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Filtering vascular flow artifacts in fMRI

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Table of content

Introduction

The work described in this report has been achieved in Strasbourg between March and August 2009 and has been performed under the supervision of Daniel Gounot from the `Neuropsychologie et Perception' team of the LINC (Imaging and Cognitive Neurosciences Laboratory) and Nicolas Passat from the `Modèle, Image et Vision' team of the LSIIT (Image Sciences, Computer Sciences and Remote Sensing Laboratory).

The field of magnetic resonance imaging (MRI) has evolved since 1990s to enable the brain functional activity study; this is named the functional MRI (fMRI). The location of activated areas is determined by statistical analysis and is a function of the considered paradigm[1]. That determination is based on the BOLD effect (Blood Oxygen Level Dependent) induced by a local increase of the MRI signal. This variation is very low (around 1%). It is then essential to reduce noises contained in fMRI images such as patient movements, respiratory or cardiac noises. In addition, Dagli *et al.* [1] have demonstrated that the heartbeat in the vascular network induces changes in the fMRI signal.

The objective of this study is to determine the influence of brain vascularization in fMRI images, based on anatomical knowledge obtained by brain angiography atlases. This work introduces a first approach to vascular atlas used to improve the detection of brain activity. The first part of this work creates a cerebral vascular atlas with the required information, that is to say only the intracranial vessel network. The second part determines the influence of the vascular Nuclear Magnetic Resonance (NMR) signal in the activity detection. This second part is a new field and is complex because of the number of ways that can be used to determine the influence level. Last but not least, this works creates a toolbox which allows reducing systematically and repeatedly the noise caused by cardiac signals in the cerebral vascular network.

The magnetic resonance phenomenon and its linked applications are presented first, followed by the way to create a brain vascular atlas and its improvements. Then the different ways to study the influence of vascular signal in fMRI detection are described. A result analysis and the toolbox usage are proposed at the end.

[1] Set of tasks realized by the subject during the experiment.

1 Magnetic Resonance Imaging: functional and angiography

1.1 fMRI: BOLD effect and acquisition

The cells increase their consumption of oxygen during cerebral activity. The local response to this oxygen consumption is the increase of blood flow in these regions. Neuronal activity is expressed as a relative increase in oxyhemoglobin compared to deoxyhemglobin in the activated regions. The variation in deoxyhemoglobin concentration can be detected by MRI because of its paramagnetic effect. This is the BOLD effect principle.

The fMRI consists of acquiring a temporal set of images in preparation of a statistical analysis of the signal variations during the test. The fMRI active areas are obtained by comparing images taken during high brain activity with low brain activity ones (see Fig. 1.1).

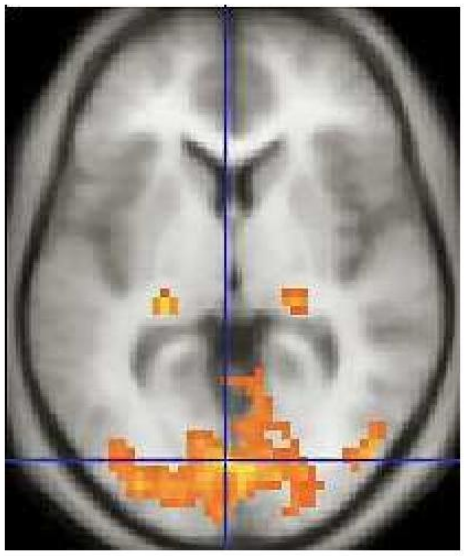
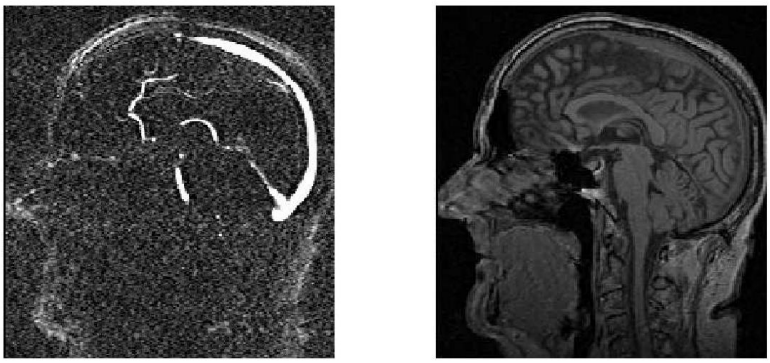


Figure 1.1 Visual activation map (in yellow) superposed to a morphological atlas

1.2 Magnetic Resonance Angiography

Magnetic Resonance Angiography (MRA) is a technique used to produce image of blood vessels to help make diagnosis and prepare for surgical operations; in particular neurosurgical ones. Those images are obtained by detection of blood flow.

The MRA used in this work is the Phase-Contrast MRA (PC-MRA) illustrated in Fig. 1.2. It is non-invasive and does not use a contrasting product. It is a specific acquisition sequence, where the phase of the MRI signal is modified in function of the blood velocity. It provides a morphological image perfectly registered to the vascular one.



(a) (b)

Figure 1.2 Phase contrast magnetic resonance angiography. Vascular image (a) and morphological image (b).

2 Vascular Atlases

Creation of brain vascular atlases is essential to determine the position of cerebral vessels in fMRI images.

2.1 Atlas creation

The vascular atlas is created from 68 PC-MRAs from different persons. The morphological images of the 68 PC-MRAs are modified to align to a reference image resulting in all brain structures having the same size and shape and being at the same place in the image. This step creates a registration field. The vascular images are then transformed using this registration field providing registered vascular images. Finally, all the registered vascular images are added on top of each other to generate a single image called the vascular atlas. A morphological atlas is created using the same method. This process is illustrated in Fig. 2.1 and detailed below.

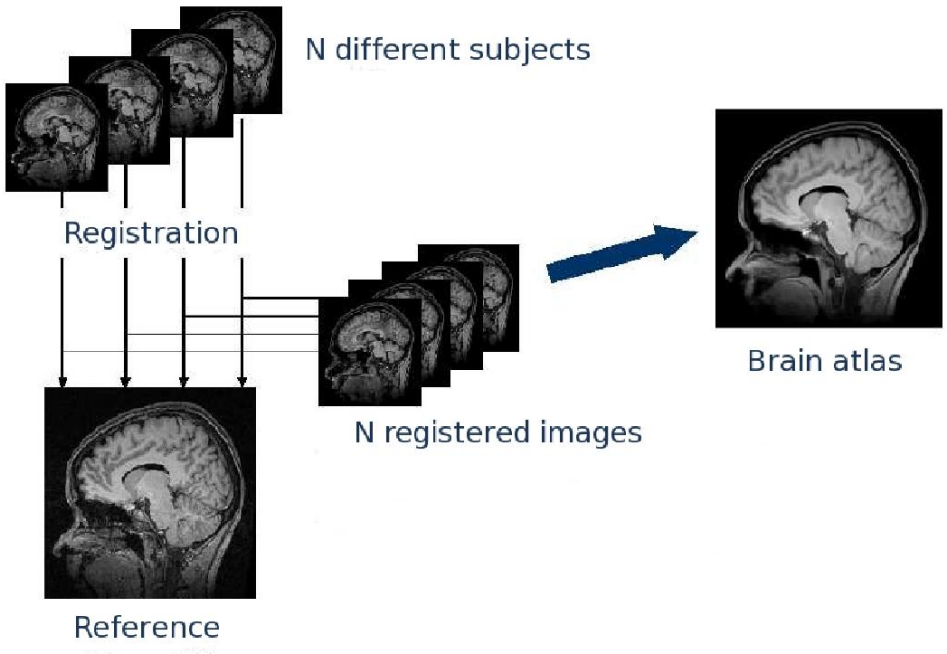
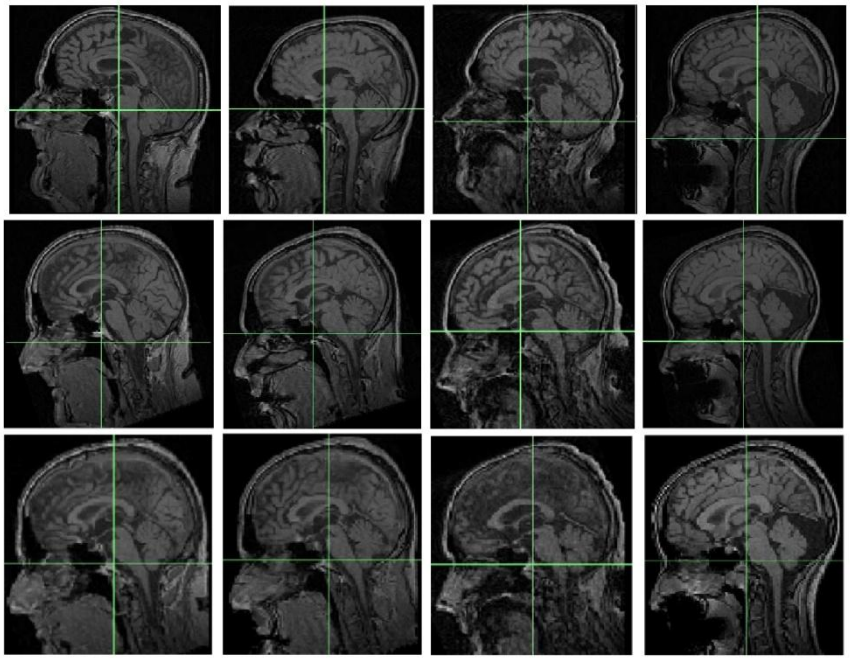


Figure 2.1 Steps to create a morphological atlas of the brain

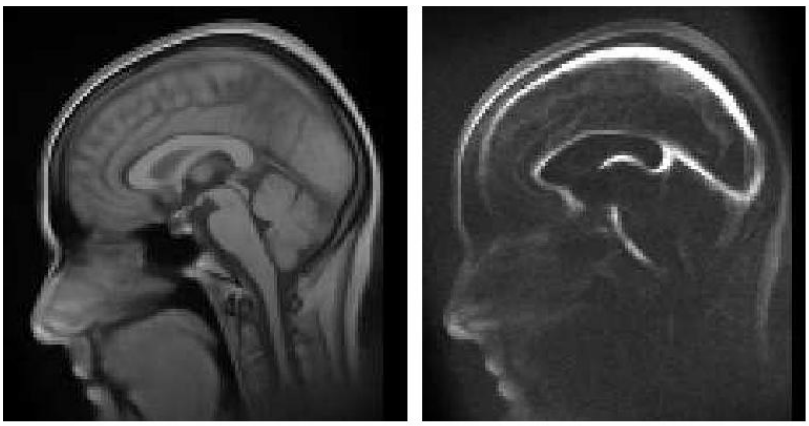
All brain structures differ from one person to another. The registration removes those differences. The method used is an affine registration followed by a non-rigid registration. The affine registration consists of rotations, translations and homotheties of the image. The non-rigid registration uses B-spline functions (see Fig. 2.2).



a

Figure 2.2 Images before registration (top). Images after affine registration (middle) and after non rigid registration (bottom). The images at the bottom are used to create the morphological atlas.

The resulting atlas (see Fig. 2.3) gives good results but has much information not useful like neck vessels or extra cranial vessels. Subsequently, some improvements are also applied to it.

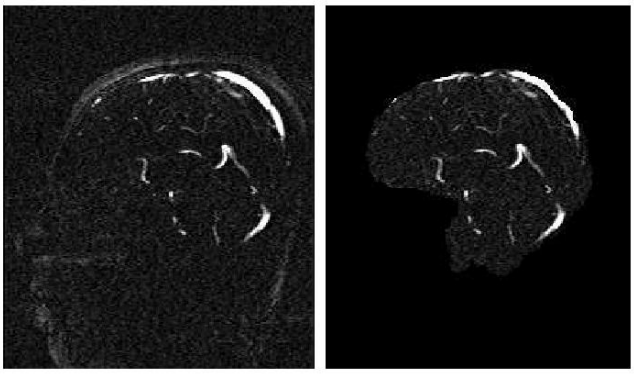


(a) (b)

Figure 2.3: (a) Morphological and (b) vascular cerebral atlas. The entire brain vascular network is presented in the vascular atlas.

2.2 Improvements to the vascular atlas

A brain mask is applied to all vascular images to keep only the intra cranial vessels information. This step reduces the size of images and also the computation time of the whole process. This mask, illustrated in Fig. 2.4, is obtained after a brain segmentation, which is realized from deformable models.



(a) (b)

Figure 2.4: PC-MRA before (a) and after (b) mask application.

Dagli *et al.* [1] demonstrated that only large brain vessels have an influence on the fMRI signal. Under these conditions, an atlas with small vessels is not interesting. Thus, a filter is applied to the vascular image to reduce the number of small vessels. It removes the connex components from the image (vessels represented with a small number of voxels[2]). The result is shown in Fig. 2.5 below.

[2] Single volume element of the image, VOlume piXEL.

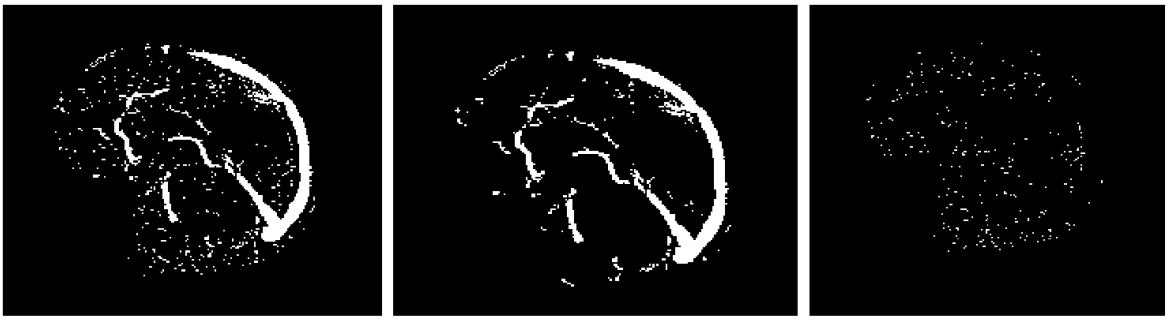


Figure 2.5: (a) vascular image before filtering and (b) after connex components filtering (20 voxels threshold). (c) Connex components with 20 voxels. It is the (b) image used to create the vascular atlas because the noise and the small vessels have been reduced.

The atlas reproduced in Fig. 2.6 is obtained after the improvements. Only the large intra cranial vessels are present. The intensity of voxels in the vascular atlas now illustrates the probable presence of vascular vessels.

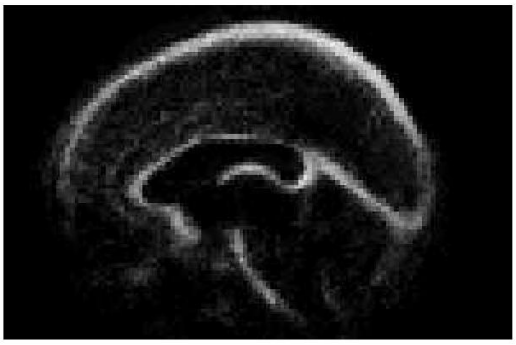


Figure 2.6: Atlas result after improvements.

2.3 Use of the atlas

The vascular atlas is used to create a new image to define the distance between voxels and vessels. The goal is to obtain an image where the voxel intensity represents its distance to the closest vessel. The image is created using the Danielson algorithm [4] (Fig. 2.7). When the intensity of the voxel is black, it means the voxel is close to one vessel. When the intensity is white, the voxel is far to a vessel.

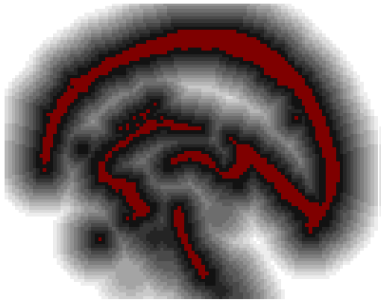


Figure 2.7: Distance map to vessels after the Danielson algorithm. The vascular network is represented in red.

The vascular atlas is also used to define the position of vessels in the fMRI images. The fMRI images are based on the Talairach coordinates system. In order to position the vascular voxel in fMRI images; the vascular atlas is transformed using a non-rigid registration. The vascular atlas is then separated into arterial atlas and venous atlas to separate the arterial and venous signals using anatomical knowledge. The new atlases are presented on Fig. 2.8.

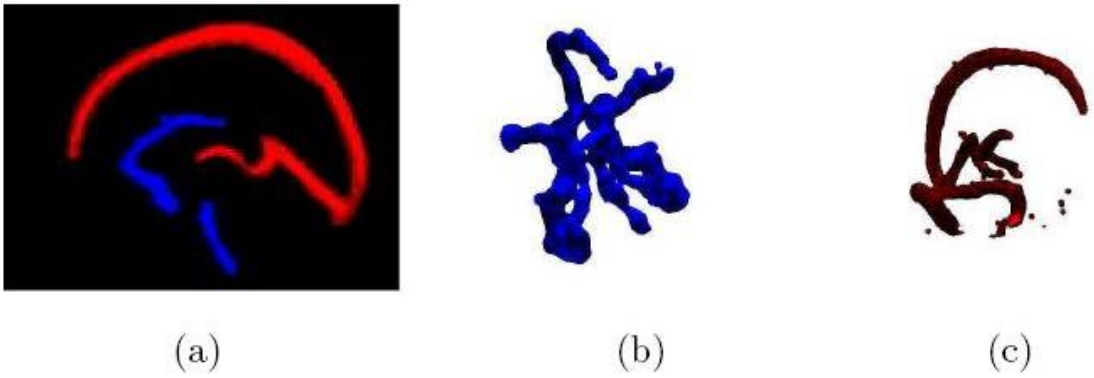


Figure 2.8: Cerebral vascular atlas, the venous network is visualized in red and the arterial network in blue. (a) is a 2D view of the atlas. (b) and (c) are 3D views of the arterial and venous atlas respectively.

3 Study of vascular fMRI signals

The fMRI study is based on a temporal analysis of MRI images implying a temporal analysis of the vascular voxels. The temporal signal of one voxel is called a `time course'. The time courses contain non-useful information and must be modified to be usable in determining their influences on the fMRI analysis. This modification is called preprocessing.

The modified time course is used to analyze its influence on the fMRI signal and to create a vascular model signal. The model signal is then used to reduce the vascular impact on the statistical detection of brain activity.

3.1 Preprocessing

The preprocessing consists of the following different possible actions:

- **Time course extraction:** fMRI images are all registered, which means a selected voxel is placed at the same place in all images. As a result, it is possible to know the NMR signal of one part of the brain during the paradigm and to extract its time course (see Fig. 3.1).

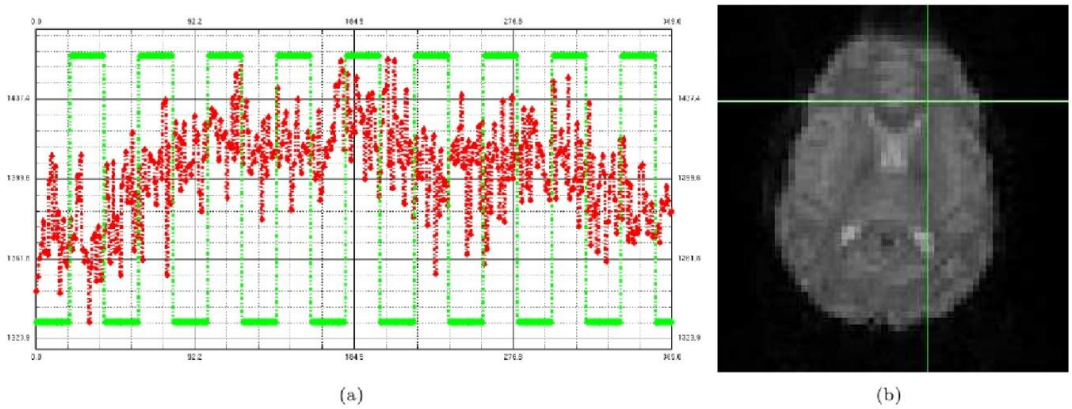


Figure 3.1: Extraction of the time course in red (a) of the voxel shown in (b). The time course corresponds to the intensity of the voxel in the difference MRI images of the fMRI series.

- **Baseline calculation (High-pass filter):** The baseline of a time course is its low frequency signal. The baseline corresponds to patient movements and must be removed. The method used to extract the baseline is the polynomial regression; the baseline being by a polynomial function (see Fig. 3.2), whose degree is variable. The useful signal corresponding to vascular activity is the difference between the real signal and the baseline.

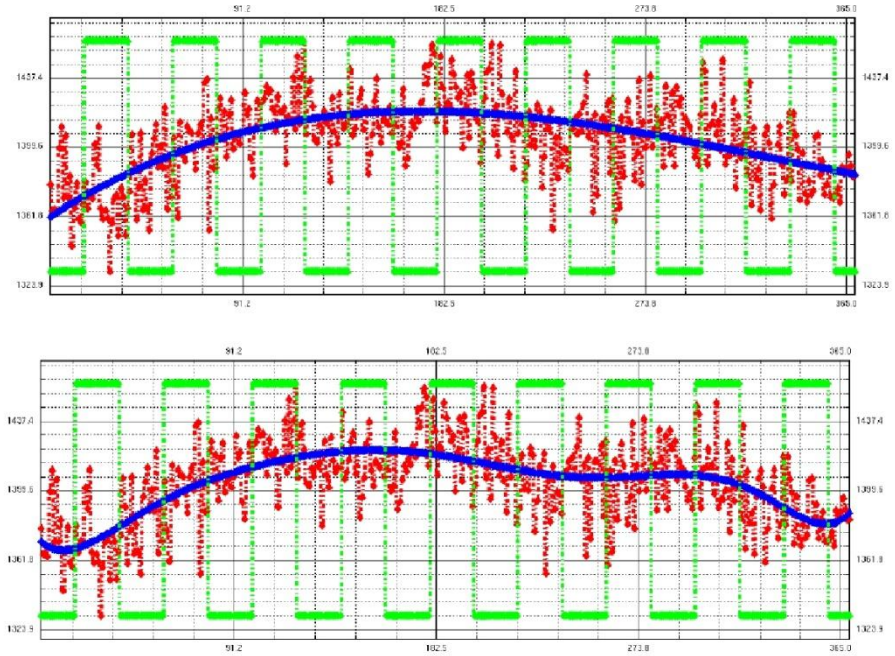


Figure 3.2: The time course is represented in red and the baseline in blue. At the top: baseline computed with a polynomial function with a degree 3. At the bottom, the degree of the polynomial function is 8. So, the degree used after is 8, because it is corresponding to the low frequencies of the vascular signals, which represent the movements of patient.

- **Temporal registration:** During the fMRI volume acquisition, the slices are taken in a non consecutive order to reduce interferences and maximize the NMR signal. Consequently the NMR signal is not continuous and the time courses should be temporally registered to use them in the right order.

Therefore, an oversampling and a temporal offset have to be applied to the set of the vascular time courses to align the vascular signals to their real time acquisition (see Fig. 3.3).

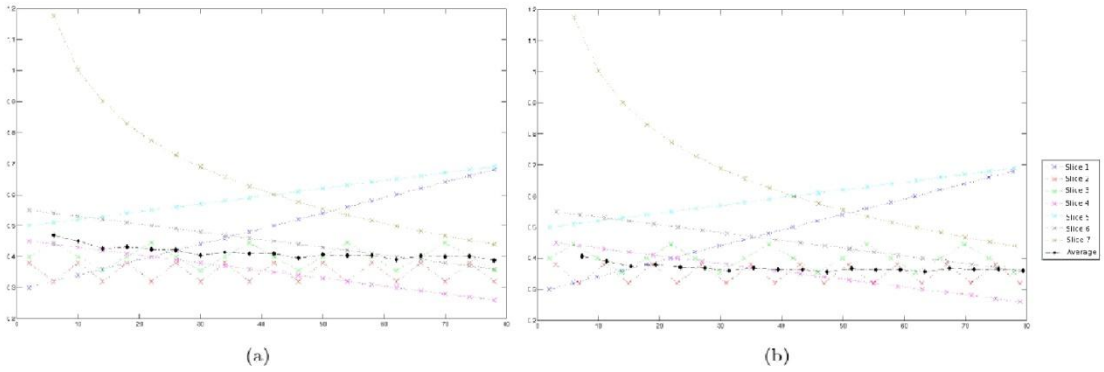


Figure 3.3: Data simulation. (a) Mean signal in black without temporal registration. (b) Mean signal (in black) with temporal registration. The error without registration is around 6%.

In addition the set of fMRI used in this work is acquired with a special procedure. The MRI acquisition is preceded by an ECG acquisition (see Fig. 3.4). Consequently the time courses are separated from one image to another by a break of 1.8 seconds. This break is removed by applying an offset.

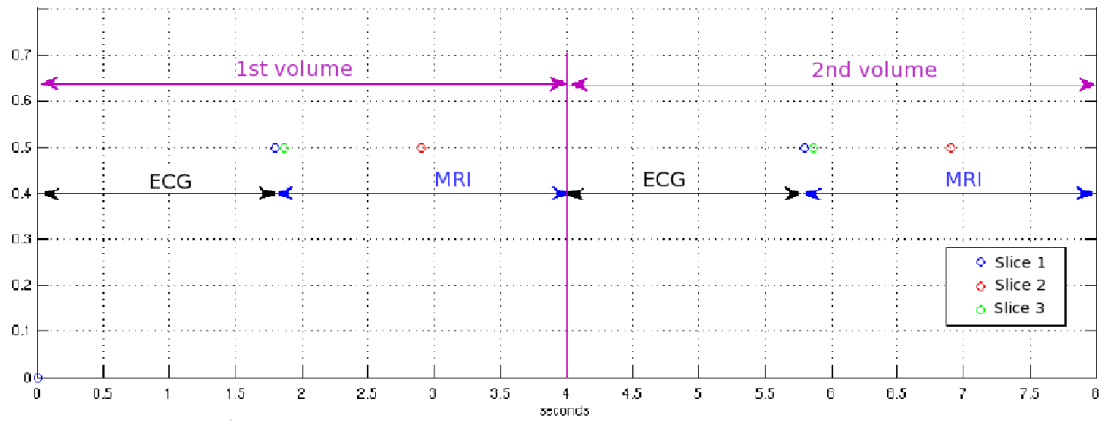


Figure 3.4: Temporal process of fMRI volumes acquisition. During the fMRI acquisition the ECG signals is also obtain. So, the acquisition of ECG signal introduces some temporal gap in the fMRI acquisition. So a temporal registration is needed.}}

- **PCA: Principal Component Analysis:** Once all signals are temporally registered, they can be compared using the Principal Component Analysis. The PCA is applied to reduce the volume of data (see Fig. 3.5), that is to say the number of temporal or frequency signals. The PCA allows selecting the right vascular information for the frequency and the temporal studies.

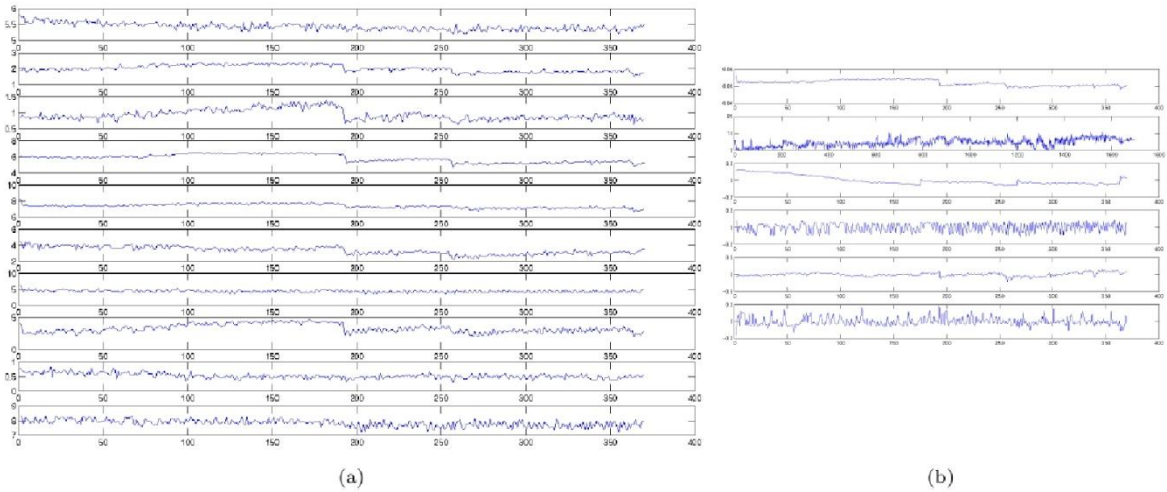


Figure 3.3: {(a) Representation of several arterial signals to be analyzed. (b) Results of the PCA with the 6 main signals. In this example, only one part of the PCA signals result corresponds to the vascular noise signals.

3.2 Frequency and temporal studies

The aim of the frequency study is to determine the frequency of the brain vascular network signals and to remove it. The steps used to complete this first analysis are illustrated in Fig. 3.6. The results of this pipeline are represented in Fig. 3.7

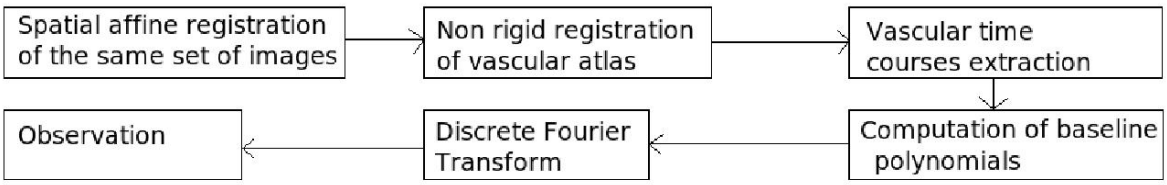


Figure 3.4: Schematization of the set of preprocessing and their order of applications use to the first frequency analysis.

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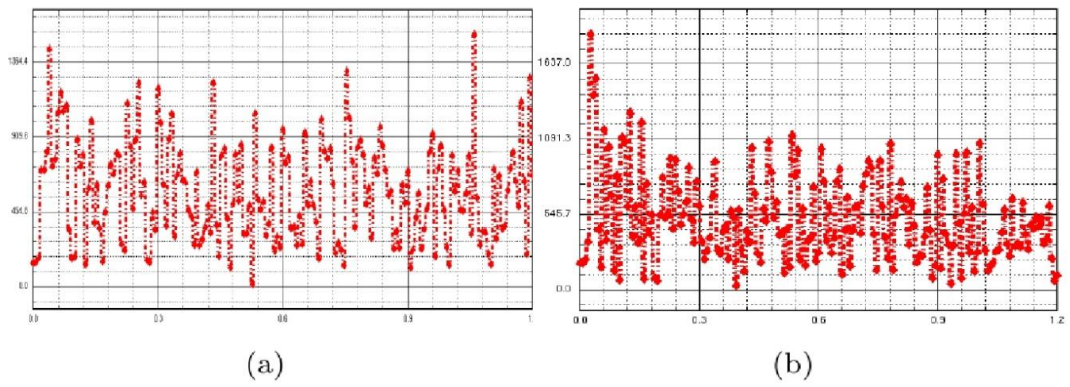

Figure 3.5: Frequency analysis of arterial signals (a) and venous signals (b). The signals is noisy, none vascular frequency is clearly visible.

The frequency signals are too different from one voxel to another one after the pipeline analysis as demonstrated on fig 3.7. They are not yet the expected results and it seems impossible to determine its frequency or a frequency set specific to the vascular signals. A frequency analysis of the averaged signals, arterial and venous is used as an alternative.

In this second frequency study, vascular signals are temporally corrected and all arterials and all venous signals are averaged respectively (see Fig. 3.8). The temporal correction is realized after the vascular voxels extraction. After the extraction, the arterial and venous signals are averaged to obtain a venous and an arterial signal. Then, a baseline polynomial function is computed and subtracted to the averaged time course. Finally, a discrete Fourier transformation is applied. The results are illustrated in Fig. 3.9.

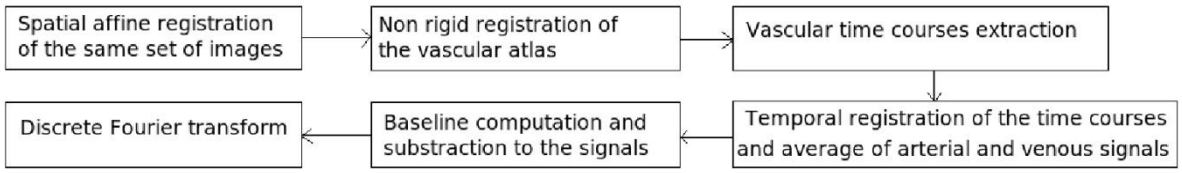

Figure 3.6: Schematization of the set of preprocessing and their order of applications use to the second frequency analysis.

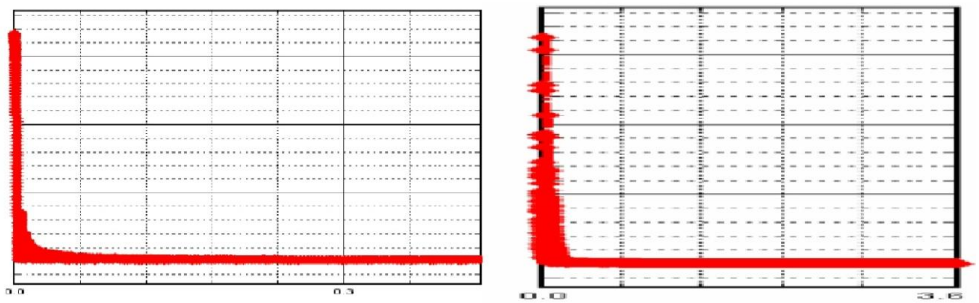

Figure 3.7: Frequency analysis of the average of arterial signals (a) and the average of venous signals (b) after temporal registration.

This is still not a usable result. Only the fMRI activity signal frequency has been detected. Therefore, the frequency analysis is discarded and a third analysis is carried out.

This third analysis is based on a temporal analysis of the vascular signals. It creates a new vascular signal model. The mean of the vascular signals is analyzed first. The mean vascular signals are obtained through the following process:

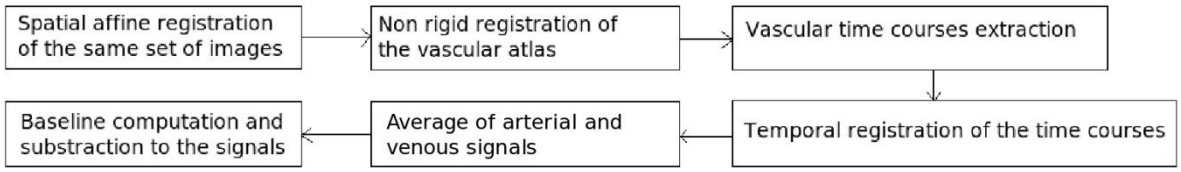

Figure 3.8: Schematization of the set of preprocessing and their order of applications.

This process is applied to the arterial and venous signals separately. The two mean signals are then entered into the SPM software (Statistical Parametric Mapping) to filter the vascular signals and improve the brain activity detection. It provides good results.

A fourth analysis based on a study of the frame of the signals is performed to try to improve the quality of the previous results. The Principal Component Analysis allows such analysis. The vascular signals are then modeled using a smaller number of signals (between 1 and 6 in this case) (see Fig. 3.12).

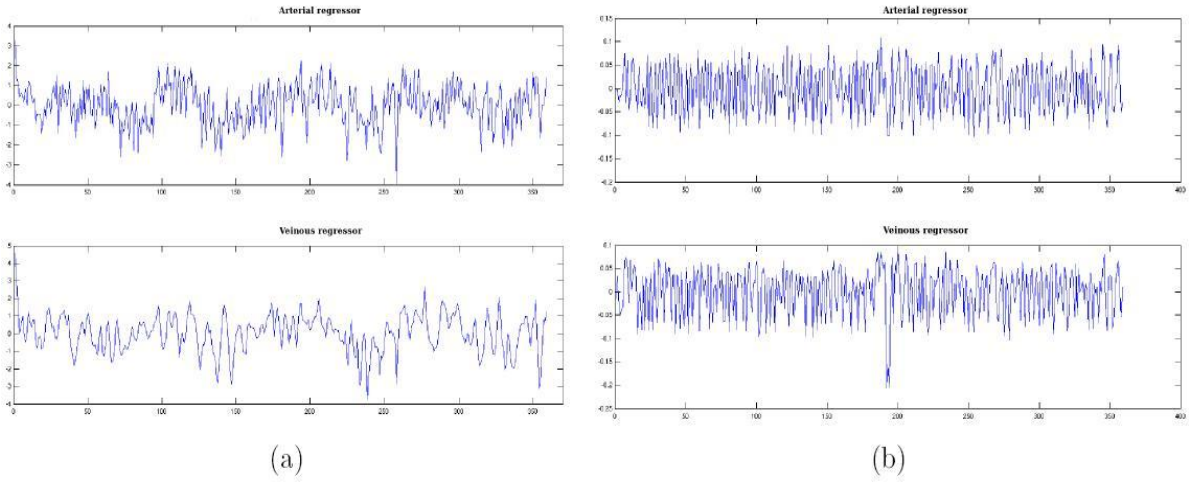

Figure 3.9: At the top, arterial signals. At the bottom, venous signal. These signals are used like a regressor in SPM method. (a) Signals resulting in the average. (b) PCA result signals.

This analysis provides improved results as shown in the comparison described in section 4.2 below.

4 Usage and comparison

4.1 Cerebro Vascular Physiology Toolbox

The analysis has demonstrated that models can be created to filter vascular signals and determine the brain activity from fMRI images. A toolbox is created to generate those models systematically and repeatedly from vascular atlas. This toolbox has been named Cerebro Vascular Physiology Toolbox (CVP toolbox). It is based on the temporal analysis of the vascular signals and the Statistical Parametric

Mapping used before. It modifies the SPM regressors to improve filtering and remove noises such as patient and eyes movements as well as vascular flow.

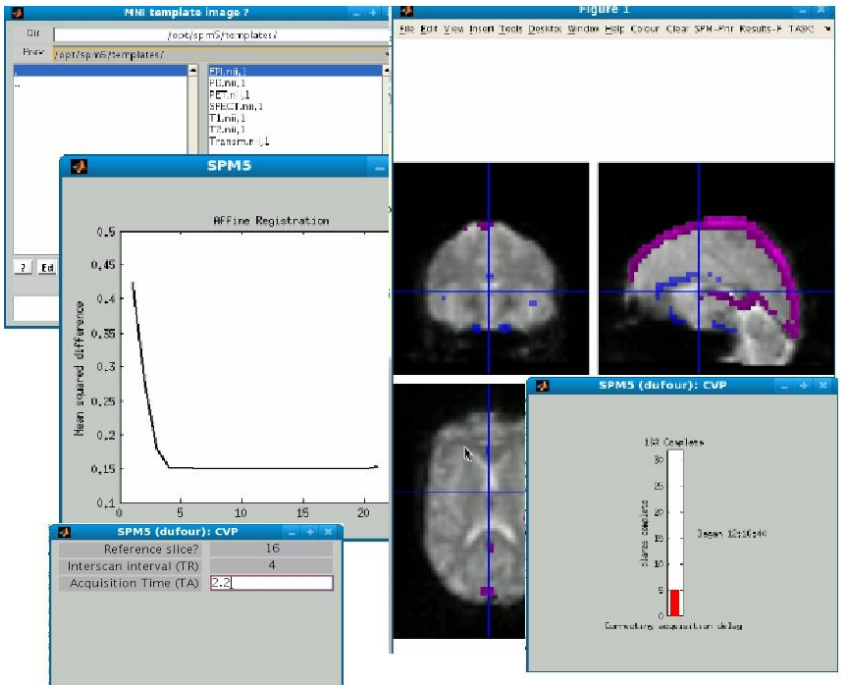

Figure 4.1: User interface of CVP toolbox.

4.2 Comparison of the best results from the analysis

The results of the filtering using the mean vascular signal analysis are compared with the PCA analysis. The PCA analysis has been conducted with 3 different sets of regressors: 2, 8 to12 and 12 regressors. The fMRI images are collected from 8 different subjects. The activation probabilities of each voxel of each image are added to produce a relative scoring and compare each method. The higher the score is the better the results are. The histogram in Fig. 4.2 presents the scores. The first column on the left shows the raw data without filtering. The second one shows the results of the mean analysis and the 3 other columns the results of the PCA tests. The best results are obtained with the 12 regressors PCA analysis.

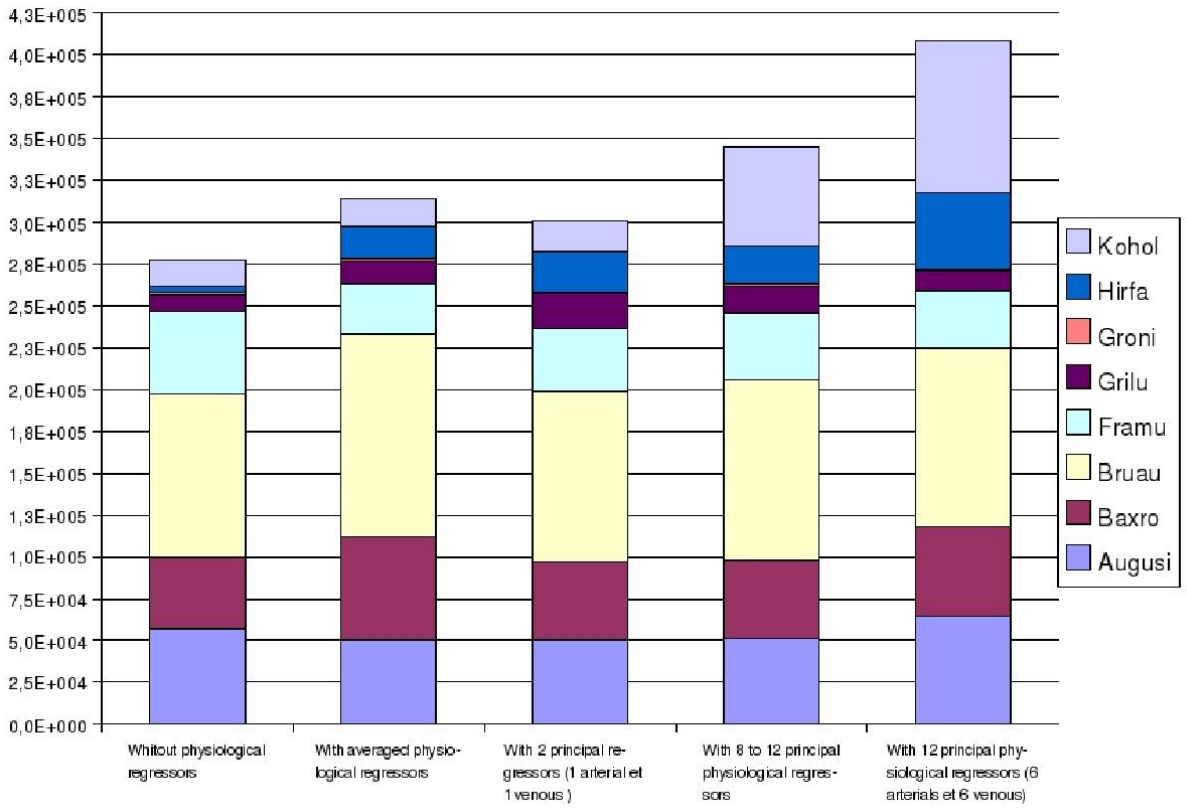

Figure 4.2: Result of the different methods used to reduce the vascular noise that fMRI images contained.

Conclusion

The results obtained in this study demonstrate a first approach to reduce vascular noise in fMRI images. This approach allows removing constraints during test such as respiratory and cardiac registering. The analysis shows improved scores for the eight subjects when the studied filtering is used. Nevertheless, even if the results are promising, the proposed method must be fully validated. It should be compared to other existing methods before being implemented.

The arterial and venous signals should also be analyzed separately to better understand their respective noise level. Likewise the analysis of the voxels closed to the vascular network should be another important step towards understanding the influence of brain vasculature in fMRI images.

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