ProFit: Two-Dimensional Prior-Knowledge Fitting of *J*-Resolved Spectra

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Introduction

In-vivo proton magnetic resonance spectroscopy is limited mainly by sensitivity and spectral overlap. In particular *J*-coupled metabolites are difficult to detect as they are often covered by stronger signals from other resonances. A powerful method to alleviate the overlap and increase specificity is two-dimensional *J*-resolved spectroscopy (*J*PRESS) [1]. The maximal information can be extracted from the data by two-dimensional fitting. In this work, a genuine two-dimensional fitting procedure is presented, capable of applying the whole amount of prior-knowledge. Previous results [2] are considerably improved by enhanced regularisation and additional verifications further support the credibility of the proposed method.

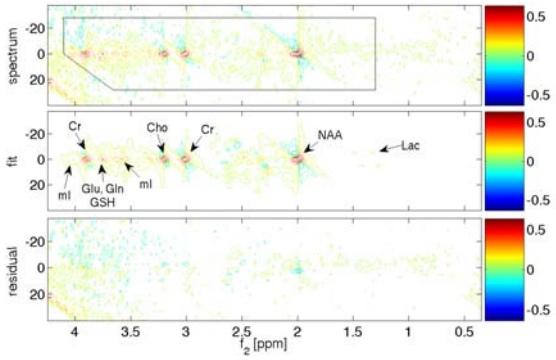

Figure 1: Typical *J*PRESS spectrum *in vivo* (top), its fit (middle) and the fit residual (bottom) plotted in logarithmically scaled contour plots. All spectra are fitted and plotted in phase-sensitive mode. The black box in the upper plot depicts the spectral region of interest used for minimising the fit residual.

Methods and Materials

ProFit [2] is based on two complementary 1D techniques: The concept of "linear combination of model spectra" (LCModel) [3] provides the maximal prior-knowledge constraint, while VARPRO [4] reduces the degrees of freedom of the fit by dividing it into a linear and non-linear part. The concentrations are determined in the cost function of the non-linear optimisation by linear least squares. The cost value is given by the sum of squared fit residual plus a term for regularisation, which guides the fit towards a typical exponential line-broadening and limits the shift in f_2. The reliability of the determined concentrations is evaluated by Cramér-Rao lower bounds and by the ratio of the two creatine peaks, which were fitted with separate basis functions.

The measurements were performed on a Philips Intera 3T whole-body scanner equipped with a transmit/receive head coil. The *J*PRESS experiment applied a maximum-echo sampling scheme and TEs ranged from 31 ms to 229 ms in steps of 2 ms and TR = 2.5 s. With a four-step phase cycling for each TE, this amounts to a total scan duration of 17 minutes. The bandwidths in f_1 and f_2 were 0.5 kHz and 2 kHz with 100 and 2048 sampling points, respectively. For validation, phantoms containing metabolites in approximate *in-vivo* concentrations [5] were measured ten times. In another experiment, the amount of GABA and GSH in this *"in-vivo"* phantom was varied and detected. The *in-vivo* experiments are described in Table 1.

Metabolites	intra-subject						inter-subject					
	*J*PRESS/ProFit			PRESS/LCModel			*J*PRESS/ProFit			PRESS/LCModel		
	inc	Cr ratio	SD [%]	inc	Cr ratio	SD [%]	inc	Cr ratio	SD [%]	inc	Cr ratio	SD [%]
NAA/NAAG	21	1.53	3.25	22	1.25	4.86	26	1.74	6.13	27	1.51	7.57
GPC/PCh	21	0.325	4.52	22	0.285	8.21	26	0.282	9.12	27	0.252	12.7
Glu	21	1.18	6.06	22	0.757	10.6	26	1.28	13.1	27	0.962	10.1
mI	21	1.06	9.89	22	0.708	8.73	26	0.99	18.4	27	0.667	15
GSH	21	0.24	14.7	22	0.221	14.8	26	0.256	11.8	26	0.263	23.7
GABA	21	0.124	16.8	0	-	-	23	0.172	22.2	0	-	-
Ala	13	0.061	18.9	0	-	-	20	0.11	47.6	0	-	-
Asc	21	0.433	20	0	-	-	26	0.468	29.1	0	-	-
Asp	21	0.349	14.7	16	0.258	15.5	24	0.412	31.3	5	0.321	11.9
Glc	21	0.348	25.2	0	-	-	25	0.368	30.8	0	-	-
Gln	21	0.187	18.7	0	-	-	20	0.213	17.1	0	-	-
Gly	21	0.101	14.1	-	-	-	24	0.123	20.9	-	-	-
Lac	19	0.072	24	1	0.084	0	22	0.12	19.5	1	0.953	0
PE	21	0.386	24.1	7	0.377	11.2	26	0.408	28.1	2	0.67	17.9
Scy	21	0.04	11.9	19	0.039	12	26	0.049	41.2	17	0.059	34.2
Tau	4	0.115	31.4	14	0.299	23.3	1	0.242	0	11	0.298	25.7
Cr 3.91	21	1.09	6.22	-	-	-	26	1.07	6.52	-	-	-

Table 1: *In-vivo* fit results. For the intra-subject comparison, one healthy volunteer (age 32 years; male) was measured eleven times in the right and left frontal lobe. No significant difference exists in between the hemispheres (t-test with a significance level of $\alpha = 0.05$) and therefore both sides are averaged. For the inter-subject comparison, 27 healthy volunteers (age 35.4±7.5 years) were measured in the occipital lobe. All voxels had a volume of ≈15 ml and contained mainly grey matter. The number of included metabolites in the analysis is denoted by "inc". Exclusion criteria are Cramér-Rao lower bounds (>20%) and ratios of Cr at 3.91 ppm to Cr at 3.03 ppm (>1.3). Gly was excluded from the LCModel fitting due to too heavy overlap with mI.

Results and Discussion

Quantification of *J*PRESS spectra with ProFit is accurate, robust and yields consistent results, both *in vivo* and *in vitro*. The intra-subject standard deviation (SD) (Table 1; left) and the SD in a repeated phantom measurement (not shown) is small for the pre-dominant singlets (≈ 4 %). Most other metabolites are usually detectable with a SD in the range of 5-25%. The inter-subject SD (Table 1; right) is larger than the intra-subject SD due to additional individual variability. The comparison to PRESS (TE = 31ms; TR = 2.5 s; n = 128 (intra-subject); n = 256 (inter-subject)) evaluated with LCModel reveals that ProFit detects more metabolites and generally decreases the SD for metabolites detectable with both methods. The SDs suggests that the number of quantifiable brain metabolites can be increased from seven with LCModel (i.e., Cr, GPC/PCh, NAA/NAAG, Glu, mI, GSH and Scy) to 16 with *J*PRESS/ProFit (additionally: GABA, Ala, Asc, Asp, Glc, Gln, Gly, Lac and PE). However, the following metabolites should be interpreted with caution: Asp, Glc and PE failed to yield reproducible results in phantom experiments, while being overestimated *in vivo* as compared to literature values [5]; Gln is too low *in vivo*; Lac is (partly) in a spectral region with many macromolecules, hence quantification might be impaired; Gly appears to be contaminated by the much larger mI resonance. The remaining three metabolites can be accurately detected with *J*PRESS/ProFit: GABA, Ala and Asc. Most importantly, the detection accuracy of the eight metabolites also detectable with LCModel is generally increased with ProFit.

Conclusion

The combination of *J*PRESS with ProFit is a viable alternative to other forms of editing, yielding a wealth of information in a single experiment. The quality of the spectra and fit can be assessed objectively by the Cramér-Rao lower bound.

References

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