	1
Input 14	5	-1	1	0	0	0	0	1
Input 15	5	0	-1	0	0	0	0	1

Setup orthogonalisations

View design Efficiency Done



Model

1							
1							
1							
2							
2							
2							
3							
3							
3							
4							
4							
4							
5							
5							
5							

	A>B	B>C	Subj1	Subj2	Subj3	Subj4	Subj5
C1 A>B	1	0	0	0	0	0	0
C2 B>C	0	1	0	0	0	0	0
C3 A>C	1	1	0	0	0	0	0



Assumptions: All subjects from the same “population”, no dependence between subjects and “compound symmetry” within subjects

假设：所有被试来自同一人群，被试间无依赖性，并且被试内“复合对称”

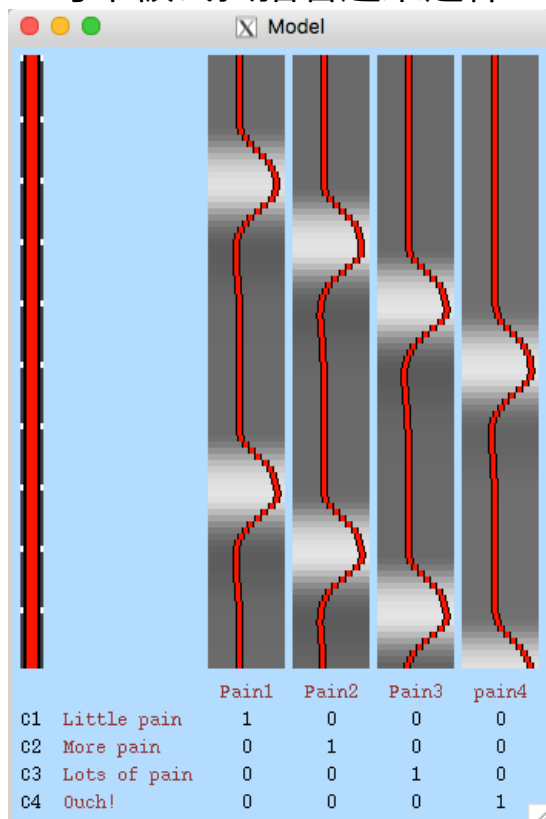


My advice: Keep it simple!

我的建议：保持简单

Each subject
scanned like this

每个被试扫描看起来这样



Taking 4 contrasts
to 2nd level

第二水平有4个对比

We want to find areas that
respond “linearly” to pain.

我们想找到对疼痛线性响应的区域。

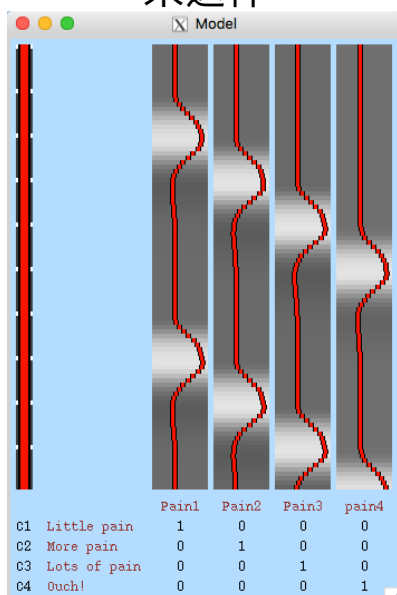


My advice: Keep it simple!

我的建议：保持简单

Each subject scanned like this

每个被试扫描看起来这样



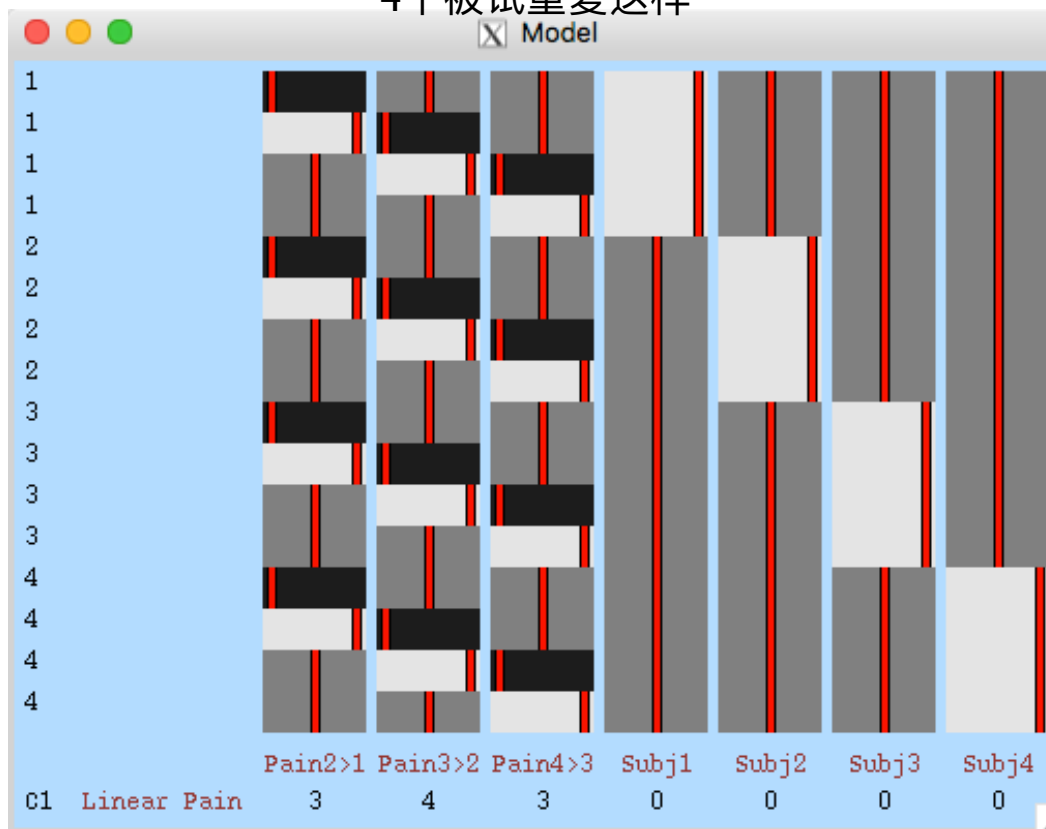
Taking 4 contrasts

to 2nd level

第二水平有4个对比

Repeating this for four subjects

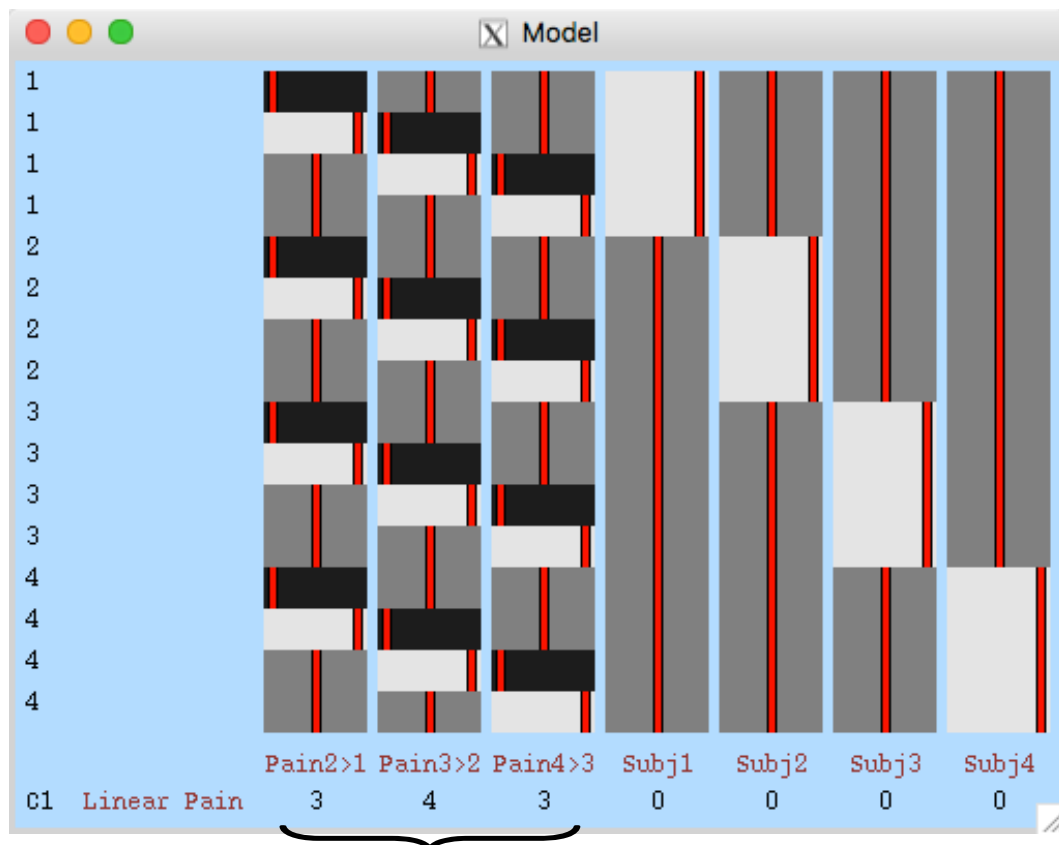
4个被试重复这样





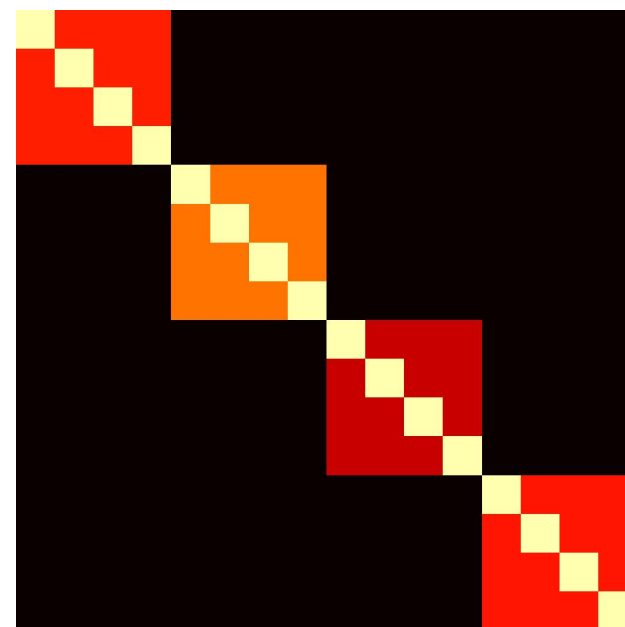
My advice: Keep it simple!

我的建议：保持简单



And figure out this contrast

推理得到这样设置对比



You have to assume this covariance matrix

必须假设这个协方差矩阵

Why put yourself through all that pain?

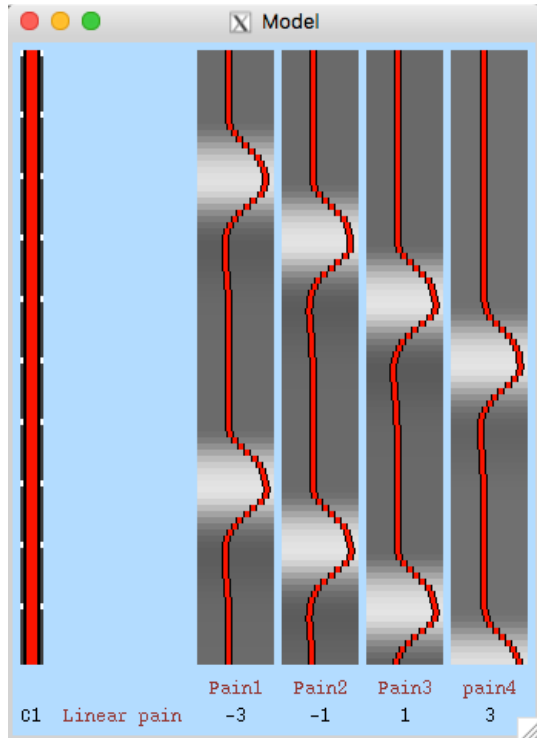
为什么要忍受所有痛苦?



My advice: Keep it simple!

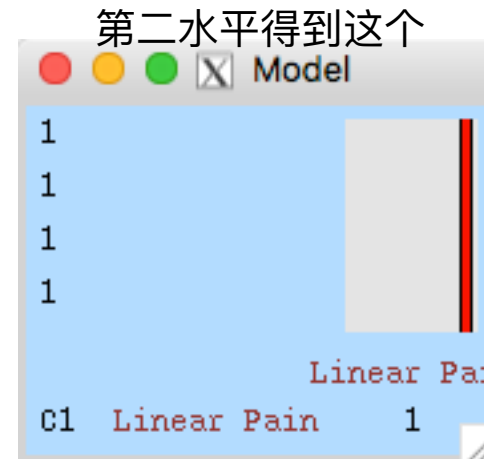
我的建议：保持简单

And get this at the second level



When you can take a single contrast from the first level

当你可以跟第一水平做简单对比时



Assuming only symmetric errors

仅假设对称误差

Much nicer, no?

更赞，不是吗？



Outline大纲

- Null-hypothesis and Null-distribution 零假设和零分布
- Multiple comparisons and Family-wise error 多重比较和族错误率
- Different ways of being surprised 惊奇的不同方式
 - Voxel-wise inference (Maximum z) 体素推断 (最大z)
 - Cluster-wise inference (Maximum size) 簇水平推断 (最大尺寸)
- Parametric vs non-parametric tests 参数vs非参检验
- Enhanced clusters 增强的簇
- FDR - False Discovery Rate FDR-错误发现率



Clustering cookbook 簇指导

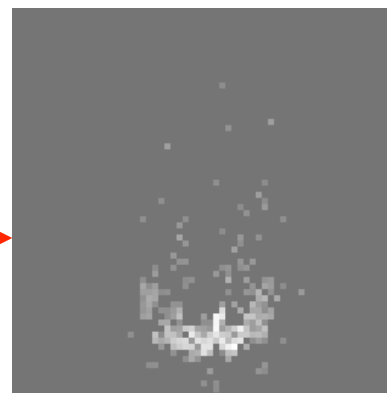
Instead of resel-based correction, we can do clustering:

除了基于resel的校正外，我么还能做簇：

z stat image z值图



Threshold at
(arbitrary!) z level
在z水平(任意)的阈值





Clustering cookbook 簇指导

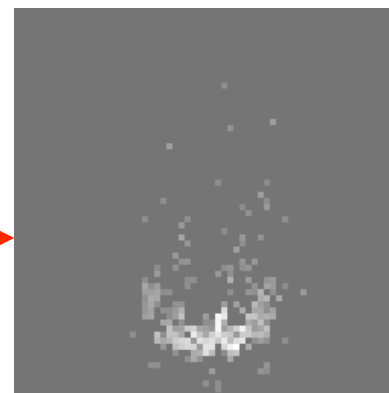
Instead of resel-based correction, we can do clustering:

除了基于resel的校正外，我们还能做簇：

z stat image z值图



Threshold at
(arbitrary!) z level
在z水平(任意)的阈值



Form clusters from surviving voxels.

从尚存体素形成簇

Calculate the size threshold $u(R,z)$.

计算大小的阈值 $u(R,z)$

Any cluster larger than u “survives” and we reject the null-hypothesis for that.

存在大于 u 的簇，我们拒绝零假设

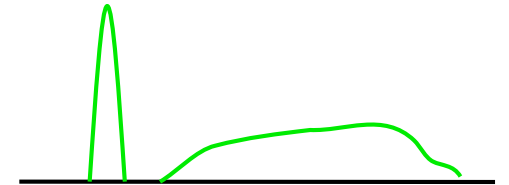




How do we choose the (arbitrary!) z-threshold?

我们是怎样(随意)选择z阈值的?

This is arbitrary and a trade-off 这是一个随意和权衡





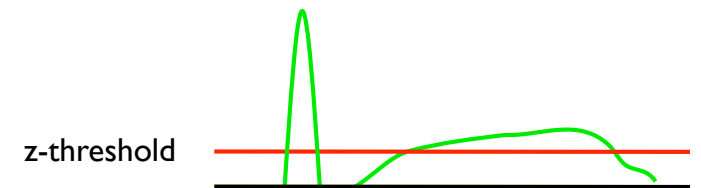
How do we choose the (arbitrary!) z-threshold?

我们是怎样(随意)选择z阈值的?

This is arbitrary and a trade-off 这是一个随意和权衡

I. **Low threshold** - can violate RFT assumptions, but can detect clusters with large spatial extent and low z

低阈值-可能违反RFT假设，但可以检测到具有较大空间范围和较低z的簇





How do we choose the (arbitrary!) z-threshold?

我们是怎样(随意)选择z阈值的?

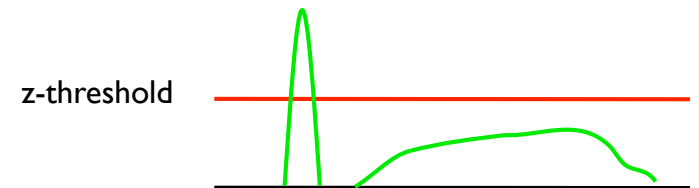
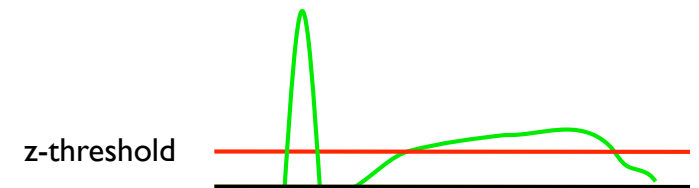
This is arbitrary and a trade-off 这是一个随意和权衡

1. **Low threshold** - can violate RFT assumptions, but can detect clusters with large spatial extent and low z

低阈值-可能违反RFT假设，但可以检测到具有较大空间范围和较低z的簇

2. **High threshold** - gives more power to clusters with small spatial extent and high z

高阈值-为空间范围较小且z较高的簇提供更多功能





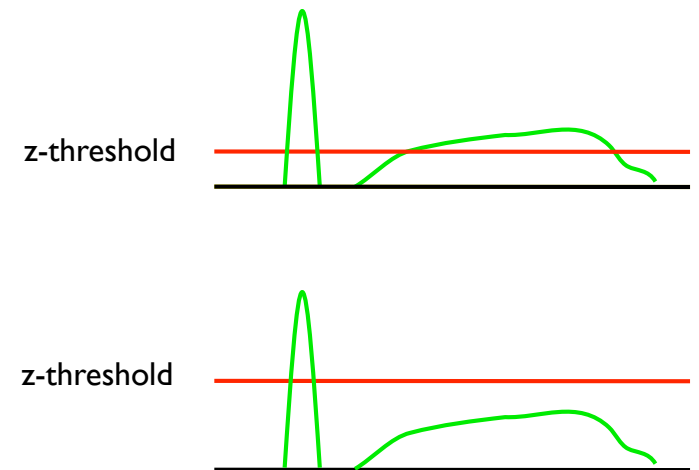
How do we choose the (arbitrary!) z-threshold?

我们是怎样(随意)选择z阈值的?

This is arbitrary and a trade-off 这是一个随意和权衡

1. **Low threshold** - can violate RFT assumptions, but can detect clusters with large spatial extent and low z
低阈值-可能违反RFT假设, 但可以检测到具有较大空间范围和较低z的簇

2. **High threshold** - gives more power to clusters with small spatial extent and high z
高阈值-为空间范围较小且z较高的簇提供更多功能



Tends to be more sensitive than voxel-wise corrected testing
倾向于比体素校正测试更敏感

Results depend on extent of spatial smoothing in pre-processing
结果取决于预处理中空间平滑的程度



TFCE

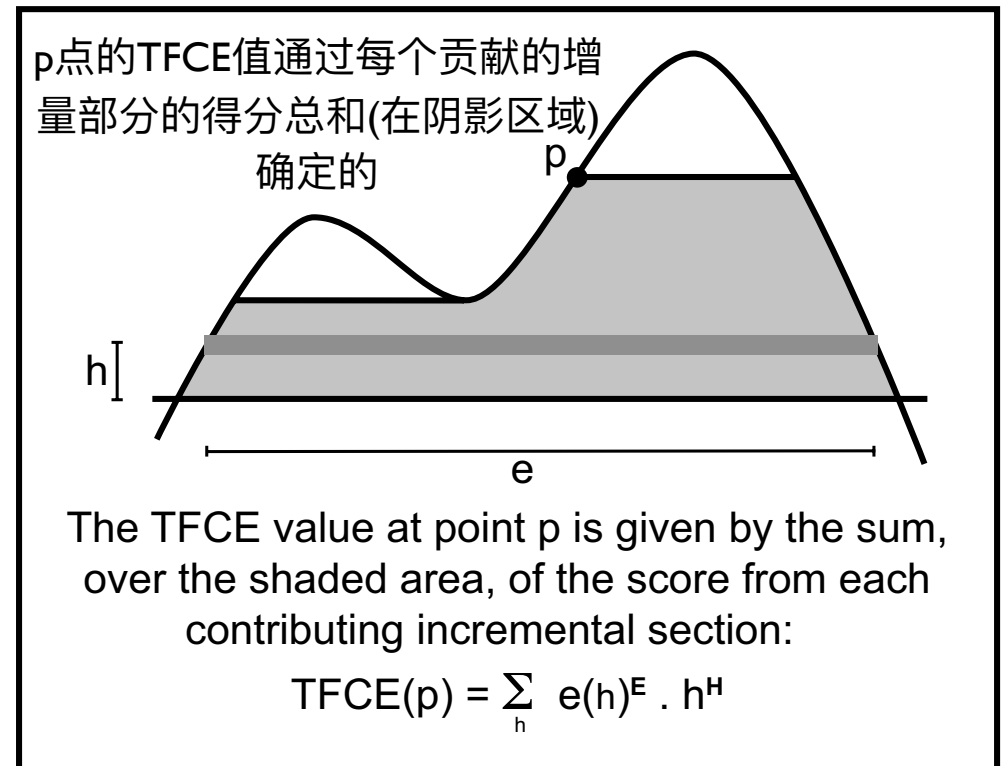
Threshold-Free Cluster Enhancement 无阈值簇增强

[Smith & Nichols, NeuroImage 2009]

- Cluster thresholding: 簇阈值
 - popular because it's sensitive, due to its use of spatial extent 因为在空间范围内的使用导致的很敏感，所以流行
 - but the pre-smoothing extent is arbitrary 但是预平滑程度任意
 - and so is the cluster-forming threshold 簇形成阈值也如此
 - ➔ unstable and arbitrary 不稳定和随意

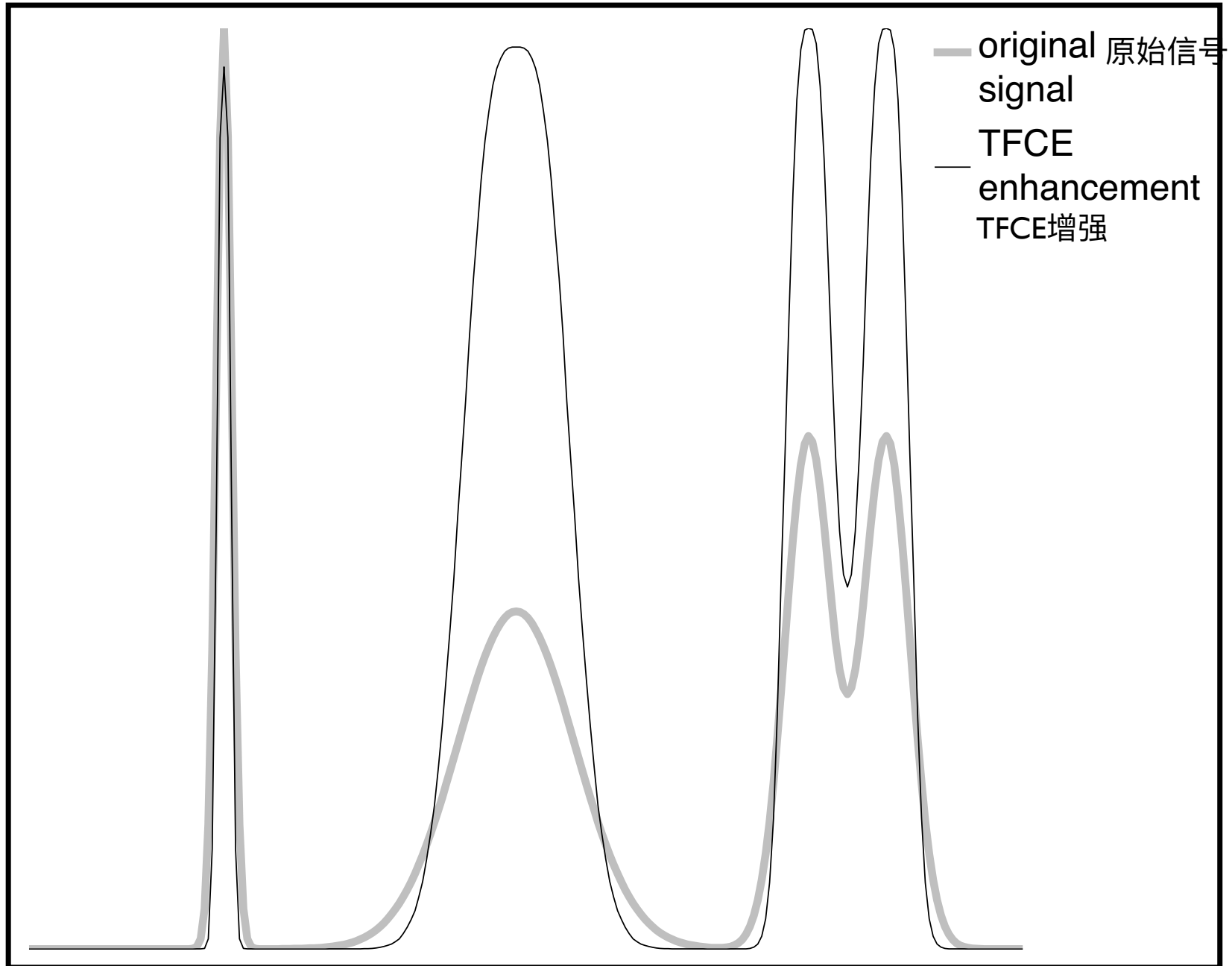
- TFCE

- integrates cluster “scores” over all possible thresholds 整合所有可能阈值的簇“得分”
- output at each voxel is measure of local cluster-like support 在每个体素输出局部簇支持的测量
- similar sensitivity to optimal cluster-thresholding, but stable and non-arbitrary 与最佳簇阈值敏感性相同，但稳定且不随意



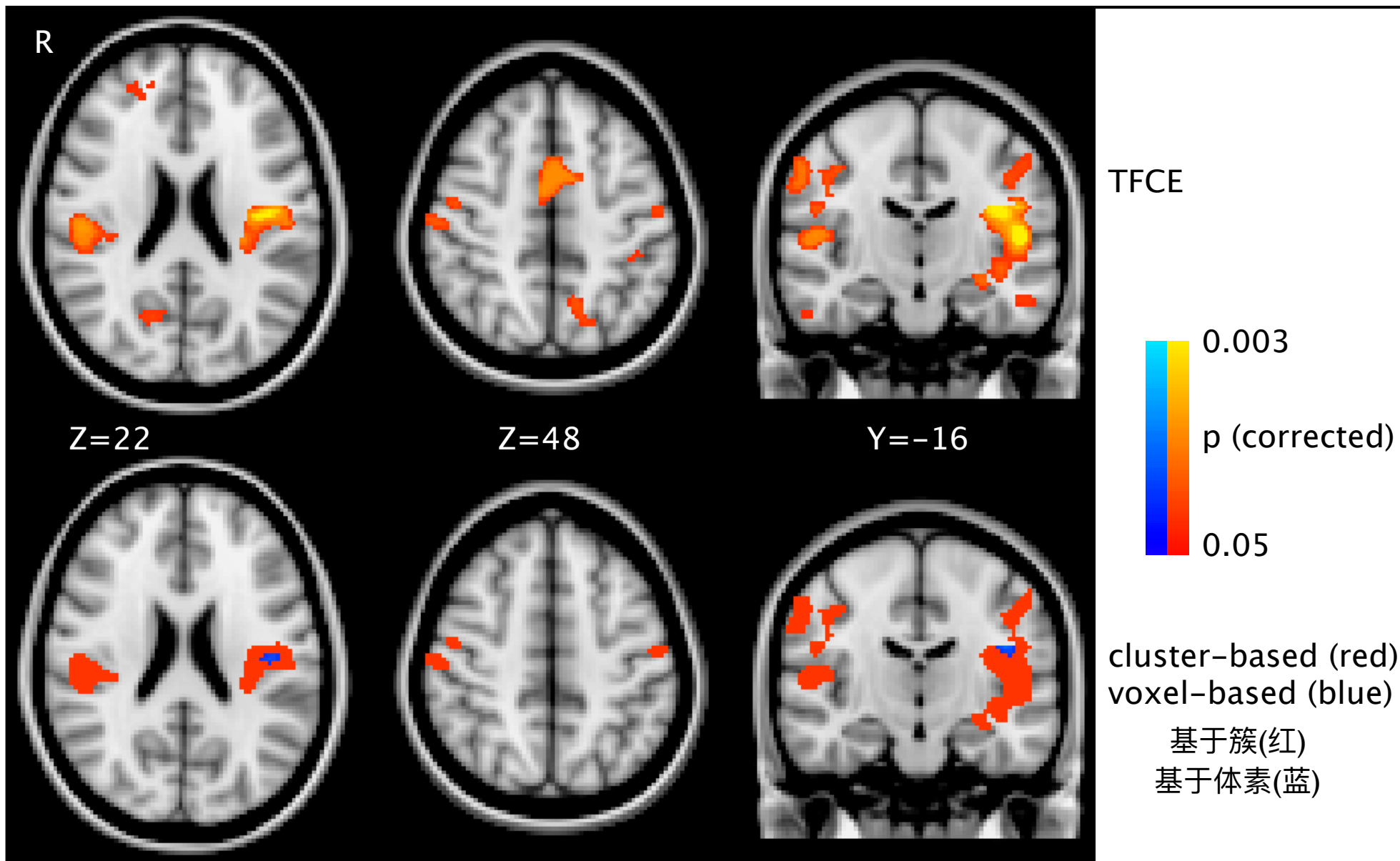


Qualitative example 定性例子





TFCE for FSL-VBM

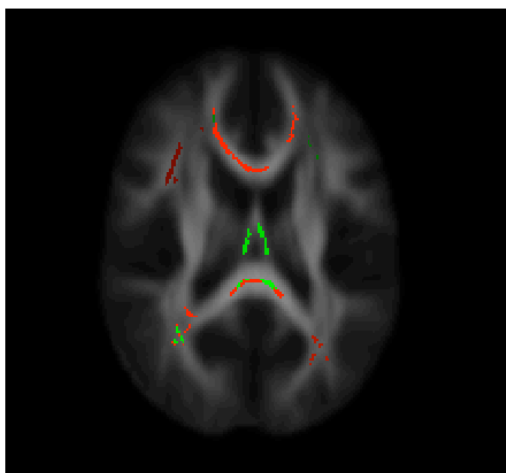
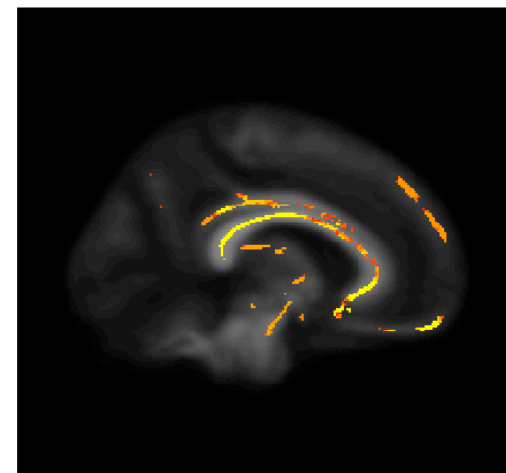
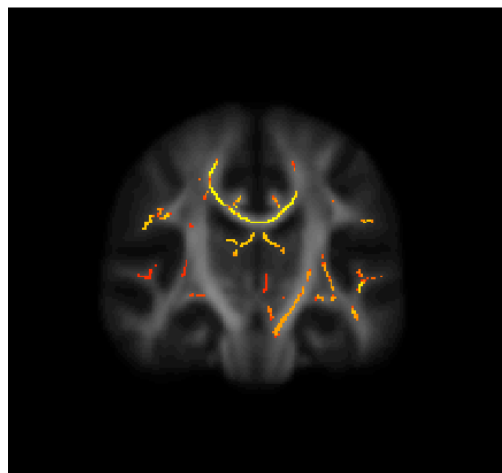
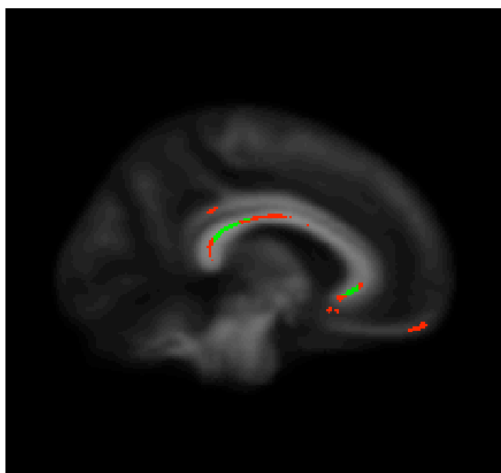
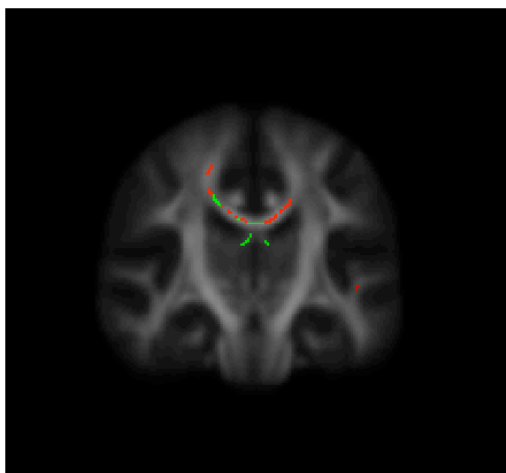




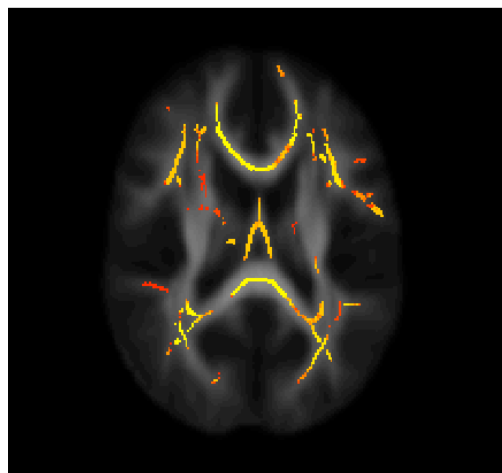
TFCE for TBSS

controls > schizophrenics 对照 > 精神分裂患者

$p < 0.05$ corrected for multiple comparisons across space, using randomise
跨空间的多重比较校正，使用randomise工具



cluster-based:
基于簇
cluster-forming
threshold =
2 or **3**
簇形成阈值=2或3



TFCE



Outline大纲

- Null-hypothesis and Null-distribution 零假设和零分布
- Multiple comparisons and Family-wise error 多重比较和族错误率
- Different ways of being surprised 惊奇的不同方式
 - Voxel-wise inference (Maximum z) 体素推断 (最大z)
 - Cluster-wise inference (Maximum size) 簇水平推断 (最大尺寸)
- Parametric vs non-parametric tests 参数vs非参检验
- Enhanced clusters 增强的簇
- FDR - False Discovery Rate FDR-错误发现率



False Discovery Rate

错误发现率



- **FDR: False Discovery Rate** 错误发现率
A “new” way to look at inference. 一种新的推断方式
- **Uncorrected (for multiple-comparisons):** 未校正(多重比较)
 - Is equivalent to saying: “I am happy to nearly always say something silly about my experiments”.
等于说: “我很乐意针对我全部实验总结一些辣鸡结论。”
- **Family-Wise Error (FWE):** 总体误差
 - Is equivalent to saying: “I am happy to say something silly about 5% of my experiments”.
相当于说: “我乐意对约5%的实验结果总结一些辣鸡结论”。
- **False Discovery Rate** 错误发现率
 - Is equivalent to saying: “I am happy if 5% of what I say about each experiment is silly”.
等于说: “如果我的实验总结只有5%很辣鸡, 我爽翻。”



False Discovery Rate

错误发现率



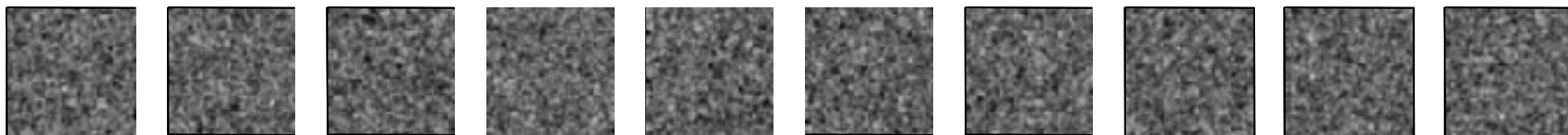
- **FDR: False Discovery Rate** 错误发现率
A “new” way to look at inference. 一种新的推断方式
- **Uncorrected (for multiple-comparisons):** 未校正(多重比较)
 - **Is equivalent to saying: “I am happy to nearly always say something silly about my experiments”.**
等于说: “我很乐意针对我全部实验总结一些辣鸡结论。”
 - **On average, 5% of all voxels are false positives**
平均而言, 所有体素中有5%是假阳性
- **Family-Wise Error (FWE):** 总体误差
 - **Is equivalent to saying: “I am happy to say something silly about 5% of my experiments”.**
相当于说: “我乐意对约5%的实验结果总结一些辣鸡结论”。
 - **On average, 5% of all experiments have one or more false positive voxels** 平均而言, 所有实验中有5%具有一个或多个假阳性体素
- **False Discovery Rate** 错误发现率
 - **Is equivalent to saying: “I am happy if 5% of what I say about each experiment is silly”.**
等于说: “如果我的实验总结只有5%很辣鸡, 我爽翻。”
 - **On average, 5% of significant voxels are false positives** 平均而言, 5%的显著体素是假阳性。



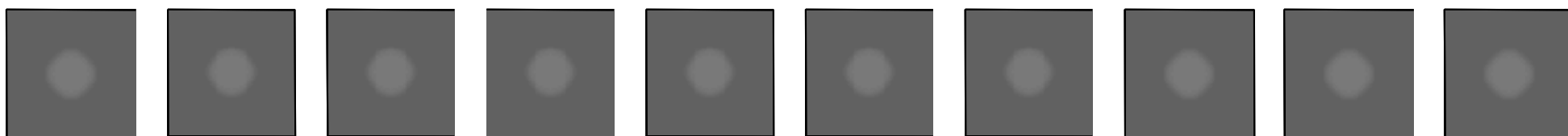
Little imaging demonstration.

影像演示

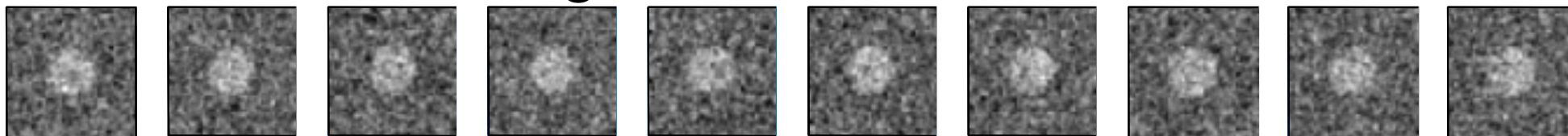
Noise 噪音



Signal 信号



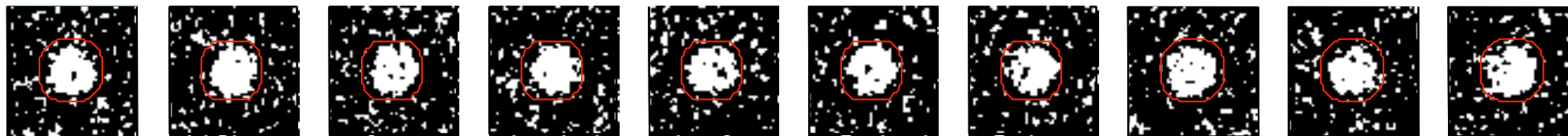
Signal+Noise 信号+噪音





uncorrected voxelwise control of FP rate at 10%

假阳性率在10%的未校正体素控制

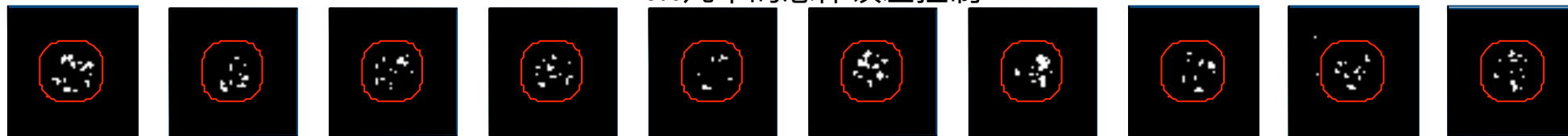


percentage of all null pixels that are False Positives

所有假阳性零像素的百分比

control of FamilyWise Error rate at 10%

10%几率的总体误差控制



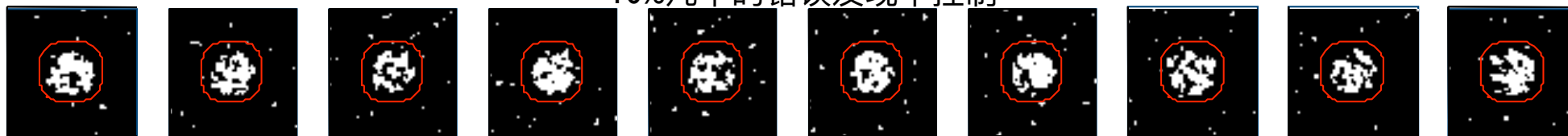
occurrence of FamilyWise Error

总体误差的发生率

FWE

control of False Discovery Rate at 10%

10%几率的错误发现率控制



percentage of activated (reported) pixels that are False Positives

报告的假阳性的激活像素百分比



FDR for dummies

傻瓜式FDR指南

- Makes assumptions about how errors are distributed (like GRT). 假设误差分布的方式
- Used to calculate a threshold. 用于计算阈值。
- Threshold such that $X\%$ of super-threshold (reported) **voxels** are false positives. 卡阈值使得 $X\%$ 超阈值(报告的)体素是假阳性。
- Threshold depends on the data. May for example be very different for $[1\ 0]$ and $[0\ 1]$ in the same study. 阈值取决于数据。同一个研究中的 $[1\ 0]$ 和 $[0\ 1]$ 可能有很大差异。