Detecting Functional Connectivity by Thresholding Correlation Random Fields

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Introduction Functional connectivity between two voxels or regions of voxels can be measured by the correlation between voxel measurements from either PET CBF or fMRI images in 3D. Singular Value Decomposition (SVD) methods[e.g. 1] characterize the connectivity indirectly by a set of 'spatial modes' or eigen vectors of the between voxels correlation matrix; Path Analysis and Structural Equations[e.g. 2] model the correlations between a small number of pre-defined regions. We propose to look at the entire 6D matrix of correlations between all voxels and search for 6D local maxima. The main result is a new theoretical formula [3], based on random field theory, for the P-value of these local maxima, that distinguishes true correlations from background noise. This can be applied to crosscorrelations between two different sets of images, such as activations under two different tasks, as well as autocorrelations within the same set of images. We present examples of both.

Methods Let $X_i(x, y, z)$ be the activation measured while performing the first task on subject i at voxel (x, y, z) in 3D. Let $Y_i(x, y, z)$ be the activation measurement made on the same subject at the same voxel while performing the second task. These activation measurements are already centred by subtracting the average over subjects, so that $\sum_i X_i = \sum_i Y_i = 0$. In general, X_i and Y_i could be the residuals from a linear model that has removed other nuisance variables such as a time trend. Then the 6D crosscorrelation field is

$$R(x_1, y_1, z_1, x_2, y_2, z_2) = \frac{\sum_{i=1}^n X_i(x_1, y_1, z_1) Y_i(x_2, y_2, z_2)}{\sqrt{\sum_{i=1}^n X_i(x_1, y_1, z_1)^2}\sqrt{\sum_{i=1}^n Y_i(x_2, y_2, z_2)^2}}.$$

We have obtained a theoretical result for the P-value of 6D local maxima of R searched over a region of arbitrary shape or size [3] so that true non-zero correlations can be distinguished from background noise.

Functional connectivity between voxels over one set of images can be assessed by setting $Y = X$ to produce the autocorrelation field between X and itself. Spatial correlation causes neighbouring voxels to be correlated, so the autocorrelation field is only evaluated for pairs of voxels separated by at least one FWHM.

If the crosscorrelation is hypothesised to be restricted to homologous voxels, that is $(x_2, y_2, z_2) = (x_1, y_1, z_1)$, this reduces the 6D crosscorrelation field to a 3D homologous correlation field. This is closely related to the t-statistic field for testing for the relation between Y and a random covariate X, rather than a fixed external covariate, in a linear model. Separate results are available for the P-value of local maxima of this field.

Results The autocorrelation field was calculated for a set of 48 PET CBF images from 8 subjects $\times$ 6 repeated scans while performing a vigilance task[4]. Computation time was reduced to 4 hours by smoothing with an 18mm FWHM Gaussian filter and resampling to 5mm voxels. The $P = 0.05$ threshold for local maxima of R for a whole brain search was 0.7981. To reduce data storage, only those correlations above the threshold were kept. Significant correlations confirmed those already reported in [4] based on correlations between pre-determined regions.

The crosscorrelation field was calculated between subtracted PET CBF data for two cognitive tasks measured on 9 subjects[5]. Computation time was reduced as before by smoothing with an 18mm FWHM Gaussian filter and resampling to 3mm voxels. It was hypothesised that ability in one task should be correlated with ability on the second task at the same location, so the homologous correlation field was also evaluated. In this case neither correlation field showed any evidence of connectivity, perhaps due to the small number of scans per task (9) which set the $P = 0.05$ threshold extremely high (0.9991 for the crosscorrelations, and 0.9818 for the homologous correlations).

Conclusions This method assesses connectivity directly rather than indirectly through SVD and spatial modes. By looking at all possible correlations, it removes the restriction of Path Analysis and Structural Equations methods to a small number of pre-determined regions. The method looks at correlations between all pairs of voxels, either between two tasks, within one task, or restricted to homologous voxels, and provides a P-value for assessing the significance of local maxima.

References

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