Separation of EMCL and IMCL in musculoskeletal 1H MR spectra by Filter-Diagonalization method (FDM)

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Introduction

Measuring intramyocellular lipids (IMCL) in 1H MRS has been popular for its relation to insulin sensitivity, diabetes and obesity (1). However, quantification of IMCLs are often difficult because they are strongly overlapped with extramyocellular lipids (EMCL)(2, 3). The time domain algorithms offer many advantages for the quantification for separating IMCL and EMCL (1,4). First, the time domain methods usually require shorter signals but still exert high spectral resolution (5). Second, background contamination of macromolecules should be minimized, while the background accommodation can be done much easier in time domain (6).

Among all the time-domain fitting methods, the Filter-Diagonalization Method (FDM) is a frequency-selective time domain method (7), which has several superior properties compared with other time-domain fitting methods. First, the fitting can be focused on a narrow frequency range other than whole spectral range. Second, its computation loading is lower than other singular value decomposition (SVD) based time-domain methods. Last year, we have demonstrated that FDM can successfully quantify three major metabolites on in vivo MRS of brain. We found that FDM perform well in extracting singlets other than multiplets even when the peaks are closely overlapped. In this preliminary study, we investigate the possibility of FDM to separate of EMCL and IMCL on in vivo MRS of muscle since lipid metabolites often have better signal to noise ratio and show simple spectra l singlet.

Theory and Method

The MRS time domain signals are modeled as sum of exponential decays: $x(n)=\Sigma d_k u_k^n + w_n$, where u_k and d_k are pole (chemical shift frequency and T2*) and amplitude (magnitude and phase) of k-th metabolite resonance; and w_n is the noise. The signals $x(n)$ form large Hankel matrices $\mathbf{X_0}$ and $\mathbf{X_1}$. Then the large $\mathbf{X_0}$ and $\mathbf{X_1}$ matrices are multiplied by the short time Fourier matrix $\mathbf{F}$ forming the $\mathbf{U_0}$ and $\mathbf{U_1}$: $\mathbf{U_0}=\mathbf{F}\,\mathbf{X_0}\,\mathbf{F}^T$, $\mathbf{U_1}=\mathbf{F}\,\mathbf{X_1}\,\mathbf{F}^T$ (where ^{T} is matrix transposition)

Here the $\mathbf{F}$ matrix can focus the solution inside the basis. The eigenvalues$\{\alpha/\beta\}$ of the generalized eigenvalue equation $\beta\,\mathbf{U_1}\,\mathbf{V}=\alpha\,\mathbf{U_0}\,\mathbf{V}$ are signal poles u_k. The amplitudes d_k s, are derived from normalized eigenvectors: $d_k=[(\mathbf{F}\mathbf{X}_{0I})\mathbf{V}_k]^2$ (the k represents the k-th column).

Data Acquisition and Processing:

The single voxel spectrum was acquired on a 3T system (Trio, Siemens Medical Solutions, Erlangen, Germany) with scan parameters: TR=1500ms, TE=35ms, NEX=64, VOI=15x15x20mm^3. Voxel was located at a healthy subject's calf. The build-in PRESS sequence with automatic shimming was used. The FDM algorithm was written by c++ language on a Linux 32-bit PC, with external netlib's LAPACK, BLAS (basic linear algebra subroutine) library, and IT++ library (patched to use the zggevx subroutine). Only the first 200 points were used for processing. No zero-filling, apodization, or noise suppression was performed before the FDM processing. The $\mathbf{F}$ matrix is constructed by 2 narrow band basis, chosen to find the EMCL's and IMCL's ethyl groups, centered at 1.49ppm and 1.28ppm (8) with 0.05ppm in width. The complex generalized eigenproblem is solved by LAPACK's zggevx subroutine. The amplifying eigenvalues ($|\{\alpha/\beta\}| > 1$) arisen from the numerical errors are deleted. The total processing time is within several milliseconds.

Results and Dicussion

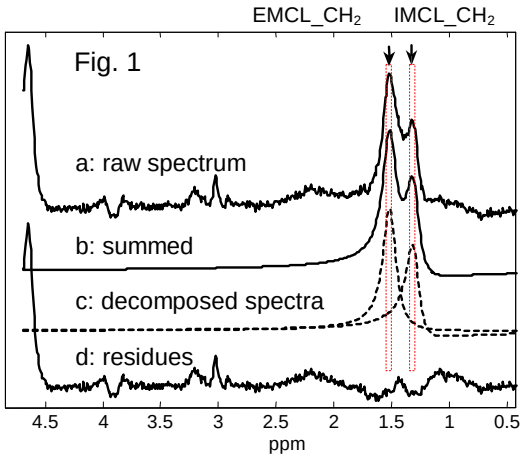

Figure 1 shows the fitting results a) raw spectrum, b) the fitted spectrum using FDM, c) the decomposed EMCL and IMCL component, d) the residues of spectrum. Arrows indicate the basis at 1.3 ppm and 1.5 ppm(red-boxed region). The CH_2 groups of EMCL (EMCL_CH_2)and IMCL(IMCL_CH_2) are located inside the basis. We found the FDM can well separate the EMCL and IMCL peaks. (Figure 1c) The basis we choose can extract the poles inside the interested region, while suppressed the poles outside. Therefore, the quantification of EMCL or IMCL is immune from outside metabolites contamination.

Several requirements have to be satisfied to successfully use FDM. First, spectra have better to be gathered in global homogenous field to full-filled the time domain exponential model. Second, the peaks have better to be located at the center of basis to prevent the distortion occurring at the edge of basis. In this study, we incorporate the frequency information of EMCL_CH_2 and IMCL_CH_2. Third, the SVD could be included into the algorithm to improve its stability. Fourth, the signal to noise ratio (SNR) and spectral bandwidth should be high enough. In this work, the data has only 64 averages; sampling frequency is only 1kHz. Higher quality spectra with more average and wider bandwidth should be obtained before we can quantify the small methyl groups (EMCL_CH_3 and IMCL_CH_3)(2). In summary, our preliminary result shows the FDM can reliably resolve the overlapping peaks. Performance of FDM should be studied by collecting more data set. The FDM may be useful not only as a preprocessing method but also as a tool directly quantifying the metabolites. In the future we will further investigate the FDM on the non-water suppressed muscular MRS where water signal can be extracted as an internal concentration reference for absolute quantification.

Ackowledgement

We thank the National Taiwan University Hospital for technical support on 3T MR system

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