

# Enhanced Motion Correction in Long TR phMRI through Dual Modified Temporal Cluster Analysis

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## Abstract.

Subject motion is a common problem in all forms of BOLD MRI and it is accepted that conventional motion correction does not remove all of this variance from the data. Hypothesis-driven approaches use the shifts from these corrections as unwanted-effects regressors, whereas data-driven analysis techniques often cannot, and so are more susceptible to this form of artefact. Modified temporal cluster analysis (MTCA) is a data-driven approach to the examination of fMRI and phMRI data. It is, however, susceptible to motion artefact, which we use here as an advantage and introduce the dual MTCA method as a means to discover when and where in the brain is being affected by motion which is uncorrected for, so that those slices may be suppressed before further data-driven analysis. This is particularly useful in experiments with long repetition times since only a subset of slices will require further correction. We apply this to placebo data from a phMRI study and conclude that it will be a useful step in the preprocessing and further analysis of such experiments.

## 1 Introduction

A wide variety of analysis techniques are applied to functional magnetic resonance imaging (fMRI) data. The most popular of these uses the general linear model (GLM) to identify voxels whose time course correlates with the *a priori* experimental procedure, implemented as statistical parametric mapping (SPM) [1]. One of the most important preprocessing steps before any analysis is the correction of any small motion that has occurred during a session. Even after this correction, a large source of variance in the data will still be correlated with this motion, and so the small shifts for each timepoint in each direction are taken and used as unwanted-effects regressors in a GLM approach [2].

Recently, pharmacological MRI (phMRI) has emerged as a development of fMRI. In conventional fMRI the experimental procedure is generally a well-defined activation task (word generation, finger tapping etc). In phMRI the experimental procedure is the administration of a drug; consequently the analysis procedure must look to identify voxel time courses correlating with the expected neural response to the drug. This can be problematic if the expected neural response is not well established or could be expected to have a number of differing spatial and temporal modes. There is correspondingly greater potential for data-driven methods in phMRI than in conventional fMRI, such as *k*-means clustering, Independent Component Analysis (ICA) or Wavelet Cluster Analysis (WCA) [3] [4].

However, data-driven approaches often cannot use anything similar to unwanted-effects regressors and will thus be more susceptible to large artefacts such as motion, which can easily drown out the much smaller variance expected from the Blood Oxygen Level Dependent (BOLD) response. In some recent designs of phMRI experiments there has been a long repetition time (TR) (effectively  $\sim 20$ s, with each volume being acquired during the first  $\sim 5$ s of this). Due to the protracted and interleaved nature of collection of slices during this time, any motion will not affect all the slices in a volume as in fast fMRI, but will only affect several across a number of slices which are non-abutting.

Temporal Cluster Analysis (TCA) is a data-driven method for discovering the time at which voxels experience their maximum value [5]. This was used originally to find the times at which the neural response to the body's uptake of glucose was maximal so that better models could be developed and tested using conventional hypothesis-driven approaches. This method is now generally called Original TCA (OTCA). An iterative version (ITCA) was introduced in [6]. The results of this form of model generation for a SPM analysis compare favourably with the results of an Independent Component Analysis (ICA) [7]. More recent work has looked at detecting extended plateaus of response using autocorrelation combined with OTCA [8].

Modified TCA (MTCA) takes into account the changes in signal intensities producing the maximal values to weight the results so that a timepoint when many voxels have a small increase to take them to their maximal value will not overshadow a timepoint where a small number of voxels have a large positive response [9]. TCA was used in [10]

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to detect epileptic activity without the use of electroencephalography (EEG). However, the results of this study were disputed and found to be difficult to reproduce due to the susceptibility of TCA to motion artefacts [11].

Here, we explore the use of TCA as a method to discover uncorrected motion at an early stage in the processing pipeline. We introduce dual MTCA, whereby both maximum and minimum times are found and weighted at each voxel, and those timepoints found to have large magnitudes in both directions are examined further, with the voxels producing these treated as undergoing motion. This is applied to a ‘resting state’ brain (placebo day of a phMRI experiment).

## 2 Methodology

Once a 4D (3D + time) dataset has been preprocessed to realign each point so that it may be confidently compared to itself over time, it may be represented as a matrix of voxels

$$\mathbf{V} = \begin{pmatrix} v_{1,1} & v_{1,2} & v_{1,3} & \cdots & v_{1,t} \\ v_{2,1} & v_{2,2} & v_{2,3} & \cdots & v_{2,t} \\ v_{3,1} & v_{2,3} & v_{2,3} & \cdots & v_{3,t} \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ v_{x \times y \times z, 1} & v_{x \times y \times z, 2} & v_{x \times y \times z, 3} & \cdots & v_{x \times y \times z, t} \end{pmatrix} \quad (1)$$

where each column represents a full 3D brain volume at one point in time and each row represents the temporal changes of one voxel.  $x$ ,  $y$  and  $z$  are the spatial dimensions of one brain volume, while  $t$  is the number of volumes in the session.

### 2.1 Original Temporal Cluster Analysis

In the original algorithm (OTCA) maximum valued timepoints are found as

$$v'_{i,j} = \begin{cases} 1 & \text{if } v_{i,j} = \max\{v_{i,1}, v_{i,2}, \dots, v_{i,t}\} \\ 0 & \text{otherwise} \end{cases} \quad (2)$$

with collation occurring as

$$\mathbf{p} = (p_1, p_2, \dots, p_t) \text{ where } p_j = \sum_{i=1}^{x \times y \times z} v'_{i,j} \quad (3)$$

$\mathbf{p}$  may then be plotted, showing the number of voxels which reach their maximal value at any given timepoint.

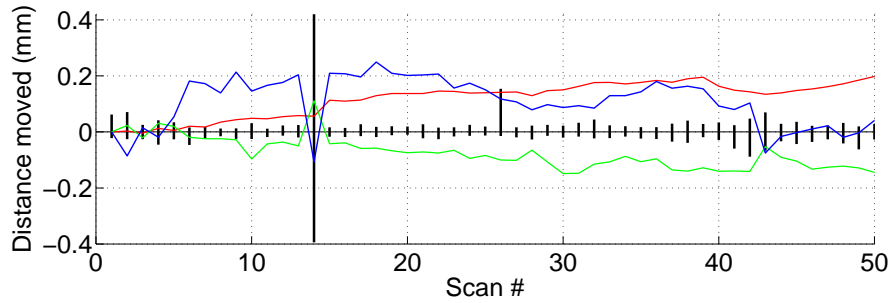
### 2.2 Dual Modified Temporal Cluster Analysis

The modified algorithm (MTCA) takes the signal change at each voxel, and we extend this to find both maximum and minimum values for each voxel as

$$v_{i,j}^{max} = \begin{cases} \% \text{ change} & \text{if } v_{i,j} = \max\{v_{i,1}, v_{i,2}, \dots, v_{i,t}\} \\ 0 & \text{otherwise} \end{cases} \quad (4)$$

$$v_{i,j}^{min} = \begin{cases} \% \text{ change} & \text{if } v_{i,j} = \min\{v_{i,1}, v_{i,2}, \dots, v_{i,t}\} \\ 0 & \text{otherwise} \end{cases} \quad (5)$$

which we refer to here as dual MTCA (d-MTCA). The percentage change used here is the percentage difference of a voxel’s value at a timepoint compared to the mean of that voxel’s values between timepoints 2 and 22 (during the baseline period). These are then collated as in Equation 3, the results of which may be plotted as seen in Fig. 1 where the shifts from the conventional motion correction step are overlaid.



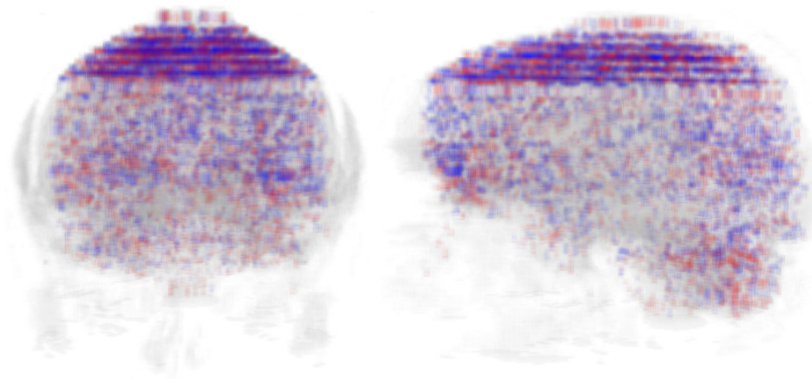
**Figure 1.** An example of d-MTCA. The bars represent collated percentage signal change from all those voxels reaching a maximum or a minimum at that timepoint (here scaled relative to timepoint 14). The coloured lines represent the shifts returned from the motion correction step (in the three orthogonal directions). If this were a real experiment one would discover which voxels are causing the dual spike at timepoint 14 and suppress those slices. The single positive spike at timepoint 25 would be examined further since positive response with no corresponding negative is much more likely to represent a true BOLD effect.

At each timepoint we also record the spatial position of each voxel reaching its maximum or minimum value. For acquisitions which are interleaved, any subject motion will manifest as concentrations of maximum and minimum points across every second (generally) transverse slice over a portion of the volume corresponding to how long the motion took place for. This is due to the motion moving a previously higher signal intensity region into a lower signal intensity region and *vice versa*. Indeed, any uniform structure such as this is extremely unlikely to have been caused by the BOLD response alone.

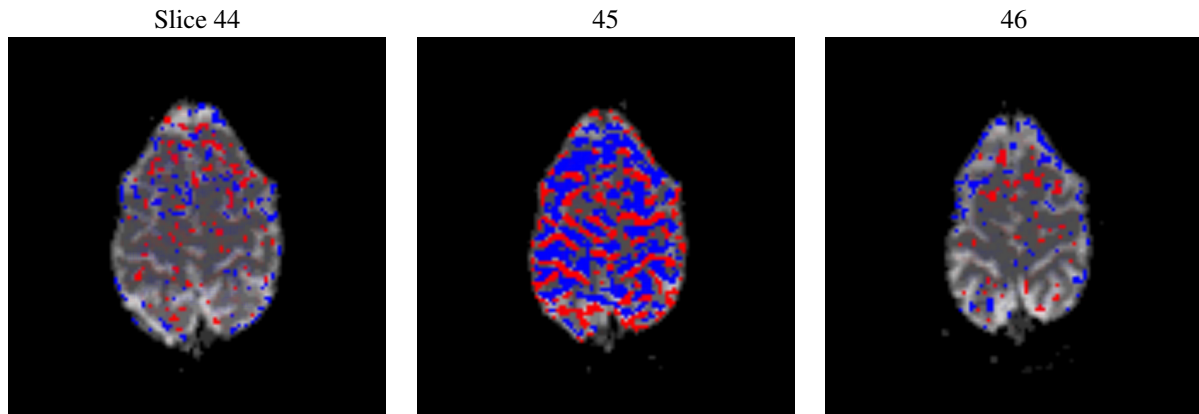
At a timepoint with large positive and negative d-MTCA results, those slices with a large number of maximum and minimum spatial points are classed as having motion artefact. The voxels in these slices are removed and replaced with the result of an interpolation of the signal intensities from the same position at the surrounding timepoints. If the motion extends over many slices, or there are two or more distinct periods of motion in a particular acquisition, the entire volume at that timepoint could be classed as having motion artefact and be suppressed. Further preprocessing techniques such as spatial transformation to a standard anatomical space and smoothing may now take place, allowing for data-driven methods to be used to analyse the data without as much risk of only discovering the smeared effects of these motion artefacts.

### 3 Results

We have used data from a BOLD pHMRI experiment where twelve healthy volunteers received an infusion of either saline (placebo) or hydrocortisone after 10 minutes of baseline (out of 100 minutes in total) on alternate days [12]. The one session from this experiment studied here is from the placebo day, of which the first 50 volumes (17 minutes) are used. Each acquisition of an entire brain volume was carried out in an interleaved fashion (to reduce susceptibility



**Figure 2.** Coronal and sagittal views of a volume rendering showing only those voxels reaching their maximum (red) or minimum (blue) values at timepoint 38. In an ideal situation these would be distributed randomly throughout the brain. Here these voxels are concentrated in the odd numbered slices from 41 to 49 inclusive indicating motion during their acquisition.



**Figure 3.** Transverse slices 44, 45 and 46 (left is true left) at timepoint 38. The d-MTCA voxels for this timepoint are overlaid on the  $T_2^*$  weighted slices. In slice 45 sulci are apparent due to the motion occurring at that point in the acquisition as previously higher signal intensity regions momentarily move into lower signal intensity regions and *vice versa*. In the absence of serious motion slice 45 should look more similar to slices 44 or 46.

distortions) over the course of 5s with 20s between the start of each full scan yielding an effective TR of 20s. Images were motion corrected using Statistical Parametric Mapping Software version 5 (SPM5, Wellcome Trust Centre for Neuroimaging, Institute of Neurology, UCL, London, UK; <http://www.fil.ion.ucl.ac.uk/spm/>). Images were aligned using a least squares framework minimising the mean square error between two images. No further preprocessing was performed since each step will smear the effects of motion across several slices.

Timepoint 38 was found to have large magnitudes in both directions using d-MTCA. Those voxels reaching their maximum or minimum value at this time are shown in Fig. 2<sup>1</sup>. When viewed individually as transverse slices, as in Fig. 3, sulci are visible, which would not be expected for this type of analysis in the absence of movement. It should be noted that the volunteer was not consciously moving.

Fig. 4 shows some of the slices from Fig. 2 together with the results of a  $k$ -means clustering (using 3 clusters) carried out before (row 2), and after (row 3) any d-MTCA driven correction was performed. For this design of experiment we should see no apparent structure as a result of the clustering since we are only examining function (the clustering algorithm also has no spatial awareness). In effect, there should be nothing sensible to cluster besides any commonality among noise. However, before d-MTCA driven correction (row 2), we see some of the structure of the cortex when this clustering is carried out. All timepoints have been used in this clustering, with the effects of the motion at timepoint 38 driving the variance. Conversely, after a temporal interpolation step has been carried out on the identified slices (odd numbers 41 through 49) at this timepoint, the clustering algorithm finds no clear spatial clusters, as would be expected in this case in the absence of motion.

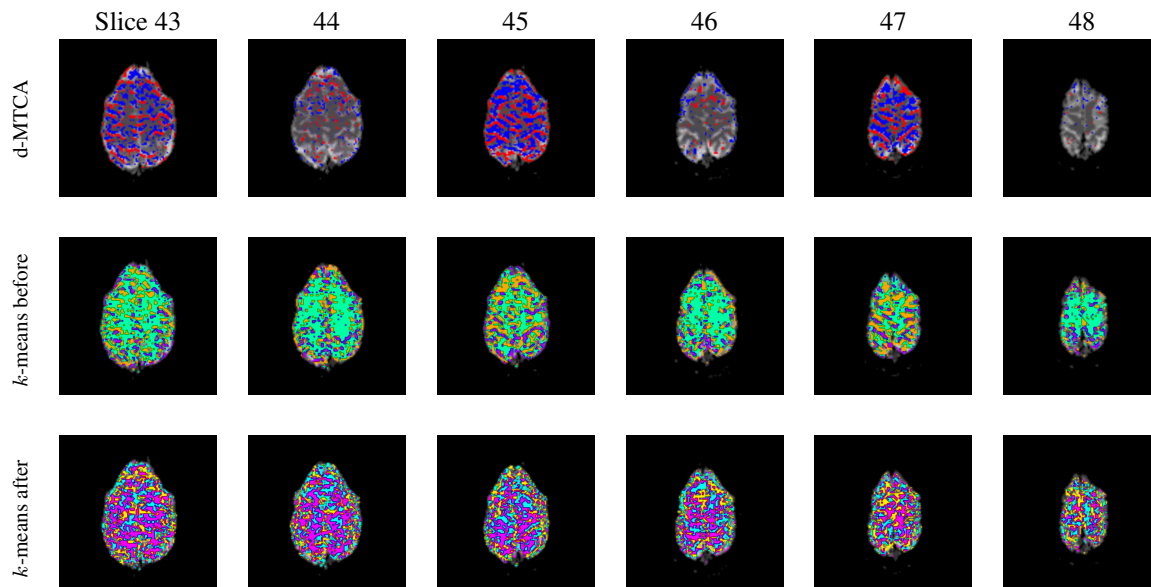
## 4 Discussion

This method is designed for the long form of experiment common in phMRI where motion becomes a problem in the later stages, the TR is quite long, and where subsequent data-driven analysis is most useful [13] [12]. It should not be confused with conventional slice timing correction which is common in event-related designs in fMRI. In an exploratory analysis it may also be useful to explore the spatial nature of any motion artefact, especially one that occurs close to important timepoints in the experiment such as the infusion of a drug. Limits could be put in place so that if there were more than a certain number of slices found to have severe motion artefact through this method, the entire timepoint could be suppressed out and replaced with an interpolation of temporally surrounding entire volumes. For most movements, however, only those slices affected need to be removed, meaning we may keep most of the information from each timepoint, without the risk of seeing this type of motion artefact affecting many more slices after further preprocessing steps.

## Acknowledgments

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<sup>1</sup>More figures of this process may be viewed in full colour at <http://www.cs.bris.ac.uk/home/mcgonigle/dualmtca/>.



**Figure 4.** Row 1 shows slices 43 through 48 with those voxels reaching a maximum value at timepoint 38 coloured red, and those reaching a minimum coloured blue. Motion is apparent in slices 43, 45 and 47, which corresponds to the interleaved nature of the acquisition. Row 2 shows the same slices with the colours corresponding to  $k$ -means clusters as the timecourse of each voxel has been examined. Sulci are apparent in slices 43, 45 and 47 here which would not be expected purely through examination of function using this algorithm in the absence of motion. It is evident that the motion at timepoint 38 is having a large effect on the clustering. Row 3 shows the same slices, again with colours corresponding to  $k$ -means clusters, after the voxels in slices 43, 45 and 47 at timepoint 38 were removed and replaced with an interpolation of the same positions from the surrounding timepoints. Colours do not correspond between rows.

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