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CRC In vivo Imaging

SPM

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Topological Inference

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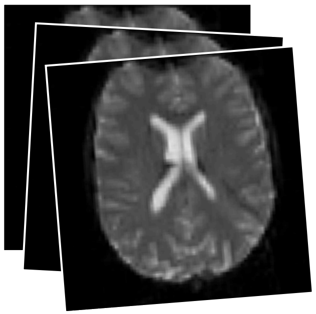
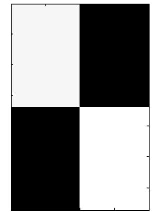
With thanks to Guillaume Flandin, Justin Chumbley and Tom Nichols

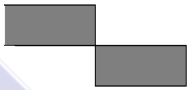
SPM Course
Woluwe, 28 November 2019

SPM

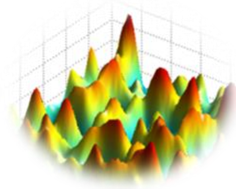


$y =$  $\beta + \varepsilon$

Contrast *c*



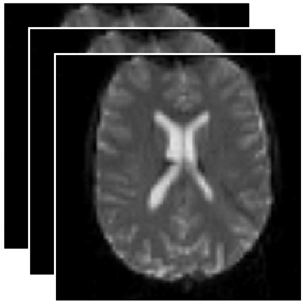
Random Field Theory



Pre-processings

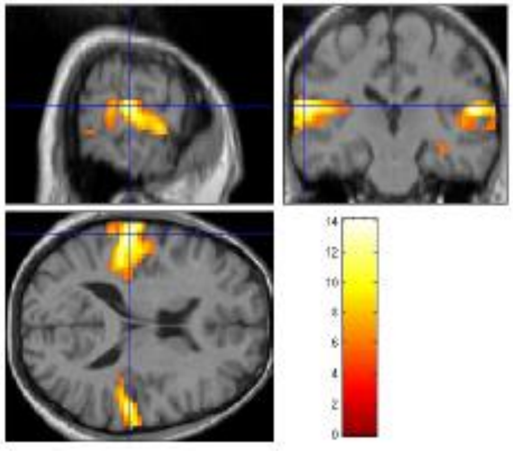
General Linear Model

Statistical Inference



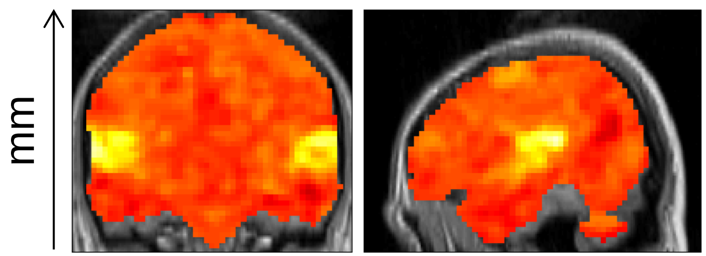
$$\hat{\beta} = (X^T X)^{-1} X^T y$$

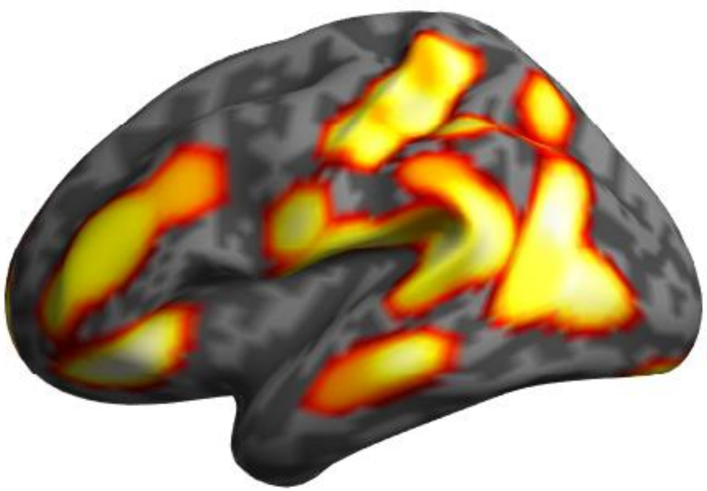
$$\hat{\sigma}^2 = \frac{\hat{\varepsilon}^T \hat{\varepsilon}}{rank(X)}$$

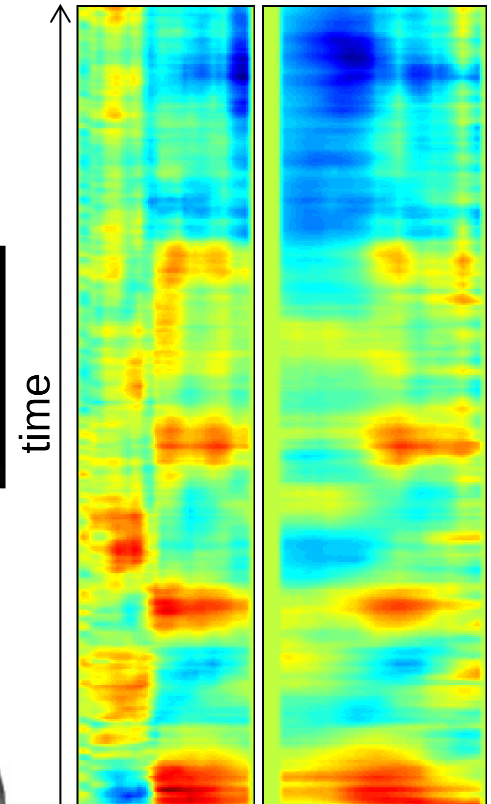


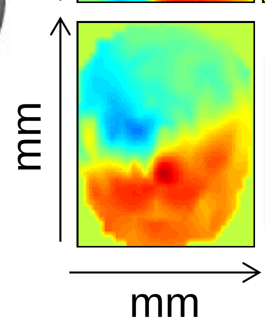
Statistical Parametric Maps

fMRI, VBM,
M/EEG source reconstruction



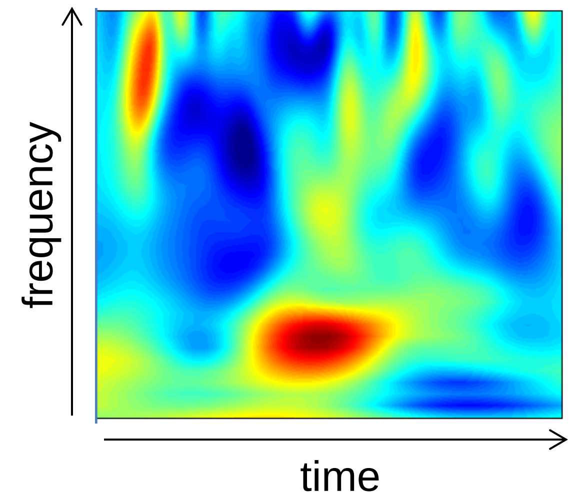




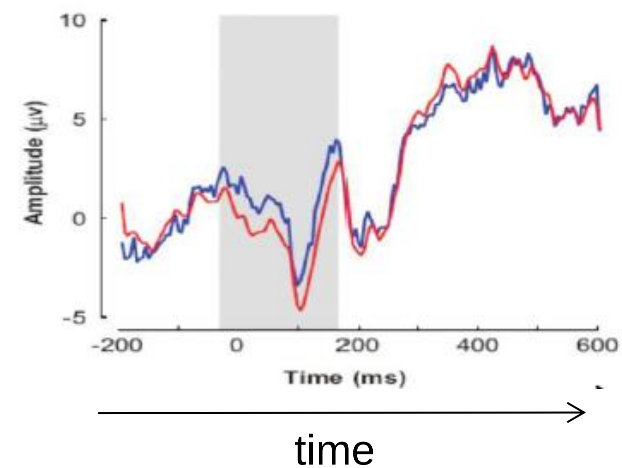


M/EEG
2D+t
scalp-time

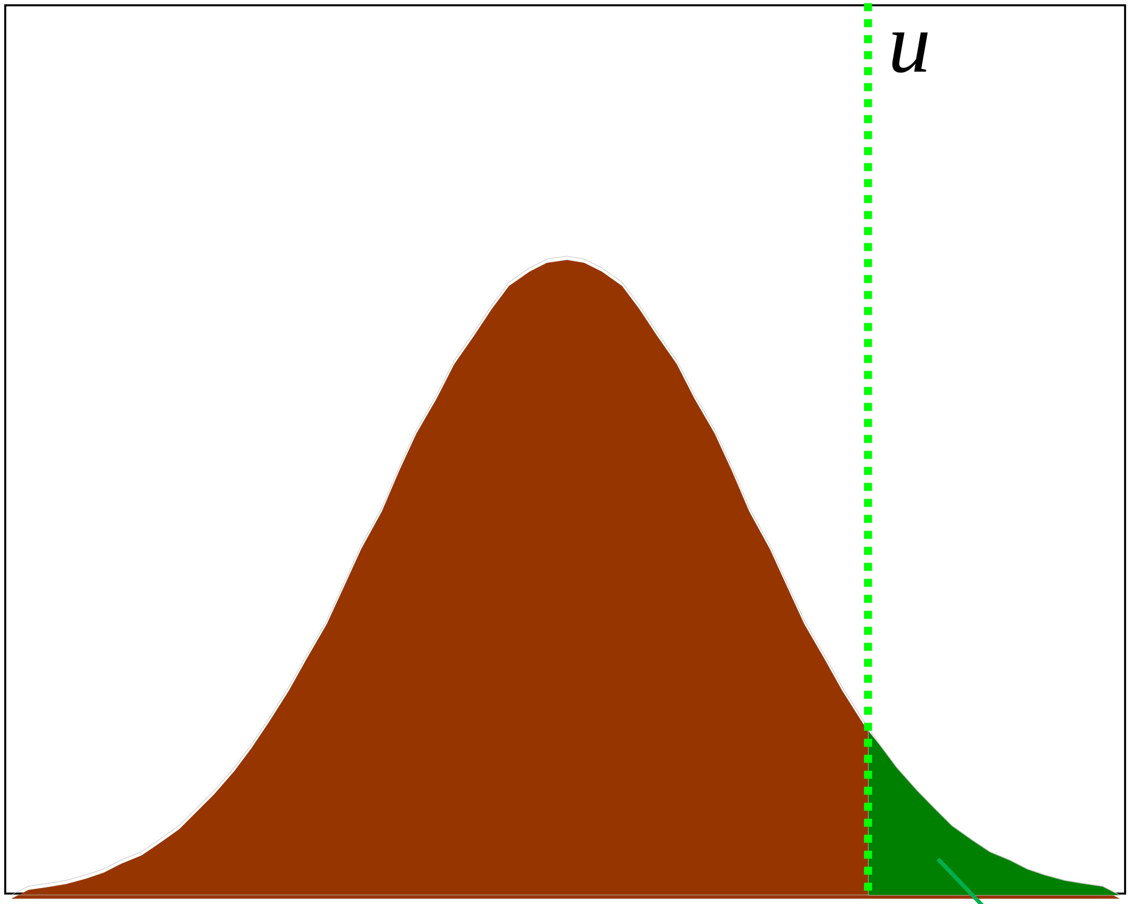
M/EEG 2D time-frequency



M/EEG 1D channel-time



Inference at a single voxel



Null distribution of test statistic T

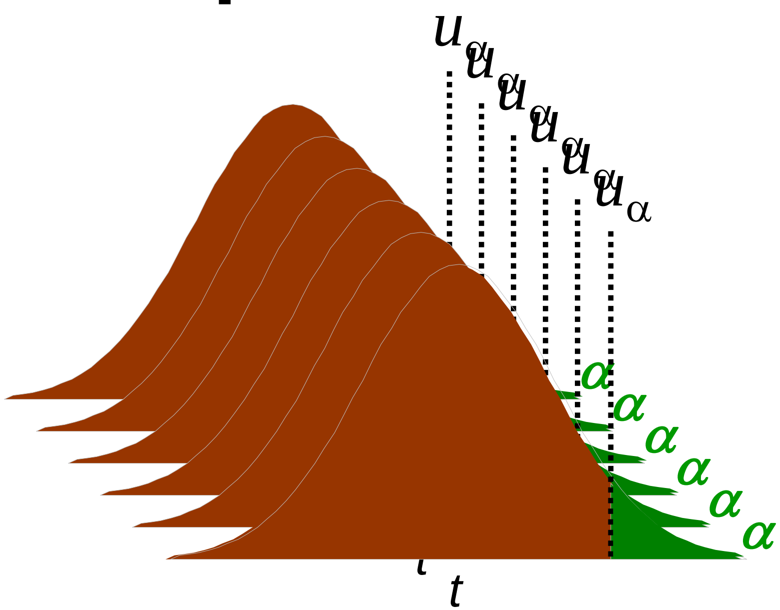
Null Hypothesis H_0:
zero activation

Decision rule (threshold) u:
determines false positive rate α

$\Rightarrow$ Choose u to give acceptable α under H_0

$$\alpha = p(t > u | H_0)$$

Multiple tests

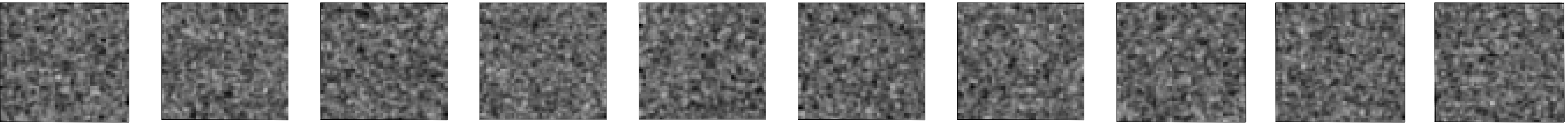


If we have 100,000 voxels,

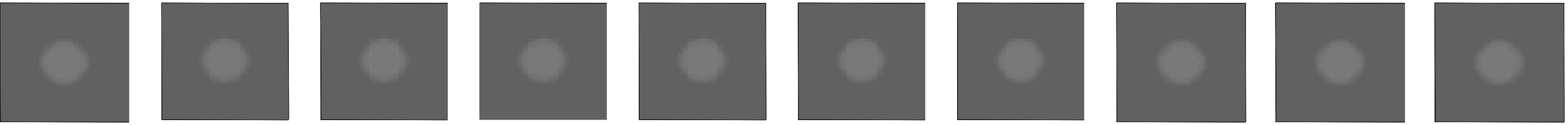
α=0.05 $\Rightarrow$ 5,000 false positive voxels.

This is clearly undesirable; to correct for this we can define a null hypothesis for a collection of tests.

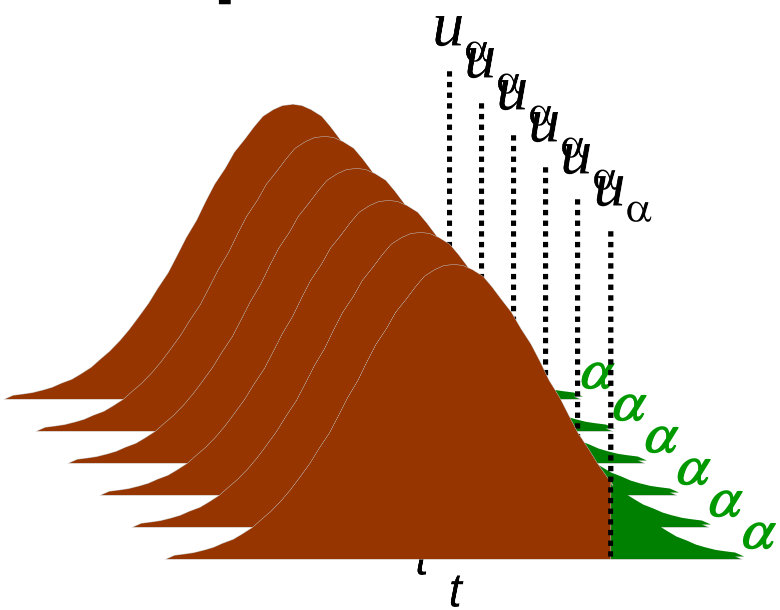
Noise



Signal



Multiple tests



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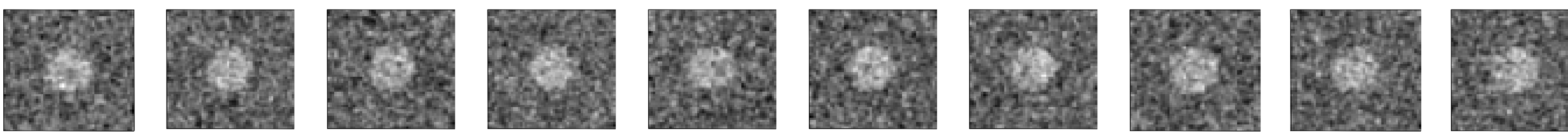
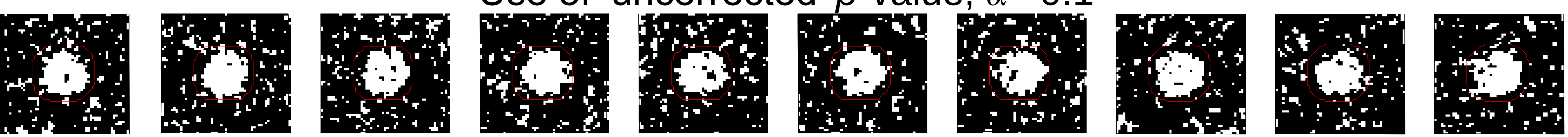


Use of ‘uncorrected’ *p*-value, α =0.1



11.3%	11.3%	12.5%	10.8%	11.5%	10.0%	10.7%	11.2%	10.2%	9.5%

Percentage of Null Pixels that are False Positives

Family-Wise Null Hypothesis

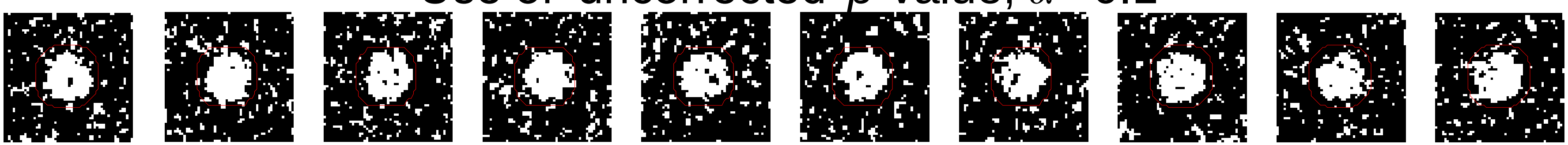
Family-Wise Null Hypothesis:
Activation is zero everywhere

If we reject a voxel null hypothesis at *any* voxel,
we reject the family-wise Null hypothesis

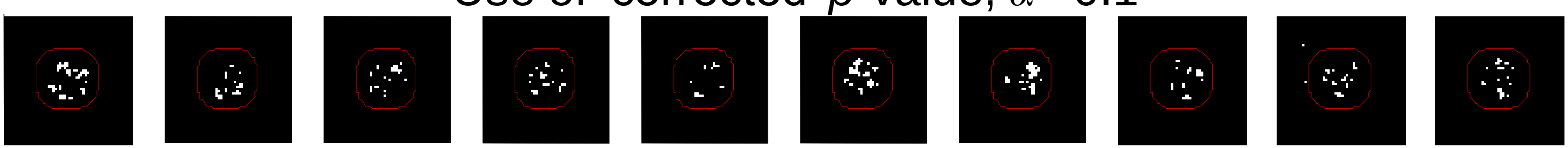
A FP ***anywhere*** in the image gives a **Family Wise Error** (FWE)

Family-Wise Error rate (FWER) = '*corrected*' *p*-value

Use of 'uncorrected' *p*-value, α =0.1



Use of 'corrected' *p*-value, α =0.1



FWE

Bonferroni correction

The Family-Wise Error rate (FWER), α_{FWE}, for a family of N tests follows the inequality:

$$\alpha_{FWE} \leq N\alpha$$

where α is the test-wise error rate.

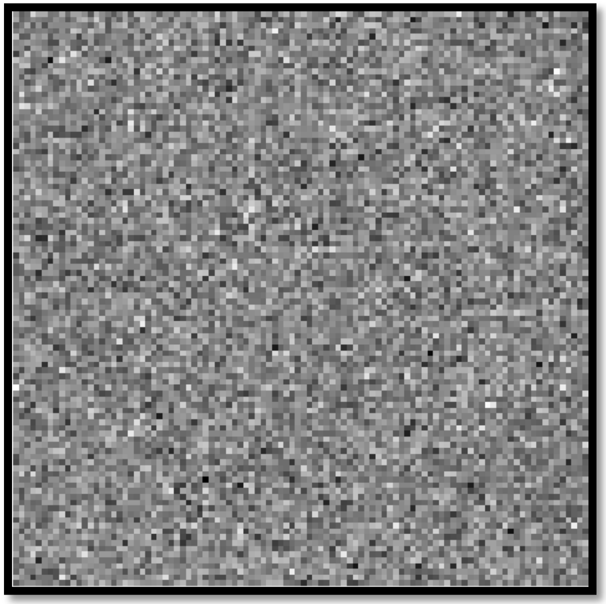
Therefore, to ensure a particular FWER choose:

$$\alpha = \frac{\alpha_{FWE}}{N}$$

This correction does not require the tests to be independent but becomes very stringent if dependence.

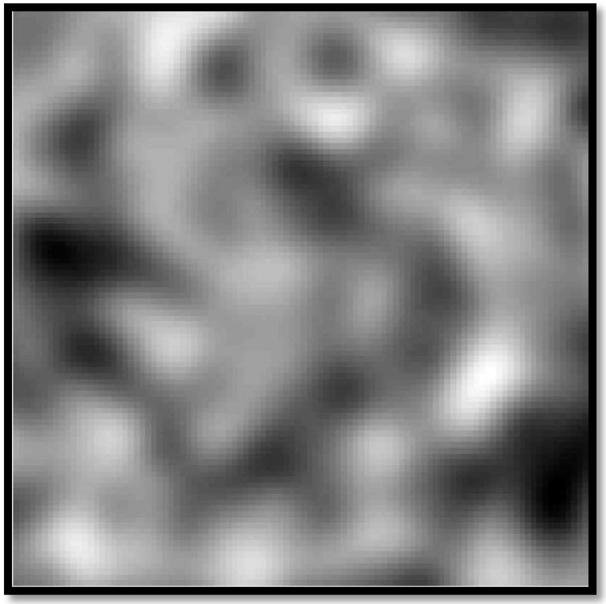
Spatial correlations

100 x 100 independent tests



Discrete data

Spatially correlated tests (FWHM=10)



Spatially extended data

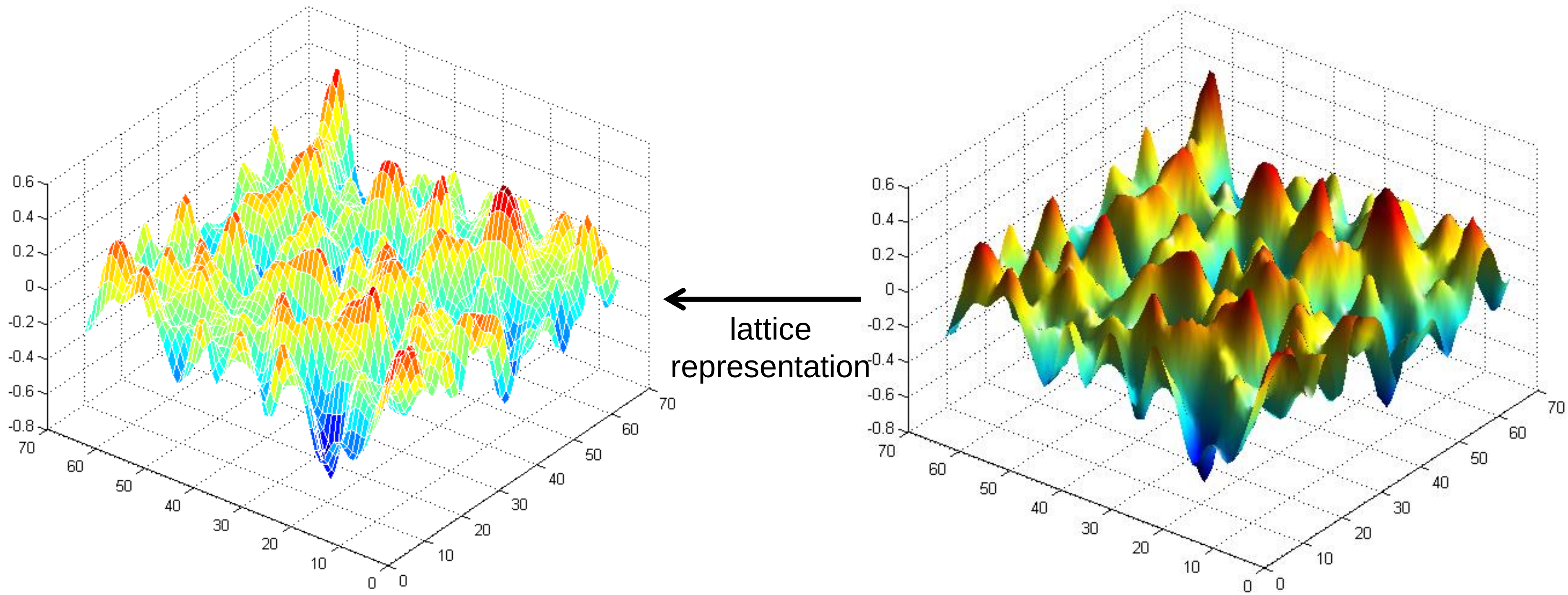
Bonferroni is too conservative for spatial correlated data.

10,000 voxels $\Rightarrow \alpha_{BONF} = \frac{0.05}{10{,}000} \Rightarrow u_c = 4.42$ (uncorrected $u = 1.64$)

Random Field Theory

⇒ Consider a statistic image as a discretisation of a continuous underlying random field.

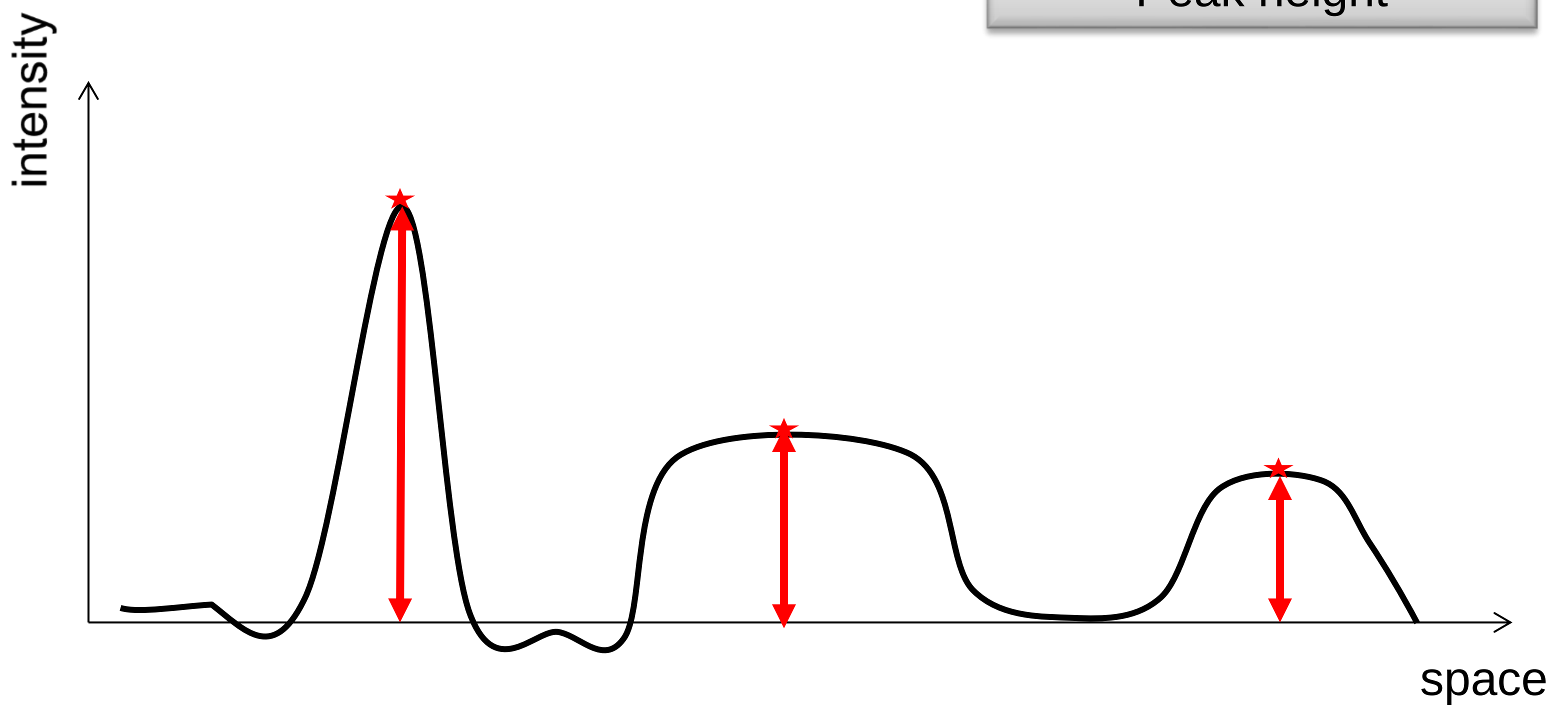
⇒ Use results from continuous **random field theory**.



Topological inference

Peak level inference

Topological feature:
Peak height



RFT and Euler Characteristic

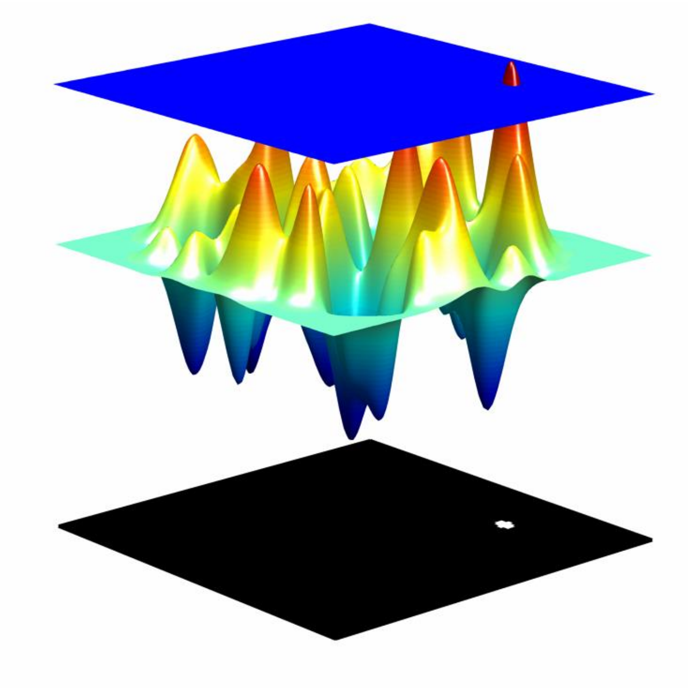
Euler Characteristic χ_u:

- Topological measure

  χ_u = # blobs - # holes

- at high threshold u:

  χ_u = # blobs



$$FWER = p(FWE) \approx E[\chi_u]$$

Expected Euler Characteristic

2D Gaussian Random Field

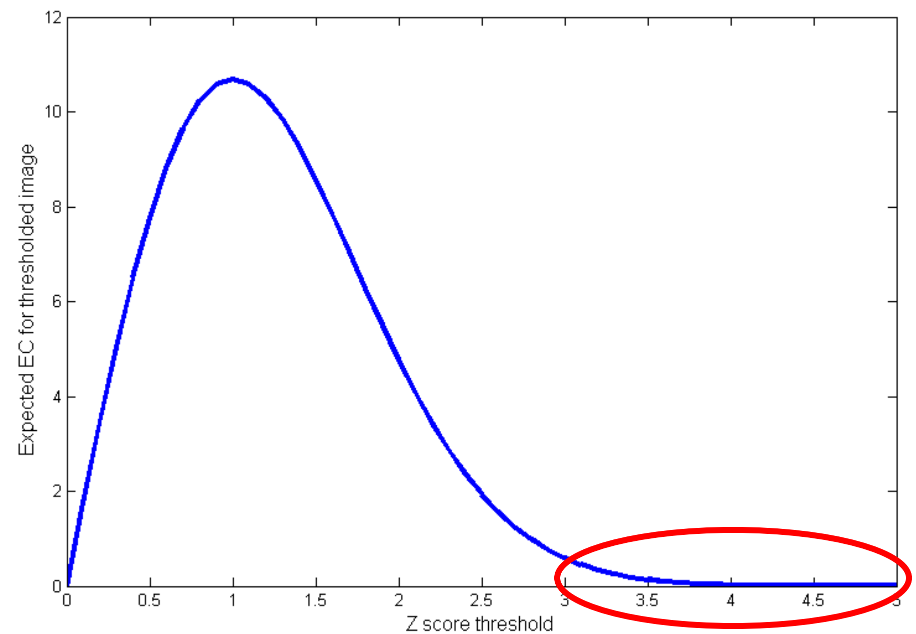
$$E[\chi_u] = \lambda(\Omega)|\Lambda|^{1/2}\, u \exp(-u^2/2)/(2\pi)^{3/2}$$

Search volume

Roughness (1/smoothness)

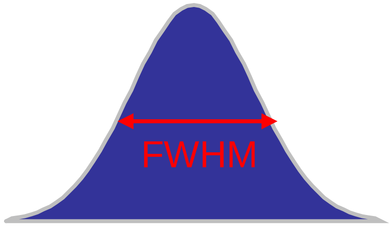
Threshold

100 x 100 Gaussian Random Field
with FWHM=10 smoothing
$\alpha_{FWE} = 0.05 \Rightarrow u_{RFT} = 3.8$
$(u_{BONF} = 4.42, u_{uncorr} = 1.64)$

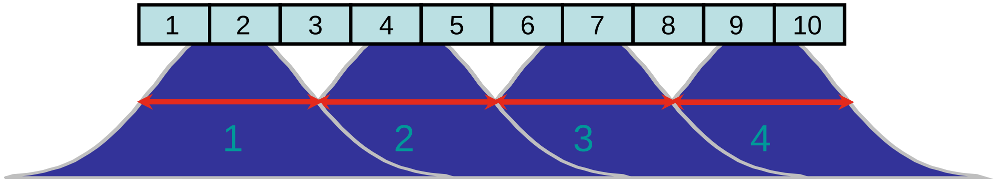


Smoothness

Smoothness parameterised in terms of FWHM:
Size of Gaussian kernel required to smooth i.i.d. noise to have same smoothness as observed null (standardized) data.



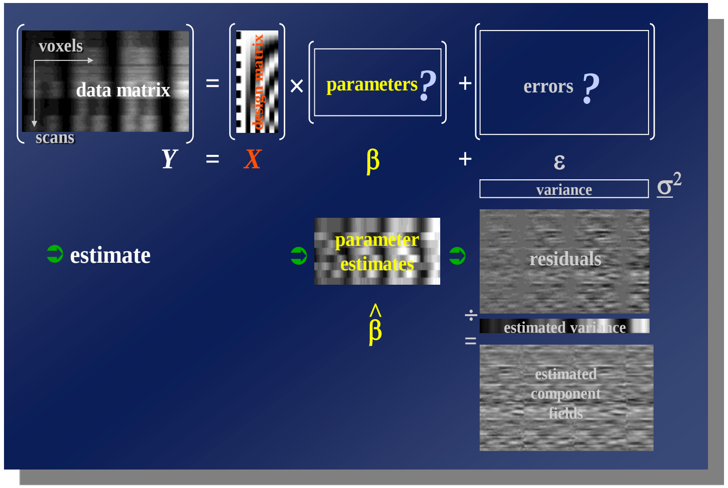
RESELS (Resolution Elements):
1 RESEL = $FWHM_x FWHM_y FWHM_z$
RESEL Count R = volume of search region in units of smoothness



Eg: 10 voxels, 2.5 FWHM, 4 RESELS

The number of resels is similar, but not identical to the number independent observations.

Smoothness estimated from spatial derivatives of standardised residuals:
Yields an RPV image containing local roughness estimation.



Random Field intuition

Corrected *p*-value for statistic value *t*

$$\begin{aligned} p_c &= p(\max T > t) \\ &\approx E[\chi_t] \\ &\propto \lambda(\Omega)|\Lambda|^{1/2}\, t \exp(-t^2/2) \end{aligned}$$

- Statistic value *t* increases ?
  - p_c decreases (better signal)
- Search volume increases ($\lambda(\Omega) \uparrow$) ?
  - p_c increases (more severe correction)
- Smoothness increases ($|\Lambda|^{1/2} \downarrow$) ?
  - p_c decreases (less severe correction)

Random Field: Unified Theory

General form for expected Euler characteristic

• t, F & χ^2 fields • restricted search regions • D dimensions •

$$E[\chi_u(\Omega)] = \sum_{d=0}^{D} R_d(\Omega)\rho_d(u)$$

$R_d(\Omega)$: d-dimensional Lipschitz-Killing curvatures of Ω ($\approx$ *intrinsic volumes*):

– *function of dimension,*
space Ω and smoothness:

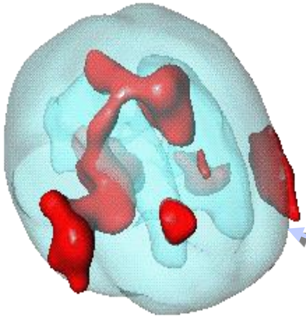
$R_0(\Omega) = \chi(\Omega)$ Euler characteristic of Ω
$R_1(\Omega)$ = resel diameter
$R_2(\Omega)$ = resel surface area
$R_3(\Omega)$ = resel volume

$\rho_d(u)$: d-dimensional EC density of the field

– *function of dimension and threshold,*
specific for RF type:

E.g. Gaussian RF:

$$\rho_0(u) = 1 - \Phi(u)$$
$$\rho_1(u) = (4 \ln 2)^{1/2} \exp(-u^2/2) / (2\pi)$$
$$\rho_2(u) = (4 \ln 2) \quad u \quad \exp(-u^2/2) / (2\pi)^{3/2}$$
$$\rho_3(u) = (4 \ln 2)^{3/2} \, (u^2 - 1) \quad \exp(-u^2/2) / (2\pi)^2$$
$$\rho_4(u) = (4 \ln 2)^2 \, (u^3 - 3u) \; \exp(-u^2/2) / (2\pi)^{5/2}$$

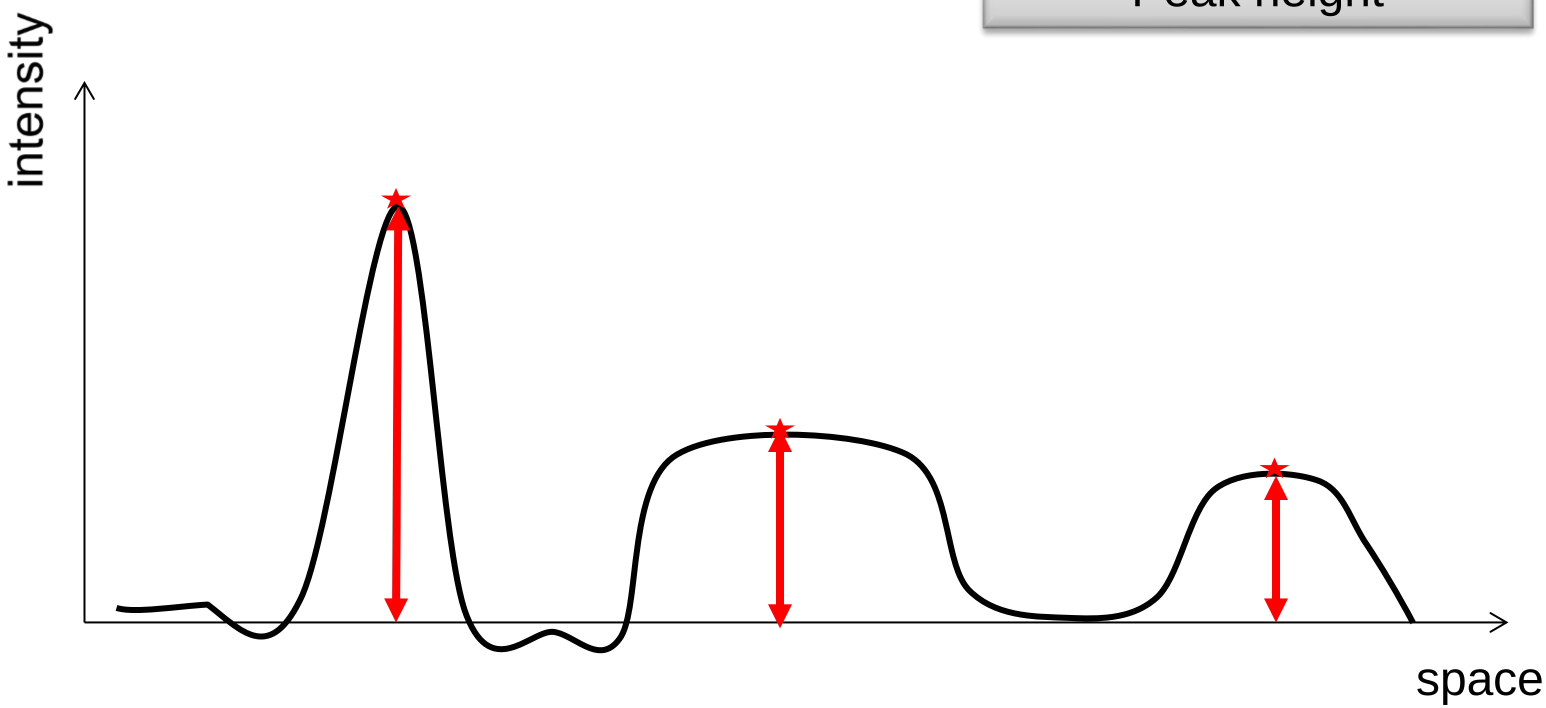


Ω

Topological inference

Peak level inference

Topological feature:
Peak height

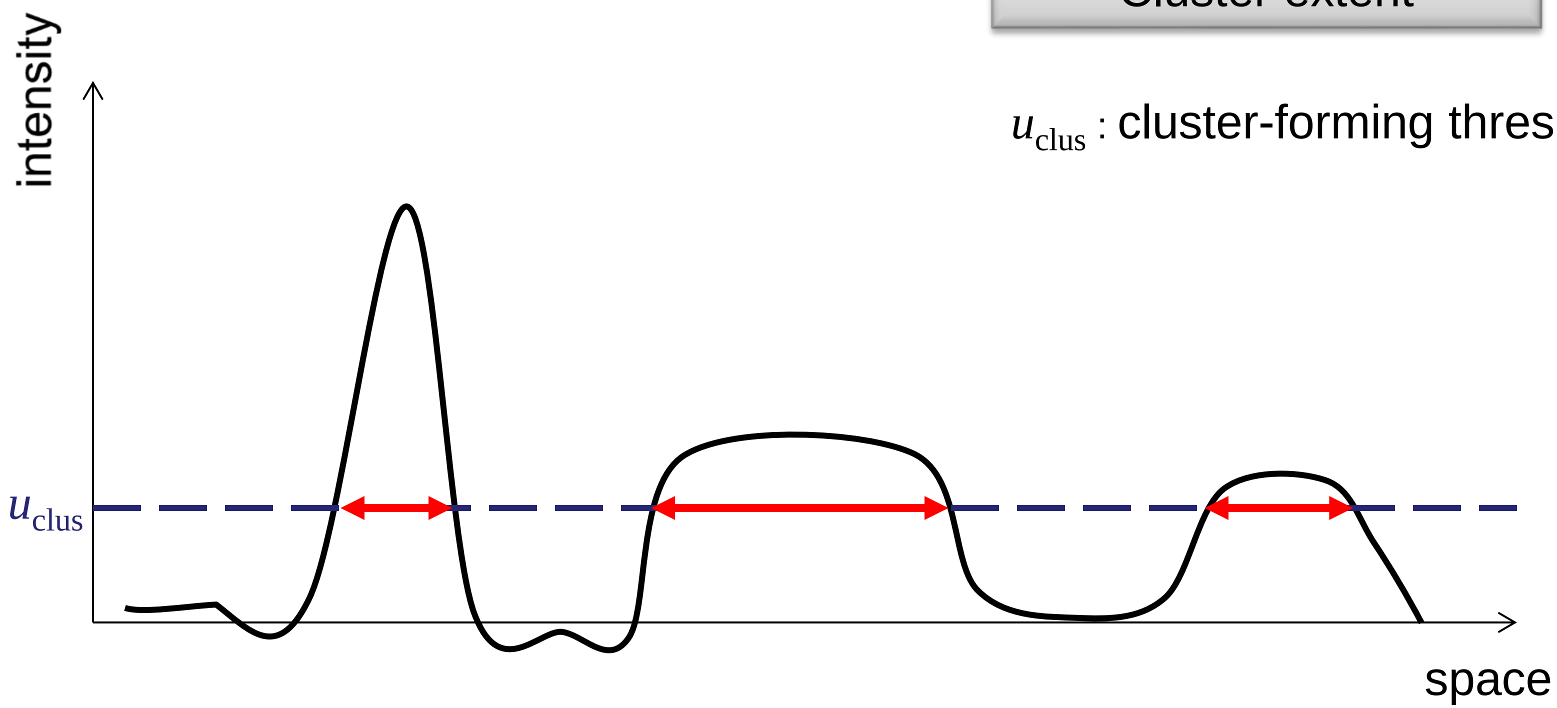


Topological inference

Cluster level inference

Topological feature:
Cluster extent

u_{clus} : cluster-forming threshold

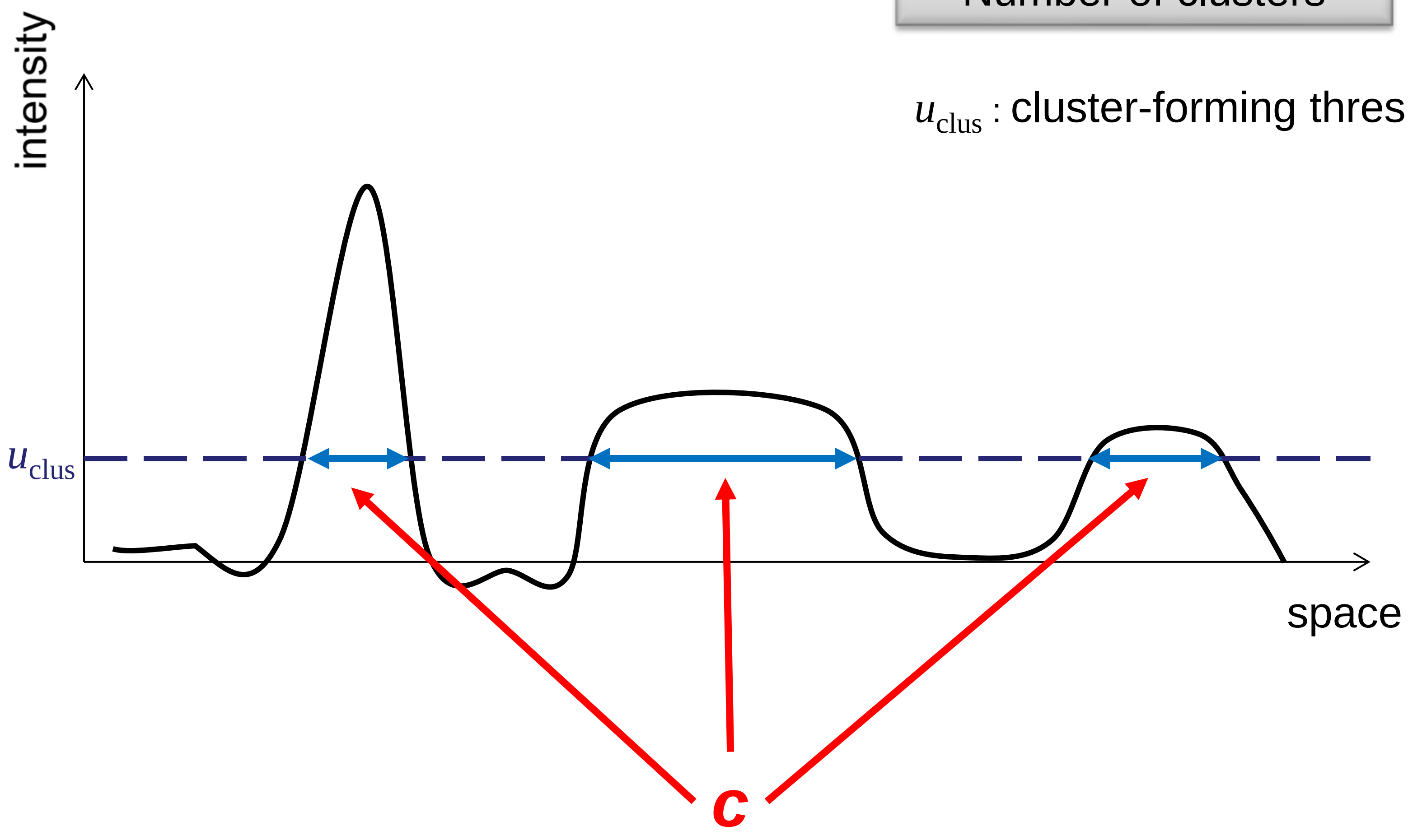


Topological inference

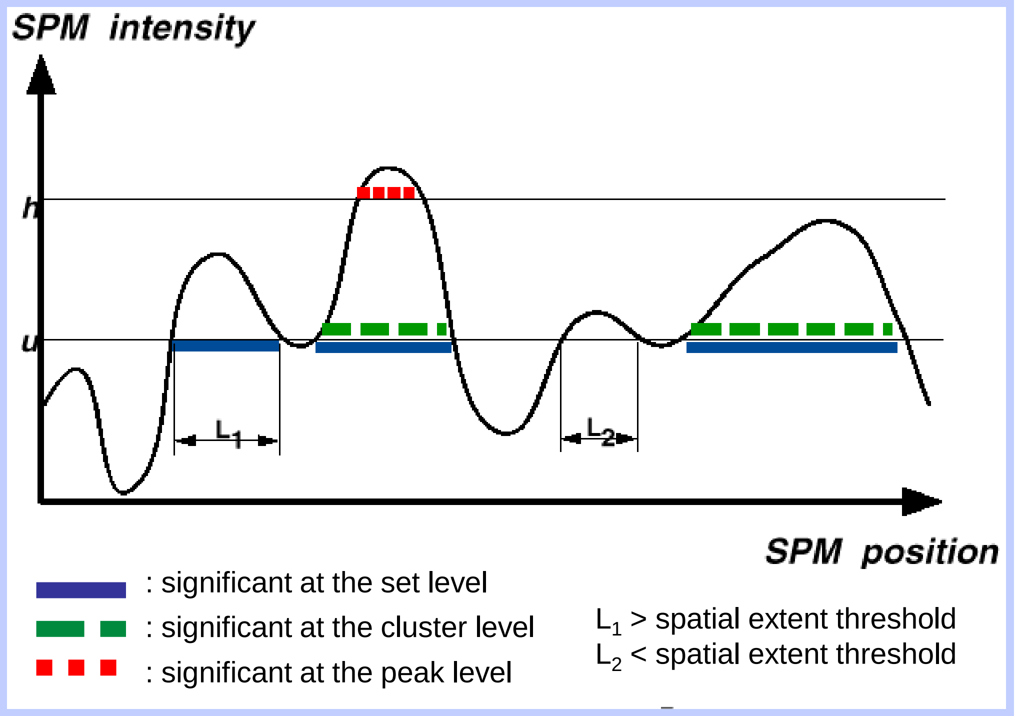
Set level inference

Topological feature:
Number of clusters

u_{clus} : cluster-forming threshold



Peak, cluster and set level inference



Sensitivity

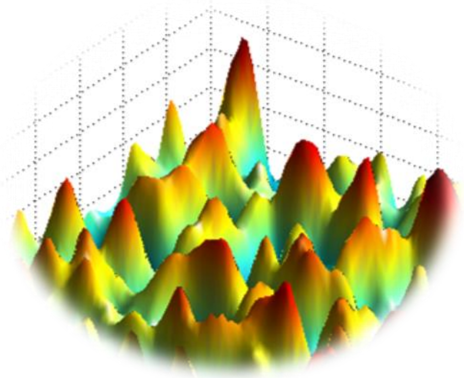
Regional specificity

Peak level test:
height of local maxima

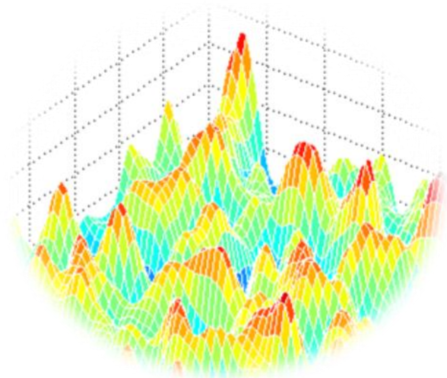
Cluster level test:
spatial extent above u

Set level test:
number of clusters above u

Random Field Theory Assumptions



- The statistic image is assumed to be a good lattice representation of an underlying random field with a multivariate Gaussian distribution.
- These fields are continuous, with an autocorrelation function twice differentiable at the origin.



- ⇨ The threshold chosen to define clusters is high enough such that the expected EC is a good approximation to the number of clusters.
- ⇨ The lattice approximation is reasonable, which implies the smoothness is relatively large compared to the voxel size.
- ⇨ The errors of the specified statistical model are normally distributed, which implies the model is not misspecified.

- Smoothness of the data is unknown and estimated:
  very precise estimate by pooling over voxels $\Rightarrow$ stationarity assumption.

Small Volume Correction

- If one has some *a priori* idea of where an activation should be, one can **prespecify a small search space** and make the appropriate correction instead of having to control for the entire search space

    - mask defined by (probabilistic) anatomical atlases
    - mask defined by separate "functional localisers"
    - mask defined by orthogonal contrasts
    - search volume around previously reported coordinates

With no prior hypothesis:

1. Test whole volume.
2. Identify SPM peak.
3. Then make a test assuming a single voxel.

Conclusion

- There is a ***multiple testing problem*** and *corrections* have to be applied on *p*-values (for the volume of interest only (see SVC)).

- Inference is made about ***topological features*** (peak height, spatial extent, number of clusters).
  Use results from the ***Random Field Theory***.

- **Control of *FWER*** (probability of a false positive anywhere in the image) for a space of any dimension and shape.

References

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