Unsupervised modelling of physiological noise artifacts in fMRI dataφ

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Introduction: It has been shown that including nuisance regressors to account for movement [1] and physiological artefacts [2] in General Linear Models (GLM) for the analysis of fMRI data provides an efficient way to reduce correlations and non-normality in the residuals [3]. In order to model the physiological effects using the RETROICOR method [2] the respiratory and cardiac phase and frequency needs to be acquired. This however may not always be feasible. In the current study we propose a way to obtain such nuisance regressors without measures of respiratory and cardiac cycles. This is based on the observation that residual variance in fMRI data is most pronounced in regions strongly contaminated by cardiac noise [4], specifically a thresholded SPM of the residual variance in fMRI studies have remarkable resemblance towards angiograms. By capturing structure of the time series within this region it may be possible to extract time functions that describe physiological noise in the specific data set.

Methods: Sixteen datasets each consisting of 381 volumes of forty slices (matrix size 64x64) was acquired on a 3T scanner (Siemens Trio) using a GRE EPI sequence: voxelsize: 3mm isotropic, TE=30ms, TR=2.37s. During the scanning the subject was stimulated visually (reversing checkerboard (expanding ring and rotating wedge). Each rotation/expansion lasted 30 seconds. Following rigid body-realignment using SPM2, each dataset was subsequently analysed with six different general linear models: "Simple" including baseline plus sine and cosine of the first three harmonics of the (1/30s) oscillation. "60sec-HP" similar to "Simple", but now including a high-pass filter modelled as a discrete cosine set with a minimum period of 60s. "SPM2-AR(1)" similar to "60sec-HP" but with whitened residuals using a global AR(1) model estimated in a mask defined by the voxels where a significant effect of the paradigm was observed (this is the recommended SPM2 procedure). "NVR-ox" similar to "60sec-HP" but including several extra nuisance regressors for modelling the autocorrelation. A Volterra expansion of the movement parameters giving was used to model residual movement effects including spin-history effects [1] (24 regressors). Respiration and cardiac noise was modelled using 16 RETROICOR [2] regressors (5 cardiac harmonics and 3 respiratory harmonics). The RETROICOR regressors are a Fourier basis spanned by the oscillations of the aliased frequencies. The cardiac frequency and phase was determined using the scanner pulsoximeter. The respiratory phase and frequency was measured using the scanner respiratory belt. "SVD+motion" similar to "60sec-HP" but including the 24 regressors to model residual movement and a variable number of nuisance SVD regressors constructed using a method described later. "SVD+NVR-ox" like "NVR-ox" but including a variable no. SVD regressors. The SVD regressors where created by fitting a model without these additional regressors and using the residual variance in this test to identify the 7.5% voxels (approx. 5000 voxels) that have the most residual variance. Singular Value Decomposition (SVD) was then performed on a filtered version of these time series (filtered using the high pass filter and the nuisance regressors from the original model but not the paradigm to reduce bias). The additional regressors are the time series corresponding to K largest singular values. In order to determine the number of nuisance regressors (K) we use the Laplace evidence approximation [5]. Because fMRI data is spatially correlated the number of independent observations is not equal to the number of samples (voxels) that entered the SVD therefore the number of time points was used as the number of independent observations (equivalent to pre-whitening using SVD).

After the analysis, Statistical Parametric Mapping diagnosis (SPMd) [6] was used to test the whiteness ("Dep" for arbitrary stationary dependence and "Corr" for AR(1)-type autocorrelation) and normality "Norm" of the residuals, from the different models.

Results: The results of the SPMd of the six different analyses of the 16 different sessions and the no. components for the "SVD+motion" model are summarized in Figure 1, and for session 8 the SPMd images from the analyses are shown in Figure 2. When comparing the SVD regressors (from the "SVD+motion" method) it was found that on average 61% of the variance of the first harmonic cardiac RETROICOR regressors was explained by the SVD regressors. For the 2., 3., 4. and 5. harmonics the corresponding numbers were 20%, 5%, 2% and 1%. Similarly the numbers for the three respiratory harmonics were 12%, 2% and 2%. When comparing these numbers it should be noted that it is impossible to explain the total variance as the RETORICOR set is an orthogonal basis set and the number of SVD regressors is lower than the no. of RETROICOR regressors. The strong correlation between the first order harmonics should be noted because this is also where the largest effect is observed in the data.

Discussion: In this study we show that the suggested method reduces non-normality and correlation in the residuals equivalent to or better than the RETROICOR method, however our method does not include measures of the respiratory and cardiac cycles. The number of regressors used in the suggested method (3-12) is significantly lower than the no. regressors in the RETROICOR method, thus suggesting that the regressors provides a more efficient way to correct for correlations and non-normality. The obtained regressors show strong correlation towards regressors obtained using the RETROICOR method. Furthermore, the effects are in fact present in regions related to the visual paradigm even though the visual cortex is normally not regarded as a region suffering from heavy contamination by cardiac and respiratory noise.

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References: [1] Friston et al. 1996, MRM, **35**, 346-355., [2] Glover et al. 2000, MRM, **44**, 162–7., [3] Lund et al. 2005, NeuroImage, Aug 10 In Press., [4] Lund et al. 2001 9'th ISMRM., [5] Minka, 2000, Techinal report 514, MIT., [6] Luo et al. 2003, NeuroImage, **19**, 1014–32., [7] Genovese et al. 2002, NeuroImage **15**, 870-878.

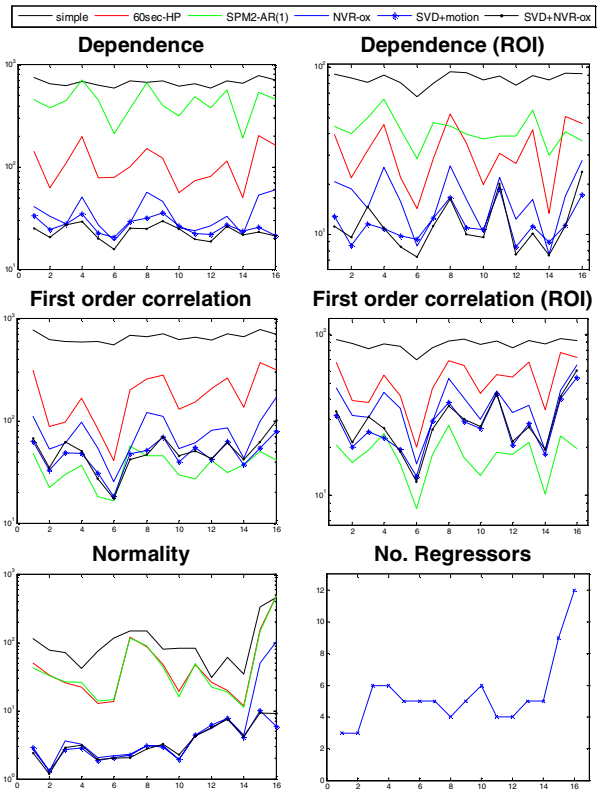

Figure 1: The three figures to the left show for the three differe tests, across the 16 datasets, the factor by which rejections exceed t expected number. The different curves correspond to several differe analysis of the same dataset. The dataset used in Figure 2 is fro session 8. The two figures to the right show the same in a region interest (ROI) defined by an F-test where the paradigm was activate ($p<0.05$ FDR corrected [7]). Due to the relative few no. voxels in t ROI's the normality test did not have enough power in this case. T figure to the bottom right shows the estimated no. regressors for t "SVD+motion" model over the 16 datasets. The no. regresso estimated where higher for sessions with more movement (session and 16) thus indicating that the method is able to correct more when is needed. It is seen that the difference between the "SVD+motio and "SVD+NVR-ox" methods are only marginal.

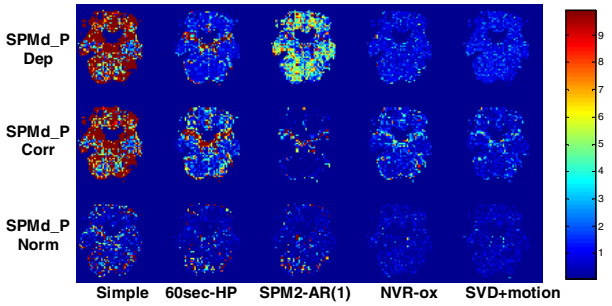

Figure 2: The figure shows the output of a SPM-diagnosis (log(values) from 5 different analyses of the same dataset (horizontal). It seen that the two rightmost models have similar and best overa performance. Only these two models are able to reduce higher ord correlations and non-normality sufficiently in problematic region The "SVD+NVR-ox" model is almost identical to "SVD+motion".