Adaptive Seeding for Resting-State Network Correlation Analysis with Empirical Mode Decomposition

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Introduction The temporal correlations in low-frequency resting-state BOLD signal suggest functional brain networks that are not related to a specific task [1]. The widely-used seed voxel correlation analysis reveals functional connectivity strength with respect to a particular seed region-of-interest (ROI). Thus it requires priori assumptions, and the result is strongly susceptible to this ROI prescription.
Empirical mode decomposition (EMD) is a data-driven approach suitable for analyzing non-linear and non-stationary signal, which is often the case of biophysical datasets [2]. It has been applied to neuronal data analysis, such as filtering event-related potential (ERP) signals [3], and in combine with independent component analysis to study the temporal characteristics of resting state networks [4]. In this study we used EMD to separate low-frequency BOLD signals into different intrinsic mode functions (IMFs) before analyzing for underlying coherent networks. Instead of performing one single correlation coefficient calculation with a pre-defined seed ROI, we propose an adaptive correlation weighted seeding scheme to determine the correlation map. Results were compared to regular band-pass filtering and seed voxel correlation analysis methods.

Methods Resting fMRI data were acquired on a 3.0 T Siemens Trio scanner (Siemens, Erlangen, Germany) using a single-shot, gradient-recalled echo planar imaging (EPI) sequence with 6 slices of 5 mm thickness and a matrix size of 112 × 112, TR/TE = 360/25 ms and scan time 185 seconds. Motion correction and spatial smoothing was performed in SPM8 (http://www.fil.ion.ucl.ac.uk/spm). Physiological noises were regressed out using parallel-acquired ECG and respiratory signals as reference. Global signal regression was also applied to reduce non-neural signal correlations [5]. The time series were then processed with two methods: 1) empirical mode decomposition. The resulted IMFs that had an instantaneous frequency outside of 0.01~ 0.08 Hz were rejected; 2) a linear phase band-pass filter was applied to extract the signals within the same 0.01~0.08 Hz frequency band.
The adaptive seeding scheme is described in Figure 1. A 4x4x5 mm^3 initial seed ROI for the default network was first prescribed at the posterior cingulate cortex (PCC). The cross-correlation coefficients between the time series of all other voxels in the 3D volume and the seed were calculated to generate an initial correlation map. Voxels with correlation coefficients below a chosen cut-off threshold were then set to zero to create a magnitude-weighting mask. A new seed was defined as the average of the whole data volume weighted by this mask. The correlation coefficients were again calculated for the whole volume with respect to the new seed. This process was repeated until the correlation map converges.

Results Figure 2 shows the functional connectivity maps from one representative subject. The correlation map of band-pass filtered time series is more dependent on the choice of cut-off threshold, while IMFs result is stable across different threshold values. An initial seed prescribed at anterior cingulate cortex (ACC) and a cut-off value of 0.6 was also tested (Fig.3). The initial correlation map was different from the one with initial seed at PCC, but after ten iterations it again converged and resembled the previous one in the bottom row of Figure 2.

Discussion We have demonstrated that the IMFs are capable of generating more consistent correlation maps, regardless of the threshold value we choose. This higher specificity can help reduce the error we might introduce into the determination of functionally correlated networks when manually selecting the threshold. It may also imply that the IMF signals more closely correspond with the underlying correlated neuronal activities. The use of adaptive seeding for multiple iterations also reduces possible correlation coefficient variations related to initial seed ROI selection, which can potentially provide a more reliable correlation map for further functional analyses.

References [1] Biswal et al., MRM 34: 537–541; [2] Huang *et al.*, Proc. R. Soc. London Ser. A 454:903-995 (1998); [3] Liang *et al.* Neurocomputing, 65-66:801-807 (2005); [4] Niazy *et al.* Proc. OHBM 2006, p.1105; [5] Hampson *et al.*, Hum. Brain Mapp. 15, 247-262 (2002).

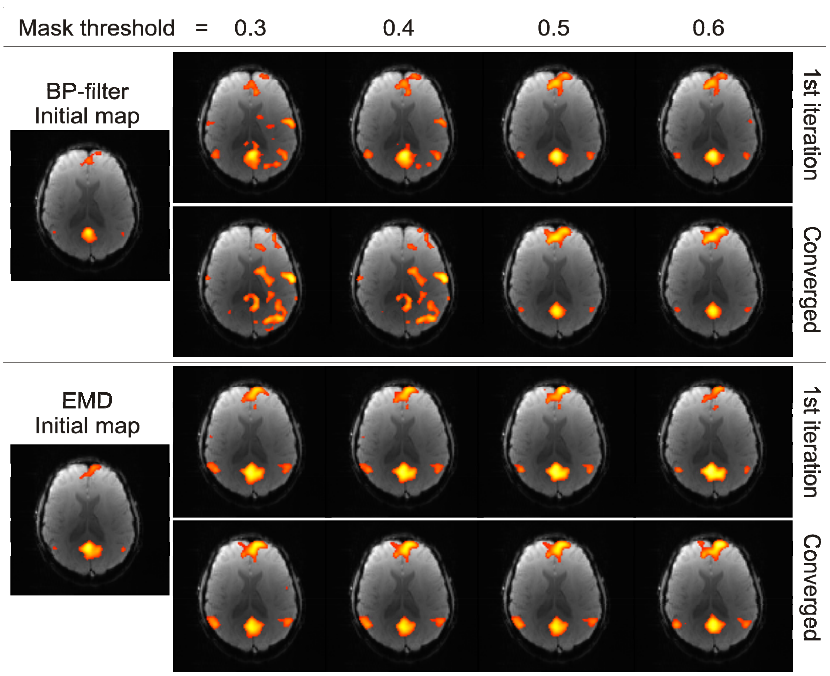

Figure 2 The correlation maps generated with different seed mask cut-off thresholds (0.3 ~ 0.6). Initial seed was prescribed at PCC. All correlation maps converged within ten iterations.

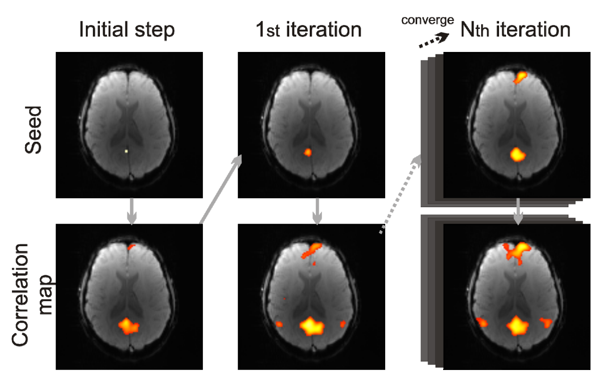

Figure 1 The adaptive correlation weighted seeding scheme. The iteration stops when the correlation map converges.

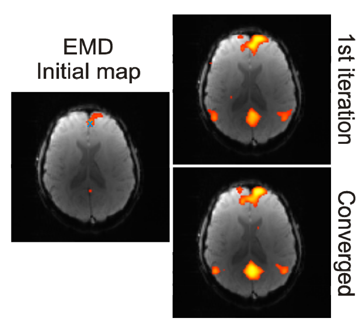

Figure 3 Correlation maps with initial seed prescribed at ACC (blue cross). After ten iterations the correlation map resembled the one with initial seed at PCC (Fig.2, bottom right).