Induced Correlation Resulting from Respiration and Motion Correction Processing Operations in fMRI

Emily M. Paulson¹, Daniel B. Rowe^{1,2} ¹Department of Mathematics, Statistics and Computer Science, Marquette University, Milwaukee, WI, USA ²Department of Biophysics, Medical College of Wisconsin, Milwaukee, WI, USA

Abstract

Slight movements of a subject cause the function magnetic resonance imaging (fMRI) signal to be affected, thus causing errors in the data. This can include small head movements or systematic movement from respiration. However, these movements can be estimated and adjusted for, so that the time series is now corrected. Although the goal of respiration and motion correction is to improve the fMRI data, it has an ancillary effect of inducing correlation between voxels that is of no biological origin. In this manuscript, these processing operations are represented in a matrix framework. With the matrix formulation of the processed voxel data are determined. It will be shown that these processing operations induce correlation in previously uncorrelated voxel data. The goal is to first quantify these statistical properties so they can be accounted for, and identify the true biological signal of interest.

Key Words: MRI, fMRI, motion correction, induced correlation

1. Background

In functional magnetic resonance imaging (fMRI), the data for each image is measured as an array of complex-valued spatial frequencies. Images are created from these spatial frequencies using an image reconstruction operator. The most common operator is the twodimensional discrete inverse Fourier transform. After the Fourier transform is applied to a series of images, the result is a time series within each voxel. Contained within a voxel's time series is true signal of interest and "noise." Noise referring to random variation and to any systematic physiological/non-physiological signal that is not of interest, such as respiration or movement [1]. Any noise reduces the accuracy of the analysis of the data. Therefore, spatial and/or temporal operators that are applied to images are represented as matrix operators and their effect estimated so that it could potentially be accounted for before any statistical analysis takes place.

These operators alter the acquired data, and potentially have a negative effect – specifically inducing correlations [2]. Some of these operators include, but are not limited to, spatial and temporal filtering processes, respiration and motion correction, global intensity normalization, and slice timing correction. These artificial correlations must be estimated so that they can be taken into consideration when performing statistical analysis. This study will focus on constructing a matrix representation for respiration and motion correction. Representing these operations in a matrix framework will help determine the changes in mean, variance, and any potentially induced correlation structure, with the goal of them being accounted for or removed in order to identify the true biological signal of interest.

1.1 Image Reconstruction

Images are created from complex-valued spatial frequencies using an image reconstruction operator. The two-dimensional inverse Fourier transform has been put into a matrix operator [1]. The complex-valued inverse Fourier transform of frequencies F_c can be written as

 $Y_c = \Omega_{Cv} F_C \Omega_{Cx}^T$

where Y_c is the complex-valued reconstructed image created by pre-multiplying the *k*-space spatial frequency matrix, F_c , by the inverse Fourier transform matrix in the dimension of y, Ω_{Cy} , and post-multiplied by the inverse Fourier transform matrix in the dimension of x, Ω_{Cx} . This is the usual way to represent the inverse Fourier transform of F_c . However, these pre- and post-multiplication of the IFT matrices can be combined into a single reconstruction matrix:

$$\Omega = \begin{bmatrix} \Omega_R & -\Omega_I \\ \Omega_I & \Omega_R \end{bmatrix}$$

where the components are derived through Kronecker products:

$$\Omega_{R} = \left\lfloor \left(\Omega_{yR} \otimes \Omega_{xR} \right) - \left(\Omega_{yI} \otimes \Omega_{xI} \right) \right\rfloor \text{ and } \Omega_{I} = \left\lfloor \left(\Omega_{yR} \otimes \Omega_{xI} \right) - \left(\Omega_{yI} \otimes \Omega_{xR} \right) \right\rfloor$$

The Kronecker product multiplies each element in the first matrix by the entire second matrix. The real-valued isomorphism by Rowe et. al. [1] makes it possible for the reconstructed image to be a product of the IFT operator, Ω , and the observed spatial frequencies in vector form, f, as:

 $y = \Omega f$

where f is formed by stacking the rows of the real frequencies on top of the rows of the imaginary frequencies in each image.

1.2 Induced Correlation

After the matrix operator is applied to the data vector, any changes in correlation structure can be observed from the covariance matrix. The spatial processing operator, O_s , is multiplied by a real-value vector, Ωf . The resulting covariance matrix is:

$$\operatorname{cov}(y) = \sum_{s} = O_{s} \Gamma O_{s}^{T}$$
(1)

To observe the induced correlation, the covariance in Eq. (1) is utilized to obtain

$$\operatorname{cor}(y) = D^{-\frac{1}{2}}O_s \Gamma O_s^T D^{-\frac{1}{2}},$$
 (2)

where D is a diagonal matrix with elements that are variances and -1/2 means to square root and invert the nonzero elements.

2. Translation Correction Operator

2.1 Introduction

Sight movements of a subject cause the fMRI signal to be affected, thus causing noise in the data. This can include small head movements or systematic movement from respiration. These movements induce signal modulations in the image time series that increase noise and degrade the statistical significance of activation signals. When statistical methods are applied to the data, it is assumed that the location of a given voxel within the brain does not change over time [3]. When a subject is in the scanner there is typically some degree of movement. Therefore, if statistical analysis takes place before correcting for motion the analysis could include various voxels. Once the image is reconstructed these fluctuations cause a spatial shift in the brain image, most noticeable near the edges of high contrast

areas [4]. If the transformation between the source image and the reference image only involves translations, a fractional shift can be used.

2.2 Methods

In two dimensions, a shift only needs two parameters, the shift in the x-direction a and the shift in the y-direction b. Estimating a and b can be performed by optimizing a cost function. A *Gauss-Newton* optimization algorithm can be used to estimate the spatial transformation parameters by optimizing the mean squared difference between the source and reference images. Once the shifts a and b have been found they can be applied to the source image with the creation of a fractional shift matrix.

As an example, assume that the source image has to be translated $a.\alpha$ voxels in the xdirection and $b.\beta$ voxels in the y-direction, where a and b are the whole number of voxels translated while α and β are the fractional translation amounts. The translation of each voxel in the x-direction can be performed by placing α of the voxel's value a voxels away and (1- α) of the voxel's value a-1 voxels away in the x-direction. Similarly, the translation of each voxel in the y-direction can be performed by placing β of the voxel's value b voxels away and (1- β) of the voxel's value b-1 voxels away in the y-direction.

Consider a 96×96 image being shifted over 5.25 and to down 2.75 - a is 5 and *b* is 2, α is .25 and β is .75. A [$N_X \times N_Y$, $N_X \times N_Y$] matrix is created by placing .25 of the voxel's value in the spot 4 away and .75 of the voxel's value would be placed 5 away both in the *x*-direction. The same idea is repeated for the *y*-direction. The values .25 and .75 are multiplied by the voxels intensities and their intensities split between two voxel locations. This process is continued until all the voxels are accounted for. This matrix can then be multiplied by the data vector. Figure 1 shows the original phantom (Left), a simulated shift (Center), and a fixed phantom using a fractional shift matrix (Right).



Figure 1:

Left: simulated reference image. Center: simulated object image. Right: corrected image using translation matrix.

2.3 Results and Discussion

Matching the source image to the reference image using a fractional shift induced a correlation. Before statistical analysis can be done on the images, the correlation must be taken into consideration. The correlation and covariance matrices can be calculated from

the operator applied to the source image. Using Eq. (1) the covariance matrix is $\operatorname{cov}(y) = \sum = P \Gamma P^T$ where *P* is the fractional shift matrix and Γ is the observed covariance in the data. Here Γ is an identity matrix. The induced correlation matrix *R* can be calculated using Eq. (2). $R = D^{-1/2} \sum D^{-1/2}$. Figure 2 shows the resulting correlation matrix when a fractional shift matrix is applied to the data and the induced correlation zoomed in. Applying a smoothing operator along with the shifting, enhances the correlation induced on the neighboring voxels. Figure 3 compares the induced correlation from just the shifting matrix and the addition of smoothing.



Figure 2: Left: correlation matrix from shifting matrix Right: induced correlation from shifting matrix



3. Rigid Body Transformation

3.1 Introduction

Most times images have to be corrected for more than just translation. If a source image has to be rotated to match the reference image, a different transformation must be used. The transformation picked depends on if the scans are inter or intra-modal. When correcting for motion within a subjects scan, the source image can be corrected by applying a rigid body transformation that will rotate and translate it to match a reference image.

3.2 Processor Implementation

The goal of a rigid-body transformation is to take a source image and rotate and translate it to match a reference image. The reference image can be the first image in the time series or an average of all the scans. Two steps are involved to get two images to match: registration and transformation [5].

3.2.1 Registration

Registration is the process of estimating the parameters for the best geometric alignment of two images [3]. The goal is to maximize the similarities between both images. To achieve this, a cost function that quantifies the differences between the two images is minimized. Intensity based cost functions are more accurate and reliable then geometric ones [6]. There are a variety of intensity-based cost functions to choose from. Choosing the right one depends on the type of registration being performed. Intramodal problems most often use least squares or normalized correlation cost functions, whereas intermodal problems use mutual information, normalized mutual information, woods and correlation ratio cost functions [3]. Optimizing the cost function using an optimization algorithm, such as a *Gauss-Newton*, will find the optimal transformation parameters to match the source image to the reference image. The transformation (T^*) that gives the minimum cost is:

$$T^* = \arg\min C(Y, T(X)),$$

where $C(I_1, I_2)$ is the cost function and T(X) is the source image after being transformed [6].

The cost function also requires an interpolation method to calculate what the intensities of the source image are at points in between original voxel locations. The interpolation method used is important because the intensities of the transformed image are used for statistical analysis. Interpolation methods commonly used include linear/bilinear/trilinear, windowed sinc, polynomial, or Fourier interpolations [5]. In motion correction, all the images acquired are from the same subject and have the same imaging parameters. Because of this, the problem can be classified as intrasubject, intramodal registration.

3.2.2 Transformation

Once the transformation parameters are found, the source image can be matched to the reference image. Since motion correction is an intrasubject intramodal problem, a rigid body transformation can be used. Rigid body transformations involve only rotations and translations. To map each point in the source image to the reference image in 2-dimensions, two translations and one rotation are used. Mapping each pixel location in the source image

 (x_i, y_i) to the reference image gives

$$\begin{pmatrix} u_i \\ v_i \end{pmatrix} = \begin{pmatrix} \cos\theta & -\sin\theta \\ \sin\theta & \cos\theta \end{pmatrix} \begin{pmatrix} x_i \\ y_i \end{pmatrix} + \begin{pmatrix} a.\alpha \\ b.\beta \end{pmatrix} \quad \text{for } i = 1, \dots, n,$$

where θ is the rotation degree, $a.\alpha$ is the translation in the x-direction and $b.\beta$ is the translation in the y-direction. If the reference image and the source image have the same number of points the parameters $a.\alpha$, $b.\beta$ and θ can be estimated by:

$$\hat{\theta} = \tan^{-1} \left(\frac{+mean(\overline{uy}) - mean(\overline{vx}) - \hat{a}\overline{y} - \hat{b}\overline{x}}{-mean(\overline{ux}) - mean(\overline{vy}) + \hat{a}\overline{y} + \hat{b}\overline{x}} \right)$$
$$\hat{a} = \overline{u} - \overline{x}\cos(\hat{\theta}) + \overline{y}\sin(\hat{\theta})$$
$$\hat{b} = \overline{v} + \overline{x}\sin(\hat{\theta}) - \overline{y}\cos(\hat{\theta})$$

where $\overline{x}, \overline{y}, \overline{u}, \overline{v}, uy, vx, ux, vy$ are the means of x, y, u, v, and uy, vx, ux, and vy points respectively. After the parameters are estimated, they can be applied to the source image.

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References

- Rowe DB, Nencka AS, Hoffmann RG. Signal and Noise of Fourier Reconstructed FMRI Data. J Neurosci Meth. 2007; 159:361–9.
 Kurren MMA, Neurola AS, David B, Parris DB, Overstification of the
- [2] Karaman MM, Nencka AS, Bruce IP, Rowe DB. Quantification of the

Statistical Effects of Spatiotemporal Processing of Nontask fMRI data. *Brain Connectivity*. 2014; 4:649–61.

- [3] Jenkinson M, Bannister P, Brady M, Smith S. Improved optimization for the robust and accurate linear registration and motion correction of brain images. *Neuroimage*. 2002; 17(2):825–41.
- [4] Birn RM, Diamond JB, Smith MA, Bandettini PA. Separating respiratoryvariation-related fluctuations from neuronal-activity-related fluctuations in fMRI. *Neuroimage*. 2006; 31:1536–48.
- [5] Ashburner J, Friston KJ. Rigid body registration. In: Frackowiak RSJ, Friston KJ, Frith C, Dolan R, Price CJ, Seki, S, Ashburner J, Penny WD, ed. *Human Brain Function*. 2nd ed. San Diego, CA. Academic Press; 2003; 635–654.
- [6] West J, Fitzpatrick JM, Wang MY, Dawant BM, Maurer CR, Kessler RM, Maciunas RJ, Barillor C, Lemonie D, Collignon A, Maes F, Suetens P, Vandermeulen D, van den Elsen PA, Napel S, Sumanaweera TS, Harkness B, Hemler PF, Hill DL, Hawkes DJ, Studholme C, Maintz JB, Viergever MA, Malandain G, Woods RP. Comparison and evaluation of retrospective intermodality brain image registration techniques. *J. Comput.Assist. Tomogr.* 1997; 21(4): 554–66.