MCDAPS V2.0

Manual

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CHAPTER 1 MCDAPS

Overview

Data Browser is a program for multichannel physiological signal display and analysis. The program was built using MATLAB 2020a-2022a. The analysis capabilities include stationary power spectral analysis, time-varying power spectral analysis, moving correlation analysis and univariate analysis. Users can also analyze multiple sets of data using the batch processing option.

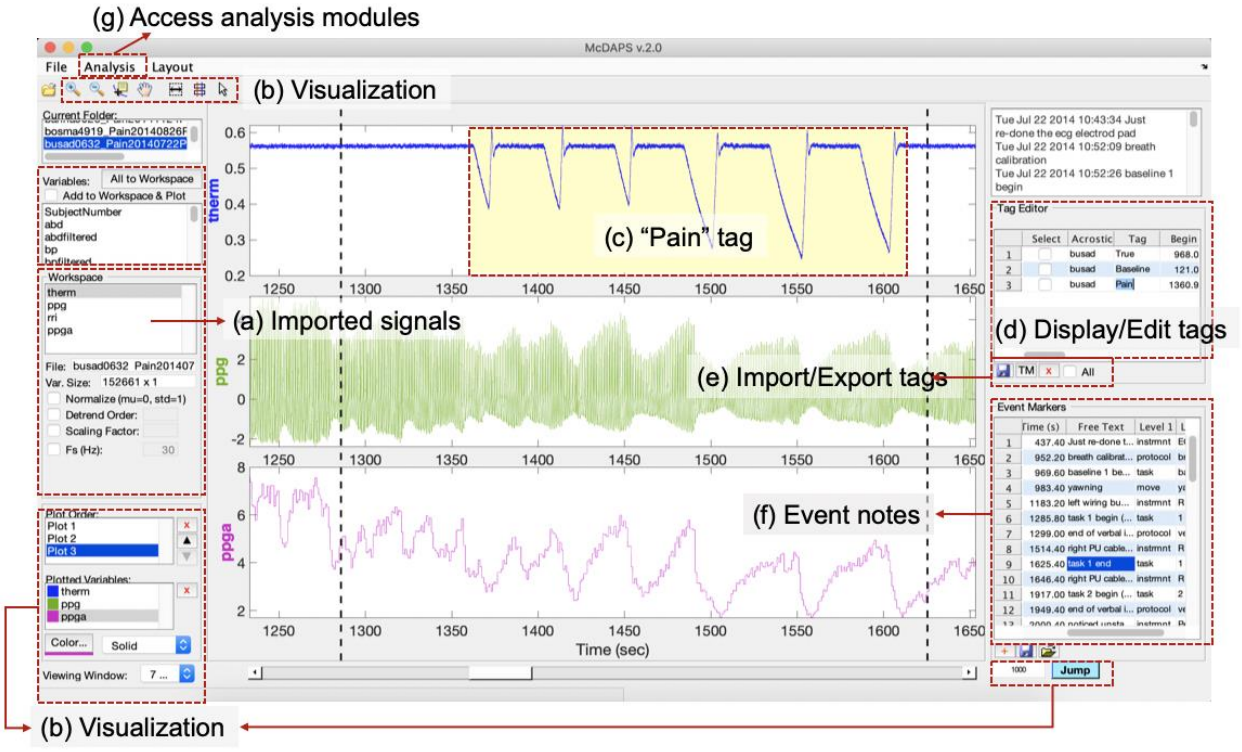


Figure 1-1. A snapshot of Data Browser visualizes the signals from the same experiment: (1) heat stimulus, (2) raw PPG, (3) beat-to-beat PPGa

As the user loads each signal to Workspace, the signal will appear automatically in the plot area by default. Each signal is plotted as a time-series, assuming default values of the sampling rate. If the assumed sampling rate is incorrect, the user can modify the value accordingly in the Transformation option

panel. Other data transformations such as normalization, shifting, scaling can be applied to each signal. These transformations do not affect the data in the original file. Additionally, we have developed visualization tools to aid the user in establishing temporal relationships among signals. Annotation of interventions introduced by the investigator during the experiment takes the form of timestamps with event descriptions, which are saved with the data file. The user can select those events displayed in the event panel: these are marked by vertical dashed lines across the plot area. Another tool is the vertical guide tool, which draws a movable vertical line across the plot area. The user can move this guide horizontally to visually align the temporal sequence of events happening across signals. For each plot panel, the user can plot multiple signals per panel. The user can also change the plotted signal colors and the plot order using the plotting option panel.

Supported data formats

Data Browser imports data as a MATLAB-binary file (MAT-file). When using McDAPS, make sure your MAT-file contains

1. each channel in a row vector format
2. the sampling frequency of all the signals. The supported variable name for sampling frequency is fs, fs_varname, fs_name.

For example, fs_ecg indicates the sampling frequency of a variable named, ‘ecg’. If all the channels are sampled at the same rate, you can use ‘fs’ as a variable to store your sampling frequency.

Example of a MAT-file supported by McDAPS

In this example, we have three sampling frequencies associated with several channels. fs_high is associated with the channels sampled at 250 Hz. fs_low is associated with the channels sampled at 30 Hz. fs_fnir is associated with the channels sampled at 2Hz.

Import	Name	Size	Bytes	Class
☑	SubjectNumber	1x1	8	double
☑	abd	152661x1	1221288	double
☑	abdfiltered	0x0	0	double
☑	bp	127217...	10177368	double
☑	bpfiltered	0x0	0	double
☑	bpmaxind	4949x1	39592	double
☑	bpminind	4949x1	39592	double
☑	calibfactor	2x1	16	double
☑	dbp	152661x1	1221288	double
☑	ecg	127217...	10177368	double
☑	ecgfiltered	0x0	0	double
☑	event	1x1	37904	struct
☑	fnirtrigger	152661x1	1221288	double
☑	fs_fnir	1x1	8	double
☑	fs_high	1x1	8	double
☑	fs_low	1x1	8	double

Figure 1-2. Example of a MAT-file structure supported by McDAPS

‘event’ variable contains the events marked during a study. To see the structure of ‘event’, please go to Event Markers section.

Data visualization

LOADING DATA

1. On the top left corner of the main window (Fig. 1-1), click Load Data icon () in the toolbar *or* go to menu File > Load Data..

   Select a Mat file (e.g. filename.mat) > Open.

2. Mat files in the selected file directory are displayed in the Current Folder listbox.

   Variables in the selected file are displayed in the Variables (the listbox above Workspace).

   *Note: at this point, variables are **not** yet added to the Workspace.*

3. To add a variable to Workspace:

   a. Double-click a variable in the Variables listbox.

   b. Right-click (ctrl + click for Mac) a variable in Variables listbox > Add to Workspace.

   c. Click All to Workspace button to add all variables in the Variables listbox to Workspace.

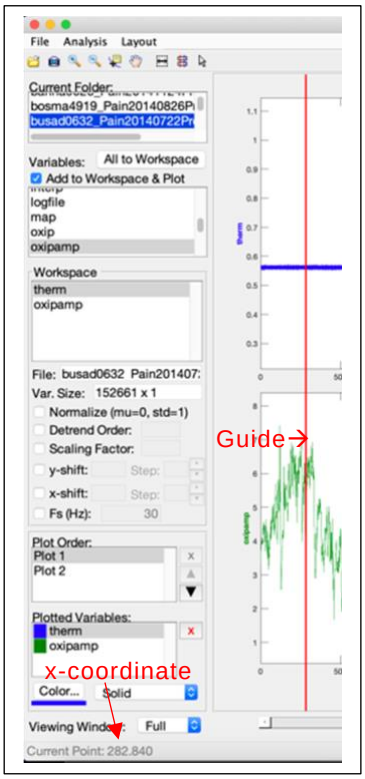
   Note: For option a. and b., the selected variable will be added to Workspace and plotted if the Add to Workspace & Plot checkbox is checked.

TRANSFORMING DATA

1. To transform a signal, left-click on a variable in the Workspace, go to transformation options underneath the Workspace, check transformation options, enter values if any detrend order, scaling.

2. A sampling frequency (fs) is a reference for plotting. One sample is displayed every 1/fs second. Changing the frequency does not re-sample a signal, but merely re-plots it. Make sure fs is correct to plot correct time-axis.

DELETING PLOTTED VARIABLES

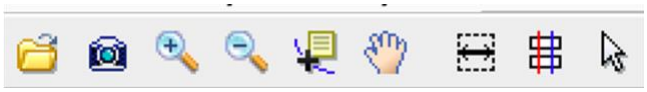


There are several ways to delete plotted variables. Choose one of the options below.

1. From Workspace, right-click on a variable > Delete.
2. Right-click on a plot > Delete. (This will delete plotted variables & the plot)

   Select a variable in Plotted Variable listbox > click X button.

TOOLBAR



a b c d e f g h

a) Load data

b) Screen shot

c) Zoom in > Toggle to activate / untoggled to deactivate

d) Zoom out > Toggle to activate / untoggled to deactivate

e) Data cursor > Click and pin on a tracing to show (x,y) coordinates.

f) Pan > Click > Left-click on a plot > drag horizontally

g) Tag > Define a new tag

h) Vertical guide > Click to display the guide > Drag the guide horizontally to display the x-coordinate.

Plot Templates

PLOT FROM PRE-DEFINED TEMPLATES

(*Warning: currently plotted variables will be removed*)

a. Go to menu Layout > Plot Template > choose a template.

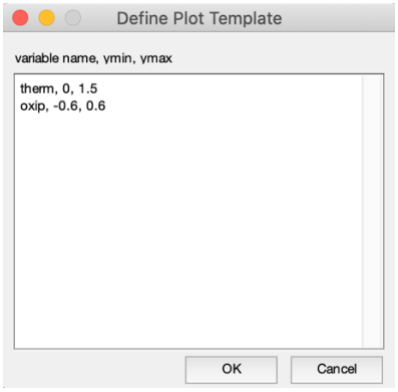
b. The variables listed in the template file are loaded from the currently selected file, added to Workspace (if they are not already there), and plotted in the Plot Area.

Note: If the variables are not found, the plots will not be generated.

DEFINE A NEW TEMPLATE

c. Go to menu Layout > Plot Template > define a template.

d. Enter one variable per line in a plotting order. The range of y-axis is limited to ymin-ymax. Click OK.



e. Save plot template window appears. Type the desired filename in the Save As text box > Save.

SAVE SCREEN AS TEMPLATE

f. Go to menu Layout > Plot Template > save screen as template... This option saves the current plots into a new template.

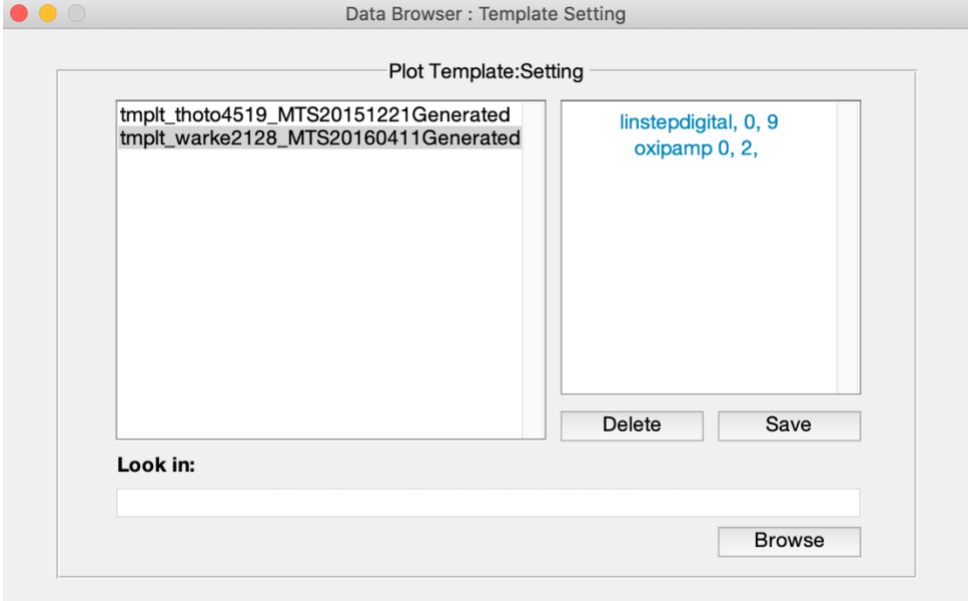


Figure 1-3. Plot Template Setting

SET THE DEFAULT TEMPLATE PATH

g. Go to menu Layout > Plot Template > Setting

h. Under “Look in”, the text box shows the current folder where the templates are. To change, click Browse, and select a new folder.

DELETE A TEMPLATE

i. Go to the template folder on a user’s computer or go to Setting.

j. Choose a template from the list, the right text box will display the variables inside the selected template.

k. Click delete button.

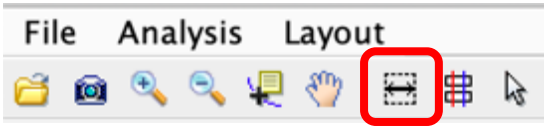
EDIT A TEMPLATE

l. Go to menu Layout > Plot Template > Setting

m. Choose a template from the list, change the variable’s name, ymin and ymax in the text box. Note that: we must put the exact syntax ‘name, ymin, ymax’ appeared in the texts.

Annotation (Tagging)

1. Click Select a Region tool in the toolbar.



2. The cursor shape changes from an arrow ( ) to a cross ( ).

   Click on a plot that you want to select a region. The selected plot will be highlighted.

3. The cursor shape changes from a cross ( ) to a thin cross ( ).

   Draw a rectangle (hold and drag a mouse button) to define a region. (Double-click to cancel)

   Once the mouse button is released, the selected region is highlight. Name a tag and enter, a new tag will be added to Tag Editor.

   Tips:

   - On the event table, Free Text column, click on an event will make a location on the plot to get better precision while tagging.
   - On the tool bar, activate the vertical guide ( ), drag along the time-axis to see a time point while tagging (bottom left corner of the main window).

   SAVING TAGS

1. Go to Tag Editor > select the rows to export or at the bottom, select All > click button.

2. If Tag Manager is being opened, go to Tag Editor in Tag Manager > select the rows to be exported or check ‘Select All’> Click  .

LOADING TAGS

1. At the bottom of Tag Editor, click TM (), Tag Manager will appear.
2. At the bottom right of Tag Viewer, click a folder icon (), choose a CSV file, then all tags will be displayed in Tag Viewer.
3. In the table, on ‘Select column’, select tags to be exported or check ‘Select All’ at the bottom, then click ‘Export’ and close the window.

Event Markers

Under Event Markers, the event table displays time-stamps and corresponding notes read from a variable, 'event' in a matfile. The program automatically looks for this variable, and if found, its contents are shown.

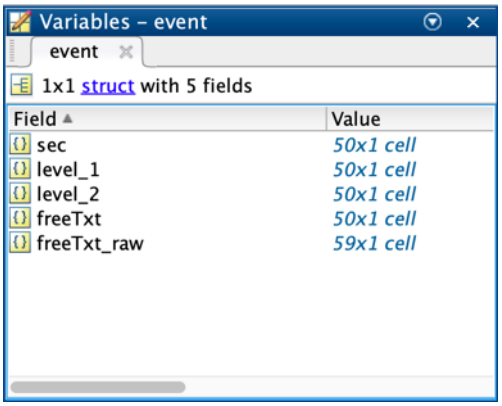


Figure 1-4. Inside 'Event' variable

1. What is 'event'?

   A structure that contains four variables 'sec', 'freeTxt', 'level1' and 'level2'.

   Each variable stores the contents to be displayed on the column, 'Time (s)', 'FreeTxt', 'level1' and 'level2' in the event table.

   'sec', 'freeTxt', 'level1' and 'level2' are cell arrays, and their size is determined by the number of events. For example, in Fig 1-4., each variable has 50 rows from 50 events.

2. Loading an 'event' variable

   If 'event' is in a separate mat-file, users may load the file into the data browser via the folder icon () located at the bottom of the event table. Note that a separate event must have the same structure as the event shown in Fig 1-4.

3. To create a compatible event matfile, > create sec, level_1, level_2 and freeTxt with the same size. Then, create a new variable ‘event’ and add sec, level_1,level_2 and freeTxt as fields. In Matlab workspace, right click on ‘event’ variable and save as .mat.
4. Saving events to a new variable

a. At the bottom of the event table, click the save icon (), choose a file location and save.

5. Markers

a. On the event table, in the FreeTxt column, click on a cell to display a vertical marker (dash line in Fig 1-1.) at the time location specified in the ‘Time(s)’ column.

b. Left-click on the dash line to remove the marker.

CHAPTER 2 BEAT-TO-BEAT PROCESSING

B2B provides three processing options to extract beat-to-beat values of ECG, BP and PPG. The beat-to-beat values available on McDAPS are R-to-R interval (RRI), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), the pulse-to-pulse interval (PPI) and the pulse amplitude of a photoplethysmogram (PPGa).

In B2B, the R-peaks are detected from the ECG using an in-house adaptive thresholding algorithm. The R-peak is the maximum point which exceeds the 90th percentile value of the ECG in 1.5-second window. Once the first R-peak in the ECG is identified, a new threshold is determined from the next 1.5-second window beginning from the most recently identified R-peak. The process repeats until the end of the signal.

The systolic peaks of BP and PPG are detected using the algorithm proposed by [1]. The detected systolic peaks are then used to search for the corresponding troughs. For BP processing, B2B extracts systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial blood pressure (MAP). The mean arterial pressure is calculated as the sum of 2/3 DBP and 1/3 SBP. For PPG processing, B2B extracts the pulse amplitude and the pulse interval of PPG.

While the processing is automatic, users can correct the algorithm detection via Add/Reject buttons. B2B exports the interpolated beat-to-beat time-series sampled at 2Hz to Data Browser. A snapshot of B2B is shown in Fig 2-1.

Sample run

The user can access the B2B module via the Data Browser's interface. Go to Analysis, then select Beat-to-Beat.

1) Then, select a signal to be processed.

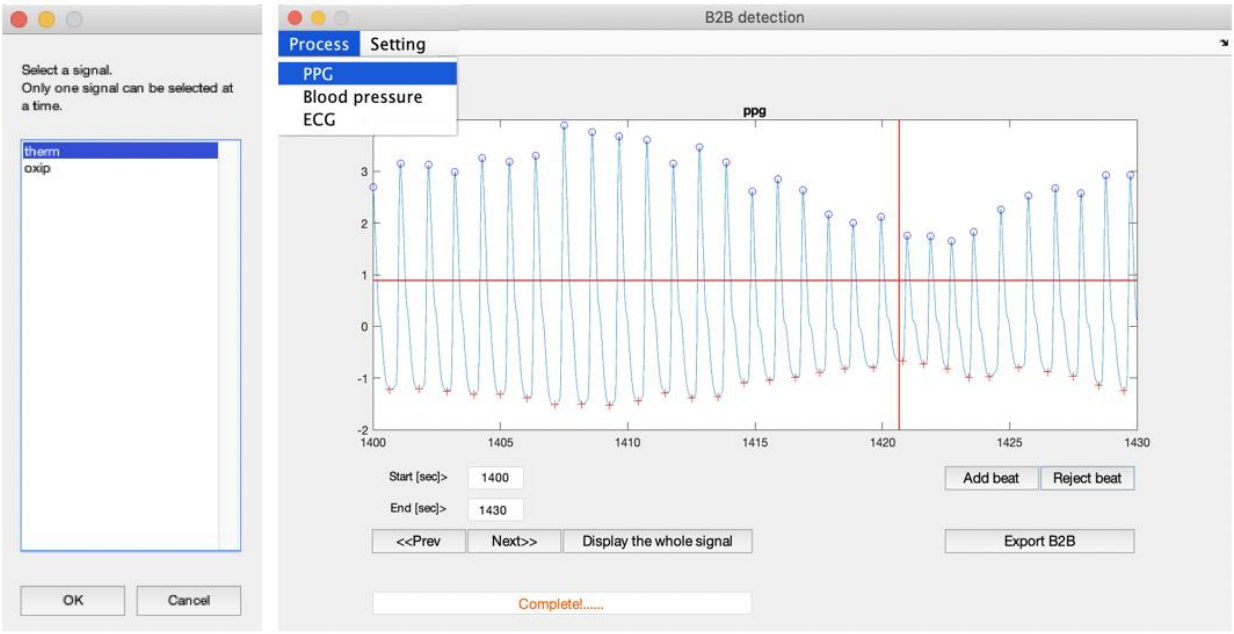


Figure 2-1. A snapshot of the B2B module. The interface provides tools to add, reject incorrect beat detection. The user can adjust the processing window. The beat-to-beat signals are exported to the main module.

2) When the B2B window is open, go to the top left of the window and select "**Process**". Choose one of the options to process PPG, BP or ECG. After, wait until the status bar says that the Detection is complete.
3) On the B2B interface, adjust the window size at Start [sec] and End [sec] for inspection.

   Navigate to the next portion of the signal using the Next>> button.

4) Click on **Add beat**, to add a new beat (one beat at a time). Do this by marking the start position (left click on the plot) and the end position (another mouse click on the plot) for the algorithm to detect the systolic peak and its corresponding trough within that region. Make sure to select the region that covers the peak and trough of that beat.
5) Click on **Reject beat**, to delete incorrect beats. Select the region to delete by marking the start position (1st click on the plot) and the end position (2nd click on the plot).

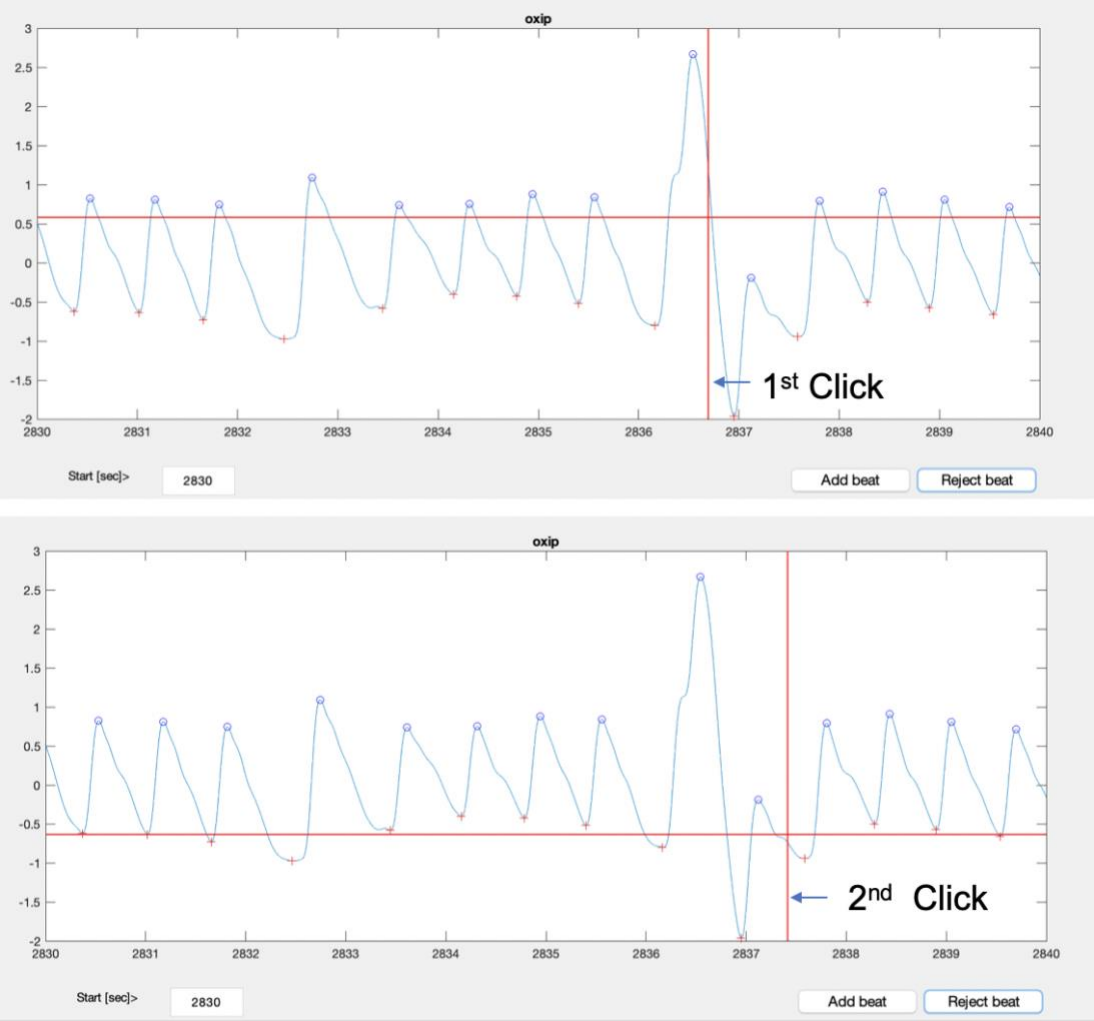


Figure 2-2. How to reject incorrect beats. *All the beats within the marked region are deleted.

6) Click the Next >> button to inspect the next window.
7) Click the Export B2B button to export beat-to-beat signals and beat locations to Data Browser.

CHAPTER 3 STATIONARY POWER SPECTRAL DENSITY (PSD)

Stationary power spectral density (PSD) analysis decomposes signal fluctuations into different frequency components and represents the components in terms of power, which is proportional to the square of the signal's amplitude. As the name suggests, it is assumed that the data being analyzed are stationary, i.e. the mean and standard deviation can be considered constant within the selected data segment. The power within a frequency range is obtained by integrating the PSD in the specified frequency range. By default, this analysis returns low-frequency (0.04 – 0.15 Hz) power, high-frequency (0.15 – 0.4 Hz) power, and total power. These frequency ranges are defined per recommendation for heart rate variability analysis but they can be redefined by the user.

The available PSD estimation methods are Welch's method [2], autoregressive (AR) model [3] and "input-adjusted" autoregressive model [4, 5]. The PSD estimate from Welch's method is the average of periodograms obtained from the overlapping and windowed data segments. The AR method assumes that the signal can be modeled as the output of an AR filter (regressed on its own past values) driven by white noise, where the AR filter coefficients are estimated and optimized using the Akaike information criterion. The PSD estimate can then be obtained by taking the Fourier transform of the optimized AR filter. The input-adjusted autoregressive method is an extension of the AR method and is used

when the influence of a correlating factor (input) needs to be adjusted. This method was originally developed to correct for the influence of non-uniform ventilatory patterns on heart rate variability – i.e. it would produce an estimate what the heart rate variability index would be under tidal breathing conditions with the same ventilation.

Using Stationary PSD

To open Stationary PSD module, select “Analysis” on the upper left of the Data Browser’s interface. Then, select “Stationary PSD…”

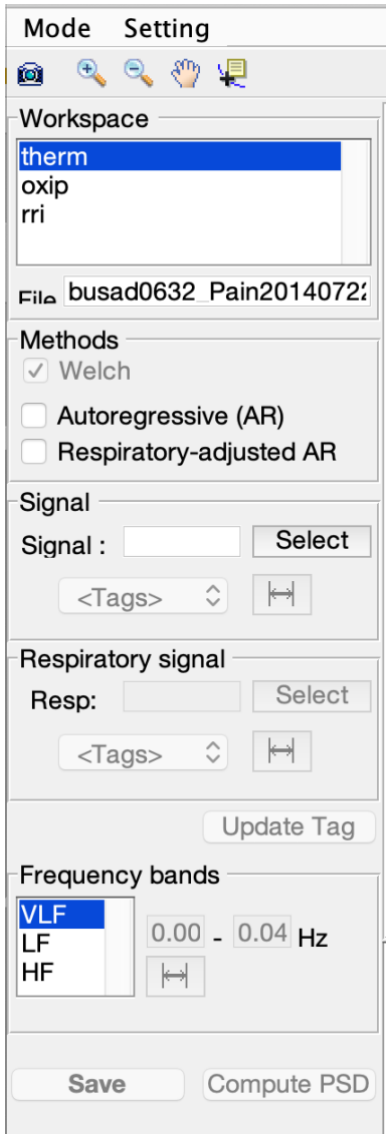


Figure 3-1. Normal analysis mode of Stationary PSD

Normal Mode

1) Select a method for the analysis.

2) Choose a signal from the workspace and hit “**Select**” in the Signal panel.
3) Select a tag for the analysis to compute.
   a. If no tags are available, you define a tag by hitting  .
4) Choose a respiratory signal if the respiratory-adjusted method is selected.
5) In case, new tags are defined in the main browser, click Update Tag to load the new tags to the Stationary PSD module.
6) Press “**Compute PSD**”
7) Computed frequency bands are shown in the Frequency band panel.
8) To define a new frequency band, click  in the Frequency band panel, and drag a rectangular on the spectrum plot.

In the bottom table of the opened stationary PSD window, the desired collected data will be displayed. To **save** the data, select rows on the output table and select “**Export**” button.

Stationary PSD Batch Processing

1) When Stationary PSD window is open, go to the top left of the window and select the tool bar titled "**Mode**".
2) Select "**Batch**", and the Batch Processing will be displayed.
3) Click on **Browse**, to select a Data Folder that contain .MAT files.
4) Click on **Browse**, to select a Tag Folder that contains .CSV files (predefined tag).
5) Choose a signal from the list, correct the sampling frequency if needed, click **Add to Signal**.
6) Choose a respiration from the list, click **Add to Respiration.**
7) From **Region of Interests** panel, choose a respiration baseline tag, **Click Respiratory Baseline** (add one tag per click).
8) From **Region of Interests** panel, choose a tag, **Click ROI** (add one tag per click) to add a region for the analysis.
    - If the tag of interest does not appear, add the tag manually using **Add Tag to Region** button**.**
9) Choose a method for the analysis.
    - Select "**Compute**"
    - After the result summary is displayed, save the results by hitting the "**Save Output**" button.
10) Select the location to save the result files.

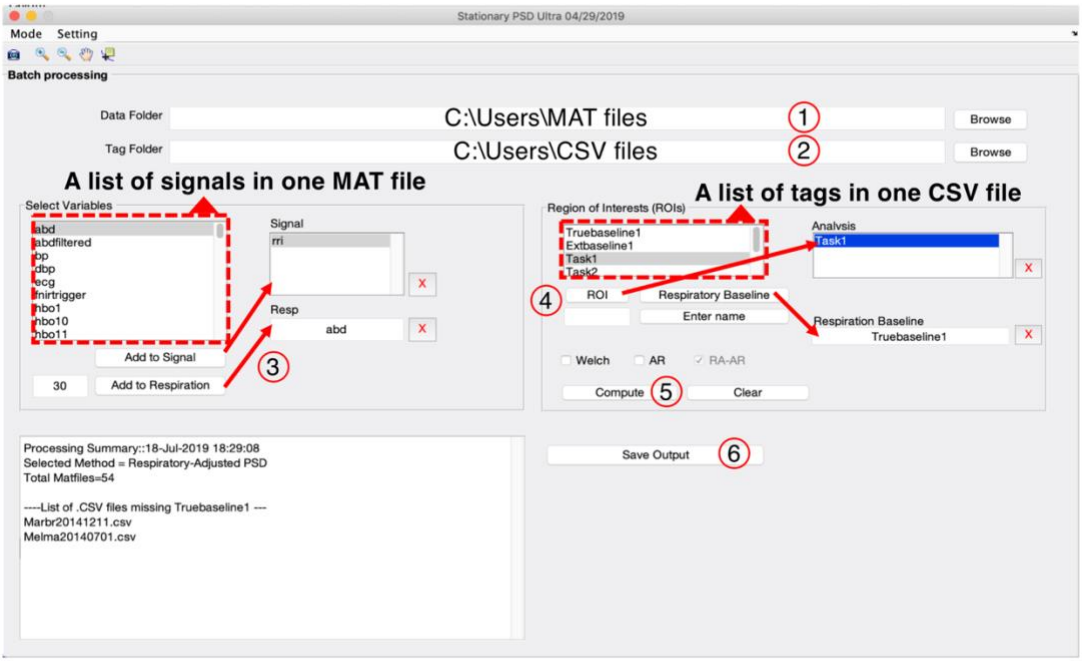


Figure 3-2. Batch analysis for Stationary PSD.

Setting

1) When Stationary PSD window is open, go to the top left of the window and select the tool bar titled "**Setting**" (Fig 3-1.).
2) Click + to add a new frequency range.
3) Select a frequency's name and click – to delete a frequency range.
4) Checkboxes indicate the default frequency ranges; the module will export.
5) At 'Downsample to', change the resampled-frequency (fs) for a signal. Note that the module plots the spectrum between 0-fs/2.
6) At Detrending order, change the polynomial order to detrend a signal before the analysis.
7) At frequency resolution, change the resolution for the frequency-axis.
8) Click "**Apply**" to save changes.

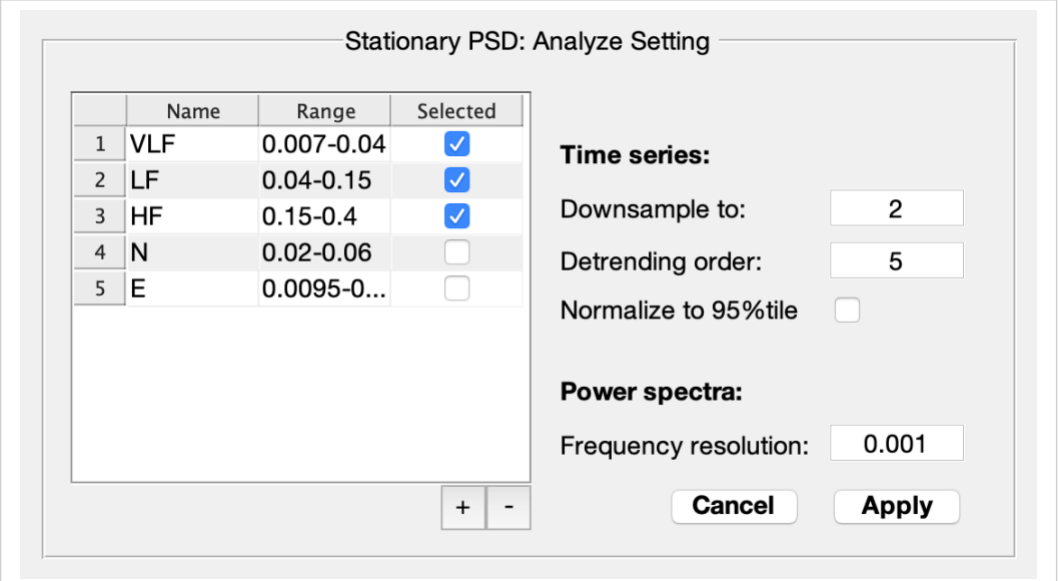


Figure 3-3. Analysis setting for Stationary PSD

Sample run

We now present an example in which heart rate variability analysis is applied to the RRI signal. From the Analysis menu of the Data Browser main interface, “Stationary PSD” is selected, which opens the window displayed in Fig 3-4. ‘rri’ is selected as the signal to be investigated, using the input-adjusted Autoregressive (AR) PSD estimation method. We first select the baseline duration for the respiratory signal, ‘abd’. Then, an estimate of the heart rate variability is corrected using the selected respiratory pattern. The analysis module plots the ‘rri’ signal and corresponding PSD after the correction. The very low-, low-, high-frequency and total powers are reported in the table, which can be exported as a CSV file. As mentioned in the Computational Methods section, the frequency ranges for power calculation can also be manually defined by user as needed.

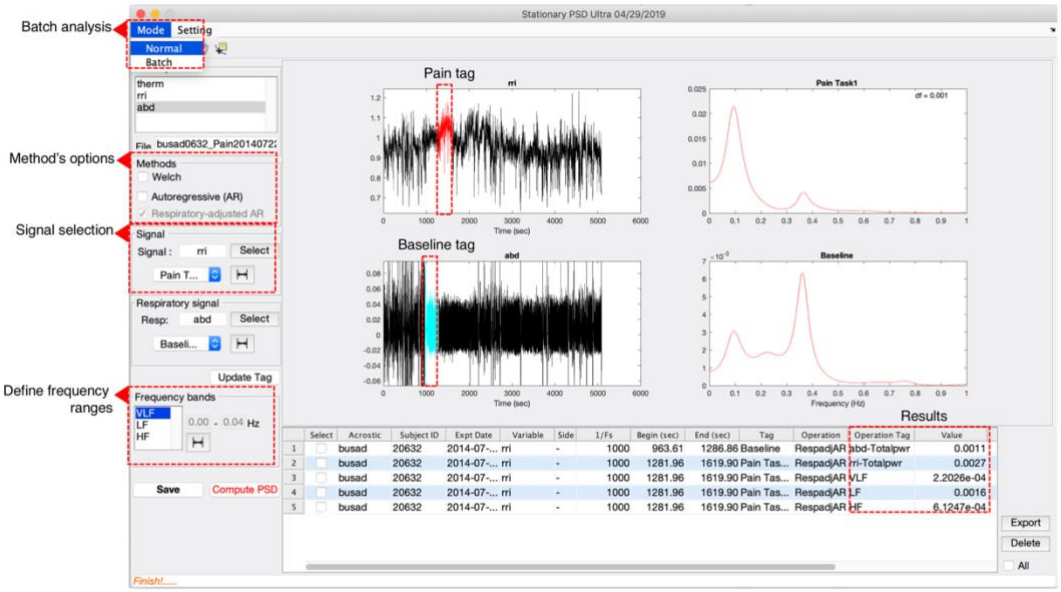


Figure 3-4. Sample run on Stationary PSD using respiratory-adjusted method.

More About

- The use of PSD analysis is not limited to heart rate variability analysis. In fact, the module is applicable to any signal when the fluctuation is of interest. For example, the very low- (0.007-0.04) and low- frequency (0.04-0.15) of PPGa may be indicative of the sympathetic control of peripheral blood flow and vascular function [6-8].
- Truncated segment suffers from spectral leakage [ref]. As long as the stationary assumption holds, the longer segment yields more accurate estimation. The length of analysis segment must be at least (1/fc) second long if the spectral component at fc Hz is of interest.
- According to the Nyquist sampling theorem, the reliable frequency components lie between 0-(fs/2) Hz, when fs is the sampling frequency. As a default, fs is set to 2 Hz and the module plots power spectrum between 0-1 Hz. To extract the spectral powers higher than 1 Hz, a user must change the sampling frequency in **Setting**.

CHAPTER 4 TIME VARYING POWER SPECTRAL DENSITY (PSD)

Time-varying PSD applies the stationary PSD analysis to a sliding 60-second window that is moved along the signal one sample at a time. For each sliding step, the low- and high-frequency powers are derived from the calculated PSD. Therefore, the outputs of this analysis are the time-series of low- and high-frequency powers of the signal under investigation. However, it should be noted that this frequency analysis only yields reliable frequency information above 1/60 Hz since the window size is fixed at 60 seconds. Users can choose one of the options listed below to estimate spectral components. Let $S(f)$ be a spectral value at f Hz. The power spectrum, S can be calculated using three methods listed below.

Fast Fourier Transform (FFT)

$$S(f) = \left(\frac{1}{fs * N} * |H(f)|^2\right) \quad (1)$$

The FFT method uses a fast Fourier transform algorithm to decompose a signal, y into a complex function of frequency, $H(f)$. The power spectrum, S is proportional to the square of the magnitude of $|H(f)|$. The low- and high- frequency components are derived by integrating area under S within 0.04-0.15 Hz and 0.15-0.4 Hz respectively.

Autoregressive (AR) Model

The AR model estimates S from the model's parameters, rather than an original signal, y. The AR method assumes that $y = \{y_1, y_2, \dots y_N\}$ can be modeled using its own past values and white noise, $\epsilon = \{\epsilon_1, \epsilon_2, \dots, \epsilon_N\}$, in which *N* is the number of samples.

$$y(n) = \sum_{i}^{m} a_i y(n-i) + \epsilon_n \tag{2}$$

Within a 60-second window, the algorithm derives the optimal model parameters, $a = \{a_1, a_2, .. a_m\}$ by minimizing the sum of square errors, J between y and one step prediction, $\hat{y}$.

$$J = \sum_{n=1}^{N} e_n^2 = \sum_{n=1}^{N} \langle y(n) - \widehat{y(n)} \rangle^2 \tag{3}$$

$$\widehat{y(n)} = \sum_{i=1}^{m} a_i y(n-i) \tag{4}$$

Then, the PSD of y is estimated using the optimal a. This way, the model can remove unwanted noise, and power spectrum is smoother in comparison to the FFT method. The PSD of y is calculated by multiplying the transfer function, $|H_{ar}|$ and the variance of $e = \{e_1, e_2, \dots, e_N\}$, in which e is the model residual.

$$S(f) = \frac{|H_{ar}(f)|^2 \sigma_e^2}{fs} \tag{5}$$

H_{ar} is a function of a that relates the input's frequency to the output's frequency. In this case, the model's input is assumed to be a white noise.

$$H_{ar}(f) = \frac{1}{1 + \sum_{i=1}^{m} a_i e^{-\frac{j2\pi if}{fs}}} \quad (6)$$

The convenience of a white noise input allows us to estimate $S(f)$ in Eq. 5 using the variance of e. However, e may not always be white, especially when the model prediction is poor. In this case, users may use the alternative method- **Pre-whitened Autoregressive Model [9],** which does not assume e to be white. Pre-whitened AR calculates the PSD of y by multiplying $|H_{ar}|$ with the PSD of e (Eq. 7).

$$S(f) = \frac{|H_{ar}(f)|^2 S_e(f)}{fs} \quad (7)$$

Input-Adjusted Autoregressive Model

The input-adjusted AR method makes use of the autoregressive model to normalize effects of an additional variable that may obscure the PSD of y [4, 5]. For example, the high frequency of heart rate variability is modulated by respiratory sinus arrhythmia. Increase or decrease in tidal volume will result in increase or decrease in the high frequency power. Breathing pattern may change regardless of a given stimulus, and we sometime want to dilute its effect on the power spectrum.

The autoregressive model is rewritten to incorporate an additional input (e.g. respiration), x (Eq. 8).

$$y(n) = \sum_{i=1}^{m} a_i y(n-i) + \sum_{k=0}^{q} b_k x(n-k) + \epsilon_n \tag{8}$$

This equation assumes that x linearly causes changes in y, and the relationship between them is carried through the model parameters, a and b. This relationship may as well be expressed in a frequency domain, through a transfer function H (Eq. 11).

$$H_x(f) = \frac{\sum_{k=0}^{q} b_k e^{-\frac{j2\pi fk}{fs}}}{1 + \sum_{i=1}^{m} a_i e^{-\frac{j2\pi if}{fs}}} \tag{9}$$

It is important to remind that x is not the only variable driving y, and white noise (ϵ) is still in effect. Part of the PSD of y affected by the PSD of x is shown in Eq. 10.

$$S_{cx}(f) = |H_x(f)|^2 S_x \tag{10}$$

Supposedly the analysis segment is during thermal pain, and x is respiration, S_x would be the power spectrum of respiration during thermal pain. In an attempt to normalize x, we replace S_x with S_{x0} which is the power spectrum of respiration during **baseline**. This justifies the requirement for the baseline tag by the respiratory-adjusted AR option.

Now, we want to focus more on what defines a proper baseline. If possible, the ideal baseline should be driven solely by resting conditions, and x must

contain all possible frequency components that may influence the PSD of y. Usually, the latter criterion is not met because a baseline (5-10 minutes) is often too short to catch them. **We may get away by selecting the baseline where x shares the same frequency as possessed during the analysis section.** Then, the input-adjusted PSD of y is described in Eq. 11.

$$S_{adjusted-y}(f) = \frac{|H_\epsilon(f)|^2 \sigma_e^2}{fs} + |H_x(f)|^2 S_{x0} \tag{11}$$

Using Time-Varying PSD

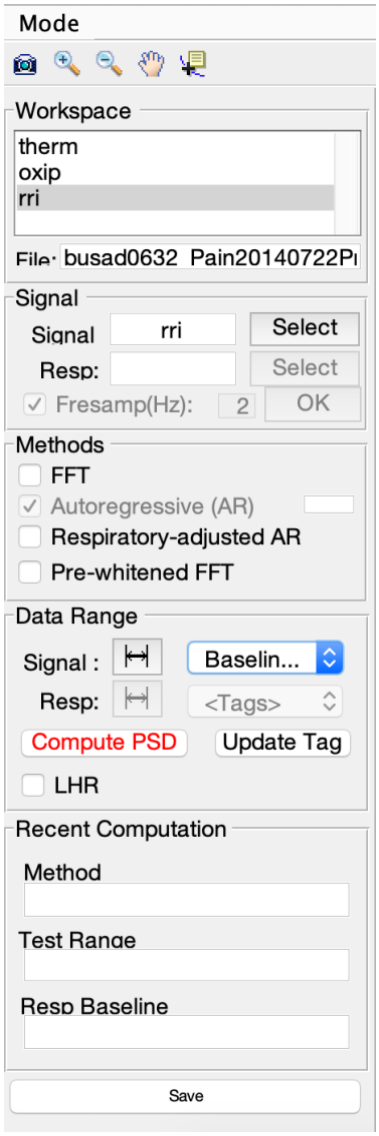


Figure 4-1. Default analysis window for Time-varying PSD module

Normal Mode

1) Choose from the workspace the signal to be inspected and hit "**Select**".
2) Next choose a respiratory signal. (respiratory signal is needed if respiratory-adjusted method selected)
3) Select the sampling frequency (default is 2Hz) and select "**OK**"
4) Select method of analysis.
5) Select a tag for the analysis to compute.
    a. If no tags are available, you can make a tag by selecting  .
6) Select a tag for baseline respiration if respiratory-adjusted is selected.
    a. If no tags are available, you can make a tag by selecting  .
7) Select LHR to show the spectrum from low-high frequency ratio.
8) Press "**Compute PSD**"
9) Select "**Save**"

Upon saving a Time Varying PSD file, a window will pop up to allow for selection of the files saved name and file location. The file is saved as a '.m' file, and can be opened using Matlab. The data will appear in the workspace under the handle TVPSDresults.

TIME-VARYING PSD BATCH PROCESSING

1) When Time Varying PSD window is open, go to the top left of the window and select the tool bar titled "**Mode**".
2) Select "**Mode**".
3) Next to Mat-file directory, click "**Browse**" to open the desired files filled with data.
4) Next to Tags directory, click "**Browse**" to open the desired files filled with tags.
5) Next to Save directory, click "**Browse**" to open the desired file to save the processed data in.
6) Under Select Variables panel, choose variables from the list, correct the original sampling frequency if needed and click "**Add to Signal**".

a. If the desired variable is not on the list, manually enter the name and click "**Add to Signal**".

7) Under Select Defined-Region Tags, choose predefined tags from the list box, then click "**ROI**" estimate power spectra within the tags. Note that tags should be at least longer than 60 second.

a. If the desired tag is not on the list, manually enter the name and click "**Add Tags to Response**".

8) Click "**Compute**".

a. The data files will be saved as '.mat' files into the selected save file. There will be a file for each sample set. Each file will provide the set's information in the workspace.

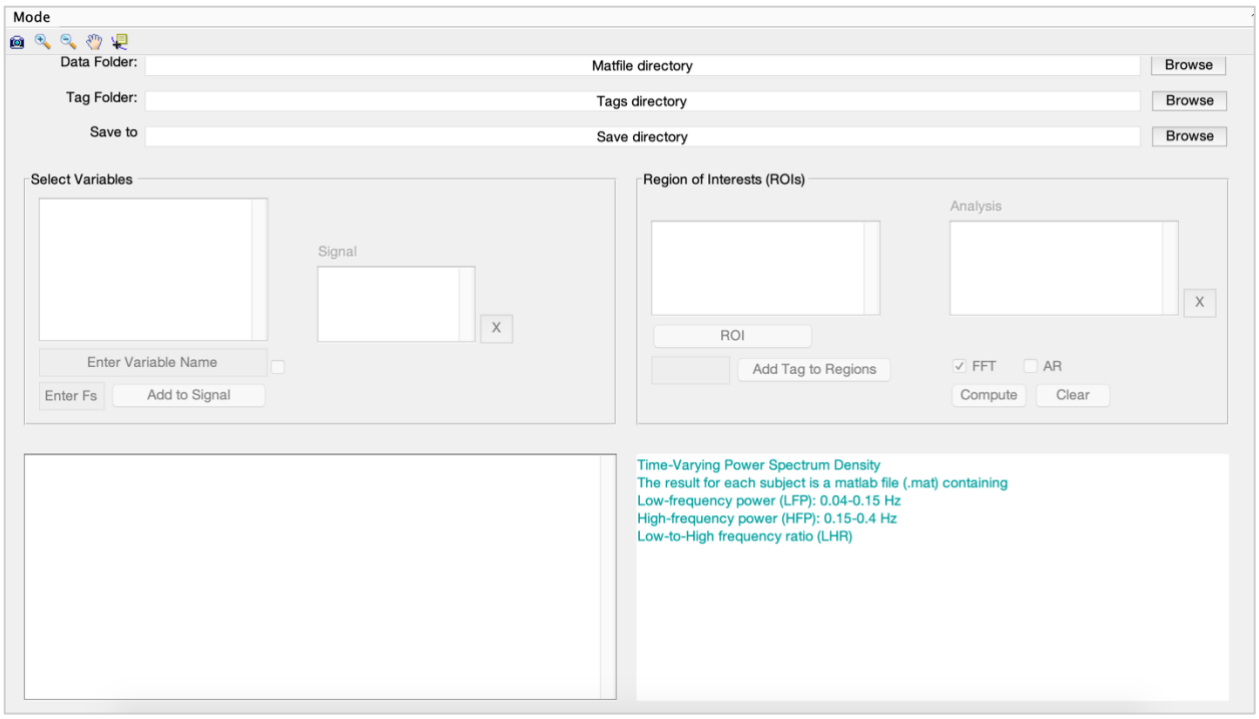


Figure 4-2. Batch analysis window for Time-Varying PSD module

More About Batch Processing

- The list of variables and defined-tags are sampled from the first MAT and CSV files in the selected folders.
- Batch processing pairs a .MAT file and a .CSV file using its filenames. For example, if there was ‘abcde9999_heatpain.mat’ in the mat-file directory, the module would pair a .CSV file whose name begins with ‘abcde’ as a corresponding a .CSV file. If there is more than one CSV file, the module will prompt a window asking a user to choose a correct CSV file.
- Predefined tags are case sensitive. Please make sure that the tags are uniformly defined across all subjects.

SAMPLE RUN

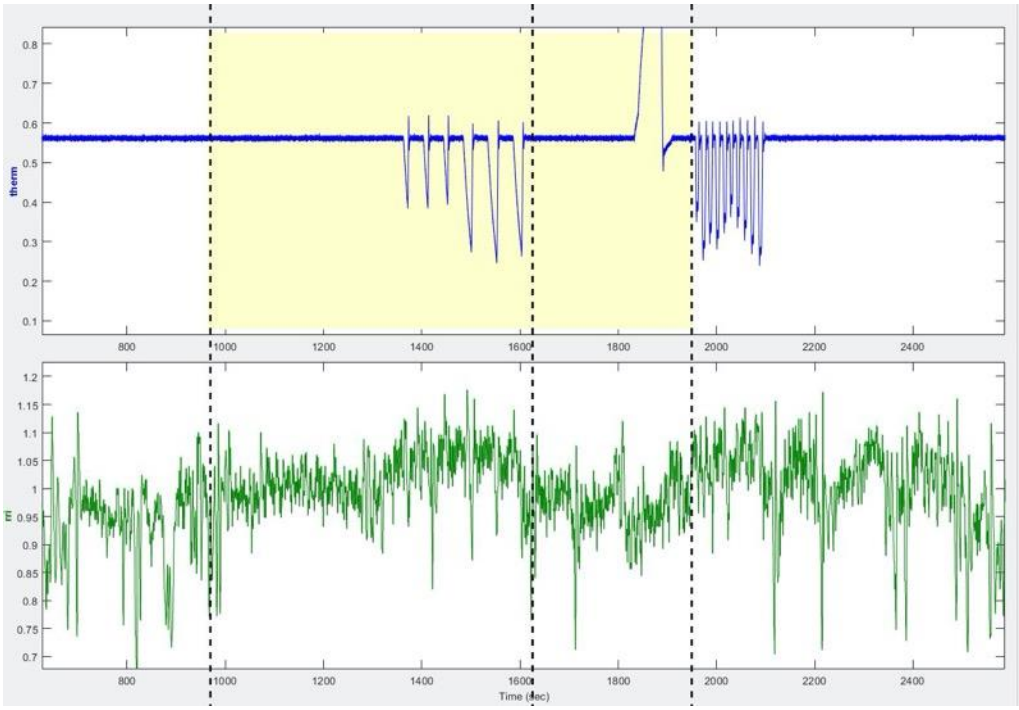


Figure 4-3. Define a tag for the Time-varying PSD module, (1st panel) heat stimulus, (2nd panel) rri.

In this section, we show how to use the Time-varying PSD module. The Time-varying PSD module plots power spectrum over time, which enables users to observe the changes in low- and high- frequency components affected by changes in external conditions. As an example, we re-analyzed the heart rate variability of the same subject presented in Fig 3-4. A new tag has been defined to cover baseline, pain task and recovery period (Fig 4-3).

From the Analysis menu of the Data Browser main interface, select “Time-Varying PSD”, which directs us to the window displayed in Fig 4-1. Then, select ‘rri’ as a signal to be investigated. Then press OK button to down-sample rri from 30 Hz to 2Hz. The Autoregressive (AR) PSD estimation method is selected for the analysis.

Under ‘Data Range’ panel, we selected the tag we recently created to calculate power spectrum of the signal within that tag region. In order for the module to calculate LHR, we also selected the low-to-high frequency ratio (LHR) checkbox to plot LHR spectrum in addition to the low- and high- frequency power spectra. After we pressed Compute PSD, three power spectra were plotted along the time-axis. The plots can be exported to Data Browser by pressing ‘Save’ button. Then, the TVPSD module will automatically generate new variables named rri_lfp, rri_hfp and rri_lhr in the workspace of Data Browser. Note that, these new variables are sampled at 2Hz. To plot the spectra (Fig 4-4), double-click a variable from the workspace and correct the sampling frequency to 2Hz if needed.

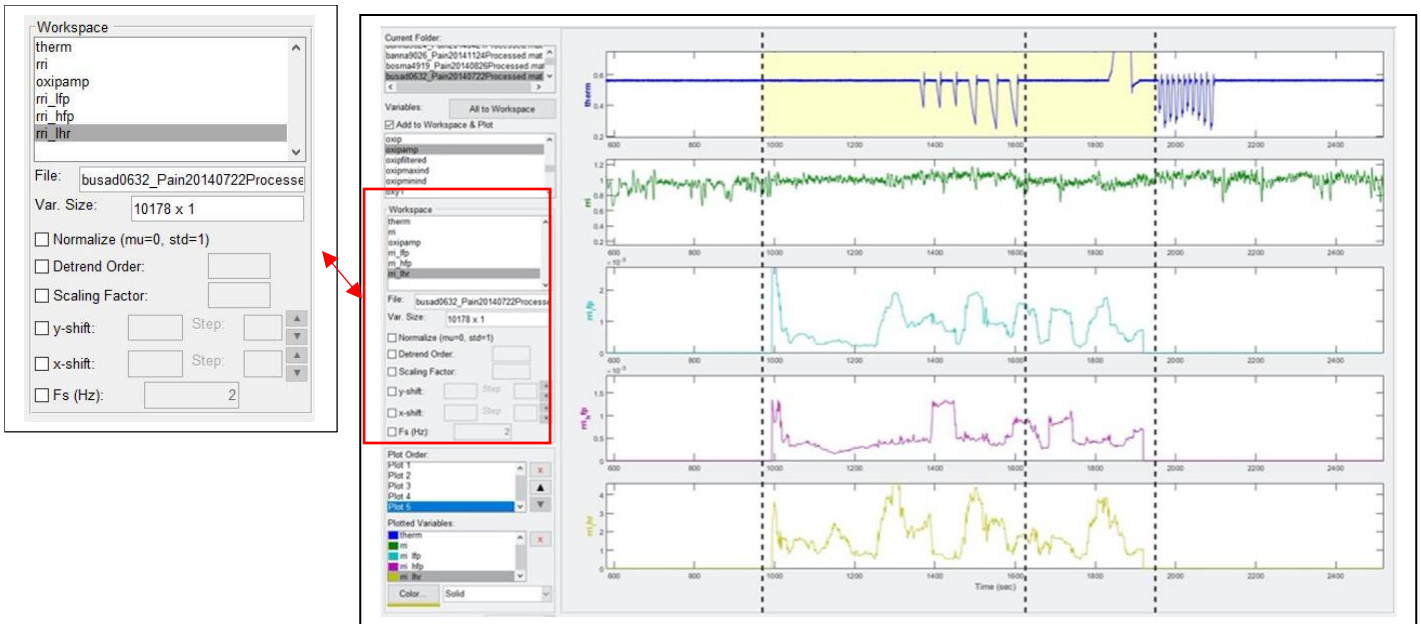


Figure 4-4. The power spectra of heart rate variability exported from TVPSD, (3rd panel) LFP, (4th panel) HFP, LHR.

More About

- Time-Varying PSD module detrends data points within the window using the fifth order polynomial. **Detrending removes the frequency components below 0.06 Hz,** and the estimation of the low frequency component below this is not accurate.
- The spectral components for the n^{th} sample is estimated using the data points 30-second before and after the n^{th} sample. The power spectrum will is always zero in the first and the last 30 second of the analysis tag (Fig 4-4).

CHAPTER 5 MOVING-CORRELATION ANALYSIS (CROSS-CORRELATION ANALYSIS)

Moving-correlation detects similarity (e.g. signal pattern) between a stimulus signal and a response signal. This analysis yields the strongest (positive or negative as specified) correlation coefficient (Pearson and Spearman) and the time lag between the two signals where the strongest correlation occurs. The follow-up significance test is used to statistically distinguish the pattern identified as a response from the pattern that may arise simply from spontaneous fluctuations in the signal that coincide with the stimulus.

Using Moving Correlation

In Data Browser, Go to Analysis and choose Moving Correlation.

Normal Mode

1) From a Workspace, choose a stimulus signal (e.g. pain), and go to 'Variables' panel, click 'Select'.
2) From a Workspace, choose a corresponding response, and go to 'Tested Signal', click 'Select'. Tips: Users can select multiple tested signals (e.g. perfusion, blood flow).
3) Select a baseline region for constructing a null distribution. Note that the baseline region must be at least 10-second (the duration of search window) longer than a test region.

a. If no tags are available, define a tag by hitting  .

4) Select a test region (e.g. during a pain task)

a. If no tags are available, define a tag by hitting  .

5) To update recent tags made in the Data Browser, click Update Tag to load the tags to the moving correlation module.

6) Select correlation option to be

a. Positive if the positive correlation is expected (One-sided hypothesis test)

b. Negative if the negative correlation is expected (One-sided hypothesis test)

c. Absolute if either direction is expected (Two-sided hypothesis test)

7) Press “Compute”

8) Statistical parameters will be shown in the result table.

In the bottom table of the opened moving correlation window, the results are reported. The detailed descriptions of parameters given by the module are listed the table. To **save** the data, select rows on the table and select “**Export**” button. Click Export All to export all the results.

Features	**Description**
Pearson r	Pearson correlation coefficient. $r = \frac{1}{N-1}\sum_{i=1}^{N}\frac{(X_i-\mu_x)}{\sigma_x}\frac{(Y_i-\mu_y)}{\sigma_y}$ N = No. of samples in the test region X = stimulus signal within the test region.

	Y = shifted response according to the delay from **Pearson correlation**. μ_x= mean of X in the test region μ_y= mean of Y in the test region
Pearson p	P-value shows statistical difference from null distribution.
Pearson delay	Delay in a response (no. of samples) identified using linear correlation.
Pearson slope	Slope of the linear regression between the stimulus (X) and the delayed response (Y) within the test region. Y = slope*X+b;
Spearman r	Spearman correlation coefficient. $r = \frac{1}{N-1}\sum_{i=1}^{N}\frac{(X_i-\mu_x)}{\sigma_x}\frac{(Y_i-\mu_y)}{\sigma_y}$ N = No. of samples in the test region X = stimulus signal within the test region. Y = shifted response according to the delay from **Spearman correlation**. μ_x= mean of X in the test region μ_y= mean of Y in the test region

Spearman p	P-value shows statistical difference from null distribution.
Spearman delay	Delay in a response (no. of samples) identified using rank-based correlation.
Spearman slope	Slope of the linear regression between the stimulus (X) and the delayed response (Y) within the test region. Y = slope*X+b;

MC Batch Processing

1) When Moving Correlation window is open, go to the top left of the window and select the tool bar titled "**Mode**", then select "**Batch**".
2) Click on **Browse**, to select Data Folder that contain .MAT files.
3) Click on **Browse**, to select Tags Folder that contains .CSV files (predefined tag).
4) Choose a test signal (stimulus) from the list, correct the sampling frequency if needed, click **Add to Test**.
5) Choose a tested signal (response) from the list, correct the sampling frequency if needed, click **Add to Tested**.
6) From **Defined-Region Tags** panel, choose a baseline tag, **Click Baseline Reg.** (add one tag per click).
7) From **Defined-Region Tags** panel, choose a test tag, **Click Test Reg.** (add one tag per click) to add a test region for the analysis.

a. If the tag of interest does not appear, add the tag manually by entering a region name and click **Baseline Reg.** or **Test Reg.**

8) Choose correlation option.

9) Select "**Compute**".

10) After the result summary is displayed, save the results by hitting the "**Save Output**" button.

Sample Run

The heat-pain stimuli were measured as changes in voltage, negatively proportional to changes in skin temperature, and are denoted as 'therm' in Fig 5-1. (top panel). The corresponding responses in peripheral blood flow were represented by changes in PPG amplitude, denoted as 'oxipamp' in Fig 5-1. (2nd panel).

The baseline and pain tags are defined using the Data Browser module accordingly to indicate the signal regions before and during pain application. The cross-correlation analysis is first applied to detect the similarity between the patterns in the pain stimuli and the peripheral blood flow. From the Data Browser main interface, "Moving Correlation" (option within the Analysis menu) is first selected. 'therm' and 'oxipamp' are selected as the stimulus and the response, respectively. The baseline tag is assigned to Baseline while the pain tag is assigned to the subsequent test segment (Fig 5-1.). The Correlation Option is specified as "Positive" since a decrease in 'therm' (increase in temperature)

results in a decrease in ‘oxipamp’ (i.e. same directional change). Clicking the “Compute” button produces the results displayed in the table below, which can be exported as a CSV file. The table entries include the identified maximum correlation coefficients (Pearson and Spearman) and the time lag between ‘therm’ and ‘oxipamp’ where the maximum correlation occurs. The third and fourth panels of Fig 5-1. display the Pearson and Spearman cumulative distribution functions constructed from correlation between “therm” (in the test region) and “oxipamp” in the baseline region. The vertical line indicates where the maximum correlation during pain is relative to the baseline “null” distribution. In this subject, the maximum correlation locates to the far left of the cumulative null distribution function. This indicates that the pattern observed in the peripheral blood flow during pain application is caused by pain rather than by random fluctuations in the peripheral blood flow.

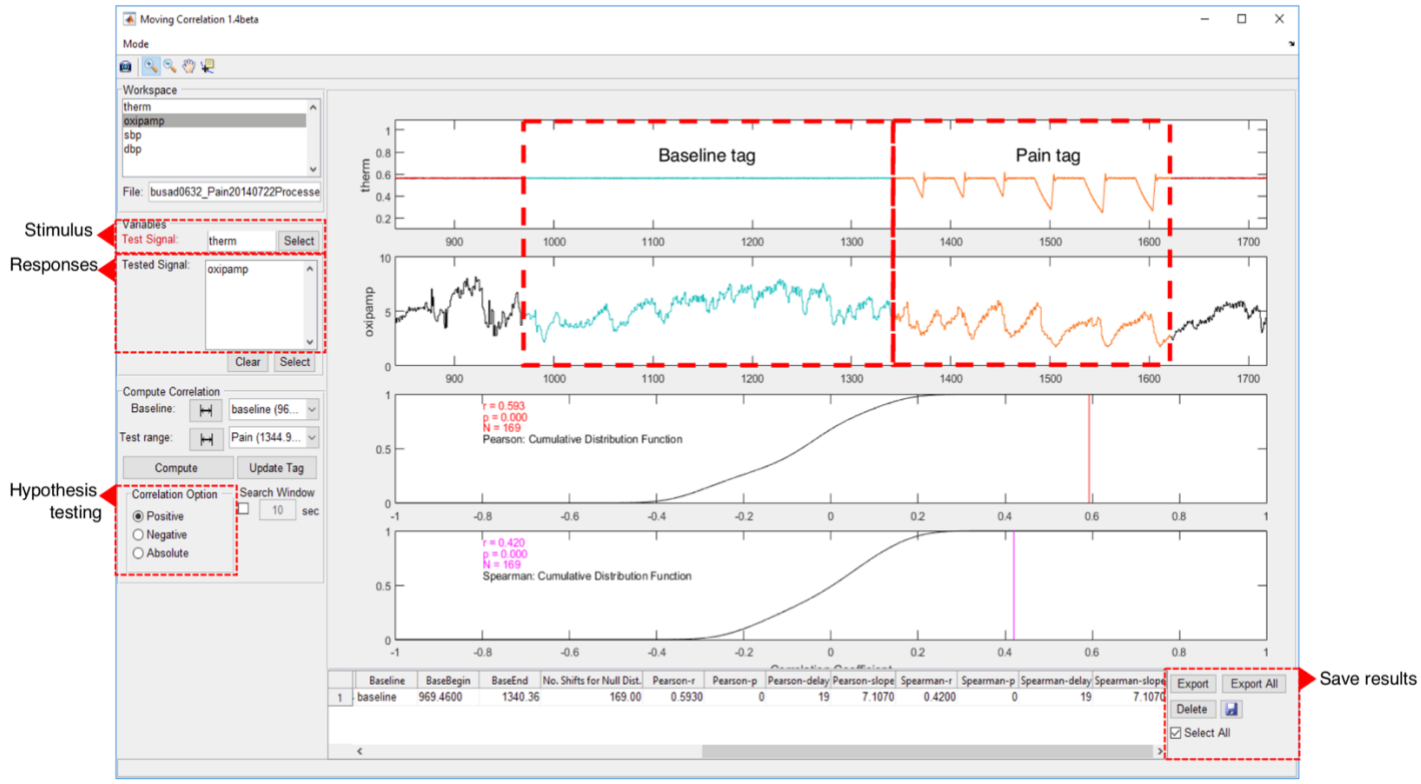


Figure 5-1. Data Browser's Moving correlation module

More About

Moving correlation statistically tests the significance of the pain-induced response against a null distribution constructed by cross-correlating the pain signal (the stimulus) with all possible sections of the baseline response. P-values show how further the correlation coefficient falls outside the 95th percentile of a null distribution. For more details see Sunwoo et al. [10].

CHAPTER 6 DESCRIPTIVE STATISTICS AND FEATURE EXTRACTION

Descriptive statistics, e.g. mean, median and variance, as well as the descriptive features, e.g. maximum and minimum, are derived from the selected tags. Prior to feature extraction, the user has options to normalize and/or filter the signal. To select exported features, go to FEX>Analyze menu>Descriptive, and select features to derive. Table 6-1. Shows available descriptive features in FEX.

FEX also allows users to fit a curve to the data within a selected tag. This function gives out response rate and response time derived from the fitted curve, rather than the original data. By default, FEX fits a curve to an entire data within a selected tag. However, users can choose to fit part of the data using percentile ranks. For example, fitting between the 5^{th} – 95^{th} percentile takes the 5^{th} percentile value as the start of a response, and the 95^{th} percentile value as the ending of a response. Table 6-2. Shows available fitting options. Initial parameters can be changed under Analyze menu>Curve Fitting. Note that the descriptive and curve features are derived after normalization or filtering is applied.

Table 6-1. Descriptive Features produced by FEX

Feature	Description
Area	Area between a response curve within selected sub-regions to a median from the baseline
Max	Maximum value of a signal within a tag
Min	Minimum value of a signal within a tag
Mean	Mean value of a signal within a tag
Median	Median value of a signal within a tag
95th percentile	The 95th percentile value of the whole selected signal
Coefficient of variation	Variance of a signal within a tag
Mvasoc [11, 12]	Mvasoc : magnitude of vasoconstriction Avasoc : vasoconstriction area Tvasoc : vasoconstriction duration Nvasoc : No. of vasoconstriction/hour

Table 6-1. Curve fitting features produced by FEX

Curve	Equation	Initial parameters	Feature
None	-	-	Time to half max Half max
Exponential	$y = ae^{-xb}$	Scaling (a), Time constant (b)	Scaling (a), Time constant (b) Time to half max Half max
Polynomial	$y = p_n x^n + p_{n-1} x^{n-1} + \cdots + p_0$	n (order)	Intercept, Coefficients
Sigmoid	$y = \frac{(y_{lower} + y_{upper} e^{(\frac{x-x_0}{k})})}{1 + e^{\frac{x-x_0}{k}}}$ $k = \frac{y_{upper} - y_{lower}}{4 * slope}$	Upper plateau (y_{upper}) Lower plateau (y_{lower})	Upper plateau Lower plateau Linear slope Midpoint

- **<u>More About</u>**
  - When Curve Fitting is enabled, FEX will pop up a figure of a fit which summarizes fitting parameters. We recommend users run this function on

one signal at a time. Using batch processing with curve fitting may generate too many figures that slow down the computation.

Using Feature Extraction

Normal (1 Subject, >1 Variables)

1. From Data Browser window, define tags, load variables into workspace, **select** Feature Extraction (FEX).
2. From FEX browser, choose a signal from Workspace, and **Click Add**.
3. From **Region of Interests** panel, choose a tag, and **Click ROI**.
   - To define an ROI, click **New ROI** and drag a region on the plot.
   - To rename, choose ROI from the list, enter a name and click Rename.
   - **Click Baseline** to add a baseline tag (**When 'Area' is selected**).
4. **To display ROI**, choose ROI from the list, a red rectangle will appear on the plot.
5. Select **Apply a filter** to apply a filter from the current setting before the analysis. If selected, the filtered signal will be displayed on top of the original signal.
6. Select **Normalized to 95% to normalize the signal to 95th percentile** before the analysis. If selected, the normalized signal will be displayed on top of the original signal. If the filter is applied, the normalization will be applied on the filtered signal.
7. Click **Extract** to analyze.

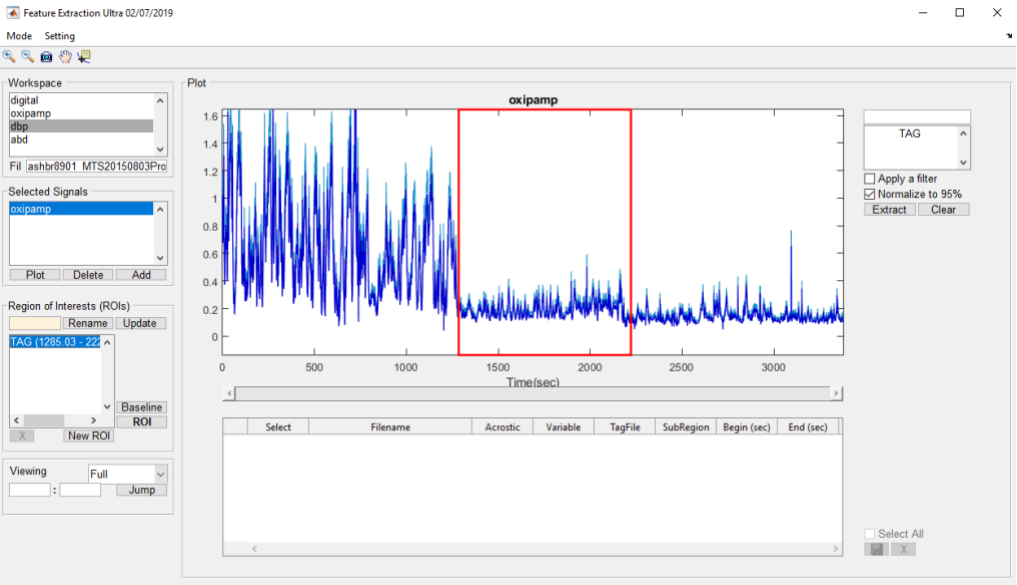


Figure 6-1. Figure 5.1. Sample run for FEX, (turquoise) oxipamp, (blue) normalized oxipamp.

FEX BATCH PROCESSING

How to run

1. From FEX browser, go to Mode menu (Above magnifying glass), and **Select** Batch
2. Click on **Browse**, to select Data Folder that contains mat-files.
3. Click on **Browse**, to select Tags Folder that contains predefined tag files (.csv).
4. Choose variable from the list, correct the sampling frequency if needed, Click **Add**.
5. From Region of Interests (ROIs) panel, choose a tag, **Click ROI** (add one tag per click).
6. From Region of Interests (ROIs) panel, choose a baseline tag, **Click Baseline** (add one tag per click). Note that, a median value of a baseline is used as a reference point to calculate an area.

7. Check **Apply a filter** to use a trend and/or check Normalized to 95% to normalize signal.
8. Click **Extract**.

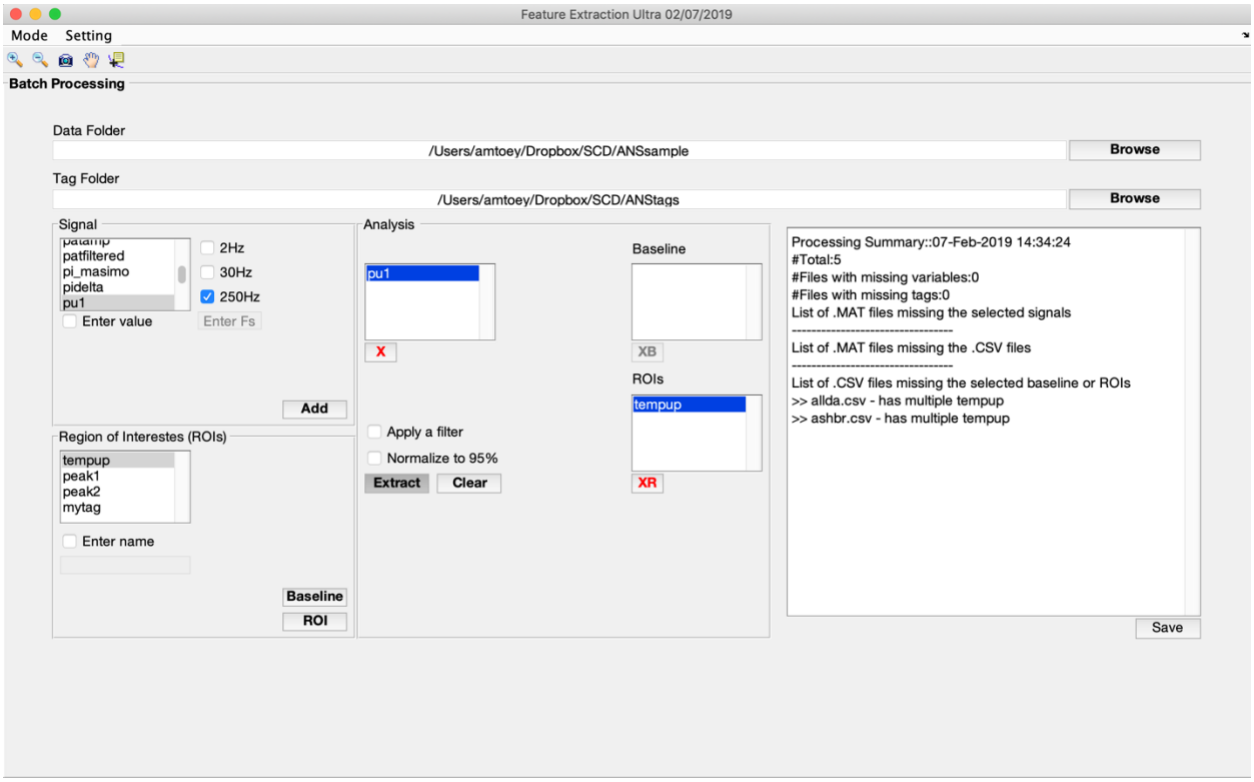


Figure 6-2. Batch processing for the univariate analysis. 1) select a MAT file's directory 2) select a CSV file's directory 3) select RR interval (rri) and systolic blood pressure (sbp) for the processing 4) select tags 5) compute and save results to a

Tips:

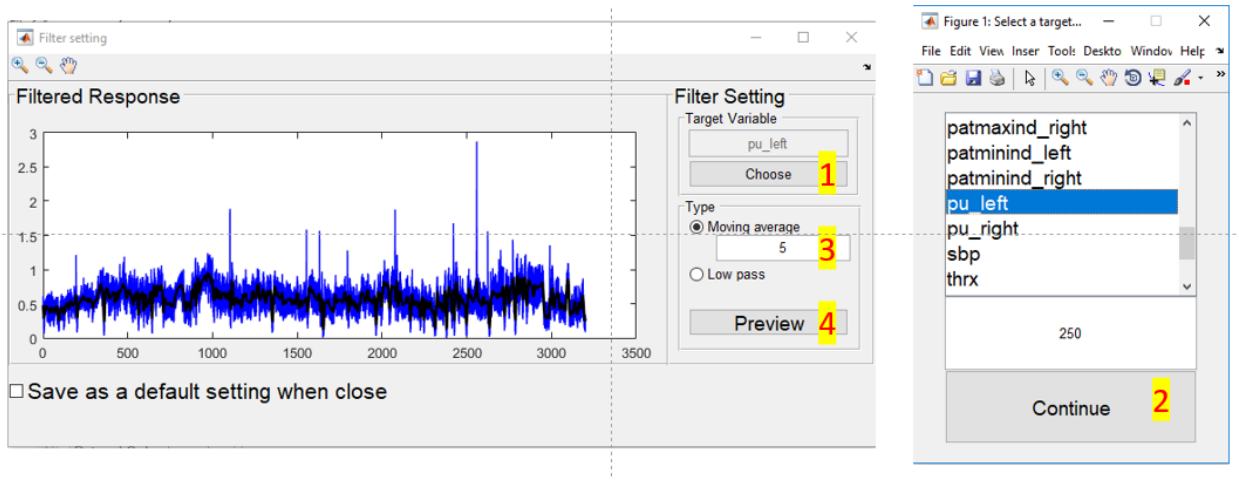
- Baseline tag is used to calculate Area. To calculate other features during baseline, click **ROI** instead.
- When selecting a signal, make sure the sampling frequency is correct. If it's incorrect, enter the frequency manually using the checkbox.
- Enter a tag manually if it does not appear in the Region of Interests panel.

FEX Setting

FILTER

By default, FEX applies a moving average filter to get a trend of data. The moving window is 5 second long. The cutoff of moving average is approximately (1/5 ~0.2 Hz). To change a filter, go to Filter menu, and change a window size, or choose a low pass filter. The lowpass filtered option removes high-frequency fluctuations above 20 Hz.

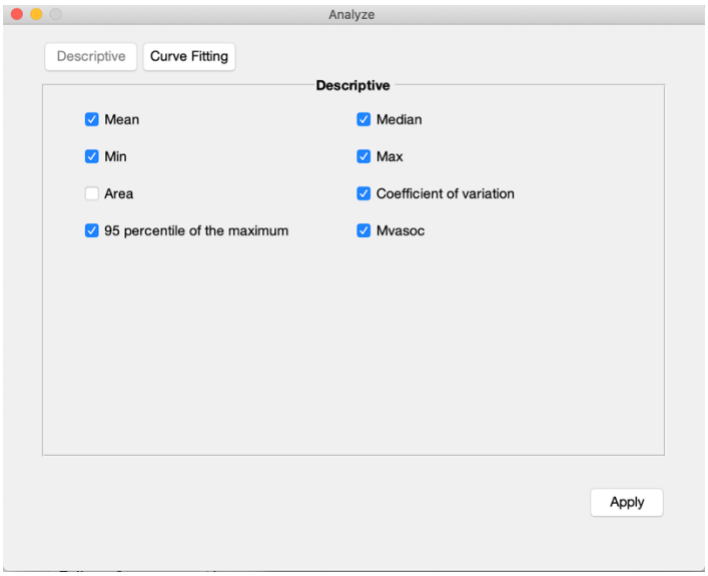
1. When FEX is being opened, go to menu, Filter.
2. Click on Choose, select one matlab file (a struct), select a variable to apply a filter
3. Enter a variable's sampling frequency and Click Continue to see a filtered signal.
4. From Type panel, select a type of filter and enter a window duration if median filter is used.
5. Click Preview to see the filtered signal.
6. Check 'Save as a default setting when close' to apply a filter.
7. Close Filter setting window


Filter setting
Filtered Response
Filter Setting
Target Variable
pu_left
Choose
1
Type
Moving average
5
3
Low pass
Preview
4
Save as a default setting when close
Figure 1: Select a target...
File Edit View Inser Tools Deskto Window Help
patmaxind_right
patminind_left
patminind_right
pu_left
pu_right
sbp
thrx
250
Continue
2

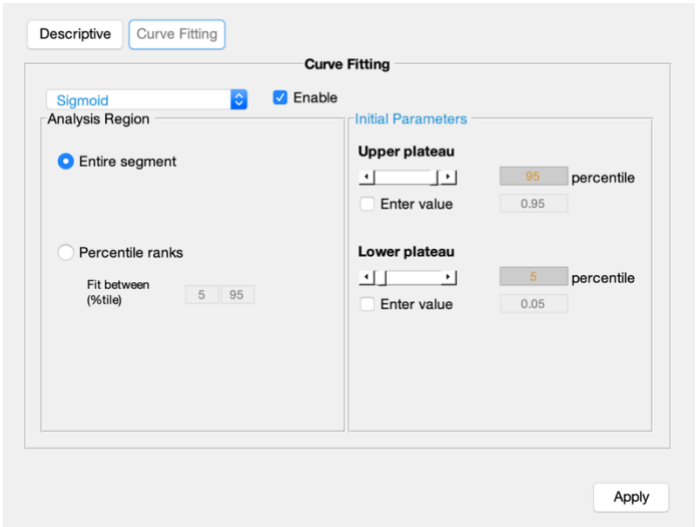
ANALYZE

To change the default features given by FEX, go to Analyze menu.

- From **Descriptive panel**, select feature for analysis by checking the feature checkboxes. Click **Apply** to save changes.



- Click **Curve Fitting** to switch to **Curve Fitting panel**.



1. From Curve Fitting panel, select a curve to fit from the pop-up menu. By default, the sigmoid curve is used.
2. From Analysis Region, choose a segment to analyze within a tag/ROI.
    - By default, FEX fits the entire segment.
    - Select the percentile ranks to fit a curve within a specified range.
3. From Initial Parameters panel, define initial values to be optimized.
    - Sigmoid : Set the initial values of the upper plateau and lower plateau to be 1) 95%-tile or 5%-tile 2) Check Enter value, and enter arbitrary numbers.
    - Polynomial : Choose the order to be 1,2 or 3.
    - Exponential : Enter initial values of the scaling factor and time constant.

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