Detecting Changes In Non-stationary Images via Statistical Flattening

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Problem

Random field theory for P-values of local maxima[1] and spatial extent[2] is not valid for non-stationary data, i.e. spatially varying FWHM

√ **OK for PET or smoothed fMRI**

× **not OK for anatomical changes via smoothed masks, GM or WM density[3], 2D surface displacements[4] or 3D warps[5]**

× **not OK for PET or fMRI projected onto a flattened or unfolded cortical surface[6,7].**

Example – 2D surface displacements

Outer cortical surfaces were extracted on $n = 151$ normal subjects[4]. As an illustration, the usual two-sample T statistic was calculated to test for a difference in cortical surface displacement between males and females:

Estimating local effective FWHM

The local *effective* FWHM ($eFWHM$) was calculated from the residuals of a linear model fitted to data at each point:

$$\text{Linear Model}: \quad Y_i = \mathbf{x}_i\mathbf{b} + e_i, \quad i = 1,\ldots,n$$

$$\text{Residuals}: \quad r_i = Y_i - \mathbf{x}_i\hat{\mathbf{b}}$$

$$\text{Normalised residuals}: \quad u_i = r_i/\sqrt{\Sigma_i r_i^2}$$

$$\text{Roughness}: \quad \Lambda = \text{Var}(\hat{\mathbf{e}}_i)/\text{Var}(e_i)$$

$$\text{Estimate}: \quad \hat{\Lambda} = \Sigma_i \hat{\mathbf{u}}_i\hat{\mathbf{u}}_i'$$

$$\text{Effective FWHM}: \quad eFWHM = (4\log 2)^{\frac{1}{2}}/|\hat{\Lambda}|^{\frac{1}{2D}}$$

If the image is stationary or 'flat' then $eFWHM$ should be constant; departures from this indicate non-stationarity:

Approximate statistical flattening via local multidimensional scaling

Can we find a warping that 'flattens' the data to stationarity, i.e. constant $eFWHM$?

$$\text{Original space}: \; eFWHM \text{ varies} \quad \begin{pmatrix} x \\ y \\ z \end{pmatrix} \overset{?}{\Longrightarrow} \begin{pmatrix} s_1 \\ s_2 \\ s_3 \end{pmatrix} \quad \text{Isotropic space}: \; eFWHM \approx \text{flat}$$

$$\text{Answer}: \text{Set } \frac{\textit{new edge length}}{\textit{old edge length}} \approx \frac{1}{eFWHM}$$

We can then apply the usual random field theory to the 'flattened' data:

P-value for local maxima[1]

$$\mathrm{P}\left(\max_{\textit{region}} T > t\right) \approx \sum_{d=0}^{D} \text{Resels}_d(\textit{region})\,\text{EC density}_d(t)$$

For D=3 dimensions:

$$\begin{aligned} \text{Resels}_0(\textit{region}) &= \textit{Euler characteristic} \\ \text{Resels}_1(\textit{region}) &= 2\,\textit{Caliper Diameter}/FWHM \\ \text{Resels}_2(\textit{region}) &= \tfrac{1}{2}\,\textit{Surface Area}/FWHM^2 \\ \text{Resels}_3(\textit{region}) &= \textit{Volume}/FWHM^3 \end{aligned}$$

For a T image with ν degrees of freedom:

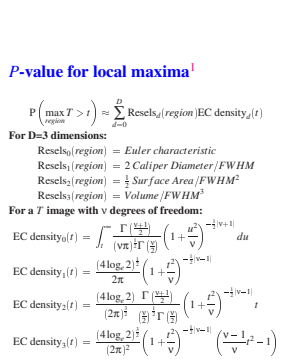
$$\text{EC density}_0(t) = \int_t^\infty \frac{\Gamma\left(\frac{\nu+1}{2}\right)}{(\nu\pi)^{\frac{1}{2}}\Gamma\left(\frac{\nu}{2}\right)}\left(1+\frac{u^2}{\nu}\right)^{-\frac{1}{2}(\nu+1)} du$$

$$\text{EC density}_1(t) = \frac{(4\log_e 2)^{\frac{1}{2}}}{2\pi}\left(1+\frac{t^2}{\nu}\right)^{-\frac{1}{2}(\nu-1)}$$

$$\text{EC density}_2(t) = \frac{(4\log_e 2)}{(2\pi)^{\frac{3}{2}}}\frac{\Gamma\left(\frac{\nu+1}{2}\right)}{\left(\frac{\nu}{2}\right)^{\frac{1}{2}}\Gamma\left(\frac{\nu}{2}\right)}\left(1+\frac{t^2}{\nu}\right)^{-\frac{1}{2}(\nu-1)} t$$

$$\text{EC density}_3(t) = \frac{(4\log_e 2)^{\frac{3}{2}}}{(2\pi)^2}\left(1+\frac{t^2}{\nu}\right)^{-\frac{1}{2}(\nu-1)}\left(\frac{\nu-1}{\nu}t^2-1\right)$$

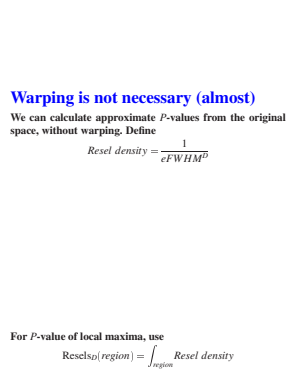
For this data:



Warped back to the original space:

P-value for cluster size

Provided the warped space is reasonably flat locally, we can apply the usual theory for P-values of cluster sizes[2]. For $T > 3$, the approximate critical cluster size ($P < 0.05$) is the size of the intersection of the balls with the warped space:



Warping is not necessary (almost)

We can calculate approximate P-values from the original space, without warping. Define

$$\textit{Resel density} = \frac{1}{eFWHM^D}$$

For P-value of local maxima, use

$$\text{Resels}_D(\textit{region}) = \int_{\textit{region}} \textit{Resel density}$$

For size or spatial extent of clustered voxels, use

$$\text{Resels}_D(\textit{cluster}) = \int_{T>u} \textit{Resel density}$$

Usual theory applies if the manifold is reasonably flat locally (need a correction for random distribution of $eFWHM$).

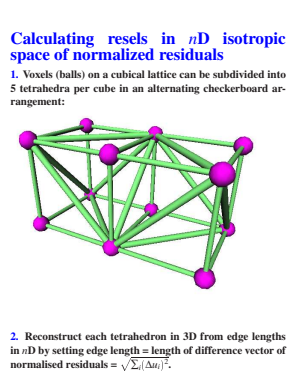
Exact statistical flattening in nD

The P-value for local maxima also works for D-dimensional manifolds embedded in a larger dimensional space, so we could warp into more dimensions to improve isotropy or statistical flatness. In fact, exact isotropy can be achieved in as many dimensions as images:

$$\text{Original space}: \; eFWHM \text{ varies} \quad \begin{pmatrix} x \\ y \\ z \end{pmatrix} \Longrightarrow \begin{pmatrix} u_1 \\ u_2 \\ \vdots \\ u_n \end{pmatrix} \quad \text{Space of normalized residuals}: \; eFWHM \text{ is flat}$$

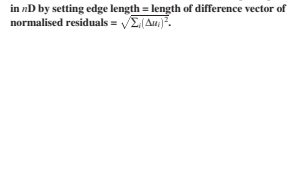
$$\text{Reason}: \frac{\textit{new edge length}}{\textit{old edge length}} = \frac{1}{eFWHM}$$

Illustration with $n = 3$:



Calculating resels in nD isotropic space of normalized residuals

1. Voxels (balls) on a cubical lattice can be subdivided into 5 tetrahedra per cube in an alternating checkerboard arrangement:



2. Reconstruct each tetrahedron in 3D from edge lengths in nD by setting edge length = length of difference vector of normalised residuals = $\sqrt{\Sigma_i(\Delta u_i)^2}$.

3. Calculate resels for all edges, triangles and tetrahedra:

$$\begin{aligned} \text{Resels}_1(\textit{edge}) &= \textit{Length} \\ \text{Resels}_1(\textit{triangle}) &= \tfrac{1}{2}\,\textit{Perimeter length} \\ \text{Resels}_2(\textit{triangle}) &= \textit{Area} \\ \text{Resels}_1(\textit{tetrahedron}) &= 2\,\textit{Caliper diameter} \\ &= \textstyle\sum \textit{edge length} \times \textit{angular deficiency}/(2\pi) \\ \text{Resels}_2(\textit{tetrahedron}) &= \tfrac{1}{2}\,\textit{Surface area} \\ \text{Resels}_3(\textit{tetrahedron}) &= \textit{Volume} \end{aligned}$$

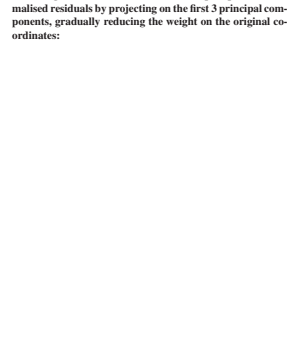
4. Combine resels of edges, triangles, tetrahedra in region:

$$\begin{aligned} \text{Resels}_0(\textit{region}) &= \#\textit{points} - \#\textit{edges} + \#\textit{triangles} \\ &\quad - \#\textit{tetrahedra} \\ \text{Resels}_1(\textit{region}) &= \textstyle\sum \text{Resels}_1(\textit{edges}) - \sum \text{Resels}_1(\textit{triangles}) \\ &\quad + \textstyle\sum \text{Resels}_1(\textit{tetrahedra}) \\ \text{Resels}_2(\textit{region}) &= \textstyle\sum \text{Resels}_2(\textit{triangles}) \\ &\quad - \textstyle\sum \text{Resels}_2(\textit{tetrahedra}) \\ \text{Resels}_3(\textit{region}) &= \textstyle\sum \text{Resels}_3(\textit{tetrahedra}) \end{aligned}$$

5. Use these resels to get the P-value for local maxima.

Visualizing the nD isotropic space

We can get an idea of the 151-D isotropic space of normalised residuals by projecting on the first 3 principal components, gradually reducing the weight on the original coordinates:



Conclusions

- **This method can be applied to any smooth image data**
- **Does not depend on whether the data is on a sphere, ellipsoid, smoothed cortex, flatmap, banana ...**
- **Original coordinates are not used, only the *connectivity***
- **Adding cuts changes connectivity, increasing resels, increasing P-value, so cuts should be avoided**
- **Only requirement is that *there exists* a higher dimensional space in which the data is isotropic**
- **BUT we don't actually have to find this space.**
- **Previous methods[1,2] which assume the data is stationary on a cubical lattice give P-values for local maxima that are approximately correct for large regions, but P-values for cluster sizes can be biased**

References

1. **Worsley KJ, Marrett S, Neelin P, Vandal AC, Friston KJ, Evans AC (1996). *Hum. Brain Map.*, 4:58-73.**
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4. **MacDonald D, Avis D, Evans AC (1996). *NeuroImage*, 7:S703.**
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