Two-Dimensional *J*-resolved Spectroscopy Fitting

R. F. Schulte[1], P. Boesiger[1]

[1]Institute for Biomedical Engineering, University and ETH Zurich, CH-8092 Zurich, Switzerland

Introduction

J-coupled metabolites are generally difficult to detect and quantify *in vivo*. Promising approaches are spectral editing and multi-dimensional spectroscopy. A simple and useful 2D sequence providing better distinction of the *J*-coupled resonances is 2D *J*-resolved spectroscopy (JPRESS) [1]. The maximum information contained in the spectra can be extracted through fitting directly in two dimensions with all the prior knowledge available. A first attempt to fit in 2D was made through the 2D Hankel singular value decomposition [2], which fails to yield satisfactory results for *in vivo* JPRESS spectra due to experimental imperfections, the impossibility to impose prior knowledge and other conceptual shortcomings. Another attempt was made through fitting 2D spectra as constrained 1D fits [3] without Fourier transforming the indirect dimension. However, this was only applied to glutamate phantoms yielding limited benefits. In this work a fully two-dimensional fitting procedure is presented, which is capable of applying the complete prior knowledge. *In vivo* T_2 relaxation times are directly obtained for a wide range of metabolites.

Theory and Methods

The 2D fitting procedure is based on two complementary approaches - LCModel [4] for providing the maximum prior knowledge constraint and VARPRO [5] for minimising the degrees of freedom. The JPRESS spectra are fitted in the frequency domain, mainly because of convenience of implementation. A linear combination of model spectra approximates the measured spectrum based on the following optimisation parameters: individual for each metabolite are the concentration, line broadening and a small chemical shift. The global parameters for the whole spectrum are the phase and a line shape distortion function. Several strategies are applied to restrict the numerous degrees of freedom. The fitting is split up (Fig.1) - similar to VARPRO [5] - into a non-linear outer loop for optimising the non-linear parameters, such as line broadening and phase. In an inner step, the basis spectra are updated to the given parameters from the outer loop. The spectrum is approximated by this basis through a linear least squares fit, yielding the individual concentrations. Since the concentrations are not optimised in the outer loop, the degrees of freedom are reduced and the robustness is increased compared to a complete non-linear fit. Further strategies for a successful fit are a good initialisation, starting close to the minimum and repeating the fitting procedure four times, each time with increasing the degrees of freedom and initialisation with the result of the preceding step.

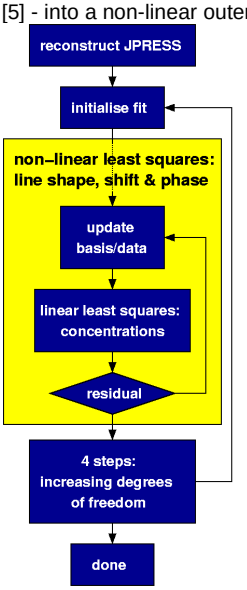

Fig. 1: Principle functioning of the 2D fitting procedure.

The basis spectra were simulated numerically with the GAMMA library [6]. All experiments were performed on a Philips Intera 3T scanner equipped with a transmit/receive head coil. Twenty-seven healthy volunteers with written informed consent (age 35.4±7.5) were measured in the parietal lobe. PRESS was acquired with T_E=31ms, T_R=2.5 s and 256 averages for comparison with LCModel [4]. JPRESS was acquired with T_E=31 to 229 ms, ΔT_E=2 ms, T_R=2.5 s, 100/2048 samples in t_1/t_2, BW=0.5/2 kHz in f_1/f_2 and a four-step phase-cycling scheme. The data was eddy current corrected, reconstructed to JPRESS, truncated to the spectral region of interest and then fitted (Fig. 1). All post-processing was implemented in Matlab. A Nelder-Mead simplex direct search algorithm (function fminsearch) was used for the non-linear fit, due to its capability of circumventing local minima.

Results

The fitting routine is robust and generally converges to a solution. The residual is usually small (Fig. 2) and reproducibility is in the range of physiological changes for the predominant singlets. Metabolites with a Cramer-Rao lower bound of more than 20% were excluded. The concentration ratios to creatine (mean ± standard deviation; number of included spectra) for the volunteers are: NAA/NAAG 1.65±0.16; n=27, total choline 0.28±0.04; n=27, glutamate 1.77±0.49; n=27, myo-inositol 1.19±0.39; n=27, glutathione 0.60±0.31; n=27, glycine 0.14±0.06; n=23, scyllo-inositol 0.046±0.024; n=20, glucose 0.39±0.25; n=12, alanine 0.22±0.12. High inter-subject standard deviations (around 100%) with many exclusions due to too high Cramer-Rao bounds were found for the other metabolites included in the fit, namely aspartate, GABA, glutamine, lactate, phospho-ethanolamine and taurine.

The T_2 relaxation times are directly given by the line widths in the indirect dimension. The times range from 60ms to 270 ms with standard deviations of 15% to around 50%. Metabolites with a long T_2 include the predominant singlets. Most of the other metabolites decay in less than 100 ms. The agreement of the averaged concentration ratios between the 2D fit and LCModel is excellent for the predominant singlets; NAA/NAAG is 9% and total choline 7% higher with 2D fitting. The concentrations determined with 2D fitting are consistently higher for glutamate (78%), glutathione (110%) and myo-inositol (81%). The other metabolites are not reliably quantified through LCModel at this field strength.

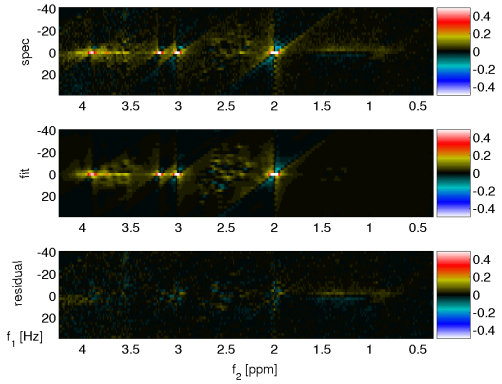

Fig. 2: Typical JPRESS spectrum in vivo (top), its fit (middle) and the fit residual (bottom row) plotted on logarithmic scale. No baseline is included in the fit.

Discussion and Conclusion

The direct 2D fitting of JPRESS is a useful and promising approach for the *in vivo* detection and quantification of many *J*-coupled metabolites, which are currently difficult if not impossible to assess. The underlying limitation in 2D is not governed by the overlap of metabolites any more, but rather by sensitivity. The whole procedure is fully automatic and easily applicable even in the clinical routine. A big advantage over other forms of editing is the estimation of the individual quantification errors through the Cramer-Rao lower bound.

The baseline in JPRESS is flat and well-behaved and was not included in the fit, hence reducing the uncertainty of the fit. This might explain the differences in concentrations to LCModel [5], where the baseline is modelled through broad singlets and splines. Furthermore, different relaxation behaviour inside the measured basis spectra might underestimate the concentrations of metabolites with short T_2 times in case of LCModel, as the PRESS echo time is about half the *in vivo* T_2 relaxation. As one usually looks at concentration changes in spectroscopy, this consistent difference is unproblematic.

References

[1] Ryner LN, et al. Magn Reson Imaging 1995; 13: 853.
[2] de Beer R, et al. Pure Appl Chem 1992; 64: 815.
[3] Slotboom J, et al. ISMRM 1999: 1561.
[4] Provencher SW. Magn Reson Med 1993; 30: 672.
[5] van der Veen JW, et al. Magn Reson Med. 1988; 6: 92.
[6] Smith SA, et al. J Magn Reson Ser A 1994; 106: 75.