Cross-Regularisation of the Frequency Domain Enables High-Resolution Inverse Laplace Transform of Human Brain Single Voxel Spectroscopy at 3 Tesla

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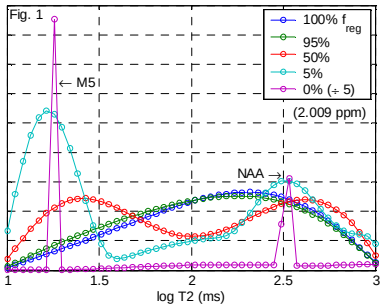
Introduction

T1-based spectral nulling using an inversion recovery preceding an MR-spectroscopy sequence with a short echo time (TE) has been increasingly suggested to estimate a basis set describing macromolecules (proteins and lipids) [1] for inclusion in an LCModel analysis [2]. This approach assumes that metabolites share a similar T1 and does not account for possible distributions of environments experienced by metabolites within a large voxel. Alternatively STEAM measurements acquired at variable mixing times (TM) may be subjected to an inverse Laplace transform (ILT) that yields a continuous distribution of T1 relaxation times (coined relaxogram [3]). Similarly T2 distributions may be obtained by varying TE. Unfortunately the ILT is an ill-conditioned computation requiring a strong regularisation of the non-negative least-square fit typically penalising non-smooth solutions [4] and consequently returning rather broad features that may prove inadequate to segregate macromolecules from metabolites. In order to achieve sufficient resolution in the relaxogram we introduce an adapted cross-regularisor [5] that imposes smoothness in the frequency domain rather than in the relaxation domain.

Methods

Acquisition: Studies were performed on a 3T scanner (Siemens Trio) using a voxel-selective STEAM sequence. Two series of in vivo human brain datasets (healthy volunteer) for T1 and T2 analysis were obtained: a.) series with 8 acquisitions, TE 20 ms, TR 6000 ms, zero prescan, 2 step-phase cycle, randomized list of 64 TM geometrically varying between 10 and 4000 ms with 50% below 490 ms to homogenously sample macromolecules and metabolites; b.) series with 24 acquisitions, TM 10 ms, TR 1700 ms, 2 prescans, 2 step-phase cycle, randomized list of 64 TE geometrically varying between 15 and 500 ms with 50% below 80 ms. Voxels of interest (25×50×20 mm^3) consisting predominantly of white matter were outlined in the high-parietal right hemisphere. Spectra were independently phase corrected with the program package LCModel without eddy-current correction [2] and later referenced to the NAA singlet at 2.009 ppm.

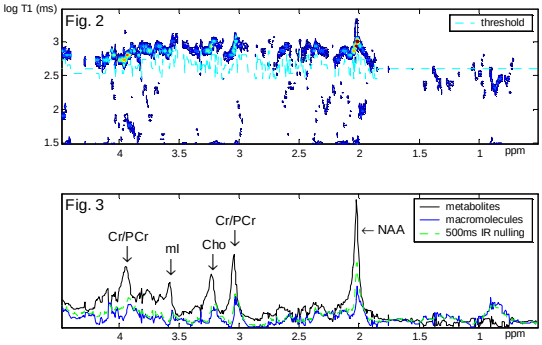
Inverse Laplace transform: The cross-regularisation was implemented with the USERRG function of CONTIN [4] such that a second-order regularisation of 4 adjacent decays down- and up-field from the target frequency was applied either along the relaxogram or across the 9 adjacent frequency points (adapted from [5]). The fraction f_{reg} depicts the ratio of regularisation weighting between the relaxation and frequency domains, with 100% being the CONTIN classical regularisation of the relaxation domain and 0% the novel cross-regularisation of the frequency domain.

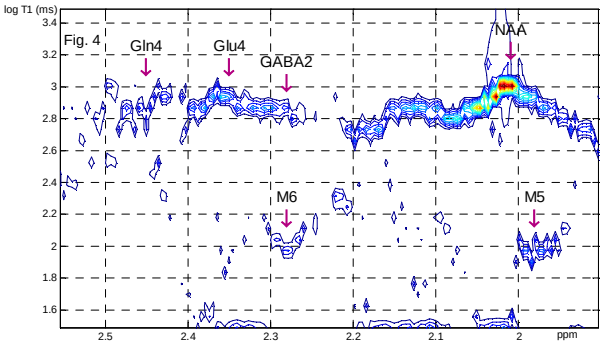


Results

Fig. 1 visualises the effect of the cross-regularisation on the T2 relaxograms (48 T2 grid points) obtained from the 64 TE of the NAA peak (2.009 ppm). The classical CONTIN T2 relaxogram (f_{reg} 100%) is made of only one broad peak that splits into two highly resolved T2-peaks at 18 ms (M5) and 329 ms (NAA) with decreasing f_{reg} fractions. These results confirm the potential of the cross-regularisation previously reported in the context of cartilage imaging with a drastic increase in the relaxogram resolution [5].

Fig. 2 presents the cross-regularised T1-relaxograms of all frequencies between 0.5 and 4.5 ppm as a contour plot (f_{reg} 0%, 30 T1 grid points). Although the T1 of metabolites are comparable, their respective contour plots highlight some degree of fluctuation that may hamper a strict metabolite spectral nulling by inversion recovery. The T1 of macromolecules are more scattered, an aspect that may be attributed to their respective molecular weights. To segregate between macromolecules and metabolites a threshold line (dashed) was placed at the base of the metabolite peaks (lower T1 relaxation side, 393 ms in average). The integration on either side of this threshold is depicted in Fig. 3: metabolites (black) and macromolecules (blue) respective proton densities. A metabolite nulling (dashed green) was simulated with a TI of 500 ms as recommended in the literature [6] and is roughly in agreement with the macromolecule proton density (blue). Fig. 4 magnifies the region between 1.9 and 2.55 ppm. The high resolution of the cross-regularisor enables to differentiate between metabolites and macromolecules (e.g. GABA2 and M6, NAA and M5) and may contribute to an improved separation of metabolites such as glutamine and glutamate (Gln4 and Glu4).





Conclusion

The cross-regularisation of the frequency domain can drastically increase the resolution of the inverse Laplace transform of localized MR spectroscopy making it possible for investigators to study multi-exponential relaxation of spectral resonances. Though the long acquisition time and the considerable processing overhead make this approach inappropriate for routine clinical applications (the computing time roughly progresses with the cube of the number of adjacent spectral points and relaxation grid points), it could contribute to study the nature of macromolecule resonances and their changes related to pathologies. With a high-resolution relaxogram one may contemplate to differentiate the relaxation time constants of metabolites and macromolecules (e.g. GABA2 and M6, NAA and M5), strongly correlated metabolites (e.g. Gln4 and Glu4) or experiencing different environments (e.g. astroglial and neuronal cells).

References

[1] Behar K. (1994) MRM 32:294-302. [2] Provencher S.W. (1993) MRM 30:672-679. [3] Labadie C. et al. (1994) J. Magn. Reson. B105:99-112. [4] Provencher S.W. (1982) Computer. Phys. Comm. 27:229-242. [5] Labadie C., S. Jarchow (2004) ISMRM Kyoto, e-poster 2707. [6] Hofmann L. (2001) MRM 46:855-863.