

Clinical MRS data processing using KBDM

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TARGET AUDIENCE: MR physicists, MR spectroscopists and clinicians.

PURPOSE: To introduce a new mathematical tool for data processing of clinical magnetic resonance spectroscopy (MRS).

INTRODUCTION: The Fourier transform (FT) theory has been used worldwide during the past decades and is a powerful mathematical tool for a broad range of applications, including the spectral analysis of NMR signals. However, there are situations in which the FT spectral analysis of a given NMR time-domain data can become a difficult task. To overcome some difficulties, techniques such as FT-based back-prediction, linear prediction, maximum entropy method, Krylov basis diagonalization method (KBDM) and filter diagonalization method (FDM) have been proposed. KBDM, in focus here, is a promising tool that can provide complementary information to the well-established FT techniques. In the present study we evaluate the feasibility of clinical MRS data processing using KBDM, paying attention to important issues related to signal-to-noise ratio (SNR) and baseline distortions. The latter is particularly critical in *in vivo* short echo-time MRS and is a well-known confounder for proper quantification of selected spectral peaks.

METHODS: KBDM is a parametric non-linear method that can be applied for fitting and spectral analysis of experimentally measured transient time signals [1-4]. A comprehensive description and a review of the algorithm for one- and multi-dimensional problems can be found in the literature [3]. To illustrate the main characteristics and performance of the KBDM we present a non-trivial example based on a numerically simulated data, generated to mimic typical experimental clinical spectra. For this purpose, the simulated spectrum was based on experimental clinical MRS brain data, as indicated by spectrum S1 in Fig. 1. To increase the complexity of the problem, we artificially added a much intense baseline composed by spectrum S2, generated with the same peaks, with same amplitudes but 10 times broader than the corresponding peaks in S1. The resulting spectrum is shown as S3 in Fig. 1. These spectra were simulated with 2048 points and a dwell time of 500 μ s. The KBDM algorithm was implemented in the code builder environment of Origin C (OriginLab, Northampton, MA). To evaluate the ability of the KBDM in dealing with noisy signals, random normally distributed noise was gradually added to the free induction decay signal (FID) corresponding to spectrum S3, before subsequent analysis. A clinical spectrum was obtained from a 26 years old healthy adult volunteer, scanned under an Institutional Review Board (IRB)-approved protocol on a 3T Philips Achieva (Philips Medical Systems, The Netherlands). Single voxel spectroscopy was performed using a point-resolved spectroscopy sequence (PRESS) with the following parameters: TE/TR = 31/2000 ms, 2048 spectral points and 2 kHz receiver bandwidth. A voxel size of 25x25x25 mm positioned at the posterior cingulum was used and a total of 96 measurements were averaged resulting in an acquisition time of 3 min and 12 sec. Before obtaining the spectra, automatic shimming and water suppression procedures were conducted by the scanner.

RESULTS: In the absence of noise the KBDM is capable to characterize exactly all spectral components present in the spectrum S3 of Fig. 1 within computer arithmetic precision (results not shown). However, some fluctuation in the spectral estimation is observed when noise is added to the simulated spectrum. Fig. 2 shows the estimated areas of some selected peaks obtained from the processing of spectra at different noise levels. Noise can impose a serious limitation for the KBDM, but, it can be depicted from Fig. 2 that the estimated areas are reasonably stable even when a relatively large amount of noise is added to spectrum S3 under analysis. Fig. 3 shows the S3 spectrum with a RMS noise level of $2E-4$, which results in a SNR of approximately 15 (measured at the highest peak), which is close to the typical SNR achieved in brain spectra obtained in clinical 1.5 T systems. The estimated spectrum obtained by KBDM is also shown, where it can be noticed the high correspondence between experimental and KBDM-edited spectra. Fig. 4 shows a clinical MRS spectrum and the KBDM-edited one. At the bottom row is shown the fitting residue illustrating the high accuracy of the KBDM estimate. From the KBDM analysis of this data we obtained NAA/Cr = 1.37, Cho/Cr = 0.55 and M-Ins/Cr = 0.56, in agreement with previously reported values [5].

DISCUSSION AND CONCLUSIONS: We have shown that quantification of MRS data by means of the KBDM can lead to accurate spectral analysis for both simulated and *in vivo* data. Despite the presence of noise in the simulated and real data, the method was capable to properly quantify each of the main selected metabolites, even when a very intense baseline was added as a confounder in the simulated spectrum. The possibility to edit the KBDM line list may be useful for the analysis of overlapping peaks, which still represents a challenge for conventional processing approaches. The KBDM-edited spectra closely reproduces the original data, even in the case of real experiments, in which the relations obtained for some of the main brain metabolites are in agreement with previously published data, corroborating the accuracy of the quantification promoted by KBDM. Another potential application of the KBDM resides in the processing of time-resolved spectroscopy data, which could be an alternative to overcome some limitations imposed by FT in functional MRS. Further studies are in progress to extend the applicability of KBDM to other fields.

REFERENCES: [1] Mandelshtam VA, Taylor HS. *Journal of Chemical Physics* 1997;107:6756-6769. [2] Mandelshtam VA, Taylor HS. *Physical Review Letters* 1997;78:3274-3277. [3] Mandelshtam VA. *Progress in Nuclear Magnetic Resonance Spectroscopy* 2001;38:159-196. [4] Magon CJ et al. *Journal of Magnetic Resonance* 2012;222:26-33. [5] Kantarci K et al. *AJNR* 2003;24:843-849.

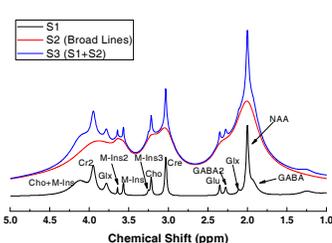


Figure 1: Simulated spectrum based on experimental clinical MRS data (S1). Broad lines spectrum (S2) generated to mimic the baseline contribution found in short echo time *in vivo* MRS. Resulting spectrum (S3) obtained from the sum of spectra S1 and S2.

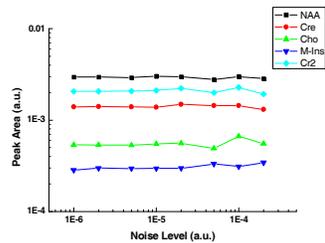


Figure 2: Peak areas obtained for different noise levels in the simulated spectrum S3.

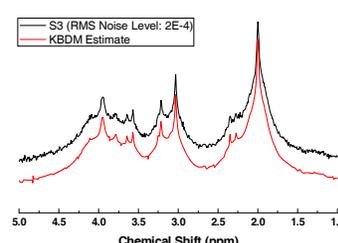


Figure 3: S3 spectrum with noise added (black line) and the KBDM-edited spectrum (red line).

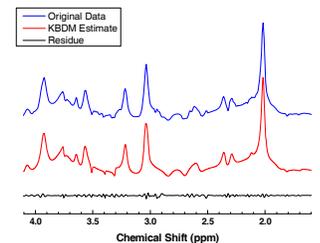


Figure 4: Clinical MRS spectrum (top row), the estimated spectrum by the KBDM (middle row) and the fitting residue (bottom row).