

BASCO User Manual

Version 2.1

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Introduction

BASCO (BetA Series COrrrelation) is a software tool for investigating inter-regional functional connectivity in event-related fMRI data. This tool is based on an approach introduced by Rissman and colleagues (2004). In contrast a standard univariate analysis, a general linear model (GLM) is fitted to the data where the evoked activity in each trial is modeled by a separate covariate. This renders a series of beta-values for each voxel which is related to a given experimental condition. The functional connectivity between brain regions is derived from correlating beta-series. Estimated movement parameters can be included in the GLM. The classical parameter estimation is performed using SPM. BASCO offers the following analysis approaches:

- i) **Seed-based functional connectivity analysis.** This yields functional connectivity maps using a defined seed-region. The mean beta-series is estimated for the seed-region and correlated to the beta-series of each individual voxel within the brain.
- ii) **ROI-based network analysis.** Given a parcellation of the brain, e.g. based on the SPM AAL template (Tzourio-Mazoyer, Landeau et al. 2002), the mean beta-series are extracted for each ROI and a network matrix is calculated correlating all ROI beta-series.
- iii) **Voxel-based whole brain network analysis.** BASCO allows you to create voxel-degree maps for a selected condition. The degree of a voxel is defined as the number of connections to other voxels in the brain which are stronger than a defined absolute threshold. The voxel-degree is a sensitive marker for altered functional connectivity providing a high spatial resolution.

Connectivity analyses are performed for a specific condition or a set of conditions on individual subjects. The modulation of functional connectivity by an experimental condition can be investigated on group-level using a paired t-test. Between-group effects can be studied performing a two-sample t-test using connectivity maps for the same experimental condition. More complex analyses can be performed applying an ANOVA or multiple regression analyses.

Details on the methods applied in this toolbox can be found in Göttlich et al. (2015). This toolbox was used to investigate the neural response to socio-emotional stimuli from a network perspective using a graph-theory based analysis approach (Göttlich, Ye et al. 2015).

This manual describes how to install the BASCO toolbox. The functionality and the handling are described in form of a hands-on tutorial. BASCO is publically available under the GNU General Public License (GPL) from the NITRC (Neuro-Informatics Tools and Resources) BASCO project pages: <http://www.nitrc.org/projects/basco>. Questions and comments may be sent directly to martin.goettlich@neuro.uni-luebeck.de or to the BASCO user forum. Please cite the following paper if you used BASCO in your analysis:

Göttlich, M., F. Beyer, U.M. Krämer (2015). "BASCO: A Toolbox for task-related functional connectivity."

Installation

BASCO is implemented in Matlab® (<http://de.mathworks.com>) and depends on SPM (<http://www.fil.ion.ucl.ac.uk/spm>) and MarsBaR (<http://marsbar.sourceforge.net>). MarsBaR is a region of interest toolbox for SPM. Carefully follow each of the following steps to install BASCO. BASCO will not work if it wasn't installed properly and if dependencies aren't resolved without conflicts.

- 1) Download and install SPM8 or SPM12 and MarsBaR (MarsBaR version 0.44 or higher; <http://marsbar.sourceforge.net>).
- 2) Make sure that you added SPM and MarsBaR to the Matlab® path (not with subfolders) and that both toolboxes are working properly. Run both SPM and MarsBaR and check that there are no error messages.
- 3) Download the latest version of BASCO.
- 4) Extract the files. You may want to use the Matlab® command 'unzip' to do this.
- 5) Add the BASCO folder to your MATLAB path (not with subfolders).
- 6) Download the tutorial data. Extract the data in your BASCO folder.
- 7) Some analysis scripts provided with the toolbox call functions implemented in the Brain Connectivity Toolbox. Download the latest version of this toolbox from <https://sites.google.com/site/bctnet>.

Tutorial

The experimental design used in the tutorial data was as follows. For the measurement of neural responses to socio-emotional stimuli, participants were presented with black-and-white drawings of five categories: emotionally neutral situations involving one person only (one person performing a neutral action, such as ironing), emotionally neutral situations involving two persons (two people interacting in a neutral manner, such as playing chess), emotionally negative situations involving one person (one person in distress, such as falling off a boat), emotionally negative situations involving two persons (two people interacting in an aversive manner, such as a man hitting a woman) and scenes with objects only (e.g. a desk). Negative emotions included anger, sadness, pain or anxiety. There were three experimental runs employing a slow event-related design. Pictures were presented in random order but with no more than two successive pictures of the same condition. Each picture was presented for 6 s, followed by a 10 s fixation cross. Each run comprised 40 drawings, 8 per condition. The tutorial data set comprises data of two subjects which was already preprocessed (slice time correction, realignment, warped to MNI space and spatially smoothed).

The BASCO GUI

1) Start BASCO (within Matlab®). The BASCO GUI should appear (Figure 1). At start-up BASCO checks if MarsBaR and SPM are installed and returns an error message if this is not the case. Note that there is a message box. New messages appear always on top.

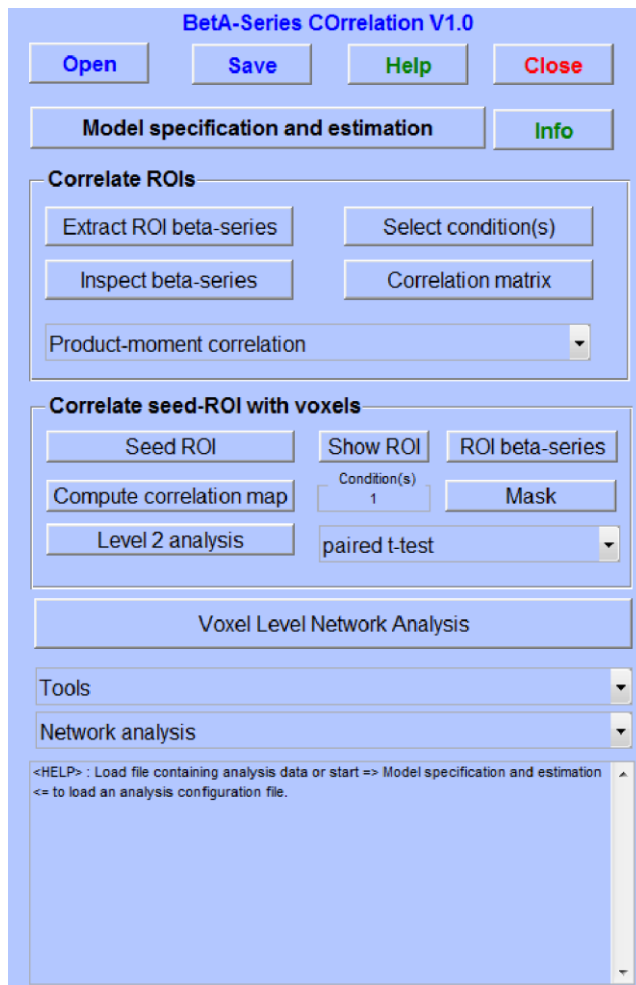


Figure 1

2) Open the file 'tutorial/empathy/anadef.m' with the Matlab® editor. This Matlab® script allows you to configure the analysis. You define the experimental design (number of conditions, the names of the conditions), configure the beta-series analysis and specify the data and onset-files for each subject. See comments for more details. For this tutorial set the variable AnaDef.ROIAnalysis to 'true'.

3) Push the button 'Model specification and estimation' and select the file tutorial/empathy/anadef.m'. BASCO now executes the analysis configuration script and performs the model specification and estimation. All data is saved to the file specified in the analysis configuration script (see step 2 of this tutorial). Depending on your hardware resources this step may take a few minutes. Please check the output in the message box and the Matlab® command window.

4) The button 'Save' allows you to save the current analysis. Analysis-files can be loaded pushing the 'Open' button. Analysis data is stored in a .mat file which can be inspected by double-clicking on the file in the Matlab® file browser).

ROI based network analysis

1) In order to select trials with emotional content push the button 'Select condition(s)' and enter '1 3'. See the analysis configuration file for details on the experimental design and the experimental conditions. Push the button 'Inspect beta-series' to inspect the regional β -series (Figure 2).

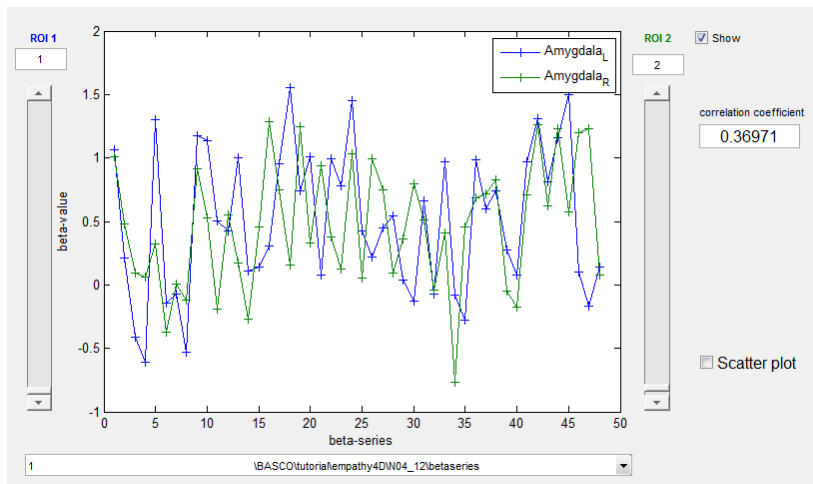


Figure 2

Shown are the two β -series for the selected condition (emotional content) and the correlation coefficient for the two selected ROIs. Other ROIs can be selected using the scroll-bars. The drop-down menu allows you to select a different subject. You may also want to inspect the scatter plot.

2) Now you calculate the network matrix (connectivity matrix) by selecting 'Product-moment correlation' in the pull-down menu. For each AAL atlas ROI a mean beta-series was calculated. These beta-series are now correlated to give a connectivity matrix. Only trials with emotional content are taken into account.

3) You may then inspect the correlation matrix. Push the button 'Correlation matrix'. A new window should appear (Figure 3). In the top left corner the correlation matrix is shown (for the present subject). Select an absolute threshold of 0.6. Use the scroll bar or enter the value directly into the edit box. In the panel 'Seed ROI' enter 13 for the posterior cingulate cortex. The table shows you the ROIs which show a strong correlation to this seed region (above 0.6). Push the button 'Show ROIs' for displaying the ROIs (Figure 4). We mainly see strong correlations to medial frontal and angular regions.

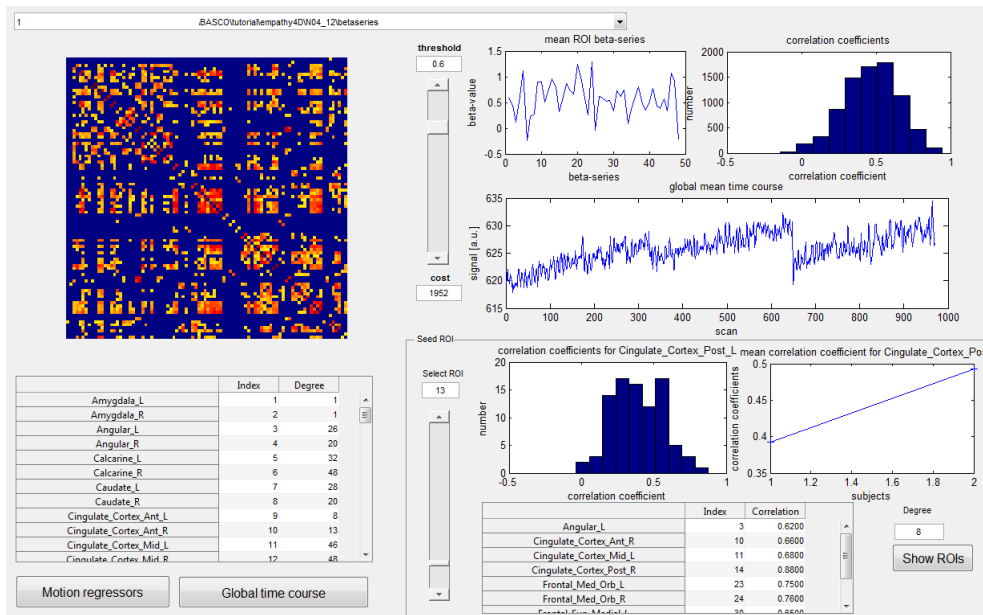


Figure 3

You can switch to another subject via the pull-down menu. The table in the left lower corner lists the ROIs included in the analysis and their degree centrality according to the selected threshold. The buttons ‘Motion regressors’ and ‘Global time course’ allow you to perform data quality checks on the data.

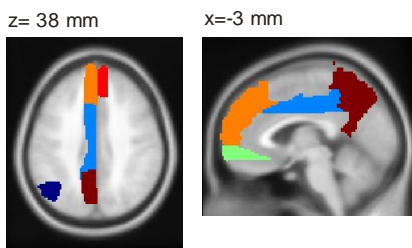


Figure 4

4) Select ‘arc-hyperbolic tangent transf.’ from the pull-down menu. This performs a Fisher z-transformation to allow for averaging of correlation coefficients and statistical testing. Then hit the ‘Save’ button and save the file to ‘empathy4D/out_estimated_AAL90_emot.mat’. This saves the analysis data with the current selection of the experimental condition.

5) The simple script ‘tutorial/ana.m’ shows you how to load the analysis data and how to access the data to perform a simple network analysis. You may run the script now.

6) Now we select only trials with neutral content. Push ‘Select condition(s)’ and enter ‘2 4’. Now the network matrix has to be recalculated. Go to the pull-down menu and select

‘Product-moment correlation’. Then select ‘arc-hyperbolic tangent transf.’. Save the file to 'empathy4D/out_estimated_AAL90_neut.mat'.

7) We now want to investigate if the connectivity between network nodes is modulated by the experimental condition, i.e. we test if the edges are significantly different comparing the emotional and the neutral condition. Here, we only have data from two subjects. This doesn't allow for reasonable statistical testing. It is enough, though, to demonstrate a very useful feature of the BASCO toolbox. Select ‘Network edges’ from the pull-down menu ‘Network analysis’. A file browser open and asks you to select two data sets. Select the two analysis files created earlier ('out_estimated_AAL90_emot.mat' and 'out_estimated_AAL90_neut.mat'). A new GUI opens. Figure 5 shows how this would look using data from 26 subjects. You can choose between different statistical tests (paired t-test, two-sample t-test and permutation test) and apply corrections for multiple testing. The table shows which edges are significantly different comparing the two experimental conditions. Hitting the button ‘View NW’ created .node and .edge files which can be parsed by the BrainNet Viewer (<https://www.nitrc.org/projects/bnv/>).

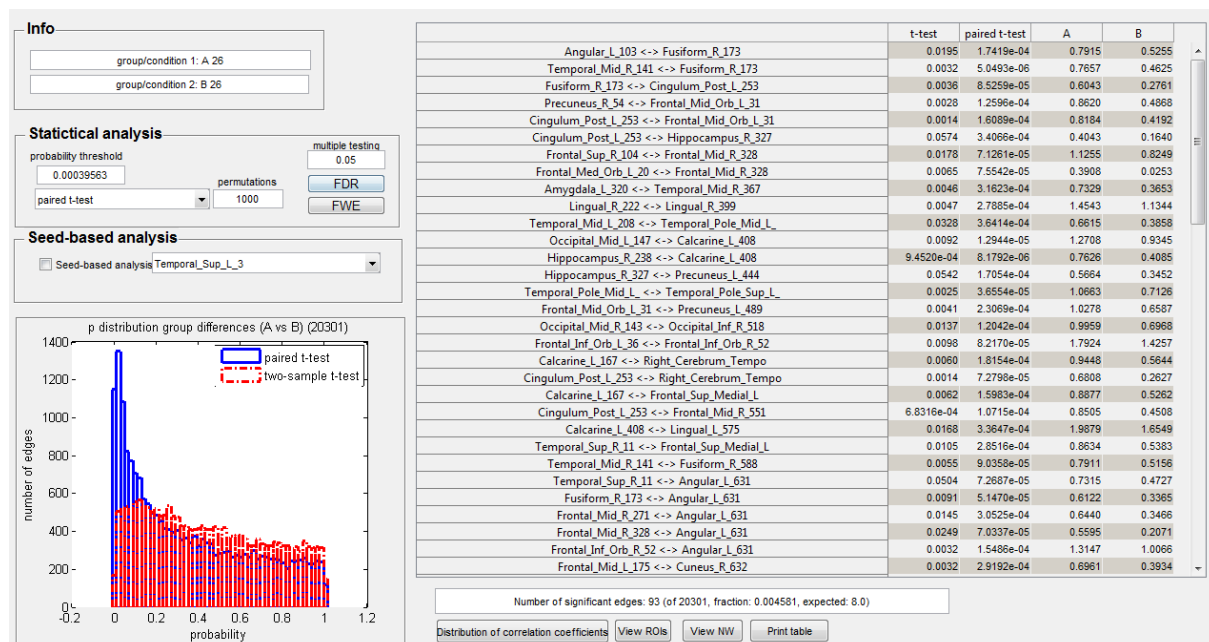


Figure 5

8) You may want to perform a network analysis based on an alternative brain atlas (set of ROIs). This can be done via the button ‘Extract ROI beta-series’. A file browser opens and

asks you to select the ROIs (MarsBaR .mat files). A second file browser opens asking you to specify the text-file indicating the ROI names. See the 'rois/AALROI90/AALROINAME.txt' for an example.

Seed-based functional connectivity analysis (seed ROI to voxel)

- 1) Push the button 'Seed ROI' to select a ROI (MarsBaR) which is used as a seed region. Select the precuneus ROI ('precuneus_sphere_6-0_-57_33_roi.mat') which can be found in the tutorial subfolder. You are asked to enter the name of the ROI. Enter 'precuneus'.
- 2) Use the button 'Show ROI' to view the ROI.
- 3) You may also inspect the ROI beta series pushing the button 'ROI beta-series'.
- 4) Now enter the conditions for the beta series in the edit box: '1 3' for trials where images with emotional content are shown to the subject.
- 5) Push the button 'Mask'. This allows you to select a mask for the seed-based functional connectivity analysis. A file browser opens. Go to the directory 'masks' and select the file 'brainmask_roi.mat'.
- 6) Press 'Compute correlation map' to start the analysis. When the analysis is done use a viewer of your choice to display the connectivity map which can be found in the subfolder 'betaseries' in the subject folder. Note that the correlation coefficients are Fisher z-transformed ('zfcmap_precuneus_1__3.nii').

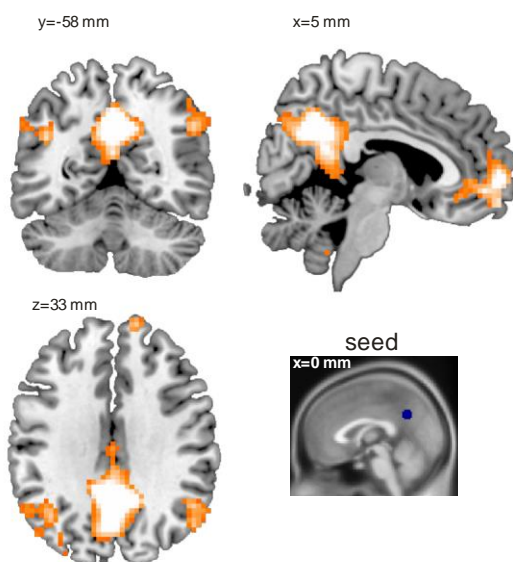


Figure 6

Figure 6 shows the seed-based functional connectivity map for a single subject. For the purpose of this illustration a threshold on the Fisher z-transformed correlation coefficients of $z > 0.7$ was applied. Also shown is the seed-ROI in the posterior cingulate cortex (button 'Show ROI').

Voxel based whole brain network analysis

BASCO allows you to calculate voxel-wise degree centrality maps. The degree centrality is a measure for the connectedness of a voxel with the whole brain and is defined as the number of outgoing connections which are stronger than a given threshold.

1) Push the button 'Voxel Level Network Analysis'. A dialog box opens where you select the experimental condition. Enter '1' for trials where images with socio-emotional content are shown. Accept the default setting for the absolute threshold which is 0.25. This sets an absolute threshold of 0.25 to the voxel-wise connectivity matrix. The string 'ID' appears in the name of the output file and allows you to uniquely name your files. The entry 'Mask' allows you to restrict your analysis to a certain brain mask ('1': use a mask; '0': no mask). Push 'OK'.

2) If 'Mask' is set to '1' you are asked to provide a mask file which is in the same space as the beta-files (this may require a resampling of mask files). Select the file 'masks/spm8/rgm_mask_p03.img'. An error message is shown and the function aborts if the mask file is in the wrong space. In the 'Tools' pull-down menu you can find a function which allows you to conveniently resample and reslice your mask image to fit the beta-files ('Reslice image').

3) Depending on your hardware performance calculating the degree centrality maps may take several minutes per map. When the calculations are done you may inspect the degree centrality map using any NIfTI viewer. You may use MRICron (<https://www.nitrc.org/projects/mricron>) or xjView (<http://www.alivelearn.net/xjview8/>). The degree centrality maps are stored as 3D NIfTI images in the subfolder 'betaseries' in the subject folder.

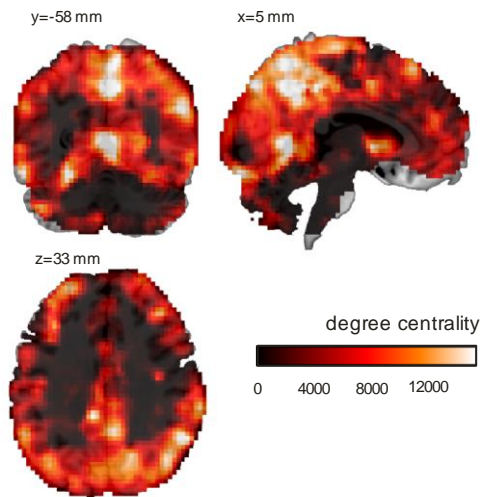


Figure 7

Figure 7 depicts the degree centrality map of a single subject for the emotional condition. We observe a low degree centrality in white matter and ventricles which is expected and useful for quality control. Brain regions showing a high degree centrality ('hubs') are the precuneus, the posterior cingulate cortex, the medial and lateral prefrontal cortex and the inferior parietal cortex.

Group-level analysis

1) BASCO allows you set up a second level analysis. In the pull-down menu right next to the button 'Level 2 analysis' you first have to select the type of analysis: paired t-test (comparing two different conditions within the same group), two-sample t-test (comparing the same condition between two different groups) and a 2x2 flexible factorial design. Select 'paired t-test'.

2) Push the button 'Level 2 Analysis'. A file browser opens which asks you to select the maps you want to include in the analysis. You only have to provide this information for one subject as BASCO knows where to find the data from the other subjects. Select the functional connectivity or degree centrality maps produced earlier (see above). A new file browser opens which asks you for the directory of the 2nd level analysis. Finally, the SPM batch editor opens. You may inspect the settings and run the analysis. Note that this makes no sense for the tutorial data as we only provide data from two subjects.

Frequently Asked Questions

1) Which brain atlases are included in the toolbox for convenience and which papers do I have to cite when I use them?

For convenience several brain atlases are included in the toolbox. The data are available in a format which can be directly used in BASCO (MarsBaR .mat files). (i) The Automatic Anatomical Labeling (AAL) atlas provides a parcellation of the brain into 116 regions (Tzourio-Mazoyer, Landeau et al. 2002). This atlas is based on an anatomical parcellation according to major sulci and gyri using a spatially normalized single subject high resolution T1 volume provided by the Montreal Neurological Institute (MNI) (Collins, Zijdenbos et al. 1998). (ii) A parcellation of the brain provided into 160 regions of interest (ROIs) derived from a series of meta-analyses of task-related fMRI studies (Dosenbach, Nardos et al. 2010). (iii) A brain atlas provided by Craddock et al. (2012) which was generated via spatially constrained spectral clustering. Craddock et al. (2012) offer several atlases which differ in their level of clustering, i.e. the number and size of the individual clusters. The atlases by Craddock et al. (2012) have been made publicly available at: http://www.nitrc.org/projects/cluster_roi/.

2) I went through the tutorial and everything worked just fine. Now I want to use BASCO on my own data. How may I start?

You should start with the pre-processed functional data which is ready for a GLM analysis. Next you have to create text-files for each run containing the stimulus onsets (one condition per row). See the tutorial data for an example. Then you copy the analysis configuration file from the tutorial and adjust it according to your experiment. If you need help please contact me directly or use the BASCO user forum.

The toolbox uses the MarsBaR region of interest toolbox (<http://marsbar.sourceforge.net>). If you want to perform ROI-based network analyses or seed-based functional connectivity analyses you need to define ROIs using MarsBaR. It is thus a good idea to get familiar with the MarsBaR toolbox.

References

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