## Marginal distributions constrained optimization (MADCO) used to accelerate 2D MRI relaxometry

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Introduction: Multidimensional NMR experiments allow us to study correlations between relaxation properties, such as T<sub>1</sub> and T<sub>2</sub> and physical parameters, such as the diffusivity (D). In the 2D case, when the kernels have an exponential form, application of a 2D inverse Laplace transform (ILT), which is a classic ill-conditioned problem, is required. The most common and efficient 2D-ILT algorithm [1] is typically used in 2D relaxometry experiments that involve a CPMG acquisition, which results in high-density sampling of the signal decay. Although multidimensional diffusion/relaxation experiments have been of great interest in recent years, preclinical and clinical applications remain infeasible. In high-field MRI scanners, specific absorption rate limits the use of multi-echo or CPMG pulse trains, and the large amounts of data required cannot be collected in in vivo experiments due to long scan times. The goal of this work is to vastly reduce the number of acquisitions required for an accurate 2D diffusion/relaxation spectrum reconstruction. Recently, a strategy was introduced that used the marginal 1D distributions of the desired 2D function as equality constraints [2] to stabilize and reduce the number of acquisitions. Here we apply the concept of marginal distributions constrained optimization (MADCO) to multidimensional NMR experiments. Methods: Although the method is equally applicable to other types of multidimensional experiments, we chose to demonstrate it on a D- $T_I$  polyvinylpyrrolidone (PVP) water solution phantom. Doped water and PVP were used to create a 3-peaks MRI phantom. Two purified water samples with 0.18 mM and 0.5 mM gadopentetate dimeglumine were prepared, along with a 20% w/v PVP water solution sample. The corresponding relaxation times and diffusivities  $(T_l, D)$ , as measured separately for each sample (referred to as ground truth, Fig. 1A). MRI data were acquired on a 7 T Bruker wide-bore vertical magnet with an inversion recovery DW EPI sequence. The full 2D experimental set had 40 diffusion gradient linear steps, and 37 inversion times ( $\tau$ ) with logarithmic spacing. A single 5 mm axial slice with a matrix size and resolution of 64x64 and 0.2x0.2 mm, respectively, acquired with 2 averages and 4 segments. For D- $T_l$  measurements, for a given recovery time the fully recovered data are subtracted from the data, and the signal attenuation can be expressed as:

$$M(\tau, b) = \sum_{n=1}^{N_{T1}} \sum_{m=1}^{N_D} \mathbf{F}(T_{1,n}, D_m) \exp(-\frac{\tau}{T_{1,n}}) \exp(-bD_m)$$
 (1)

In this work we suggest a simple way to stabilize the estimation of  $F(T_1,D)$  in Eq. 1, while significantly reducing the number of required acquisitions and improving accuracy, by constraining the solution according to the following relations:

$$\sum_{n=1}^{N_D} \mathbf{F}(T_1, D_n) = F(T_1) \quad and \quad \sum_{n=1}^{N_{T1}} \mathbf{F}(T_{1,n}, D) = F(D)$$
 (2)
These marginal distributions can be separately estimated from 1D experiments, which require an order of magnitude less data

than a conventional 2D acquisition.

Results and Discussion: The performance of MADCO was determined and compared with the conventional method by estimating the D-T<sub>1</sub> distribution by using 500 random subsamples from the full data at 19 logarithmically distributed acquisitions, from 7 to 1480. 2D distributions and their 1D projections obtained from MADCO and conventional analyses of the signal using 7 and 1480 acquisitions, respectively, are shown in Figs. 1 B and C. Purposely oversampled, the full acquisition scan time in the 2D experiment was  $\sim$ 37 h. As shown, the D- $T_I$  distribution estimated with the conventional method was far from accurate, even when the full data set was used (Fig. 2C). Conversely, applying the proposed method led to very good agreement with the ground truth distribution, even when only 7 randomly sampled data points were used (Fig. 2B). This immense improvement in accuracy and efficiency translates to a reduction in the required 2D scan time from 37 h to 10 min.

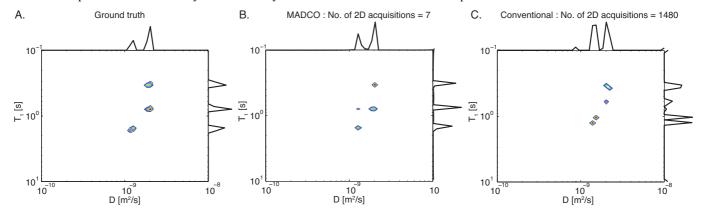


Figure 1 – D-T<sub>1</sub> distributions. (A) Ground truth, estimated using (B) MADCO with 7 acquisitions, and (C) conventional using 1480 acquisitions.

Conclusion: The potential impact of this work is directed towards preclinical and clinical applications, where it would allow a comprehensive investigation in a reasonable time frame by using the MADCO method in conjunction with a variety of 2D MRI experiments. Furthermore, our work may be extended beyond 2D, since application of the marginal distributions constrained optimization principle in higher dimensions enables the main limitation of experimental time to be lifted.

## References

- [1] Y.-Q. Song et al., J. Mag. Res. 154 (2002) 261-268.
- [2] D. Benjamini and P. J. Basser, J. Chem. Phys. 141 (2014) 214202.