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A Wavelet-based Method for the Metabolite Detection and Quantification in Proton Magnetic Resonance Spectroscopy

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Abstract

Purpose: In healthy tissue, metabolites are present in steady-state concentrations typical for that specific tissue. Metabolite concentrations may shift due to stress, functional disturbances, tumors or metabolic diseases. These changes are detectable with MRS, and provide valuable information for both diagnosis and therapeutic surveillance. Various methods have been developed to quantify the metabolite concentrations using methods ranging from the simple integration of spectral peak to complex algorithms.

Theory and Methods: The purpose of this work is to develop an analysis system for in vivo NMR spectroscopy for brain metabolites quantification based on continuous wavelet transforms without prior knowledge. Tests are done on both simulated and real in vivo MRS signals using spectroscopic data acquired in 16 healthy subjects (range 20-50) using 3T MR system.

Results: Results show that even with the presence of low SNRs and baseline, the proposed method is able to derive the parameters such as the frequencies, the amplitudes and the damping factors of metabolites directly from the raw data and without any beforehand preprocessing or prior knowledge.

Conclusion: The CWT analysis has shown to be accurate, robust and in agreement with the time domain fitting method AMARES for the quantification of short echo time in vivo MRS data.

Keywords: Magnetic resonance spectroscopy (MRS), signal processing, continuous wavelet transforms, quantification, peak detection.

Introduction

Nowadays, Magnetic Resonance Spectroscopy is a non-invasive diagnostic test commonly used in medicine for measuring the biochemical changes in the brain, precisely in localizing tumors and consequently helping clinicians to detect tissue changes in stroke and epilepsy and to optimize the appropriate treatment. The first in vivo MRS was applied on Phosphorus, 31P, but now many other nuclei are detected by this modality such as Proton, 1H, Carbon, 13C, Fluorine, 19F, Sodium, 23Na and others, however 1H MRS predominates because of the high natural abundance of protons in human body, and also due to the high number of information contained in 1H MRS spectrum [12].

There are different metabolites, or products of metabolism, that can be measured to differentiate between tumor types: Amino Acids, Lipid, Lactate, Alanine, N-acetyl aspartate, Choline, Creatinine, Myoionisotol.

In order to use the MRS tool in clinical environment, a reliable quantization method is fundamental. Unfortunately, in vivo studies of MRS has a number of drawbacks such as low Signal to Noise Ratio (SNR) due to the weak concentrations of the detected metabolites, poor homogeneity of the magnetic fields, macromolecular baseline and many other imperfections which make it very difficult to achieve accurate measurements [8].

The choice of an appropriate quantification method is crucial to estimate the intrinsic parameters of the signals and convert them into biochemical quantities. In fact the quantification methods can be divided into three main categories: time-domain methods, frequency-domain methods [19, 14] and time-frequency domain methods [25]. In the time domain, the quantification methods can be classified into two main categories: iterative and non-iterative methods [18]. The iterative approaches, such as the NLLS (Non-linear least square) methods, use the local or global optimization to reduce the difference between the model function and the MRS data. These methods allow the inclusion of prior knowledge such as the frequencies, the damping factors and the phases of certain metabolites. VARPRO (VARiable PROjection) is one of these time-domain methodologies [27] which in turn was improved by AMARES (Advanced Method for Accurate, Robust and Efficient Spectral) [28, 15]. This latter allows the inclusion of more prior knowledge, extracted either from phantoms or in vitro data, in order to enhance the efficiency and the overall accuracy. AMARES performs fitting of Lorentzian, Gaussian or Voigt models to the signal [26]. This method is supposed to give good results for a spectrum where the peaks are well separated. However if the spectrum is corrupted with noise and the nuisance peaks have large amplitude or are close to the metabolic peaks, this method will fail [9]. Other iterative methods exists, they rely on a metabolic basis set [21] for example the AQSES (Accurate Quantitation of Short Echo time domain Signals) [17] or QUEST (QUantum ESTimation). On the other hand, the non-iterative methods use either the linear prediction principle or the state space theory to derive the amplitudes of the metabolites present in the MRS spectrum [3].

In the frequency domain, the quantification of metabolites can be also divided into two classes: the non-interactive methods which are based on the integration of areas under the peaks of interest; these tools allow good quantification when the peaks in the spectrum are well separated, however this is not the case in the in vivo studies. Therefore, in the frequency domain, the interactive methods which use the nonlinear least square fitting approach are more used [20]. Many frequency domain fitting algorithm exist, such as the LC-Model, which also allow the inclusion of prior knowledge [11, 6].

All the time domain and frequency domain methods require lots of preprocessing steps and strong prior knowledge to provide good quantification of the metabolites and many of them are user dependent. Therefore the main goal of this work is to develop an automatic analysis system for in vivo MRS based on continuous wavelet transform allowing good quantification of the metabolites and operating directly on the raw data without any preprocessing beforehand or user interaction. This method is divided into two main parts: peak detection and quantification. To evaluate its performance both simulated and real MRS signals were used. Note that this tool is totally automatic and does not require any prior knowledge.

The paper is organized as follows. In the next section, the proposed automatic peak detection algorithm is introduced along with the mathematics behind the Continuous Wavelet transform used for MRS quantification and the result obtained for some simulated MRS signals used to evaluate the robustness of this method in different conditions. In the following section, the results for in vivo MRS signals are presented and discussed. These tests were conducted in order to validate the proposed algorithm. Finally the main conclusion and the perspectives were formulated.

Theory

Time-Frequency Methods

Methods based on the time-frequency domain have been developed for analyzing MRS signals and present some advantages over the previous mentioned methods. These techniques are based either on the WT (Wavelet Transform) or on the STFT (short time Fourier transform); both will give a time-frequency representation of the FID signal [24]. A number of methods based on wavelet transform have been suggested for MRS quantification by different authors; Continuous wavelet transform (CWT) have been proposed by [1, 25] and discrete wavelet transform (DWT) such as the wavelet packet decomposition has been proposed by [13]. Nevertheless the DWT is not well adjusted to the underling physics of MRS, using it will lead to some difficulties. The principle of the discrete wavelet transform computation is indeed based on downsampling and upsampling operators in a filter bank. This operators do not allow to the transform to be translation-invariant [22].

While the CWT is primarily a tool for analysis and feature determination, the DWT is the preferred technique for data compression and signal synthesis. Since the applications in NMR spectroscopy consist mainly in detecting particular features in the spectra, the CWT will be in

general better adapted than the DWT [5, 2].

Wavelets Principles

A wavelet is a normalized function $\psi \in L^2(\mathbb{R})$ with a null mean. A family of time-frequency elements can be obtained by dilating with a factor a and by translating the wavelet with a factor τ:

$$\psi_{a,\tau}(t) = \frac{1}{\sqrt{a}}\psi\left(\frac{t-\tau}{a}\right) \tag{1}$$

The wavelet coefficient $W_s(a,\tau)$ of $s \in L^2(\mathbb{R})$ at time a and scale τ is obtained by projecting the signal s onto the family $\{\psi_{a,\tau}(t)\}$ of functions obtained by dilatation of a and by translation of τ of the mother wavelet ψ :

$$W_s(a,\tau) = \int_{\mathbb{R}} s(t)\psi^*_{a,\tau}(t)dt \tag{2}$$

The wavelet transform denoted in the Eq. 1 is equivalent to a filter process. And the obtained coefficients indicate the correlation between the signal and the selected mother wavelet. Several families of mother wavelets exist and each type has its own time-frequency structure.

Simulated MRS Signals

To assess the performance of the suggested method in both ideal and contaminated environment where noise and baseline are present, we used simulated MRS signals with a Lorentzian lineshape denoted by Eq. 3.

$$s(t) = Ae^{-Dt}e^{-i(\omega t+\phi)}, \tag{3}$$

where A is the amplitude, D the damping factor, ϕ and ω are the phase and the frequency of the signal respectively.

Methods

Theoretically, the spectrum of MRS is composed of pure Lorentzian profiles. Nevertheless, in real environment, the MRS spectrum might be corrupted by a wideband baseline signal generated by macromolecules and by the noise. Therefore the actual equation of the MRS signal containing one frequency component, in time domain, is represented by the following equation Eq. 4:

$$y(t) = s(t) + B(t) + \epsilon(t), \tag{4}$$

where $y(t)$ is the experimental MRS signal in time domain, $s(t)$ is the Lorentzian signal containing one frequency component, $B(t)$ is the modeled baseline and $\epsilon(t)$ is the added Noise.

The baseline is characterized by a wide range of frequency in the MRS spectrum caused by the contribution of the macromolecules and thus it is supposed to decay faster than the pure signal. It can be modeled using 50 Lorentzian profiles with random amplitudes and large damping factor or using the cubic spline interpolation.

MRS signals quality could be affected by several sources of noise, such as the body noise, the noise originating from the electronics of the receiver and the thermal noise created by the coils. The body noise, which is the result of electrolytes thermal variations inside the body, is considered as the main source of noise in MRS. This type of noise is usually characterized as being white, additive and Gaussian distributed [16].

Real in vivo MRS Signals

In order to validate the proposed algorithm, real in vivo signals are tested. 1H-MRS were performed on a sample of 16 healthy subjects (7 women, 9 men), their age was 32 years (range 20-50) for three different brain regions: Posterior Cerebral Cortex (CCP), Anterior Cerebral Cortex (CCA) and Striatum.

The MRS data considered in this project were acquired by a 3T whole-body system (Verio, Siemens, Erlangen, Germany) and were provided by the radiology department of CHU Poitiers (France). The MRS sequence was performed with a monovoxel short TE (TE: 35ms, TR: 1500ms) using a point-resolved single voxel spectroscopy (PRESS). A multiplanar reconstruction of 3D T1 volume was used to position the voxel in the region of interest. The sequence parameters were 156 signal averages, a number of samples of 1024, and a bandwidth of 1200 Hz. The voxel size was of 3.375 cm^3. The common measures usually done in MRS studies, such as automatic shimming and eddy-currents compensation, were carried out for these acquisitions. Note that this data type is ideal for comparing and validating the proposed algorithm. Quantification for MRS data was attempted for N-acetylaspartate (NAA), Creatine (Cr), Choline (Cho) and Myo-inositol (Myo).In this study we examined the ratio of these metabolite to compare at the real value.

Automatic Peak Detection

The frequencies of the different metabolites could be considered as prior knowledge, however, in order to make the quantification method more suitable for real MRS signals analysis, where the frequency of each peak could slightly drift from the theoretical one, an automatic peak detection algorithm was proposed.

The aim of this method is to identify the location of each peak, using the continuous wavelet transform. For peak detection, the mother wavelet needs to have the main characteristics of a peak which consists of:

- Approximate symmetry,
- One main positive peak.

So for this analysis, we picked the Mexican hat wavelet (or Ricker wavelet) as mother wavelet [7]. In fact the Mexican Hat is very suitable for edge detection, it is widely used to characterize the singularities of a signal and therefore it allows a geometric analysis. It is defined as the negative normalized second derivative of a Gaussian function.

The procedure of the peak detection is described as follow: First a continuous wavelet transform of the MRS spectrum is performed using the Mexican hat as mother wavelet and well-adapted scales to detect the peaks of interests then the scalogram is constructed and for every indices column the sum of the coefficients is calculated. The obtained values are used to build a 1D function. After that a standard peak detection is performed on this 1D function with one threshold: the peak height.

To choose the threshold, we used the noise level calculation method proposed by AUTOPSY [10]; all the peaks with an amplitude below this level are ignored. The noise level calculation algorithm is described as follow: First, the 1D function is splitted into small windows and for each window a noise level value is computed. The length of each slice is usually 5 percent of the total length of the spectrum so that the standard deviation inside the window takes minimal value. After that we distinguish between two noise levels: the base noise level $\theta_b = \min(\theta_i)$, where θ_i is the standard deviation of slice i, and the additional noise levels, $\theta'_i = \sqrt{\theta_i^2 - \theta_b^2}$. The first exist in the entire spectrum and the latter can exist in each window. Next, the noise level is computed from the base noise level and the additional noise levels, and this value is considered the threshold

for the peak detection:

$$\Delta = \sqrt{\sum_{i=1}^{n} \theta_i'^2 + \theta_b^2}, \tag{5}$$

where n is the number of slices.

Note that, this peak detection algorithm, based on the CWT, could be used directly on the raw MRS signals without any preprocessing steps and without removing the baseline. In fact, the baseline is assumed to be slow changing and monotonic around the peak area, therefore it will be directly suppressed while computing the CWT coefficients using a symmetric and zero-mean wavelet function, such as the Mexican Hat wavelet [7]. To evaluate the robustness and the accuracy of this peak detection algorithm, a simulated signal of known frequency components was used.

The different steps of the proposed algorithm are summarized in the following Fig. 1 shows a simulated signal S(t) in the frequency domain, composed of 11 peaks with frequency values of 15, 250, 320, 380, 500, 643, 950, 1332, 2000, 3037 and 4000 rad/sec and contaminated with noise (low SNR=10) and baseline, along with its scalogram where the peaks are clearly observed.

By comparing the known frequencies of the 11 peaks and the identified one, as shown in Tab. 1, we can clearly see that the we were able to identified all the peak with an error range between 0.03 % and 23 %. Even with the high level of error (23 %), which occurs when the frequency of the peak is very low (at 15 rad/s), the algorithm seems to be applicable even when the MRS signals are buried in noise and contaminated with macromolecular baseline. Note that the statistics were done on 50 simulated MRS signals corrupted with random white Gaussian noise and baseline modeled using the cubic spline interpolation.

Quantification of a Lorentzian Signal

Identification of the Lorentzian signal by the Morlet wavelet

Among the different types of wavelet transforms, using the continuous wavelet transform will allow the estimation of signals amplitudes directly from the modulus and the phase of the WT [24] and thus no linear model will be required as in the discrete wavelet transform [4] . Next we will explain the mathematics behind the Morlet wavelet transform and how it is used to extract the different parameters of in vivo MRS signals [25].

Lets take a Lorentzian signal s(t), that models the time decay signal for one a specific metabolite

which has only one frequency:

$$s(t) = Ae^{-Dt}e^{-i(\omega_s t+\phi)}. \tag{6}$$

The 1D Fourier transform of the time signal is represented in Eq. 7 as

$$S(\omega) = 2\pi Ae^{i\phi}\delta\left(\omega - \omega_s + iD)\right), \tag{7}$$

where D is the damping factor, ϕ the phase of the signal, ω_s the frequency of the signal, A the amplitude of the signal and δ the Dirac delta function[1].

The Morlet wavelet denoted in Eq. 8 by $g_M(t)$:

$$g_M(t) = \frac{1}{2}\pi\sigma e^{-\frac{t^2}{2\sigma^2}}e^{i\omega_0 t}, \tag{8}$$

and

$$G_M(\omega) = e^{\frac{\sigma^2}{2}(\omega-\omega_0)^2} \tag{9}$$

where $g_M(t)$ is Morlet wavelet equation in time domain, $G_M(\omega)$ is Morlet wavelet equation in frequency domain, ω_0 its frequency and σ its width. Morlet is considered among the wavelets which are well localized in the frequency space, it is build form a windowed Fourier atom and is very adapted to analyse the local energy distribution along the time or signal indice. The wavelet transform of a signal s(t) is given by the following equation Eq. 10:

$$S(\tau, a) = \frac{1}{2\pi}\sqrt{a}\int_{\mathbb{R}} S(\omega)G_M^*(a\omega)e^{-i\omega\tau}d\omega, \tag{10}$$

where a is the dilation parameter that represents the frequency of the signal, $\tau \in \mathbb{R}$ is the translation parameter that specifies the time localization and G_M^* is the complex conjugate of $G_M(\omega)$. Suvichakorn et al prove in [25] that the modulus of the WT at a_r is defined by:

$$|S_{a_r}(\tau)| = \sqrt{a_r}e^{\left(\frac{\sigma a_r D}{\sqrt{2}}\right)^2}|s(\tau)|, \tag{11}$$

where $|s(\tau)| = Ae^{-D\tau}$. Note that the scale here is computed according to the frequency of the metabolite.

[1]The Dirac delta function is defined by: $\delta(x) = +\infty$ if $x = 0$ else $\delta(x) = 0$ and $\int_{\mathbb{R}}\delta(x)dx = 1$.

We so have:

$$\ln |S_{a_r}(\tau)| = \frac{1}{2} \ln a_r + \left(\frac{\sigma a_r D}{\sqrt{2}} \right)^2 + \ln A - D\tau. \tag{12}$$

Therefore the damping factor D is indicated by Eq. 13,

$$D = \frac{\partial}{\partial \tau} \ln |S_{a_r}(\tau)| \tag{13}$$

The derivative is computed as the differences between adjacent elements of $\ln |S_{a_r}(\tau)|$ along τ. After computing the damping factor D we can now obtain the amplitude A of the signal denoted by the equation Eq. 14, [25]:

$$A = |s(t)| \, e^{Dt} \tag{14}$$

Illustration of the method robustness

To work closer to real acquisitions, experiments were done on a simulated signal containing 4 metabolites; Creatine (Cr) which is composed of two peaks at w=1332 rad/s and w=643 rad/s, Lipid (Lip09) at w=3037 rad/s, Glycerophosphocholine (GPc) at w=320 rad/s and Glycine (Gly) at w=2246 rad/s and to evaluate the robustness of this method in noisy environment and in the presence of macromolecular baseline both white Gaussian noise with SNR=10 dB, which almost matches the SNR measured in vivo and baseline model were added to the signal. Fig. 2 show the original spectrum before and after adding the noise and the baseline.

Fig. 3 shows the extracted amplitude versus the actual values. The results show that using a simple CWT method allows good estimation of the amplitudes of different metabolites contained in a single MRS spectrum.

Results

In this section, CWT analysis is applied to the acquired in vivo MRS signals, and the amplitudes of the four metabolites; NAA, Creatine, Choline and Myo-inositol, are derived using the following algorithm:

- The described peak detection algorithm is applied directly on the raw data.
- The analyzed signal contains more than 20 metabolites, therefore only the frequencies corresponding to the peaks of interest are automatically selected from the values obtained by the peak detection algorithm.

- MWT analysis is performed using Lorentzian lineshape.
- The parameters are derived and averaged in time in order to obtain smoother results. Then the amplitude of each metabolite is estimated.
- The metabolites ratios are calculated.

The bar charts in Fig. 4 show the metabolite ratios for the 16 patients obtained using the CWT approach and the mean value of these metabolite ratios along with their normal values in these three brain regions [23]. Statistics are provided for comparison in Tab. 2.

Discussions

The values of the metabolite ratios extracted using the CWT analysis from the 16 healthy volunteers are very homogeneous and very closed to the normal values. Here the CWT analysis shows its ability to extract the physical parameters directly from the raw in vivo MRS data without any preprocessing steps even when contaminated with noise and macromolecular baseline.

In the Tab. 2 we observe that standard deviations of computed metabolite ratios in the CCP and the Striatum are low. The t-tests shows that the distributions of patient values are similar at the distributions of the normal values except for Naa/CR in the CCP.

In addition this method is totally automatic and does not require any user interaction therefore it is well suitable for clinical applications and it has many advantages over the other MRS quantification methods such as the AMARES. In fact an AMARES analysis of the same data for the CCA region, presented in Tab. 3 and Fig. 5, shows less homogeneity compared with the CWT approach. Note that strong prior knowledge is required by AMARES to obtain these ratios estimation along with numerous pre-processing steps. We also observe in Tab. 2 that the standard deviations of metabolite ratios in the CCA with our method is lower than those computed with AMARES presented in Tab. 3. Note that our method allows a good estimation for Naa/CR unlike AMARES which t-test rejects its estimation.

In addition, it is important to mention that these preprocessing steps used before the quantification might severely affect the analysis process, furthermore, removing the baseline beforehand and reducing the noise are unrecoverable, therefore if one of the peaks of interest in the MRS spectrum was removed by these preprocessing tools, it can never be recuperated in the later analysis, during

the quantification.

In some cases, such as in the Striatum results for patient n°5, the ratios diverge severely from the normal values and this is normal because in this spectrum the peaks are buried in noise. Note that, all the quantification method will give similar results in this case and the noise level here is considered unacceptable. So even though the analysis using this method could be performed automatically, this doesnt assure good results for severely distorted MRS acquisitions, hence the examination of results by a qualified spectroscopist or radiologist is necessary before interpreting the metabolic ratios.

1 Conclusions

In this work, an automatic MRS analysis system based on the Continuous Wavelet Transform was proposed. This method starts with a peak detection algorithm that identifies the location of each peak in the MRS spectrum. After that, the amplitudes of the metabolites of interest are estimated and the ratios are computed. Note that to select the right mother wavelet, the Mean Square Error (MSE) was computed and based on the results, two different mother wavelets were considered, which gave the lowest values of the MSE: Mexican Hat for peak detection and Morlet for the quantification. According to the results, the CWT analysis has shown to be accurate, robust and in agreement with the time domain fitting method AMARES for the quantification of short echo time in vivo MRS data without any preprocessing beforehand or user interaction. As future work, we aim to compare this method to other existing methods such as Tarquin, AMARES, QUEST using data acquired from healthy patients and patients suffering from different pathologies and finally we aim to improve this method and make it suitable for Multivoxel studies. Moreover we propose introducing an adapted denoising method to increase the robustness of this method against the noise.

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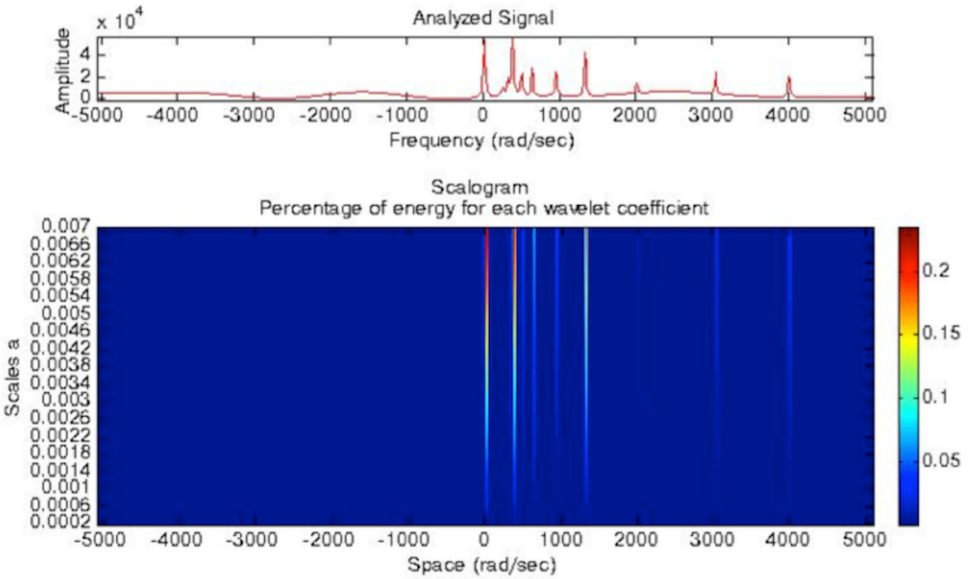
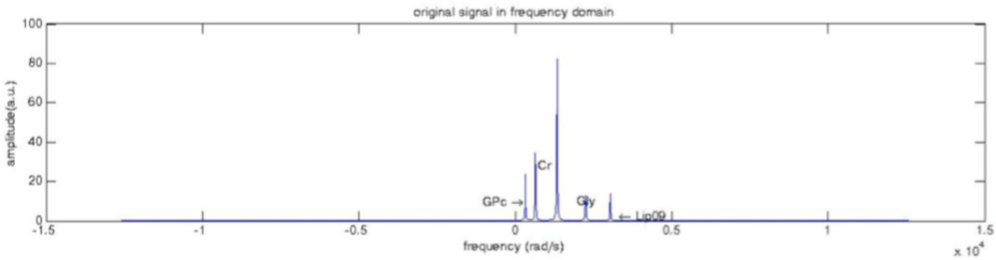
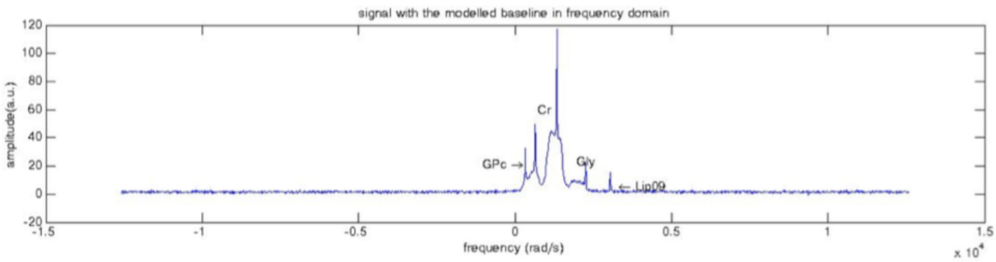


Figure 1:



(a)



(b)

Figure 2:

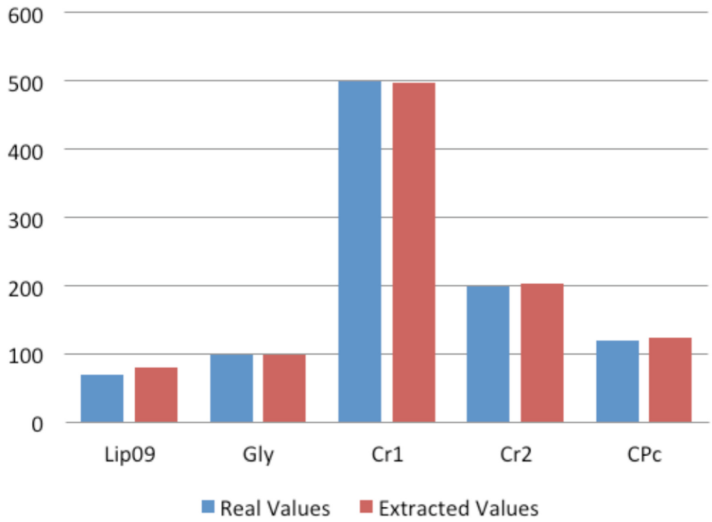
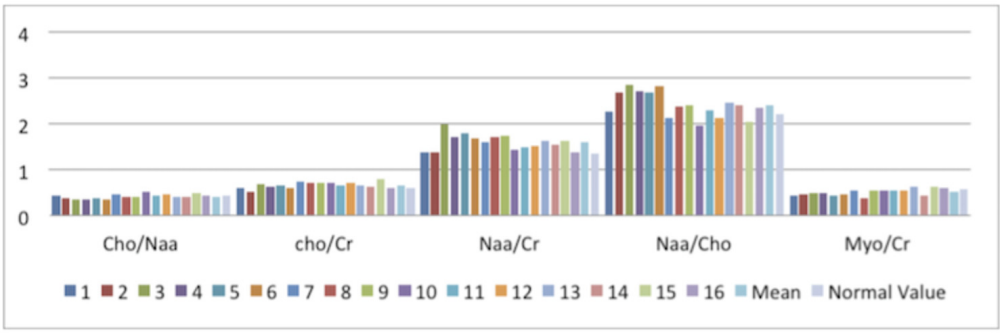
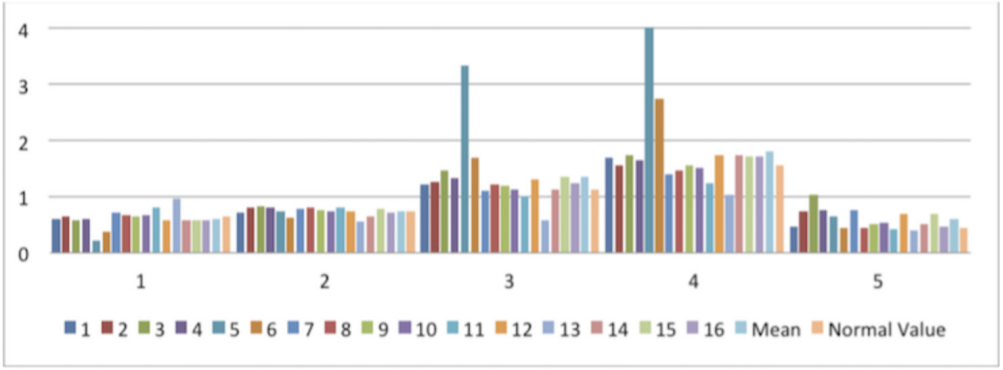


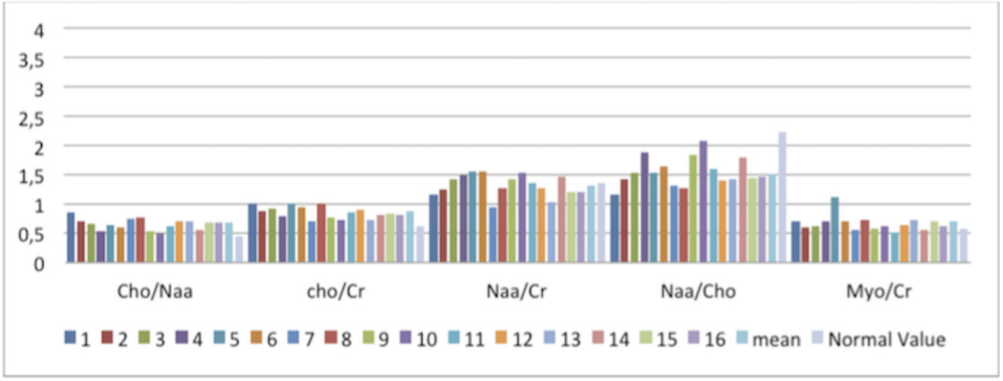
Figure 3:


4
3
2
1
0
Cho/Naa
cho/Cr
Naa/Cr
Naa/Cho
Myo/Cr
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 Mean Normal Value

(a)


4
3
2
1
0
1
2
3
4
5
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 Mean Normal Value

(b)


4
3,5
3
2,5
2
1,5
1
0,5
0
Cho/Naa
cho/Cr
Naa/Cr
Naa/Cho
Myo/Cr
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 mean Normal Value

(c)

Figure 4:

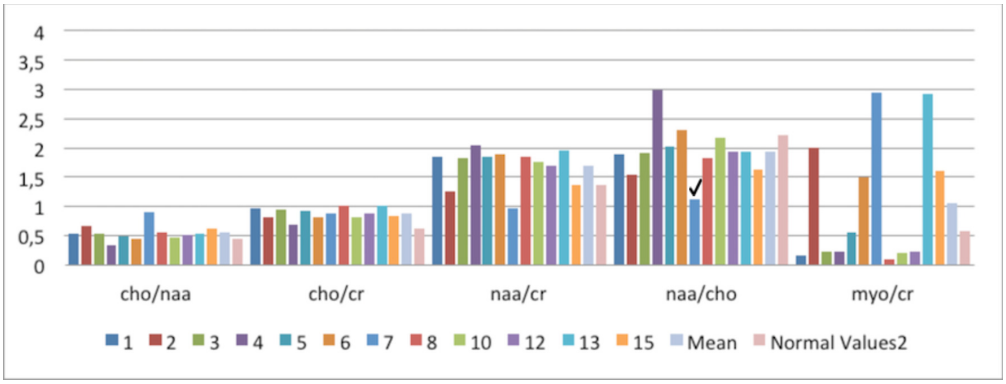

4
3,5
3
2,5
2
1,5
1
0,5
0
cho/naa
cho/cr
naa/cr
naa/cho
myo/cr
1
2
3
4
5
6
7
8
10
12
13
15
Mean
Normal Values2

Figure 5:

Table 1: Comparison between the real values of the frequencies of the peaks and the detected ones.

	Detected Values [2]	Real Values	Error (in %)
1	18.4462749	15	22.96
2	239.801573	250	4.08
3	313.586673	320	2.00
4	387.371772	380	1.94
5	510.346938	500	2.07
6	657.917137	643	2.32
7	953.057535	950	0.322
8	1346.57807	1332	2.10
9	2000.559998	2000	0.03
10	3043.881305	3037	0.27
11	4002.841648	4000	0.07

Table 2: Metabolite ratios for the 16 healthy subjects in the CCP, Striatum and CCA, obtained using the CWT algorithm.

	CCP				Striatum			
	Patients Values Mean ± SD	Normal Values Mean ± SD	T-test	Similarity 99%	Patients Values Mean ± SD	Normal Values Mean ± SD	T-test la	Similarity 99%
Cho/Naa	0.42 ± 0.05	0.45 ± 1.12	0.07694	True	0.61 ± 0.17	0.65 ± 1	0.1060	True
Cho/Cr	0.67 ± 0.07	0.61 ± 0.09	1.3989	True	0.74 ± 0.08	0.73 ± 0.06	0.4085	True
Naa/Cr	1.61 ± 0.17	1.36 ± 0.08	3.6180	False	1.35 ± 0.58	1.13 ± 0.06	1.0240	True
Naa/Cho	2.42 ± 0.28	2.23 ± 0.8	0.6118	True	1.82 ± 0.81	1.5	0.9084	True
Myo/Cr	0.51 ± 0.07	0.57 ± 0.05	1.7113	True	0.6 ± 0.18	0.44 ± 0.04	2.3646	True

	CCA			
	Patients Values Mean ± SD	Normal Values Mean ± SD	T-test	Similarity 99%
Cho/Naa	0.66 ± 0.10	0.45 ± 1.12	0.5078	True
Cho/Cr	0.86 ± 0.10	0.61 ± 0.09	5.1142	False
Naa/Cr	1.32 ± 0.18	1.36 ± 0.08	0.4892	True
Naa/Cho	1.55 ± 0.25	2.23 ± 0.8	2.2158	True
Myo/Cr	0.67 ± 0.14	0.57 ± 0.05	1.9387	True

Table 3: Metabolite ratios for the 16 healthy subjects in the CCA, obtained using the AMARES.

	Patient Values Mean ± SD	Normal Values Mean ± SD	T-test	Similarity 99%
Cho/Naa	0.54 ± 0.14	0.45 ± 1.12	0.2266	True
Cho/Cr	0.88 ± 0.1	0.61 ± 0.09	5.5856	False
Naa/Cr	1.69 ± 0.32	1.36 ± 0.08	2.7402	False
Naa/Cho	1.94 ± 0.47	2.23 ± 0.8	0.8634	True
Myo/Cr	1.05 ± 1.1	0.57 ± 0.05	1.2015	True

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