Iterative improvement of lineshape estimation

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Abstract— **Magnetic Resonance Spectroscopy (MRS) is an effective diagnostic technique for monitoring metabolic and biochemical changes within an organism or sample. Static and dynamic inhomogeneity of the magnetic field applied to the patient distorts the function that governs the natural damping of the MRS signals. This damping function can be expressed in the frequency domain as a Lorentzian, Gaussian, or Voigt function; however, using these approximations, estimation of the desired *in vivo* metabolite concentrations may be biased.**

We investigate by means of simulations whether estimation of the unknown distorted damping function can improve the overall result. Using an improved damping function decreases bias, but increases variance because more parameters are involved. It is, therefore, important to find a suitable bias-variance trade-off. Our method improves on that in Ref [1] by including iterations, consisting of applying Hankel Singular Value Decomposition (HSVD) and Nonlinear Least Squares (NLLS) to estimate a common damping function that is finally applied to a metabolite database [2]. For our simulations we use a signal with 11 undamped Lorentzian components inspired by the benchmark signal of ^{31}P provided by [3]. Results show that by identifying the right model complexity using a convenient number of Lorentzians, the iterative method improves the parameter estimates significantly.

Keywords— **Magnetic Resonance Spectroscopy (MRS), lineshape, inhomogeneity, damping.**

I. Introduction

In vivo MRS is a unique technique that enables noninvasive monitoring of metabolites anywhere in a patient. It is an indispensable tool for diagnosis of major diseases. MRS signals are measured in the time domain. A permanent point of concern is that static and dynamic inhomogeneity of the magnetic field applied to the patient distorts the function that governs the natural damping of the signals.

Ideally, the damping function of metabolites in a liquid solution is exponential. But, under *in vivo* conditions, the damping function is *a priori* unknown due to the mentioned inhomogeneity of the applied magnetic field, which in turn is due to heterogeneity of the tissue of a patient. This complicates analysis of the signals. Traditionally, one assumes the damping function to be $\exp(-d_1 t)$ or $\exp(-d_2 t^2)$, or a combination of the two, $\exp(-d_1 t - d_2 t^2)$. In these functions, t is time, and d_1 and d_2 are positive constants. In the frequency domain, the spectral shapes corresponding to these damping functions are called Lorentzian, Gaussian, and Voigt, respectively. Using these approximations, estimation of the wanted *in vivo* metabolite concentrations will be biased. In this work, we investigate by way of simulations whether estimation of the unknown distorted damping function applying an iterative method, can improve the overall result. Using an improved (*i.e.*, estimated) damping function will reduce bias, but variance will increase because more parameters are involved.

II. Materials and Methods

A. Simulated signal: Distortion of the damping function

The distortion of the damping function of *in vivo* MRS signals depends on the scanner at hand and on tissue heterogeneity at the chosen location in a patient. The more the tissue is heterogeneous, the faster is the decay of the damping function. Moreover, geometric asymmetry of tissue distribution results in asymmetry of the spectral shape. In view of the diversity of local geometry in a patient, a spectral shape that represents all cases cannot be given. In this study, the spectral shape of the distortion was chosen to be asymmetric, so as to better mimic *in vivo* conditions. For easy handling of the degree of asymmetry we adopted a triangle, as shown in Fig. 1. For frequency f in the region $f_1 \leq f \leq f_2$ the shape is $(f - f_1)/(f_2 - f_1)$ and for $f_2 \leq f \leq f_3$, the shape is $(f_3 - f)/(f_3 - f_2)$; outside these regions the shape is zero. Asymmetry is achieved by setting $f_2 - f_1 \neq f_3 - f_2$.

An MRS signal is measured in the time domain. Hence we must calculate the Fourier transform of the shape function to arrive at the wanted damping function for the simulation. The Fourier transform of the triangular shape in Fig.1 is

$$g(t) = \frac{2}{f_3 - f_1} * \frac{1}{2\pi j t}\left(\frac{e^{x_1} - e^{x_2}}{x_2 - x_1} + \frac{e^{x_3} - e^{x_2}}{x_3 - x_2}\right) \text{ for } t > 0 \quad (1)$$

where $g(t)$ is the damping function, $j=\sqrt{-1}$ and $x_i = 2\pi j f_i t$, for $i = 1, 2, 3$. $\mathrm{Lim}_{t\to 0}\, g(t) = 2/(f_3 - f_1)$. Eq. (1) is then transformed to be smoothed using a Lorentzian e^{-dt}.

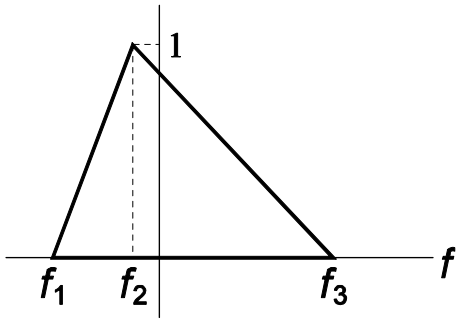

Fig.1 Simulation of the distortion of the spectral shape caused by heterogeneity of the patient. The present choice can easily be made asymmetric by setting $f_2 - f_1 \neq f_3 - f_2$. Asymmetry brings along an extra challenge for spectral shape estimation. In this work we used f_1= −0.003, f_2= -0.001, f_3= 0.005.

Finally, we emphasize that Eq. (1) constitutes the dominant contribution to the damping of all spectral components of the MRS signal. In the frequency domain this means that the spectral shapes of the metabolite peaks to be introduced in the next Sections are all equal. See Ref. [4] for an example of an alternative lineshape.

B. Simulated signal: Metabolites Signal

Baseline contributions of macromolecules are known to be largely present in short-echo-time spectra of human brain. However, we do not take into account this contribution. Traditionally, a metabolite signal is approximated by Eq. (2), assuming that the damping can be described by a Voigt function. Our simulated signal was derived from a benchmark ^{31}P signal provided by Ref. [3].

$$y_{old}(t) = \sum_{m=1}^{M} \alpha_m e^{-d_{1m}t - d_{2m}t^2 + 2\pi j f_m t + j\varphi_m} \qquad (2)$$

where $y_{old}(t)$ is the MRS signal, M=11, α the amplitude, d_1 and d_2 the positive damping factors, f the frequency and φ the phase of the mth spectral component. Using now that g(t) dominates all other contributions to the damping - as mentioned in the previous section - we can replace exp(-$d_{1m}t$- $d_{2m}t^2$) by $g(t)$ for all m. This results in:

$$y_{new}(t) = g(t) \sum_{m=1}^{M} \alpha_m e^{2\pi j f_m t + j\varphi_m} \qquad (3)$$

where the factor $2/(f_3 - f_1)$ serves as normalization because $g(0)=(f_3-f_1)/2$. Eq. (3) enables us to write:

$$g(t) = \frac{y_{new}(t)}{\sum_{m=1}^{M} \alpha_m e^{j2\pi f_m t + j\varphi_m}} \qquad (4)$$

which can be used as estimator of the unknown damping function, directly in the time domain. Note that starting values are needed for the parameters in the denominator.

The final simulated signal is described by (5), where $n(t)$ corresponds to some added Gaussian noise.

$$y_{sim}(t) = y_{new}(t) + n(t) \qquad (5)$$

C. Algorithm

The present method extends that in [1], by introducing iterations. It consists of the following steps:

Step i. Modeling of the metabolite signal of Eq. (5) with HLSVD-PRO [5], a State Space algorithm based on Singular Value Decomposition. The model order used in this case was 11 and the resulting model parameters α_m, f_m, φ_m are used as starting values in the next step.

Step ii. Estimation of $g(t)$ with Eq. (4).

Step iii. Modeling (denoising) of $g(t)$ obtained in step ii. with HLSVD-PRO, using an appropriate model order. The model order was selected after comparing several model orders and obtaining the one with the smallest Root Mean Squared Error (RMSE), related to the initial amplitudes. $RMSE = b^2 + \sigma^2$; where b represents the bias and σ^2 the variance. .

$Bias, b(\hat{\varphi}) = \varphi - E[\hat{\varphi}]$

$Variance, (\sigma^2) = E[(\hat{\varphi} - E[\hat{\varphi}])^2]$

Step iv. Estimating the metabolite parameters α_m, f_m, φ_m with an NLLS fitting algorithm.

Step v. Iterative application of Steps ii-iv until convergence is reached.

Step v constitutes the extension of the method of [1]. The success of the method hinges on obtaining good parameter values in the formula in Step i. Hence the extension of the original method consists of:

1. Step i is improved so as to obtain better starting values for the next steps.
2. Step i to iii are iterated so as to gradually improve the parameter values further. The convergence behavior is investigated.

Finally, the simulated metabolite signal is rather different from that in [1], due to the fact that here we do not include the eddy current effects.

III. Results

Results showed that applying this iterative method which using the denoised damping signal of Fig.2, provides good parameter estimations that will be finally used for improving quantification. We analyze the response of our algorithm by checking the results of estimations and the corresponding residuals, as shown in Fig.3.

Table 1 shows a summary of the comparison between the RMSE of different choices of HLSVD-PRO model orders that were investigated for SNR=50. The model order was selected to denoise $g(t)$. The 2 digits in the HLSVD-PRO subtitle indicate that the method is used two times for denoising. We use model orders 1 to 6 to be evaluated in different combinations and calculating the RMSE of all of them. Finally, we chose 1-6 (i.e. model order=1 and =6 for denoising), which ever has the lowest RMSE. The analysis was done using an SNR=50; however the results at low SNR are still under investigation.

Table 1. RMSE for the first amplitudes applying different model orders for modeling $g(t)$. SNR=50.

HLSVD-PRO 1-6	HLSVD-PRO 4-6	HLSVD-PRO 6-6	HLSVD-PRO 6-3	HLSVD-PRO 2-3
2.9546	4.8748	4.9036	4.7556	5.1184
5.6564	9.9173	9.9190	9.8915	10.5973
4.0552	5.5111	5.4868	5.6549	5.9733
5.4132	9.8197	9.7759	9.6707	10.4002

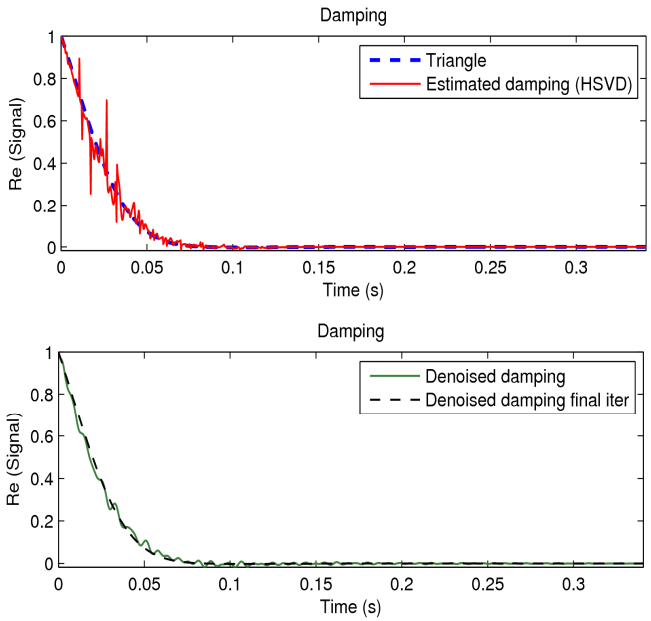

Fig.2. Top: Time domain signal of the triangular damping function with the estimated damping in an initial approach. Bottom: Denoised damping in the first and last steps, where the estimation has already reached convergence.

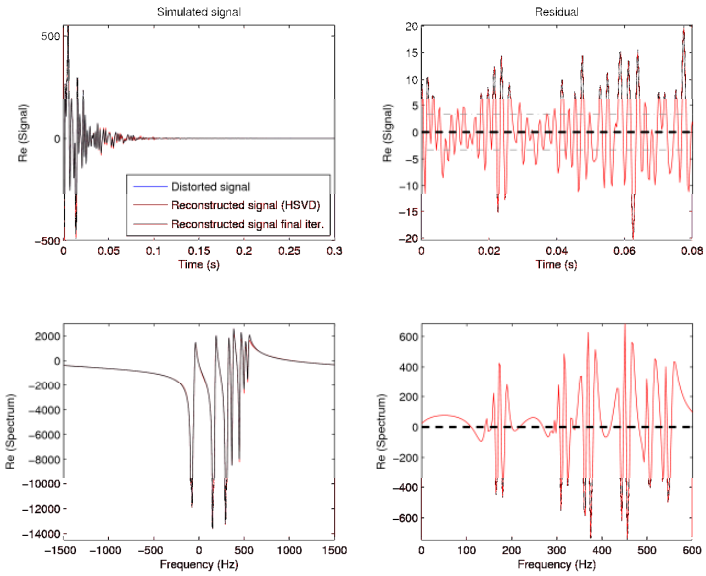

Fig.3. Final fitting of the signal using the damping function estimated in Step iv. Left: real part of the signal in the time domain (top), and the corresponding real part of the spectrum (bottom). Right: residuals for the first (solid line) and the last (dashed line) iterations.

IV. Discussion

The parameters of the denoised damping signal are the ones used for estimating every new fit; therefore, a bad initial estimation will influence the final results because improvements will depend on them. Results are obtained with the chosen HLSVD-PRO parameters applied to the signal; however, we look for an appropriate bias-variance trade-off based on the number of parameters used for that method.

Our simulations differ from those in [1] in the sense that a simulated signal with 3 overlapping metabolites is used; additionally, the distortion of the damping function includes eddy currents effects. Here, we use a simulated signal of ^{31}P with 11 metabolites and as distorted damping we use only an asymmetric triangle. In addition, the first estimated parameters are calculated in [1] using NLLS while we use a combination HLSVD-PRO–NLLS. Finally the iterative improvement using Eq. (5) is the main difference that makes our method a more consistent procedure.

V. Conclusions

Our results show that estimation of the lineshape for acquiring more realistic MRS signals is a useful method for acquiring more accurate quantification results. We confirm that the estimated lineshape can be used for obtaining more realistic spectral distortions caused by the field and tissue heterogeneities, yielding thereby more accurate estimates. Finally, we emphasize that simulations are important for studying estimation of an *a priori* unknown lineshape in a semi-parametric setting.

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References

1. Rabeson H, Capobianco E, de Beer R, van Ormondt D, Graveron-Demilly D (2008) Correction for B0 inhomogeneity and Eddy Current effects without using a reference line. 12ème congrès du GRAMM, Lyon, France, 2008, Proc. pp.101.
2. Poullet J-B., Sima D.M., Simonetti A.W., De Neuter B., Vanhamme L., Lemmerling P., Van Huffel S.,. (2007) An automated quantitation of short echo time MRS spectra in an open source software environment: AQSES. NMR in Biomed, vol. 20(5): 493-504.
3. Vanhamme L., Van den Boogaart A., Van Huffel S., (1997) Improved Method for Accurate and Efficient Quantification of MRS Data with Use of Prior Knowledge. J Mag Reson, 129: 35-43.
4. Stancik A.L., Brauns E.B, (2008) A simple asymmetric lineshape for fitting infrared absorption spectra. Vibrational Spectroscopy, 47: 66-69.
5. Laudadio T., Mastronardi N., Vanhamme L., Van Hecke P., Van Huffel S., (2002) Improved Lanczos Algorithms for Blackbox MRS Data Quantitation. J Mag Reson 157 (2): 292–297.