Analysis of MRS Signals with Metabolite-based Autocorrelation Wavelets

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THE ANALYSIS SO FAR

- Time-domain and frequency-domain are traditional methods to quantify metabolites;
- Also Time-Frequency (Scale) methods have been used to analyzing MRS signals;
- The CWT using Morlet was presented in [4]. An example of pure Creatine using the Morlet wavelet:

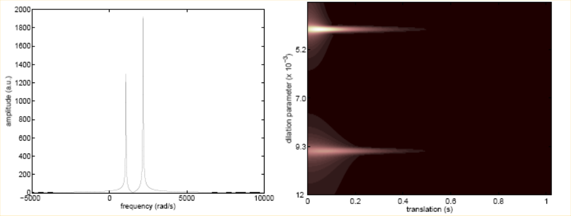
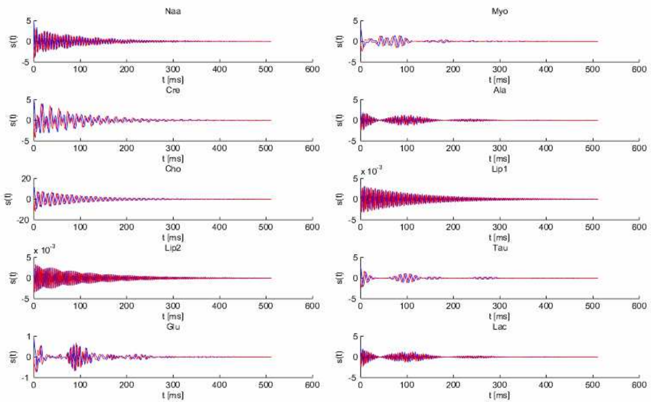


Fig. Freq. response of CRE at 4.7 T and its Morlet CWT ($w_0 = 10$ rad/s, $\sigma = 1$, $F_S = 4006, 41\ s^{-1}$). Extracted from A.-Suvichakorn and J.-P. Antoine, *The Continuous Wavelet Transform in MRS*, e-book FAST website, 2009

QUESTIONS MADE BY THE AUTHORS

- Questions made by the authors:
  1. Can one make a Wavelet function with its spectrum "Matched" with some MRS metabolite signal?
  2. Can one estimate this metabolite's parameters using the CWT with such a wavelet function?



THE AUTOCORRELATION FUNCTION

- One answer can be the use of the concept of Autocorrelation Functions.
- The autocorrelation function estimator $R_{xx}(\tau)$ of an ergodic process time series $x(t)$ is ([3]):

$$R_{xx}(t) = \int_{-\infty}^{\infty} x(\tau)\overline{x(\tau - t)}\,\mathrm{d}t = \int_{-\infty}^{\infty} \overline{x(\tau)}x(\tau + t)\,\mathrm{d}\tau, \qquad (1)$$

  where $\overline{x(t)}$ means the complex conjugate of $x(t)$.
- In the frequency domain, the Fourier transform of R_{xx}, called $S_{xx}(\omega)$ can be evaluated by the Wiener-Khintchine relation:

$$S_{xx}(\omega) = \mathcal{F}\left\{R_{xx}(\tau)\right\} = \left|X(\omega)\right|^2. \qquad (2)$$

OBJECTIVES AND OUTLINE

- Objectives:
  1. Create a wavelet from a MRS pure metabolite signal autocorrelation function;
  2. Perform the CWT of a complex MRS signal using this wavelet;
  3. Estimate the metabolite parameters.
- Outline:
  1. Find an Analytical Solution for CWT using classic MRS models and autocorrelation wavelets form this model;
  2. Create the discrete versions of signals and wavelets presented in the analytical part and analyze them with YAWtb Matlab Toolbox(Lorentzian Models);
  3. Create discrete versions of signals and wavelets now based on the metabolite database and analyze them with Matlab (Metabolite-based Models);

Lorentzian Lineshape

- A simple classical FID MRS signal model $x(t)$: The Lorentzian lineshape.

$$x(t) = A_1 e^{-D_1 t} e^{i(\omega_{s_1} t + \phi_1)} \; A_1 > 0,\; D_1 > 0. \quad (3)$$

- In the frequency domain this signal is defined by

$$X(\omega) = 2\pi A_1 e^{i\phi_1} \delta(\omega - (\omega_{s1} + iD_1)), \quad (4)$$

where δ is the Dirac delta function.

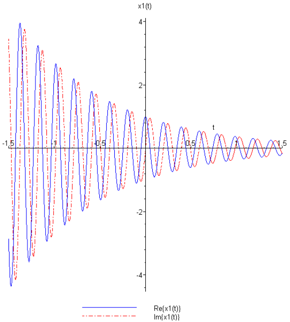


Fig. Real part (blue line) and imaginary part (red dash) of $x(t)$ for $A_1 = 1$, $D_1 = 1$ s, $\omega_{s1} = 32$ rad/s, $\phi_1 = 0$ rad.

- What is the autocorrelation function of this signal?
  NOT a CLUE!!!

Modified Lorentzian Lineshape

- A slightly modified FID MRS signal model $x_1(t)$ can be:

$$x_1(t) = A_1 e^{-D_1 t} e^{i\omega_{s_1} t}\,\theta(t),\;\; D_1 > 0, \tag{5}$$

  where $\theta(t)$ is the Heaviside function (or step function).
- In the frequency domain this signal is defined by

$$X_1(\omega) = \frac{A_1}{[D_1 + i(\omega - \omega_{s_1})]}\,. \tag{6}$$

- Now, the autocorrelation function (on freq. domain) is easily computed:

$$S_{xx}(\omega) = \left|\frac{A_1}{D_1 + i(\omega - \omega_{s_1})}\right|^2 = \frac{A_1^2}{D_1^2 + (\omega - \omega_{s1})^2}\,. \tag{7}$$

THE ADMISSIBLE WAVELET FUNCTION

- Is this function admissible? PROBABLY NOT.
- What to do, then? As with Morlet, use a correction term. Then the admissible wavelet function $\Psi_{\mathrm{adm}}(\omega)$ becomes:

$$\Psi_{\mathrm{adm}}(\omega) = \frac{A_1^2}{D_1^2 + (\omega - \omega_{s_1})^2} - \frac{A_1^2}{D_1^2 + (\omega^2 + \omega_{s_1}^2)} \,. \tag{8}$$

- Is this term really necessary?
- As with Morlet, in practice the appropriate choice of D_1 and ω_{s1} make its value numerically negligible, so that the correcting term can indeed be omitted.

$$\Psi(\omega) = \frac{A_1^2}{D_1^2 + (\omega - \omega_{s_1})^2} \,. \tag{9}$$

THE WAVELET FUNCTION:

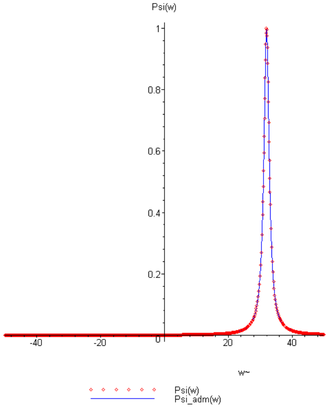


Fig. $\Psi_{\mathrm{adm}}(\omega)$ (blue line) and $\Psi(\omega)$ (red dot) for $A_1 = 1$, $D_1 = 1$ and $\omega_{S_1} = 32$ rad/s.

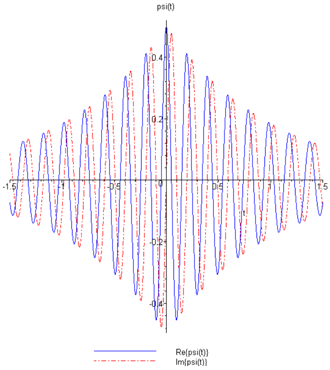


Fig. $\psi(t)$, for $A_1 = 1$, $D_1 = 1$ and $\omega_{S_1} = 32$ rad/s: real part (blue line) and imaginary part (red dash).

THE CWT OF A LORENTZIAN MRS SIGNAL

- Then, the CWT of the the Lorentzian lineshape signal $x(t)$ using $\Psi(\omega)$ is:

$$S(b,a) = \frac{1}{2\pi}\sqrt{a}\int_{-\infty}^{\infty} 2\pi A_1 e^{i\,\phi_1}\,\delta(\omega-(\omega_{s_1}+i\,D_1))\,\frac{A_1^2}{D_1^2+(a\omega-\omega_{s1})^2}\,e^{i\omega b}\,\mathrm{d}\omega$$
$$= \sqrt{a}\;x(b)\;\frac{A_1^2}{D_1^2+[\omega_{s_1}(a-1)+i\,a\,D_1]^2}\,. \quad (10)$$

- $S(b,a)$ diverges for $a=1$ cause signal and wavelet have the same “damping factors" D_1. It cannot be used to estimate parameters, as in the Morlet case, but...
- Using different “damping factors" D_1 for the wavelet function and D_{11} for the signal, then $|S(b,a)|$, for $a=1$ will become:

$$|S(b,1)| = |x(b)|\;\left|\frac{A_1^2}{D_1^2-D_{11}^2}\right|$$
$$= |A_1|\,|e^{-D_{11}b}|\;\frac{|A_1^2|}{|D_1^2-D_{11}^2|}\,. \quad (11)$$

- So the signal’s damping factor can be calculated by:

$$D_{11} = -\frac{d}{db}\ln|S(b,1)| \quad (12)$$

THE (BEAUTIFUL) GRAPHICS

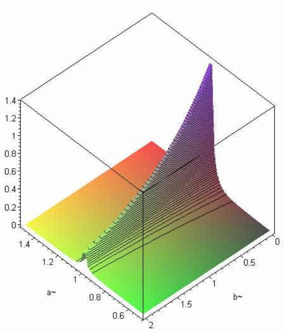


Fig. $|S(b,a)|$ for $A_1 = 1$, $D_1 = 1$, $\omega_{s_1} = 32$ rad/s,$b = [0,2]$ s and $a = [0.5, 1.5]$, $a \neq 1$.

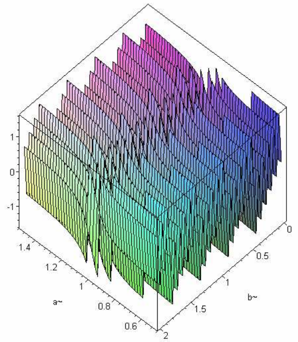


Fig. arg $S(b,a)$ for $A_1 = 1$, $D_1 = 1$, $\omega_{s_1} = 32$ rad/s,$b = [0,2]$ s and $a = [0.5, 1.5]$, $a \neq 1$.

Generalizing for N-peaks signals

- As many metabolites are multipeaked, we will generalize for N-peaks Lorentzian signals.
- The signal $x_N(t)$, a weighted sum of N Lorentzian components:

$$x_N(t) = \sum_{n=1}^{N} A_n e^{-D_n t} e^{i(\omega_n t + \phi_n)}; \, D_n > 0. \tag{13}$$

The Fourier transform of $x_N(t)$:

$$X_N(\omega) = 2\pi \sum_{n=1}^{N} A_n e^{i\phi_n} \delta(\omega - (\omega_{sn} + iD_n)). \tag{14}$$

The left truncated version of $x_N(t)$:

$$x_N^{'}(t) = \sum_{n=1}^{N} A_n e^{-D_n t} e^{i(\omega_{sn} t)} \theta(t), \; D_n > 0\,, \tag{15}$$

where $\theta(t)$ is the Heaviside function.

Now the Fourier transform of $x_N^{'}(t)$

$$X_{1N}(\omega) = \sum_{n=1}^{N} \frac{A_n}{[D_n + i(\omega - \omega_{sn})]}. \tag{16}$$

The N-peak wavelet function and CWT

- The autocorrelation of (15) in the frequency domain is:

$$S_{x'_N x'_N}(\omega) = \left| \sum_{n=1}^{N} \frac{A_n}{D_n + i(\omega - \omega_{sn})} \right|^2 \approx \sum_{n=1}^{N} \frac{A_n^2}{D_n^2 + (\omega - \omega_{sn})^2}. \tag{17}$$

- Under the considerations made, the autocorrelation wavelet function is:

$$\Psi_N(\omega) = \sum_{n=1}^{N} \frac{A_n^2}{D_n^2 + (\omega - \omega_{sn})^2} \tag{18}$$

- The CWT of the signal (13) using (18) as wavelet function is given by:

$$\begin{aligned} S_N(b,a) &= \sqrt{a} \int_{-\infty}^{\infty} \sum_{k=1}^{N} A_k e^{i\phi_k} \delta(\omega - (\omega_{s_k} + iD_k)) \sum_{n=1}^{N} \frac{A_n^2}{D_n^2 + (a\omega - \omega_{s_n})^2} e^{i\omega b}\, \mathrm{d}\omega \\ &= \sqrt{a} \sum_{k=1}^{N} x_k(b) \sum_{n=1}^{N} \frac{A_n^2}{D_n^2 + [a(\omega_{s_k} + iD_k) - \omega_{sn}]^2} \end{aligned} \tag{19}$$

(Also beautiful)graphs of 2 and 3 peaks CWT

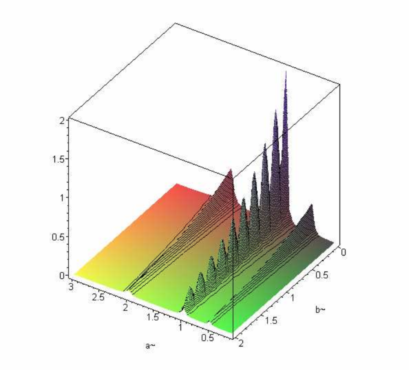


Fig. $|S_2(b,a)|$ for $A_1 = A_2 = 1$, $D_1 = D2 = 1$, $\omega_{s1} = 32$ and $\omega_{s2} = 64$ rad/s, $b = [0,2]$ s and $a = [0.1, 3]$, $a \neq 1.0$;

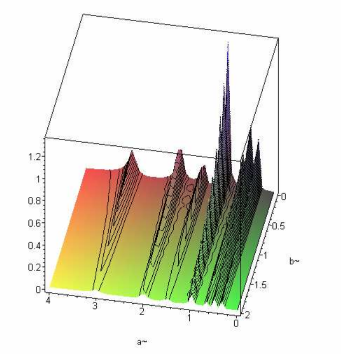


Fig. $|S_3(b,a)|$ for $A_1 = A_2 = A_3 = 1$, $D_1 = D_2 = D_3 = 1$, $\omega_{s1} = 30$, $\omega_{s2} = 60$ and $\omega_{s2} = 90$ rad/s, $b = [0,2]$ s and $a = [0.1, 4]$, $a \neq 1.0$;

THE N-PEAK DAMPING FACTORS ESTIMATION

- An "oscillating" local maxima at $a = 1$;
- Also, $|S_N(b,a)|$ have horizontal ridges at $a = \omega_{s_n}/\omega_{s_k}$, $k \neq n$; $k, n = 1, 2, ..., N$.
- Estimation of the damping factors:
  1. Consider the wavelet function have damping factors D_n and the signal have D_{nn}, $D_n \neq D_{nn}$ for any n.
  2. Choosing one of the other local maxima $a = \omega_{s_n}/\omega_{s_k}$, and considering that the other factors are small enough in this scale, so only one term of (19) will be significative and we can estimate the damping factor as:

$$\frac{d}{db}\ln|S(b,\frac{\omega_{s_n}}{\omega_{s_k}})| \approx \frac{d}{db}\ln|e^{-D_{kk}b}| + \frac{d}{db}\ln|A_k A_n^2| - \frac{d}{db}\ln|D_n^2 + [(\omega_{s_k} + iD_{kk}) - \omega_{s_n}]^2| \\ \approx -D_{kk}\,. \qquad (20)$$

- Summarizing: if (a) peaks are far enough from each other and;(b) damping factors provide sharp peaks, the damping factors can estimated by $D_{kk} \approx -\frac{d}{db}\ln|S(b,\frac{\omega_{s_n}}{\omega_{s_k}})|$.

What happens with more realistic signals?

- What happens when one analyzes limited, discretized, noisy and more realistic signals?
- Two procedures proposed:
  1. Create Discrete versions of signals and wavelets presented before and analyze them with Matlab and YAWtb Toolbox (Lorentzian Models);
  2. Finally, create Discrete versions of signals and wavelets based on the metabolite database and analyze them with Matlab (Metabolite-based Models);
- Next, in the Numerical Analysis section.

NUMERICAL ANALYSIS WITH 1 PEAK LORENTZIAN FUNCTION

- A MATLAB© function which implements $\Psi(\omega) = \left| \sum_{n=1}^{N} \frac{A_n}{D_n + i(\omega - \omega_{s_n})} \right|^2$ were created (called"LorentzNd.m") and added to YAWtb toolbox ([5]);
- A N component discrete exponential signal was defined by:

$$x1[n] = \begin{cases} 0, & 0 \le n \le (\frac{N}{4} - 1), \\ \sum_{n=1}^{N} A_n \, e^{-D_1(n-\frac{N}{4})t_s} \, e^{i\omega_{s_n}(n-\frac{N}{4})t_s}, & (\frac{N}{4}) \le n \le (\frac{3N}{4} - 1), \\ 0, & (\frac{3N}{4}) \le n \le N - 1, \end{cases}$$

where $t_s = 1/f_s$ is the sampling period in seconds.

- The CWT of this signal using the "LorentzNd" function, with the same frequency and damping factors as the signals, for $n = 1, 2, 3$ was performed;

THE CWT RESULTS FOR 1 COMPONENT

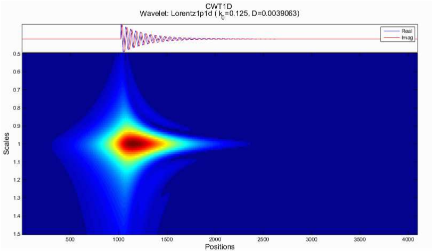


Fig. $|CWTx_1[n]|$ for $A = 1$, $D_1 = 1$, $\omega_{s1} = 32$ rad/s, $n = [1, 4096]$ and $a = [0.5, 1.5]$ using the "Lorentz1d" wavelet.

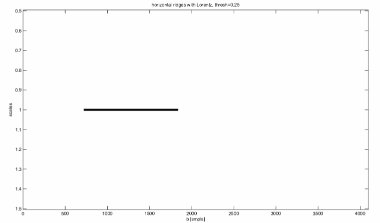


Fig. Skeleton of the CWT, for $A = 1$, $D_1 = 1$, $\omega_{s1} = 32$ rad/s, $n = [1, 4096]$ and $a = [0.5, 1.5]$ using the "Lorentz1d" wavelet.

THE CWT RESULTS FOR 2 COMPONENTS

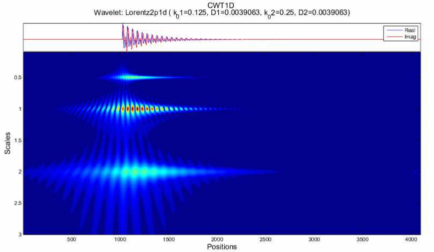


Fig. $|CWTx_2[n]|$ for $A_1 = A_2 = 1$, $D_1 = D_2 = 1$ 1/s, $\omega_{s1} = 32$ and $\omega_{s2} = 64$ rad/s, $t_s = 1/256$ s and $N = 4096$ for “Lorentz2Pk1d" wavelet.

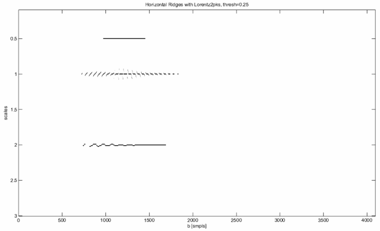


Fig. Skeleton of CWT for $A_1 = A_2 = 1$, $D_1 = D_2 = 1$ 1/s, $\omega_{s1} = 32$ and $\omega_{s2} = 64$ rad/s, $t_s = 1/256$ s and $N = 4096$ for “Lorentz2Pk1d" wavelet.

...AND THE CWT RESULTS FOR 3 COMPONENTS:

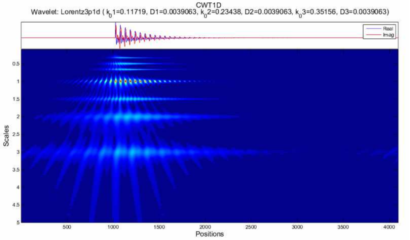


Fig. $|CWT x_3[n]|$ for $A_1 = A_2 = A_3 = 1$, $D_1 = D_2 = D_3 = 1$ 1/s, $\omega_{s1} = 30$, $\omega_{s2} = 60$ and $\omega_{s2} = 90$ rad/s, $t_s = 1/256$ s, $N = 4096$ and $a = [0.5, 5]$ for “Lorentz3Pk1d" wavelet.

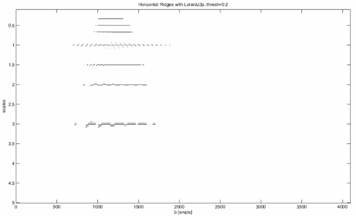
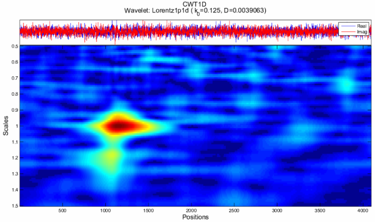


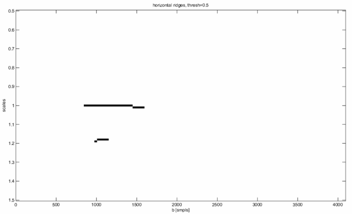
Fig. Skeleton of CWT for $A_1 = A_2 = A_3 = 1$, $D_1 = D_2 = D_3 = 1$ 1/s, $\omega_{s1} = 30$, $\omega_{s2} = 60$ and $\omega_{s2} = 90$ rad/s, $t_s = 1/256$ s, $N = 4096$ and $a = [0.5, 5]$ for “Lorentz3Pk1d" wavelet.

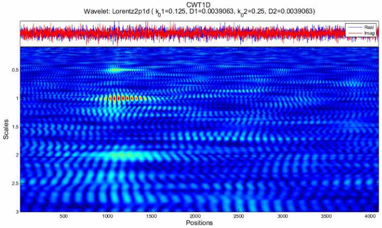
Numerical Analysis for signals with noise

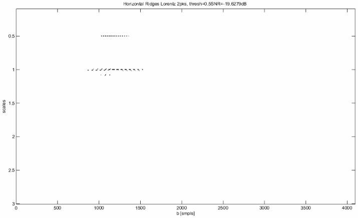
- Here the goal was to find the limit of signal detection in presence of noise by means of autocorrelation wavelets ;
  1. White gaussian noise was added to signals at different SNR levels;
  2. The CWT was performed (N peak was analyzed by its related N autocorrelation wavelet;
  3. The results are in the limit of signal detection by its wavelet (still have the horizontal ridge);
  4. The SNR of this limit were in average ≈ -20dB

Some noise results









Creating and using Metabolite-based wavelets

- Numerical analysis with Metabolite-based wavelets:
  1. Take signals from one *in vitro* metabolite database;
  2. Create its related Autocorrelation Wavelets;
  3. Analyze a mixture of metabolites by one related autocorrelation wavelet with Matlab;

The Algorithm:

1. Calculate autocorrelation function R of metabolite profile ϕ:

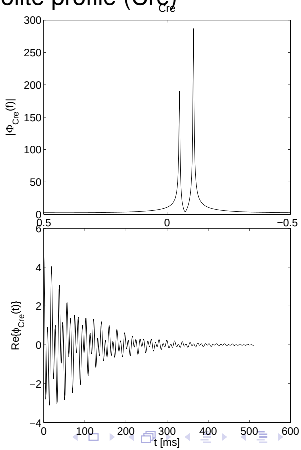
$$R[n] = \sum_{k=-N}^{+N} \phi[k]\,\overline{\phi[n-k]} \qquad (21)$$

   using Matlab function xcorr;

2. Subtract its mean value:

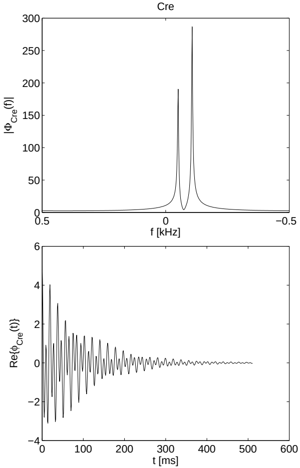
$$\psi[n] = R[n] - E\{R[n]\} \qquad (22)$$

Metabolite profile (Cre)

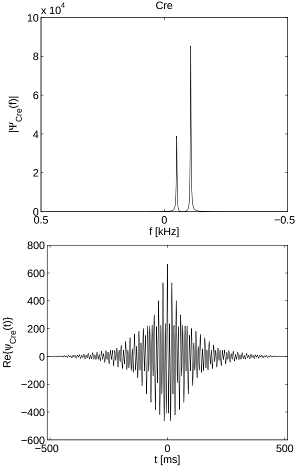


WAVELET CONSTRUCTION RESULT

Metabolite profile (Cre)



Cre-based wavelet



HOW TO DILATE DISCRETE WAVELETS?

- PROBLEM: Mother wavelet is Discrete , no analytical expression;
- SOLUTION: An discrete upsampler/downsampler system was used.

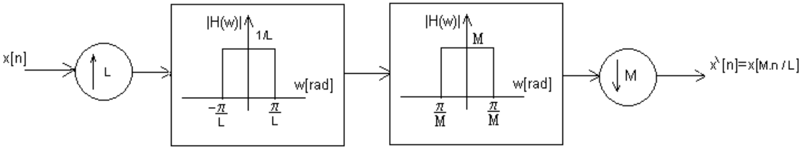


Fig. Block diagram of Upsampler/downsampler system. $L, M \in (Z)$.

- Wavelet will be expanded by an integer factor of L and contracted by an factor of M.
- $a = L/M$.

Example of dilated wavelet

Cre-based wavelet (real part) at different scales:

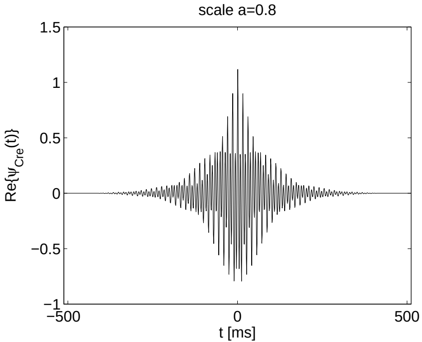


Fig. scale $a = 0.8$

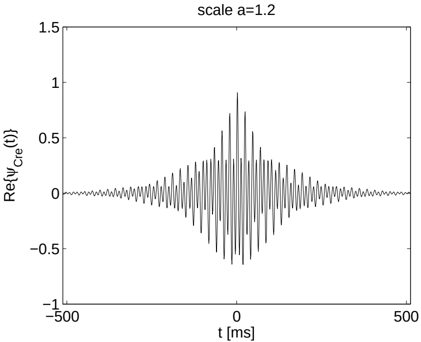


Fig. scale $a = 1.2$

Signal 1: Combination Naa + Cre without Lac

Sum of pure Naa and Cre signals, no noise:

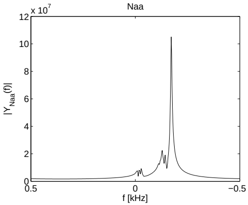


Fig. Naa part

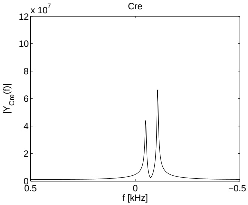


Fig. Cre part

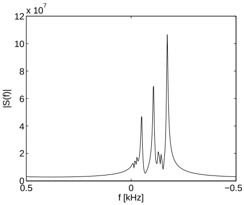


Fig. Naa + Cre

Signal 2: Combination Naa + Cre + Lac

Sum of pure Naa and Cre signals PLUS Lac, no noise:

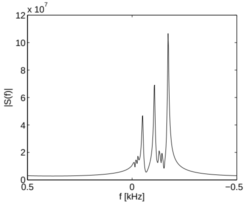


Fig. Naa + Cre

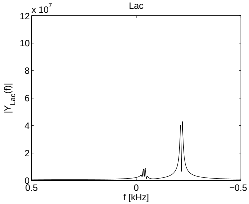


Fig. Lac part

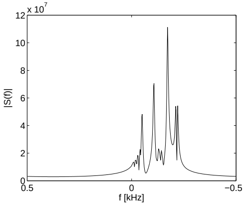


Fig. Naa + Cre + Lac

CWT analysis of signal 1 with Naa-based wavelet

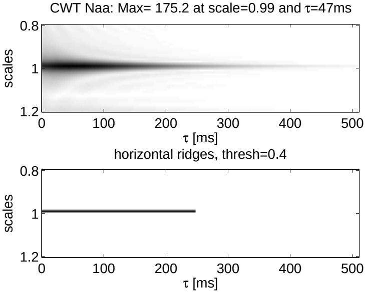


Fig. Naa-wavelet CWT of Naa reference signal

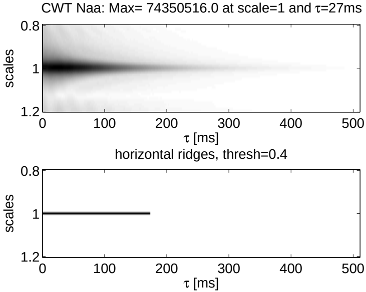


Fig. Naa-wavelet CWT of Naa+Cre composed signal

CWT analysis of signal 2 with Naa-based wavelet

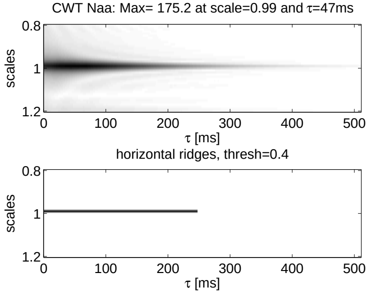


Fig. Naa-wavelet CWT of Naa reference signal

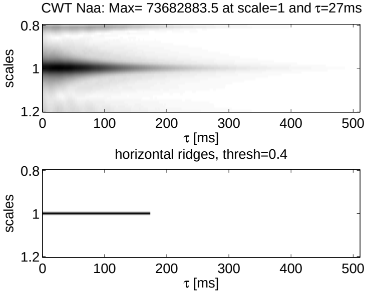


Fig. Naa-wavelet CWT of Naa+Cre+Lac composed signal

CWT analysis of signal 1 with Cre-based wavelet

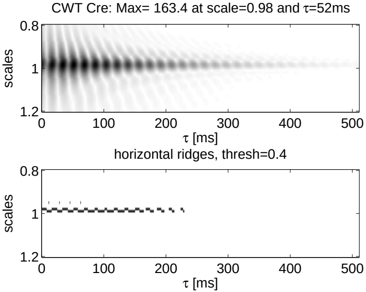


Fig. Cre-wavelet CWT of Cre reference signal

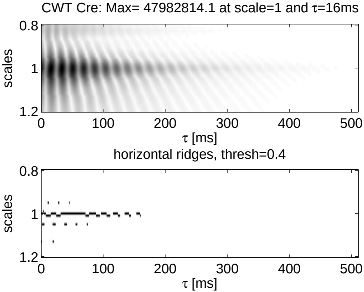


Fig. Cre-wavelet CWT of Naa+Cre composed signal

CWT analysis of signal 2 with Cre-based wavelet

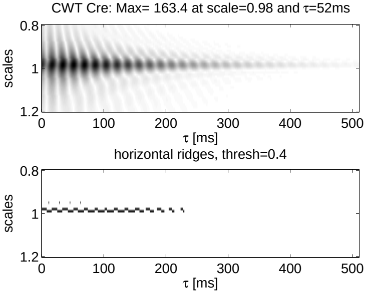


Fig. Cre-wavelet CWT of Cre reference signal

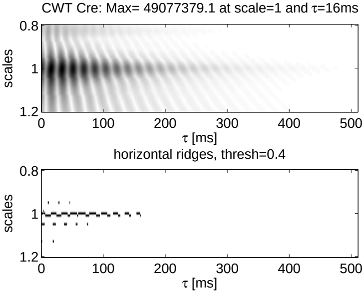


Fig. Cre-wavelet CWT of Naa+Cre+Lac composed signal

CWT analysis of signal 1 with Lac-based wavelet

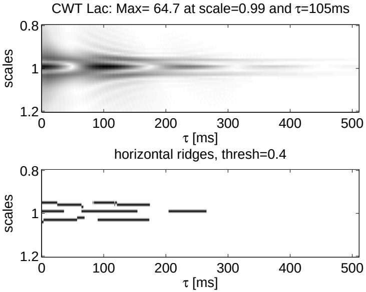


Fig. Lac-wavelet CWT of Lac reference signal

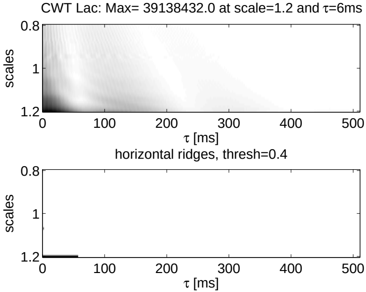


Fig. Lac-wavelet CWT of Naa+Cre composed signal

CWT analysis of signal 2 with Lac-based wavelet

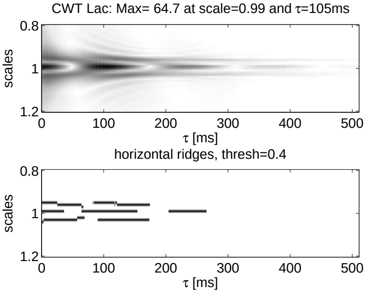


Fig. Lac-wavelet CWT of Lac reference signal

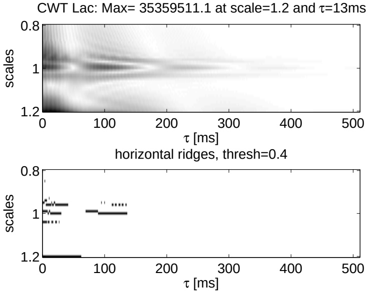


Fig. Lac-wavelet CWT of Naa+Cre+Lac composed signal

THE CONCLUSIONS SO FAR

- Analytical analysis:
  1. Analytical expressions for Wavelet function and CWT, using Lorentzian models were made;
  2. Horizontal ridges at $a = 1$ means Presence of Metabolite which generated the autocorr.wavelet;
  3. For 1 peak, the Damping factor can be found. For more than one peak, the Damping factors can be approximated from horizontal ridges at $a \neq 1$;
- Numerical analysis with Lorentzian signals:
  1. Discretization and time limitation of signals changed a little the results (“lateral" Ridges are not smooth);
  2. With multi-peaked signal/autocorr. wavelet, the damping estimation is harder;
  3. Single signals could be detected at ≈ -20dB SNR;
- Numerical analysis with metabolite-based signals:
  1. Algorithms for autocorrelation wavelet creation, dilation and CWT were made;
  2. The metabolites presence could be detected in the mixture by its related wavelet;
  3. Parameters estimation is almost done (so wait a little bit more).

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REFERENCES

J-P. Antoine and R. Murenzi and P. Vandergheynst and S.T. Ali.
Two-Dimensional Wavelets and their Relatives.
Cambridge University Press, 2004.

A. Oppenheim and R.W. Schaffer with J. R. Buck.
Discrete-time signal processing, 2nd Ed..
Prentice-Hall, Inc., 1999.

A. Papoulis and S. U. Pillai.
Probability, random variables and stochastic processes, 4th ed..
McGraw-Hill, Inc., 2002.

A. Suvichakorn and H. Ratiney and A. Bucur and S. Cavassila and J-P. Antoine.
Toward a quantitative analysis of *in vivo* proton magnetic resonance spectroscopic signals using the continuous Morlet wavelet transform.
Meas. Sci. Technol., 20:104029–104040, 2009.

L. Jacques and A. Coron and P. Vandergheynst and A. Rivoldini.
YAWTb toolbox : Yet Another Wavelet Toolbox.
http://rhea.tele.ucl.ac.be/yawtb, 2009.