TEMPORAL PROCESSING OF FMRI DATA INDUCES FUNCTIONAL CORRELATIONS AND POTENTIALLY ALTERS FUNCTIONAL ACTIVATIONS

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Purpose: Temporal processing, such as dynamic B-field correction, slice timing correction, image registration and temporal filtering, is a common practice in fMRI and functional connectivity MRI (fcMRI). Although such processing yields "improved" results, the processing may fundamentally alter the signal and noise properties of the data. This work mathematically models time series and spatial preprocessing as linear operators by further expanding the previous work that considered the effects of individual preprocessing.[1] The effects of intra-acquisition decay (T_2^*) and longitudinal relaxation (T_1), the Fourier anomalies (FAs) that the signal is subject to, are also corrected by being incorporated into the Fourier reconstruction. The model allows one to compute exact image-space statistics to be included into the statistical fMRI models, and thus contributes to produce more accurate activation statistics.

Theory: The vector of reconstructed image, y, has been computed with $y = Os$, where O signifies the series of linear operators, and $s=(s_1, \dots, s_p)'$ is the vector of k-space observation for an image of p voxels.[1,2] This linear framework can be extended to include temporal processes by considering $s_T = (s_{11}, s_{12}, \dots, s_{12p}, s_{21}, \dots, s_{n2p})'$, which is a stack of n k-space signal vectors, with each n of them representing one $2p$ dimensional time point image vector. The vector, y_t, can then be computed by $y_T = O_T s_T$, where O_T is the product of k-space operators, K, reconstruction operators, R, image-space operators, I, and time-series operators, T, as $O_T = TIRK$. The time series operators can be calculated as a Kronocker product between the individual processing operators and an identity matrix matching n. With the known spatial covariance matrix, Γ, the image-space covariance matrix can be computed as $\Sigma = O_T \Gamma O_T^T$. Σ is of dimension $2pn \times 2pn$ with diagonal covariance matrix blocks of the individual images. The image time series covariance matrix, Σ_ρ, can be estimated as the average of the blocks of Σ. The voxel time series covariance matrix, Σ_v, of the i^{th} voxel that is used in fMRI activation models can be calculated by first reordering Σ, and then extracting the corresponding i^{th} diagonal block of the ordered Σ.

Methods: The implemented operators for a 6×6 ROI in a single slice in a time series of 8 repetitions are: censoring, permuting the acquired real (Re)/imaginary (Im) pairs, Nyquist correction, and apodization (in K); reconstruction, dynamic B-field, motion and FA correction (in R); smoothing (in I); temporal filtering (in T). T_1 (>0.042s, <4s), T_2^* (> 0.832s, < 2.2s), and ρ (>1e-6, <1) were considered as Shepp-Logan phantom at 3.0 T. ΔB was a linear gradient from 0 to 2.5×10^{-6}T. An echo planar pulse sequence (eesp=0.72ms, TE=40.4ms, TR=1s) was assumed. Γ is assumed to be identity. Motion was modeled as a cumulative shift of one-pixel in both directions, and rotation of 2°. A temporal band pass filtering from 0.01 and 0.1 Hz was utilized. Gaussian smoothing with fwhm of 4 pixels was utilized. Spherical simulated phantom data with $N(0,1)$ real-imaginary noise and ρ being 1 inside and 0 outside was generated with the same tissue and imaging parameters.

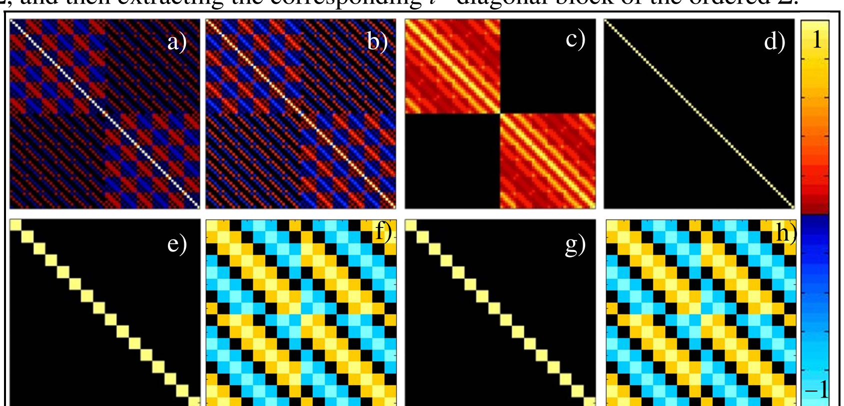

Fig. 1: (a)-(d): Σ_v for the centered voxel. (e)-(h): Σ_ρ. The considered operators: T_2^*correction (a and e); T_1correction(b and f); apodization (c and g); filtering (d and h).

Results & Discussion: Figs. 1(a)-(b) and Figs. 1(e)-(h) show $\Sigma_{\rho s}$ and $\Sigma_{v s}$ for the center voxel derived from Σ resulting from the operators: a, e) T_2^*correction; b, f) T_1 correction; c, g) apodization; d, h) filtering. T_1 and T_2^* correction leads to spatial correlations as shown in Figs. 1(a) and (b). Apodization yields increased spatial correlation of a voxel with its neighbors within Re and Im parts. Temporal filtering does not alter spatial correlations since the process itself is temporal. Correcting T_2^* effects and apodization does not induce time series correlations whereas alterations arise in the voxel time series correlations with T_1 effects correction and temporal filtering. Figs. 2(a) and (b) show the sample image-space correlations of the center voxel of the simulated agar phantom data, and sample temporal correlation matrix resulting from smoothing.

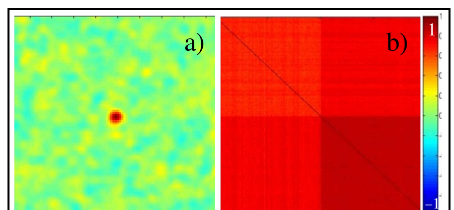

Fig. 2: a) Sample spatial correlation map of the center voxel, b) Sample temporal correlation matrix when spatial smoothing is considered.

Conclusion: This exact, analytical method provides researchers to prospectively evaluate the effects of a selected data pipeline. As such, the optimal performing of data processing steps may be determined. With the knowledge of the correct noise properties of the reconstructed, corrected and processed fMRI data, the computed activation statistics can also be improved.

References: **1.** Nencka AS, Hahn AD, Rowe DB. A mathematical model for understanding the statistical effects of k-space (AMMUST-k) preprocessing on observed voxel measurements in fcMRI and fMRI. J. Neurosci. Methods. 2009;181:268-282. **2.** Rowe DB, Nencka AS, Hoffman RG. Signal and noise of Fourier reconstructed fMRI data. J. Neurosci. Methods. 2007;159:361-369.

Temporal Processing of fMRI Data Induces Functional Correlations and Potentially Alters Functional Activations

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INTRODUCTION

Temporal processing is a common practice in fMRI and functional connectivity MRI (fcMRI) studies as a way to "improve" the resulting images. However, such processing alters the signal and noise properties of the data and could have severe effects on the statistical maps, including functional activations, computed from the processed images. This work mathematically models time series and spatial preprocessing as linear operators by further expanding the work that considered the effects of individual preprocessing.[1] The effects of intra-acquisition decay (T_2^*) and longitudinal relaxation (T_1), the Fourier anomalies (FAs) that the signal is subject to, are also corrected by being incorporated into the Fourier reconstruction process. The model allows one to compute exact image-space statistics to be included into the statistical fMRI models, thus contributes to more accurate functional activation statistics.

METHODS

The vector of a single reconstructed image, y, has been computed with $y = Os$, where O signifies the series of linear operators, and $s=(s_1,\ldots,s_{2p})'$ is the vector of k-space observation for an image of $p = mn$ voxels.[1,2]
This linear framework can be extended to include temporal processes and the vector, y_T, can be computed by $y_T = O_T s_T$, as shown in Fig. 1.[3]

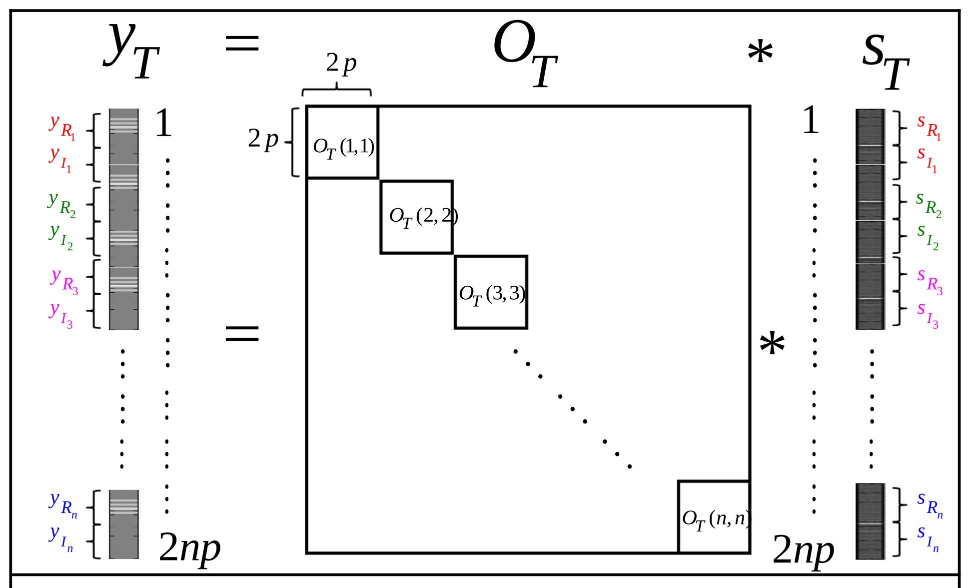

Fig. 1: Illustration of $y_T = O_T s_T$.

$$O_T = TIRK$$

- K: k-space ops.,
- R: reconstruction ops.,
- I: image-space ops.,
- T: time-series ops.

T include:

- Slice timing correction (STC),
- Temporal filtering (TF),
- Image registration (IR),
- Dynamic B-field correction (BFC).

STC and TF can be included into T with the use of the Fourier shift theorem:

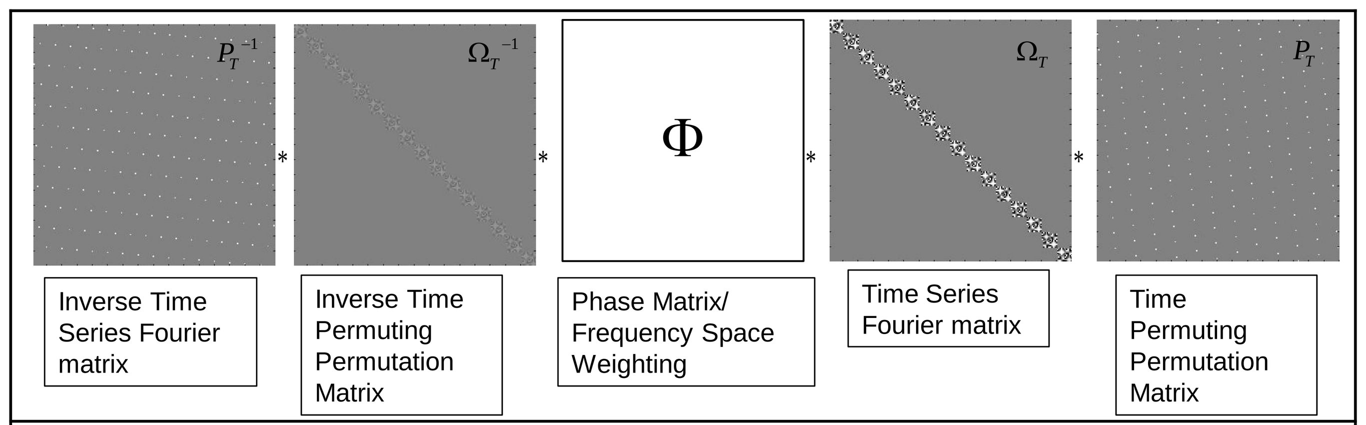

Fig. 2: Slice timing correction and temporal filtering operators for a 6×6 example.

IR as well as BFC and FA correction can also be performed through incorporation into the time-series reconstruction operator, R.

With the known $E(s_T)=s_0$ and $\mathrm{cov}(s_T)=\Gamma$, the expected value and covariance of y_T can be determined by $E(y_T)=O_T s_0$ and $\Sigma=O_T\Gamma O^T_T$, respectively.

Image time series cov. matrix:

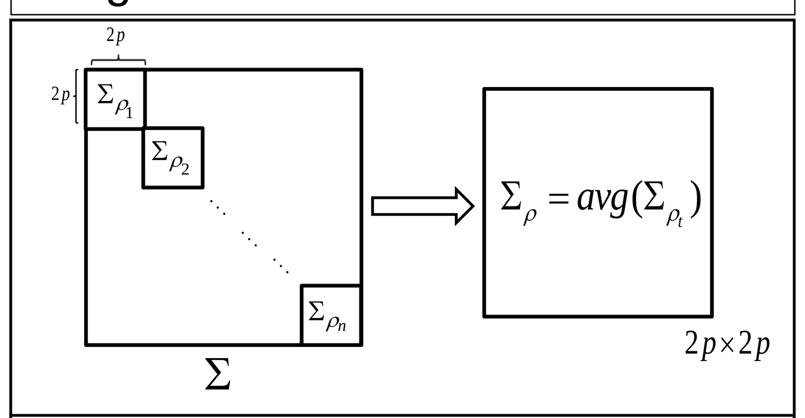

Fig. 3: Illustration of computing Σ_ρ for a 6×6 example.

Voxel time series cov. matrix:

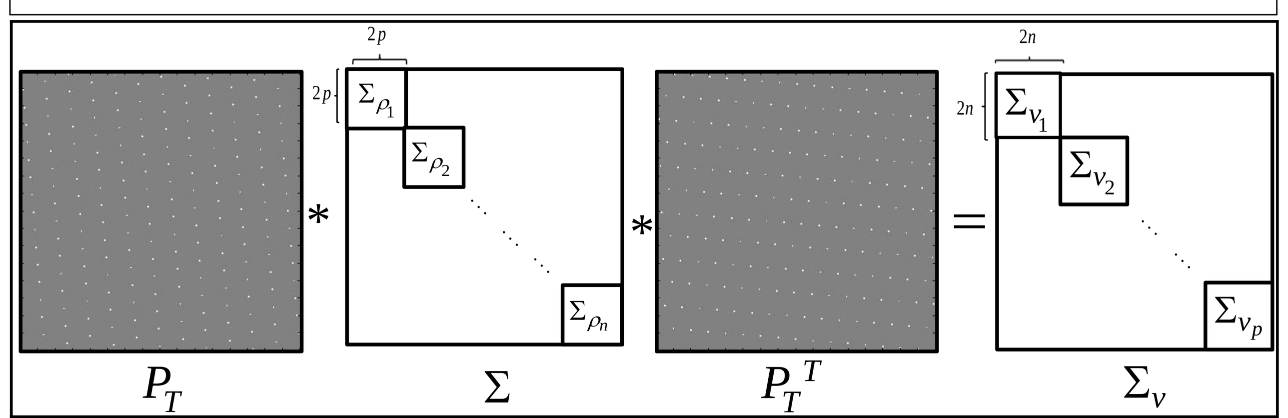

Fig. 4: Illustration of $\Sigma_v=P_T\Gamma P_T^T$ for a 6×6 example.

RESULTS AND DISCUSSION

The theoretical results, given in Fig. 5 were computed for a 6×6 ROI in a single slice in a time series of 8 repetitions. The implemented operators are: censoring, permuting the acquired Re/Im pairs, Nyquist correction, and apodization (in K); reconstruction, dynamic B-field, motion and FA correction (in R); smoothing (in I); temporal filtering (in T). T_1 (>0.042s, <4s), T_2^* (> 0.832s, < 2.2s), and ρ (>1e-6, <1) were considered as Shepp-Logan phantom at 3.0 T. ΔB was a linear gradient from 0 to 2.5×10^{-6}T. An EPI pulse sequence (eesp=0.72ms, TE=40.4ms, TR=1s) was assumed. Γ is assumed to be identity. A temporal band pass filtering from 0.01 and 0.1 Hz and Gaussian smoothing with FWHM of 4 pixels was utilized.

Fig. 6 shows the effects of smoothing on the computed correlations of a spherical simulated phantom data that was generated with $N(0,1)$ Re-Im noise and ρ being 1 in and 0 out. The same imaging parameters were used.

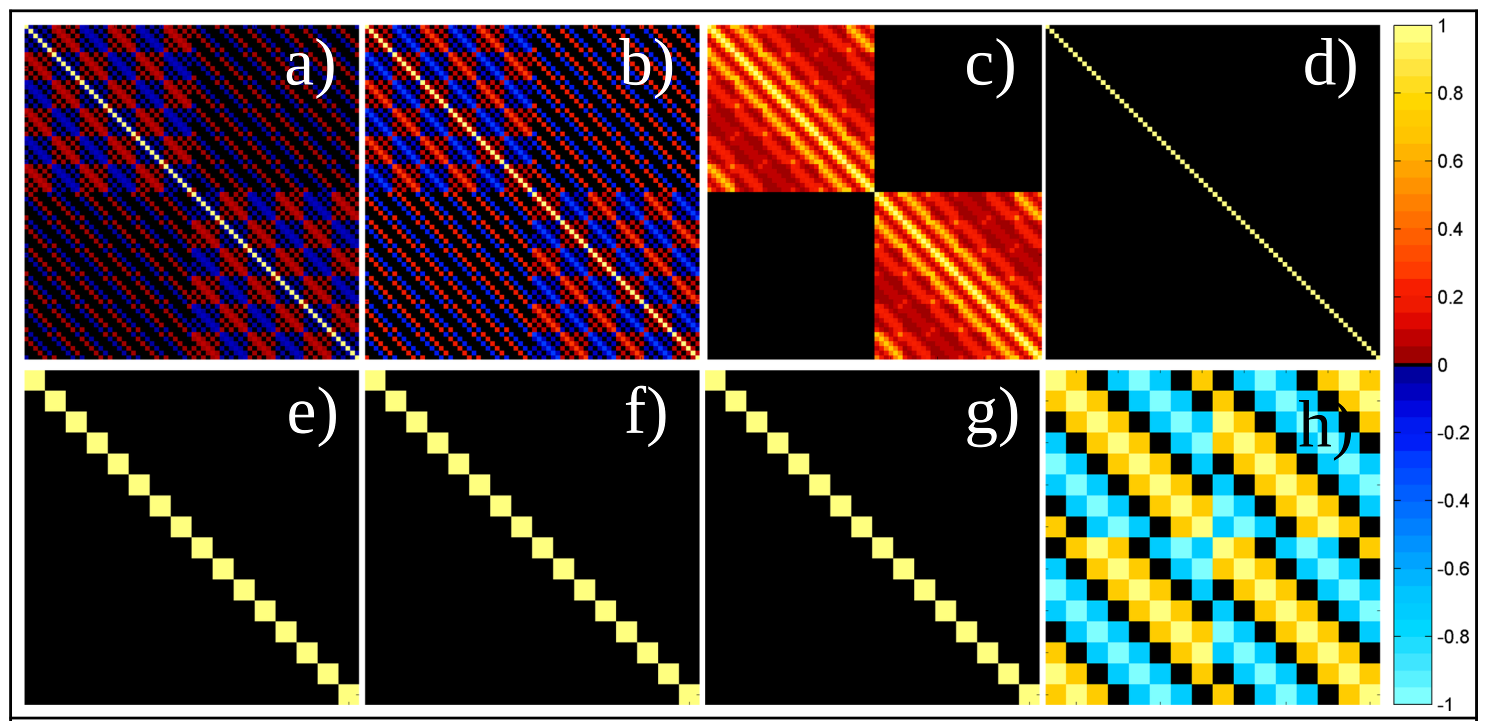

Fig. 5: a)-(d): Voxel time series correlation matrix for the centered voxel. (e)-(h): Image time series correlation matrix. The considered operators: T_2^* correction (a and e); T_1 correction (b and f); apodization (c and g); filtering (d and h).

- Correcting T_1 and T_2^* effects changes the noise structure and induces local spatial correlation as shown in Figs. 5(a) and (c).
- Apodization yields spatial correlation within Re and Im pairs as given in Fig.5(c).
- Temporal filtering induces temporal correlation as illustrated in Fig. 5(h); and does not alter spatial correlation as given in Fig. 5(d) since the process itself is temporal.
- Smoothing yields to spatial correlation of a voxel with its neighbors as well as temporal correlation as given in Figs. 6(a) and (b).

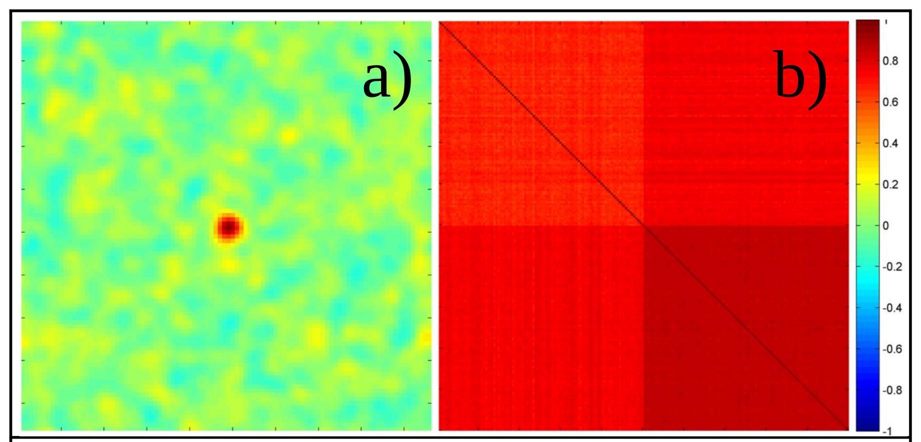

Fig. 6: a) Sample spatial correlation map of the center voxel, b) Sample temporal correlation matrix when spatial smoothing is considered.

CONCLUSION

This exact, analytical method provides researchers a prospective evaluation of the effects of a selected data pipeline. With the knowledge of the correct noise properties of the reconstructed, corrected and processed fMRI data, the computed activation statistics and the medical statements that may be drawn can also be improved.

REFERENCES

1. Nencka AS, Hahn AD, Rowe DB. A mathematical model for understanding the statistical effects of *k*-space (AMMUST-*k*) preprocessing on observed voxel measurements in fcMRI and fMRI. J. Neurosci. Methods. 2009;181:268-282. **2.** Rowe DB, Nencka AS, Hoffman RG. Signal and noise of Fourier reconstructed fMRI data. J. Neurosci. Methods. 2007;159:361-369. **3.** Nencka, A.S. Improving fcMRI blood oxygenation level dependent (BOLD) signal through the characterization of processing effects. Medical College of Wisconsin Ph.D. Thesis, 2009.