T_2 relaxation times of seven individual macromolecules in rat brain ^{1}H MR Spectra at 9.4T: single inversion recovery and AMARES post processing

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Synopsis

At short echo times 1H-MR spectra contain the contribution of mobile macromolecules (MM), i.e. broader resonances characterized by shorter relaxation times (T_1,T_2) which underlie the narrower peaks of metabolites. There are very few studies assessing MM T_2 relaxation times, with only one study reporting T_2-s of individual MM peaks in the full ppm range at 9.4T in the human brain. In this work we present a new approach: single inversion recovery with an optimized inversion time combined with AMARES post-processing. Using this technique we quantified 10-MM components and estimated T_2 relaxation times (for 7-MM components) in rat brain at 9.4T.

Introduction

At short echo times (TE) ^{1}H-MR spectra contain the contribution of mobile macromolecules (MM), i.e. broader resonances characterized by shorter relaxation times (T_1 and T_2) which underlie the narrower peaks of metabolites. There are very few studies assessing the MM T_2 relaxation times[1–3], with only one study reporting T_2-s of individual MM peaks in the full ppm range at 9.4 T in the human brain[4]. Otherwise, only the peaks till 1.7ppm have been reported or full MM[2] or grouped MM[3] T_2s, since measuring T_2 of all individual MM is not straightforward due to the overlapping metabolites and requires more complex and sophisticated approaches. In this work we present a new approach: a single inversion recovery (IR) with an optimized inversion time combined with AMARES post-processing, allowing to quantify 10 MM components and estimate T_2 relaxation times for 7 MM components in the rat brain at 9.4 T.

Methods

For measuring the *in vivo* spectrum of macromolecules, the SPECIAL[5] sequence was extended with a 2 ms non-selective hyperbolic secant inversion pulse, applied at an inversion time (TI) of 750 ms before starting the localization part of the sequence[6]. All the *in vivo* MM spectra were acquired in rat brain (9.4 T system Magnex Scientific) in a voxel of 3x3x3 mm^3 centered on the hippocampus (n=5). This VOI was selected in order to increase the SNR while it is well accepted that MM do not substantially change between brain regions in rodents[7,8]. The metabolite residuals present in the acquired MM spectrum were identified using: 1) a series of IR spectra using a full range of TI (i.e. 420-1000 ms); and 2) and IR spectrum with a longer echo time (TE around 40 ms) to confirm the presence of the residual metabolite signals (Figure 1A-B).
For the measurement of MM T_2 relaxation times the TE was varied from 2.8 to 150 ms (TE=2.8, 4, 6, 8, 10, 12, 16, 20, 40, 60, 100, 120 and 150 ms, TI=750 ms).

Data processing

Elimination of metabolite residuals

The spectra were phased individually in jMRUI (http://www.mrui.uab.es/mrui/) and 2 Hz of line broadening was applied. Each MM spectrum was manually inspected to determine the presence of metabolite residuals based on the spectra acquired at different TIs (TE=2.8 ms) and at the TE=40 ms (TI=750 ms) (Figure 1A-B). Using AMARES algorithm[9] (advanced method for accurate, robust and efficient spectral fitting) the constraints on the peak frequency, phase, linewidth (lw) and amplitude were fixed to fit the residual metabolites (Ins, tCr, Glx, Tau, NAA) and thus their contribution was removed from the MM spectra (Figure 1C).

Quantification of the MM and T_2 fits

MM were then divided into 10 components (Figure 2) and quantified using AMARES. Each MM component was quantified using several Lorentzian lines in order to obtain the best possible match with the original spectra. Figure 2 shows the constraints in frequency, number of peaks and linewidth which were given to AMARES as prior knowledge for quantification, while the amplitude was left to be estimated freely by the algorithm. After each quantification, the spectra were manually inspected. In some cases (longer TEs) soft constraints on the amplitudes of the peaks were additionally imposed to avoid over or underestimation. Since the spectra were acquired from 5 different animals, the obtained MM amplitudes for all the TEs were normalized to one rat always using $M_{0.94}$ component. $M_{0.94}$ was used since it is reliably quantified and does not overlap with metabolite resonances. The quantified and normalized amplitudes were fitted to a single exponential decay across the TE series to estimate the T_2 relaxation times.

Results and discussion

The excellent quality of the in vivo acquired MM is shown in Figure 1. All acquired spectra showed excellent SNR. The proposed post-processing method was efficient and robust in removing all the residual metabolites providing clean MM spectra for quantification and fitting. All the 10 components were quantified (at different TEs). For 7 components reliable exponential decay fits were obtained (standard deviation of the fit was lower than 20%), leading to reliable T_2 estimations. The MM at 0.94, 1.22, 1.43 and 3.00 ppm all presented similar T_2 relaxation times in-between 22-24 ms, the ones at 1.70, 2.05, 3.21 were in-between 12-15 ms. The obtained fits and T_2 values are shown in Figure 3A,B and are in good agreement with previously reported values[1,4].

Conclusion

This study proposed a novel methodological approach allowing reliable post-processing and quantification of the MM spectra, together with T_2 relaxation time estimates of 7 individual MM components in the rat brain at 9.4 T. The described method also provides an efficient tool for a potential parametrization of individual MM. The information obtained by parametrization can be further used as an individual MM basis set for spectral quantification and detection of individual MM changes in pathologies. Furthermore, this approach can fully characterize the MM spectra at different TIs and TEs and this can provide a comprehensive set of information necessary in a MM dictionary for MR fingerprinting[10].

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Figures

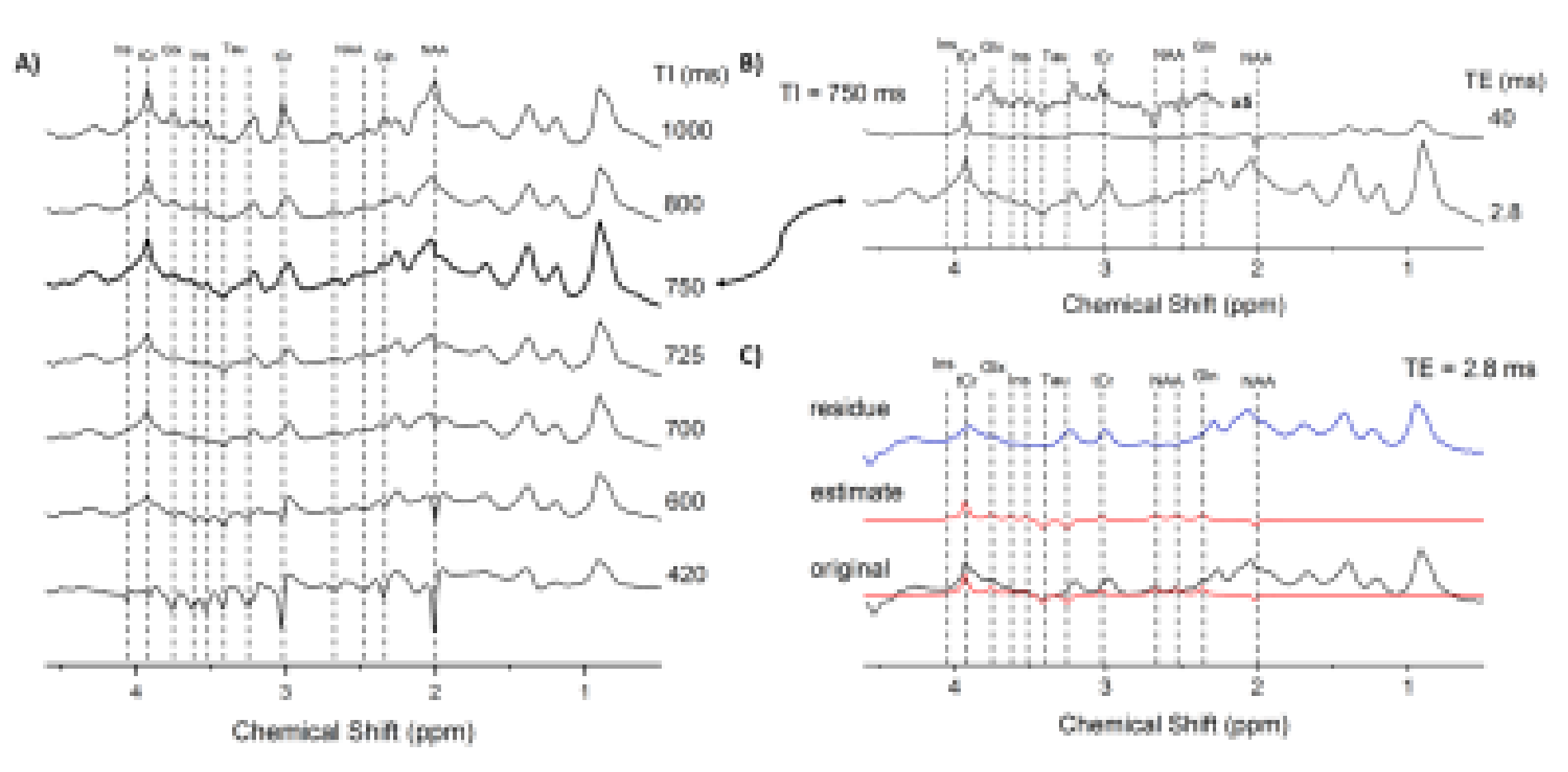
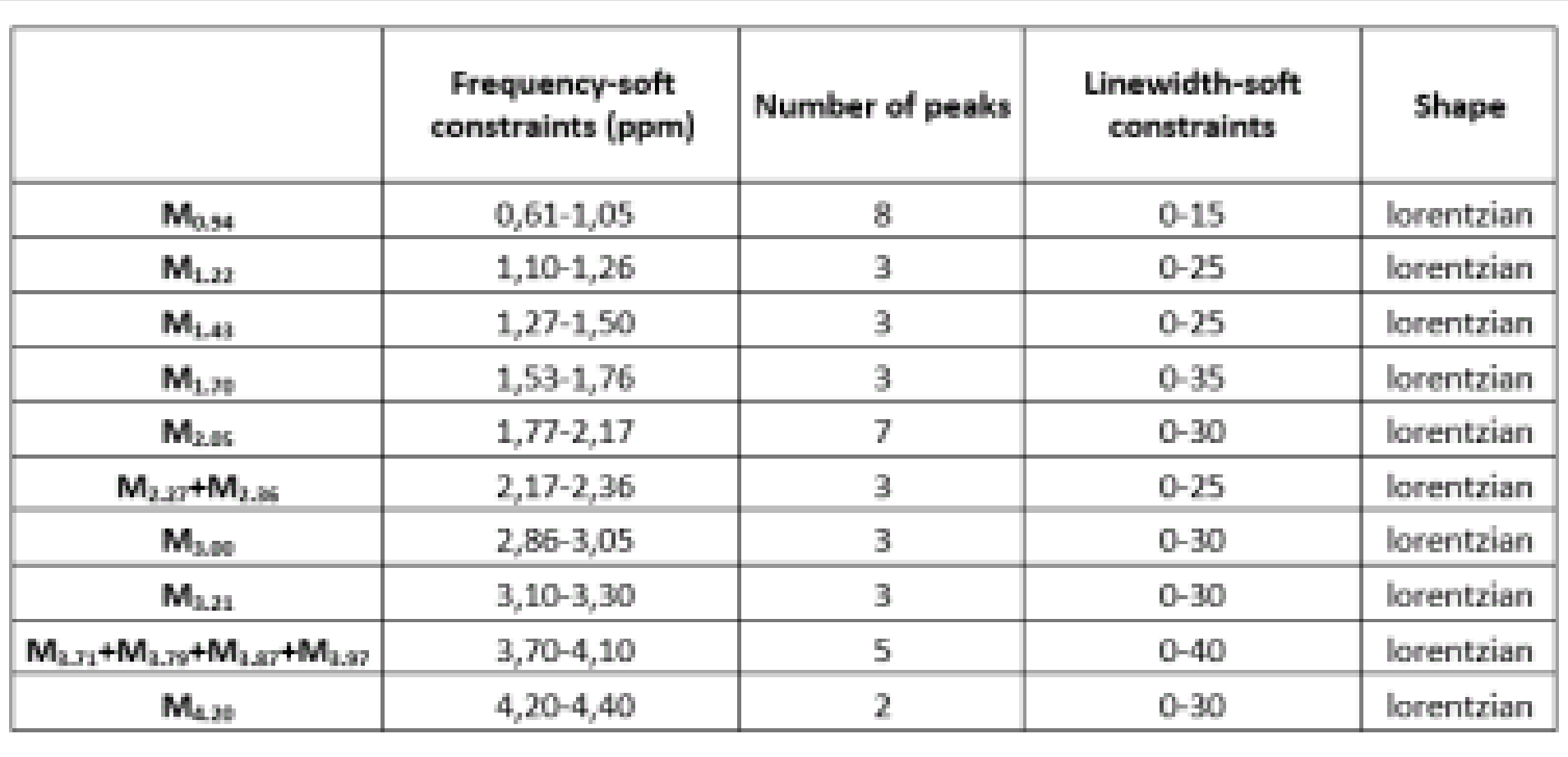
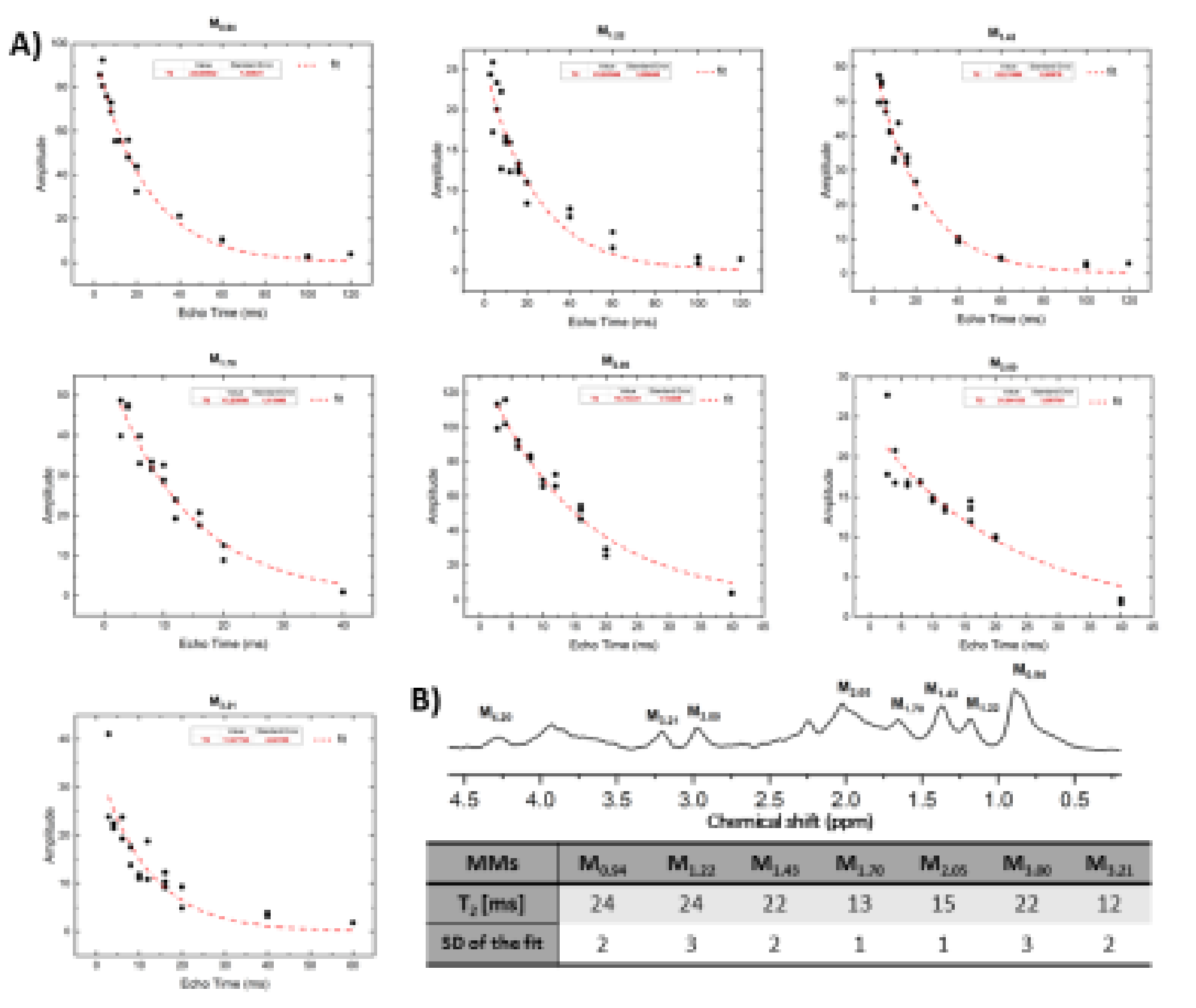


Figure 1: A) In vivo rat brain series of IR spectra with TI ranging from 420 to 1000 ms revealing the evolution of metabolite intensities over a series of different TIs (acquisition parameters TE/TR=2.8/2500 ms); B) Spectra acquired with a selected TI=750 ms and TE=2.8 ms as well as with TE=40 ms (5x magnified); C) Original spectra acquired at TI=750 ms and TE=2.8 ms (shown in black), estimated fits of the residual metabolites using AMARES (shown in red) and the residue obtained after subtraction of the estimated metabolites signals remaining from the original spectrum (shown in blue).



	Frequency-soft constraints (ppm)	Number of peaks	Linewidth-soft constraints	Shape
$M_{0.94}$	0,61-1,05	8	0-15	lorentzian
$M_{1.22}$	1,10-1,26	3	0-25	lorentzian
$M_{1.43}$	1,27-1,50	3	0-25	lorentzian
$M_{1.70}$	1,53-1,76	3	0-35	lorentzian
$M_{2.05}$	1,77-2,17	7	0-30	lorentzian
$M_{2.27}$+$M_{2.36}$	2,17-2,36	3	0-25	lorentzian
$M_{3.00}$	2,86-3,05	3	0-30	lorentzian
$M_{3.21}$	3,10-3,30	3	0-30	lorentzian
$M_{3.71}$+$M_{3.79}$+$M_{3.87}$+$M_{3.97}$	3,70-4,10	5	0-40	lorentzian
$M_{4.20}$	4,20-4,40	2	0-30	lorentzian

Figure 2: Table containing prior knowledge given to AMARES for the MM quantification: constraints in frequency, number of peaks, linewidth and line shape.



MMs	$M_{0.94}$	$M_{1.22}$	$M_{1.43}$	$M_{1.70}$	$M_{2.05}$	$M_{3.00}$	$M_{3.21}$
T_2 [ms]	24	24	22	13	15	22	12
SD of the fit	2	3	2	1	1	3	2

Figure 3: A) Exponential fits which provide T_2 relaxation estimates, B) The MM spectra with marked components for which the relaxation times were estimated (up) and a table reporting the T_2 estimates from the fit and its standard deviations (down).