Wavelet-based cluster analysis (WCA): data-driven identification of temporal profiles in MRI time series

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Introduction: Data-driven or exploratory algorithms have begun to be applied to fMRI data as a complement to hypothesis-driven analyses based on the experimental design[1]. Modelling of phMRI data poses some different problems; in experiments with acute compound administration the resulting transient signal changes can vary with location in the brain and may not be known *a priori*. The ability to rapidly identify regions of similar temporal profile can play an important role in highlighting underlying biological relationships and in the design of subsequent analyses, e.g., involving general linear modelling or non-linear regression.

Methods: A Wavelet-based Cluster Analysis (WCA) algorithm was implemented, comprising (1) a discrete wavelet transform (DWT) of each voxel time course, (2) a filtering operation retaining p wavelet coefficients (cf. denoising), (3) determining clusters of voxels in the space $\mathbf{R}^p$ formed by the remaining wavelet coefficients. In order to validate this approach, WCA was applied to both simulated and *in vivo* time series data from well-characterised time series experiments, namely phMRI of acute cocaine challenge and perfusion-weighted MRI following middle cerebral artery occlusion (MCAO) in the rat. Here, step (2) involved retaining the lowest 31 or 15 wavelet coefficients (phMRI or perfusion respectively), and in step (3) we used the k-means clustering algorithm. The results and performance were compared with both spatial and temporal ICA as implemented in the fast-ICA algorithm[2]. The phMRI data comprised a Cerebral Blood Volume (CBV) time series (dt=10s, Nt=128) with an acute 0.5mg/kg i.v. cocaine injection over 1 minute covering time points 26-32. The MCAO data comprised a series of 50 images acquired in 32 seconds, with a 200ul bolus of Gd-DTPA injected into the jugular vein over 1 second at image 20.

Results: Our results were found to be insensitive to the choice of wavelet generating function – here we used Daubechies. Applied to the phMRI data, WCA was able to identify subtly different time courses in different brain regions[3]. Figure 1 illustrates the results in one slice (approx. 2-4mm from bregma) showing a rapid onset and decrease in the frontal cortex (#1), and broader temporal profiles in the prefrontal/cingulate and orbitofrontal cortices (#3,4). ICA identified the primary positive cocaine response time course, and also the transient dip during injection, but did not distinguish the different time courses associated with different brain regions. Applied to the MCAO perfusion data WCA differentiated healthy tissue and different regions within the damaged contralateral hemisphere, highlighting differences in cerebral perfusion (Figure 2).

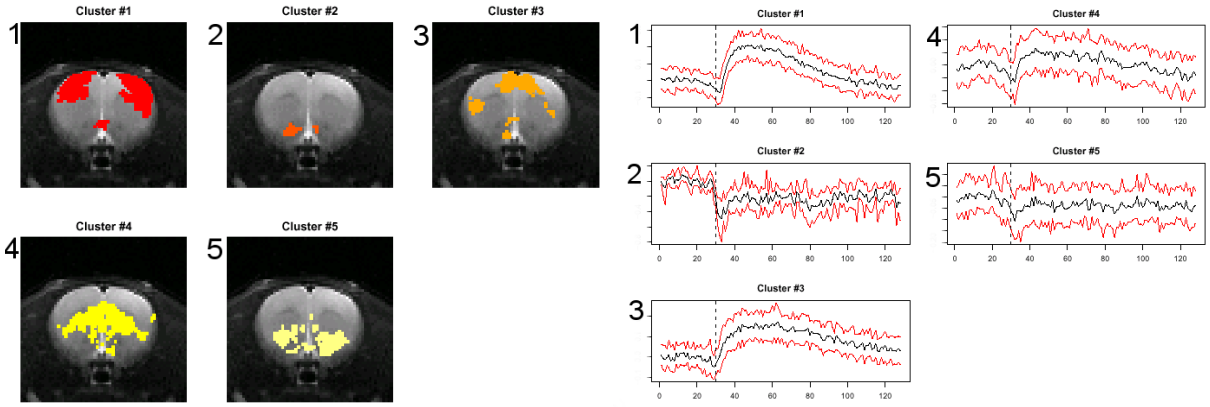

Figure 1: WCA applied to cocaine challenge phMRI data (5 clusters). (a) Spatial maps, and (b) associated time courses (10/50/90%) for each cluster.

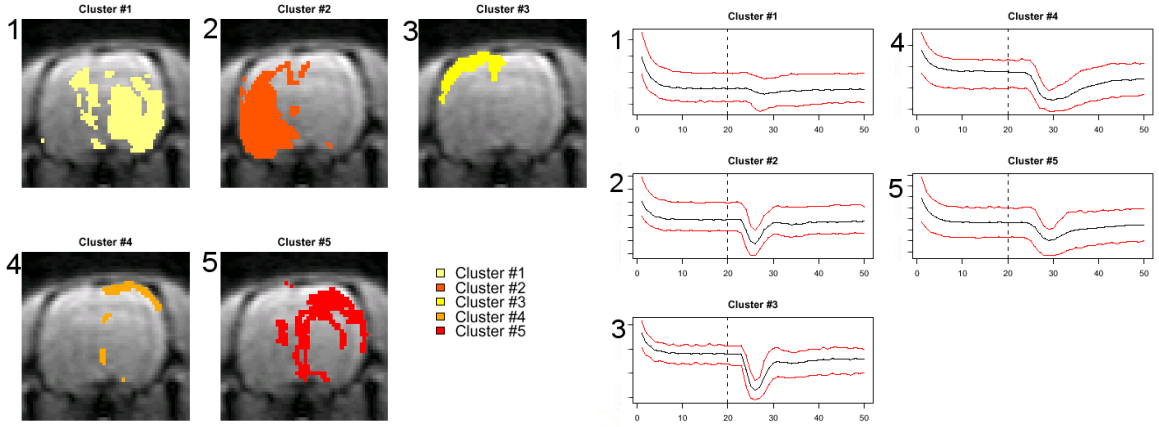

Figure 2: WCA applied to MCAO perfusion data (5 clusters). (a) Spatial maps, and (b) associated time courses (10/50/90%) for each cluster.

Discussion: WCA provides a useful exploratory algorithm for the identification of different temporal responses within massively univariate time-series data. Application to perfusion-weighted MCAO and cocaine challenge phMRI data validated the algorithm's ability to identify subtly different time course variations. Data-driven approaches such as this are likely to prove valuable in highlighting spatiaotemporal patterns in phMRI and related time series data, for example when applied to novel compounds that induce responses that are less widespread, weaker and of unknown temporal characteristics.

References

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