# Gram-Schmidt Orthogonalization to Reduce Aliased Physiologic Noise in Low Sampling Rate fMRI data.

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**Introduction**

When timeseries fMRI data are sampled below the Nyquist frequency for respiratory and cardiac fluctuations, these effects can alias into the resulting data, increasing the temporal variance(1). Although it has been shown there are correlations in low-frequency temporal fluctuations between functionally related brain regions (1,2), these aliased effects of cardiac and respiratory noise reduce the specificity of the observed correlations in low sampling rate, multi-slice data.

In this study, we show that Gram-Schmidt orthogonalization can be used to remove the aliased effects of respiratory and cardiac-cycle noise. The cross correlation coefficient can be expressed in a vector formalism in the following way: Assume that the N time points which constitute independent measurements of the MR signal of a given pixel in the brain form an N-dimensional vector (where the basis vectors are not necessarily orthogonal). Then, the cross correlation between two pixels can be described as the normalized dot, or inner-product of the two vectors.

$$cc(r_i, R) = \frac{\vec{r_i} \bullet \vec{R}}{|\vec{r}_i||\vec{R}|}$$

where R is the reference pixel and $r_i$ is the pixel for which we wish to calculate the correlation coefficient. If two pixels have no correlation, this is equivalent to saying that they are orthogonal in our vector framework.

If we wish to remove the projection of respiratory and cardiac-cycle dependent effects from our cross-correlation calculation, we can simply subtract the projection of these effects from the reference function:

$$\vec{R}' = \vec{R} - (\vec{R} \bullet \vec{C})\,\vec{C} - (\vec{R} \bullet \vec{P})\,\vec{P}$$

where $\vec{C}$ is a timeseries which represents cardiac effects and $\vec{P}$ is a timeseries which represents respiratory effects. In this case, the corrected correlation coefficient becomes:

$$cc'(r_i, R) = \frac{\vec{r_i} \bullet [\vec{R} - (\vec{R} \bullet \vec{C})\,\vec{C} - (\vec{R} \bullet \vec{P})\,\vec{P}]}{|\vec{r}_i \| \vec{R} - (\vec{R} \bullet \vec{C})\,\vec{C} - (\vec{R} \bullet \vec{P})\,\vec{P}|}$$

$$= \frac{\vec{r_i} \bullet \vec{R}}{|\vec{r}_i \| \vec{R}|} - \frac{\vec{R} \bullet \vec{C}}{|\vec{R} \| \vec{C}|} \frac{\vec{r_i} \bullet \vec{C}}{|\vec{r}_i \| \vec{C}|} - \frac{\vec{R} \bullet \vec{P}}{|\vec{R} \| \vec{P}|} \frac{\vec{r_i} \bullet \vec{P}}{|\vec{r}_i \| \vec{P}|}$$

$$= cc(r_i, R) - cc(r_i, C) \bullet cc(R, C) - cc(r_i, C) \bullet cc(R, C)$$

**Methods**

To validate this method, it is necessary to determine $\vec{C}$ and $\vec{P}$ for the expression above. Tissue near large arteries shows a large coupling to the cardiac cycle, while pixels near large veins show large coupling to the respiratory cycle. Thus, we can take a pixel in the region of a large artery to be an *estimator* of $\vec{C}$ and a pixel in the region of the superior sagittal sinus to be an estimator of $\vec{P}$.

Using a 1.5T GE Echospeed MRI scanner (GE Medical Systems, Waukeshau, WI), timeseries BOLD-weighted data were acquired in four single slice axial scans on the same subject with the following parameters: acquisition: Gradient-recalled echo echoplanar, echo time=50ms, matrix= $64 \times 64$, field-of-view= $24\text{cm} \times 24\text{cm}$, receiver bandwidth=125kHz, slice thickness=5cm. The axial slice was through primary motor cortex and was selected such that both a sizeable artery and vein were apparent in the slice (this was verified with a MR angiography scan taken of the chosen location). Four resting state scans were taken, varying the repetition time from 133.4ms, which samples both cardiac and respiratory-related noise directly, to 4s, where cardiac and respiratory-related effects will be aliased. All data were digitally filtered to remove fluctuations greater than 0.08Hz.

It has been shown that the remaining temporal fluctuations are highly correlated between right and left precentral gyrus in rapidly sampled scans(1,2). Regions-of-interest were drawn in right precentral gyrus (rPrG), left precentral gyrus (lPrG), and right middle frontal gyrus (rMFG). A pixel near the large artery in the slice was chosen as $\vec{C}$, and a pixel near the large vein was chosen as $\vec{P}$. The standard correlation coefficient and the cardiac and respiratory-effect orthogonalized correlation coefficient were then calculated between left precentral gyrus and right precentral gyrus, and between left precentral gyrus and right middle frontal gyrus, for all four scans.

Table 1A Table of cross-correlation (cc) and corrected cross-correlation ($cc'$) between left precentral gyrus and right precentral gyrus (rPrG) and left precentral gyrus and right middle frontal gyrus (rMFG).

| Repetition time | $cc_{rPrG}$ | $cc_{rMFG}$ | $cc'_{rPrG}$ | $cc'_{rMFG}$ |
|---|---|---|---|---|
| 133.4ms | 0.55 | 0.19 | - | - |
| 600ms | 0.66 | 0.36 | 0.55 | -0.18 |
| 2000ms | 0.77 | 0.25 | 0.68 | -0.11 |
| 4000ms | 0.51 | 0.04 | 0.51 | 0.00 |

**Results and Discussion**

Table 1 shows the resulting standard correlation coefficient and the corrected correlation coefficient. Columns 2 and 3 of Table 1A shows that the uncorrected correlation coefficient becomes less specific to the right precentral gyrus as the sampling rate becomes lower than cardiac (~1Hz) and respiratory (~.3Hz) rates. Column 4 and 5 of Table 1 was calculated using our correction technique and shows that specificity to the homologous region of motor cortex is preserved while effectively reducing the correlation to the right middle frontal gyrus, which is putatively uninvolved in simple motor function. Presumably, the correlations observed between lPrG and rMFG were from aliased cardiac and respiratory noise.

**Conclusion**

We have shown that temporal fluctuations from brain regions with a high coupling to cardiac and respiratory-cycle noise can be used as estimators of the aliased effects from these sources in low-sampling rate BOLD-weighted timeseries data. Gram-Schmidt orthogonalization technique can be used effectively to remove the aliased effects. Although the illustration here was directed at resting-state data, this technique is equally applicable in fMRI data as well.

**References**

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2. Biswal, B., *et al., Magn. Res. Med.*, 34,537, 1995.