Protein Quantitatation by Field-Cycling MRI

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Introduction:

It is well known that "quadrupole dips" occur in the T_1-dispersion plots of samples containing immobilised protein molecules [1,2]. The markedly-reduced T_1 values are due to enhanced ^{1}H relaxation at those field strengths where the ^{1}H NMR frequency coincides with one of the ^{14}N NQR frequencies.

When T_1-dispersion data is plotted as relaxation rate ($R_1 = 1/T_1$) versus magnetic field, peaks occur at the "quadrupole dip" field strengths. Jiao and Bryant [2] previously showed that the size of these peaks, ΔR_1, is proportional to a sample's protein concentration, where

$$\Delta R_1 = R_1^{QD} - R_1^{0} \qquad (1)$$

Here, R_1^{QD} is the measured R_1 value at the field where a dip should occur (e.g. 65 mT) and R_1^{0} is the predicted R_1 value at the same field in the absence of the effect (obtained by interpolation).

In this work we have extended these ideas in order to generate "ΔR_1" images, the intensity of which should be proportional to the concentration of immobilised protein [2].

Methods:

A field-cycled inversion-recovery imaging pulse sequence was used. An initial polarisation period at 450 mT was applied, at the end of which the magnetisation was inverted by a 10 ms adiabatic fast passage (AFP). (AFP was used for inversion, to provide immunity from B_1 and B_0 field inhomogeneity.) The field was then switched to its evolution value, around 65 mT, for approximately 150 ms. Then the field was returned to 450 mT and the signal was read out using a 90° pulse. In imaging experiments, gradients were also applied during this detection period. In order to generate a ΔR_1 image, k-space data was collected with and without inversion at three evolution magnetic field values: 56 mT, 65 mT and 75 mT. The R_1^{0} value at 65 mT was calculated by linear interpolation of the R_1 values measured at 56 mT and 75 mT. R_1^{QD} was calculated directly from the data obtained at an evolution field of 65 mT, and a ΔR_1 image was generated via Eq. 1, using software written in IDL.

The imager used for these experiments was a new home-built field-cycled MRI system with signal detection at 450 mT [3], suitable for samples up to 60 mm diameter.

Figure 1: Measured R_1 dispersion of heat-treated hen's egg albumin.

Results and Conclusion:

Figure 1 shows an R_1 dispersion curve obtained from a sample of heat-treated hen's egg albumin; the peaks at 49 mT and 65 mT are clearly visible. The dashed line indicates the linear fit of R_1 between 56 mT and 75 mT, from which ΔR_1 was calculated. Figure 2 shows a calculated ΔR_1 image of a test-object composed of tubes (11 mm i/d) filled with protein-containing gels (various concentrations of BSA or egg albumin). Initial results show good correlation between ΔR_1 (from the image) and protein concentration.

In conclusion, our initial results confirm the feasibility of non-invasive quantitative protein concentration imaging.

References:

[1] Kimmich R. *et al.*, Phys. Med. Biol. **29**, 593 (1984).
[2] Jiao X. & Bryant R.G., Magn. Reson. Med. **35**, 159 (1996).
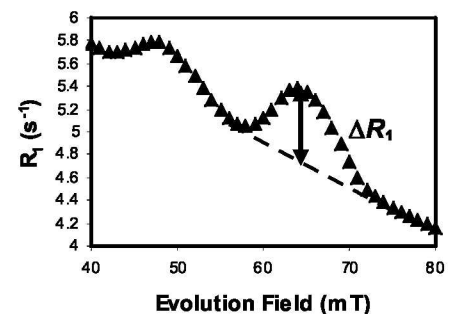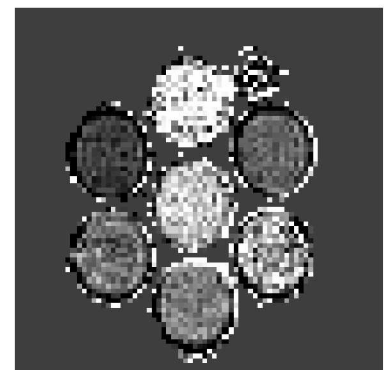[3] Lurie D.J. *et al.*, Magn. Reson. Imaging **23**, 175-181 (2005).

Figure 2: Section from calculated ΔR_1 image of multi-sample gel sample.