making functional MRI easy

NordicNeuroLab

nordicBrainEx

Tutorial – BOLD Module

Please note that this tutorial is for the latest released nordicBrainEx.
If you are using an older version, please upgrade.

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Contents

1 Introduction to BOLD analysis

The nordicBrainEx BOLD computation can analyze functional BOLD data acquired with all major MR vendors. The BOLD analysis includes basic pre–processing steps (slice time correction, motion correction, spatial and temporal smoothing, high-pass filtering), voxel based statistical analysis using the General Linear Model (GLM) and visualization of statistical output maps.

The GLM is a well-established method for analyzing BOLD data. The method, as it is implemented in nordicBrainEx, is described in Kiebel and Holmes: *The general linear model* in Ashburner et al (eds.): *Human Brain Function*, 2nd ed, 2003.

2 BOLD design files

2.1 Running the analysis

After loading a BOLD series, nordicBrainEx automatically tries to connect a design file to the dataset. The name of the associated design file for the series is shown in the *Settings* column in the *Select patient data* window. You should check that the correct design file has been chosen. If a design file is connected to the BOLD series, the analysis starts automatically after the loading and co–registration has finished.

You can choose a different design file by right clicking on the chosen BOLD series in the *Series* tab in the *Select patient data* window (see Figure 3). Only fitting design files will appear in the list. Fitting design files are those that match regarding "Number of volumes" and "Repetition time".

If no design file is associated with the scan, the *Settings* column in the *Select patient data* window will be empty. If you try to run the analysis when there is no design file associated with the scan, the analysis will stop after the co-registration procedure, and warning message will appear (see Figure 1), telling you that no design file was found. You then have to import or create a new design file (see 'Importing BOLD design files' on page 5 or 'Edit or create new design files' on page 5).

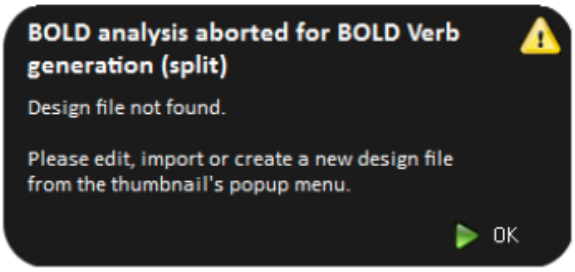

Figure 1: If you try to run the analysis when there is no design file associated with the scan, this warning will appear.

If you want to display the BOLD settings for a dataset whose analysis is running, you must wait until the computation has finished or you abort the computation. This is to avoid that parameters can be modified while they are used for the analysis.

2.2 Accessing BOLD design files

BOLD design files can be accessed from two different locations in nordicBrainEx.

- In the *Visualization* interface, right click on the selected BOLD series' thumbnail in the *Data panel* and choose *BOLD settings* (see Figure 2).
- In the *Select patient data* window, right click on the selected BOLD series in the *Series* tab and choose *BOLD settings* (see Figure 3).

This will open the *List of design file* menu. The current design file can then be edited, a new design file can be made, or design files can be imported. Also, a list of all available design files is shown, all of which can be selected to be used as current design, edited or deleted.

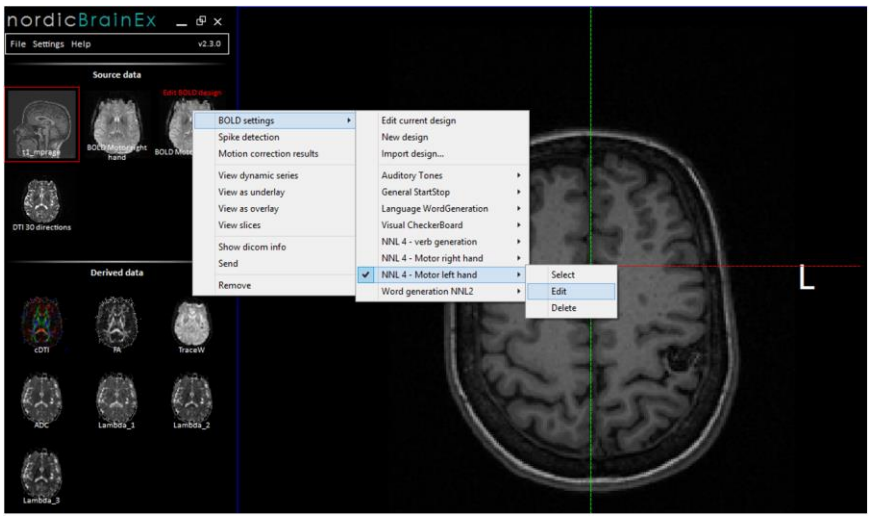

Figure 2: In the Visualization interface, right click on the series' thumbnail in the Data panel

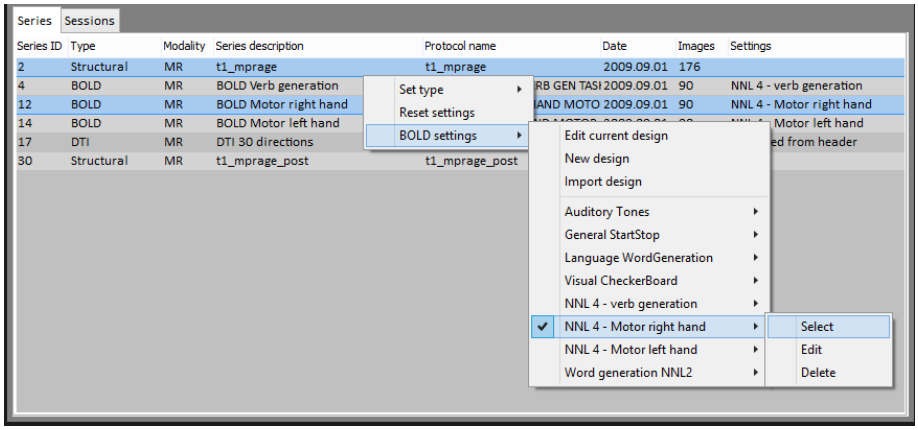

Figure 3: In the Select patient data window, right click on the selected series and choose BOLD settings.

2.3 Importing BOLD design files

If you use *nordicAktiva* as your stimulus presentation software, you can push the design file from nordicAktiva to nordicBrainEx. The design file will then automatically be connected to the patient's BOLD series, see Figure 4

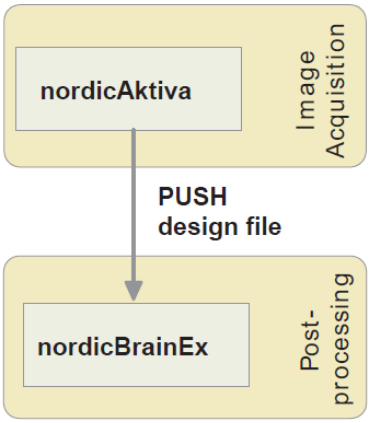

Figure 4: Push the design file from nordicAktiva to nordicBrainEx.

If design files that you would like to use already exist on your computer/network, they can be imported into nordicBrainEx. In the *List of design files* menu (see Figure 2 and Figure 3), select *Import design*. The imported design file will appear in the list of all designs. When choosing a different design file, the BOLD analysis will be automatically redone.

2.4 Edit or create new design files

In the *List of design files* menu, accessed either from the *Select patient data* window or the *Visualization* interface (see Figure 2), choose *Edit current design* or *new design*. A four-tab window with acquisition parameters will appear (see Figure 11). Note that you can view all tabs simultaneously by clicking on the *View all tabs* button on the bottom.

Start creating a new design file by entering the design name in the *Design name* field and enter acquisition parameters, preprocessing steps, paradigm and contrasts. The different parameters are described in 'Details on BOLD design file settings' on page 12.

3 Interacting with BOLD results

3.1 General use

When the BOLD analysis is completed, the resulting activation maps will automatically be added as overlays on the structural volume, and the *Visualization* interface will open (Figure 5).

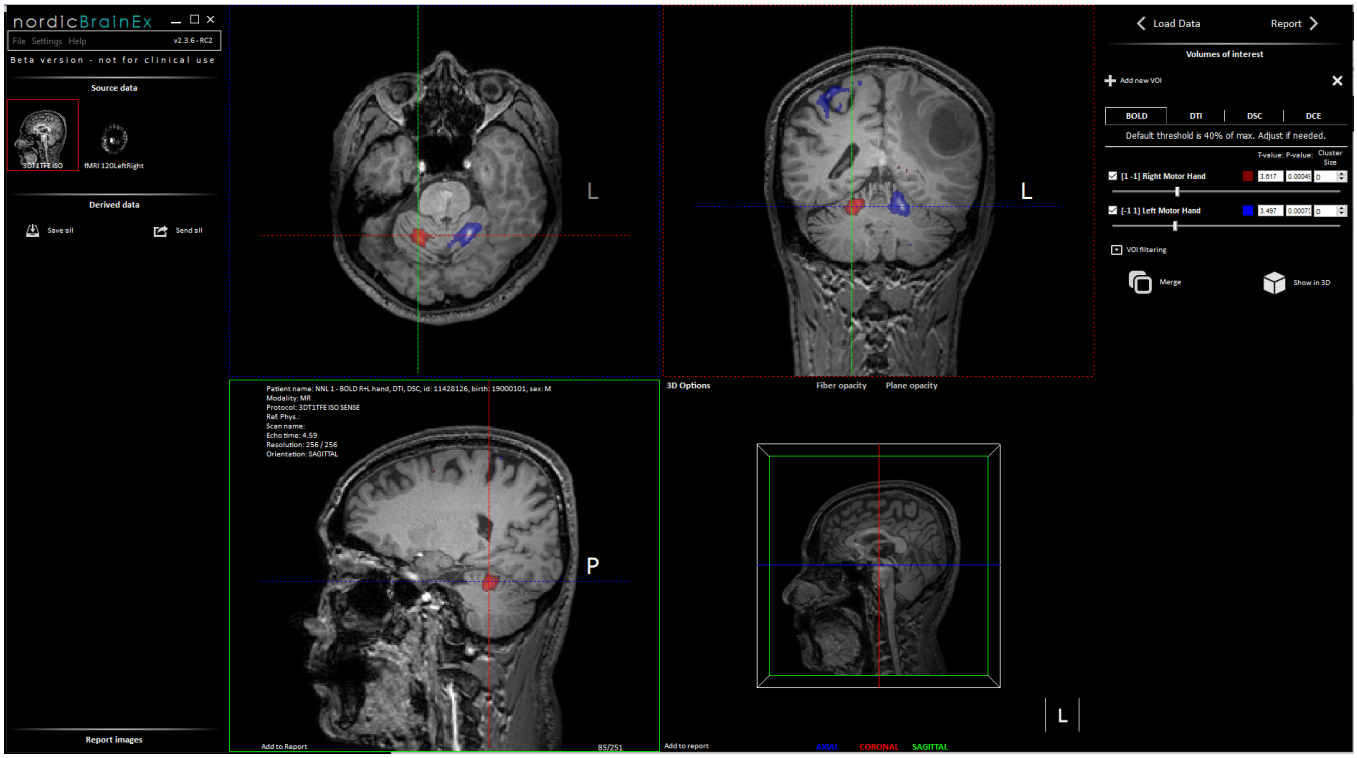

Figure 5: Visualization and interaction with the BOLD results in nordicBrainEx.

The statistical output maps will initially be shown as overlays on the structural data with a threshold set to 40% of the maximum T-value. An adjustment of the threshold is probably necessary. This can be done from the *BOLD tab* in the interaction panel (see Figure 5 and Figure 6). Each contrast will be listed with their names (corresponding to the description assigned in the design file). Click on the color indicator box next to the contrast name to expand and show options for selecting BOLD overlay color and opacity (Figure 6).

The cluster size entry that exists for each individual statistical map allows for setting a minimum number of contiguous voxels in the statistical map, i.e. all visualized voxels must be in a group of at least this minimum number of other contiguous voxels with a T-value above the threshold value.

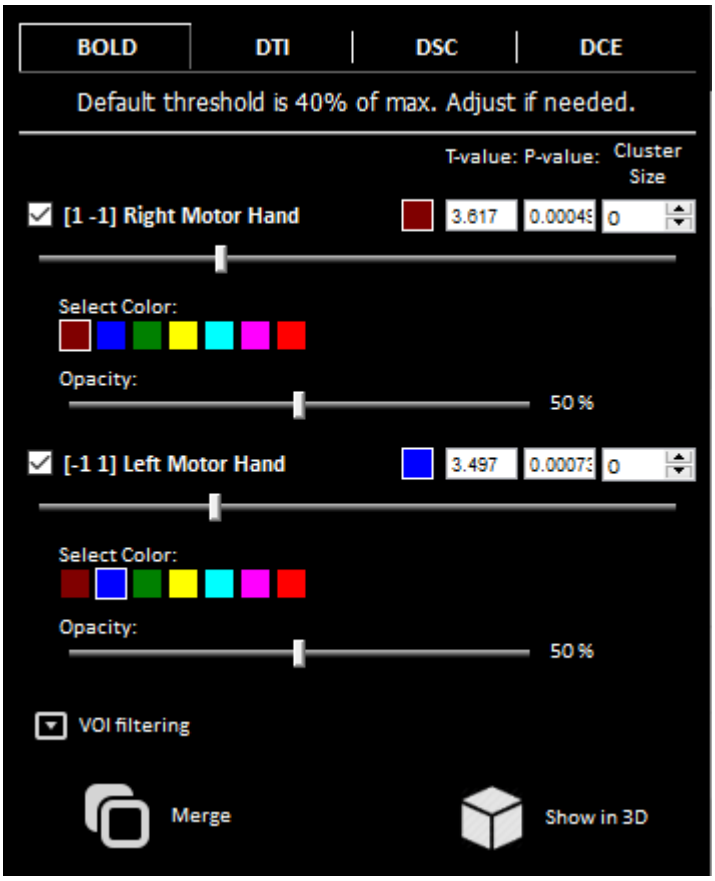

Figure 6: Thresholding the contrasts. Click on the color indicator box to expand options for selecting BOLD overlay color and opacity.

Merge will create an export of each of the selected activation maps on a format chosen in *Export results as...* under the *Settings* menu in the upper left corner of the *Visualization* interface. The different export formats are suitable for different neuronavigation devices.

- *Color export*
  The BOLD activation maps will be exported as a new DICOM image series with a geometry equal to that of the underlay series.
- *White pixels on greyscale*
  The output is a copy of the underlay series with the values of the pixels inside the volumes with BOLD activations, as defined by the thresholding of the activation map, set to the highest possible value (white).
- *Vector format*
  Output is a file containing the coordinates of the pixels in the underlay series that are inside the volume with BOLD activation as defined by the thresholding of the activation map. The file also contains the geometry information. The validity of the visualization of the vector format in an external viewer must be verified by the user of the viewer. For further details about this format, please contact NordicNeuroLab.

Figure 7 shows an example of the different export formats.

The new series (using *Color export* or *White pixels on greyscale*) can be saved to the local database and sent to remote entities such as PACS or a neuronavigation system. Please note that neither saving to the database nor sending is done automatically but must be done by right-clicking on the thumbnail or by selecting *Save all* or *Send all* in the left panel of the interface.

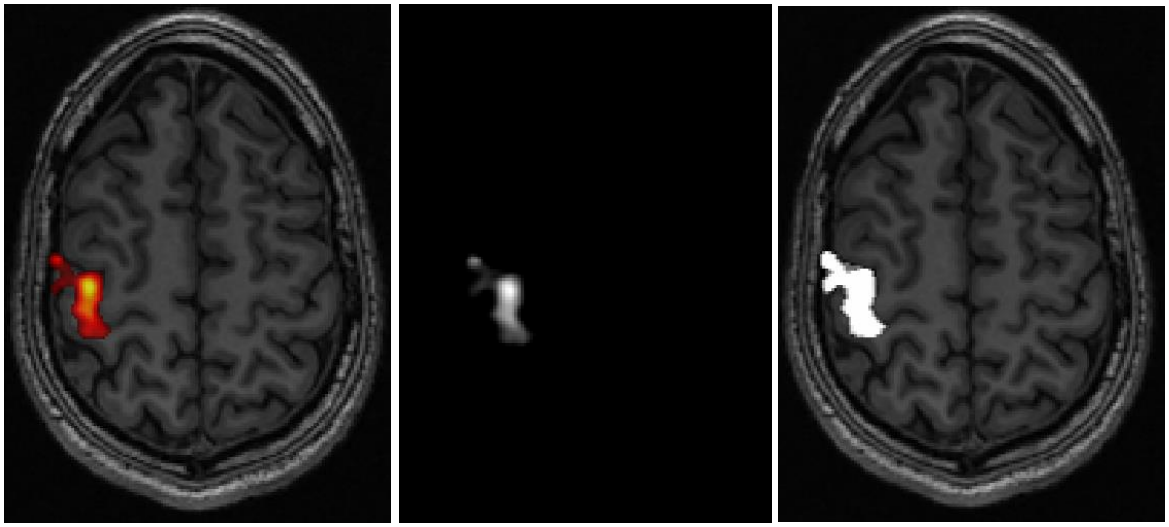

Figure 7: Left: original BOLD contrast, with a given threshold, middle: merged series as 'color' export, right: merged series as 'white pixels on greyscale' export. Both merged series show the same BOLD threshold.

Show in 3D will visualize the selected activations in the 3D viewing window (Figure 8). *Please note* that this operation can take some time, depending on your computer's graphic card and system specification. A tip is to adjust the threshold relatively high (high T–value/low P–value) before choosing *View in 3D*.

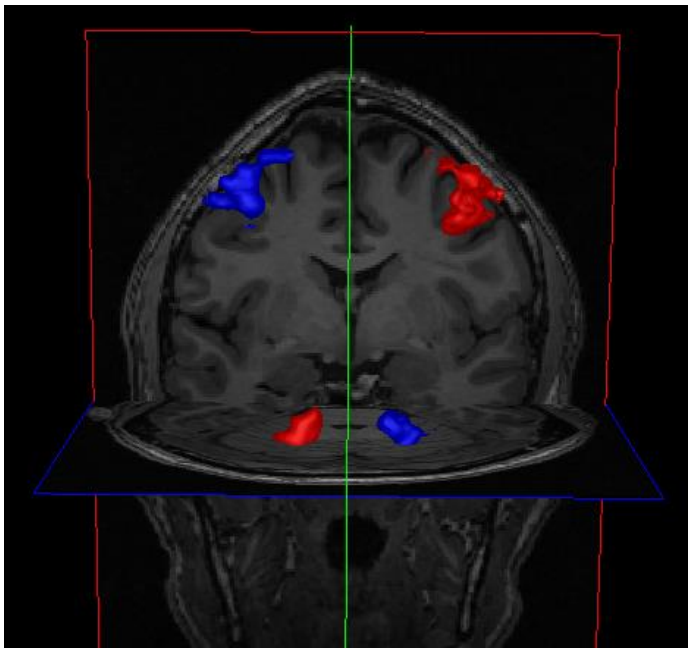

Figure 8: 3D view of two BOLD contrasts, displayed as red and blue overlays in 3D.

More details on how to work with the 2D and 3D MPR views in nordicBrainEx are described in 'Visualization panels and thumbnails' in 'Tutorial – Visualization and Interaction'.

3.1.1 Using VOI filtering to remove unwanted areas before merge and export

To remove regions of noise or other unwanted regions before merging for neuronavigation, the VOI filter functionality can be used. This will use VOIs to select regions that one wants to include or exclude from the merged output. Multiple VOIs can be included or excluded to include/exclude multiple regions from the merged series. An example is shown in Figure 9, where only one VOI has been used.

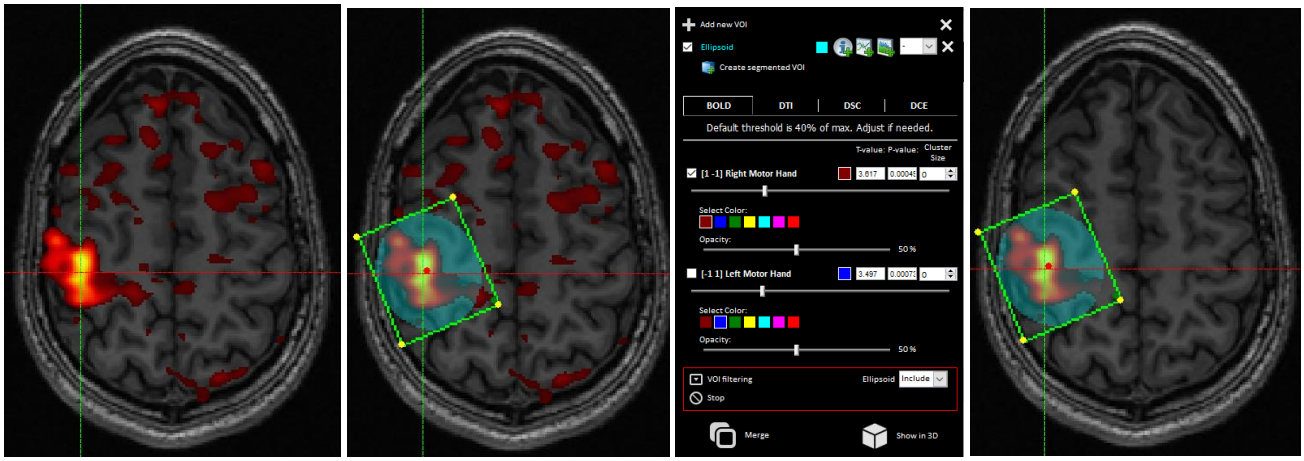

Figure 9: Using VOI filtering to exclude regions before merging. A) BOLD results with a given threshold. B) A VOI is drawn around the activation of interest. C) VOI filtering is activated and the VOI is set to 'include'. This will remove all activations outside this VOI (D).

To use the VOI filtering, adapt your workflow to these following steps:

1. Set the threshold and locate the area(s) of interest.
2. Add VOI(s).
3. Select VOI filtering and select include/exclude on the VOI(s).
4. Verify the output in real time in the MPR.
5. Merge for neuronavigation.
6. Stop VOI filtering to continue.

While in VOI filtering mode, some of the application's functionality is blocked. To access all functionality, VOI filtering mode must be stopped (hit 'Stop', see Figure 9 C).

3.2 Spike detection in BOLD

Spike detection is a BOLD quality check by visual inspection of the BOLD series, which can be performed by the user. The user can exclude those slices or volumes from the analysis which contain spikes. The spike detection is

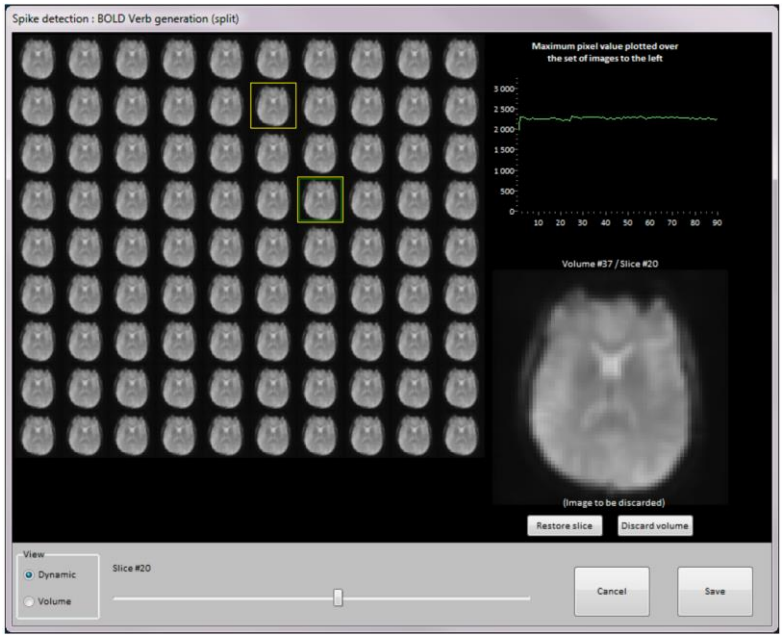

Figure 10: The BOLD quality check interface.

normally done when the results of the BOLD analysis have not induced the expected results. In that case you can have a closer look at the BOLD series and exclude spike slices or volumes.

The spike detection interface (see Figure 10) can be opened by right clicking on the BOLD series' thumbnail in the Data panel of the Visualization interface, and selecting *Spike detection* (see Figure 2). The BOLD series can be displayed *dynamically* (all volumes (the entire dynamic BOLD time series) for one selected slice) or as a *volume* (all slices for a chosen volume). Use the slider to easily change the slice/volume.

The curve in the upper right corner shows the maximum pixel value of all the images to the left. If you have a slice/volume with high pixel values, this will show on the curve.

If you have detected a spike slice, click on the slice in order to mark it, and then choose *Discard slice*, or *Discard volume* if you want to discard the entire volume at the specific time point. The following border colors are used in the *Spike detection* interface:

- A *green* border indicates the current slice/volume.
- A *yellow* border indicates that a slice/volume is marked to be discarded.
- A *red* border indicates that this slice/volume has been saved as discarded in a previous session.

Slices/volumes can be restored by choosing *Restore slice* or *Restore volume* (please note that after you re-run the analysis, the slices/volumes cannot be restored). When you have marked all slices/volumes you would like to

discard, click on *Save (see* Figure 10*)*. You will first be prompted with a warning telling you that discarding slices will modify the pixel values, and then a question if you want to re-run the analysis. If answering *yes*, the analysis will be redone without the discarded slices. All marked slices will then be replaced by the average of the corresponding slice from the two neighboring volumes.

3.3 Motion correction results

Right click on the BOLD series' thumbnail in the *Data panel* of the *Visualization* interface and choose *Motion correction results*. Motion graphs will be displayed for the chosen series. This option will only be available if motion correction was done as part of the BOLD preprocessing steps. You can read more about motion correction in 'Motion correction (BOLD/DTI/DSC)' in 'Tutorial – Visualization and Interaction'.

3.4 Saving BOLD data

There are several different ways of saving the data derived from the BOLD analysis.

- If choosing *Merge* in the *Interaction panel*, the selected BOLD activity maps overlaid on the structural datasets can be merged into a new DICOM series (see Interacting with BOLD results on page 6).
- In the *Slice editor* window (See 'Tutorial – Visualization and Interaction'), accessed by right clicking on any of the three planes in the MPR and choosing Slice selection (and clicking on Slice) or Slice all, slices can be:
  - Saved to the database
  - Saved and sent to a remote entity (for example PACS)
  - Added to report (Select 'View slices' by right-clicking on the new thumbnail after saving to database)
  - Saved as AVI-file (Select 'View slices' by right-clicking on the new thumbnail after saving to database)
- By right clicking on any of the three planes of the current volume in the MPR, choosing
  - *Create snapshot* will open the *Slice editor window* of the current slice.
  - *Create snapshot of MPR* will open the *Slice editor window* of the three current planes of the MPR, as well as the visualized activations in the 3D viewer.
  - *Copy* will copy the current slice to the clipboard, so it can be pasted into other programs (like word etc.).
- *Send*, accessed by right clicking on series' thumbnail in the *Data panel* will send the series to a remote entity (for example PACS). Read more about saving sessions in 'Saving data to database and PACS' in 'Tutorial – Handling Image data'.
- In the 3D viewer, animations can be made by right clicking in the 3D viewer and choosing *Create snapshots/animations*. This will create a new thumbnail that can be saved, for example as an AVI-file. How to make and save animations are described in more details in 'Interacting with the 3D viewer' in 'Tutorial – Visualization and Interaction'.
- *Add to report* (bottom left of any plane in the MPR) can be chosen to add the current slice to Report (see 'Report' in 'Tutorial – Visualization and Interaction').

- *Saving the session* can be done by choosing *File -> Save Session*. This will save the entire session (all loaded and acquired datasets) to the database. The session name that you entered will appear in the session table on the Select patient data window. Read more about saving sessions in 'Saving, loading and sending a Session' in 'Tutorial – Handling Image data'.

4 Details on BOLD design file settings

4.1 Acquisition parameters

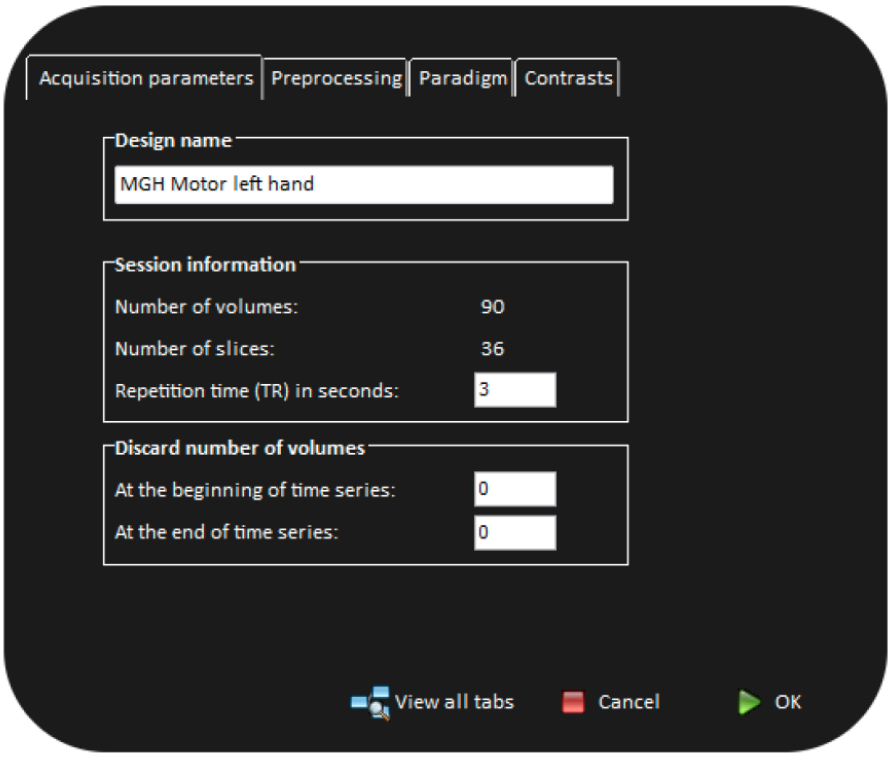

Figure 11: The BOLD settings interface in nordicBrainEx

The acquisition parameters define the imaging protocol settings needed for the BOLD analysis (Figure 11):

- *Number of volumes*
  Number of volumes in the BOLD series. This value is automatically deduced from the BOLD series and cannot be changed.
- *Number of slices*
  Number of slices in the BOLD series. This value is automatically deduced from the BOLD series and cannot be changed.
- *Repetition time (TR) in seconds*

TR–time is the time difference from when a given slice is acquired in one volume, to when it is acquired in the next volume.

- *Discard number of volumes at the beginning of the time series*
  Discard a given number of volumes at the beginning of the image time–series. The default value is 0.
- *Discard number of volumes at the end of the time series*
  Discard a given number of volumes at the end of the image time–series. The default value is 0.

4.2 Preprocessing

The preprocessing options define which steps will be performed before the BOLD GLM computation starts (see Figure 12):

- *Slice time correction*
  Slice time correction is done to correct for the fact that for a given volume in the image time–series, each slice is acquired at slightly different times. The correction is done using spline interpolation. For blocked designs, slice time correction might not be necessary.
- *Motion correction*
  Apply motion correction to the BOLD data to correct for patient movement during scanning. For details see 'Motion correction (BOLD/DTI/DSC)' in 'Tutorial – Visualization and Interaction'.
- *Gaussian smoothing (Spatial)*
  Gaussian spatial smoothing is performed to blur and reduce high–frequency spatial noise in the images.
- *High–pass filter*
  A temporal high–pass filter (Butterworth filter) is applied to reduce low frequency drifts in the image time series.
- *Auto–detect noise threshold / Noise level*
  Toggle on/off whether automatic detection of noise threshold should be done to the data. If checked, the current noise threshold will be estimated automatically. If unchecked, a static threshold will be applied, that can be defined manually by using the *Noise Level* slider bar.
- *Show advanced options*

  Can be toggled on/off and provides additional parameters for most of the preprocessing steps listed above.

  – *Slice time correction*: If used, the slice time correction parameters must correspond to the order in which the slices of the image acquisition were collected. For example, if there are 10 slices, an ascending interleaved sequence with odd start would correspond to 1–3–7–9–2–4–6–8–10 (the slices are numbered from 1).

  – *Gaussian smoothing* can be done by applying either a two–dimensional (within slice) or a three-dimensional (within volume) filter. Also, the full–width–half–maximum (FWHM) of the filter can be specified (in millimeters). By default, the FWHM is about twice the voxel size in all directions.

– The *high-pass filter* can be specified either by the filter's wavelength in seconds or the cutoff frequency in Hz. If editing one, the other will be automatically updated. *Please note* that setting

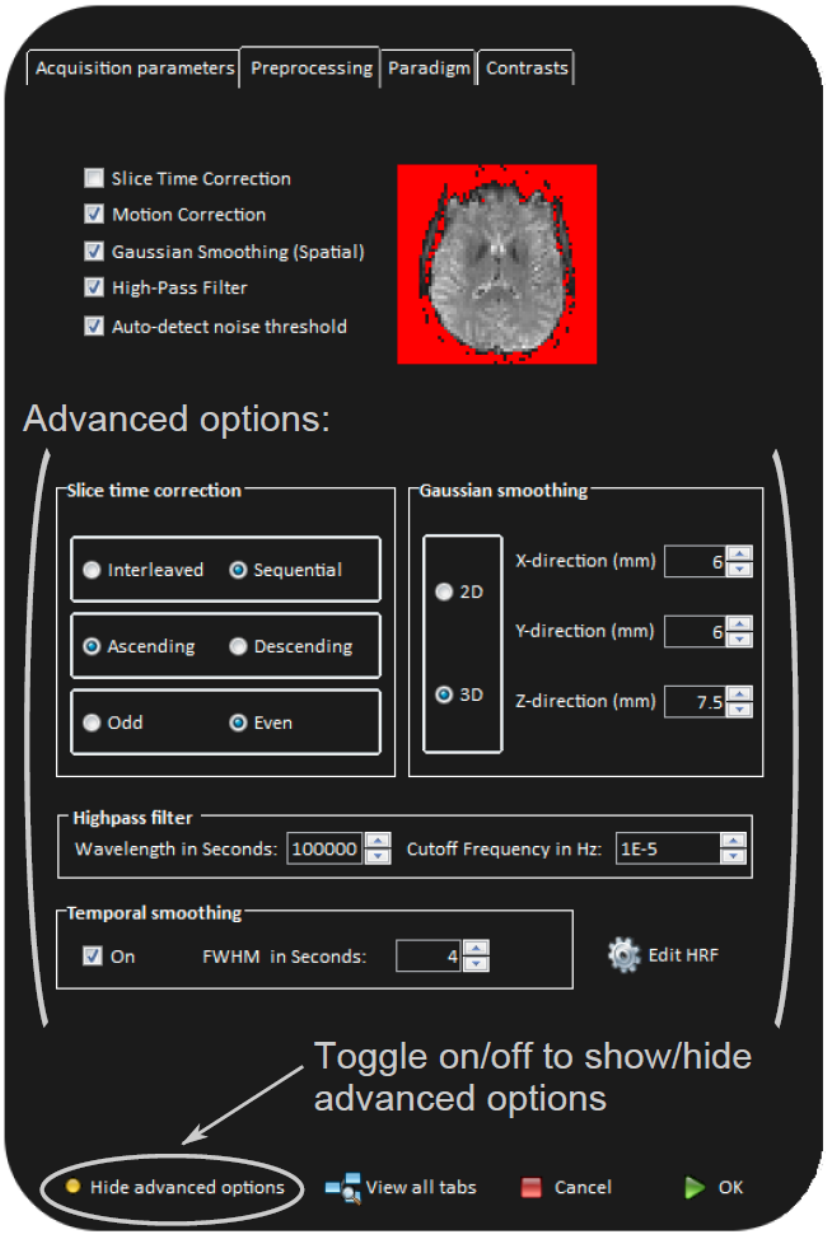

Figure 12: BOLD settings for preprocessing before GLM computation. Advanced options (in brackets) can be toggled on/off by selecting Show/hide advanced options

the wavelength in seconds too low might result in filtering out the BOLD response. If used, it is *crucial* that the correct wavelength/cutoff frequency is specified. It is the user's responsibility to set up the correct wavelength.

– *Temporal smoothing* using a Gaussian filter is performed for the GLM estimation. It will influence the degrees of freedom used in statistical analysis. By default, the temporal smoothing is on with a FWHM default value of 4 seconds.

– *Edit HRF:* By clicking here, the hemodynamic response function is shown, and can be edited. Please note that in most cases, it should not be necessary to edit the default values of the HRF.

4.3 Paradigm

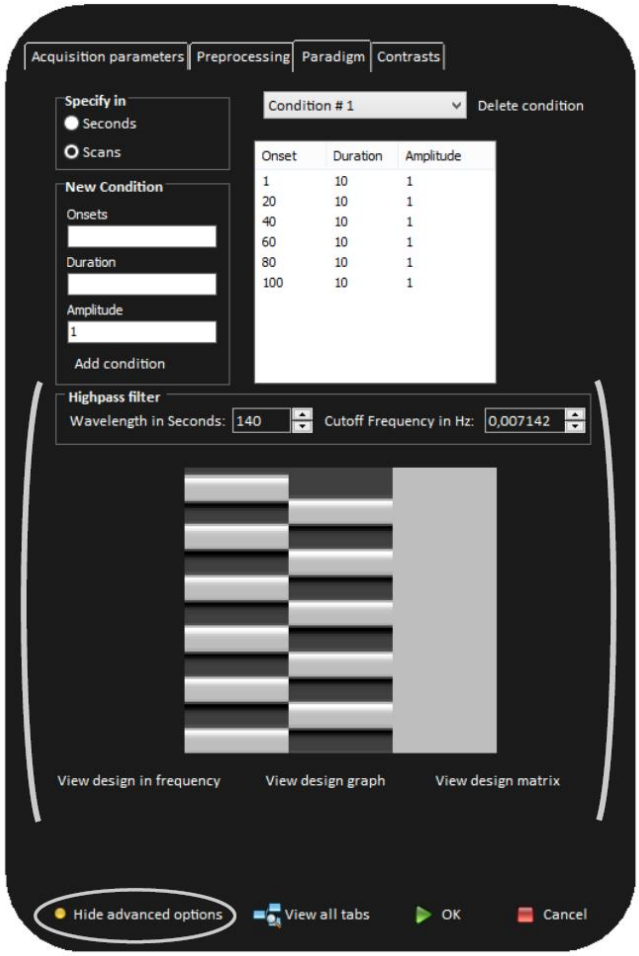

Figure 13: BOLD settings describing the paradigm. Advanced options are shown in brackets and can be toggled on/off by choosing show/hide advanced options. To add several paradigms, first define onset and duration, and then click on Add condition.

Define all conditions, their *onset* and *duration* depending on the stimulation paradigm and specify it in *Seconds* or *Scans*. The *amplitude* can be used to weight conditions individually and is by default set to 1.

After you entered the values for the first condition click on the *Add condition* button and the first condition will be added. Enter all the other conditions in the same way.

Example for a block design that is defined in seconds, with a block duration of 30 seconds:

- *Specify in*: "Seconds".
- *Onset*: "0 60 120 180 240 300".
- *Duration*: "30" (indicate all durations if they are not equal in length).

- *Amplitude*: "1".

Alternatively, if the spacing between the onset times is the same throughout the condition, you can write "start time" : "spacing" : "end time" in the *Onset* field (corresponding to 0:60:300 being written as onset in the above example).

If choosing the *Show advanced options*, you can choose between viewing the design in frequency, viewing the design graph, or viewing the design matrix.

- The *high-pass filter* can be specified either by the filter's wavelength in seconds or the cutoff frequency in Hz. If editing one, the other will be automatically updated. *Please note* that setting the wavelength in seconds too low might result in filtering out the BOLD response. If used, it is *crucial* that the correct wavelength/cutoff frequency is specified. It is the user's responsibility to set up the correct wavelength. This is the same parameter as described under *Advanced options* in the *Preprocessing* tab. The cut–off value is visualized as a vertical line if choosing *View design in frequency* (see below). If editing the wavelength in seconds, click in the frequency window to update the display.
- *View design in frequency* will display the magnitude response of the design matrix (frequency vs magnitude response).
- *View design graph* will display the paradigm as a design graph or as a boxcar graph (time vs amplitude). The design graph is the boxcar graph convolved with the HRF.
- *View design matrix* will show the paradigm's design matrix. This is the default view when opening advanced options.

4.4 Contrasts

Contrasts are used to generate statistical output maps of the BOLD general linear model (GLM) analysis. Each condition is described by an *element* in a *contrast vector*.

If you want to add more elements to the contrast vector, you first have to define more conditions under the *Paradigm* tab (and the paradigm must of course correspond to the actual acquired BOLD MR scan of the patient). For each condition, a corresponding element in the contrast vector will be added

Edit each contrast element by clicking up/down on the slider corresponding to each condition (Figure 14). After you have defined all conditions, several *contrasts* (or *contrast vectors*) can be added by clicking on the *Add* button (Figure 14). By doing this, you can investigate interaction between the stimulations (see example below).

Example: Two conditions (Figure 14): finger tapping with left hand and finger tapping with right hand (the contrast vector has two elements).

- Contrast vector = [1 0] will show where there is an increased response due to the first condition (finger tapping with left hand).

- Contrast vector = [0 1] will show where there is an increased response due to the second condition (finger tapping with right hand).

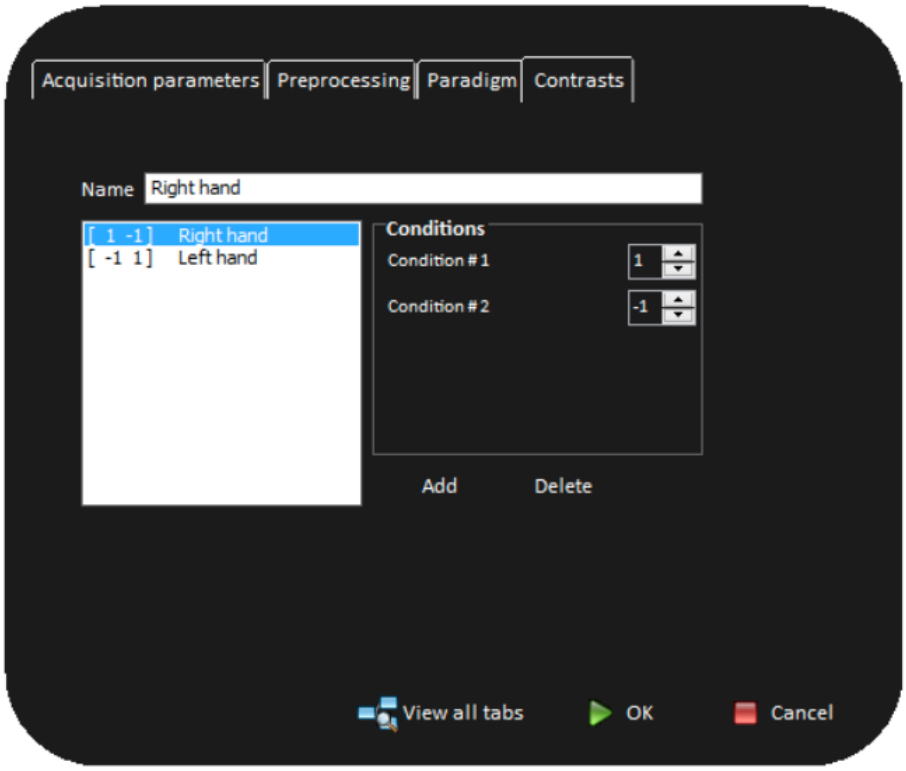

Figure 14: Contrasts for the BOLD design can be added and edited here

4.5 Saving new settings in the BOLD design file

After defining all parameters in the design file, click on *OK*. The BOLD analysis will now run with the new settings. If you have made changes to the design, you will be asked if you want to save the new design, or run with the new settings, but not save them. If you have not already chosen a different name for the new design, you will get a chance to do this now.

Note that you can edit the BOLD design file settings and run the analysis with or without saving the new settings in a new design file. If you run the analysis without saving, the edited settings will be remembered if *Edit current design* is re-opened. *Note however*, that if you change the preprocessing settings, the dataset might have to be re-loaded for the new settings to be active. This requires that these settings are saved in a new design file.