

Empirical and Theoretical FDR Analyses for fMRI Data

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Abstract

The multiple comparisons problems encountered in statistical analysis of functional neuroimaging data are well known. As an alternative to conservative methods for Family Wise Error Rate correction (e.g., Random Field Theory (RFT), Bonferroni tests), procedures that control the False Discovery Rate (FDR, Benjamini et al, 2004) have been proposed as alternatives (Genovese et al, 2002). While these procedures are usually described in terms of sorted p-values, they can also be described using the ratio of two distribution functions: one null and one "observed" from the data (Storey et al, 2004). The null distribution function is usually just the voxelwise null distribution of the statistical parametric map (SPM) (e.g., t with 10 degrees of freedom).

A common problem we have observed with this method is a shift in the modes of the two distributions (Figure 1). The mode of the theoretical distribution is fixed at zero while that of the observed histogram is typically shifted away from zero. This shift can lead to misleading (and non-reproducible) results from the analysis.

As a possible solution to the above mismatch, we used an empirical (local) FDR procedure (Efron, 2004), which replaces the theoretical null distribution function with an empirically-derived null distribution. This procedure also replaces the ratio of distributions with the ratio of densities (hence the name "local"), though this usually has little effect on the results. The procedure assumes that the large number of voxels in a typical fMRI study make it possible to derive an empirical null distribution from a given SPM. Although the empirically-derived function matches the distribution of the data more closely than the theoretical distribution, the analysis does not typically produce significant activations, contradicting the results of RFT analyses. In other words, the empirical null is unable to partition the SPM into "active" and "null" regions.

To address this problem, we propose using a different null distribution than the one used by Efron (2004). In an fMRI experiment with many trial types, we define the variation of null voxels by computing random contrasts and matching the mode of null voxels to the mode of the observed density.

We find that the variability of a typical random contrast is approximately that of the theoretical distribution. Hence, a conservative estimate of this null distribution can be attained by a simple compromise consisting of shifting the theoretical density so that the modes match. These results suggest that the shifted theoretical distribution is a simple and effective compromise between empirically-derived and purely theoretical distributions used in FDR calculations, producing more consistent FDR-thresholded fMRI results.

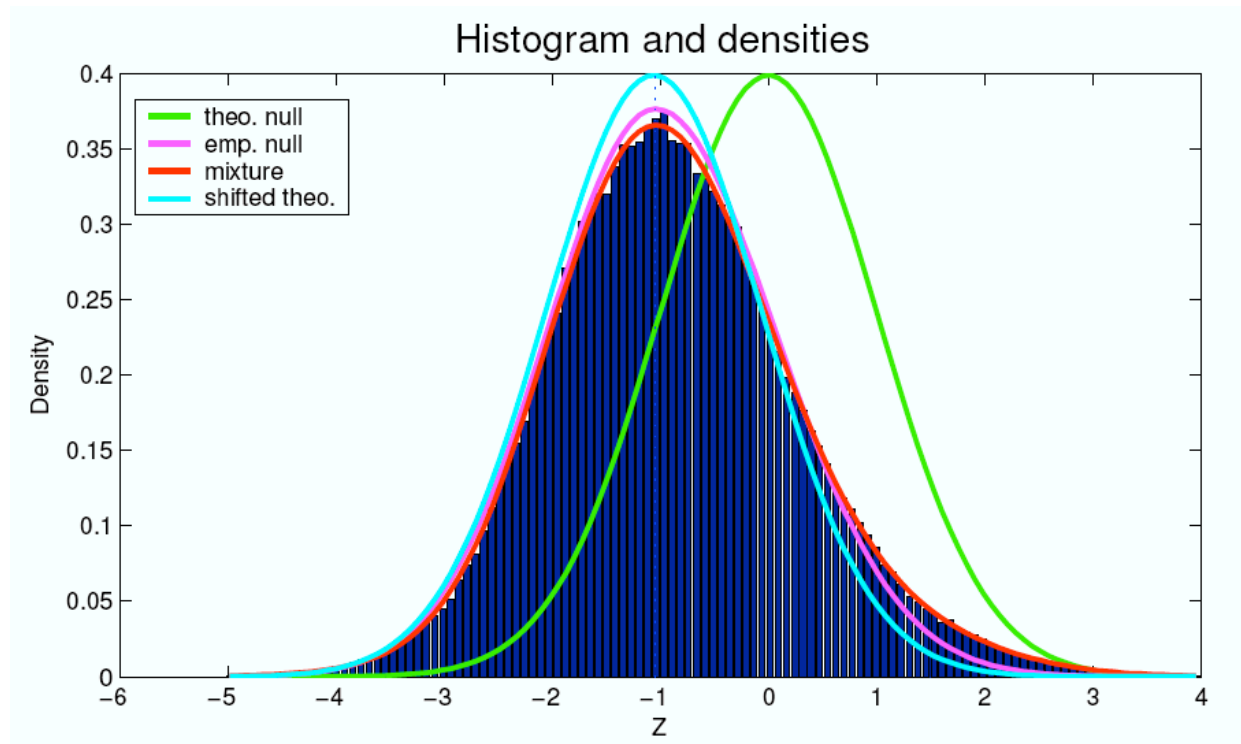


Figure 1. Plot shows four distributions: (1) observed histogram of the z-statistic from a group level contrast (n=18) along with a plot of its density ("mixture"), (2) the theoretical density ("theo. null"), (3) the empirically-derived distribution using local FDR ("emp. null"), and (4) the shifted theoretical distribution ("shifted theo.").

References

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