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FWER Correction

Family-Wise Error Rate

- The **family-wise error rate** (FWER) is the probability of making one or more Type I errors in a family of tests, under the null hypothesis.
- FWER controlling methods:
 - Bonferroni correction
 - Random Field Theory
 - Permutation Tests



Problem Formulation

- Let H_{0i} be the hypothesis that there is no activation in voxel i , where $i \in V = \{1, \dots, m\}$.
- Let T_i be the value of the test statistic at voxel i .
- The **family-wise null hypothesis**, H_0 , states that there is no activation in any of the m voxels.

$$H_0 = \bigcap_{i \in V} H_{0i}$$



- If we reject a **single** voxel null hypothesis, H_{0i} , we will reject the family-wise null hypothesis.
- A false positive at any voxel gives a **Family-Wise Error (FWE)**
- Assuming H_0 is true, we want the probability of falsely rejecting H_0 to be controlled by α , i.e.

$$P\left(\bigcup_{i \in V} \{T_i \geq u\} \mid H_0\right) \leq \alpha$$

Bonferroni Correction

- Choose the threshold so that

$$P(T_i \geq u | H_0) \leq \frac{\alpha}{m}$$

- Hence,

$$FWER = P\left(\bigcup_{i \in V} \{T_i \geq u\} | H_0\right)$$

$$\leq \sum_i P(T_i \geq u | H_0)$$

Boole's Inequality

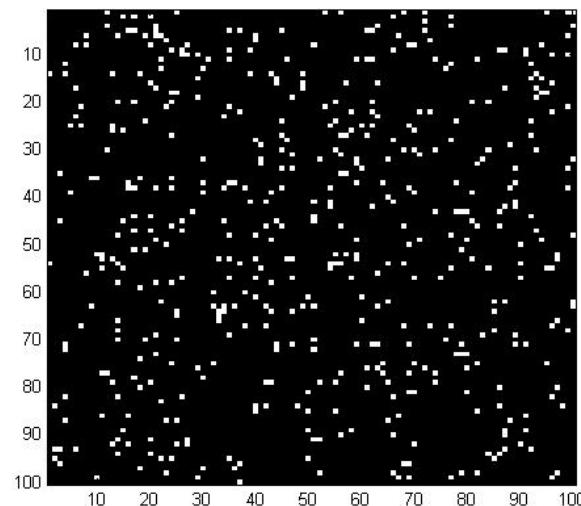
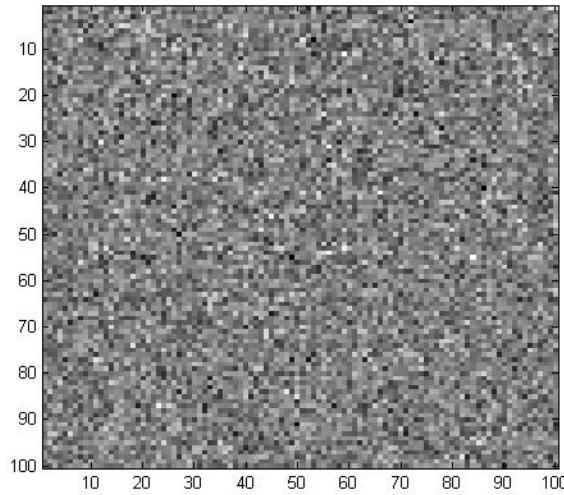
$$\leq \sum_i \frac{\alpha}{m} = \alpha$$



Example

Generate 100×100 voxels from an iid $N(0, 1)$ distribution

Threshold at $u=1.645$



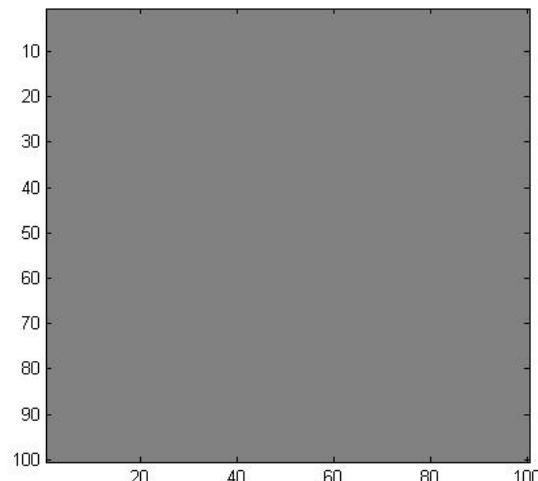
Approximately 500 false positives.



Example

To control for a FWE of 0.05, the [Bonferroni correction](#) is 0.05/10,000.

This corresponds to $u=4.42$.



No false positives

On average only 5 out of every 100 generated in this fashion will have one or more values above u .

Bonferroni Correction

- The Bonferroni correction is very **conservative**, i.e. it results in very strict significance levels.
- It decreases the power of the test (probability of correctly rejecting a false null hypothesis) and greatly increases the chance of false negatives.
- It is not optimal for correlated data, and most fMRI data has significant **spatial correlation**.



Spatial Correlation

- We may be able to choose a more appropriate threshold by using information about the spatial correlation in the data.
- Random field theory allows one to incorporate the correlation into the calculation of the appropriate threshold.
- It is based on approximating the distribution of the maximum statistic over the whole image.



Maximum Statistic

- Link between FWER and max statistic.

$$\text{FWER} = P(\text{FWE})$$

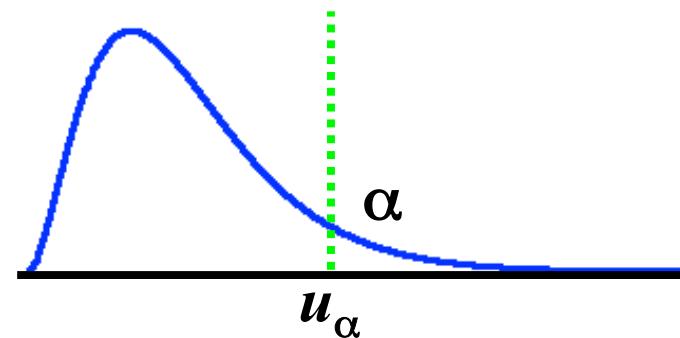
$$= P(\bigcup_i \{T_i \geq u\} \mid H_0)$$

$P(\text{any t-value exceeds } u \text{ under null})$

$$= P(\max_i T_i \geq u \mid H_0)$$

$P(\text{max t-value exceeds } u \text{ under null})$

Choose the threshold u
 such that the max only
 exceeds it $\alpha\%$ of the time



Random Field Theory

- A **random field** is a set of random variables defined at every point in D-dimensional space.
- A **Gaussian random field** has a Gaussian distribution at every point and every collection of points.
- A Gaussian random field is defined by its mean function and covariance function.



Random Field Theory

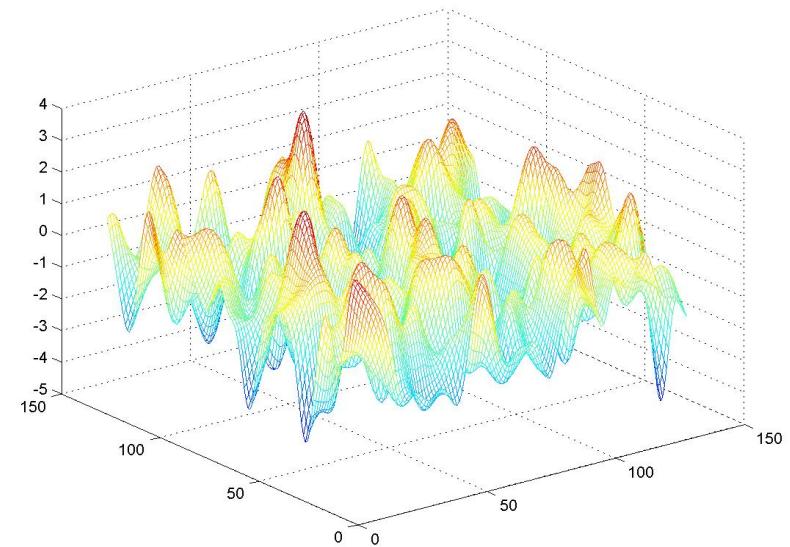
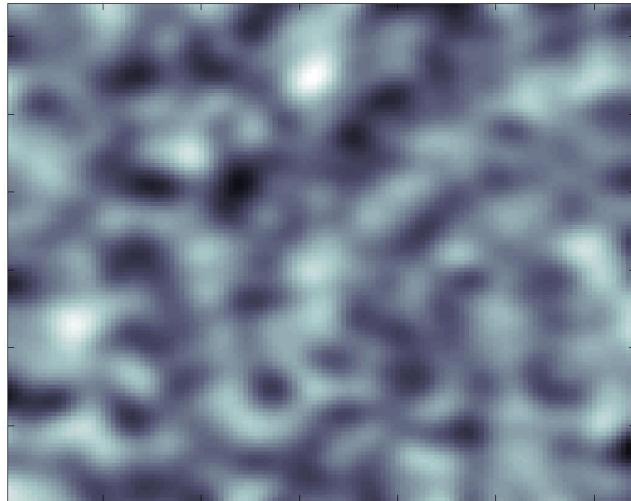
- Consider a statistical image to be a lattice representation of a **continuous random field**.
- Random field methods are able to:
 - approximate the **upper tail** of the maximum distribution, which is the part needed to find the appropriate thresholds; and
 - account for the spatial dependence in the data.

Random Field Theory

- Consider a random field $Z(s)$ defined on

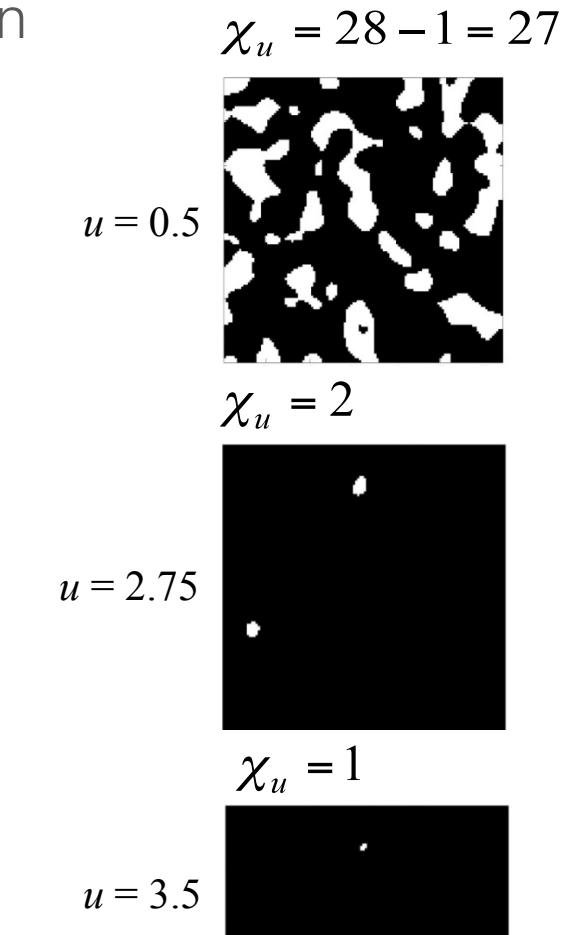
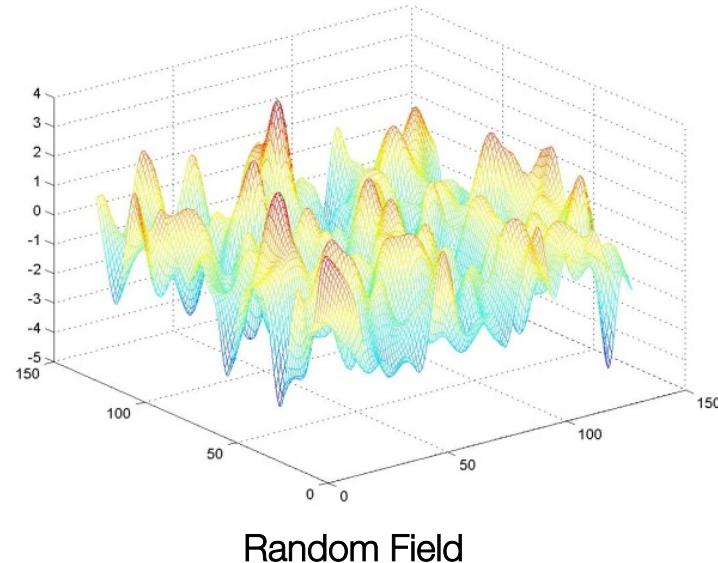
$$s \in \Omega \subset R^D$$

where D is the dimension of the process.



Euler Characteristic

- Euler Characteristic χ_u
 - A property of an image after it has been thresholded.
 - Counts #blobs - #holes
 - At high thresholds, just counts #blobs



Controlling the FWER

- Link between FWER and Euler Characteristic.

$$\text{FWER} = P(\max_i T_i \geq u \mid H_0)$$

$$= P(\text{One or more blobs} \mid H_0)$$

no holes exist

$$\approx P(\chi_u \geq 1 \mid H_0)$$

never more than 1 blob

$$\approx E(\chi_u \mid H_0)$$

- Closed form results exist for $E(\chi_u)$ for Z, t, F and χ^2 continuous random fields.

3D Gaussian Random Fields

- For large search regions:

$$E(\chi_u) \approx R(4 \log 2)^{3/2} (u^2 - 1) e^{-u^2/2} (2\pi)^{-2}$$

where

$$R = \frac{V}{FWHM_x FWHM_y FWHM_z}$$

- Here V is the volume of the search region and the full width at half maximum (FWHM) represents the smoothness of the image estimated from the data.

R = Resolution Element (Resel)



Controlling the FWER

- For large u :

$$FWER \approx R(4 \log 2)^{3/2} (u^2 - 1) e^{-u^2/2} (2\pi)^{-2}$$

where

$$R = \frac{V}{FWHM_x FWHM_y FWHM_z}$$

Properties:

- As u increases, FWER decreases (Note u large).
- As V increases, FWER increases.
- As smoothness increases, FWER decreases.



RFT Assumptions

- The entire image is either multivariate Gaussian or derived from multivariate Gaussian images.
- The statistical image must be sufficiently smooth to approximate a continuous random field.
 - FWHM at least twice the voxel size.
 - FWHM smoothness $3\text{-}4 \times$ voxel size is preferable.
- The amount of smoothness is assumed known.
 - Estimate is biased when images not sufficiently smooth.
- Several layers of approximations.

End of Module



@fMRIstats