Physiological noise correction for the GE scanners at CFMRI
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Overview:

This document describes the procedure of using **PHYSIO©** program to remove cardiac and respiratory noise from fmri datasets. The fmri datasets can be either BOLD data acquired with GE product EPI or ASL data acquired with our in-house SPEP. A previously reported retrospective image-based method (RETROICOR)[1,2] is used for correcting the GE BOLD data, and extensions[2] of this method are used for the reduction of physiological noise in ASL data.

The output of the **PHYSIO©** program can be either an AFNI brik containing the physiological noise corrected dataset or a set of physiological noise regressor files. The latter is designed for users who wish to regress out physiological noise using their own deconvolution algorithms.

NOTE:
1. <u>We currently do NOT support event related design for ASL</u>.
2. <u>The efficacy of respiratory noise removal based on CO2 data has NOT been fully tested.</u>

System Requirement and Software Installation
1. SYSTEM REQUIREMENTS:
   - Redhat linux 8.0 or above recommended.
   - Matlab v.14 service pack 1 or above is required. Afni v2.55j above is required.
   - Minimum 512Mb available system memory required, 1Gb recommended.

2. DOWNLOAD and INSTALLATION:
   If on **cfmri** or **fmriserver**, include in your startup.m the following line:
   - addpath /var/www/html/fmap/physio
   Otherwise
   - Download physio.tar from http://cfmri.ucsd.edu/download/ .
   - Untar the file (on Linux: tar –xvf physio.tar).
   - Add the physio folder to Matlab path.
     (To do so, you can add a line "addpath yourpath/physio" in your startup.m)

Required Data Files
1. fMRI data sets
   - For GE EPI: DICOM files or AFNI BRIKs
   - For ASL: Pfiles or AFNI BRIKs

2. The following two physiological data files (containing pulsox, respiratory effort, or CO2 data):
   - SubjectID_real_data.txt

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[1] Glover et al , Magn Reson Med 44(1): 162-7, 2000
[2] Khaled Restom, Yashar Behzadi and Thomas T Liu, submitted for review,2005 (ttliu@ucsd.edu)

- SubjectID_kHzdata.txt

Physiological Noise Correction (Step-by-step Instructions)

1. Create AFNI Briks for your fMRI dataset
   - for GE EPI : **to3d -prefix prefixname -time:zt #slices #reps TR alt+z i***
   - for ASL: **gr Pfilename prefixname** , then **a3** or **d3** as desired
     (for information on a3 and d3, please attend an ASL training session at the center.)

2. Pre-process physiological data (combine real_data.txt and kHzdata.txt)
   - Start Matlab
   - ***physioDataProcess(real_data, kHzdata);***
     Example:
      physioDataProcess('subject1_real_data.txt','subject1_kHzdata.txt')
   - Follow the instructions (see Appendix A)

3. Remove physiological noise
   - OPTION 1: Deconvolution
     graphical user interface GUI (Appendix B)
      physioGUI;

     or, command line command (Appendix C)
     physio(brikIn, physiofile, brikOut, dummy, ref, TR, model, [pflag], [anatmask]);

   - OPTION 2: No deconvolution
     This option is designed for users who wish to regress out physiological noise using their own deconvolution algorithms. Thus the program does not perform deconvolution. The outputs are a set of text files (.1D extension), each of which containing a physiological noise regressor for one slice.
     physioRG(brikIn, physiofile, fileOut, dummy, TR, [pflag]);

APPENDIX A: physioDataProcess

1. You will see the following message in MATALB command window:
   >> physioDataProcess('real_data.txt','kHzdata.txt')
   Data check complete! (kHz data matches 40 Hz data duration)
   Output written to File: real_dataProc.txt

   If your physiological data file contains data from multiple scans,
   it will need to be parsed into separate files, each containing one scan only!

   Would you like to proceed to parsing the physiological data? y/n [y]

   Visually check the TTL plot on the screen. If it contains TTL pulses from more than one scan (e.g. Figure on the right contains 6 individual scans), choose "y" and go to step 2; otherwise choose "n" and go to step 5. Often times, TTL plot also contains TTL pulses from prescans, you will then need to choose "y" and go to step 2.
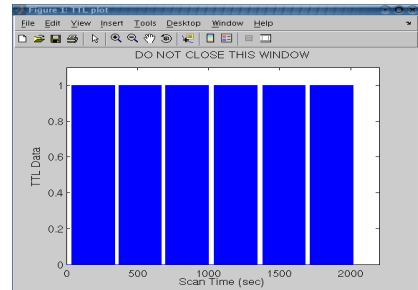
2. In MATLAB command window:
   >> Parsing scan 1: real_dataProc_1.txt
   --
   Use left mouse button to choose the START and END points of scan 1
   *(right mouse button to zoom)*

   With LEFT mouse button, click on an empty area before the start of the first scan, then click again on an empty area after the end of the first scan.

   If the empty area is too small to put the mouse pointer, you can use ZOOM. To ZOOM IN, with RIGHT mouse button, click the start of the desired zooming area, then click the end of the desired zooming area. To ZOOM OUT, with RIGHT mouse button, click the left margin of the figure window, then right margin.

   Tips: Warning or error messages will be displayed in MATLAB command window to alert you of illegal clicks.

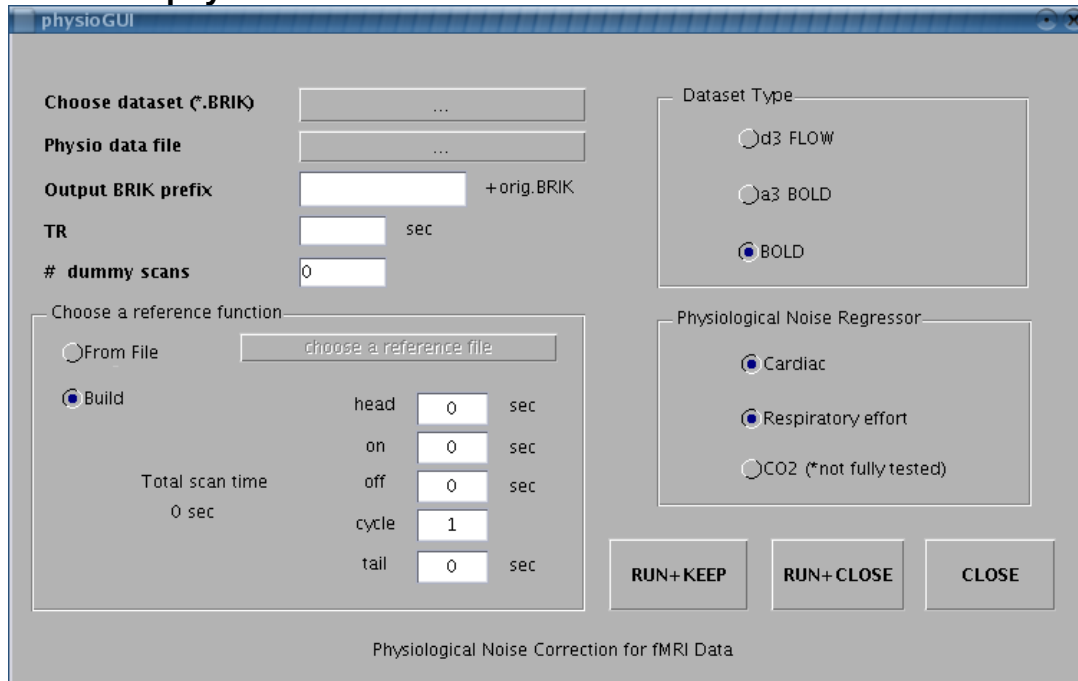3. In the pop-up SAVE window, make a choice:

   - *SAVE and NEXT*: save the current selection into a file and continue to the next scan.
   - *SAVE and FINISH*: save the current selection into a file and exit.
   - *NO*: discard the current selection and go back to select again.
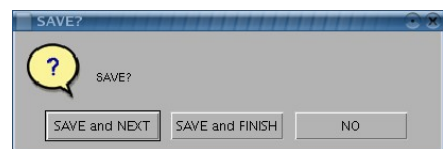
4. Repeat step 2 and 3 until finish.

5. Visually check the data quality in the pop-up figure windows.

APPENDIX B: physioGUI

- *Choose dataset (*.BRIK): choose an input dataset (3D+time)*
- *Output BIRK prefix: the prefix of the output BRIK name*
- *Physio data file: pre-processed physio data file*
- *TR: scan repetition time*
- *# Dummy scans:*
  - o *For EPI BOLD: # of dummy acquisitions specified in the fMRI screen*
  - o *For ASL: # if images discarded during a3 or d3*
- *Choose a reference function*
  - o *From File (multiple selection allowed by holding the Shift key): text files containing columns of stimulus pattern (or predicted hemodynamic response). Each column represents one stimulus, and each row is one time point. The time points must fall on the same grid as the input dataset.*
  - o *Build:*
    - – *head: initial off period (sec)*
    - – *on: on period (sec)*
    - – *off: off period (sec)*
    - – *cycle: # of on-off repeats*
    - – *tail: end off period (sec)*
- *Dataset Type:*
  - o *d3 FlOW : if data is ASL FLOW obtained from d3*
  - o *a3 BOLD: if data is ASL BOLD obtained from a3*
  - o *BOLD: if data is GE EPI BOLD*
- *Physiological Noise Regressor*
  - o *Cardiac: remove cardiac noise using pulsox data*
  - o *Respiratory Effort: remove respiratory noise using respiratory effort data*
  - o *CO2*: remove respiratory noise using CO2 data (* no fully tested).*

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APPENDIX C: physio

physio(brikIn, physiofile, brikOut, dummy, ref, TR, model, [pflag],[anatmask]);

Inputs:
brikIn   - prefix of the input AFNI brik (3D+time);
physiofile   - pre-processed physiological data (.txt);
brikout   - prefix of the output AFNI brik;
dummy   - # of dummy scans;
- *for EPI BOLD: # of dummy acquisitions specified in the fMRI screen;*
- *for ASL: # if images discarded during a3 or d3;*

ref   - reference function:
Either a vector: [head on off cycles tail]
- *total scan time = (head + (on+off)*cycles + tail)*

Or a cell array :{'file1', 'file2', 'file3', ...}
- *must be text files containing columns of stimulus pattern (or predicted hemodynamic response). Each column represents one stimulus, and each row is one time point. The time points must fall on the same grid as the input dataset.*

TR   - scan TR (sec);
Model   - 'raw' : if data is GE EPI BOLD;
*   'd3' : if data is ASL FLOW obtained from d3;*
*   a3' : if data is ASL BOLD obtained from a3 ;*
pflag   - (Optional) default 3
*   1 : remove cardiac noise using pulsox data;*
*   2 : remove respiratory noise using respiratory effort data ;*
*   3 : remove cardiac and respiratory noise (pulsox + respiratory effort) ;*
*   4 : remove respiratory noise using CO2 data;*
*   5 : remove cardiac and respiratory noise (pulsox + CO2 data);*
Anatmask   - (Optional)
*   Prefix of the anatomical mask brik ;*
*   (The mask must be down-sampled to match the size of the input dataset)*

Output: *An AFNI brik (3D+time) with physiological noise removed.*

Example:
physio('subject1','subject1_Proc.txt','subject1_Corr',4, [0 20 40 5 0], 2, 'raw');
or
physio('subject1','subject1_Proc.txt','subject1_Corr', 4, 'subject1_ref.txt', 2, 'raw', 1);
or
physio('subject1','subject1_Proc.txt','subject1_Corr', 4, {'Stim1.1D', 'Stim2.1D', 'Stim3.1D'}, 2, 'raw',3);

APPENDIX D: physioRG

physioRG(brikIn, physiofile, fileOut, dummy, TR, [pflag]);

Inputs:

brikIn	*- prefix of the input AFNI brik (3D+time);*
physiofile	*- pre-processed physiological data (.txt);*
fileout	*- prefix of the regressor file (fileout.1D.slice#);*
dummy	*- # of dummy scans (TRs);*

- *for EPI BOLD: # of dummy acquisitions specified in the fMRI screen;*
- *for ASL: # if images discarded during a3 or d3;*

TR	*- scan TR (sec);*
pflag	*- (Optional) default 3*

    1 : remove cardiac noise using pulsox data;
    2 : remove respiratory noise using respiratory effort data ;
    3 : remove cardiac and respiratory noise (pulsox + respiratory effort) ;
    4 : remove respiratory noise using CO2 data;
    5 : remove cardiac and respiratory noise (pulsox + CO2 data);

Outputs: *Physiological noise regressor per slice saved in a text file (.1D.slice#).*

Example:

    physio('subject1', 'subject1_Proc.txt', 'subject1_preg', 0, 2);

    Output files:
        Subject1_preg.1D.01
   *Subject1_preg.1D.02*
        Subject1_preg.1D.03
          .
   *.*
          .
          .

APPENDIX E: Sample images before and after physiological noise correction
The following images are generated from an ASL flow dataset acquired at the visual cortex. Physiological noise correction is done using measured pulsox and respiratory effort data.

1. Using the same correlation threshold of 0.4, the number of activated voxels after correction is increased compared to before correction (only showing slice 2 out of 4 slices).
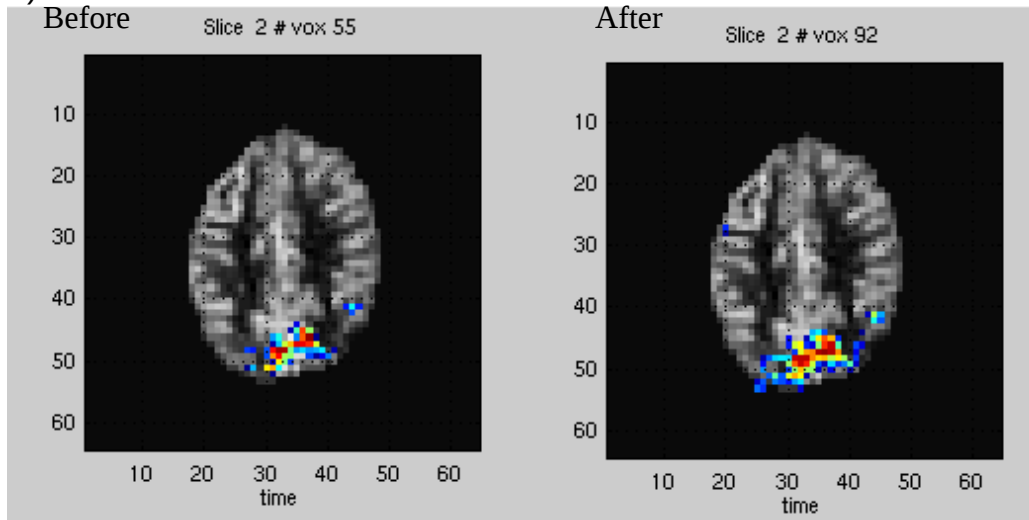
2. Using the same anatomical mask (visual cortex, 145 voxels), physiological correction cleans up the time course compared to without physiological correction.
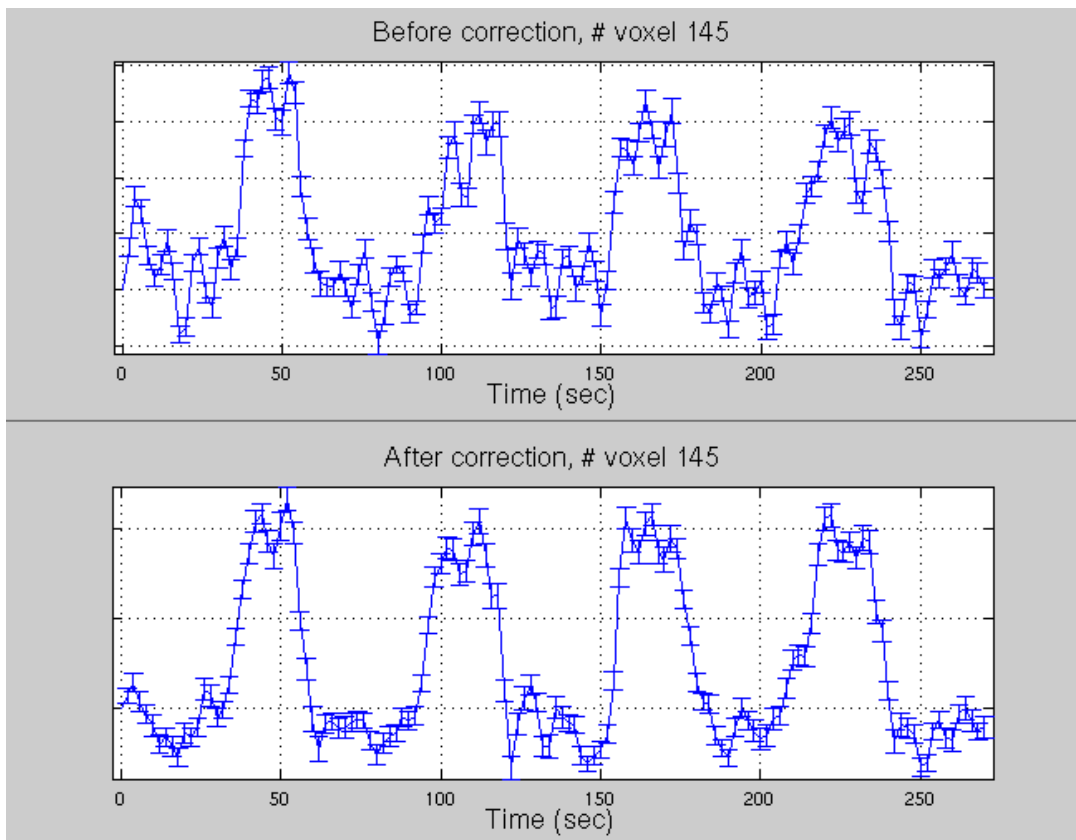
APPENDIX F: Trouble Shooting

1. If when running physioGUI or physio, the following error msg occurs:
??? Error using ==> mtimes
Out of memory. Type HELP MEMORY for your options.

Solution: Depending on your system memory, it usually happens when your dataset has a matrix size of 128*128 or higher. Use anatomical masks to reduce the total number of voxels to be analyzed.

3.   The following error msg occurs
??? Index exceeds matrix dimensions.
Error in ==> genPregs at 30
        PhysData   = PhysData((ttlInd(1)-Indoffset):(ttlInd(end)+Indoffset), :);

Solution: Open globalvar.m and reduce Indoffset value (default =120) until the error goes away (e.g. Indoffset=100, 80, or 40, etc).