Spatial Modeling: What do we want?

- We want to find the signal
  - ⇀ Where is it?
  - ⇀ How big is it?
- Explicit Model
  - ⇀ Each blob parameterized
    - – x,y,z location
    - – Volume
  - ⇀ Standard errors & confidence intervals on location, volume

Spatial Modeling: What do we get?

- Sorry
  - ⇀ While naive estimates available...
    - – Location of local maximum
    - – Volume above a threshold
  - ⇀ ... no standard errors, no inference
- What is available?
  - ⇀ Massively Univariate Modeling

Spatial Modeling: Massively Univariate Modeling

- Massively Univariate Models
  - ⇀ Fit temporal model at every voxel
    - – No information shared across space
  - ⇀ Create statistic at each voxel
    - – GLM & contrast
- How to threshold the statistic image?
  - ⇀ Usual $\alpha = 0.05$ threshold?
  - ⇀ Yields 5% false positive rate
  - ⇀ Yet we're performing 100,000 tests!
  - ⇀ Is 5,000 false positives OK?

Multiple Comparisons: Overview

- Multiple comparisons problem
  - ⇀ Usual threshold produces too many false positives
- What to control?
  - ⇀ Control *per-voxel* false positive rate
    - – That is, do nothing
  - ⇀ Control *FamilyWise false positive Error* rate (FWE)
    - – FWE one or more false positives, anywhere
    - – FWER is chance of getting *any* false positive
- Adjust threshold to control FWER
- Other false positive measure
  - ⇀ *False Discovery Rate* (FDR)

Multiple Comparisons: FWER-Controlling Methods

- Bonferroni
  - ⇀ An old friend, but stingy
- Random Field Theory
  - ⇀ Hi tech, Hi maintenance
- Nonparametric Permutation Test
  - ⇀ Lo tech, trustyworthy

MCP: Bonferroni

- Usual approach to MCP
- Use α/S as critical value instead of α
  - ⇀ S = Number of tests
- Controls FWER
  - ⇀ But is conservative, especially for (spatially) correlated data

MCP: FWE & Maximum Statistic

- Important connection between FWE & Maximum

$$\begin{aligned} \mathsf{P}(FWE) &= \mathsf{P}(\cup_i \{T_i > u\} | \mathcal{H}_0) \\ &= \mathsf{P}(\text{One or more voxels} > u | \mathcal{H}_0) \\ &= \mathsf{P}(\text{Maximum is above threshold } u | \mathcal{H}_0) \end{aligned}$$

- Distribution of maximum is key
  - ⇀ Just as 95%ile of null dist^n gives 5% α threshold, 95%ile of null max dist^n gives 5% α *FWE-controlling* threshold!

D:Nrm;Mx

MCP: FWE & Maximum Statistic

- If we can find the distribution for the max statistic we're done!
- Two approaches
  - ⇀ Random field theory
  - ⇀ Nonparametric permutation

RFT: That spells Random Field Theory

- Random Field is statistical process
  - ⇀ Ocean surface
  - ⇀ Temperature map of USA
  - ⇀ A fMRI statistic image
- Rich theory available for continuous random fields

RFT: Getting at the Max with the Euler Characteristic

- Euler (say "oiler") Characteristic (EC)
  - ⇀ Take continuous random field
  - ⇀ Threshold it at level u
  - ⇀ EC = #blobs - #holes

N:Wor92

- At high thresholds, no holes
  - ⇀ EC then just counts blobs
- At very high thresholds
  - ⇀ EC is just zero or one
  - ⇀ Either one or no blobs

RFT: Getting at the Max with the Euler Characteristic

- Expected EC
  - ⇀ Mean or average
  - ⇀ By definition

$$\mathsf{E}(EC) = \sum_k k\mathsf{P}(EC = k)$$

- For high thresholds, expected EC is just what we want!

$$\begin{aligned} \mathsf{E}(EC) &= \sum_k k\mathsf{P}(EC = k) \\ &= 0\mathsf{P}(EC = 0) + 1\mathsf{P}(EC = 1) + 2\mathsf{P}(EC = 2) + \cdots \\ &\approx \mathsf{P}(EC = 1) \\ &= \mathsf{P}(\text{“Maximum is above threshold } u\text{”}) \end{aligned}$$

- The expected EC approximates the max dist^n

RFT: Getting at the Max with the Euler Characteristic

- So we can obtain p-values using
  - ⇀ $\mathsf{P}\{\max_{i=1}^{S} T_i > u\} \approx \mathsf{E}(EC_u)$
- Expected EC formula for Gaussian random field
  - ⇀

$$\mathsf{E}(EC_u) = (\text{RESELs})(u^2 - 1)\exp(-u^2/2)/(2\pi)^2(4\log(2))^{3/2}$$

  - ⇀ Where
    - u is the threshold
    - RESELs is the RESolution ELement
- RESEL is search volume in units of resolution

RFT: RESELs

- Smoothness described in terms of FHWM
  - ⇀ FWHM = Full Width at Half Maximum D:fwhm
- RESEL formula

$$\text{RESEL} = \frac{S}{f_x f_y f_z}$$

  - ⇀ Where
    - S is search volume, in mm^3
    - f_x, f_y, f_z is FWHM smoothness in mm in x, y, & z

RFT: Intuition

- Get a feel for corrected p-values!
- Say I observe a statistic with value u

$$\mathsf{P}\{\max_{i=1}^{S} T_i > u\} \approx \mathsf{E}(EC_u) = (\text{RESELs})(u^2-1)exp(-u^2/2)\cdots$$

All other things equal...

- ... as u increases
  - ⇀ Corrected p-values go ____, i.e. ____ significance
    - – Hint: As u gets higher, can ignore u^2 term
- ... as number of RESELS increases
  - ⇀ Corrected p-values go ____, i.e. ____ significance

RFT: Intuition

$$\mathsf{P}\{\max_{i=1}^{S} T_i > u\} \approx \mathsf{E}(EC_u) = (\text{RESELs})(u^2-1)exp(-u^2/2)\cdots$$

- ... as search volume S increases
  - ⇀ Corrected p-values go ____, i.e. ____ significance
  - ⇀ Remember RESEL $= \frac{S}{f_x f_y f_z}$
- ... as resolution f increases
  - ⇀ Corrected p-values go ____, i.e. ____ significance
  - ⇀ Remember RESEL $= \frac{S}{f_x f_y f_z}$
  - ⇀ Remember resolution is measured in FHWM, so bigger f means [sharper | fuzzier] statistic images

RFT: Assumptions

- Raw image data are multivariate Gaussian
  - ⇀ Can check Normality at each voxel
  - ⇀ Impossible to check multivariate Normality for every pair of voxels
- Smoothness
  - ⇀ Images are sufficiently smooth to approximate continuous field
    - – Rule of thumb: FWHM 2-3 times voxel size
  - ⇀ Insufficient smoothness results in
    - – Conservative voxel-wise p-values
    - – Liberal cluster-size p-values

RFT: Assumptions

- Stationarity
  - ⇀ Smoothness the same *everywhere*
  - ⇀ Assumption needed for cluster size p-values
  - ⇀ *Not* needed for voxel size p-values

Spatial Inference: SPM

- The following slides are addendum to the SPM intro slides

Spatial Inference: “Scopes of Inference”

- SPM’s framework on inference
- Define Clusters
  - ⇀ Use intensity *and* cluster size threshold
- Consider 4 “levels”
  - ⇀ Average, Set, Cluster, & Voxel
- Each has successively greater spatial specificity
  - ⇀ Though successively less sensitivity

Spatial Inference: “Scopes of Inference”

- Average
  - ⇀ Assesses $\bar{F}$, average of F image
  - ⇀ Small p-value rejects $\mathcal{H}_0$: No activation anywhere
    - – No localization power
- Set
  - ⇀ Assesses c, number of clusters
    - – Given intensity & cluster size threshold
  - ⇀ Small p-value rejects $\mathcal{H}_0$: No activation anywhere
    - – No localization power

Spatial Inference: “Scopes of Inference”

- Cluster
  - ⇀ Assesses k, number of voxels in a cluster
    - – Given intensity threshold
  - ⇀ Small p-value rejects $\mathcal{H}_0$: No activation in cluster
    - – Localization to blob
    - – However, can’t point to particular voxel
- Voxel
  - ⇀ Assesses z or t or F statistic at a voxel
  - ⇀ Small p-value rejects $\mathcal{H}_0$: No activation here
    - – Localization to precise voxel

Spatial Inference: SPM

- Important to understand each component of SPM p-value results page
- Top
  - ⇀ Interactive MIP
    - – Drag & Drop to move
    - – Right click to get menu
  - ⇀ Interactive Design Matrix
    - – Click to get values
- Middle
  - ⇀ Interactive table of corrected & uncorrected p-values
    - – Click on x,y,z to move cursor
    - – Click on number to show it in Matlab window
    - – Right click in margin to get menu

Spatial Inference: SPM

- Bottom
  - ⇀ Details on results
  - ⇀ Key key key!
    - – Smoothness must be $>\approx$ 2-3 voxel size
    - – This is needed for

      ______________________ to be valid

Spatial Inference: SPM etc

- `SPM.mat`
  - ⇀ Contains essentials of fitted model results
  - ⇀ Design matrix, number of voxels, etc
- `SPMcfg.mat`
  - ⇀ “SPM Configuration file”
  - ⇀ Input to ‘Estimate’ button
  - ⇀ Specifies everything necessary to fit a model

Spatial Inference: SPM etc

- `SPM_fMRIDesMtx.mat`
  - ⇀ Specification of fMRI design
  - ⇀ Does *not* contain any filenames
  - ⇀ If identical design is used, can copy these into other analysis directories
  - ⇀ For example
    - – I could have created one `SPM_fMRIDesMtx.mat` that the whole class could use, since all of our subject's had identical paradigms
- “Explore Design button works with any of these.