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Improvement of lineshape estimation for MRS signals

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***Abstract*— Magnetic Resonance Spectroscopy (MRS) is an effective diagnostic technique for monitoring biochemical changes in an organism. The lineshape of MRS signals can deviate from the theoretical Lorentzian or exponential lineshape due to inhomogeneities of magnetic field applied to the patient and to patient's tissue heterogeneity. We call this deviation a distortion. Using an improved damping function, we estimate the lineshape with an iterative method that finds optimal parameters. In our simulations we investigate whether estimation of the unknown distorted damping function can improve the overall result. Our method improves on that in [1], by including iterations, consisting of applying Hankel Singular Value decomposition (HSVD) and Nonlinear Least Squares (NLLS) to calculate the frequencies, amplitudes and phases that are used to estimate a common damping function finally applied to a metabolite database; the method is applied iteratively until the parameters' convergence is reached. For our simulations we used a signal with 11 undamped Lorentzian components inspired by the benchmark signal of ^{31}P provided in [2]. Results show that identifying the right model complexity using a convenient number of sinusoids improves significantly the iterative method. Comparison of residuals for the first and last iterations show a clear improvement. We consider the bias-variance trade-off because increasing the number of sinusoids decreases the bias but increases the variance and vice versa, so we look for an optimal order that leads to the best possible results. Although perfect estimation of the lineshape distortion is difficult, simulations are important to find a good approximation. Since parameters estimated in the first iteration are used for the next ones, a bad initial estimate will affect the final result. Iterations provided the expected successive improvements, due to the enhancement of estimations.**

Keywords*— *Magnetic Resonance Spectroscopy (MRS), Lineshape, damping

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I. INTRODUCTION

In vivo Magnetic Resonance Spectroscopy (MRS) is a noninvasive technique for monitoring metabolites in a tissue. It is an effective tool for diagnosis of major diseases. MRS signals are measured in the time domain and a quantification method like the one in [3] is used to determine the concentration of the metabolites present in the region of interest. A perennial point of concern is that static and dynamic inhomogeneity of the magnetic field distorts the natural lineshape 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 mainly due to heterogeneity of patient's tissue. This complicates signal analysis. The aim is to estimate a lineshape to improve quantification of MRS signals. This work extends the original method [1] by adding iterations.

II. MATERIALS AND METHODS

A. 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; however, there are an infinite number of shapes that can be used to simulate this asymmetry. See [4] for an example of an alternative lineshape. 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.

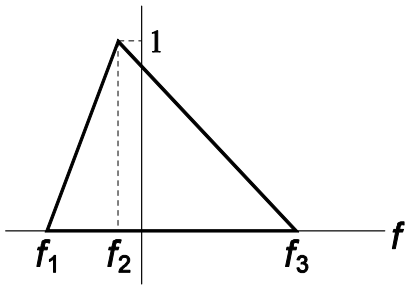

Fig.1 Simulation of the distortion of the spectral shape caused by heterogeneity of the patient. The present choice can easily be made asymmetric by setting $f_2 - f_1 \neq f_3 - f_2$. The vertical axis indicates that the first two frequencies are negative. Asymmetry brings along an extra challenge for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

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. $\text{Lim}_{t\to 0}\, g(t) = 1$. The factor $2/(f_3 - f_1)$ serves as normalization. Eq. (1) is then transformed to be smoothed using a Lorentzian e^{-dt}.

Finally, we emphasize that (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.

B. *Simulated 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 (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 [2]. This signal comprises 11 spectral components and is modeled by:

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

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:

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

Then (3) enables us to write:

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

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.
Finally, the simulated signal is composed by y_{new} plus some added Gaussian noise:

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

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

Step ii. Estimation of the damping function $g(t)$ with (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 true 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 a 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.

Iterative algorithm

Initialization

1. Simulated signal multiplied by the triangular function plus some added Gaussian noise:
$$y_{sim}(t) = g(t) \sum_{m=1}^{M} \alpha_m e^{2\pi j f_m t + j\varphi_m} + n(t)$$
2. HLSVD-PRO to calculate the parameters α_m, f_m, φ_m.
3. Calculate damping function:
$$g(t) = \frac{y_{sim}(t)}{\sum_{m=1}^{M} \alpha_m e^{j2\pi f_m t + j\varphi_m}}$$
4. Denoise $g(t)$ using HLSVD-PRO

Iterative procedure

5. Calculate new parameters α_m, f_m, φ_m using the denoised $g(t)$ with an **NLLS** method
6. Calculate a new $g(t)$:

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

7. Denoise $g(t)$ using HLSVD-PRO
8. Calculate reconstructed signal:

$$y_{reconst}(t) = g_{denoised}(t) * \sum_{m=1}^{M} \alpha_m e^{j2\pi f_m t + j\varphi_m}$$

9. *If* abs(error new param.)<2*variance(last 24 p. $y_{reconst}(t)$)
   $y_{reconst}(t)$ is final signal with parameters α_m, f_m, φ_m
   else
   Go to 5

III. RESULTS

Results showed that the reconstructed lineshape improves significantly when applying this iterative method. Fig.2 shows the effectiveness of denoising applied to the damping function. On the other hand, the improvement of the method can be observed in Fig.3 by comparing the residuals of the first and the last iterations. The Euclidean norm of the residuals was calculated as 127.5846, 0.7574, 0.0175 for the initial, second and last iterations, respectively.

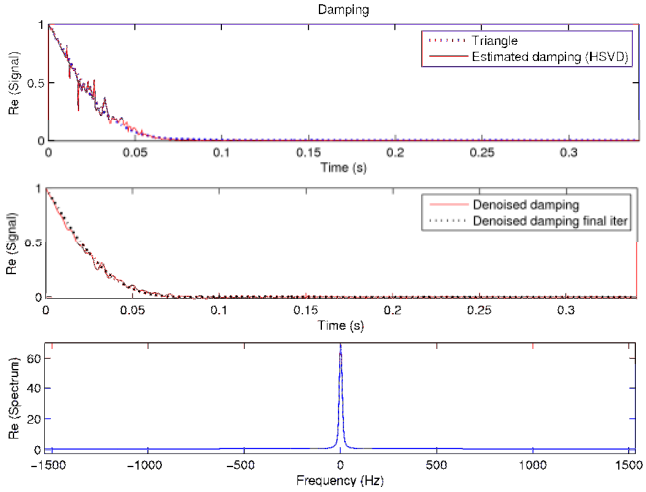

Fig.2. Top: Time domain signal of the triangular damping function with the estimated damping in an initial approach. Middle: Denoised damping in the first and last steps, where the estimation has already reached convergence. Bottom: Frequency domain of the damping function which resembles a Lorentzian shape characteristic for MRS signals.

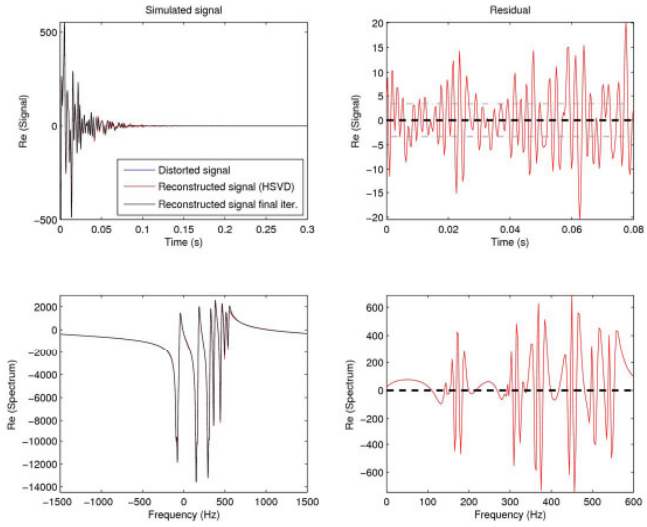

Fig.3. Final fitting of the signal using the damping estimated in Step iii. Left top: real part of the signal in the time domain, left bottom: corresponding real part of the spectrum. Right: Residuals for the first (solid line) and the last (dashed line) iterations. The norm of the residuals for the initial, second and last iteration are 127.5846, 0.7574, 0.0175, respectively.

Table I shows the results of convergence of the first 5 amplitudes and frequencies calculated using a Signal to Noise Ratio (SNR) of 50 and model orders 1 and 6 in HLSVD-PRO. When selecting the number of sinusoids to be used for the HLSVD-PRO method, we run our algorithm using different combinations of model orders, as it is applied at least 2 times for the denoising part. For this we consider 1 to 6 sinusoids to be evaluated in different combinations and calculating the RMSE of all of them. The RMSE of this model orders was compared and the minimum was selected. Finally, we chose 1-6 (i.e. model order=1 and =6 in step 4 and 7 of the algorithm respectively), which ever has the lowest RMSE. The first row indicates the true parameters and the following values are the estimates obtained in the successive iterations until convergence.

Table II 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 $g(t)$ 2 times as can be seen in the algorithm in Section II.C, for that reason there are 2 numbers in the HLSVD-PRO subtitle. The method was done using 1 to 6 sinusoids in different arrangements; The analysis was done using an SNR=50 to 10; however the stability at low SNR is still under investigation.

TABLE I. CONVERGENCE OF PARAMETER ESTIMATES

Results for the first five amplitudes and frequencies estimated using SNR=50 and HLSVD-PRO order 1-6				
Amplitudes				
Ampl.1	***Ampl.2***	***Amp.3***	***Amp.4***	***Ampl.5***
75.0000	150.0000	75.0000	150.0000	150.0000
82.6216	164.6005	134.2865	127.1447	223.4241
65.0874	158.0970	94.8358	147.6927	174.3433
63.4788	154.0152	92.4455	143.9448	169.8871
73.1479	154.2447	83.5502	151.2525	160.7305
75.8608	154.6093	78.7521	152.8109	157.2310
76.3930	154.5854	77.9131	153.7389	155.9945
77.6189	154.8951	76.9361	155.5419	155.5516
77.3898	154.8799	77.2298	155.3686	155.2685
77.5512	155.1123	77.4754	155.2634	155.1773
77.5944	155.1662	77.5466	155.1866	155.1746
77.6014	155.1733	77.5619	155.2128	155.1862
77.5997	155.1982	77.5889	155.1965	155.1858
77.5970	155.2010	77.5998	155.1982	155.1984
77.5994	155.2024	77.6011	155.2017	155.2032
77.6012	155.2034	77.6011	155.2026	155.2034
77.6015	155.2034	77.6016	155.2030	155.2035
77.6015	155.2033	77.6015	155.2030	155.2032
77.6015	155.2030	77.6014	155.2027	155.2029
77.6015	155.2026	77.6012	155.2024	155.2025
77.6014	155.2023	77.6011	155.2021	155.2022
Frequencies				
Freq.1	***Freq.2***	***Freq.3***	***Freq.4***	***Freq.5***
-86.0000	-70.0000	-54.0000	152.0000	168.0000
-87.5629	-74.4156	-49.8417	147.6822	170.0192
-86.3254	-71.2759	-56.7079	151.8834	166.9222
-86.1058	-71.0562	-56.4899	152.1023	167.1429
-85.7965	-70.2578	-54.9946	152.0118	167.5235
-86.0024	-70.1045	-54.5315	152.0003	167.8406
-85.9562	-70.0178	-54.3305	152.0945	168.1174
-85.8382	-69.9058	-54.0501	152.0747	168.0855
-85.8451	-69.8773	-53.9351	152.1330	168.1157
-85.8490	-69.8602	-53.8824	152.1460	168.1383
-85.8549	-69.8579	-53.8674	152.1444	168.1387
-85.8551	-69.8570	-53.8625	152.1426	168.1408
-85.8561	-69.8567	-53.8582	152.1439	168.1421
-85.8563	-69.8567	-53.8573	152.1438	168.1430
-85.8563	-69.8565	-53.8568	152.1438	168.1435
-85.8563	-69.8564	-53.8566	152.1436	168.1435
-85.8563	-69.8564	-53.8565	152.1437	168.1436
-85.8563	-69.8564	-53.8564	152.1437	168.1436
-85.8563	-69.8563	-53.8564	152.1437	168.1436
-85.8563	-69.8563	-53.8563	152.1437	168.1436
-85.8563	-69.8563	-53.8563	152.1437	168.1436

TABLE II. COMPARISON OF RMSE

RMSE for first parameters 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
6.9338	10.4493	10.4620	10.4722	11.12757

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 specific parameters applied to the signal; however, we look for an appropriate bias-variance trade-off based on the number of parameters used for the HLSVD-PRO method. By increasing the number of parameters, bias will decrease but variance will increase, and vice versa, we used the RMSE to find the best combination.

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 current effects. Here we use a simulated signal of ^{31}P with 11 metabolites and as distorted damping we use an asymmetric triangle. In addition, the first estimated parameters are calculated in [1] using NLLS while we use a combination HSVD–NLLS. Finally the iterative improvement using (5) is the main difference that makes our method a more consistent procedure.

V. CONCLUSIONS

Our results show that estimation of the lineshape for obtaining more realistic MRS signals is a useful method for obtaining 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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