DECREASING FALSE POSITIVES AND NEGATIVES FROM SPATIOTEMPORAL PROCESSING OF FMRI

M. Muge Karaman[1], Daniel B. Rowe[1,2], and Andrew S. Nencka[2]
[1]Department of Mathematics, Statistics, and Computer Science, Marquette University, Milwaukee, WI, United States, [2]Department of Biophysics, Medical College of Wisconsin, Milwaukee, WI, United States

Purpose: In fMRI and fcMRI, many studies have aimed to attenuate the noise through spatial and temporal data processing operations. Although such processing improves the appearance of the data, recent studies[1,2] show that such processing induces artificial correlations that are not of any biological origin. The traditional fMRI and fcMRI models often assume independence between voxels and therefore do not account for the spatial correlation between voxels or temporal correlation within each voxel's time series. As these induced correlations are of no biological origin, they may result in increased Type I/II errors in fMRI and fcMRI if unaccounted for. In this work, we use novel computational tools to theoretically determine these induced correlations through the use of linear operators that can be integrated into the fcMRI analysis; and expand the current complex-valued (CV) fMRI activation model to incorporate an analytically derived exact spatiotemporal covariance structure of the processed time series.

Methods: The development of linear matrix representations of processing operations makes it achievable to determine the exact spatiotemporal covariance (*cov*) structure of the reconstructed images after processing[2]. In such a framework, the vector of the processed time series images, y_T, can be calculated by $y_T=O_Ts_T$, where $s_T=[s_1,s_2,\ldots,s_n]^T$ is a stack of n k-space signal vectors, with each of the n vectors representing a $2p\times1$ image frequency vector, and O_T is the product of the applied operators. With an estimate of the inherent *cov* in acquired data, Γ, the image-space *cov* matrix can be computed by $\mathrm{cov}(y_T)=\Sigma=O_T\Gamma O_T^T$. The image time series correlation (*corr*) matrix, Σ_ρ, (representing the spatial *corr*) and the voxel time series *corr* matrix, Σ_ν (representing the temporal *corr*), which are both considered in fcMRI studies can then be estimated from Σ. The conventional fMRI models detect activations on a voxel-by-voxel basis with the assumption of an identity *cov* structure. In order to incorporate the spatiotemporal *cov* matrix, Σ, into the final analysis, the CV-fMRI model[3] can be expanded as given in Eq. 1, where C_i and S_i are matrices with the cosine and sine of the i^{th} voxel's modeled phase along the diagonal, X_i and β_i are the design matrix and the magnitude regression coefficient vector of the i^{th} voxel.

$$\begin{pmatrix} y_{1R} \\ y_{1I} \\ \vdots \\ y_{pR} \\ y_{pI} \end{pmatrix} = \begin{pmatrix} C_1X_1\beta_1 \\ S_1X_1\beta_1 \\ \vdots \\ C_pX_p\beta_p \\ S_pX_p\beta_p \end{pmatrix} + \begin{pmatrix} \eta_{1R} \\ \eta_{1I} \\ \vdots \\ \eta_{pR} \\ \eta_{pI} \end{pmatrix} \quad (1)$$

This model can be represented in matrix form as $y_T=JX\beta+\eta_T$, where $\eta_T\sim N(0,\Sigma)$. The model's parameters can then be derived through a CV weighted least squares estimation. The matrix representations of processing operations can be very computationally intensive, requiring large amounts of memory. An efficient implementation with the use of matrix partitioning, sparse matrix multiplication techniques, and utilization of the block diagonal forms in matrix multiplication was used to present the results in this study. To theoretically compute the induced *corr*s by smoothing (Sm), Gaussian Sm with fwhm of 3 pixels; and temporal filtering (TF), band pass filtering from 0.01 and 0.1 Hz, a single slice 64×64 image was considered in a time series of 84 repetitions. To illustrate the effects of such processing in fMRI activation statistics, a 64×64 slice is selected with two ROIs designated to have bilateral activation similar to a finger tapping experiment (20s rest, 4 epochs of 8s on, 8s off). CV fMRI data is generated by a multiple regression model with i.i.d. noise $N(0,0.01)$ for 1000 simulations.

Results: The induced spatial *corr*s (in real data), Σ_ρ, of the center voxel (*cv*) by a) Sm, b) TF, c) Sm and TF in the presence of a nonidentity spatial k-space *cov* are given Fig. 1. The spatiotemporal *corr* plots of the *cv* of a 12×12 slice in 16 repetitions are illustrated in Figs. 2a-c. Figs. 3a-b show the activation z-statistics of the processed data (Sm and TF) from voxel-based CV-fMRI model[3], and the generalized CV-fMRI model in Eq. 1.

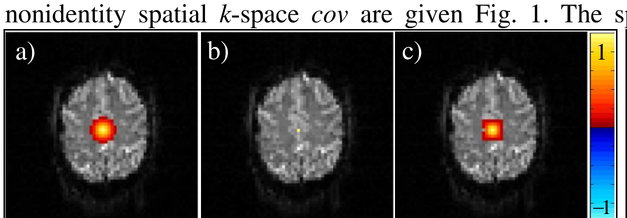

Fig. 1. Spatial correlations induced in real data under different settings.

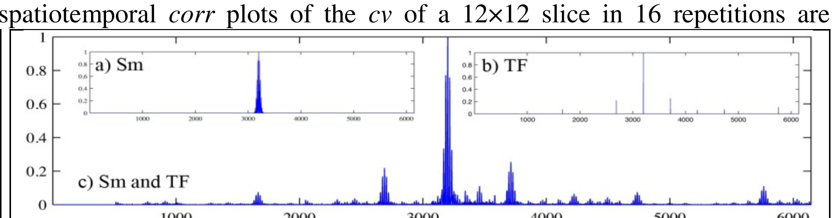

Fig. 2. The computed spatiotemporal correlation plot for the centered voxel.

Discussion: Figs. 1a-1c show that Sm and inherent spatial *corr* result in induced *corr*s in the neighborhood of the *cv*. As expected, Sm induces non-negligible spatial *corr*s whereas TF induces only temporal *corr*s as given in Figs. 2a and 2b. When combined, Sm and TF induce notable spatiotemporal *corr*s in the originally spatially correlated data. Not accounting for the induced *corr*s in the fMRI model produces false negatives as presented in Fig. 3a, and such errors can be avoided with the above generalized fMRI model that accounts for these effects.

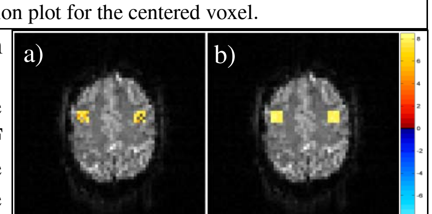

Fig. 3. Activation maps (with Bonferroni correction at α level of 0.05) from the processed data (Sm and TF) with the assumption of a) $\eta_T\sim N(0,\sigma^2 I_2\otimes I_n)$, b) $\eta_T\sim N(0,\Sigma)$.

Conclusion: The proposed model with its application to fcMRI and fMRI analyses enables researchers to analytically quantify artificial correlations induced by data processing, and draw more accurate and reliable functional connectivity and cognitive brain activity results.

References: **1.** Nencka et al. J. Neurosci. Meth 2009;181:268-282. **2.** Karaman et al. ISMRM. 2013;21:2232. **3.** Rowe, Logan. NeuroImage 2004;23:1078-1092.