

# Voxel-wise Regressor Selection for Physiological Noise Correction with RETROICOR

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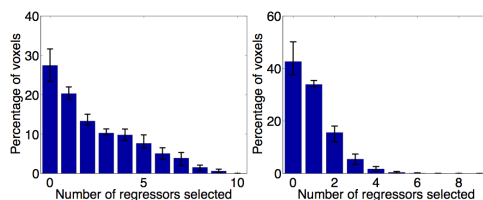
**Introduction:** Correcting physiological noise is important for the analysis of functional images, especially at higher fields. The RETROICOR method [1] is a common and effective way of removing physiological noise based on regressing out signals using a set of Fourier series constructed from independent physiological recordings (e.g. pulse-oximeter, respiratory bellows). However, the best set of regressors to use depends on the region of the brain being studied [2] and the acquisition used. Furthermore, several new types of regressors have recently been proposed (e.g. cardiac-respiratory interactions [3], RVT [4], heart-rate [5]) leading to a very large set of potential regressors. Using all these regressors is problematic due to loss of degrees of freedom and correlation with stimulus-related regressors. We propose a method that uses the Bayesian Information Criterion to adaptively select the most suitable set of regressors for each voxel, thus reducing the number of regressors needed per voxel.

**Methods:** The Bayesian Information Criterion (BIC) is defined as  $BIC = -2 \ln(L) + k \ln(N)$ , where  $N$  is the number of samples (timepoints),  $k$  is the number of parameters (regressors) and  $L$  is the (maximized) likelihood. Different models, with different sets of regressors, can be compared where the preferred model has the lowest BIC. For two GLM models, one with  $k$  regressors and the other with  $k+1$  regressors, the latter model is preferred by BIC when  $RSS_{k+1} / RSS_k < N^{-1/N}$ , where  $RSS$  is the residual sum of squares. This is used to iteratively create a set of selected regressors where, in each iteration, a new regressor is added as long as it passes the BIC test. The candidate regressor at each iteration is the one that explains the greatest amount of the remaining variance. In this way the set of regressors is built up for each voxel, one regressor at a time, until the BIC test fails.

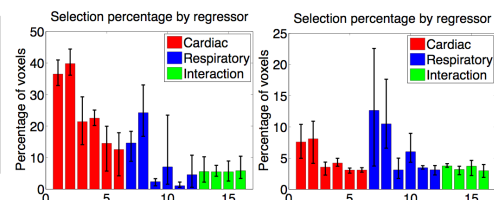
The method, written in MATLAB, was tested using resting (eyes closed) FMRI datasets (from a Siemens 3T Trio) with very different TRs: Dataset 1 is GE-EPI, 1 slice, 128x128 matrix, 2x2mm, TE/TR=30/152ms, 2000 timepoints, 7 healthy subjects; Dataset 2 is GE-EPI, 128x128 matrix, 44 slices, 2x2x3.125mm, TE/TR=30/3000ms, 100 timepoints, 3 healthy subjects. Physiological recordings using pulse-oximeter and respiratory bellows were made and processed to create 16 regressors from cardiac and respiratory phase ( $\phi_C$  and  $\phi_R$ ) [1]: three orders of Fourier series for both cardiac and respiratory and first-order interactions [3];  $\sin/\cos(A.\phi_C)$ ,  $\sin/\cos(A.\phi_R)$ ,  $\sin/\cos(\phi_C \pm \phi_R)$ , with  $A=1,2,3$ . The method was run at each voxel separately to select a subset of the 16 regressors, based on the BIC, as described above.

**Results:** Figure 1 is an example image from Dataset 2 showing the number of selected regressors at each voxel. It can be seen that it is extremely rare for more than 6 regressors to be chosen, and that often 2 or less regressors are used. This is confirmed in Figure 2 where the histograms of number of selected regressors are shown for each dataset. The maximum number of regressors that are ever chosen is 10 and this only occurs in 0.014% of voxels. Figure 3 shows how often each regressor is selected as part of the BIC subset. It can be seen that each regressor contributes to some subsets, with the most commonly selected being the cardiac regressors, the low-order respiratory regressors and the interaction regressors. However, even the least favoured regressors are chosen by a significant fraction of voxels. Finally, Figure 4 shows example images of the relative proportion of explained variance by the BIC-selected and full sets of regressors. A very

similar amount of variance is explained, especially in the areas of high physiological noise, even though the full set of regressors is substantially larger. The amount of variance explained per regressor in the different datasets is given in table 1, which shows that the regressors excluded by the BIC-selected set explain much less variance than included ones, and in dataset 2 they explain less variance than a



**Figure 2: Number of regressors selected by BIC (left=dataset 1; right=dataset 2). Errorbars give total range**



**Figure 3: Percentage of voxels selecting individual regressors (left=dataset 1; right=dataset 2). Errorbars give total range.**

randomly constructed regressor would be expected to explain.

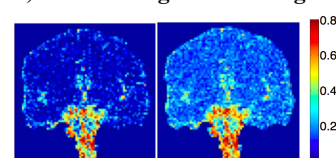
**Discussion:** Results show that a substantially smaller subset of regressors can be used to explain the majority of the physiological noise at each voxel. There is a high degree of consistency in the number of selected regressors across subjects and datasets, and it is also clear that each regressor serves a useful function at some locations. Consequently, no regressors should be eliminated from the potential set of regressors. Furthermore, a very similar amount of variance is explained using either the full or BIC-selected set, with the excluded regressors explaining less variance on average than would be expected by a randomly constructed regressor (which would on average explain  $1/(N-k)$  of the remaining variance).

Selecting a small subset of regressors from a larger set is advantageous because it (a) reduces the loss of degrees of freedom in the statistics, which can be considerable for higher-order terms, (b) makes overlap between the stimulus-related regressors and the physiological noise regressors less likely, and (c) allows a wider range of potential regressors to be used. It is therefore feasible with this method to consider higher-order interaction regressors (number of regressors is quadratic in order) and different delayed versions for RVT and heart-rate regressors, all of which may be crucial for brainstem or spinal studies and work at higher fields. Investigating the use of these regressors, and the incorporation of this method with pre-whitened statistical estimation, are topics of ongoing work.

**References:** 1. Glover et al, MRM 44(1), 2000; 2. Harvey et al, JMRI, 2008 (early view); 3. Brooks et al, NeuroImage 39(2), 2008; 4. Birn et al, NeuroImage 31(4), 2006; 5. Chang et al, NeuroImage, 2008 (early view).

Regressors	BIC-selected	All	Unselected	Random
Dataset 1	1.59	0.52	0.10	0.05
Dataset 2	4.27	1.22	0.83	0.96

**Table 1: Mean variance explained per regressor**



**Figure 4: Amount of explained variance in dataset 2 (left=BIC-selected; right=all)**