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Optimising magnetic resonance sampling patterns for parametric characterisation

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ABSTRACT

Sampling strategies are often central to experimental design. Choosing efficiently which data to acquire can improve the estimation of parameters and reduce the acquisition time. This work is focused on designing optimal sampling patterns for Nuclear Magnetic Resonance (NMR) applications, illustrated with respect to the best estimate of the parameters characterising a lognormal distribution. Lognormal distributions are commonly used as fitting models for distributions of spin-lattice relaxation time constants, spin-spin relaxation time constants and diffusion coefficients. A method for optimising the choice of points to be sampled is presented which is based on the Cramér–Rao Lower Bound (CRLB) theory. The method's capabilities are demonstrated experimentally by applying it to the problem of estimating the emulsion droplet size distribution from a pulsed field gradient (PFG) NMR diffusion experiment. A difference of <5% is observed between the predictions of CRLB theory and the PFG NMR experimental results. It is shown that CLRB theory is stable down to signal-to-noise ratios of ~10. A sensitivity analysis for the CRLB theory is also performed. The method of optimizing sampling patterns is easily adapted to distributions other than lognormal and to other aspects of experimental design; case studies of optimising the sampling scheme for a fixed acquisition time and determining the potential for reduction in acquisition time for a fixed parameter estimation accuracy are presented. The experimental acquisition time is typically reduced by a factor of 3 using the proposed method compared to a constant gradient increment approach that would usually be used.

1. Introduction

All experiments are to some degree limited by the amount of data that can be acquired. Choosing which acquired data will give the most statistically accurate parameters has long been a central topic in experimental design [1]. Recently, in the quest to achieve higher resolution (e.g. temporal resolution), mathematical techniques have been developed, of which the most prominent is Compressed Sensing [2,3], which guarantee the accurate reconstruction of parameters from far fewer samples than was previously possible. As the number of samples acquired decreases significantly, the choice of which data are acquired becomes critical. The design of optimal sampling strategies depends on the application and it has been approached differently for example in Magnetic Resonance Imaging (MRI) [4], Nuclear Magnetic Resonance (NMR) spectroscopy [5], NMR relaxation time analysis [6,7], electronic spectroscopy [8], X-ray ptychography [9] and Helium Atom Scattering [10].

This work is concerned with designing optimal sampling patterns for the most accurate estimate of parameters characterising a lognormal distribution. Lognormal distributions are ubiquitous in science and engineering, ranging from the description of the population distribution of organisms [11] to the size distribution of materials produced from particle processing techniques, such as in the food industry [12] and nanotechnology [13]. In NMR applications, lognormal distributions have been assumed to be a good approximation for polymer size distributions [14], molecular aggregate length distributions [15] and reverse micelle size distributions [16] obtained from pulsed field gradient (PFG) diffusion experiments; the spin-lattice relaxation time distribution of heavy oils obtained from fast-field cycling [17] and inversion recovery experiments [18]; and the spin-spin relaxation time distribution of heavy oils obtained from CPMG experiments [18,19].

A systematic, statistical method is presented for designing sampling patterns when the distribution sought can be approximated by a lognormal distribution. The developed method is based on the Cramér–Rao Lower Bound (CRLB) theory [20]. The CRLB theory gives the theoretical minimum uncertainty in the estimation of the parameters of a model. This minimum uncertainty is the accuracy

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limit with which the parameters can be estimated, given the experimental data. The CRLB theory has previously been used to obtain optimal sampling patterns for mono-exponential decays in NMR relaxation time analysis [21,22], multidimensional COSY experiments [23] and diffusion-weighted MRI [24].

The proposed method is validated against PFG NMR diffusion experiments of an emulsion of toluene in water. The accurate measurement of the emulsion droplet size distribution is important in the food, pharmaceutical and oil recovery industry, among other areas [25]. Since its development [26], the measurement of the emulsion droplet size distribution using PFG NMR diffusion experiments has become an established characterisation technique [27–29]. The emulsion droplet size distribution obtained from PFG NMR diffusion experiments is commonly approximated to a lognormal distribution [26,30–32]; this is supported by population balance statistics between droplet breakage and coalescence during emulsification [33] and by experimental results from other characterisation techniques such as dynamic light scattering [34] and confocal scanning laser microscopy [35].

The complete optimisation of an NMR experiment would also require the optimisation of specific NMR acquisition parameters and reconstruction techniques, which are separate from the optimisation of the sampling pattern considered in this work. The optimisation of specific NMR acquisition parameters and reconstruction techniques for PFG NMR diffusion experiments have been covered in detail elsewhere [24,29,36] and will not be addressed here.

Although the sampling method strategy presented here is illustrated with respect to improving the accuracy of estimation of lognormal distribution parameters, it can be easily adapted to other types of distributions, with the most obvious extension being distributions that can be approximated by the sum of lognormal distributions [16,17,29]. Of particular interest could be the optimization of sampling schemes for bi-exponential decays, the fitting of which is a long-standing challenge and remains a subject of debate [37–41]. In a related study [42], the application of CRLB theory to bi-exponential decays has been validated against experimental data.

The paper is structured as follows. Section 2 introduces the theory behind obtaining the emulsion droplet size distribution from PFG NMR diffusion experiments and the application of the CRLB theory to these experiments. The experimental sampling methods and PFG NMR setup are described in Section 3. The comparison between the predictions of the CRLB theory and PFG NMR experimental results is presented in Section 4. The limitations, sensitivity and potential of the CRLB theory are also discussed in Section 4.

2. Theory

The structure of this Section is as follows. Section 2.1 briefly reviews the theory behind the extraction of the emulsion droplet size distribution from PFG NMR diffusion experiments. Section 2.2 introduces the CRLB theory in its generality, and in Section 2.3 the CRLB theory is applied to the problem of optimizing the sampling pattern for the PFG NMR diffusion acquisitions of emulsion droplet size distributions.

2.1. PFG NMR diffusion of emulsion systems

The ideal NMR signal attenuation acquired from a PFG NMR diffusion experiment of an unconstrained component, for a range of pulsed field gradient amplitudes, g_i ($i = 1, 2, \ldots, n$), is described by the Stejskal-Tanner equation [43]:

$$y_i = A\exp\left(-\gamma^2 g_i^2 \delta^2 D\left(\Delta - \frac{\delta}{3}\right)\right), \tag{1}$$

where γ is the gyromagnetic ratio of the NMR-active nucleus, δ is the pulsed field gradient duration, Δ is the diffusion time, D is the unconstrained diffusion coefficient and A is a scaling factor.

If the component is constrained in the dispersed phase of an emulsion and the diffusion time is such that the root mean square distance travelled due to Brownian motion is larger than the characteristic size of the droplet, the apparent diffusion coefficient is smaller than the unconstrained diffusion coefficient, with the apparent value depending on the droplet size. Since the emulsion is characterized by a distribution of droplet sizes, the PFG NMR signal attenuation is a multi-exponential decay, from which the droplet size distribution can be extracted. The ideal NMR signal attenuation acquired from the dispersed phase of an emulsion with droplet number size distribution $f_0(a_j)$, has been calculated by Murday and Cotts [44]:

$$y_i = A\sum_{j=1}^{p} a_j^3 f_0(a_j) R(g_i, a_j), \tag{2a}$$

where a_j ($j = 1, 2, \ldots, p$) is the discretized list of droplet radii and A is a scaling factor. The standard notation for the number size distribution, $f_0(a_j)$, [45] has been used. The factor a_j^3 could be combined with $f_0(a_j)$ to give the volume size distribution, $f_3(a_j)$, but we choose to focus on the number size distribution, for ease of interpretation. In Eq. (2a):

$$R(g_i, a_j) = \exp(-2\gamma^2 g_i^2 \sum_{k=1}^{\infty} \frac{1}{\alpha_k^2(\alpha_k^2 a_j^2 - 2)} r(\alpha_k)), \tag{2b}$$

where:

$$r(\alpha_k) = \frac{2\delta}{\alpha_k^2 D} + \frac{-2 - \exp\left(-\alpha_k^2 D(\Delta-\delta)\right) + 2\exp(-\alpha_k^2 D\Delta) + 2\exp(-\alpha_k^2 D\delta) - \exp(-\alpha_k^2 D(\Delta+\delta))}{(\alpha_k^2 D)^2}. \tag{2c}$$

In Eqs. 2(b, c), D is the unconstrained diffusion coefficient of the dispersed phase and α_k are the solutions to the equation:

$$J_{3/2}(\alpha_k a_j) = \alpha_k a_j J_{5/2}(\alpha_k a_j), \tag{2d}$$

where J_k is the Bessel function of the first kind and of order k. As discussed in Section 1, the droplet number size distribution, $f_0(a_j)$, is typically well approximated to a lognormal distribution:

$$f_0(a_j) = \frac{1}{a_j s_g \sqrt{2\pi}} \exp\left(-\frac{(\ln a_j - \bar{a}_{0,0})^2}{2s_g^2}\right), \tag{3}$$

where $\bar{a}_{0,0}$ is the geometric mean of the droplet size distribution and s_g is the geometric standard deviation of the droplet size distribution, following standard notation (the arithmetic mean of the droplet size distribution is $\bar{a}_{1,0}$ and the standard deviation of the droplet size distribution is s). If the droplet number size distribution is lognormal, the volume size distribution is also lognormal [45,46]. As a result, a similar analysis of what follows in the next sections can also be applied to the volume size distribution, $f_3(a_j)$.

The ideal NMR signal, therefore, depends on three parameters: the scaling factor, A, the geometric mean, $\bar{a}_{0,0}$, and the geometric standard deviation, s_g, of the lognormal droplet size distribution. The accurate estimation of these parameters is the objective of the PFG NMR diffusion experiment.

2.2. CRLB theory

All signals are to some degree corrupted by noise. As a result, the acquired signal, $\hat{y}_i$, is composed of the ideal signal, y_i, and an unknown noise term, ϵ_i, according to:

$$\hat{y}_i = y_i + \epsilon_i \tag{4}$$