

Extension of the double-wave-vector diffusion-weighting experiment to multiple concatenations

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ABSTRACT

Experiments involving two diffusion-weightings in a single acquisition, so-called double- or two-wave-vector experiments, have recently been applied to measure the microscopic anisotropy in macroscopically isotropic samples or to estimate pore or compartment sizes. These informations are derived from the signal modulation observed when varying the wave vectors' orientations. However, the modulation amplitude can be small and, for short mixing times between the two diffusion-weightings, decays with increased gradient pulse lengths which hampers its detectability on whole-body MR systems. Here, an approach is investigated that involves multiple concatenations of the two diffusion-weightings in a single experiment. The theoretical framework for double-wave-vector experiments of fully restricted diffusion is adapted and the corresponding tensor approach recently presented for short mixing times extended and compared to numerical simulations. It is shown that for short mixing times (i) the extended tensor approach well describes the signal behavior observed for multiple concatenations and (ii) the relative amplitude of the signal modulation increases with the number of concatenations. Thus, the presented extension of the double-wave-vector experiment may help to improve the detectability of the signal modulations observed for short mixing times, in particular on whole-body MR systems with their limited gradient amplitudes.

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1. Introduction

Experiments where two diffusion-weighting periods are applied successively in a single acquisition [1–4] (Fig. 1a) have gained interest due to their sensitivity to tissue structure on a microscopic level. Because of the analogy of a diffusion-weighting period to a scatter event for short gradient pulses [5], these experiment often are referred to as two- or double-wave-vector (DWV) experiments, in contrast to standard, single-wave-vector diffusion-weighting. In these experiments, the dependency of the signal amplitudes on the angle between the two wave vectors is usually exploited since it offers information beyond that of a single-wave-vector experiment. Because the averaging over the sample is performed for the accumulated phase difference each spin experiences during the two successive diffusion-weightings with, in general, different directions, the correlation of the diffusion-related displacements are reflected in the acquired signal. This information can be used to assess the size and shape of the compartments in which the spins diffuse [3].

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Which property can be investigated depends on the experimental parameters, in particular on the mixing time between the two diffusion-weightings. For long mixing times and diffusion in isotropically orientation-distributed pores or cells, an angular modulation occurs only for anisotropic, e.g. ellipsoidal, cells yielding a signal difference between parallel and perpendicular orientations of the wave vectors [3]. This is in particular interesting as such a sample in a standard, single-wave-vector experiment appears isotropic and cannot be distinguished from a sample of spherical pores. Experiments showing this effect have been reported for yeast cells [6], model systems [7], and, *ex vivo*, for monkey brain gray matter [7] and pig spinal cord [8]. The observations have been supported by theoretical considerations [6] and numerical simulations [9,10].

For short mixing times, a signal difference between parallel and antiparallel wave vector orientations is expected [3] which has been demonstrated for biological model systems and pig spinal cord *ex vivo* on a whole-body MR system [11]. Furthermore, experimental evidence of this signal difference in the cortico-spinal tract in the living human brain has been provided recently [12]. Because the initial description of this effect [3] assumed infinitely short gradient pulses and mixing times, infinitely long diffusion times, and was focused on isotropically orientation-distributed pores or cells, some theoretical extensions have been provided which cover

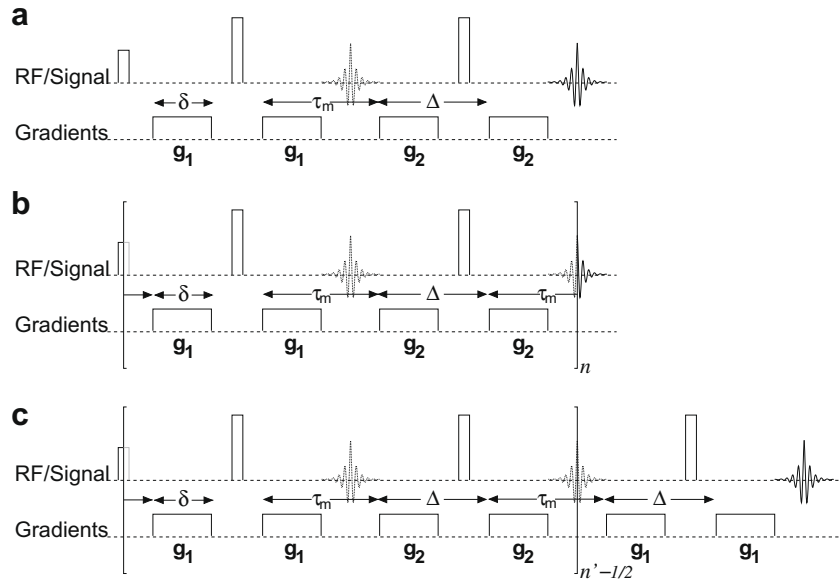


Fig. 1. Basic pulse sequences for the double-wave-vector (DWV) diffusion-weighting experiments considered. (a) Standard DWV experiment, (b) extension with n concatenations of the two wave vectors which involves an even number of diffusion-weightings, and (c) extension with concatenations of the two wave vectors and a final diffusion-weighting with the first wave vector, i.e. an odd number of diffusion-weightings, which can be considered as an experiment with a half-integral number n' of concatenations.

signal expressions for finite timing parameters [13] and a tensor approach to describe the signal behavior for arbitrary orientation-distributions and obtain a rotationally-invariant pore size measure [14].

The amplitude of the signal differences observed in the mentioned experiments is rather small and limits their detectability. This in particular holds for whole-body MR systems with their weaker gradient systems and the experiment with short mixing time to determine cell or compartment sizes where the signal modulation has been shown to decay with the gradient pulse length [9,10,15,16].

In this work, an extension of the DWV experiment is investigated which involves multiple concatenations of the two diffusion-weightings. The theoretical framework derived for fully restricted diffusion is adapted yielding expressions for the signal in such experiments. The corresponding tensor approach for short mixing times and the derived pore or cell size measure [14] are extended and verified by numerical simulations. It is shown theoretically and in numerical simulations that the relative amplitude of the signal modulation for short mixing times increases with the number of concatenations which may help to improve the detectability of the signal modulation experimentally and to increase the accuracy of the derived cell parameters.

2. Theory

A first analysis of the MR signal in experiments involving multiple wave vector diffusion-weighting (e.g. see Fig. 1a) was presented by Mitra [3]. In the short-pulse approximation, i.e. assuming that the gradient pulse duration δ approaches 0, the phase difference $\Delta\varphi$ for a particle diffusing along the trajectory $\mathbf{r}(t)$ in the experiment shown in Fig. 1a is given by

$$\Delta\varphi(\mathbf{q}_1, \mathbf{q}_2) = \mathbf{q}_1[\mathbf{r}(0) - \mathbf{r}(\Delta)] + \mathbf{q}_2[\mathbf{r}(2\Delta + \tau_m) - \mathbf{r}(\Delta + \tau_m)] \quad (1)$$

where \mathbf{q}_1 and \mathbf{q}_2 represent the two wave vectors and are given by $\mathbf{q}_i = \gamma\delta\mathbf{g}_i$ with the gyromagnetic ratio γ and the gradient pulse duration and amplitude δ and \mathbf{g}_i , respectively. The corresponding MR signal then obeys

$$M(\mathbf{q}_1, \mathbf{q}_2) \propto \langle e^{i\mathbf{q}_1[\mathbf{r}(0) - \mathbf{r}(\Delta)] + i\mathbf{q}_2[\mathbf{r}(2\Delta + \tau_m) - \mathbf{r}(\Delta + \tau_m)]} \rangle \quad (2)$$

where the average is taken over the spin ensemble within the sample.

Considering spins diffusing in isolated pores, i.e. fully restricted diffusion, and assuming furthermore that the diffusion time Δ is large compared to $\tau_D = \frac{a^2}{2D}$ ($\Delta \gg \tau_D$), i.e. the time a spin with diffusion coefficient D typically requires to cross a pore with diameter a , some simplifications of Eq. (2) can be achieved. Thereby, two limiting cases for the mixing time τ_m between the two diffusion-weightings, a vanishing and a very large τ_m , were considered in more detail [3].

For a long mixing time ($\tau_m \gg \tau_D$), the individual \mathbf{r} for a spin's trajectory at the individual time points in Eq. (2) are independent and their ensemble averages are identical. This yields

$$M(\mathbf{q}_1, \mathbf{q}_2) \propto \sum_i |\tilde{\rho}_i(\mathbf{q}_1)|^2 |\tilde{\rho}_i(\mathbf{q}_2)|^2 \quad (3)$$

with

$$\tilde{\rho}_i(\mathbf{q}) = \int_{\text{pore}} \rho_i(\mathbf{r}) e^{i\mathbf{q}\mathbf{r}} d\mathbf{r} \quad (4)$$

being the Fourier transform of the spin density $\rho_i(\mathbf{r})$ in the i th pore.

For a very short mixing time ($\tau_m \rightarrow 0$), the positions at Δ and $\Delta + \tau_m$ are identical while those at 0, Δ , and 2Δ are independent and yield the same ensemble average. Thus, an MR signal of

$$M(\mathbf{q}_1, \mathbf{q}_2) \propto \sum_i \tilde{\rho}_i(\mathbf{q}_1) \tilde{\rho}_i(\mathbf{q}_2) \tilde{\rho}_i(-\mathbf{q}_1 - \mathbf{q}_2) \quad (5)$$

is obtained.

2.1. Signal for multiple concatenations of two wave vectors

Now the experiment sketched in Fig. 1b is investigated which involves a concatenation of diffusion-weightings where the wave vector alternates between \mathbf{q}_1 and \mathbf{q}_2 . This experiment represents a special case of the general multiple-wave-vector experiment

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