An Automatic Time-Domain Algorithm for the Quantification of In Vivo Non-water-suppressed MR Spectroscopy: the Filter-Diagonalization Method (FDM)

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Introduction

The water suppression (WS) pulses in MRS scans may distort metabolite signals, making it difficult to accurately quantify the metabolites. On the other hand, it has been shown feasible to perform absolute metabolite quantification using non-water-suppressed (NWS) MRS techniques [1,2] in which the water signals are fit and then removed in post-processing. The un-suppressed water signal in NWS MRS can then serve as an internal reference for reliable metabolic quantification. Several time-domain methods based on singular value decomposition (SVD) have been developed to extract water signals from NWS MRS data [4]. However, the existing SVD-based methods are not well suited for quantifying metabolites due to several limitations. First, the optimal number of resonances (rank) to be fitted needs to be determined in advance for the whole spectral range, making existing methods less general. Second, the computational cost for the current time-domain data processing methods is high, particularly for MR spectroscopic imaging. Here we propose to use the Filter-Diagonalization Method (FDM) [6], an algorithm originally developed for quantum dynamic computation, to reliably and automatically quantify the metabolite signals in NWS MRS with a very economic computational cost. In comparison to the existing methods, FDM has a much better localization property and can be applied to analyze a selected spectral range, greatly reducing computational cost [6].

In our studies, we first compared with computer simulations the performance of three different time-domain MRS data processing methods: FDM, matrix-pencil method (MPM) and LPSVD. The FDM-based metabolic quantification was then verified with a spectroscopic calibration phantom, which contained lactate solution of different concentrations. Furthermore, the FDM was used to process *in vivo* NWS MRS data. N-Acetyl aspartate (NAA), Creatine (Cre) and Choline (Cho) were quantified using unsuppressed water signal as a reference.

Theory and Methods

FDM Algorithm: MR signals in the time domain can be modeled as a summation of complex exponential decays: $y(n)=\Sigma d_k u_k^n + w_n$, where u_k and d_k are poles (chemical shift frequency and T2*) and amplitudes (magnitude and phase) respectively of each metabolite resonance; and w_n is the noise. This function can be rewritten using a time-correlation function, and u_k can be solved in a generalized eigenvalue equation $U^{(1)}B_k=u_k U^{(0)}B_k$, where u_k are the eigenvalues and B_k are the eigenvectors. The $U^{(1)}$ and $U^{(0)}$ matrices are constructed from a local basis set in the selected spectral range and d_k can be calculated from B_k and $U^{(0)}$. This process is repeated several times until the whole spectral range is covered [6]. The FDM algorithm was implemented using Matlab in a Linux-based Intel PC (P-M 1.7GHz CPU) with an optimized blas-atlas library.

Simulation: MR spectra with a water peak and a triplet at different SNR values were simulated. The SNR definition is $SNR \equiv 10\ log_{10}(A/\rho)$, where A represents the amplitude of triplets and ρ is the standard deviation of the random noise. Three algorithms, FDM, MPM, and LPSVD, were applied to extract the triplet peaks and the errors of the extracted amplitudes were calculated for different SNR values (100 simulations in each SNR value).

NWS MRS Experiments (phantom and human): Four spherical spectroscopic phantoms containing lactate solution with concentrations of 5mM, 10mM, 50mM, and 250mM were scanned in a 3T scanner using the single voxel PRESS sequence without water suppression (TE/TR=288/2000 ms, spectral bandwidth = 3003Hz, sampling points = 4096, and NEX=32). FDM was applied to quantify the concentration of lactate using water scaling method. The Lactate/H_2O ratio was then compared with the known lactate concentrations. For *in vivo* MRS experiments, a 2x2x2 cm^3 volume located at the white matter in the parietal lobe was acquired from a healthy subject using single voxel PRESS with parameters TE/TR = 40/2000 ms, spectral bandwidth = 2 KHz, sampling points= 2048, and NEX= 128. Concentrations of NAA, Cre, and Cho were calculated using the unsuppressed water signal as a reference.

Results and Discussion

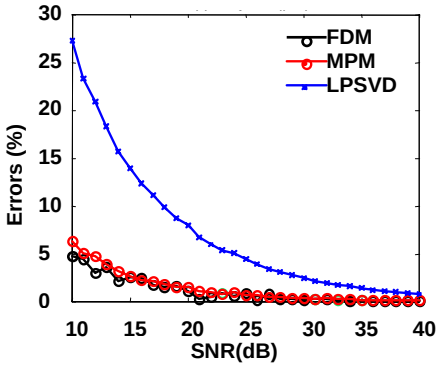

Figure 1 (Simulation): Averaged errors of three algorithms, FDM, MPM, and LPSVD, in 100 simulations at different SNR values.

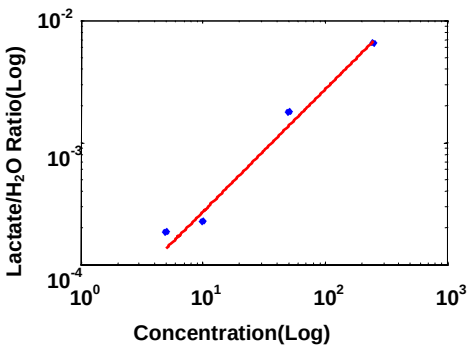

Figure 2 (Phantom scan): The lactate-to-water signal ratio (lactate/H_2O) against the lactate concentrations in a logarithmic scale. Strong correlation was found between concentrations and the signal ratio (R^2=0.993)

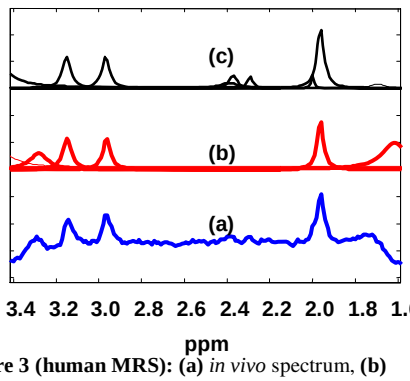

Figure 3 (human MRS): (a) *in vivo* spectrum, **(b)** synthetic spectrum using MPM, and **(c)** synthetic spectrum using FDM. Note that the water signal is fitted and subtracted from the NWS MR spectrum.

Figure 1 shows that, in the simulation study, the FDM and the MPM reach similar accuracy levels in quantification, while the errors in LPSVD are larger. The computation time for FDM was 2.2 seconds for 400 points, and 4.7 seconds for 600 points. The results of our phantom study are shown in Figure 2. It can be seen that the lactate concentrations can be calculated with FDM with high accuracy (R^2=0.993). The results of our *in vivo* MRS study are shown in Figure 3. The FDM analysis is capable of automatically resolving glutamate and glutamine peaks between 2.3 to 2.4ppm (Fig.3(a)), which were not detected by the MPM algorithm (Fig.3(b)). The calculated values of NAA, Cre, and Cho concentrations are 13.8, 8.6 and 2.63 mM in our study, which are in a good agreement with values reported by other groups using the water scaling method (14.26±1.38, 7.1±0.67 and 2.65±0.25 mM for NAA, Cre and Cho respectively) [7]. In conclusion, we have demonstrated that FDM can reliably and automatically quantify the metabolite signals for *in vivo* NWS MRS. Our data show that the FDM, with its capability of automatically detecting all peaks including glutamate and glutamine, is superior to the state-of-the-art MPM algorithm and should prove a useful tool for *in vivo* MRS studies.

Acknowledgment

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References

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