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Communication

Use of marginal distributions constrained optimization (MADCO) for accelerated 2D MRI relaxometry and diffusometry

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ABSTRACT

Measuring multidimensional (e.g., 2D) relaxation spectra in NMR and MRI clinical applications is a holy grail of the porous media and biomedical MR communities. The main bottleneck is the inversion of Fredholm integrals of the first kind, an ill-conditioned problem requiring large amounts of data to stabilize a solution. We suggest a novel experimental design and processing framework to accelerate and improve the reconstruction of such 2D spectra that uses *a priori* information from the 1D projections of spectra, or marginal distributions. These 1D marginal distributions provide powerful constraints when 2D spectra are reconstructed, and their estimation requires an order of magnitude less data than a conventional 2D approach. This marginal distributions constrained optimization (MADCO) methodology is demonstrated here with a polyvinylpyrrolidone-water phantom that has 3 distinct peaks in the 2D D-T_1 space. The stability, sensitivity to experimental parameters, and accuracy of this new approach are compared with conventional methods by serially subsampling the full data set. While the conventional, unconstrained approach performed poorly, the new method had proven to be highly accurate and robust, only requiring a fraction of the data. Additionally, synthetic T_1-T_2 data are presented to explore the effects of noise on the estimations, and the performance of the proposed method with a smooth and realistic 2D spectrum. The proposed framework is quite general and can also be used with a variety of 2D MRI experiments (D-T_2, T_1-T_2, D-D, etc.), making these potentially feasible for preclinical and even clinical applications for the first time.

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1. Introduction

Multidimensional NMR experiments allow us to study correlations between relaxation properties, such as T_1 and T_2, and physical parameters, such as the diffusivity (D). These correlations can be used to identify and characterize microstructure-related water dynamics in many applications [1–3]. The following general expression [4] describes the signal attenuation from 2D NMR experiments with separable kernels:

$$M(\beta_1,\beta_2) = \iint F(\omega_1,\omega_2)\,K_1(\beta_1,\omega_1)K_2(\beta_2,\omega_2)\,\mathrm{d}\omega_1\,\mathrm{d}\omega_2, \qquad (1)$$

β_1 and β_2 are experimental parameters that are determined by the data acquisition scheme, and ω_1 and ω_2 are the relaxation/diffusion variables. Eq. (1) is an example of a broad class of Fredholm integrals of the first kind. When the kernels have an exponential form, application of a 2D inverse Laplace transform (ILT), which is a classic ill-conditioned problem [5], is required. The most common and efficient 2D-ILT algorithm [6] is typically used in 2D relaxometry experiments that involve a Carr-Purcell-Meiboom-Gill (CPMG) acquisition, which results in high density sampling of the signal decay. This algorithm greatly improved the efficiency of the inversion by compressing the 2D signal without losing useful information, revealing a redundancy in some basis representations.

Although multidimensional diffusion/relaxation experiments have been of great interest in recent years, preclinical and clinical applications are infeasible. In high-field 3 T and 7 T MRI scanners, the total number of 180° pulses that can be applied per unit time is limited by safety concerns, primarily due to the high specific absorption rate (SAR) [7]. Fast spin-echo, multi-echo, or CPMG pulse trains are therefore not clinically applicable, and the large amounts of data required cannot be collected in *in vivo* experiments due to long scan times. Each acquisition – whether D-T_1 or, for example, T_1-T_2 measurements absent a CPMG pulse train – would only result in a single experimental data point. An additional experiment where the 2D data surface is sampled point by point is the diffusion–diffusion exchange spectroscopy (DEXSY) [2]. When a potentially lengthy imaging block is added, shortening the scan time becomes the primary challenge.

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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 a joint diameter-length distribution of a porous material comprised of capped (finite) cylinders as equality constraints to stabilize and reduce the number of acquisitions needed to invert a discrete Fredholm equation [8]. Applying the concept of marginal distributions constrained optimization (MADCO) to 2D relaxometry/diffusometry NMR, we note that the 1D projections of a 2D correlation function of two relaxation/diffusion parameters are directly related to it, and if obtained *a priori*, can be used to greatly constrain the solutions space of $F(\omega_1, \omega_2)$.

We suggest here a novel experimental design and reconstruction framework: instead of sampling the entire experimental parameters space, (β_1, β_2), and directly estimate the 2D distribution $F(\omega_1, \omega_2)$ (Fig. 1A), using MADCO would only require sampling along β_1 and β_2 axes (i.e., 1D data), complemented with a small number of acquisitions in the 2D space (Fig. 1B). The 2D reconstruction would then have two steps: (1) estimate $F(\omega_1)$ and $F(\omega_2)$ from the 1D data, and then (2) use these 1D spectra to constrain the estimation of $F(\omega_1, \omega_2)$ from the remaining 2D data.

Although the method is equally applicable to other types of multidimensional experiments, we chose to demonstrate it experimentally on a D-T_1 polyvinylpyrrolidone (PVP) water solution phantom. A clinically applicable inversion recovery diffusion-weighted imaging pulse sequence was used to observe D-T_1 correlations. Additionally, synthetic T_1-T_2 data are presented to explore the effects of noise on the estimations, and the performance of the proposed method with a smooth and realistic 2D spectrum. The suggested and the conventional established methods were investigated to determine the generalizability of our analyses.

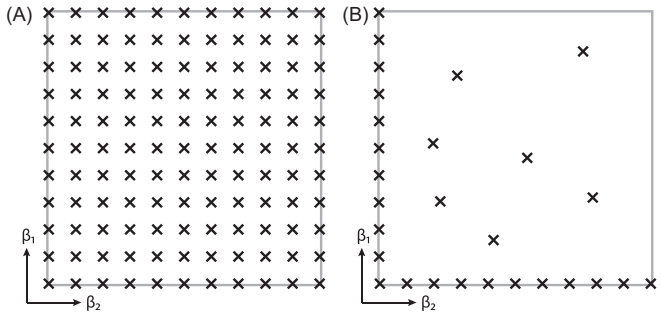

Fig. 1. Illustration of the (A) conventional and (B) MADCO experimental design schemes used to obtain a 2D correlation function, $F(\omega_1, \omega_2)$.

2. Experiments

2.1. D-T_1 phantom preparation and data acquisition

Doped water and PVP (Sigma-Aldrich, *K* value 29–32) were used to create a D-T_1 phantom with three distinct peaks. Aqueous solutions of PVP were shown to make good diffusion MR phantoms since their measured diffusivity is independent of the diffusion time, indicating Gaussian diffusion of a single population of spins [9]. In addition, increasing PVP w/v concentration is negatively correlated with both the diffusivity and T_1. Two purified water samples with 0.18 mM and 0.5 mM gadopentetate dimeglumine (Magnevist, Bayer, Germany) were prepared, along with a 20% w/v PVP water solution sample. The corresponding weighted geometric means (gm) of the relaxation times and diffusivities (gmT_1, gm$D$), as measured separately for each sample (see Section 3) are shown in Fig. 2A. Each sample was placed in a 4 mm NMR tube; these were then inserted together into a 15 mm NMR tube.

Imaging data were collected on a 7 T Bruker wide-bore vertical magnet with an AVANCE III MRI spectrometer equipped with a Micro 2.5 microimaging probe. MRI data were acquired with an inversion recovery spin-echo diffusion-weighted echo planar imaging (IR–DWI–EPI) sequence, with an adiabatic 180° inversion pulse applied before the standard spin-echo diffusion weighted sequence. The full 2D experimental set had 40 diffusion gradient linear steps (G) ranging from 0 to 900 mT/m, 37 inversion times (τ_1) with logarithmic temporal spacing ranging from 100 to 3000 ms, and an additional magnetization equilibrium scan with an inversion time of 10 s. The 1D experiments were a subset of the full 2D data set. The 1D IR data set included all of the 37 inversion times with $G = 0$, and the 1D diffusion data set included all of the odd diffusion gradient linear steps (total of 20) with $\tau_1 = 10$ s. Other acquisition parameters were diffusion gradient duration and separation of $\delta = 3$ ms and $\Delta = 15$ ms, respectively, leading to a b-value range of 0–6200 s/mm^2 ($b = \gamma^2\delta^2G^2(\Delta - \delta/3)$, where γ is the gyromagnetic ratio), TE = 50 ms, and TR = inversion time + 10 s. A single 5 mm axial slice with a matrix size and resolution of 64×64 and 0.2×0.2 mm^2, respectively, acquired with 2 averages and 4 segments. The experimental signal-to-noise ratio (SNR) in the full 2D experiment was ~700.

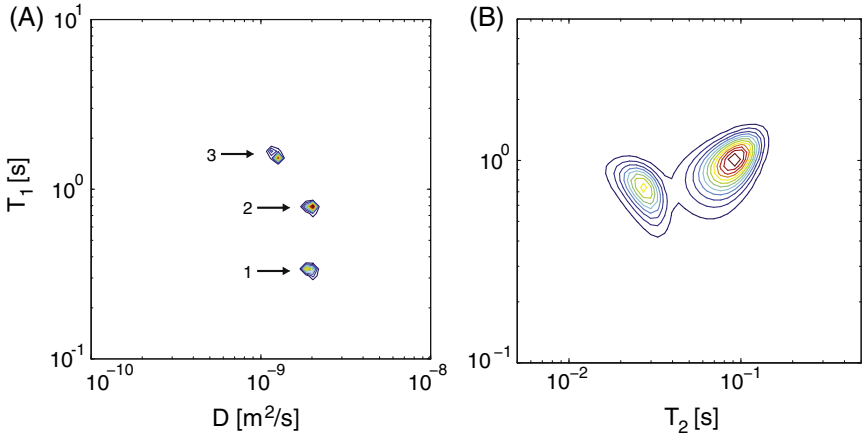

Fig. 2. (A) Ground truth T_1-D distribution obtained from a separate analysis of each (T_1, D) sample and averaging according to the relative spin density. The 3 peaks are identified and numbered for future reference, and their (gmT_1, gm$D$) values were 1. (293 ms, 2.26 μm^2/ms), 2. (782 ms, 1.99 μm^2/ms), and 3. (1596 ms, 1.24 μm^2/ms). (B) T_1-T_2 relaxometry of the simulated ground truth, with peaks centers (T_1, T_2) at (921 ms, 27.1 ms) and (1013 ms, 73.6 ms).