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Ultrafast T_1–T_2 relaxometry using FLOP sequences

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ABSTRACT

By periodically flipping the longitudinal magnetisation with a chain of 180° pulses it is possible to establish a steady-state of longitudinal polarisation that effectively stores the information of T_1 relaxation. The pulse sequence for achieving this, called steady-state Flipped LOngitudinal Polarisation (FLOP) can be used for the fast acquisition of a two-dimensional T_1–T_2 relaxation time spectrum in both periodic and a-periodic modes. We have therefore called this new class of sequences periodic or a-periodic FLOP–T_1–T_2.

1. Introduction

2D T_1–T_2 relaxation spectra based on the fast 2D inverse Laplace transformation algorithm developed by Song and Hurlimann [1,2] have proved invaluable as microstructural probes of a wide variety of complex, heterogeneous systems including porous rocks [1,3], cellular tissue [4,5], protein systems [6] and even nano-structured synthetic hydrogels [7]. There is also reason to believe that T_1–T_2 spectra could act as biomarkers in clinical diagnosis [8,9]. However the development of routine clinical T_1–T_2 relaxometry requires that it is both fast and volume-selective. A number of approaches to fast T_1–T_2 data acquisition have been proposed, including reducing the recovery delay [8] and multislicing [10]. We have also proposed a number of strategies for volume-selective T_1–T_2 relaxometry [11]. However steady-state methods based on the periodic inversion of longitudinal magnetisation have yet to be explored and have the potential of being faster than both the multislicing and reduced recovery delay methods.

Periodic inversion of the longitudinal magnetisation with a chain of 180° pulses eventually establishes a steady-state in the longitudinal magnetisation such that the magnetisation is periodically restored to some constant value. The CPMG sequence, that is routinely used to measure transverse relaxation, itself comprises a chain of equally spaced 180° pulses and will also establish a steady-state in the longitudinal magnetisation provided sufficient pulses (or spin-echoes) are used. In this paper we show how this fact can be used to output a discrete two-dimensional T_1–T_2 relaxation spectrum. We also show how the idea can be generalised into periodic and aperiodic pulse sequences and further sub-classified into those periodic sequences with separate or combined preparation and acquisition steps. The class of sequences based on repeated application of 180° inversion pulses can be called "FLOP" for "Flipped LOngitudinal Polarisation". Following this nomenclature, the present paper analyses the class of periodic and aperiodic FLOP–T_1–T_2 sequences. Elsewhere [12] we have reported that the FLOP methodology can be used for fast imaging with image contrast based on the degree of steady-state longitudinal magnetisation.

For clinical applications FLOP–T_1–T_2 methods need to be not only fast but also volume-selective where the volume selectivity needs to destroy longitudinal magnetisation outside the volume of interest (VOI) while preserving longitudinal and transverse magnetisation within the VOI. We have called the new sequence for achieving this the 'magic-SPACE box' because it can be inserted into a periodic FLOP sequence and is a simple variation of the well-known SPACE sequence [13].

This paper focuses mainly on the theoretical development of the FLOP–T_1–T_2 method, which is discussed at length in Section 2 and the experimental verification is performed only on simple doped water and oil phantoms in Section 4. The application to complex heterogeneous biological samples in clinical MRI scanners will be the subject of future work.

2. Periodic FLOP sequences

2.1. Theoretical analysis of periodic FLOP sequences with separate preparation and acquisition

Any periodically repeating pattern of 180° inversion pulses will eventually establish a "steady-state" in the longitudinal magnetisation whereby the magnetisation is periodically returned to some

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value that can be called, M_s. In this steady-state the magnetisation will have lost all memory of its initial state and can be regarded as being at equilibrium at a new spin temperature that differs from the laboratory value [12]. The simplest pulse sequence for achieving this comprises a train of equally spaced 180° pulses such that, starting from the equilibrium state, the longitudinal magnetisation eventually enters a steady-state with a saw-tooth pattern of inversion and recovery. This steady-state situation is straightforward to calculate with the well-known expression derived from the Bloch equations for the recovery of single exponential relaxation from an initial state $M(0)$,

$$M(t) = M_\infty + [M(0) - M_\infty]\exp(-R_1 t) \quad (1)$$

Here R_1 is the longitudinal relaxation rate, $1/T_1$, and M_∞ is the equilibrium longitudinal magnetisation. Consider the situation in the steady-state created by a train of 180° pulses with a spacing, t_e. At a time t_e after a 180° inversion pulse we have an increase in the longitudinal magnetisation from the inverted steady-state, $-M_s$, to a new value,

$$M(t_e) = M_\infty - (M_s + M_\infty)exp(-R_1 t_e) \quad (2)$$

This magnetisation is flipped by the next 180° pulse and the magnetisation now increases again such that after another t_e period we have,

$$M(2t_e) = M_\infty + [-2M_\infty + (M_s + M_\infty)exp(-R_1 t_e)]\exp(-R_1 t_e) \quad (3)$$

But in the steady-state $M(t_e) = M(2t_e)$, so equating (2) and (3) gives

$$m = \{1 - \exp(-R_1 t_e)\}/\{1 + \exp(-R_1 t_e)\} \quad (4)$$

where t_e is the pulse spacing, and m is the steady-state magnetisation, M_s, divided by the equilibrium magnetisation, M_∞. The modulus of m is plotted as a function of t_e for several values of T_1 in Fig. 1 and shows that there is no maximum or minimum and that the steady-state magnetisation approaches zero (or is 'nulled') only at very short pulse spacings such that $t_e \ll T_1$. Fig. 2 shows how a two-dimensional T_1–T_2-spectrum can be acquired by combining the steady-state situation described by Eq. (4) with a standard CPMG pulse sequence. The first box in Fig. 2 represents the standard

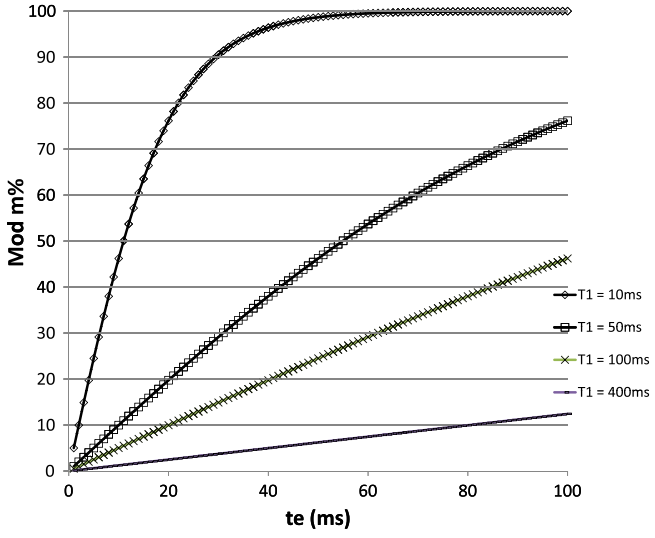

Fig. 1. The theoretical dependence of the steady-state magnetisation ratio M_s/M_∞ (i.e. modulus m%) on echo spacing, t_e, for four values of the longitudinal relaxation time, T_1, using the periodic pulse sequence in Fig. 2, having separate acquisition and preparation and a single pulse spacing (t_e). Curves have been calculated using Eq. (4).

CPMG sequence starting with equilibrium longitudinal magnetisation and acquired with a short echo spacing, 2τ, typically a few hundred microseconds. This "acquisition" CPMG sequence uses sufficient spin-echoes to reach the base-line and thereby accurately characterises the transverse relaxation for both long and short T_2 components. By the end of this CPMG echo train the longitudinal magnetisation will have attained a steady-state value given by Eq. (4) with 2τ replacing t_e. Because $R_1\tau \ll 1$ for all transverse relaxation times longer than a few milliseconds this steady-state magnetisation can be neglected. This initial "acquisition" CPMG pulse sequence is followed by a "preparation" or "dummy" sequence comprising a train of 180° inversion pulses with a longer pulse spacing, t_e, but with no data acquisition. The purpose of this preparation sequence is to establish a new steady-state in the longitudinal magnetisation, as described by Eq. (4) for each T_1 component in the sample. This preparation sequence is followed by a repeat of the first "acquisition" CPMG sequence obtained by replacing one of the preparation 180° pulses with a 90° pulse and using the same echo spacing, 2τ, and number of spin-echoes as in the first acquisition CPMG. The bottom part of Fig. 2 illustrates the time-evolution of the envelope of the longitudinal magnetisation for the sequence ignoring the saw-tooth pattern created by the chain of 180^0 inversion pulses. Analysing the echo decay envelopes from the first and second "acquisition" CPMG sequences with a standard deconvolution programme, such as UPEN [14,15] gives two, one-dimensional T_2 spectra comprising discrete peaks such as those shown in Fig. 3(top). The two spectra will, ideally, have the same T_2-peak positions but the areas of the peaks will, in general, differ because the first was acquired starting with equilibrium magnetisation, the second with steady-state magnetisation in each of the components contributing to the peaks in the T_2-spectrum. The ratio of corresponding peak areas in the two T_2 spectra is therefore a direct measurement of the normalised, steady-state magnetisation, m, for each T_2-peak so the T_1 characterising a particular T_2-peak can be calculated using Eq. (4) and the results displayed as a discrete two-dimensional T_1–T_2-spectrum, such as that illustrated in Fig. 3 (bottom). As Eq. (4) shows, the steady-state magnetisation for a T_2-peak characterised by a long T_1 is severely suppressed at short echo spacing so requires a long, t_e, in the preparation CPMG part of the sequence to give a measurable peak area. For this reason it may be necessary to run the pulse sequence several times with increasingly long preparation echo spacings, t_e, to properly characterise both the short and long T_1 components in the sample. In principle this can be done in a fast single-shot sequence by simply extending the pulse sequence to include the desired set of preparation t_e values. The fact that the steady-state magnetisation of components with long T_1's is suppressed more than those with short T_1's can be an advantage in some water-rich biological samples because it suppresses the water peak and enhances the more interesting solute and biopolymer peaks in the spectrum. Of course, any prior knowledge of the likely range of T_1 values in the sample will allow a suitable choice of preparation echo spacing(s) to be estimated with Eq. (4).

If there are two peaks with the same T_2 but different T_1's, the separate T_1's would require measurements at two different t_e so that the separate T_1's can be obtained by solving the pair of simultaneous equations comprising Eq. (1) for two sets of t_e and T_1 values. It should also be noted that Eq. (1) neglects the possible effects of magnetisation transfer on the steady-state magnetisation established in a sample having several proton pools exchanging longitudinal magnetisation. This aspect will be the subject of future theoretical analysis but lies outside the scope of this initial development.

The same periodic FLOP–T_1–T_2 methodology can be extended to trains of periodically repeating 180 pulses having different pulse spacings. Consider, for example, the situation when the preparation