Accurate voxelwise FWER control in fMRI using Random Field Theory

Samuel Davenport, Armin Schwartzman, Thomas E. Nichols and Fabian Telschow

University of California, San Diego

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Performance of Traditional RFT

In 2016 (Eklund, Nichols, & Knutsson, 2016) showed that clusterwise RFT had massively inflated false positive rates. However they actually showed that the opposite held true for voxelwise RFT.

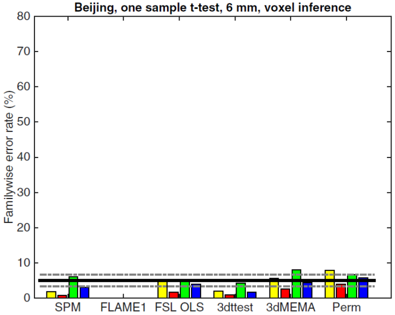


Figure 1: (Eklund et al., 2016) Figure 1c: voxelwise RFT is conservative.

Also observed in (Worsley, 2005) in simulations.

Good Lattice Assumption

Given a test-statistic T_L on the lattice $\mathcal{L}$, suppose that a random field T exists on a set S such that for all v, $T(v) = T_L(v)$ then

$$\max_{l \in \mathcal{L}} T_L(l) = \max_{l \in \mathcal{L}} T(l) < \sup_{s \in S} T(s).$$

Thus for any threshold u

$$\mathbb{P}(\max_{l \in \mathcal{L}} T_L(l) > u) < \mathbb{P}(\max_{l \in \mathcal{L}} T(l) > u)$$

so choosing thresholds for T_L based on T leads to conservativeness.

Assumptions of traditional RFT in SPM

- Good Lattice Assumption (i.e smoothness)
- Stationarity (needed for LKC calculation)
- Gaussianity (questionable validity in fMRI)

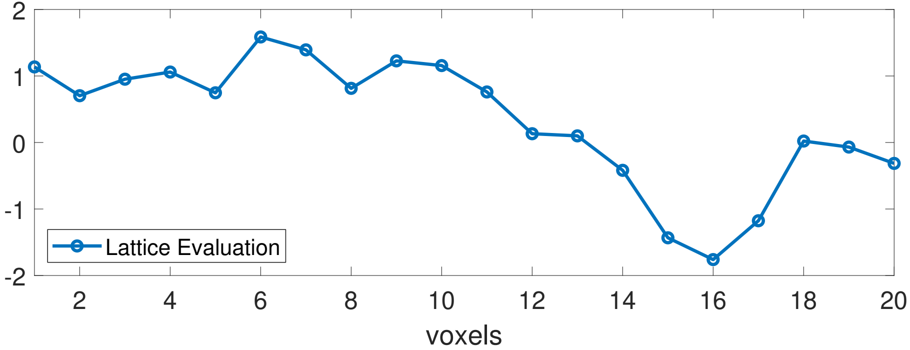
We will show that the good lattice assumption and stationarity can be dropped. We shall show that the assumption of Gaussianity of the underlying fields can be reduced by applying a transformation that accelerates the convergence of the Central Limit Theorem.

Lattice smoothing

To understand how smoothing works in fMRI, let $X(l)$ be random at every point l of a lattice $\mathcal{L}$. Then smoothing X with a kernel K gives

$$Y(v) = \sum_{l \in \mathcal{L}} K(v-l)X(l)$$

at every voxel $v \in \mathcal{L}$. Y is plotted below.

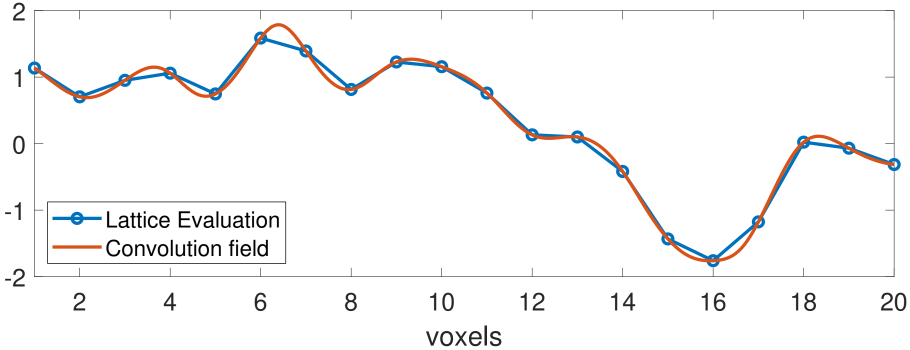


Convolution Random Fields

Definition

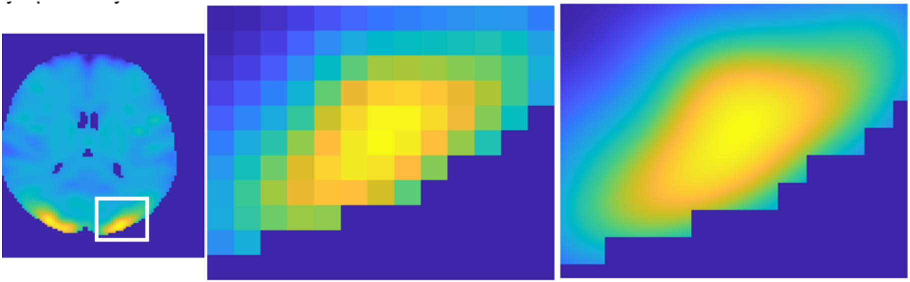
Given random data X on a lattice $\mathcal{L} \subset \mathbb{R}^D$ for $s \in \mathbb{R}^D$ and some kernel K, define the convolution field $Y : \mathbb{R}^D \to \mathbb{R}$, s.t. for all $s \in S$,

$$Y(s) := (K \star X)(s) = \sum_{l \in \mathcal{L}} K(s-l)X(l).$$



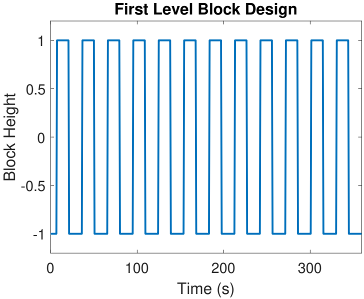
Convolution Fields in Brain Imaging

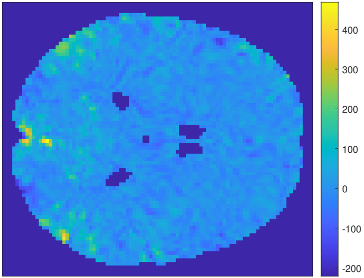
Taking slices through a 3D convolution field generated from brain imaging data, you get the following images!



Resting State Validation

We processed data from 7000 subjects from the UK biobank. Each subject has a time series of 490 images. Combine these into one contrast image using a block design at each voxel.





The results is 7000 contrast images (one for each subject). These have mean zero by construction as we randomized the blocks.

Resting state LKCs

We can estimate the true EEC distribution using the resting state data. For $j = 1, \ldots, 5000$ we draw $N = 10, 20, 50$ subjects with replacement and compute

$$u \mapsto \frac{1}{5000} \sum_{j=1}^{5000} \chi(\mathcal{A}_u(T_{j,N})).$$

were $T_{j,N}$ is the jth test-statistic based on the N random subsamples. We compare this to 3 EEC estimation approaches:

- Using non-stationary LKCs adapted to convolution fields (based on (Telschow & Davenport, 2023) and (Adler & Taylor, 2007))
- Two stationary approaches: Kiebel and Forman.

For other comparisons see (Telschow & Davenport, 2023).

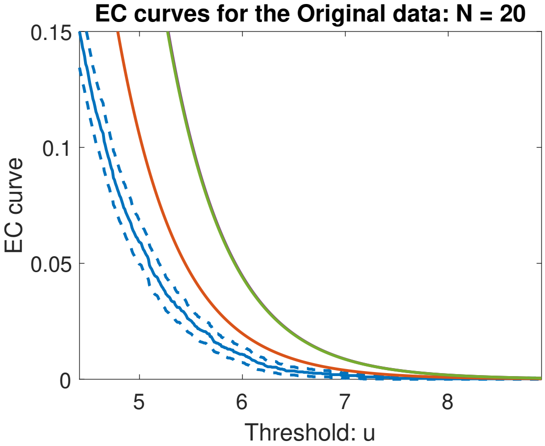
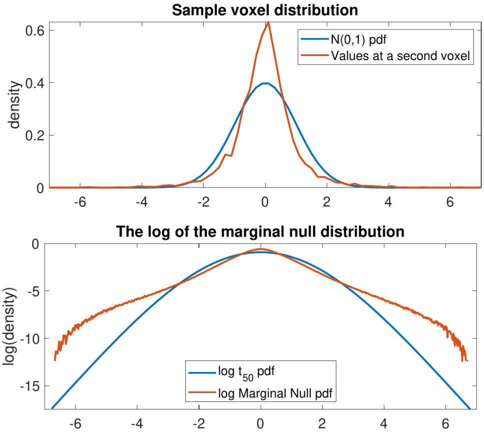


Figure 2: Blue: resting estimate EEC + 95% uncertainty, Red: SuRF LKC approximation. Green: Stationary LKC estimates (Kiebel + Forman).

Why doesn't it work? - fMRI data is highly non-Gaussian

Well the crucial and really only assumption left (as smoothness is no longer necessary nor is stationarity) is Gaussianity.



Gaussianized SuRFs

We estimate the marginal null distribution of the data Ψ_v from the data and use the transformation

$$X_n^G(v) = \Phi^{-1}\hat{\Psi}_v(X_n(v)).$$

For details see (Davenport, Schwarzman, Nichols, & Telschow, 2023). From these we can calculate the Gaussianized convolution fields

$$Y_n^G(s) = \sum_{v \in \mathcal{L}} K(s-v) X_n^G(v) \tag{1}$$

and generate corresponding t-fields in order to perform FWER inference.

Expected Euler characteristic curve - Gaussianized data

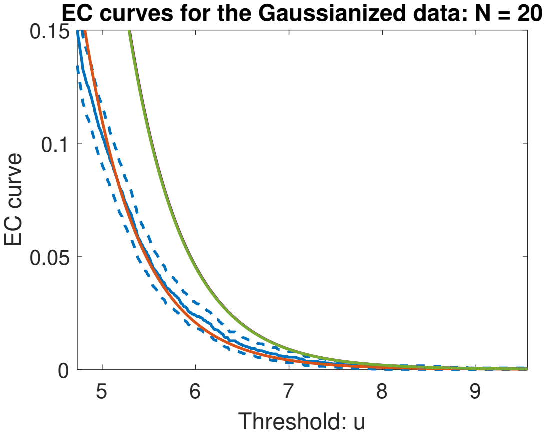


Figure 3: Blue: resting estimate EEC + 95% uncertainty, Red: SuRF LKC approximation. Green: Stationary LKC estimates (Kiebel + Forman).

Bootstrap validation

- We followed (Eklund et al., 2016) and randomly drew 5000 subsets (of size $N = 10, 20$ and 50) from the data to test the methods from the 7000 subjects.
- Apply RFT in each subset and determine use this to estimate the FWER for convolution fields and on the lattice.
- We use 7000 images instead of the between 100-200 samples used in (Eklund et al., 2016) meaning that we don't suffer from the same level of bias due to dependence between the draws.

FWER control on the Gaussianized data, $\alpha = 0.01$

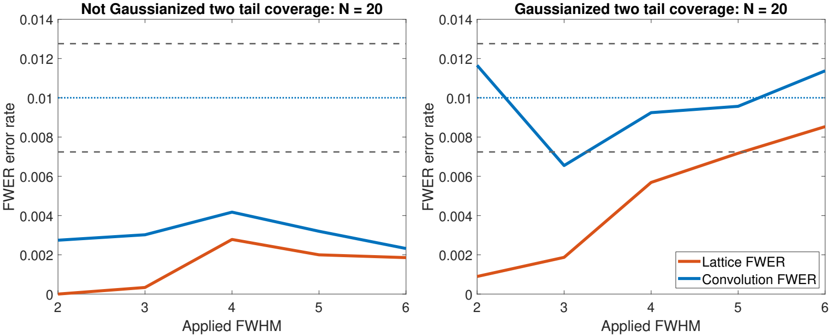


Figure 4: Red: original lattice and Blue: Convolution field

Conclusion

- Existing software (SPM, FSL, AFNI etc) only has LKC implementations under stationarity but the framework is more general as (Taylor & Worsley, 2007) showed.
- Using convolution fields accurately controls the FWER at the right level and allows you to drop the good lattice assumption. As such RFT can be applied at any level of applied smoothness.
- fMRI data is (highly) non-Gaussian and we should be careful about making this assumption.
- Using a transformation can accelerate convergence of the CLT allowing for improved LKC estimation and control of the FWER.
- Future of RFT? Combining with non-parametric methods to ensure validity.

Papers and Software

- This talk summarizes the work in two papers: (Telschow & Davenport, 2023) and (Davenport et al., 2023). Both will soon be available on arxiv.
- If you would like to read more about it, more details are available in my thesis found on my website, see: `sjdavenport.github.io/research/`.
- Software in MATLAB to perform RFT inference is available in the RFTtoolbox (Davenport & Telschow, 2023).
- Slides available at `sjdavenport.github.io/talks`.

Bibliography

Adler, R. J., & Taylor, J. E. (2007). *Random fields and geometry.* Springer Science & Business Media.

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Davenport, S., & Telschow, F. (2023). RFTtoolbox. Retrieved from `https://github.com/sjdavenport/RFTtoolbox`

Eklund, A., Nichols, T. E., & Knutsson, H. (2016). Cluster failure: Why fmri inferences for spatial extent have inflated false-positive rates. *Proceedings of the national academy of sciences*, *113*(28), 7900–7905.

Taylor, J. E., & Worsley, K. J. (2007). Detecting sparse signals in random fields, with an application to brain mapping. *Journal of the American Statistical Association*, *102*(479), 913–928.

Telschow, F., & Davenport, S. (2023). Riding the SuRF to continuous land: precise FWER control for gaussian random fields. *Preprint.*

Worsley, K. J. (2005). An improved theoretical p value for spms based

Gaussianization transformation

More formally, at each voxel v we standardize and demean the underlying (pre-smoothing) fields X_n . This yields standardized fields:

$$X_n^{S,D} = \frac{X_n - \hat{\mu}}{\hat{\sigma}}. \tag{2}$$

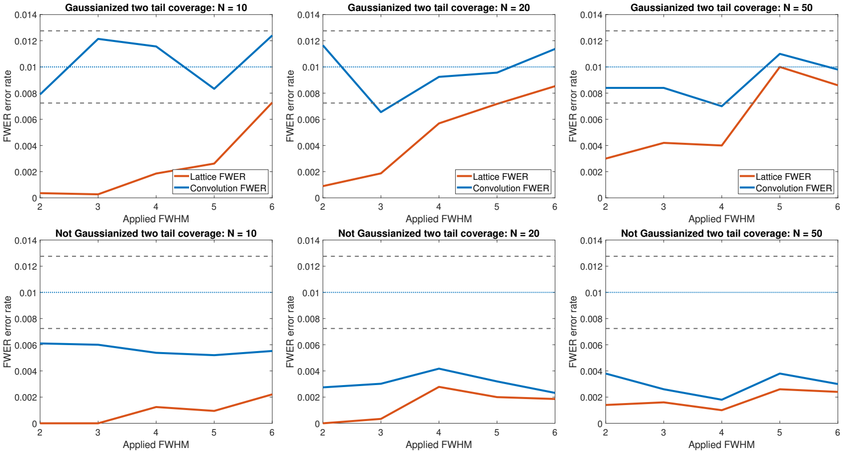
Going back to the original data we standardize it (without demeaning) to yield:

$$X_n^S = \frac{X_n}{\hat{\sigma}}$$

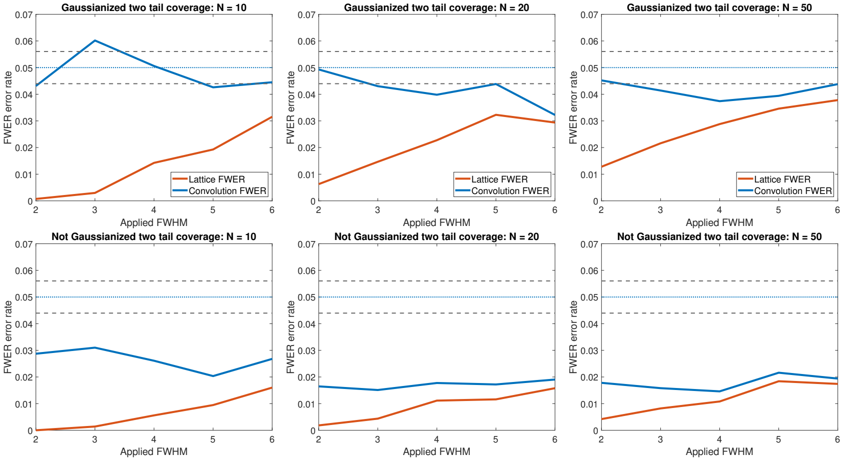
and for each voxel v and subject n we compare $X_n^S(v)$ to the null distribution to obtain a quantile

$$q_n(v) = \frac{1}{N|\mathcal{L}|}\sum_{n=1}^{N}\sum_{v'\in\mathcal{L}} 1[X_n^S(v) \leq X_n^{S,D}(v')].$$

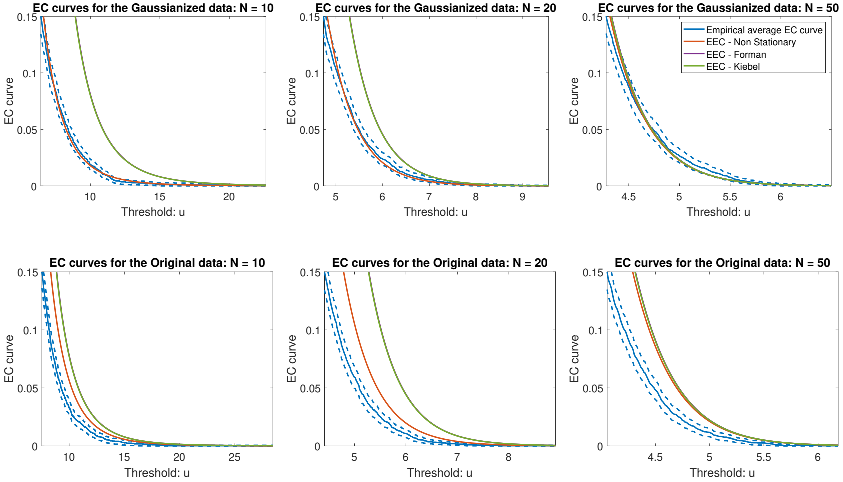
Controlling at $\alpha = 0.01$



Controlling at $\alpha = 0.05$



Expected Euler characteristic curve



LKC estimation results

We run 2D simulations, of white noise smoothed with a Gaussian Kernel. Kiebel and Forman are designed to estimate the LKCs under stationarity but they are biased. HPE and bHPE are unbiased but have a higher variance.