Quantification Method using the Morlet Wavelet for Magnetic Resonance Spectroscopic Signals with Macromolecular Contamination

Aimamorn Suvichakorn, Hélène Ratiney, Adriana Bucur, Sophie Cavassila and Jean-Pierre Antoine

***Abstract*— We study the Morlet wavelet transform on characterizing Magnetic Resonance Spectroscopic (MRS) signals acquired at short echo-time. These signals contain contributions from metabolites, water and a baseline which mainly originates from large molecules, known as macromolecules, and lipids. The baseline signal decays faster than the metabolite ones. Therefore, by making use of the time-scale representation of the wavelet, the two signals can be distinguished without any additional pre-processing. This is confirmed by the experimental results which show that the Morlet wavelet can correctly quantify the metabolite contributions even when a baseline is embedded in the MRS signals.**

I. INTRODUCTION

Magnetic Resonance Spectroscopy (MRS) is a unique non-invasive tool for detecting metabolites and quantifying their concentrations. The MRS signal comes from the interaction between atomic nuclei and radio-waves when an external static magnetic field is applied. The signal is made of several frequencies typical to the active nuclei and their chemical environments. The amplitude of these contributions in the time domain, i.e., the area in the frequency domain, depends on the amount of those nuclei, which can then relate to the concentration of the chemical substance [1]. Several quantification methods have been proposed either in the frequency domain or in the time domain (see [2], [3]). However, an MRS signal acquired at short echo-time usually contains contributions from metabolites, water and a 'baseline' which mainly originates from large molecules, known as macromolecules, and lipids. Therefore, one of the major obstructions to *in vivo* short echo-time MRS quantification is the baseline accommodation. As its shape and intensity are not known *a priori*, the baseline poses a problem if one wants to accurately quantify the overlapping signals from the metabolites; therefore, a good detection and quantification technique is required to characterize any substances present in an MRS signal.

In this paper, we present the advantage of analyzing the short echo-time MRS signals with the wavelet transform, which gives a time-scale representation of the considered signal. Analyzing the signal in the two domains simultaneously is beneficial to the MRS quantification with macromolecular contamination, where the two components have different decaying times due to the different size of the molecules. In addition, a small perturbation of a signal will result only in a small, local modification of the wavelet transform. Among several types of the wavelet transforms, the continuous wavelet transform technique [4], [5] can estimate the frequency and amplitude of the spectral lines directly from the phase and modulus of the wavelet transform and no linear model is needed, as in the techniques based on the discrete wavelet transform [6]. Therefore, we focus only on the continuous wavelet transform, with the Morlet wavelet, in particular.

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II. METHODOLOGY

A. Quantification

In order to characterize a signal, the wavelet-based techniques first detect the frequencies in MRS signals and then estimate the amplitude at each detected frequency.

The wavelet transform of a signal $s(t)$ with respect to a mother wavelet $g(t)$ is

$$S(\tau, a) = \frac{1}{2\pi}\sqrt{a}\int S(\omega)G^*(a\omega)e^{i\omega\tau}d\omega, \qquad (1)$$

where $S(\omega)$ is the Fourier transform of the signal, $a > 0$ is a dilation parameter, $\tau \in \Re$ is a translation parameter and $G^*(\omega)$ is the complex conjugate of the Fourier transform of $g(t)$. Given a Lorentzian signal $s(t)$, namely,

$$\begin{aligned} s(t) &= Ae^{-Dt}e^{i(\omega_s t+\phi)} \\ S(\omega) &= 2\pi Ae^{i\phi}\delta(\omega-(\omega_s+iD)), \end{aligned} \qquad (2)$$

where D and ϕ are the damping factor and the phase of the signal, the Morlet wavelet transform of $s(t)$ is

$$\begin{aligned} S(\tau, a) &= \sqrt{a}Ae^{i\phi}e^{-D\tau}e^{i\omega_s\tau}G_M^*(a(\omega_s+iD)) \\ &= s(\tau)G_M^*(a(\omega_s+iD)), \end{aligned} \qquad (3)$$

where

$$\begin{aligned} g_M(t) &= \frac{1}{2\pi\sigma}e^{-\frac{1}{2\sigma^2}t^2}e^{i\omega_0 t}+\epsilon \\ G_M(\omega) &= e^{-\frac{\sigma^2}{2}(\omega-\omega_0)^2}+\epsilon^*, \end{aligned} \qquad (4)$$

is the Morlet wavelet whose frequency and width are denoted by ω_0 and σ. The correction term ϵ is negligible when $\sigma\omega_0 \geqslant 5.5$, and will be omitted henceforth. It can be seen that the modulus of $S(\tau, a)$ is maximum, i.e., $\frac{\partial}{\partial a}S(\tau, a) \to 0$, when $\frac{\partial}{\partial a}G \to 0$.

Since $a \in \Re$ and, with the assumption that $\omega_s \gg D$, the maximum can be found at the scale $a_r = \omega_0/\omega_s$, which then gives

$$G^*(a_r(\omega_s + iD)) = \exp\left(\frac{\sigma a_r D}{\sqrt{2}}\right)^2, \tag{5}$$

and consequently

$$S_{a_r}(\tau) = \sqrt{a_r}\exp\left(\frac{\sigma a_r D}{\sqrt{2}}\right)^2 s(\tau), \tag{6}$$

is also identical to the signal $s(t)$ scaled by a coefficient depending on a still-unknown D. Next, consider the phase of the Morlet wavelet transform along the translation axis at the scale a_r,

$$\begin{aligned} \angle S_{a_r}(\tau) &= \omega_s \tau + \phi \\ \omega_s &= \frac{\partial}{\partial \tau}\angle S_{a_r}(\tau). \end{aligned} \tag{7}$$

That is, the instantaneous frequency at the scale a_r of the Morlet transform is ω_s. By (7), the phase ϕ can also be recovered, if needed. This method is also applicable to an n-frequency signal if its frequencies are *sufficiently* far away from each other that $G^*(a\omega)$ can treat each spectral line independently [7]. Whenever two frequencies are very close to each other (this also depends on the sampling frequency), increasing ω_0 can better localize and distinguish the overlapping frequencies. However, ω_0 should not be too high that the transform becomes noisy and unreliable. Next, consider the modulus of the wavelet transform at a_r,

$$\begin{aligned} |S_{a_r}(\tau)| &= \sqrt{a_r}\exp\left(\frac{\sigma a_r D}{\sqrt{2}}\right)^2 |s(\tau)| \\ \ln|S_{a_r}(\tau)| &= \frac{1}{2}\ln a + \left(\frac{\sigma a_r D}{\sqrt{2}}\right)^2 + \ln A - D\tau. \end{aligned}$$

That is,

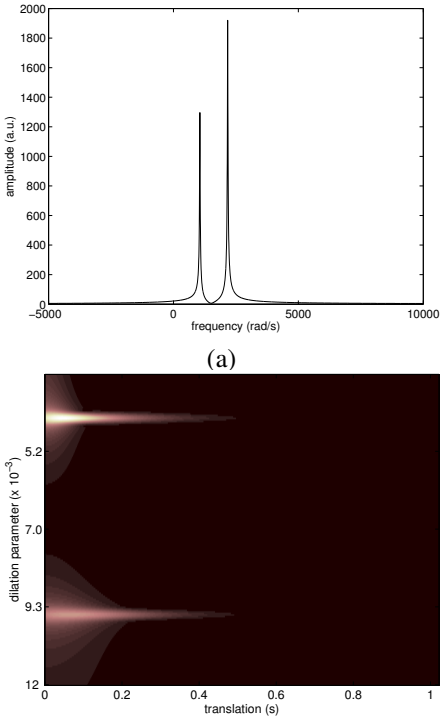
$$D = -\frac{\partial}{\partial \tau}\ln|S_{a_r}(\tau)|. \tag{8}$$

Knowing D can now lead to the estimation of the amplitude resonance A of the signal, i.e.,

$$A = |s(t)|e^{Dt}. \tag{9}$$

A simulated signal of creatine (Cr) at 4.7 Tesla, shown in Fig. 1, is used to illustrate the signal analysis by the Morlet wavelet. The instantaneous frequency of the Morlet wavelet transform converges to two frequencies as shown in Fig. 2 (a). It also shows that (7) works not only at $a_r = \omega_0/\omega_s$ but also for a wide range of a. The amplitudes of the two frequencies of the simulated Cr derived by (9) remain stationary for most of the acquisition time whereas the transient period occurs at both ends, as illustrated in Fig. 2 (b). This is possibly due to the boundary effect. The damping factor is 10.016 Hz for both frequencies.

The Morlet wavelet is the most frequently used in practice because of its simple numerical implementation and the vanishing of the third-order differentiation of its phase can also simplify the computation [5]. Note that (6) differs from the literature which approximates the wavelet transform by its Taylor series and omits the term D.



(a)

(b)

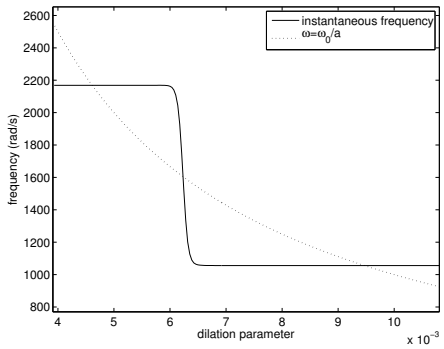
Fig. 1. (a) Frequency response of creatine at 4.7 Tesla and (b) its Morlet wavelet transform ($\omega_0 = 10$ rad/s, $\sigma = 1$)

B. Dealing with baseline

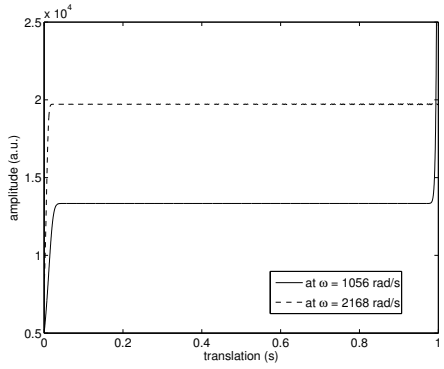
The baseline corresponds to large molecule contributions with broad pattern frequency response in the MRS spectrum. As a consequence, we modeled the baseline by cubic splines to study the performance of the wavelet transform. The modeled baseline has no effect on the instantaneous frequency derived from the wavelet transform, as shown in Fig. 3. In fact, Fig. 4 tells us that the baseline affects only the edge of the transform. Therefore, if the real baseline satisfies the assumption that it decays faster than the actual signals, it should still be possible to use the wavelet transform to derive the frequency and amplitude of a MRS signal without removing the baseline beforehand. Such an assumption has been widely used in spectroscopic signal processing [8], where several authors proposed truncation of time domain initial data points, which are believed to contain a major part of the baseline. However, some information of the metabolites could be lost and a strategy for properly selecting the number of data points is needed (see [9] for examples and further references).

III. EXPERIMENTS

In order to study the characteristics of the baseline by the Morlet wavelet, an *in vivo* macromolecule MRS signal was acquired on a horizontal 4.7T Biospec system (BRUKER BioSpin MRI, Germany).

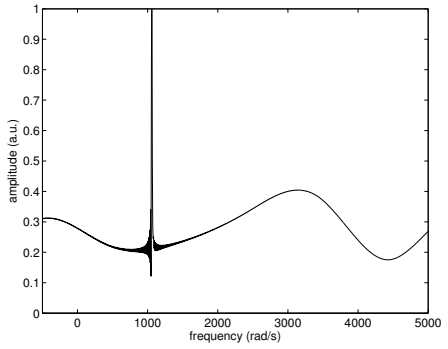


(a)

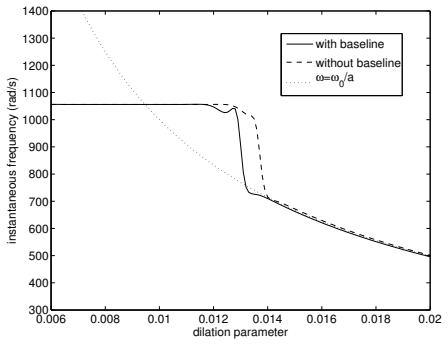


(b)

Fig. 2. (a) Frequencies and (b) amplitudes of the simulated signal creatine in Fig. 1. The amplitudes are in arbitrary unit (a.u.).



(a)



(b)

Fig. 3. (a) The Fourier transform of a 1056-rad/s signal with baseline and its instantaneous frequency in (b). The baseline is modeled by a cubic spline. ($\omega_0 = 10$ rad/s, $\sigma = 1$)

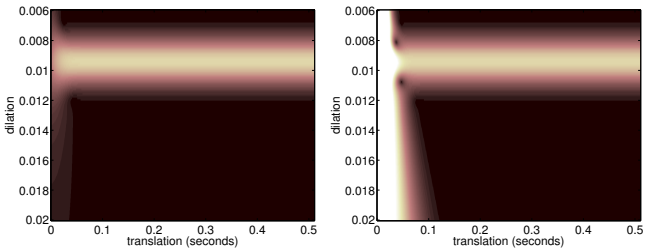


Fig. 4. The magnitude of the wavelet transform of a pure 1056-rad/s signal (left) and the signal with baseline (right).

To acquire a macromolecule-only signal, the acquisition sequence plays on the differences in spin-lattice relaxation times (T1) between low molecular weight metabolites and macromolecules, which are relatively immobile and have shorter T1 than those of metabolites. That is, by optimizing the inversion time (IT), which represents the delay between the inversion pulse and the first pulse of the PRESS sequence, the metabolites are nullified while the others are maintained [10], [11].

As seen in Fig. 5, the metabolite-nullified signal from a volume-of-interest (VOI) centered in the hippocampus of a healthy mouse[1] was a combination of residual water, baseline and noise. Compared to the simulated signal of creatine, the signal decays much faster, making it suitable to use the Morlet wavelet to analyze the MRS signal as described earlier. However, the residual water is large and could cover other details. Here, the Morlet wavelet transform can also be used to magnify and unveil these details as follows. By its time-scale representation, an integral of the scaled wavelet coefficients in both time and scale[2] is proportional to the energy of the signal. That is,

$$\int \frac{1}{\sqrt{a}} \int |S(a,\tau)|^2 d\tau d(\ln a)$$

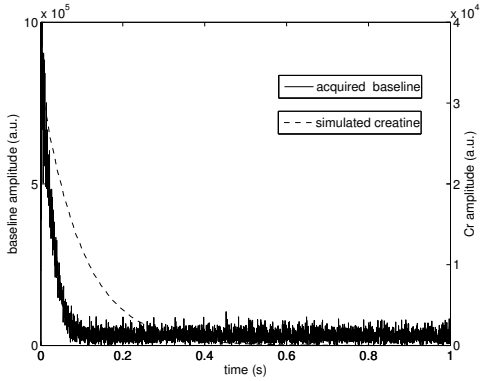
$$= A^2 \int e^{-\sigma^2\omega_s^2\left(a-\frac{\omega_0}{\omega_s}\right)^2} d(\ln a)$$

$$= A^2 \int \frac{1}{a} e^{-\sigma^2\omega_s^2\left(a-\frac{\omega_0}{\omega_s}\right)^2} da \;=\; A^2 C,$$

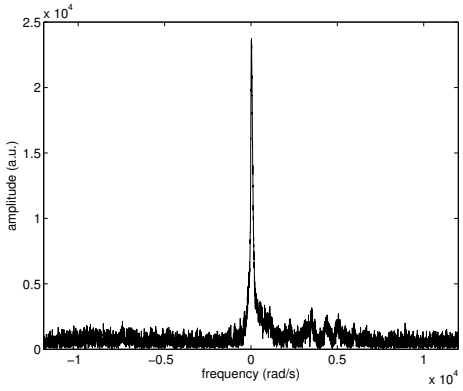
where C is a constant and does not depend on frequencies of the signal. Therefore, if we average the Morlet wavelet coefficients in time, i.e., along the translation axis, and properly adjust ω_0 to separate the frequency of the solvent from others, the averaged amplitude of the baseline (and noise) in the frequency domain should be obtained. The result is illustrated in Fig. 6. Finally, we tried to recover the (simulated) creatine at different amplitudes after adding

[1]An Inversion-Recovery module was included prior to the PRESS sequence (echo-time = 20ms, repetition time = 3.5s, bandwidth of 4kHz, 4096 data-points) in order to measure the metabolite-nullified signal. The water signal was suppressed by variable power RF pulses with optimized relaxation delays (VAPOR). All first- and second-order shimming terms were adjusted using the Fast, Automatic Shimming technique by Mapping Along Projections (FASTMAP) for each VOI ($3\times3\times3$ mm^3). IT = 700ms.

[2]Since the scale a increases multiplicatively, the natural variable (e.g. for linear sampling) is $\ln a$.



(a)



(b)

Fig. 5. The signal of baseline+residual water in time domain (a) and in frequency domain (b).

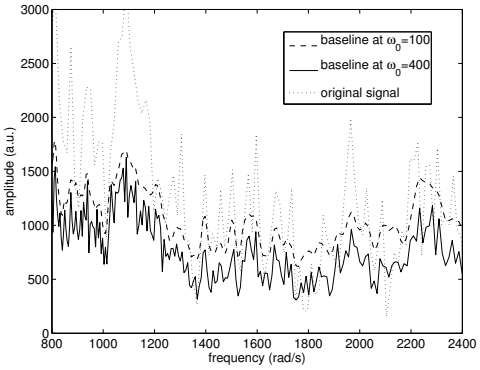


Fig. 6. The baseline derived by the Morlet wavelet transform.

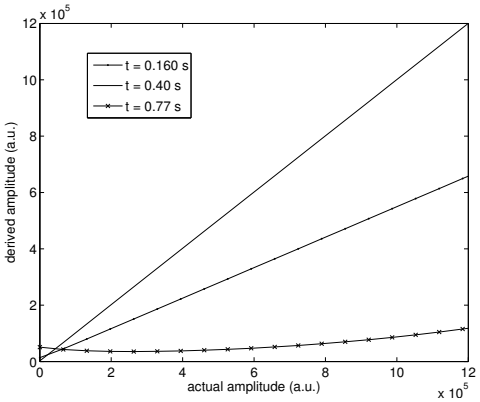


Fig. 7. Derived amplitude at $\omega = 1056$ rad/s, using ω_0 = 100 rad/s and $\sigma = 1$.

it to the signal in Fig. 5. The result, shown in Fig. 7, reveals that the amplitude of the metabolite can be correctly derived whereas at earlier time ($t < 0.2$s) the derived amplitude still has an effect of the baseline. Although one might expect some left-over creatine from the nullifying process, the simulated signal of creatine possibly has a different decaying time from that of the residual creatine in the baseline, giving a correct quantification when (9) is used. However, the metabolite was later covered by noise, giving an inaccurate amplitude. Therefore, the time to monitor the amplitude of the metabolite should be properly selected.

IV. CONCLUSION

This paper presents an analytical analysis of the Morlet wavelet transform to quantify Lorentzian MRS signals. The experimental results show that the wavelet works well even in the presence of baseline, which commonly embeds in *in vivo* MRS signals, without using any pre-processing. However, the proposed method was applied on Lorentzian signals only and still needs further development to cope with non-Lorentzian lineshapes and more complex signals.

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