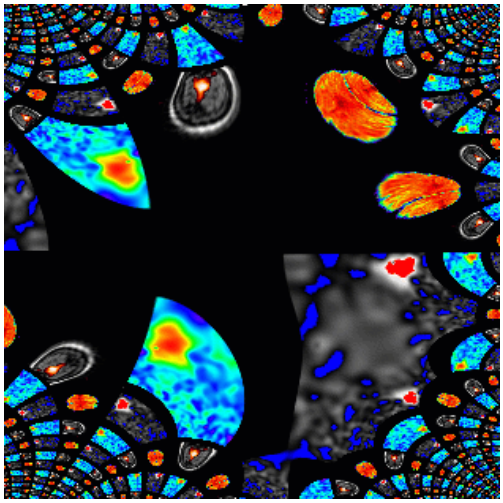
BioMAP 3_x



Medical Image analysis and visualization

Preface

In-vivo imaging of compound effects in animal models or humans is of increasing importance for the development and optimization of new drugs. Readouts are usually based on one of two general strategies: Structural analysis is employed e.g. for the quantification of lesion size and can be supported by tools allowing efficient definition of ROIs or automated segmentation of image data. Secondly, techniques acquiring multi-parametric or dynamic imaging data have been developed that allow assessment of physiological parameters, which are closely linked to the disease process or the effect of a drug. Their quantification requires complex physiological modeling and a variety of mathematical tools, which are usually not integrated in standard software packages provided for image acquisition or scanner control. With BioMAP it was intended to setup an image analysis platform that can be used for a large range of imaging modalities, and which allows efficient and flexible modeling and quantification of imaging data in pharmacological research and development.

BioMAP was written in IDL. It provides a common visualization and storage platform, which can be used for visualization of data from any source, provided that an import filter exists for this format. This platform can be extended by various software packages, individually designed for analysis of specific data sets. Visualization is based on multi-planar reconstruction allowing extraction of arbitrary slices from a 3D-volume. Other features linked to visualization are overlying of two individual data sets or displaying of ROIs. BioMAP uses a 4-dimensional representation of imaging data. The first three dimensions are used for describing the position of a voxel in space, the fourth dimension is reserved for independent parameters such as time, mass, wavelength or diffusion weighting. In addition to the voxel data, a header is used to store information for scan identification, the physical position of the object in space (important for coregistration of multiple scans) or the imaging protocol. Image data can be imported from several sources (the table). Processed data, however, will always be stored in Analyze-format. This format was used since it is widely distributed and can be loaded by several other tools, like ANALYZE (Mayo clinics) or SPM (Welcome department of cognitive neurology, London).

BioMAP comprises all tools, which are required to process single-subject-data, to combine results from several subjects or sessions and to document the final result of a study. Import and export of partially processed data to other software-tools can therefore be avoided.

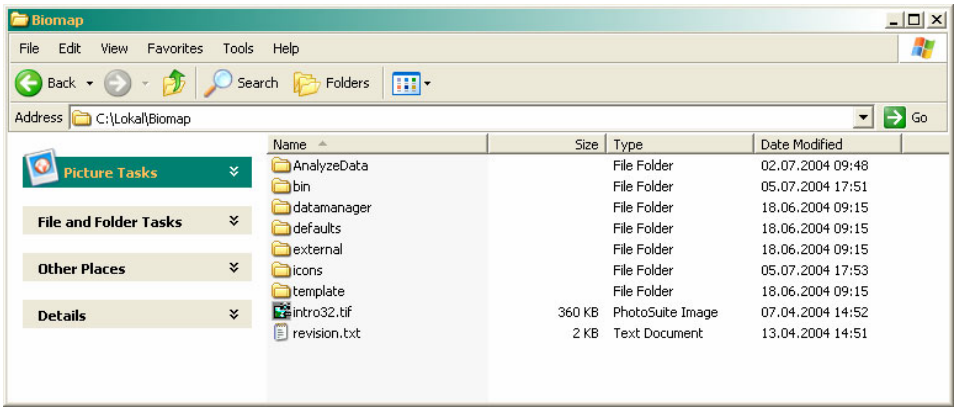
1 Installation

The following hardware and software configuration is required for using BioMAP:

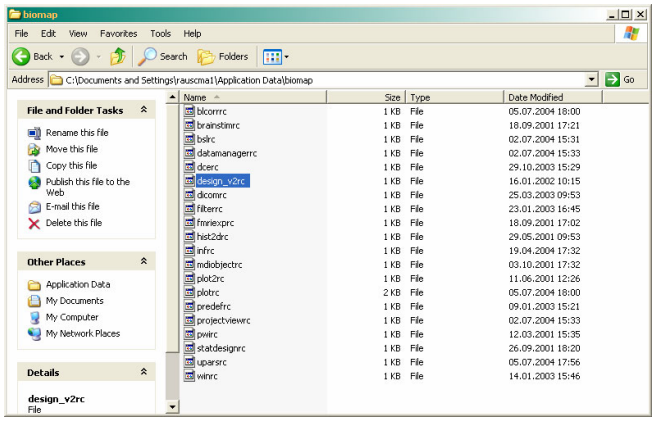
- Computer running on a UNIX operating system (LINUX, Solaris, Irix, …) or Windows XP.
- IDL software installed (version 5.4 or higher)
- Display providing a 24-Bit visual and a resolution of 1280 x 1024 or higher.
- 256 MB of RAM or more

BioMAP is an application, which was developed under IDL. In order to use BioMAP, you must have IDL installed on your system. You can either purchase a license for this software for having full access to all features. Or one can use the IDL virtual machine, which can be used without a license. This software can be downloaded e.g. from the Creaso Web-site (www.creaso.com).

The following instructions will create an installation for a multi-user system. The program files will be available for all users. First, copy the program files from the CD-ROM to a folder on your local PC.

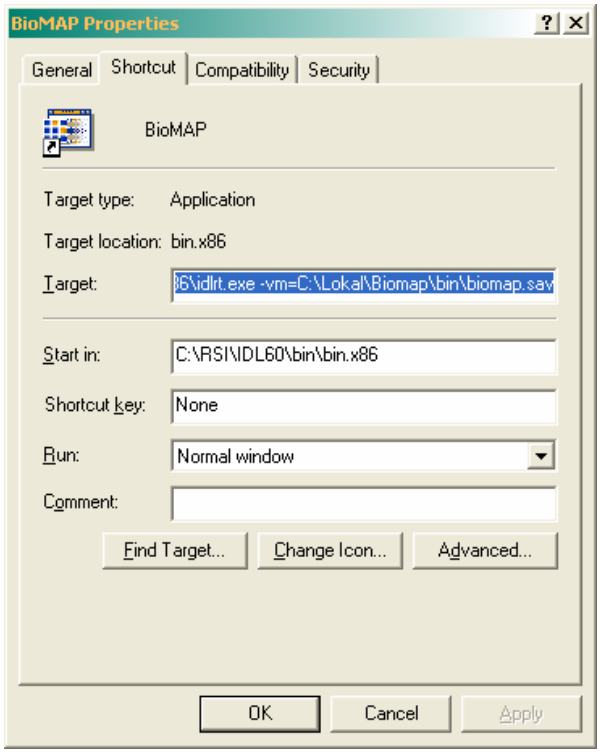


Beside this, user specific configuration files must be copied to ~/.biomap for UNIX systems. Windows XP users should copy the files to the “application and settings” folder. An example is given below.



To start BioMAP you must create a link to the following command:

C:\RSI\IDL60\bin\bin.x86\idlrt.exe -vm=C:\Lokal\Biomap\bin\biomap.sav



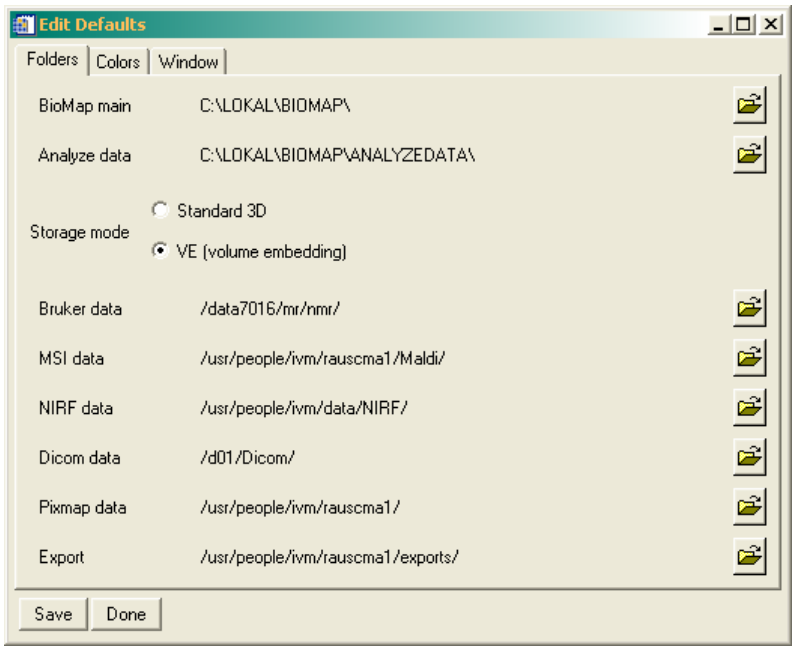
You can store this link on your desktop from were you can then start the software. After starting BioMAP for the first time, one has to setup the folders, to which data should be stored and from where image data can be retrieved. There are three important folders:

- Analyze data: In this folder all processed image data will be stored. While you can view images without having them stored to this folder, you can apply a lot of operations only to image data, which is stored in this place. The Analyze-folder is the root of the

BioMAP database.

- Users of Bruker MRI-systems will load there data from the Bruker folder.
- Users of other MRI or in general imaging equipment will retrieve data from the DICOM folder

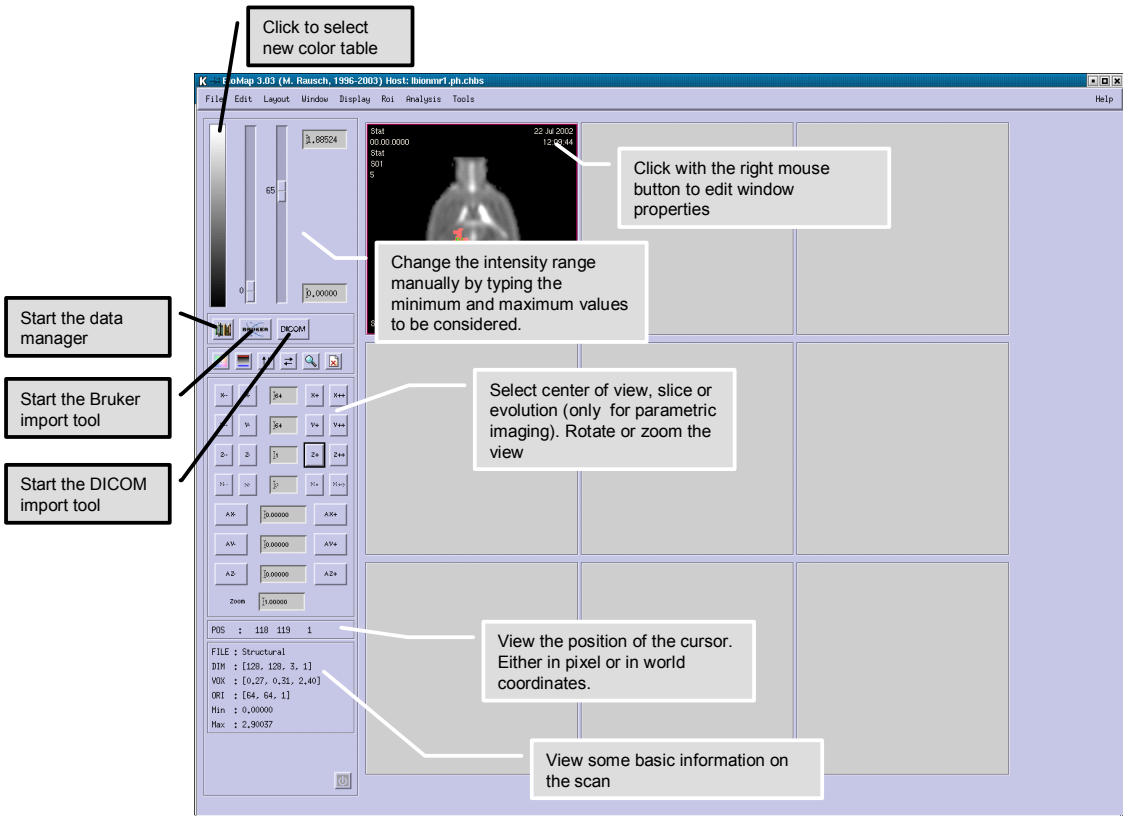
All folders can be defined by the Edit/defaults command:



2 Contents

3 Introduction and Basics

BioMAP provides functions for the visualisation and analysis of tomographic data sets. Images can be of any origin, MR, CT, SPECT and others. However, they must be loaded into the program before they can be analysed. The basic input/output format used by BioMAP is ANALYZE. This format is employed by a variety of other imaging tools, like SPM (Welcome Institute of Cognitive Neurology, London), AIR (Automatic Image Registration by Roger Woods) or Analyze (Mayo Clinics). ANALYZE is also used to store results of calculations, overlays or ROIs.



BioMAP uses a 4D representation of data in memory. This object will be denoted as MDIO (Multi-dimensional-image-object). The first three indices are used to encode the three spatial dimensions, while the fourth index is used as a free parameter, which could be time, diffusion weighting or echo number. This parameter is called an evolution. The general nomenclature for a data set in BioMAP is the following: The whole data set is termed a scan, which in general comprises four independent dimensions. A single 3D-data set (or one evolution of the scan) is called a volume, also if it comprises just one slice. In such a case, the third dimension is one. Finally, a volume can contain one or more images or slices. This structure is maintained also if a data set contains just one single slice and its size would be express as (xsize, ysize, 1,1).

3.1 Using BIOMAP

When BioMAP was started, a user interface appears on the screen, which contains a menu bar, a control panel and a set of windows. A window can be selected by a click of the left mouse button, which will then be marked by a frame. Some other input fields are shown below. BioMAP uses multi-planar reconstruction (MPR) to select the view. This means that one can in general select the slice and the evolution (or 4^{th} parameter) and if the scan comprises more than one slice, each volume can be rotated.

The menu of BioMAP comprises the following items:

- File: Load data, ROIs. Print and exit.
- Layout: Select the number of visible windows and their size.
- Window: Select the view, the color table and many other characteristics of the currently active window.
- Display: View all images from the currently active window or create a movie.
- Roi: Define, modify and delete ROIs. Display histograms or statistics of ROIs
- Analyze: Plot profiles of voxels or ROIs or perform complex types of analysis like modeling or perfusion analysis and statistics.
- Tools: Perform image calculations on scans or modify intensity and geometry.

Scans must be loaded to a window before the data can be processed or visualized. BioMAP will determine the functions, which are applicable to a certain geometrical structure. These functions, which are generally controlled by GUIs (Graphical user interface), can either block the whole program (this means all other functions become unavailable or insensitive) or they can run in parallel with other program modules. However, it is important note that some functions can block the start of other functions, without making the BioMAP-menu insensitive. These so-called compound-widgets must be stopped by pressing the Done-button at the bottom of the control-panel. Hence, if one recognizes that no functions can be started from the menu, it has to be checked, if the Done-button is sensitive. This would indicate that a compound-widget like the plot-tool is active.

3.2 Error recovery and handling

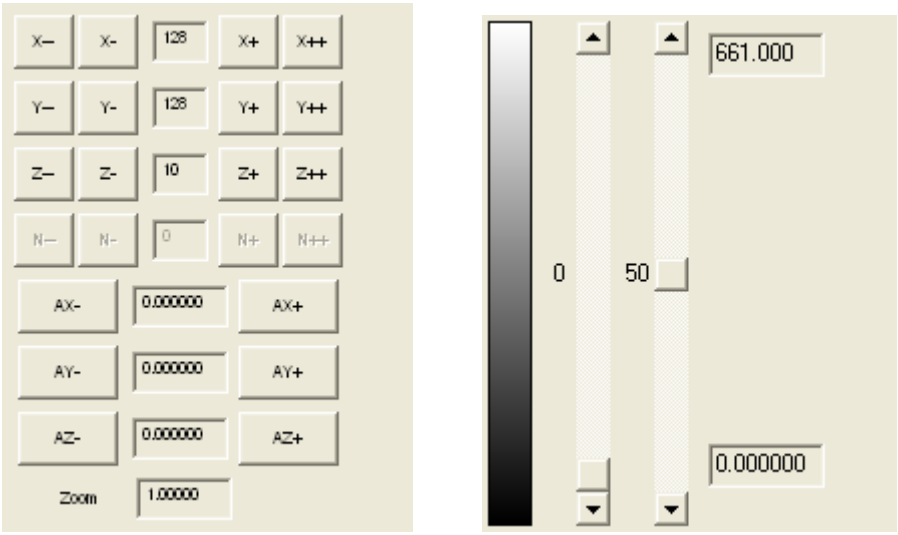
Most errors can be handled by BioMAP. After Pressing the OK-button in the error message window the program will resume. However, some errors can stop IDL's event handler, which will lead to insensitivity of all widgets. If you encounter missing responses of BioMAP you should take a look at the terminal from which the program was started. If you see an error message as shown below, you should type the command "retall". "Retall" returns control to the main program level. This will hopefully restart event handling.

3.3 The BioMAP-window

Images of a scan are shown in one of the BioMAP-windows together with identification-tags. The slice can be selected by clicking on the z-buttons in the control panel. The plane can be shifted in x- and y-direction by the corresponding buttons in same area on the panel or rotated around the x-, y- and z-axis. Instead of clicking on the buttons, it is also possible to enter the

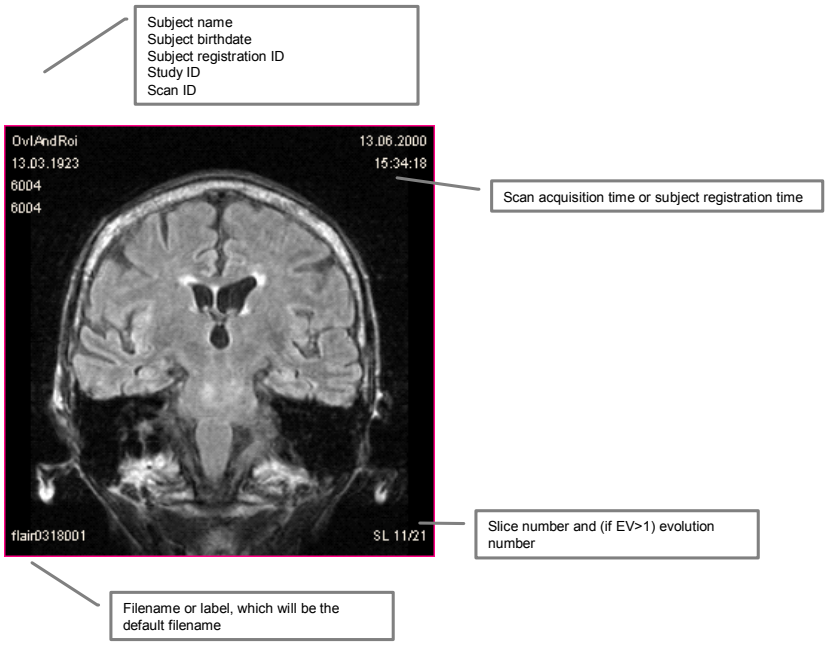
desired values into the input fields followed by pressing <Return>. The same applies for the zoom-function.

The two sliders on the top of the control panel allow adjusting the minimum and maximum voxel-values to be displayed. In the following these values will be denotes as WIN_{min} and WIN_{max}.



Values can again also be entered into input fields on the right of the sliders. The color scale used for displaying the image is indicated on the left of the sliders. It can be changed by clicking into the color-scale-area. This will allow selecting one of IDL's built-in color tables. In addition, color tables can be selected from Window/ColorTable.

All tags are stored in the header of a MDIO and can be viewed by Edit/Header. If the MDIO was retrieved from the Database the scan name is the same as the filename of the scan (without the folder information). If the scan was loaded from another source it was set according to the rules of the respective import-tool.



3.4 Functions to change the window output

3.4.1 Color scale

- Click into to the color bar on the control panel and select on of the IDL color scales
- Click on the color button  to select on of the BioMAP color scales
- Click on the range button  to select the color scale “RANGE”

3.4.2 Zooming

- Click the zoom button  to start zooming
- Click the left mouse button to define the center from which to zoom in or out.
- Keep the mouse button pressed and drag the mouse down to zoom in or drag it upward to zoom out.

- End zooming by pressing the right mouse button. A context window will appear.

3.4.3 Flipping

You can flip the image in vertical or horizontal direction.

- Press  to flip the image in vertical direction
- Press  to flip the image in horizontal direction.

The operations will not affect to data. They will only change the output.

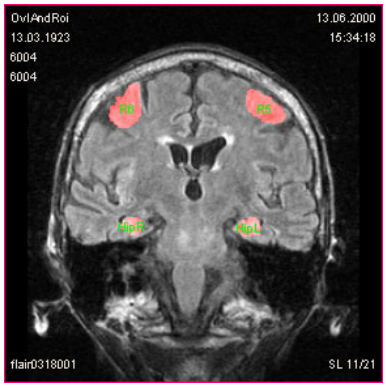
3.5 Display-options

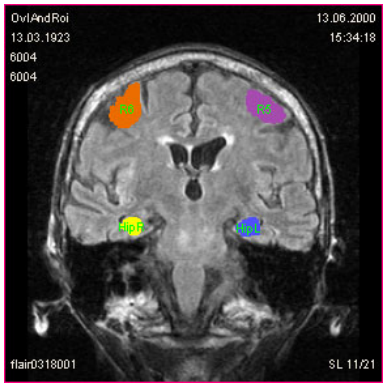
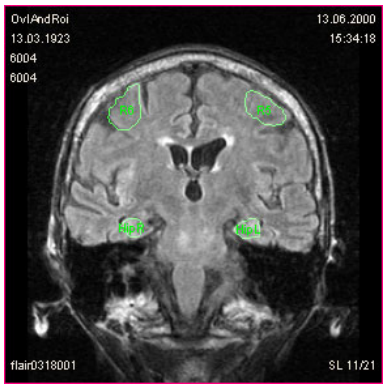
By pressing the right mouse button in a window, the window-option-GUI will appear, allowing setting several display options:

Display method: Can be “voxel” or “interpolated”. “Voxel” shows individual pixel of the scan, while “interpolate” creates an interpolated, smoother looking image.

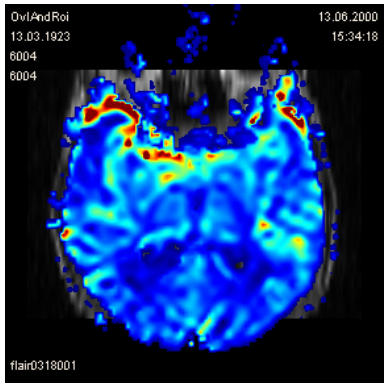
ROI display method: The same above. However, this parameter should also be set to voxel; otherwise ROI-identification might be wrong.

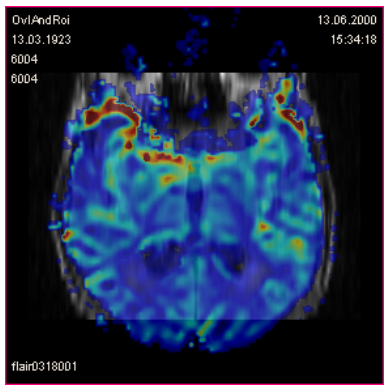
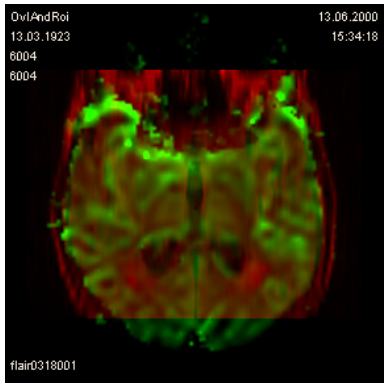
3.5.1.1 ROI display mode

Transparent red	Show the ROI as transparent overlays on the image. The ROI-names are also shown. 
Transparent red (NN)	Same as above but no names are shown

Solid	Display ROIs as solid patches in different colors. The colors will be shown as a stack in the right corner of the window. 
Outline	Draw just a ribbon around the ROI 

3.5.1.2 Overlay display modes

Solid color:	Display overlay as a completely opaque image 

Transparent:	The image will shine through the overlay 
Bicolor:	The base-image will be shown as red, the overlay as green. 

It is possible to mask out pixels from the overlay by checking the Mask-Overlay-flag and setting the intensity-minimum above a value of undesired voxels of the basis-scan.

Example: A functional scan was calculated, which contains undesired spikes outside the organ.

- Increase the window-minimum to suppress the noise around the structural scan.
- Check the Mask-overlay flag.
- Copy the functional image as an overlay onto the base-image
- Adjust the intensity-range of the overlay.

Display units: One can select between the units of image coordinates, shown in the control panel of BioMAP. Selecting “mm” will show the coordinates in world-space, selecting “voxel” will show the index of the voxel in space.

Tracking window: Allows selecting a second window, in which the three principal planes of the referred scan will be shown. The center of three planes corresponds to the physical position of the active window.
Gird: Width of the display grid in mm

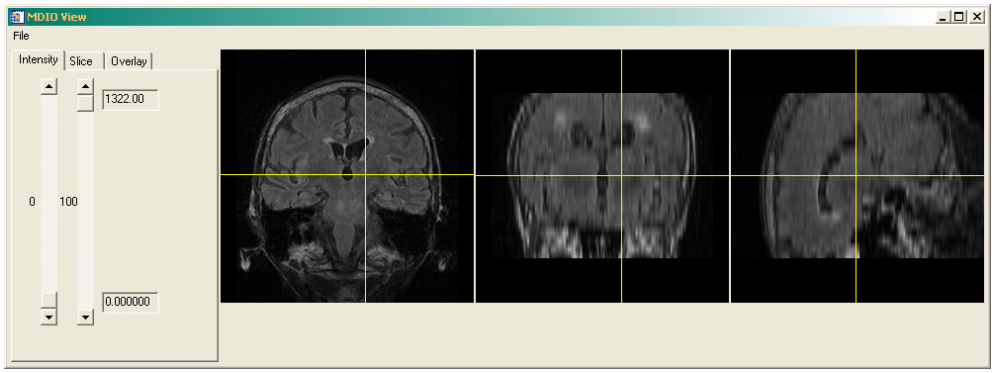
Minimum and maximum of the overlay: Set the minimum and maximum of the overlay. The same can be done by **Window/Overlay control**.

Show info	Show subject info
Scale bar	Show a scale bar, either representing the display range and color-scale of the base image or if assigned, for the overlay.
ROI list	Display basic statistical data (mean and standard deviation) for the ROIs
Mask Ovl:	Show only those parts of the overlay, were the values of the underlying scan are within the range selected by WIN_{min} and WIN_{max}.
Fix range	If selected, the window range will not be changed if a new scan is loaded to a window.

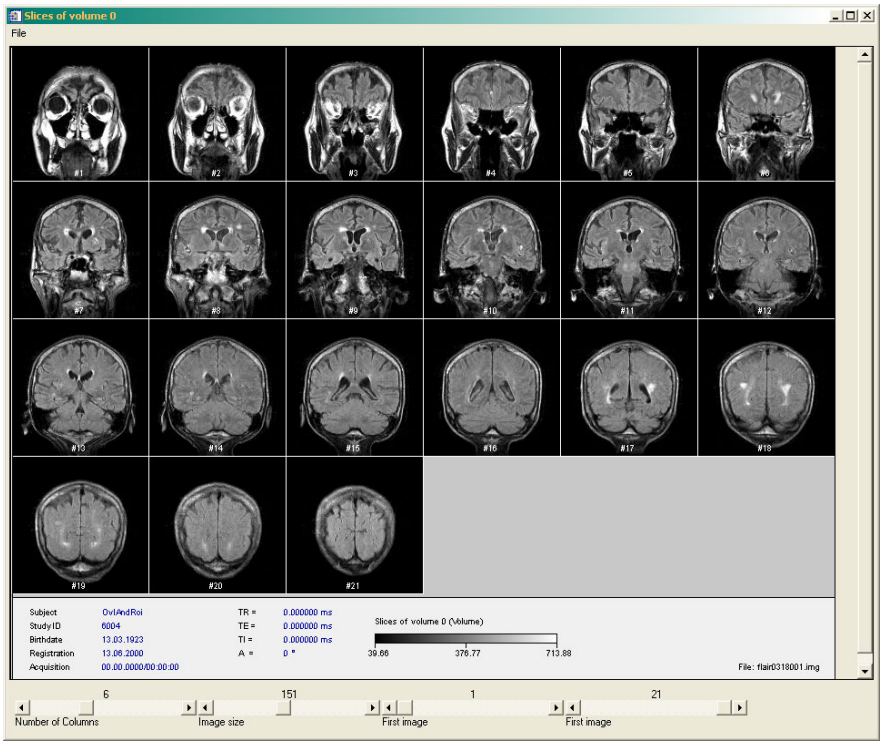
4 Windows

There are also other output windows available, which allow special visualizations. They are available from the display menu.

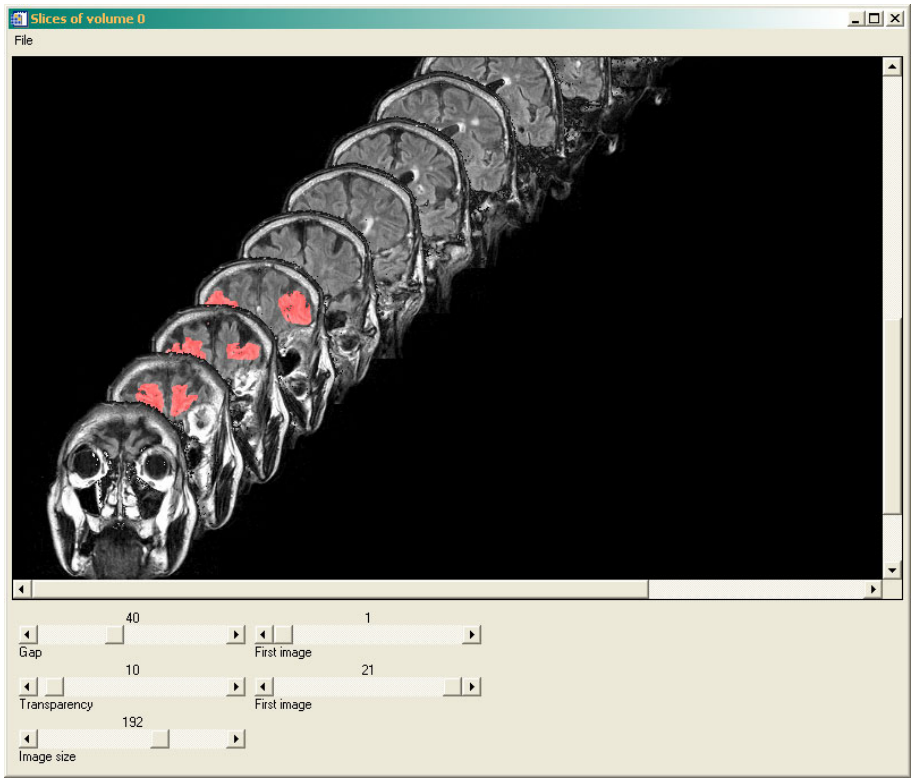
- The Multi-view (View3D)-window allows to scroll through 3 multi-slice dataset and observe the orthogonal projections



- The MultiImage –window lists all slices or all evolutions of a dataset. One can select the output format by the sliders.



- The image stack displays the slices overlaid and to some extent shifted

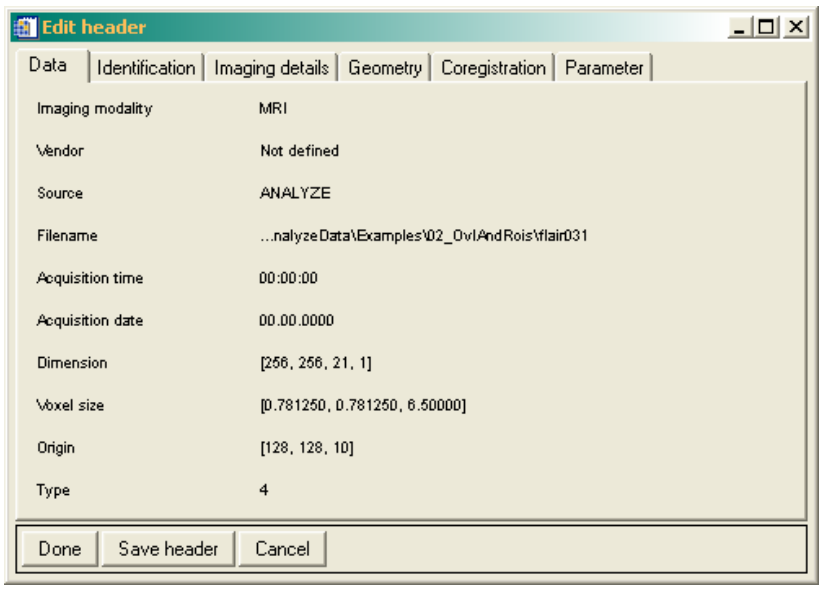


5 Scan properties

Scans represent the data elements of the image data. In BioMAP they have three spatial and one parametric dimension. The parametric dimension can be used for any purpose defined by the user. It is stored in the dat-file in text form and can be modified with the program.

5.1 Edit the header

Properties, such as scan parameters can be modified with the Edit/header command. Usually, all parameters are derived from the source of the data (e.g. the DICOM header). An exception is the "parameter". Here, the information about the 4th dimension is stored. This can be a time point, a mass or an inversion time, which could not b derived automatically from the source. The parameter is an array having as many elements as the scan volumes.



The option to save the modified header will only be available, if the scan has been stored in the database. Otherwise the changes will only be applied to the data in memory.

5.2 Events

Events are associated with the 4th dimension of the scan. Assume you have recorded a dynamic scan and every volume corresponds to a certain time-point. Then you can associate events like "injection of contrast agent" to the data. These will then shown e.g. in the plot window. Every event has a name and a time-point, given in the units of the parameter (e.g. seconds).

6 The BioMAP-datamanager

There are two ways to load image data to a window. One is to import images from sources, like DICOM, BRUKER, or PIXMAPs like TIF-images. The other is to load data from the central image database. Here, images are stored in ANALYZE format, which was extended to handle some additional information, which is used by BioMAP.

Important: Before can use most of the complex functions of BioMAP (like fitting, statistical processing, exporting) an imported scan has to be transferred to the ANALYZE+ database.

To store or retrieve data in or from the datamanager select  or File/Load/Scan+

ANALYZE stores images in files with the suffix “ima”. Additionally, a header, which has the same name as the data file, but has the suffix “hdr” is stored on disk. This header provides information about the dimensionality, the voxel size, the storage type, the scaling and other basic parameters of the image. Generally, each ANALYZE-file can contain scans with up to three dimensions. Therefore, if time series have been acquired, each volume of the scan is stored in a separate file. In such a case files are numbered as <BasicFilename>-001.img. Images can also be stored in one file (this mode is termed “VE”). This mode might be preferred, if a scan consists of a very large number of volumes. E.g. in mass spectroscopy imaging, thousands of images might have been acquired, each corresponding to a specific mass. If those would be stored in normal ANALYZE format, the directory would be filled with many thousand files, which would make data handling slow and uncomfortable.

Beyond this basic parameters additional information is stored in <BasicFilename>.dat. This information comprises the physical orientation of the scan, patient name, birthdate, registration date and time and some other important items. ANALYZE files can be loaded from disk in two ways. The first method uses a simple file-dialog method (selected by File Scan). The directory can be changed on the right side of the panel. Scans can be selected by a double click, multiple files can be selected by keeping the Control-Key pressed. Additionally, filenames with wildcards can be used. A second method to load image data is provided by the ANALYZE+ explorer (started by FILE Scan+). The data explorer uses the full capacities and information provided by the dat-files and helps to organize the data. Data organization is a very important point before any analysis is started.

6.1 The database

The BioMAP data manager is not really at database. It is in principal a front-end, which collects important information from the image data and presents it in a user-friendly way.

The general, arrangement of data in BioMAP is Project : Subject : Scan. Hence, unlike in clinical practice, we store scans of one subject in one subfolder and disregard the possibility that they might have been recorded in different sessions. This ordering generally improves grouping of the scans, since they come from the same subject and generally not more than three or four scans

will be recorded within one session. This hierarchy corresponds to the different levels of folders and subfolders.

In the main area of the front end one can find a stack of folders, which contain either the scans, the ROIs, the films or optionally information related to the subject. In general, scans are displayed in the scan-folder. However, if the name contains the string "_Roi" or "_roi", it will be assigned to the ROI-folder. All TIFF, PS or TEXT-files will be displayed in the Films-folder. Information on the subject can be entered in the Info-folder. This text will be stored in a README file to the current folder.

6.2 Commands provided by the ANALYZE+-Front-End

Project/New	Create a new project. One must enter the name of the project, which is also the name of the folder, which will be created.
Subject/New	Create a new session or subject. The session name, which has to be entered, is used as the name of the folder on disk, which will contain the data. The name must therefore be conforming to the operating system.
Subject/Edit	Enter or change the subject name and subject ID or other relevant parameters. These are stored in all DAT-files contained in this session.
Subject/Remove	Remove the session from disk.
Scan/Remove	Remove the specified scan from the session directory

Scans or ROIs can be loaded by a double click or by pressing the "Load"-button. The content of a BioMAP window can be saved on disk by pressing Save. A double-click on a film will either start the xv-application to display the image or a text-viewer if a text object was selected.

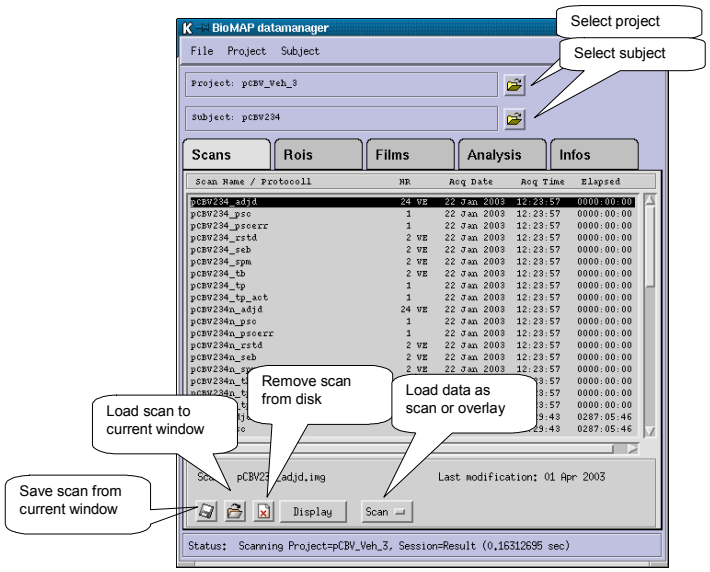


Figure 1: Commands available for storage and retrieval of image data.

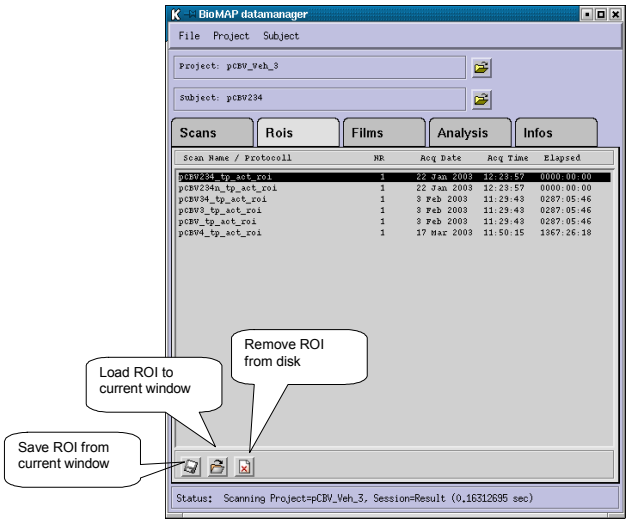


Figure 2: Commands available for storage and retrieval of ROI data. Note: ROIs are stored in the same format as scans. They are recognized as ROIs by the data manager by their suffix _Roi. Hence it is important that you do not remove this suffix from the name when storing a ROI.

Figure 3: Commands available for storage and retrieval of films. Films are either images in tiff or jpg-format or text files containing results from data analysis in list form.

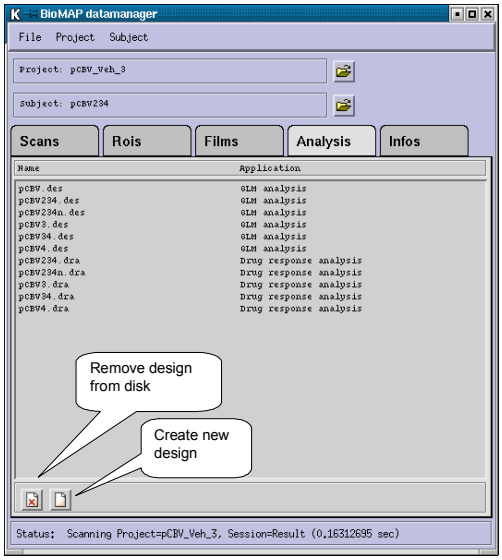


Figure 4: This folder contains batch- or parameter files, which are used to define complex analysis steps. Currently, one can generate GLM (general linear model) analysis files or analysis files for multiple subject pCBV analysis

7 Importing scans from Bruker-Imagers

Data from Bruker-imagers are usually stored as 2dseq-files together with subject-information (in the subject-file) and protocol-information (in the imnd, acqp and reco-files). The tool to load this data format can be found in the BioMAP-menu under File/Import/Bruker.

After initialization of the tool, the patient list will be shown. A double-click on a patient will show the studies for that patient. A double-click on the respective study will show the scan list. One can go back one level (e.g. from the scan list to the study list) by pressing the button on the left.

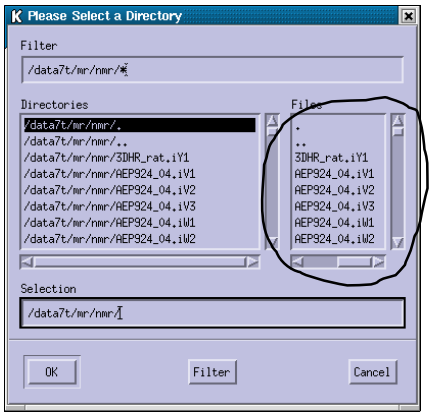
7.1 Options

Read PARX: Read the scan information from the imnd, reco and subject files. Otherwise the id of the scan will be shown.

Auto update: Automatically update the scan-list if a new data set was generated by the scanner. Otherwise, one has to press the update-button.

7.2 Configuration

Folders to look for images
The path to search for images has to be defined in Edit/Defaults in the BioMAP-GUI. If your images reside e.g. in /u/data/nmr/MyImage.dF1/ the search path has to be /u/data/nmr. It is also possible to add folders to the path-history by selecting a folder by File/Path in the Bruker-GUI. Those can then be selected from the drop list at the top of the GUI.



The study folders must appear in this window!

7.3 Mapping subject information

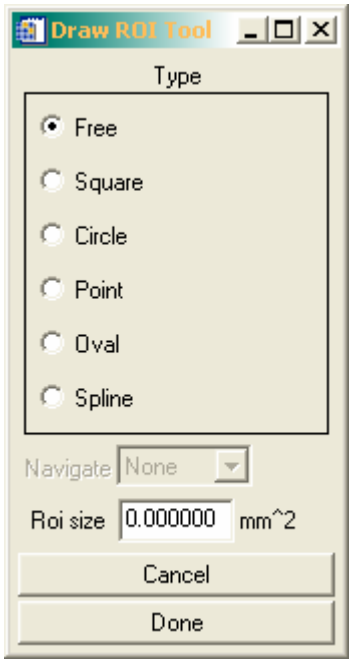
In Bruker-Paravision-Software scans are usually organized according to the scheme Subject-Study-Scan. However, to reduce the amount of typing work and the number of folders, which will be created by Paravision, a different scheme can be used, which was developed for longitudinal studies. In this scheme, the Subject-name is used to define the whole study or program, the study-name defines the subject and the session and the scan-level is defined as before. This scheme requires a special naming-format on the Paravision-scan-control:

Subject name: As desired
Study name: SubjectCodeSxx, where xx is the id of the session. E.g. lew05s01 would denote subject lew05 in session s01.
During the load process this information would be mapped to the appropriate fields in the MDIO:
PatientName =lew05
PatientId = lew05
StudyId = s01
To switch from the traditional to the modified scheme one has to set the value of SUBJECTIDENT from 0 to 1 in the file bslrc (found in the folder (~/.biomap/)

8 ROI-Analysis

8.1 Drawing ROIs

ROI can be used to perform readouts in image substructures. Internally, a volume is created for a scan, which has the same dimensions. If a voxel of a scan belongs to ROI X, the corresponding voxel in the ROI-volume is set to this value. ROIs can be defined geometrically by the ROI-tool, which will be started by Roi/Draw. Other functions that can be used are listed below:



Note: It is possible to reset the drawing by clicking into the type-box.

Init	Delete all ROIs currently defined for this window.
Clip	Remove all voxels from the ROI, where the value of the scan is larger than the maximum display value and lower than the minimum display value. The maximum and minimum are defined by the sliders on the left. You can use the color scale “RANGE” to label the voxels, which should be removed as blue and red, respectively. This function can be used e.g. to remove all voxels from the ROI, which are located outside the organ.
Name	Assign a name (e.g. tumor) to a ROI. Names are usually initialized as R1,R2,…
Delete	Delete ROIs
Merge	Combine two or more ROIs to one. The name is taken from the ROI with the lowest index.

After creation of a set of ROIs, they can be stored by File/Save/Roi or using the datamanager.

This will store tem as a scan in the same folder as the scan, on which they where defined. The scan name combined with the suffix "_roi" is used as default filename for saving of the ROI.

General remarks on ROIs:

- If you define a new ROI, which overlaps with one, which was defined before, the first ROI will loose these data points.
- Hence you cannot define overlapping ROIs.
- You can define the display mode for ROIs by starting the window-parameter-dialog with the right mouse button.
- You should always use "Voxel" as RoiDispMethod
- Viewing the ROI with outline can sometimes be difficult, because it is calculated on-the-fly.

8.2 Analyzing ROI-data

Groups of voxels defined by a ROI can be analysed in several ways. Statistical analysis of voxel values provides information about the mean and the standard deviation of values belonging to the ROI. Histogram analysis shows the distribution of values and finally, plotting ROI data from dynamic or spectroscopic scans allows visualising temporal or spectroscopic profiles.

8.2.1 Statistical analysis

Statistical analysis of data comprises calculation of parameters like mean, standard deviation, minimum or maximum of values with in a defined region. Statistical analysis can be started by Roi/Statistics. This function will calculate the parameter and will display them within a window. If more than one ROI is defined a bar-plot will be shown representing the mean values for each ROI. The analysis will only include voxels of the current evolution, if the scan comprises more than one volume.

The contents of the window can be exported to the database as a text- or TIFF-file by pressing the respective button at the bottom of the window.

8.2.2 Histogram analysis

By histogram analysis (Roi/Histogram) the distribution of values within a ROI can be calculated. The window will show a bar-plot for each ROI, which can be exported either as a text-file or a TIFF-image to the database. The histogram will be shown for the specified range. The range will be divided into N bins.

8.2.3 Plotting the profile of voxels defined by a ROI

The profile of a 4-dimensional data set can be plotted by selecting Analysis/Plot/Roi from the

menu. The plot-tool will show a line for each ROI and the actual contents of the window.

8.2.4 Plotting averaged profiles from multiple scans

Profiles from different scans can be averaged by the multi-subject-ROI-tool (Analysis/mSUB ROI). This type of analysis can be used to combine temporal profiles from different animals.

Data can only be combined, if the number of volumes is equal. The GUI allows selecting the windows, which should be included into the analysis. The dropdown-lists at the bottom allow selecting the mode of analysis.

ROI plot:

Traces	Plot the temporal profile for each data set seperately. If N windows were selected, N lines will be shown in the plot-window. The index of the ROI must be entered into the input field “Specific ROI”
Mean	Calculate the mean profile from the selected scans. The error for each data point can be calculated in addition.
Error plot	Select the error type to be calculated. SEM (standard error of mean) and standerd deviation can be selected. To see the error bars in the plot window, one has to select this option in the plot tool.

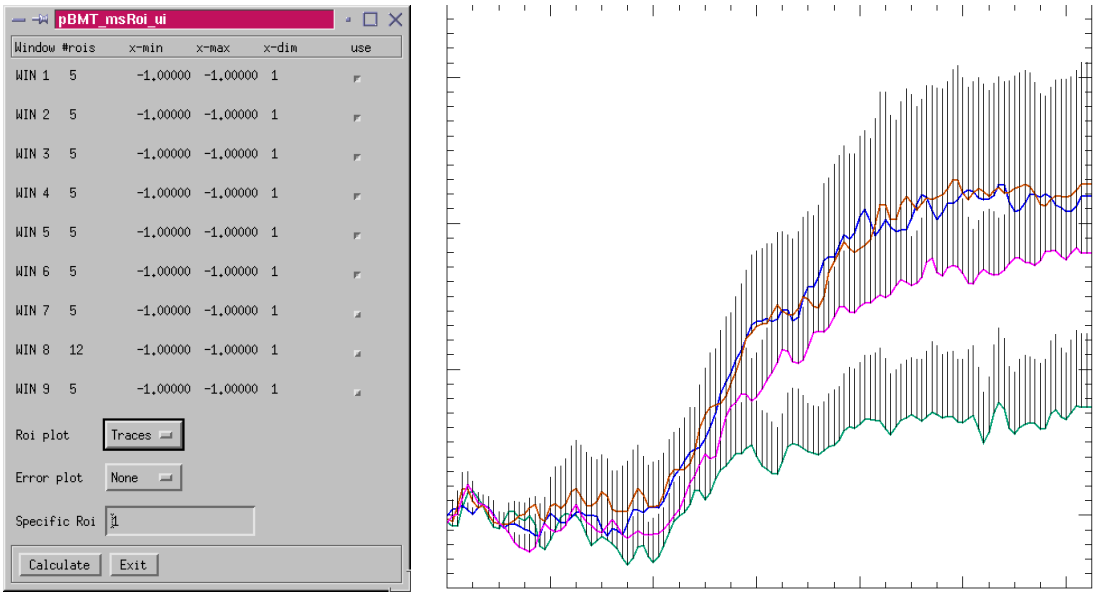


Figure 5: Basic layout of the mSUB-ROI-tool. The user must select the windows to be included into the analysis and the type of processing. A typical output of a mSUB-analysis is shown on the right.

9 Plotting

The plot-GUI is used by most applications to display profiles along the 4th dimension of the scan. The profiles can be derived from ROIs, which were defined prior to the start of the tool or plots can be generated dynamically by moving the mouse across the window.

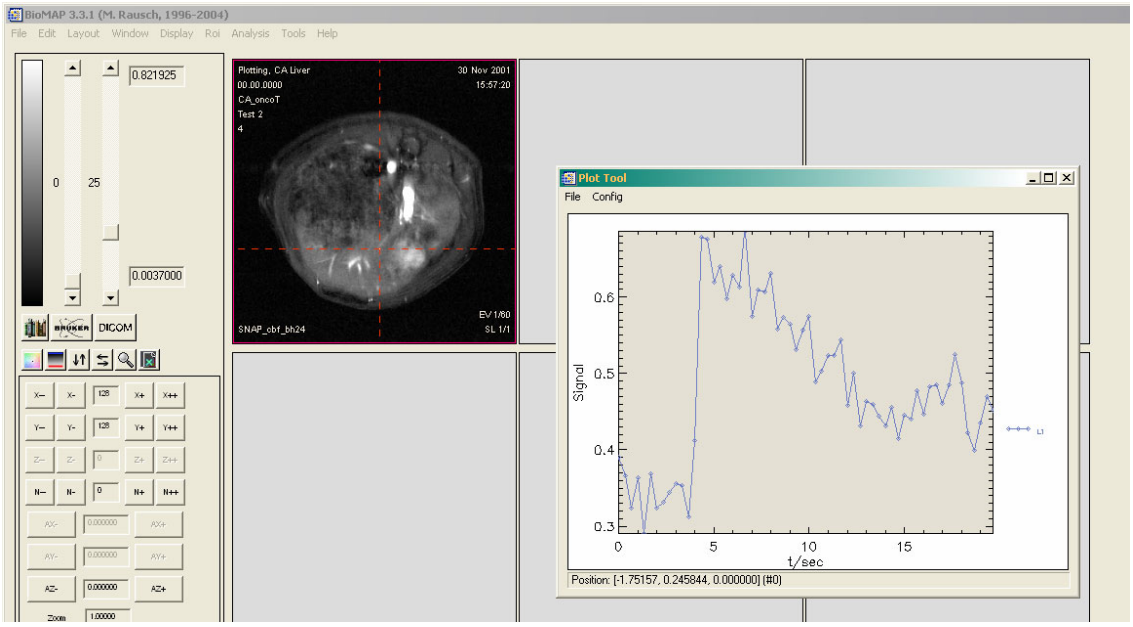


Figure 6: Layout of the plot tool. In this example dynamic plotting is performed by selecting Analysis/Plot/Point

9.1 Dynamic plotting

Dynamic plotting can be selected from Analysis/Plot/Point. While this function is active no other tools can be started. The profile along the 4th dimension will be plotted for a voxel selected by pressing the left mouse button. Pressing the right mouse button allows to increase or decrease the number of points around the cursor position to be averaged. This will increase the SNR of the profile.

9.2 Mouse functions within the plot window

Left mouse button: Select the x-range of the plot. Press the mouse button, drag the mouse over the area, which should be displayed and release it for update of the display.

Middle mouse button: Integrate or average volumes as selected. The function to be applied can be selected from Config/Mouse.

Middle mouse button: Makes the crosshair visible. If the option “N follows X” is active the N

will be updated for the scan according to the selected value on the x-axis of the plot window.

- Double-click with left mouse button left to the y-axis: The properties of y-axis
- Double-click with left mouse button below the x-axis: The properties of x-axis
- Shift+left mouse button below the x-axis: Scroll x-axis
- Shift+right mouse button below the x-axis: Expand x-axis around center
- Shift+left mouse button right to the y-axis: Scroll y-axis
- Shift+right mouse button right to the y-axis: Expand y-axis around center

9.3 Other options

Window Ev follows x	As explained above.
Baseline correction	Make the baseline correction active. The parameters can be set in the Config-menu.
Plot as bars	If only one profile is shown, bars can be plotted in addition to the line. This option generates only good results if the number of points is not larger than 10-20.
Show numbers	Display the values of individual points in the plot.
Display error bars	If values for the error of individual points were supplied by the calling function they can be displayed by selecting this option.

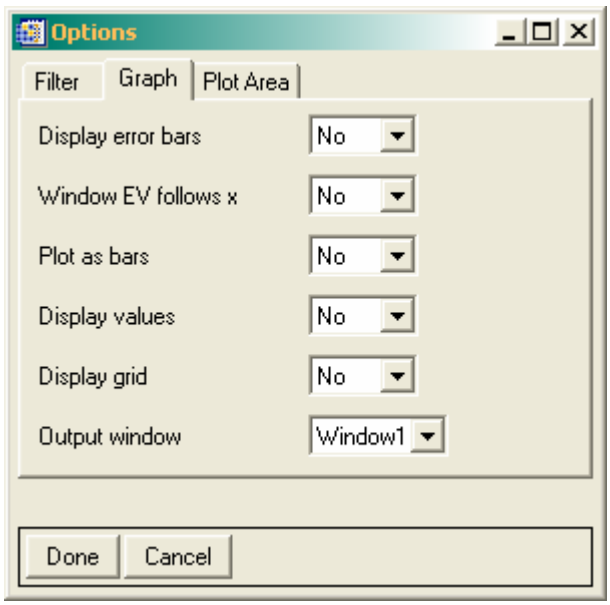


Figure 7: Plot options

9.4 Data export

Data can be exported as a Tif-image. This will simply generate a snapshot of the window.

Ascii export generates a text file in which the first line corresponds to the x-values and each of the following lines to one profile. If error-values were supplied, they will also be exported.

10 Calculations

The calculations-menu comprises routines to perform simple calculations on images like subtraction, division, etc.

10.1 Spatial filtering

Apply spatial filtering to the scan. Spatial filtering is always carried out in a two-dimensional way. This means, if the scan contains multiple slices, there will be no filtering across slices. For more information about the filter-tool see chapter 13.1

10.2 Temporal filtering

This function carries out filtering along the temporal dimension (or in general the fourth dimension of the scan).

10.3 Baseline-correction

This function applies a baseline-correction to the selected scan. The parameters, which are used in the tool will be described in more detail in chapter 13.3.

10.4 Volume subtraction

This function will subtract the current volume of a scan from all others. It is helpful if one wants to observe the dynamic change of image intensity (e.g. contrast enhancement)

10.5 Temporal derivative

This function calculates the temporal derivative from a dynamic imaging data. The result will have the same dimension as the source.

10.6 Temporal Integration

This function calculates the integral for each voxel along the fourth dimension. The boundaries of integration (given as volume indices) have to be defined within the user-interface. The result has the same spatial dimension as the source, but contains only one volume. The x-values are taken from PARAMETER1 of the scan.

10.7 Attenuation map

This function calculates the logarithmic ratio of two scans. This function can be used e.g. for calculation of blood-volume from a pre- and post-contrast scan under steady-state-condition. They must have the same dimension. The user-interface asks for the reference scan. This is the scan, which was acquired before the signal was attenuated by e.g. contrast agent. The object scan refers to the scan acquired after administration of contrast agent.

The calculation carried out is

$$Y = -\ln\left(\frac{\text{Object}}{\text{Refernce}}\right)$$

Before starting the tool, the window-minimum should be adjusted in order to suppress noise from outside the organ. For this, one should change the color table to “Range” (either with Window/Color table or by pressing the icon on the left of BioMAP’s main window). Hence, all points, which should be excluded from analysis will be shown in blue.

10.8 Divide

This function simply divides to scans by each other. The calculation carried out is

$$Y = \frac{\text{Current scan}}{\text{Refernce}}$$

If the selected (“Current scan”) contains more than one volume, each of the volumes is divided by Reference. If “Reference” contains more than one volume, their number must be the same as that of “Current Scan”.

10.9 Detrending

Detrending allows removing a linear drift of the signal from individual pixels. The linear signal drift is calculated from a series of baseline volumes by linear regression. This function is very helpful in experiments where a signal change is induced on a slow temporal basis (e.g. Pharmaco-fMRI or when slow clearance blood pool agents a re used for fMRI. The figure below shows the result of detrending for a pharmaco-BOLD experiment. A slow drift of the signal can already be seen in the first 10 to 20 baseline images before injection of the drug. Using this baseline images for regression analysis and subtracting the linear function from the native data leads to a flat baseline. Note the effect of stimulation is preserved on a qualitative level.

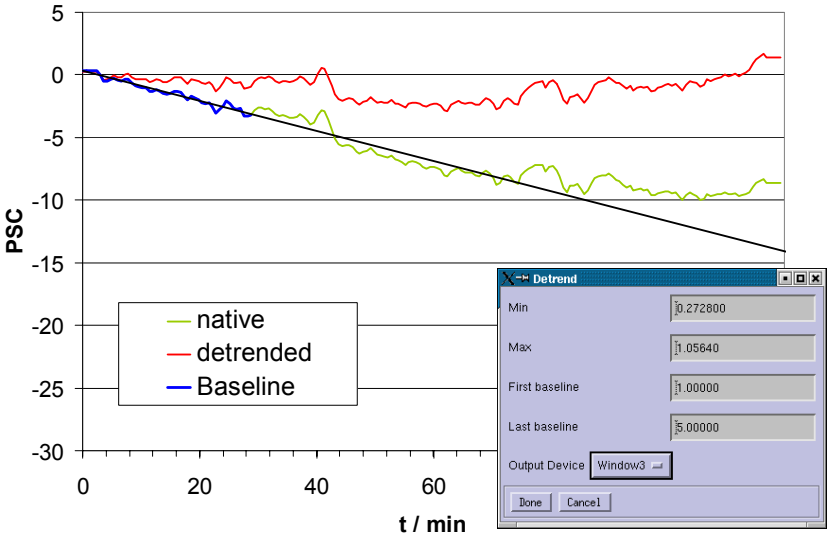


Figure 8: The principle of linear detrending

BioMAP provides two modes for linear detrending. The first takes the global mean of relevant voxels and performs a linear regression on this profile (Tools: Detrend: Linear baseline (global)). Parameters to entered are:

1. Minimum voxel value to be used for calculation of the global mean
2. Maximum voxel value to be used for calculation of the global mean
3. First baseline image, which should be used for determination of the slope
4. Last baseline image, which should be used for determination of the slope

The second mode performs the operation on a voxel-by-voxel basis (Tools: Detrend: Linear baseline (voxel)). Here the same parameters are used. The minimum voxel value is used to exclude voxels with lower values from the analysis. Figure 5 shows the results of detrending for

an experiment, where a signal decrease was induced by injection of a drug. The blue curve corresponds to the unprocessed data, for which a pronounced negative drift can be observed. Moreover, the slope of the curve decreases after some time. Hence a linear correction might not be ideal. Using the first volumes for regression analysis overestimates the slope and leads to a signal overshoot in the last volumes. In contrast to that, ROI2 shows no signal drift. If the drift correction is based on a global analysis and if a majority of voxels shows a drift, an overcompensation of the drift will follow for this ROI. Hence the local based correction is appropriate here.

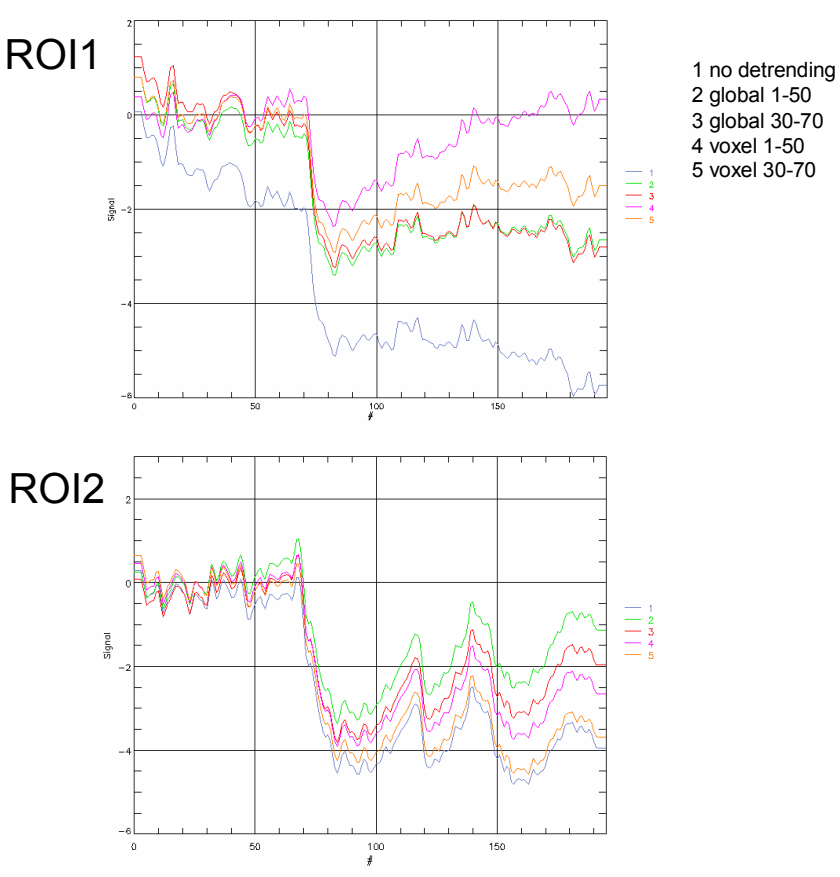


Figure 9: Comparison of different detrending operations for two different ROIs.

Therefore it is recommended to use voxel-based detrending with the last 30-40 volumes before injection of drug for drift determination.

11 Geometry

11.1 General principles on geometry

BioMAP's geometrical concept Images, volumes and scans are data sets, which consist of sets of voxels, which have a predefined size. Therefore the spatial relationship between voxels is clearly defined. However, each voxel corresponds to a certain position in space. This position is defined by a coordinate system of the imaging device. The relationship between voxel space and world space is given by a affine transformation matrix G. Therefore the position of a voxel in world space (P) can simply be calculated by matrix multiplication of the voxel coordinates (I) with this matrix. The inverse of G allows to calculate the voxel coordinates from the world coordinates:

$$\begin{pmatrix} P_x \\ P_y \\ P_z \\ 1 \end{pmatrix} = \begin{pmatrix} a_{11} & a_{12} & a_{13} & t_x \\ a_{21} & a_{22} & a_{23} & t_y \\ a_{31} & a_{32} & a_{33} & t_z \\ 1 & 1 & 1 & 1 \end{pmatrix} \begin{pmatrix} I_x \\ I_y \\ I_z \\ 1 \end{pmatrix}$$

or

$$P = GI$$

The matrix G is automatically generated when the data is imported from a source, which provides this information (like Bruker or Siemens imagers). Additionally, it is possible to modify this information by application of a second affine transformation matrix A. This might be of interest if scans, which were acquired in different sessions, should be combined:

$$P = AGI$$

The approach used by BioMAP, allows finding pixels from a second scan, which correspond geometrically to the first scan in a very simple way by the calculation of:

$$I_2 = (A_2 G_2)^{-1} (A_1 G_1) I_1$$

Therefore, it is possible to overlay scans of different orientation, or to transfer ROIs between scans. However, in the current version of BioMAP, only one matrix A is considered for each scan. This means that all volumes are regarded as having the same spatial orientation and therefore realignment of volumes (e.g. from functional MRI experiments) is not possible per se.

Note: Geometry is sometimes incorrectly extracted by the Bruker and Dicom-import-tools. This is due missing direction-cosines in the headers supplied by the image formats.

11.2 Coregistration

Coregistration of two scans is based on finding an affine transformation matrix, which describes the difference in orientation of the images. Assuming that a pixel P1 of the first scan (target) corresponds to the same anatomical position as P2 in scan 2 (object) the following relation must hold:

$$I_2 = (A_2 G_2)^{-1} G_1 I_1$$

This is a simplification of the equation shown above. In the coregistration procedure used by BioMAP only the affine transformation of the object scan is modified.

Coregistration of two scans can be carried out manually by automatically using the coregistration tool shown in Figure 1. Different display modes can be selected and landmarks can be set by clicking with the left or right mouse-button into the windows. The orientation of the object scan can be adjusted by the twelve parameters related to translation, rotation and scaling. After pressing the done-button, the parameters will be written to disk. Pressing the cancel-button will discard all changes. Automatic coregistration is working only on scans, which have the same geometry and dimensionality. To obtain optimal results it is required to adjust the lower thresholds for the two scans to values above the noise level. Moreover, if the shape of the body of the animal has changed from one session to the other, also these structures should be suppressed by adjusting the thresholds properly.

Coregistration will only change he geometrical parameters but will not affect the image data itself. The parameters can be reviewed by the Edit-Header-Tool, where they can also be set to zero. To re-slice the scan to the target, the reslice-procedure has to be applied (Tools/Geometry/Reslice). This operation will change the orientation of the object-scan and also the resolution, if this is different for the target. Re-slicing is carried out by bilinear interpolation.

Note: If the object-scan comprises only one slice, the coregistration must be carried out by using “voxel” as display mode for the target scan (to be selected by the window-options-dialog). This is because the interpolation procedure, which is used to extract a slice from 3D-dataset, reads the voxel-value from the position defined by the target scan. If this position is located outside the slice in z-direction in the object scan, zero will be returned. The problem can partly be eliminated by using the “extrapolate”-option in the coregistration-tool. However, in this case no coregistration in z-direction will be possible, because the interpolation-function will always return the same image, independently of the shift in z-direction.

Coregistration of data must be carried out prior to multi-subject-analysis. After coregistration it is possible to define ROIs on one scan and transfer them to the others. The location of the ROIs will automatically changed in pixel-space during the transfer process.

For multi-subject-analysis with the GLM-tool, scans must also be resliced.

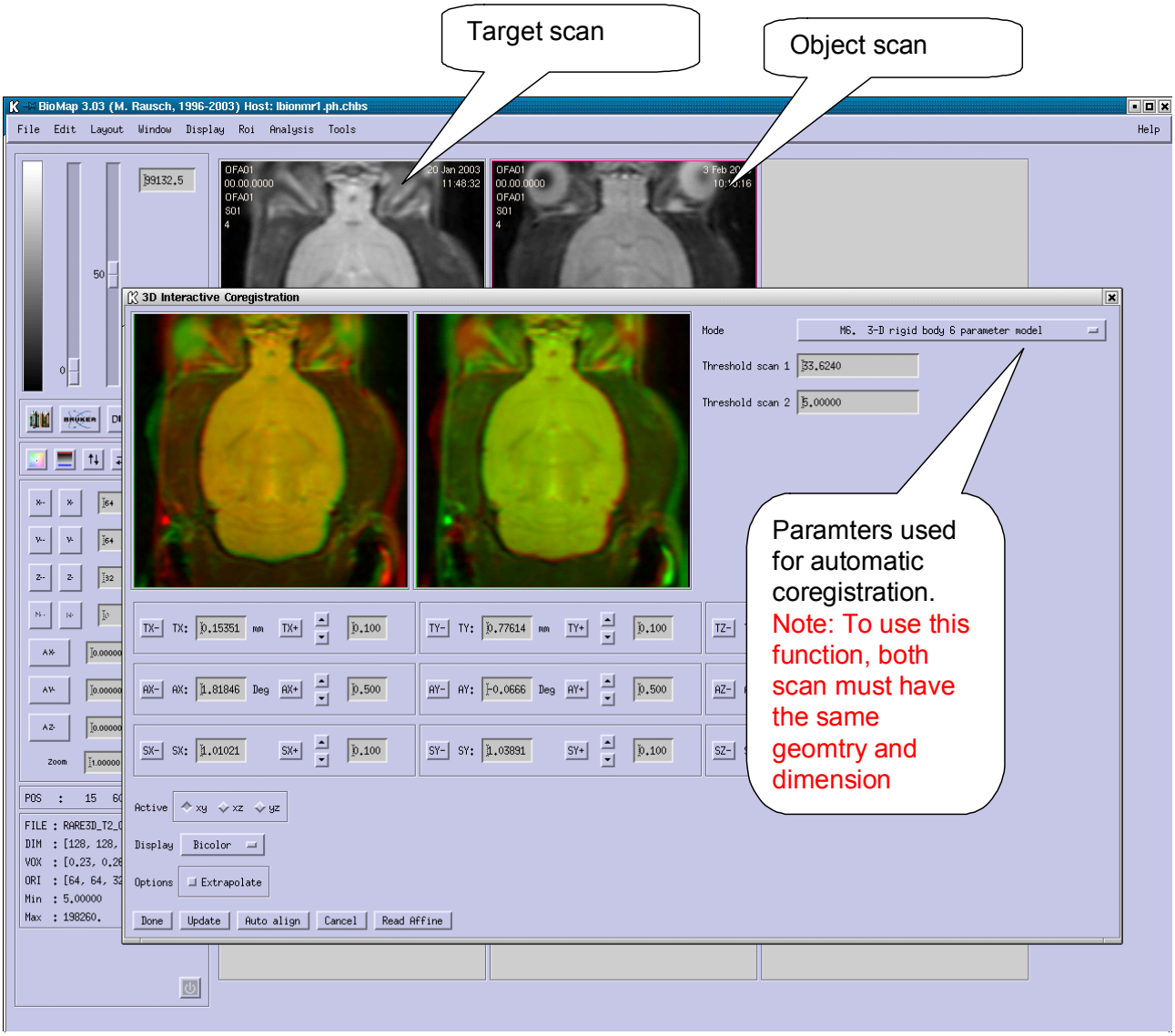


Figure 10: The coregistration tool. It can be used to modify the affine transformation matrix according to translation, rotation and scaling.

11.3 Realignment

Realignment of volumes within scans is necessary for the analysis of several dynamic imaging data where movement of the organ can interfere with certain experimental signal changes. The major application of intra-scan realignment is functional brain imaging.

The realignment-procedure of BioMAP is derived from Roger Woods C-library AIR (automatic image registration).

The importance of realignment is illustrated below for a 2D-RARE-fMRI dataset. Due to continuous movement of the animal, edge artifacts become visible at the end of the experiment.

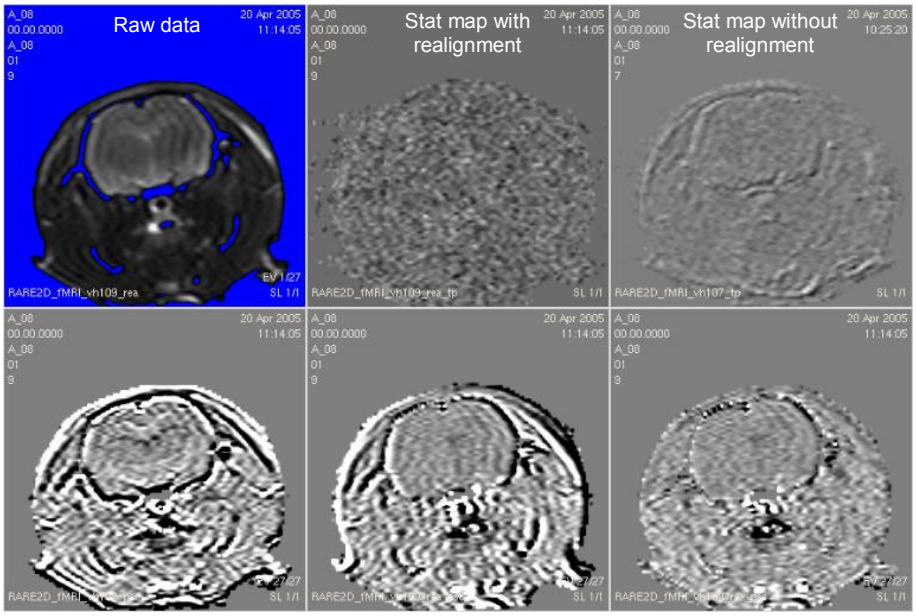
The optimal realignment parameters in this example were:

Model: 2-D affine 6 parameter model

Cost function: Least squares with intensity rescaling

The rigid body model did not provide sufficient accuracy. It can be assumed that even little tilting of the imaging around the z-axis might lead to distortions, which cannot be eliminated by rotation and translation of the image.

As a consequence, the statistical map showed fewer artifacts.



No Realignment 2D-Rigid Body 2D-Affine

12 Analysis of Magnetic-Resonance-Imaging data

12.1 Analysis of perfusion-data

MRI based perfusion imaging can be carried out by two different sequence protocols. The first and most commonly used one is based on T2- or T2*-weighted imaging and is also called DSC-imaging (dynamic susceptibility contrast). FLASH (Fast low angle shot) or EPI (echo planar imaging) sequences can provide the required temporal and spatial resolution. However, one also use T1-weightes sequences. These are superior in tissue structures with low intrinsic field homogeneity (like the kidneys).

Dynamic-susceptibility-contrast MRI is based on the measurement of the effect of a paramagnetic or super-paramagnetic contrast agent on a T2- or $T2^*$-weighted image. It is assumed that the relaxation rate R2 changes linearly with the concentration of a contrast agent:

$$R_2 = R_2^0 + C_m \cdot r_2$$

Here, the relaxivity of the contrast agent is denoted as r_2 and C_m is the concentration of the agent in tissue or blood plasma. In a T2-weighted MR-sequence, the signal-intensity at echo time TE can be calculated from

$$S = S_0 \cdot e^{-R_2 \cdot TE} = S_0 \cdot e^{-\left(R_2^0 + C_m \cdot r_2\right) TE} = S_0 \cdot e^{-R_2^0 \cdot TE} \cdot e^{-C_m \cdot r_2 \cdot TE}$$

The concentration of the tracer can therefore be calculated from S(t). Provided that the plasma concentration is constant for every vessel, C_m reflects the blood volume within a voxel.

The perfusion analysis tool can be used for the analysis of dynamic image data, which usually contains 30 to 100 volumes. The typical experimental procedure comprises the following steps:

- Acquisition of 10-15 baseline images
- Injection of a paramagnetic contrast agent
- Acquisition of the first pass of the agent

The number of slices can be one or more. Before any perfusion maps can be calculated the data must be stored in the database and the design of the experiment has to be entered. These are:

12.1.1 Basic parameters

Intensity threshold	The smallest pixel value, which is considered for analysis. This threshold is used to suppress noise from outside the organ. The voxel is just considered for analysis if The intensity of this voxel in the baseline image is larger than the threshold and The intensity in one of the volumes is larger than 10% of the threshold. The last test is used to remove voxels, where the signal intensity becomes virtually zero at the time of contrast agent passage.

Time to steady state	The first scans are discarded, since the magnetization needs some excitations to reach the steady state. The time is entered in seconds. The number of volumes, which will be discarded, can be calculated by dividing this time by the acquisition interval. Removing volumes from the scan will also affect time related parameters such as MTT, TTP or fitting of gamma-variate functions.
Baseline end	Acquisition time of the last scan, which is used to calculate the baseline map.
Cut curve at	Acquisition time of the last scan, which is included into the perfusion analysis. Typically, all scans are included.
Scan interval	Time between the beginning consecutive measurements. It should not be much larger than 2 seconds.
Contrast	Select the contrast or weighting of the images. One can select either T2/T2* or T1. The equations used to calculate the concentration time curve are used according to this parameter.
Order of excitation	If more than one slice was acquired, it is important to know the exact acquisition time of a scan (e.g. for calculation of the TTP-map). One of three schemes must be selected: • Descending: Slice #0 was acquired first. • Ascending: The topmost slice was acquired first. • Parallel: All slices were acquired at the same time. The acquisition time of a slice can only be calculated accurately, if there was no temporal gap between consecutive measurements.
TE of tissue slices	Echo time of the slices, which contain the tissue.
TE of AIF-slice	Echo time of one slice, from which the arterial input function can be derived.
AIF-slice position	Index of the slice. If no AIF-slice was acquired or should be specified, “None” must be selected.

These parameters will also be stored in the file pwirc in the current directory and will be restored whenever the PWI tool will be started for this scan.

Note: If perfusion analysis for a specific scan is performed for the first time, default parameters are loaded from ~./pwirc.

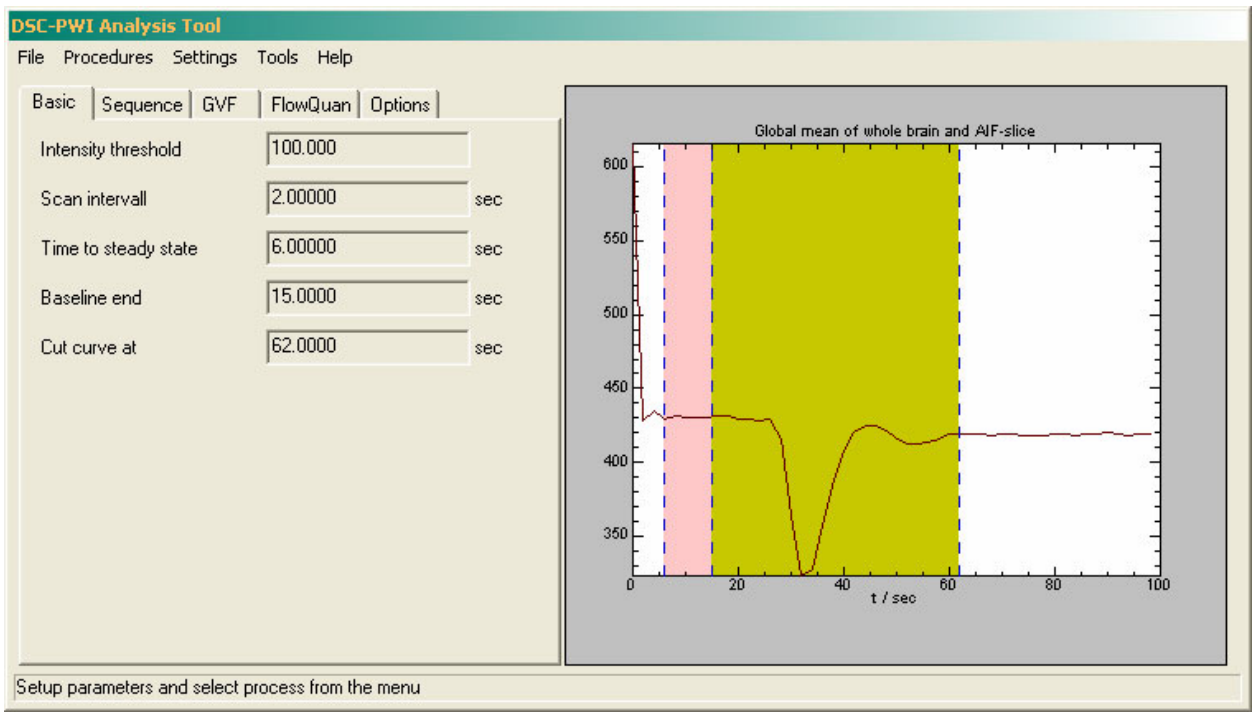


Figure 11: GUI for analysing perfusion data based on the DSC-MRI-method. Parameters are described in text. The graph on the right of the GUI shows the signal loss during the passage of the contrast agent. The pink colour marks the interval used for calculation of the baseline image, the green colour marks the interval, which is also included into calculation of the CTC. The rest of the scan is disregarded.

12.1.2 Direct methods

Here, all methods can be found, which allow calculating perfusion maps directly from the data without further parameterization.

12.1.2.1 CTC for T2 or T2*-weighted images

The CTC describes the relative concentration of the contrast agent in tissue. It is calculated by the following formula:

$$CTC(n) = -\frac{100.0}{TE} \cdot \ln\left(\frac{S(n)}{Baseline}\right),$$

where Baseline is the mean of all baseline scans. Before calculation, scans can be smoothed temporally and spatially. These options can be selected from the Options-menu. The volumes outside the pink or green interval (see Figure 6) are removed from the series, which therefore contains fewer volumes than the original data. Note that a scaling factor of 100.0 is used to calibrate the CTC. This factor was introduced, because normally the values of the CTC are very small (10^{-3} or less) and the display range is difficult to set. This parameter has no physical meaning.

12.1.2.2 CTC for T1w scans

This procedure calculates the relative concentration of contrast agent by a first order approximation of the signal change:

$$C_m^{rel}(t) = \frac{S(t)}{Baseline} - 1$$

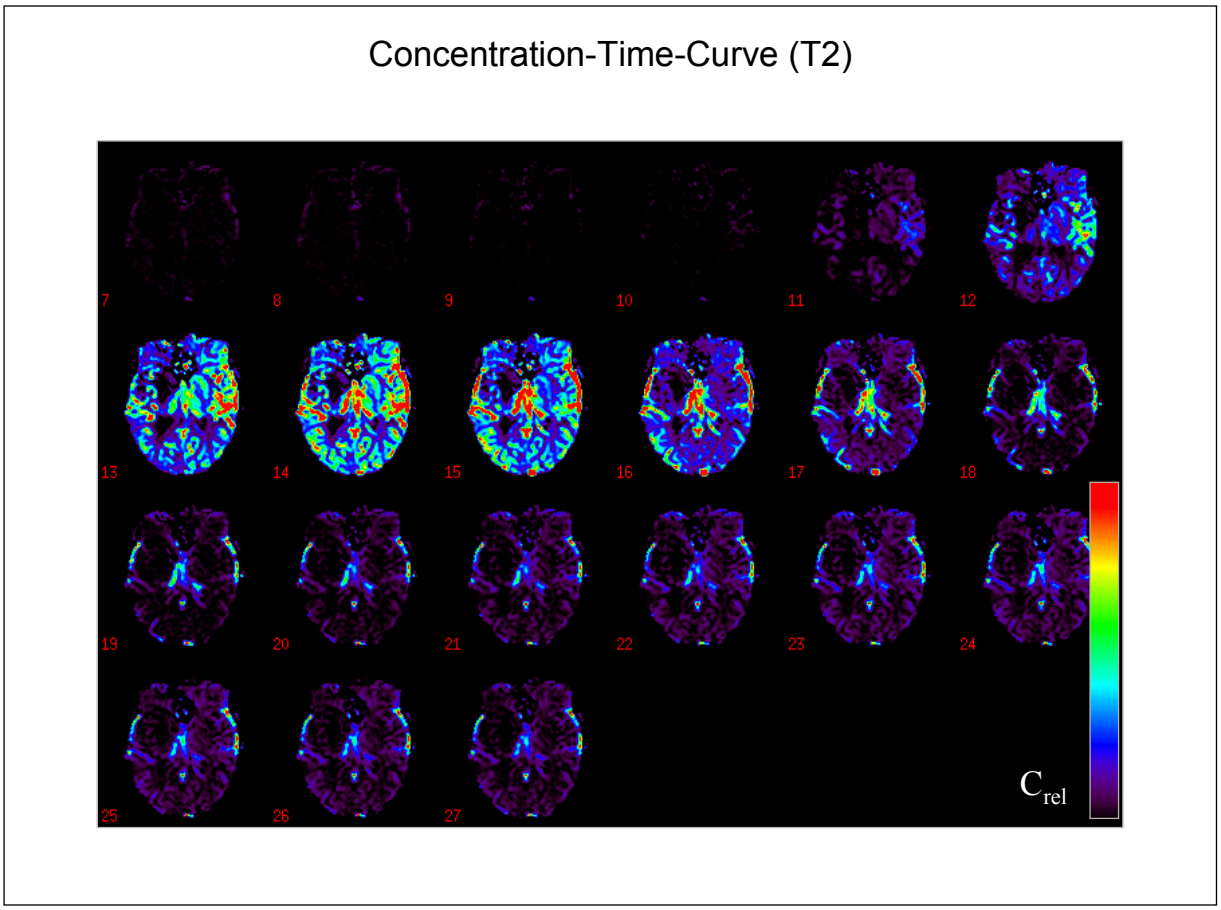
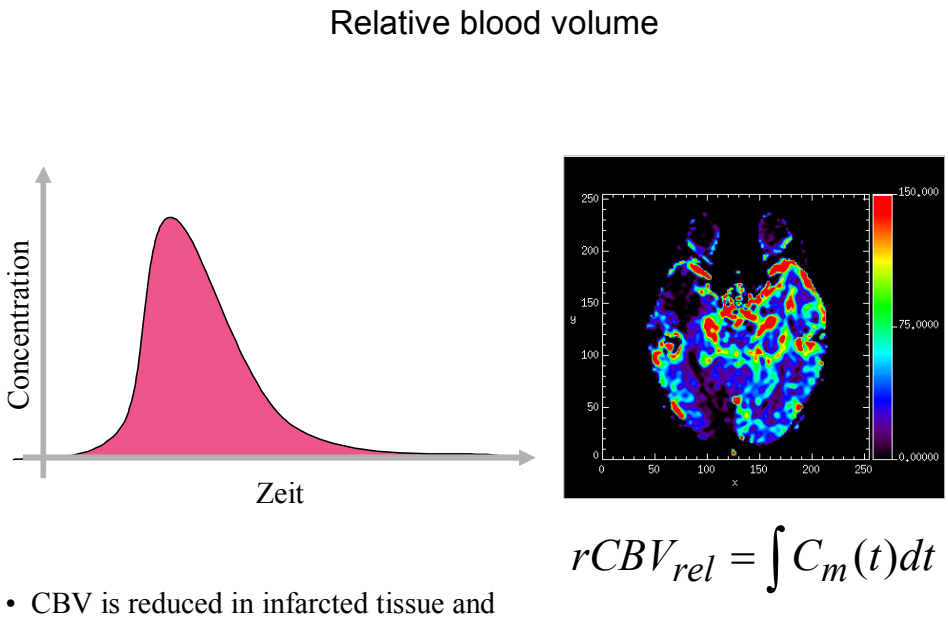


Figure 12: Concentration time curve of a human DSC-dataset

12.1.2.3 rCBV (regional cerebral blood volume)

Regional cerebral blood volume is calculated by numerical integration of the CTC. There are no corrections applied to exclude re-flow or leakage from the results. However, this approach provides good results for the analysis of data where blood flow might be severely reduced like in stroke patients, where modeling of data might fail.



- CBV is reduced in infarcted tissue and increased in inflammation
- Acute ischemia can lead to increased CBV (reactive hyperemia)

Figure 13: Relative CBV map of a human DSC-dataset

12.1.2.4 TTP (Time to peak)

Time to peak is the time, when the contrast agent shows the maximum concentration in a pixel. The time is given in seconds after the first volume, which was acquired under steady-state-conditions. The temporal resolution is limited by the time between two scans, which is approximately two seconds. Therefore the pixel values appear to change in a step-wise manner.

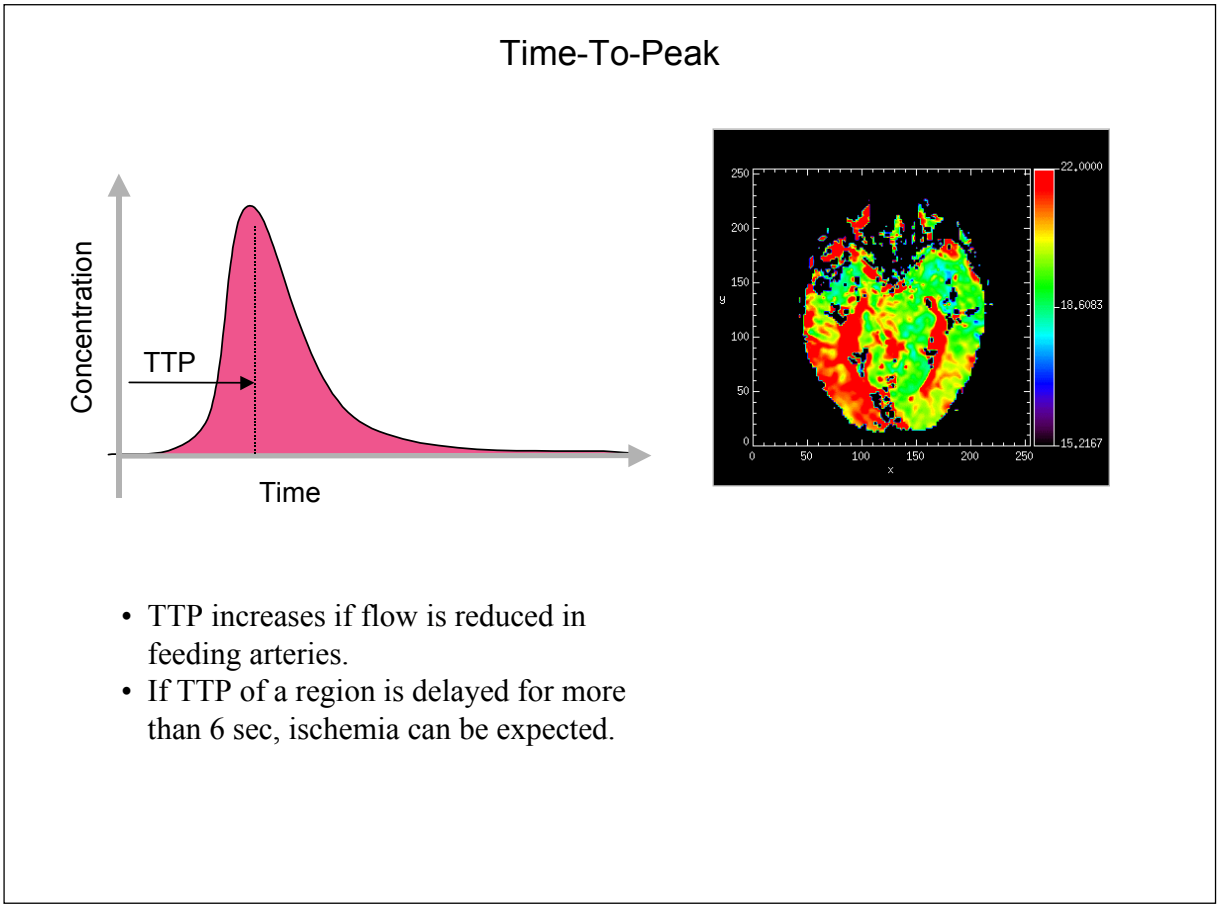


Figure 14: Time-to-peak analysis of a human DSC-dataset

12.1.2.5 MTT (Mean transit time)

The mean transit time is often defined as the first moment of the CTC:

$$MTT = \int_{t_0} t \cdot CTC(t)\, dt$$

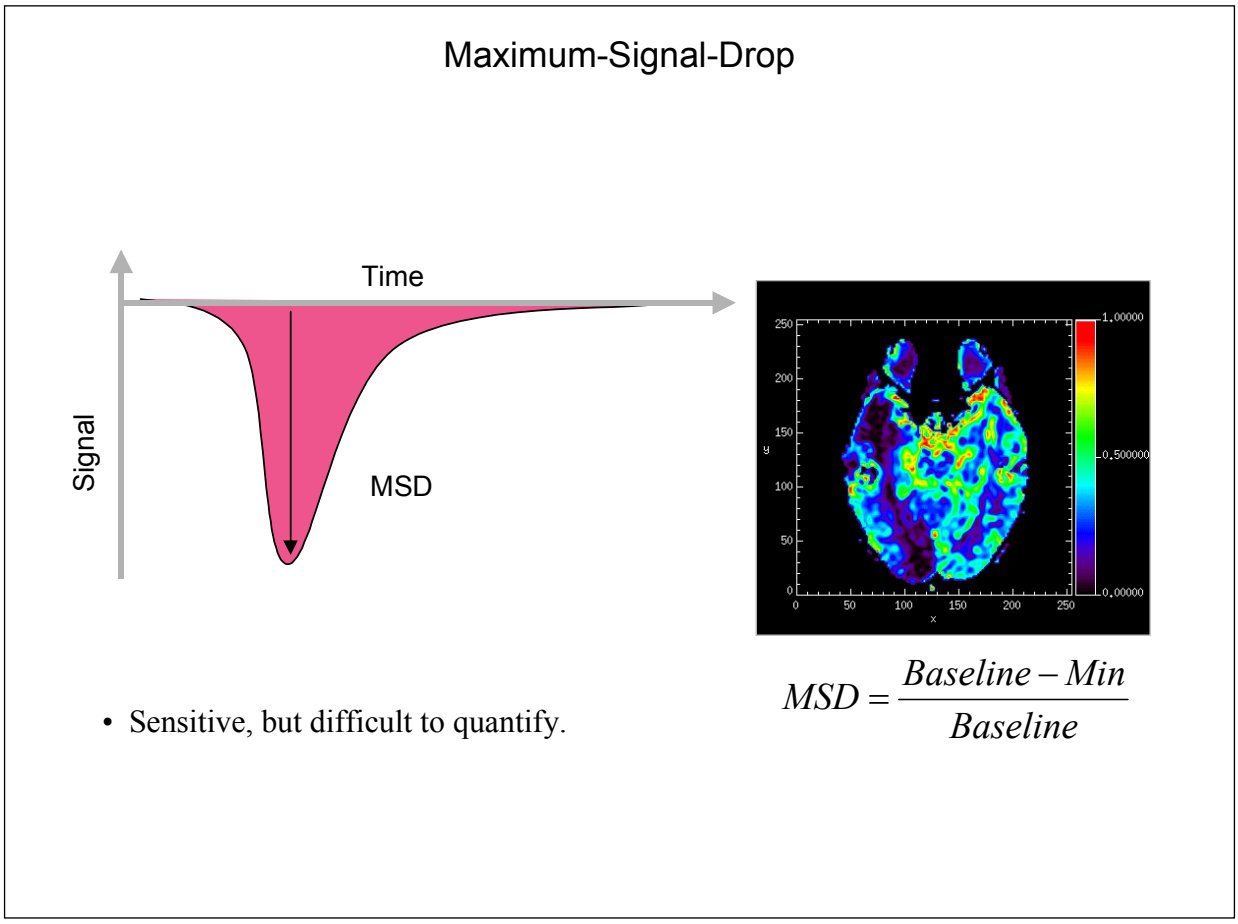
This quantity gives misleading results, since it does only measure the width of the curve if t_0 is set to the arrival time of the bolus. Otherwise, MTT is not very different to TTP.

12.1.2.6 MSD (Maximum signal drop)

The maximum signal drop is a quantity, which describes the local effect of the bolus on the MR signal. It does not provide reproducible data and it is very dependent on the shape of the bolus. If e.g., the bolus is more dispersed due to collateral blood supply MSD would indicate lower values, although the blood volume might be the same compared to the contra-lateral hemsiphere. MSD is calculated as:

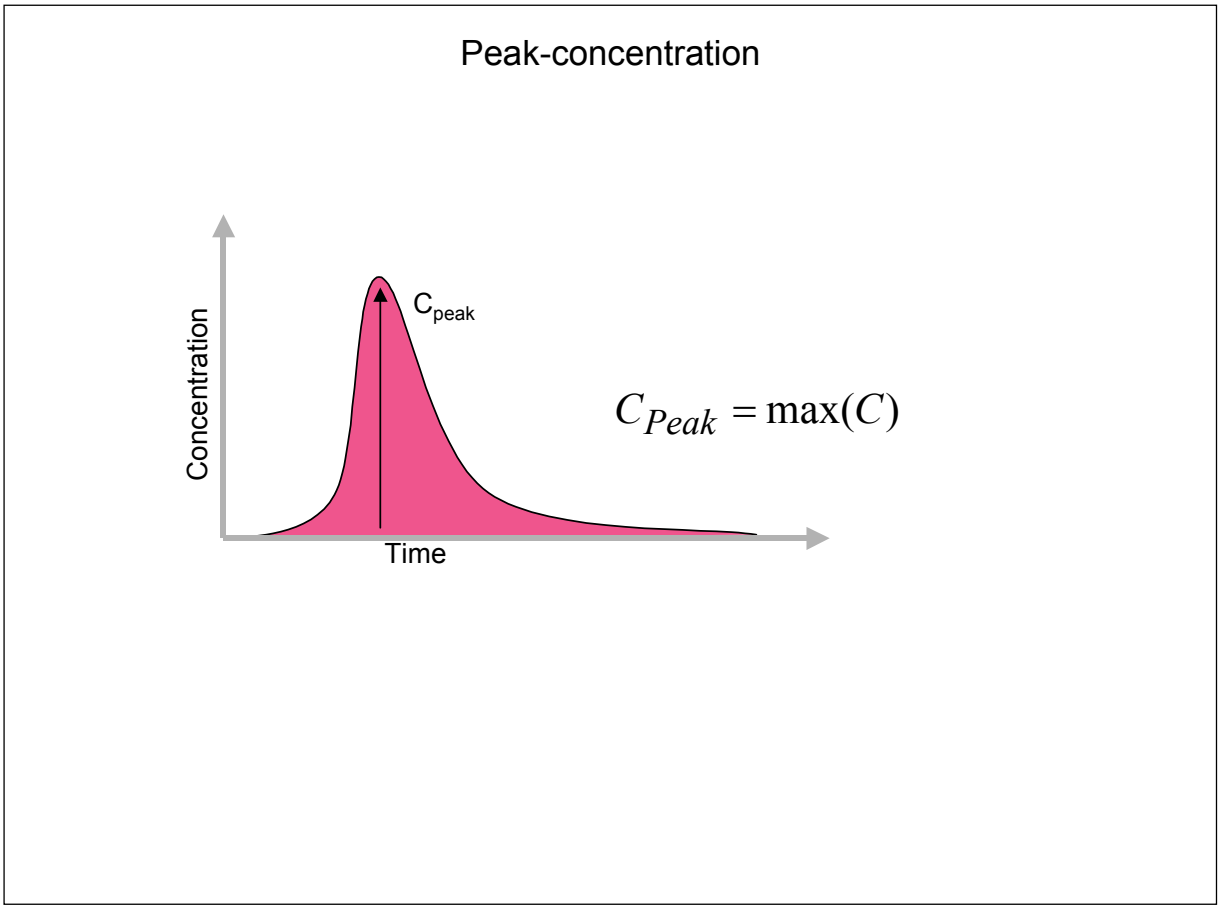
$$MSD = \frac{Baseline - Min(S(n))}{Baseline}$$

The MSD function will directly be calculated from the time-domain data. Hence, it can only be applied to T2-weighted sequences.



12.1.2.7 Peak concentration

The peak concentration reflects the maximum tracer concentration within a voxel. Numerically, the CTC will be calculated and the maximum value is taken. It is closely related to the MSD function, which can only be used for T2-weighted sequences.



12.1.3 GVF-based parameter maps

12.1.3.1 Calculating the ATD-Model

For calculation of relative blood volume it is important to eliminate re-flow and leakage of contrast agent into the extra-vascular space. This can be achieved by modeling the CTC by an function, which resembles the temporal profile of the bolus-curve.

Here, the measured CTCs can be modeled by a γ-probability-density-function (GVF) for each pixel separately. Three parameters are derived from the fit, which describe one aspect of the curve separately, namely amplitude a, peak time p and the sharpness s:

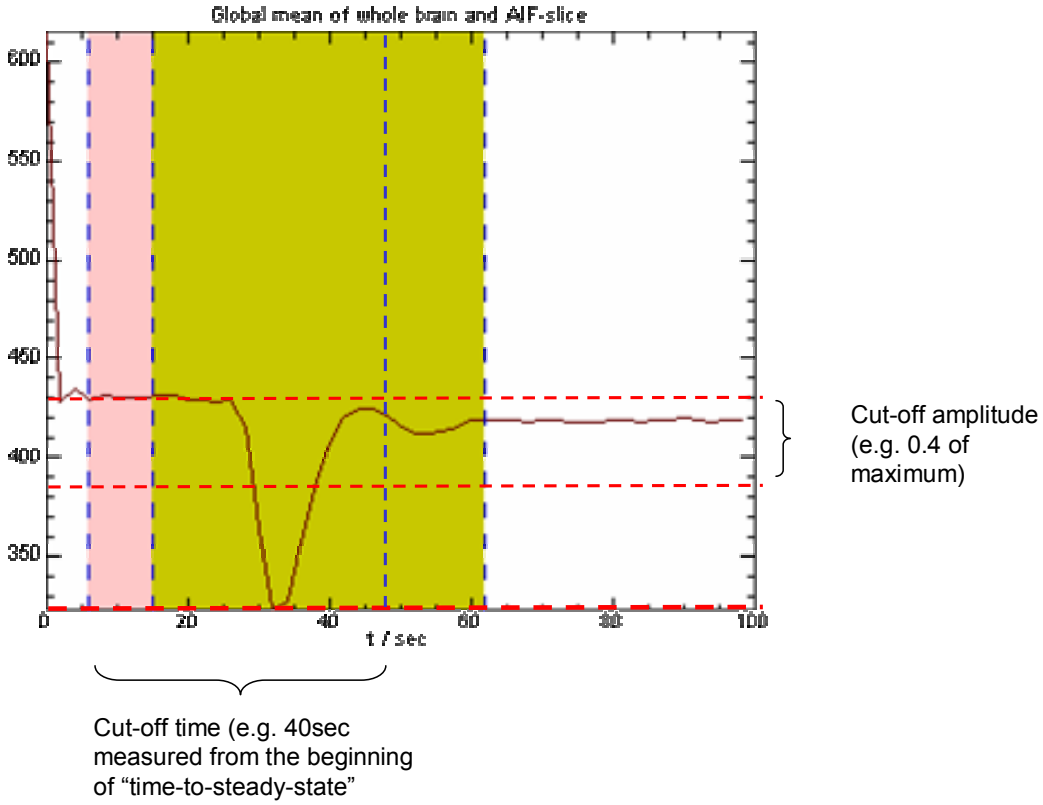
$$\gamma(t) = \frac{a}{p^{s \cdot p}} \cdot t^{s \cdot p} \cdot e^{-s \cdot (t-p)}$$

As $CTC(n)$ might not return to zero after the bolus passage only those scans acquired before and a few seconds after the bolus peak are used for the fit. This is achieved using a search algorithm, generating a weighting vector W(t) for the least square fit with the following structure:

$$W(n) = \begin{cases} 1 & \text{CTC(n)} > \text{c} \cdot \max(\text{CTC}) \vee \text{n} < \text{y} \\ 0 & \text{else} \end{cases}$$

The cut-off parameters c and y can be entered in the “Gamma Fit Parameter” tab of the toolbox window. The parameter “c” reflects the cut-off amplitude (0.0-1.0) with respect to height and the parameter “y” with respect to time (see also Figure below). This means that the algorithm will only consider those data points after the first pass with amplitude of larger than c of the maximum. To handle also data points with no significant decrease of signal a temporal cut-off can be set. In such a case, the fit is carried out according to the signal increase towards the CTC maximum of the first pass.

The parameter maps are stored on disk as GpDF_a, GpDF_t, GpDF_d and GpDF_c.



12.1.3.2 Calculating relative rCBV

Relative rCBV is simply calculated by numerical integration of the GVF.

12.1.3.3 Flow-quantification by including the arterial input function

For absolute quantification of blood flow and blood volume, measurement of the arterial input function is required. This function is used as a reference to calibrate the temporal profile of the tissue signal. The calculations are based on the tracer-dilution-theory.
Absolute quantification of blood volume just requires calibration of the integral under the CTC-curve:

$$rCBV = \frac{k_H}{\rho} \cdot \frac{\int_0^\infty CTC_{Tissue}(t)dt}{\int_0^\infty CTC_{AIF}(t)dt}$$

For absolute quantification of blood flow the residual function has to be calculated by deconvolution of the tissue concentration and the AIF:

$$C_m(t) = \kappa \cdot AIF(t) \otimes R(t)$$

The mean transit time (MTT) is then defined by:

$$MTT = \int_0^\infty R(t)\,dt$$

Using the central-volume-principle blood flow CBF can be calculated from

$$CBF = \frac{CBV}{MTT}$$

Absolute quantification of blood volume, blood flow and MTT is obtained in two steps. First the parameters of the GVF for pure vessel signal are selected. This can be achieved either manually or by using cluster analysis. The method can be chosen in FlowQuan parameter area.

- ROI: Use the pixels defined by ROI n
- CA: Perform a cluster analysis on the GpDF-maps and select the cluster with the largest signal amplitude.
- Actual: Use the values of the parameter field

The output of the calculation is written to rCBV, rCBF and MTT.

12.1.4 Special perfusion parameters

12.1.4.1 K1-K2-Model

The K1-K2-model allows to estimate the blood volume and permeability of the blood vessels and therefore eliminate T1-shine-through from the blood volume data. It was proposed by RM. Weisskoff (Proc. ISMRM 1994, p279) and applied to measurement of tumor blood volume.

It is assumed that prominent leakage occurs only in a small volume of the organ. Therefore it is possible to calculate a global mean $\overline{CTC}(t)$,which is not influenced by leakage and model the local CTCs by this function (reflecting the blood flow devoid of T1-shine-through, K_1) and the integral of the global CTC (reflecting the leakage, K_2):

$$CTC(t) = K_1 \cdot \overline{CTC}(t) - K_2 \cdot \int_0^t \overline{CTC}(t)\,dt$$

12.1.4.2 Calculation of Initial slope maps

Initial slope maps can be used to estimate the leakage of a contrast agent across a membrane. Here, several steps of data processing are combined. It is assumed that the scan was acquired

using a T1 weighted imaging sequence. From this scan the relative concentration of the contrast agent will be calculated by:

$$C_m^{rel}(t) = \frac{S(t)}{Baseline} - 1.$$

Secondly, a model function of the form

$$Y = \begin{cases} a_0 \cdot e^{b(t-t_0)} + c & ;t \geq t_0 \\ a_0 + c & ;t < t_0 \end{cases}$$

is fitted to the measured data. It is important to select a sufficiently large maximum χ^2, since all points for which the fit is not accurate enough would be discarded. The initial slope of the signal increase then becomes:

$$IS = \left(\frac{dY}{dt} \right)_{t=t_0} = a_0 \cdot b$$

12.1.5 Calculation of blood-flow-indices from muscle or tumor data

Measurement of blood-flow or blood-volume in other organs as the brain requires different analysis strategies. Unlike the brain, tissue of other organs or tumors shows venous pooling. Hence, the concentration of the tracer does not decrease significantly after the first pass. Concentration-time-curves can be modeled by sigmoid functions instead of GVF, as used for brain data:

$$gi(x) = \frac{1}{\sqrt{2\pi}} \cdot \int_{-\infty}^{x} e^{-\frac{t^2}{2}} dt$$

$$F = A_0 \cdot gi(x, \frac{(x - A_1)}{A_2})$$

The three coefficients correspond to the amplitude (A_0), the center of the sigmoid (A_1) and the slope (A_2). Large A_2 correspond to a slow signal increase and vice versa. One can relate A_2 to the MTT, which is required for the calculation of blood flow. Although there is no direct link between these two quantities, the rate of signal increase is related to the speed of contrast agent transit. Or with other words: The larger A_2, the longer MTT. The amplitude A_0 of the fit is proportional to the blood volume. Hence a blood flow index can be calculated from

$$BFI = \frac{A_0}{A_2}$$

This blood-flow-index function is helpful for the analysis of tumor data, where a blood-pool-agent (BPA) was used as tracer. The experimental protocol should follow the following steps:

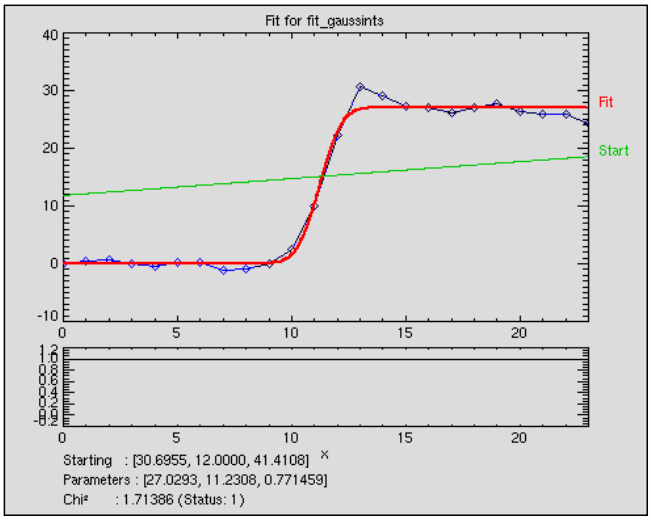
- Acquisition of T2 or T2*-weighted images, with a temporal resolution of 5 sec less.
- Administration of a BPA after acquisition of a series of baseline images.
- Continuation of the measurement until a steady-state has evolved.

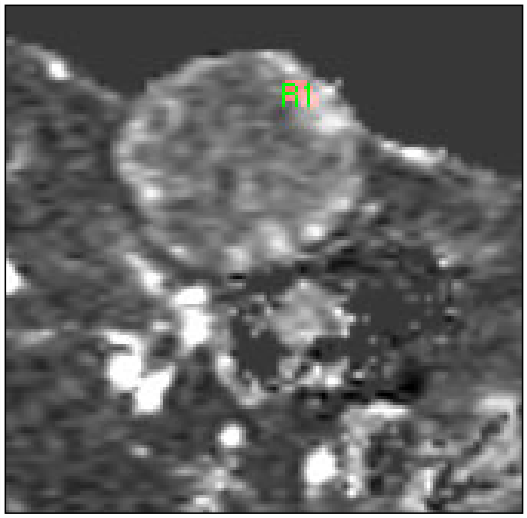
Analysis comprises the following steps:

- Calculation of the CTC(t)
- Fitting the sigmoid-function the the CTC(t)
- Calculation of BFI and blood volume

Files written to disk are:

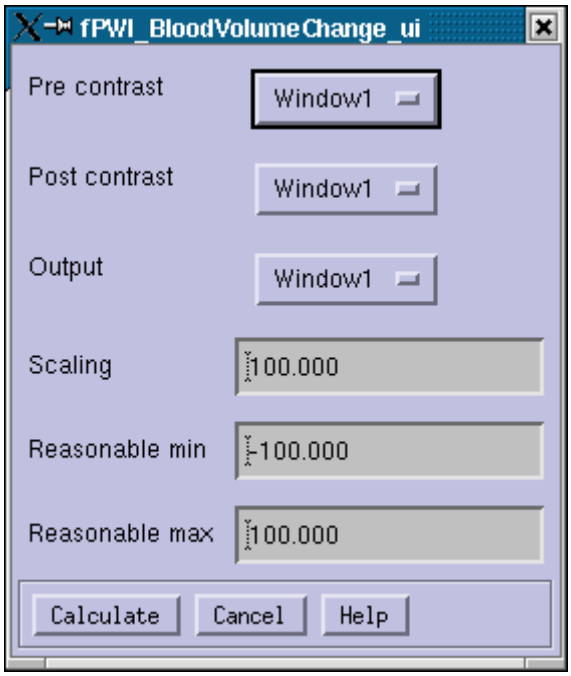
- BasicFilename_ctc (concentration time curve)
- BasicFilename_GaussIntS (parameter files generated by the fit)
- BasicFilename_bpabv (blood volume)
- BasicFilename_bpabf (blood flow index)





12.1.6 Calculating ΔCBV-maps

The MR signal can not only be changed by changing the concentration of contrast agent, but also by changing the cerebral blood volume. This effect can be exploited in fMRI-experiments using blood pool agents. In order to calculate the relative change of blood volume induced by a stimulus, the image intensity before and after application of contrast agent has to be measured. The experiment should therefore consist of two scans, separated by a period during which a steady state of contrast agent concentration can develop. The following formula is used to calculate the ΔCBV-maps:



$$\frac{\Delta CBV(t)}{CBV(t)} = \frac{\ln\left(S(t)/S(0)\right)}{\ln\left(S(0)/S_{pre}\right)}$$

The CTC of the dynamic scan, which was acquired during stimulation, should be selected as the active window.

The tool is located in Analysis/MRI/BloodVolumeChange. The following input is expected:

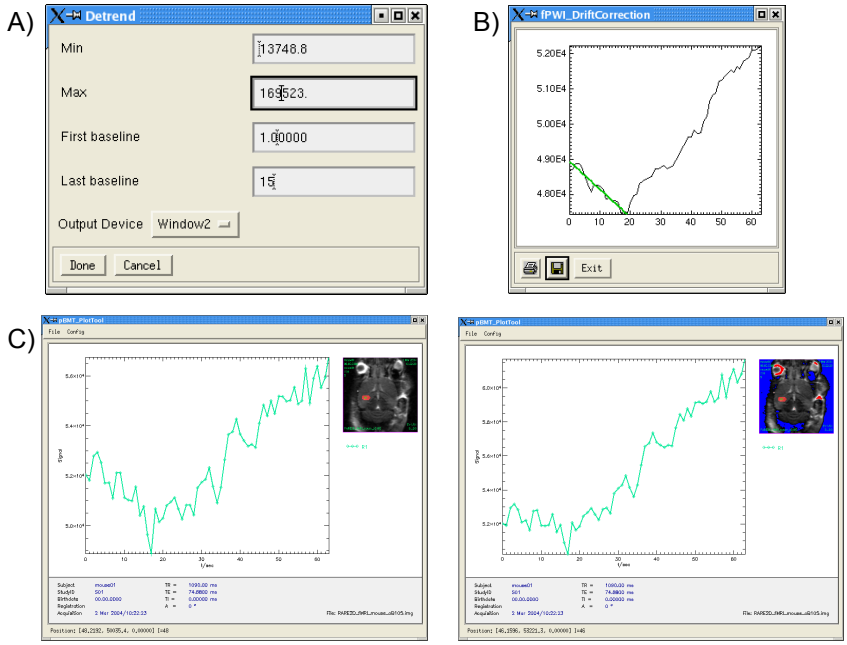
Pre contrast scan	A reference scan containing only one single volume, which was acquired before administration of contrast agent.
Post contrast scan	A reference scan containing only one single volume, which was acquired after administration of contrast agent.
Output	The window, to which the result will be copied.
Scaling	A scaling factor, which must be set to TE (as used for calculation of the CTC)

If the scaling factor is adjusted as stated above the DCBV-map reflects changes of blood volume in percent.

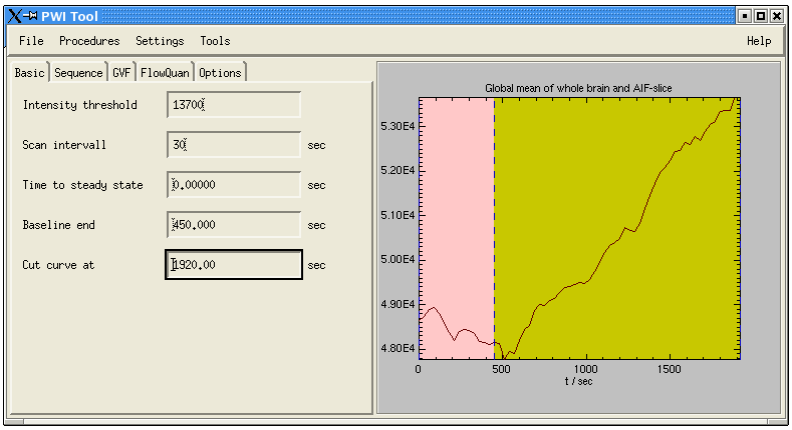
12.1.6.1 Calculation of ΔCBV induced by bicuculline

This example lists all steps, which are needed to analyze a bicuculline-stumulation experiment in mice.

1. Load the pre-contrast scan to a window. This often contains more than one volume. Therefore you must calculate an average to obtain one single volume. Use Tools/calculation/Average Volumes for this purpose. The input fields are automatically initialized to calculate an average of all volumes.
2. Load to post-contrast scan (the time series) into the next window. Since contrast agent concentration will slowly decrease over time, one has to perform a detrending:
    a. Selection of an appropriate threshold: Select the RANGE-Colortable and adjust the slider for the minimum so that the background appears blue.
    b. The detrending-function can be found under Tools/Intensity/Detrend (global). The result of this procedure is shown in the figure below. Save the result with the suffix "_dtr".



3. Calculation of the concentration time curve: Open the PWI-DCE tool from the Analysis/MRI-menu. Enter the values as shown below. The intensity threshold must be entered manually and can be selected from the minimum of the window. Select Procedures/Native/CTC to calculate the CTC. Close the tool.



4. Calculation of the ΔCBV-maps
    a. Extract the first volume from the post-contrast time series. Use Tools/Geomtry/ExtractVolumes for that.
    b. Now you should have loaded three data sets
        i. A pre-contrast scan comprising one volume
        ii. A post-contrast scan comprising one volume
        iii. The CTC-scan comprising a set of volumes (e.g. 64 as in this example)
    c. Select as CTC-scan as the active window. Start the ΔCBV-tool from Analysis/MRI and select the windows as described before.

12.2 Calculation of T1- and C_m-maps from dynamic IR-data

The relative concentration of a MR-contrast agent can be calculated from T1-weighted scans. This imaging approach is often used to assess the vascular permeability of tumors or inflamed tissue. T1-weighting can either be achieved by using a fast gradient echo sequence using a high flip angle or by preparation of the same sequence (the flip angle must be low in this case) with an inversion-recovery (IR) or saturation recovery (SR) pulse module. The analysis described here refers to the IR-prepared sequence, which provides a higher sensitivity to the injected contrast material. The protocol consists of a reference image followed by a dynamic IR-prepared scan, which is acquired during the administration of a contrast agent. The reference image must be proton-density weighted and thus reflects the longitudinal magnetization $M_{z,eq}$ in the equilibrium state. The reference scan is usually Turbo-FLASH-scan. The same imaging sequence is used for the dynamic scan, which is in addition IR-prepared. Inversion time should be larger than 70% of the longest tissue T1, so that longitudinal magnetization is positive for all spins.

The longitudinal magnetization can be calculated from

$$M_z(TI) = M_{z,eq} \cdot \left(1 - 2 \cdot e^{-TI/T_1}\right),$$

where TI is the inversion time, $M_{z,eq}$ the proton density image, T_1 the longitudinal relaxation time of the tissue and $M_z(TI)$ the longitudinal magnetization at time point TI. Reorganization of this equation leads to

$$T_1 = \frac{-TI}{\ln\left(\frac{1}{2} \cdot \left(1 - \frac{M_z(t)}{M_{z,eq}(t)}\right)\right)}.$$

In a second step, the relative concentration of the contrast agent can be calculated. Assuming a linear contribution of the contrast agent to the longitudinal relaxation rate of the tissue

$$R_1 = R_1^0 + C_m \cdot r_1^{CA},$$

the concentration can be calculated from

$$C_m = \frac{R_1 - R_1^0}{r_1^{CA}}$$

Performing the analysis:

- Load the reference scan and the IR-prepared scan to a window.
- Adjust the WIN_{min} of the reference scan to suppress background noise
- Select the window containing the dynamic scan
- Start either **Analysis/MR/T_1 from IR** or **Analysis/MR/C_m from IR** (if C_m is selected, the first fife volumes are taken to calculate a mean baseline image)

- Select the output window
- Press the Done-button to start the calculation

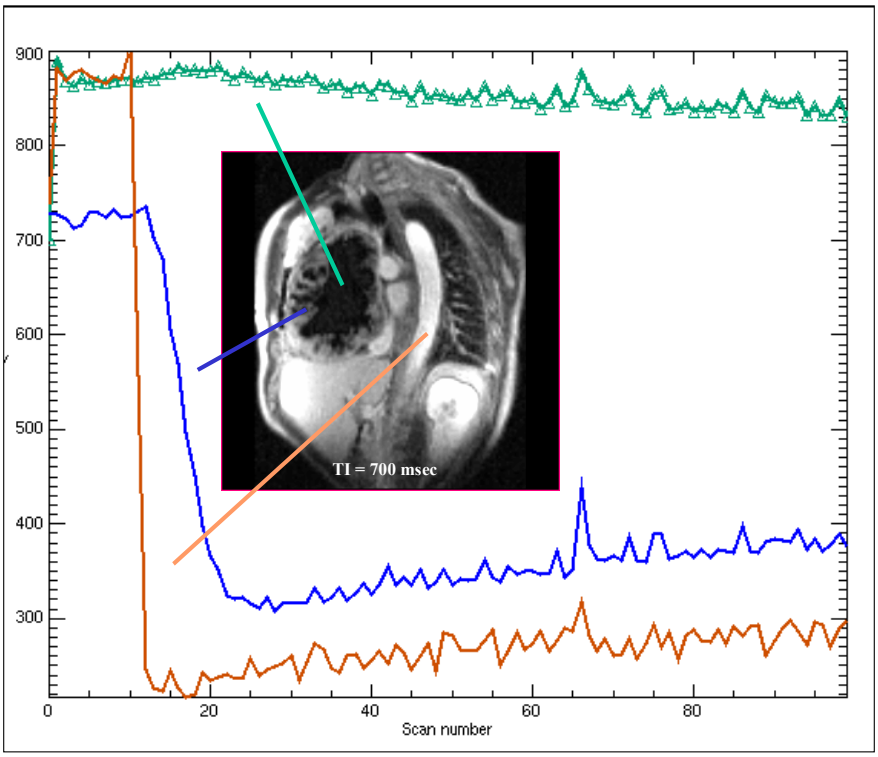


Figure 15: Example for a data set of a quantitative T1-measurment using dynamic IR-imaging. Temporal profiles are shown for three ROIs, one comprising the Aorta, the other two are representing necrotic and vital tumour tissue. Temporal resolution was 3 seconds.

12.3 Calculation of vascular permeability from DCE-data

12.3.1 Basic theory of permeability imaging using MR

Permeability of blood vessels can be assessed by measurement of the diffusion of contrast material form the vascular lumen into the tissue. The theoretical description is based on a two-compartment model. One compartment is the blood volume, the other the tissue. The driving force of the diffusion is the concentration gradient between the two compartments. The rate of diffusion depends on the permeability of the membrane and the surface. The parameter describing the rate is k, which is also called the permeability-surface-product. A typical enhancement curve is shown in Figure 9 together with the result of the least square-fit, which will be discussed below.

$$\frac{dQ_e}{dt} = \underbrace{\frac{PS}{V}}_{k} \cdot \left(C_p - C_e\right)$$

Rearrangement of this equation using

$$Q_e = v_e \cdot C_e$$

$$\frac{dC_t}{dt} = v_p \frac{dC_p}{dt} + v_e \frac{dC_e}{dt}$$

$$C_t = v_p C_p + v_e C_e$$

leads to

$$v_e \frac{dC_e}{dt} = k \cdot \left(C_p - C_e\right)$$
$$\Leftrightarrow \frac{dC_t}{dt} = -\frac{k}{v_e} C_t + k\left(1 + \frac{v_p}{v_e}\right) C_p + v_p \frac{dC_p}{dt}$$

This differential equation has the general solution

$$C_t(t) = k \int_0^t e^{-k/v_e (t-t')} C_p dt' + v_p C_p$$

Provided that the tissue concentration, the vascular concentration, the leakage space and the

blood volume are know, k can be calculated by a least square fit.

12.3.2 Estimating *k* using the EndoPerm-Tool

The EndoPerm-tool allows estimating k for c_m-maps calculated before by the procedures described in 9.2. The analysis will be carried out for temporal profiles defined by ROIs. Usually, two ROIs must be defined, one describing the tissue-concentration $C_p(t)$, the other the concentration of the tracer in blood plasma $C_p(t)$. However, in many cases, $C_p(t)$ is not known, because either the image does not contain a large blood vessel, or the signal from the blood vessel is corrupted by pulsation, movement or saturation effects. In such a case, a theoretical $C_p(t)$ can be used, which is a bi-exponential function with the parameters

$$Cp(t) = D \cdot \left(A_1 \cdot e^{-m_1 \cdot t} + A_2 \cdot e^{-m_2 \cdot t} \right)$$

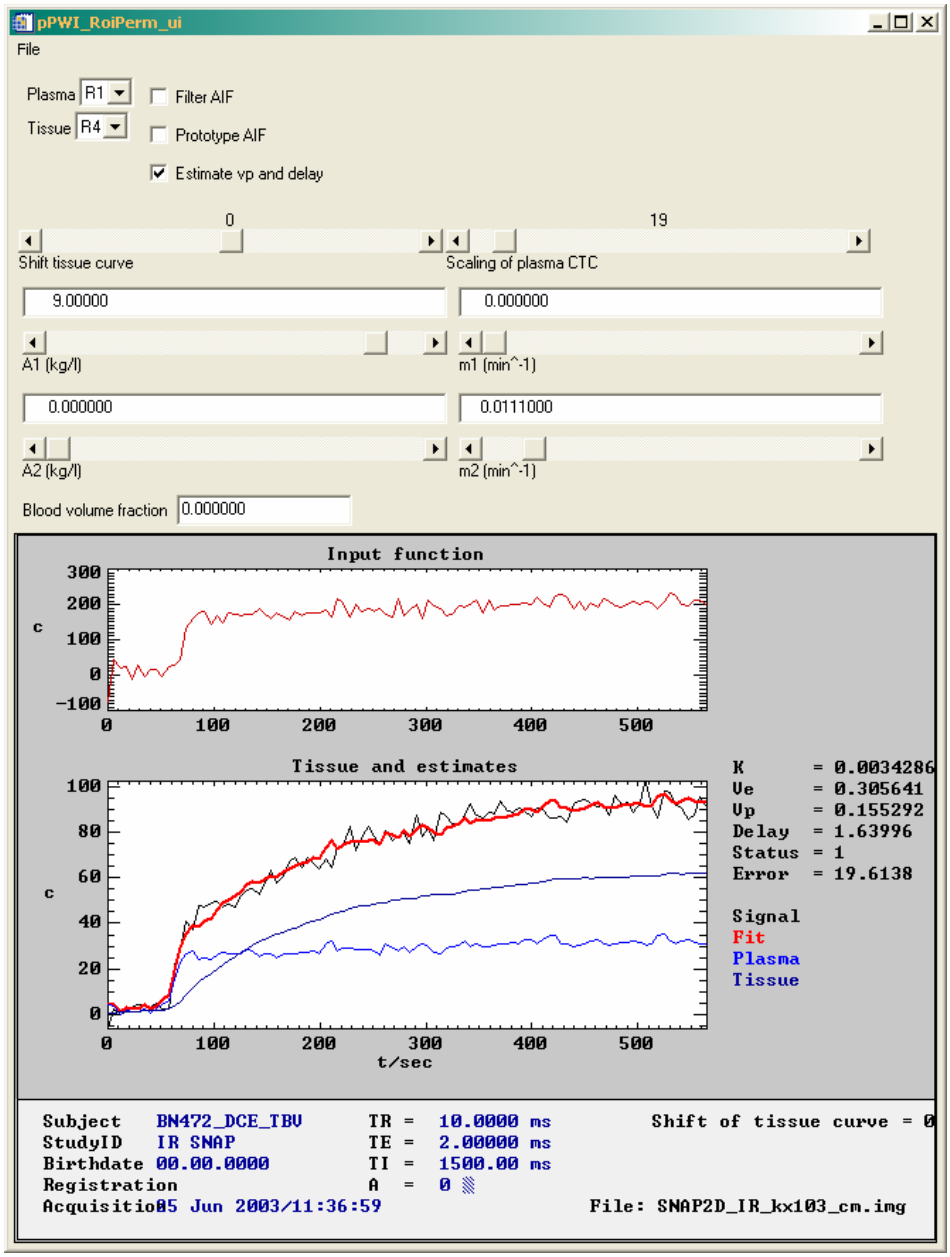
The parameters (see Tofts et al.) of this function are initialized as follows but can be changed using the slides of the tool:

a_1 = 3.99 kg/liter
a_2 = 4.78 kg/liter
m_1 = 0.144 min^{-1}
m_2 = 0.0111 min^{-1}
D = 1.0 mmol/Kg

The parameter D is used as a parameter, which will scale the result. If only relative changes are of interest, D can be set arbitrarily. If absolute values for k are required, D must be quantified.

Options available for designing the $C_p(t)$-function are:

Prototype AIF	Use Toft's $C_p(t)$-function and not the profile selected on the left.
Filter AIF	Filtering the C_p by a Savitzky-Goley-Filter produces smoother input functions.
Estimate v_p	If this option is selected, v_p will be estimated by the least square fit. Otherwise its value will be taken from the input field below.



Note: Measurement of the plasma-concentration is often difficult using single-slice-IR-sequences. Data from vessels is often corrupted by pulsation artifacts. Moreover, saturation of the longitudinal magnetization can lead to underestimation of C_p especially for long TI (see Figure below).

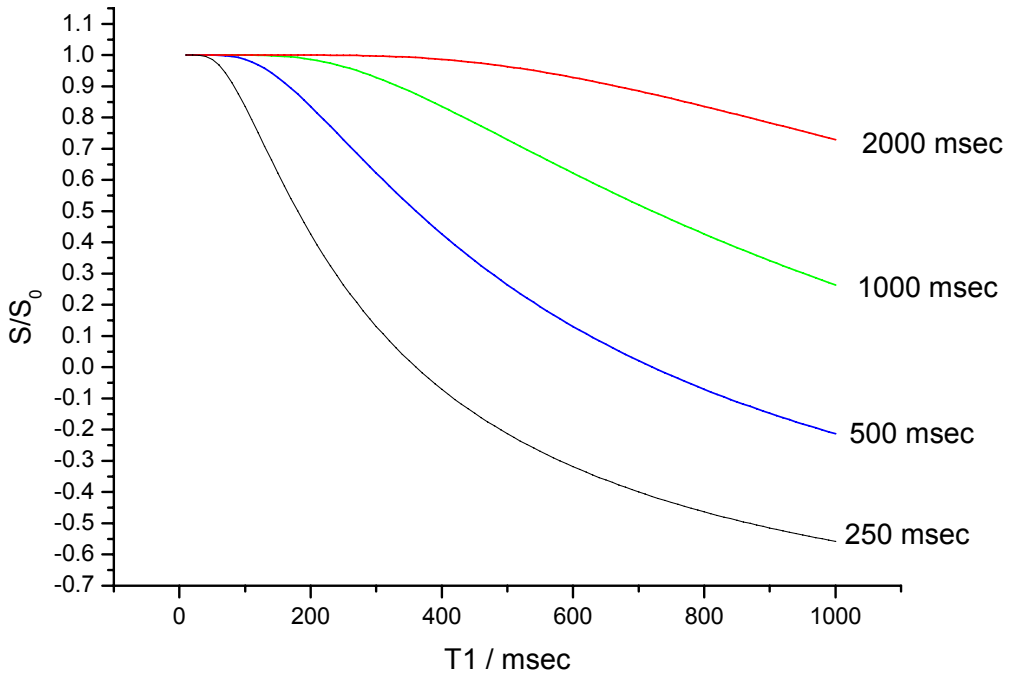
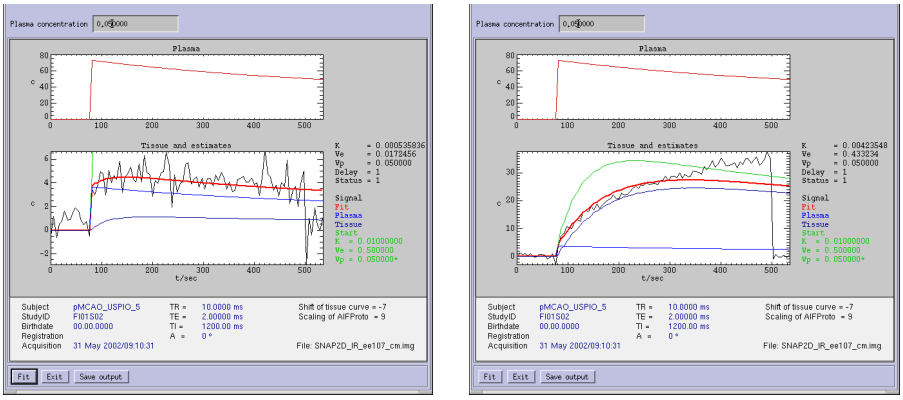


Figure 16: Calculation of the signal ratios for an IR-measurement. For very long TI, the inversion pulse will have less effect on the magnetization at time TI especially for short T1. Hence, the vascular relaxation, for which T1 drops below 300msec after injection of contrast media, will be difficult to assess. The profiles were generated by using the relation

$$S(TI) = S_0 \cdot \left(1 - 2 \cdot e^{-\frac{TI}{T_1}} \right).$$



D adjusted from profile
comprising tissue with intact BBB

Tissue comprising disrupted BBB
k=0.0042, V_e=0.43,V_p=0.05

Tissue comprising disrupted BBB
k=0.0052, V_e=0.48,V_p=0.00

Tissue comprising disrupted BBB
k=0.0047, V_e=0.45,V_p=0.025 (estimated)

Figure 17: Comparison of results obtained from different analysis for two different temporal profiles. The data was taken from a brain-study on an animal with unilateral pMCAO. Top left: Toft's $C_p(t)$-prototype. D was adjusted for an assumed v_p of 0.05. Top right: Parameters were applied to a temporal profile for tissue with compromised BBB-integrity. Bottom left: Same parameters but v_p=0. Same $C_p(t)$ but v_p was estimated by the least square fit.

12.4 Calculation of enhancement maps

This function can be used to calculate the relative signal enhancement after administration of contrast agent. The following relation is used:

$$\mathrm{Enh} = \frac{S_{pre} - S_{post}}{S_{pre}}$$

Note that this equation is similar to the one used for calculation of MTR-maps.

12.5 Calculation of magnetization-transfer-ratios (MTR)

For calculation of MTR-maps, two scans are required. One has to be acquired without, the other with magnetization-transfer-suppression. The calculation is carried out on a pixel-by-pixel-basis using the following relation:

$$MTR = \frac{S_0 - S_{MTR}}{S_0}$$

13 Fitting functions to measured data

Four-dimensional data can be modeled by analytical functions. The most frequently functions are implemented in the Function-fit-module.

Model (as named in the GUI)	Function name	Equation	Remarks
ExpDec, T2, ADC	Fit_exp	$F(x) = A_0 \cdot e^{A_1 \cdot x}$	
Exp3P	Fit_exp3	$F(x) = A_0 \cdot e^{A_1 \cdot x} + A_2$	
	Fit_exp4	$F(x) = A_0 \cdot e^{A_1 \cdot (x - A_3)} + A_2$	
ExpEnh	Fit_expenh	$F(x) = \begin{cases} A_0 \cdot \left[1 - e^{A_1 \cdot (x - A_2)}\right] & ; x \geq A_2 \\ 0 & ; x < A_2 \end{cases}$	This function should be used for exponential enhancement e.g. after injection of contrast media. A1 is negative in that case and F is set to zero before CM is arrives in the tissue.
	Fit_expelim	$F(x) = \begin{cases} A_0 \cdot e^{A_1 \cdot (x - A_2)} & ; x \geq A_2 \\ 0 & ; x < A_2 \end{cases}$	This function can be used to model an exponential decay, which is delayed by A2. It is in principal the same function as Fit_exp.
	Fit_gauss	$g(x, C, FWHM) = e^{-\frac{(x-C)^2}{k}}$ $k = \frac{(FWHM/2)^2}{\ln(2)}$ $F = A_0 \cdot g(x, A_1, A_2) + A_3$	

GaussIntS	Fit_gaussints	$gi(x) = \frac{1}{\sqrt{2\pi}} \cdot \int_{-\infty}^{x} e^{-\frac{t^2}{2}} dt$ $F = A_0 \cdot gi(x, \frac{(x - A_1)}{A_2})$	A1 is associated to the center of the sigmoid function and A2 is the slope. This function can be used to model the rate of CM enhancement and therefore something which is related to blood flow.

For function fitting the fit tool shown in the figure shown below (Analysis/Function fit) has to be used. It allows entering the model, the weighting vector used for performing the fit and the destination for the calculated maps (window or file). The x-axis can be changed by editing the header of the scan (Edit/Header from the main menu). The maximum χ^2 value is important for calculation of the maps. The result of those pixels is set to zero for which the fit reveals larger χ^2 than the given maximum. This allows to control the accuracy of the fit and discard those points, for which the model might not be appropriate or the signal to noise ration to low. If the fit tool is active, it is possible to click into the data window in order to check if the fit leads to accurate result. If the data cannot be described be the model function correctly or if the data is partly corrupted, the weighting vector (also shown as a green line in the graph) can be changed in order to select the interval, in which the fit should be optimal. High values in the weighting vector have to be selected for important data points. The values can be entered manually or weighting models can be selected by the specific button:

13.1 Modifying the weighting-vector:

Equal: Equal weighting for all points
Decreasing: Exponentially decreasing weighting.
Use even only: Use only samples 0,2,4...
Use odd only: Use only samples 1,3,5...

Three modes of operation are implemented:

Dynamic: Select individual pixels from the image by moving the mouse across the window and perform the LSF.

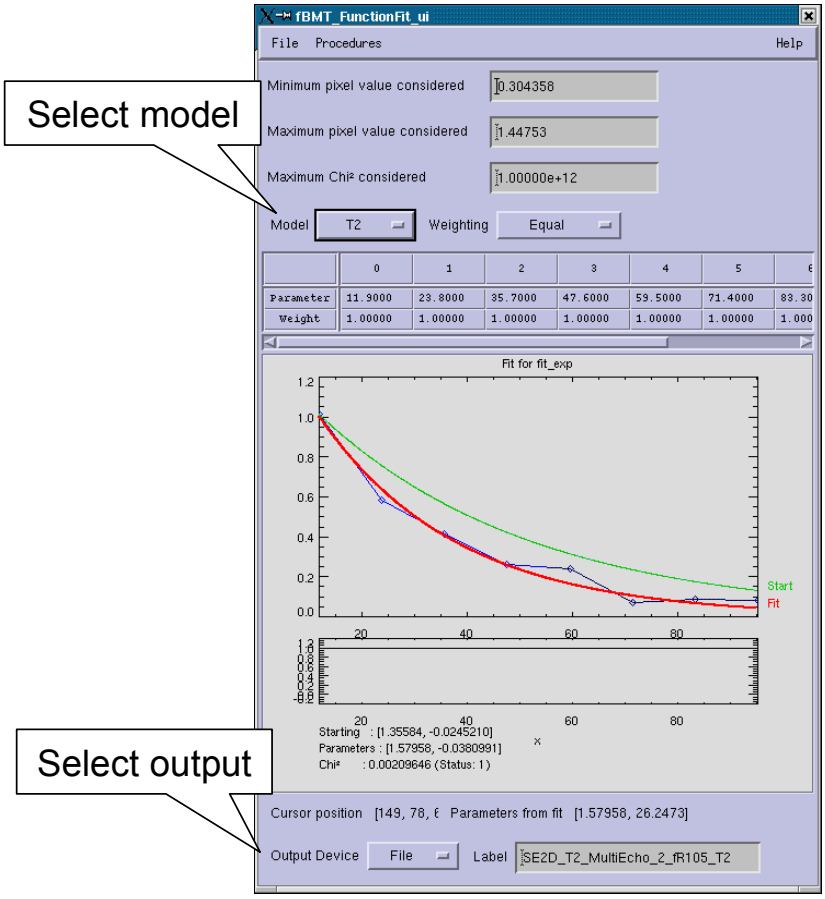
ROI: Perform the LSF for the selected ROI

Calculate maps (selected from the Procedures menu): Perform the LSF for each voxel of the scan and write the result to a file or to a window.

Before the LSF is carried out for a data point, appropriate starting values will be calculated. If a map was calculated the result can be loaded and (File/Load map) and can be used as a starting values for interactive fitting. This option allows also checking the accuracy of the result.

13.2 Example: Calculation of a T_2-map

- Load data to a BioMAP-window. If the data will be imported from e.g. Bruker, one has to store them in the database prior to analysis.
- Adjust the lower threshold. For this, one should change the color table to “Range” (either with Window/Color table or by pressing the icon on the left of BioMAP’s main window). Hence, all points, which should be excluded from analysis will be shown in blue.
- Start the tool from Analysis/Function fit.
- Set the Model to T2
- By default, the result will be copied to the database
- Now one can browse through the data by clicking into the BioMAP window.
- The T2-map will by generated by selecting Process/Generate maps



13.3 Remarks

- If the Function-fit-tool is active, no other functions can be used.
- The result of the fit will be set to zero if the error (given by Chi^2) of the LSF exceeds the maximum value defined in the user interface. This value is set to 10^{12} by default.
- The T2-model will only generate the T2-map. No proton-density map will be generated.
- The relaxation-rate can be calculated by the ExpDec-model.
- If the values of the x-axis are not set correctly, one can adjust them by Edit/Header.

14 Singular value decomposition

Singular value decomposition (SVD) is a method, which was developed for the analysis of multi-dimensional data sets. The main goal of this method is to extract the most important features of the time-series data. It is often used for the analysis of time-series data, where information was recorded from multiple channels. For example, one could record EEGs from multiple electrodes and try to find temporal patterns, which are similar across electrodes. The approach implemented in BioMAP considers a scan as a two dimensional data set. One dimension describes the position of the pixel and the other dimension is used for time or any other parameter, which was varied during the measurement. The exact position of the pixel in x, y and z is therefore not important and is exchanged by an one-dimensional index.

This 2-dimensional matrix will be decomposed according to

$$M = USV^T .$$

The matrix U contains the spatial modes, which are also, Eigenvectors of M^TM. S is a diagonal matrix of singular values. The matrix V corresponds to the temporal profile of the contribution of an Eigenvector to the time series data of M. Finally U will be reordered to the original matrix structure: $U(s,t) \rightarrow U(x,y,z,t)$

15 The GLM Tool

The General Linear Model (GLM) can be used to analyze multi-parametric imaging data on a pixel-by-pixel basis. One of the most important applications is the analysis of functional imaging data using fMRI, PET or SPECT methods. In contrast to conventional group comparisons using the t-test or other parametric or non-parametric tests, the GLM allows to model interactions of several parameters, which have been defined to describe the model or to remove confounding effects.

15.1 About the GLM

The general linear model as implemented in the GLM-tool allows to model datasets by multiple linear regression. Hereby, the values of a voxel Y are described by a linear combination of n factors:

$$Y = a_1 B_1 + a_2 B_2 + \ldots + a_n B_n$$

The B_i are vectors of the same length as Y. They are called factors. E.g. a categorical design with two levels could be described by the following parameters:

N=2
m= 8=number of volumes.

$$B_1 = (0,1,0,1,0,1,0,1)$$
$$B_2 = (1,1,1,1,1,1,1,1)$$

B_1 indicates that the first volume was acquired during rest, the second activation and so on. B_2 is used as a dummy variable, which represents the offset of the data. Using a matrix formulation the first equation can be rewritten as:

$$\begin{pmatrix} y_1 \\ \vdots \\ y_m \end{pmatrix} = \begin{pmatrix} b_{11} & \ldots & b_{1n} \\ \vdots & \ddots & \vdots \\ b_{m1} & \ldots & b_{mn} \end{pmatrix} \begin{pmatrix} a_1 \\ \vdots \\ a_n \end{pmatrix},$$

where B is the so called design matrix of the experiment:

$$Y_{m1} = B_{mn} A_{n1}$$

The goal of the GLM is to find the best estimate for the coefficients a_i. For that the matrix-formulation has to be inverted, which leads to the least square solution

$$A_{n1} = (B'B)^{-1}_{nn} B'_{nm} Y_{m1}$$

The error of the fit can be described by the following parameters:

15.1.1.1 Sum of squares for error:

$$SSE = \sum_{i=1}^{n} (y_i - \tilde{y}_i)^2 ,$$

$$s^2 = \frac{SSE}{\mathrm{DOF}} = \frac{SSE}{m-n},$$

which is the distance of the measured Y and the Y calculated from the estimate of A and the design matrix B.

15.1.1.2 Standard error of mean for b_i:

This parameter allows assessing the significance of a factor. E.g. for the categorical design shown above it has to be shown the a_1 is significantly different from zero. For that the error of an estimate can be calculated from:

$$C_{nn} = (B'B)^{-1}_{nn}$$

$$SEb_i = \frac{s}{\sqrt{c_{ii}}}$$

t-value for a parameter bi:

$$t_i = \frac{b_i}{SEb_i}$$

After solving the equations for a given design, the GLM-tool will write the following scans to the database:

*DesignName*_spm: Paramter estimates (containing n volumes)
*DesignName*_sse: Sum of squares for error (containg 1 volume)
*DesignName*_seb: Standard error for b_i (containging n volumes)
*DesignName*_tb: t-value for each b_i (containing n volumes)
*DesignName*_tp: t-value for the projections
*DesignName*_sep: Standard error for the projections

15.2 Using the tool

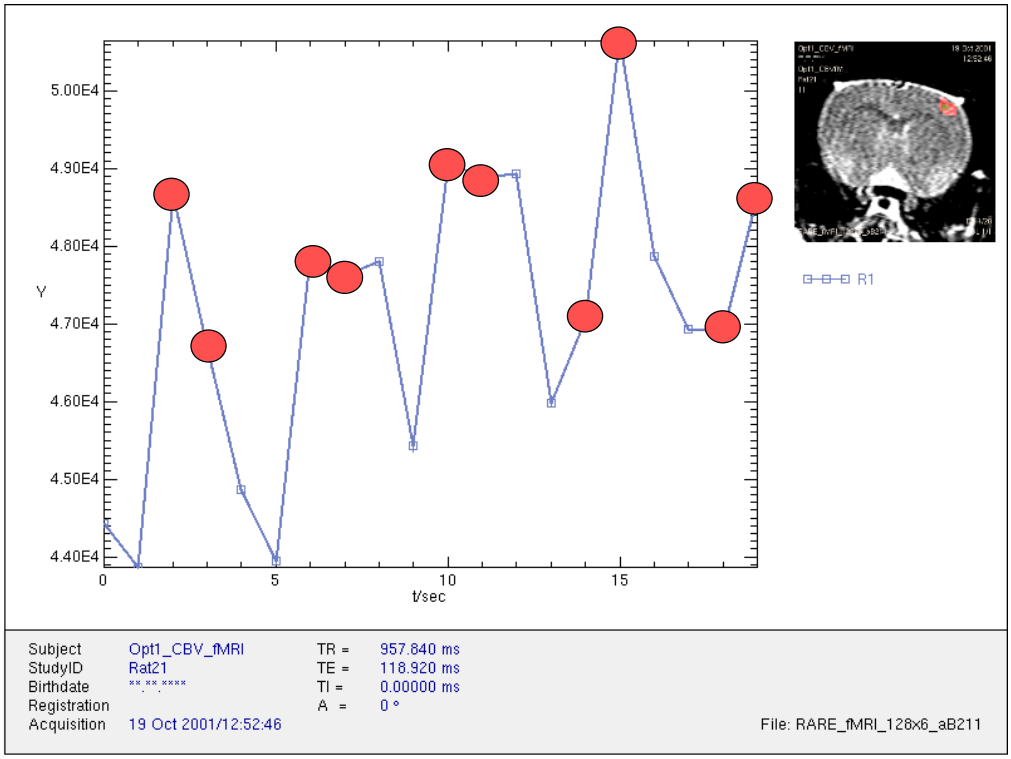
When the tool was started it takes the path of the scan in the active window as the default to store results. If one wants to create a new design, the following steps are required:

a. Select volumes/scans to be included in the analysis. This can be achieved either by selecting **File/Select scans** or by the "Add scans" button.
b. Change the name of the design (see B in Figure below). This name will be used for writing

the results to the database.

c. Select the folder, where the results should be stored (see A in Figure below).
d. Add factors to the design or change single values in the design matrix by selecting **Setup/Design matrix**.
e. Calculate the estimates and errors by selecting **Process/Solve**.

Example: Electrical stimulation of the forepaw of a rat; 20 volumes acquired in total; alternating order of two scans of rest and two of stimulation.



The temporal profile of the BOLD-response is shown below. Scans, which were acquired during stimulation are marked by red circles. Although the signal apparently increases during stimulation, a drift of the signal is visible, which can affect the analysis. This drift can be removed by different techniques.

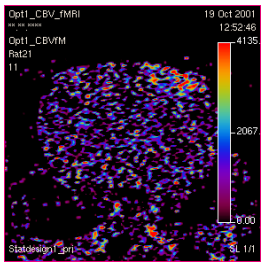
Proportional scaling: The value of each voxel will be divided by the global mean of the volume. All voxels, whose values are larger than the threshold, are considered for calculation of the global mean. This technique works well, if the signal drift is global. It should also be used if multiple sessions are analyzed together using a fixed effect assumption.

Drift correction: A series of cosine-functions are used to model the drift of individual voxels. This technique can be also in combination with proportional scaling.

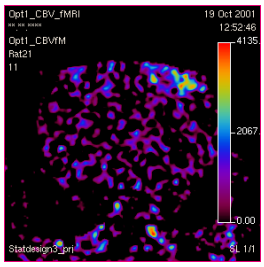
Using the global mean as factor: This technique is similar to proportional scaling. It again has the disadvantage that individual drifts cannot be eliminated.

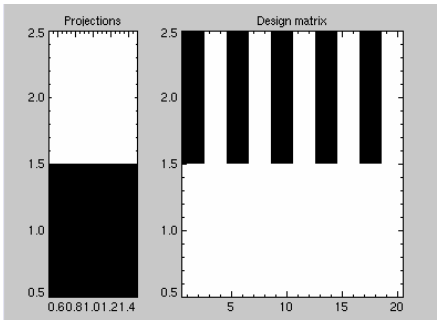
The result of the experiment can be affected by the definition and use of the confounding factors in the design matrix, filtering and scaling. Different approaches are shown below

Linear

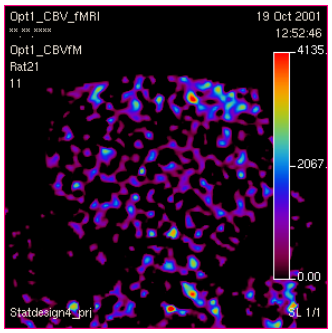


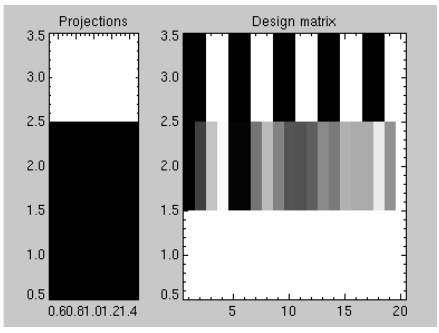
Linear+SpFilter



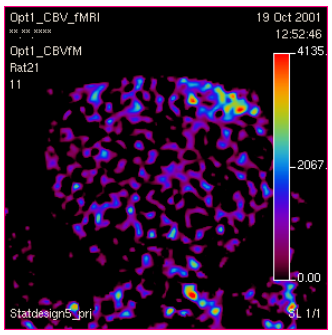


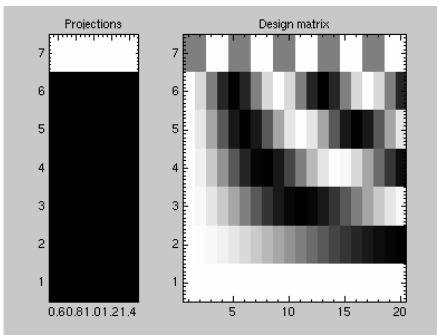
Linear+SpFilter+GlobalMean





Linear+SpFilter+DriftFilter





16 Filtering

16.1 Spatial and temporal filtering

16.1.1 Fourier-filtering

Fourier-filtering works in Fourier-space. The filter will be multiplied, point-by-point with the data.

$$S'(i) = F^{-1}\left[F\left[S\right] \cdot K\right]$$

Cut-off problems at the edges of the data can lead to oscillation-artifacts.

16.2 Baseline correction

The algorithm used for baseline correction takes the first and second derivative of a profile and derives the positions of local minima and maxima from these functions.

Modes of operation:

Mode 1: The 1st derivative of Y is calculated. Each point where the derivative is less then DerivThres is used as point for interpolation.

Mode 2: The 2nd derivative of Y is calculated. Each point where the magnitude of the 2nd derivative is less then Deriv2Thres is used as basepoint for interpolation.

Mode 3: This mode is a combination of Mode 1 and Mode 2. The second derivative of a valid point must be larger than a given threshold (maximums of peaks have to be excluded) and the absolute value of the first derivative must be less than a given threshold. Additionally, the minimum distance of two points is MinRasterDistance and points which are too close will be removed. Finally, points will be inserted for interpolation if the distance between two points is too large as defined by MaxRasterDistance (if MaxRasterDistance is not set not equal 0).

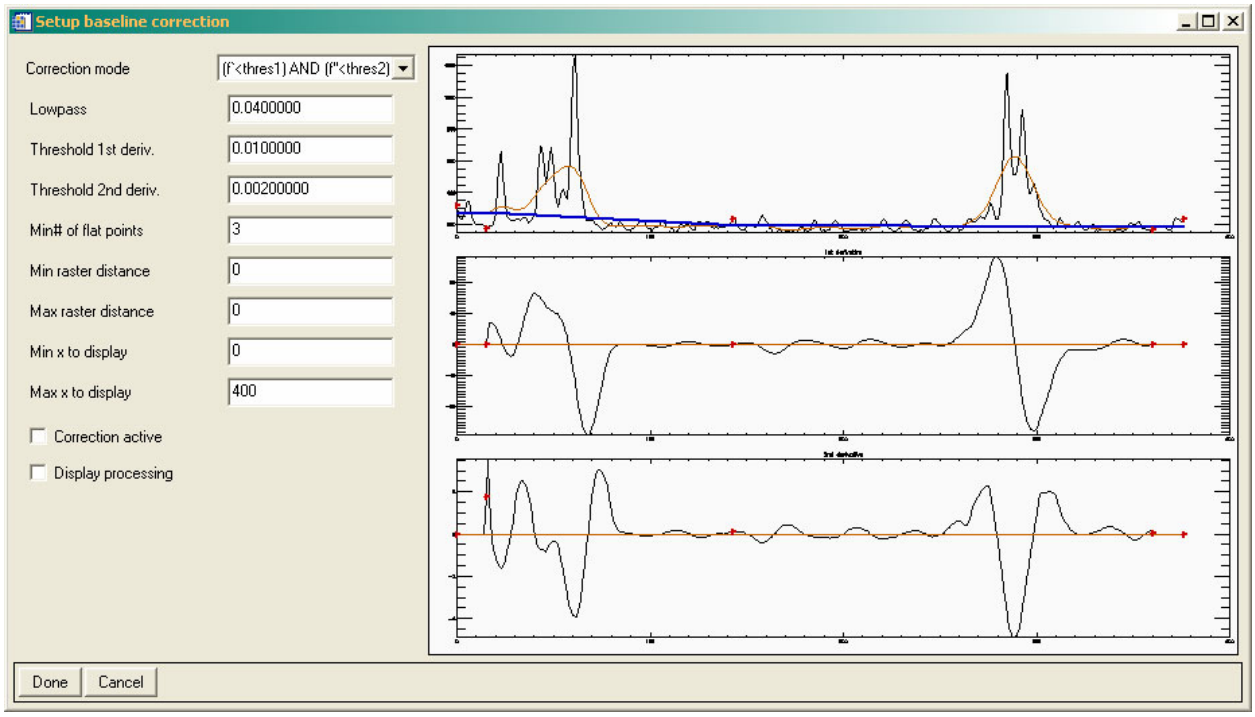
Options:

Low-pass filtering: If the cut-off frequency is set to 0, no filtering is performed. Otherwise, the parameter is the fraction of the Nyquist-frequency. Low-pass filtering eliminates spikes, which could be interpreted as minima and is esential for baseline correction.

Below an example is shown for a typical parameter setting:

MODE = 3

ACTIVE = 0
LOWPASS = 0.00200000
DERIVTHRES = 0.0200000
DERIV2THRES = 0.00200000
MINFLATPOINTS = 5
MAXRASTERDISTANCE = 0
DISPLAYFLAG = 0
DISPLAYMIN = 0
DISPLAYMAX = 9517
OFFSET = 0



17 Programming and extending BioMAP

17.1 Importing data from different formats

Importfilter for sources not yet handled by BioMAP can be added by using the interface commands:

```
Pro ImportMyData, WinNo

File = dialog_pickfile()
Openr, unit, …..
Readu, unit, ImageData
Close, unit
Free_lun, unit

; Do something with the data…..

pLIB_MatrixSize, ImageData, xs,ys,zs,n

Y = fBMT_CreateMDIObject(dim =[xs,ys,zs,n], type=16)
*Y.Data =ImageData
pMDIO_SetMinMax, Y

pBMT_CopyScanToWindow, Y, -1, WinNo, /Center

end
```

17.2 Accessing data from windows

To access data from a window and to perform some calculations, one can use the following commands:

```
Y1=fWIN_GetMDIO(WinNo1)      ; Get first scan
Y2=fWIN_GetMDIO(WinNo2)      ; Get second scan
Y = fMDIO_Subtract(Y1,Y2)    ; Perform subtraction and copy the result to a third window.

pBMT_CopyScanToWindow, Y, -1, WinNo, /Center, /Remove
```

17.3 Accessing specific data from scans

All information on a scan is stored in tags of the MDIO-structure. Once the MDIO has been generated, individual tags can be retrieved and printed or processed.

MDIO.Parameter1 contains the parameter-values, which are assigned to each volume. It is comparable to the values on the x-axis. E.g. it could contain TEs, diffusion weights, masses, or others. Parameter1 is a pointer. Hence, its values must be retreived by a command like

X=*MDIO(N).Parameter1

One can also extract values of individual pixels by

V=(*MDIO(N).Data)(23,45,2,*)

This command will copy all values of the desired pixels along the 4th dimension to V.

17.4 Reading and writing data in ANALYZE format

The data must be stored in a MDIO, which can be created by

MyScan=fMDIO_Create(Type=4, dim=[128,128,64,100])

The type formats are the same as in analyze. The data can then be loaded to the scan by

*MyScan.Data=MyArray

MyArray should have the same size as defined above. Moreover, other Meta data can be set. E.g. MyScan.Vox=[0.3,0.3,2] (in mm)

This scan can be written to a file by

pASL_WriteScan, Filename, MyScan

It can be retrieved by

MyScan2=fASL_ReadScan(Filename)

For more information refer to the routine list.

18 Apendix

18.1 Known bugs

Installation

- You must copy biomap.sav to the folder /usr/local/biomap/bin, because the installation-check will search for the file in this folder and not in the version specific folder.

Data-manager

- An error message will appear, after the first project was created. It can be ignored. You will find the project in the list, by pressing the browse button.
- If errors occur during the initialization of the data-manager, a README file will be generated on the project level. This file should be erased manually.
- The subject name is not always updated correctly after editing the subject-parameters.

18.2 FAQ's

What does the option CPeak calculate in the program? Is it the largest value over all events of the CTC-curve in a voxel?

Yes, the concentration will be calculated and the maximum is detected for each voxel.

When using the PWI-tool, the intensity treshold (initially put on 100) is used to only concentrate on the voxels that have an intensity of over 100 (and doing so reduce the influence of background and other structures). But what is meant with an intensity of above 100? Is it that the voxel has an intensity of above 100 on EVERY time-point of the 4D data? Or is it the average intensity (averaged over all time-points) of the voxel that has to be above 100?

It is the intensity of the voxel in the baseline image.

If we calculate the CTC curve for a T1 weighted series we get a 4D mdio with a number of time-points that is lower then the number of time-points of the original T1 series. In our case the series has 100 time-points and the ctc has 63. For which timepoints of the original series is the CTC calculated?

Is that for all the timepoints between the start of the baseline to the cut-off time, or something like that?

The program removes all volumes, which were not acquired during steady state conditions

The ctc curve for a T1 weighted series is calculated from:

c(t) = ((s(t) - baseline) / baseline).
We would also like to have the difference between the maximal intensity and the baseline (for each voxel of the tumor). So we need the (s(t)-baseline) - part. Is there a way to have the exact baseline that u use in your calculations, so we can calculate this ourselves?

You can apply either volume subtraction (Tools: Calculation) or percent signal change (Tool: Calculation) to the concentration time curve to do this.

Example for a manual installation of BioMAP

As root:

```
lbionmr2:/usr/local # mount /cdrom
mount: block device /dev/cdrom is write-protected, mounting read-only

lbionmr2:/usr/local # ls /cdrom/install/
.  ..  bin  defaults  external  help  icons  intro2.tif  packages  temp
template

lbionmr2:/usr/local # mkdir biomap

lbionmr2:/usr/local # cp -r /cdrom/install/* biomap/
lbionmr2:/usr/local # chmod -R +w biomap
lbionmr2:/usr/local # cd biomap/

lbionmr2:/usr/local/biomap # cd defaults/
lbionmr2:/usr/local/biomap/defaults # ls
.    brainstimrc  filterrc   infrc        plotrc        uparsrc
..   bslrc        fmriexprc  mdiobjectrc  pwirc         winrc
Idl  design_v2rc  hist2drc   plot2rc      statdesignrc

lbionmr2:/usr/local/biomap/defaults # which xv
/usr/X11R6/bin/xv

lbionmr2:/usr/local/biomap # cd bin/
lbionmr2:/usr/local/biomap/bin # ls
.  ..  5.4  5.5  5.5a

lbionmr2:/usr/local/biomap/bin # cp 5.4/biomap.sav .

lbionmr2:/usr/local/biomap/bin # /usr/local/rsi/idl/bin/idl -rt=biomap.sav
IDL Version 5.4 (linux x86). (c) 2000, Research Systems, Inc.

% PBMT_READPARAMETER: Reading /root/.biomap/winrc from disk failed
% PBMT_READPARAMETER: Reading /root/.biomap/uparsrc from disk failed
% PBMT_READPARAMETER: Reading /root/.biomap/infrc from disk failed
% XMANAGER: The MODAL keyword to the XMANAGER procedure is obsolete. It is
superseded by the MODAL keyword to the
            WIDGET_BASE function.
% FBMT_CHECKLICENSE: No license file found in /license.dat
% BIOMAP: Host  is not licensed for BioMap
% BIOMAP: License for host  will expire in 0 days
base=39600.000
pwi=39916080.
fit=39916080.
plot=-600.00000
tools=-718.00000
impmed=4.7900088e+08
impsci=39600.000
stat=-718.00000
Please copy the license file to your local biomap distribution

lbionmr2:/usr/local/biomap/bin # mv license.dat ..
```

```
lbionmr2:/usr/local/biomap/bin # ls
.  ..  5.4  5.5  5.5a  biomap.sav
```

As user:

```
Directory: /home/rausch
/home/rausch> mkdir .biomap

/home/rausch> cp /usr/local/biomap/defaults/*rc .biomap/
/home/rausch> alias biomap "idl -rt=/usr/local/biomap/bin/biomap.sav"

/home/rausch> mkdir mydata
/home/rausch> cd .biomap/
Directory: /home/rausch/.biomap

rausch/.biomap> xedit uparsrc

rausch/.biomap> biomap

IDL Version 5.4 (linux x86). (c) 2000, Research Systems, Inc.

HOST: 00001cb5a234 FEATURE: base=39600.000 status = 1
HOST: 00001cb5a234 FEATURE: pwi=39916080. status = 1
HOST: 00001cb5a234 FEATURE: fit=39916080. status = 1
HOST: 00001cb5a234 FEATURE: plot=-600.00000 status = 1
HOST: 00001cb5a234 FEATURE: tools=-718.00000 status = 1
HOST: 00001cb5a234 FEATURE: impmed=4.7900088e+08 status = 1
HOST: 00001cb5a234 FEATURE: impsci=39600.000 status = 1
HOST: 00001cb5a234 FEATURE: stat=-718.00000 status = 1
% BIOMAP: License for host 00001cb5a234 will expire in 365 days
% PBMT_READPARAMETER: Reading /home/rausch/.biomap/datamanagerrc from disk
failed
% FASL_GETSCANS: No scans found in
% PWID_DISPLAYFILE: Error occured, exiting...OPENW: Filename argument must be
a scalar string: FILENAME.
% XMANAGER: The MODAL keyword to the XMANAGER procedure is obsolete. It is
superseded by the MODAL keyword to the
            WIDGET_BASE function.
% BIOMAP: Layout no possible
rausch/.biomap>
```