Diffusion Weighted Signal at Short Times in the Presence of Impermeable Interfaces

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Introduction

The nonlinear dependence between the logarithm of the diffusion weighted signal, ln*S*, and the b-value has often been interpreted as a manifestation of two physically distinct compartments. This model results in a biexponential description of the signal. It fits experimental data well, but fails to yield realistic weights of the compartments. An alternative interpretation suggest that it is the restricted nature of the diffusion in biological tissue that results in the biexponential behavior of the signal. This hypothesis has been supported by several theoretical works (1,2). In this relation we discuss the role of the cumulant expansion of the signal (3) which is valid *ab initio* and yields ln*S* in the form of a power series in the b-value. We use the basic model of an isolated impermeable interface in order to assess the usefulness of the cumulant expansion in comparison with the exact signal and its biexponential approximation.

Method

We consider diffusion between two impermeable planes separated by the distance *2a* in the limit of diffusion lengths smaller than *a*. We analyze diffusion measurements with the spin-echo sequence with narrow pulses. The exact signal is known as an expansion in eigenfunctions (4). We find the coefficients in its cumulant expansion, terminate this expansion and analyze the accuracy of such an approximation to the exact signal. The convergence radius of the cumulant expansion is found by searching for singularities in the complex plane of *b*.

Theoretical Results

The exact normalized signal for short times from a rectangular compartment is illustrated in Fig.1 as a function of the b-factor (solid lines). It shows two different regimes which will be referred to as the small and large b-values. The position of the cross-over between them is determined by the convergence radius of the cumulant expansion.

The signal for small b-values decreases exponentially as a function of *b*. The cumulant expansion of ln*S* can be expressed in terms of the b-factor:

$$\ln S = -A\cdot bD + B\cdot (bD)^2 + C\cdot (bD)^3 + \ldots, \qquad [1]$$

where *D* is the microscopic diffusion constant. *A*=1 in the case of free, unrestricted diffusion, while all other coefficients are zero. All terms are present in the case of restricted diffusion. The first three coefficients in the model considered take the form

$$A = 1 - \frac{4}{3\sqrt{\pi}}\alpha,\ B = \frac{4}{15\sqrt{\pi}}\alpha,\ C = \frac{2}{35\sqrt{\pi}}\alpha, \quad \text{where} \quad \alpha \equiv \frac{\sqrt{Dt}}{a} << 1. \qquad [2]$$

The convergence radius of the cumulant expansion, Eqs. [1], lies within the range *bD*>*6* depending on α. The accuracy of terminating the series after the second term is illustrated in Fig.2. The absolute error for α=0.02 is below 1% of the signal magnitude without diffusion weighting for *bD*<6 (Fig.3). This threshold of 1% is selected in line with the typical noise level in real experiments. The error is below 0.1% for *bD*<2. The absolute error of the biexponential fit, which has three adjustable parameters, is shown for comparison. For *bD*-values smaller than 1 it is less accurate than Eq. [1] with two deterministically calculated terms. The fitted parameters of the biexponential function are subjected to large correlated fluctuations, which are driven by both the noise and the initial guess. This agrees with the above finding that the signal is accurately defined by only two parameters.

The cumulant expansion diverges in the cross-over region between the two regimes (Fig.1). For large b-values, the signal takes the form

$$S_{1D} = \frac{\sqrt{Dt}}{a\sqrt{\pi}}\cdot\frac{1}{bD}, \qquad S_{2D} = \frac{\sqrt{Dt}}{2\pi}\cdot\frac{\sigma}{(bD)^{3/2}}, \qquad S_{3D} = \frac{\sqrt{Dt}}{4\sqrt{\pi}}\cdot\frac{\sigma}{(bD)^2}, \quad \text{for } \alpha << 1. \qquad [3]$$

Here S_{1D}, S_{2D} and S_{3D} denote the signal in one-, two- and three-dimensions, respectively, and σ is the surface-to-volume ratio. As it is seen from Fig. 1, the large-b behavior sets up at *bD*≈8. Such a strong diffusion weighting is achievable in spectrometers and animal scanners, see for example Ref.(5). The biexponential function is sufficiently flexible to be fitted to the signal even in this range, such as shown in Fig. 1, but a systematic deviation from the exact signal reminds about its incorrect functional form (data not shown).

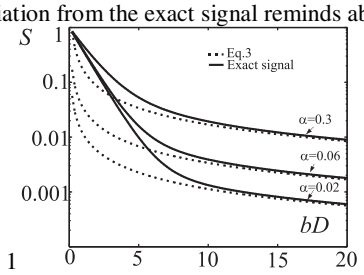

Fig. 1

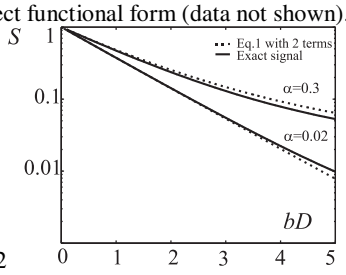

Fig. 2

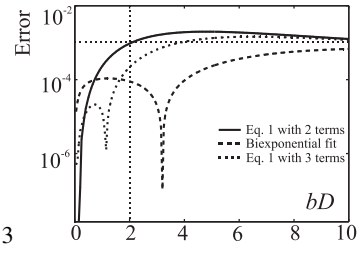

Fig. 3

Discussion/Conclusion

The cumulant expansion of the diffusion-weighted signal in the presence of impermeable boundaries converges for practically important b-values. The first two terms, which are linear and quadratic in *b*, provide for a sufficiently accurate approximation to the exact signal in the model considered. For more complex systems, fitting of the two parameters of the terminated cumulant expansion is expected to be more stable than for the three parameters of the biexponential function. Further advantage of the cumulant expansion is a better understanding of its biophysical correlates, in particular to the geometry of restrictive boundaries as in Eq. [2] and to the statistical properties of molecular motion (6). The signal at large b-values is described by a power-law in *b*, Eq. [3]. The biexponential function is a flexible tool to fit data, although the relation to microscopic parameters remains unclear.

References: (1) Sukstanskii, A.L. *et al.; MRM* **50**: 735-742, 2003. (2) Sukstanskii, A.L., Yablonskiy, D.A.*; JMR* **170**: 56-66, 2004. (3) N. van Kampen; *Elsevier Science* B.V., 1997. (4) Tanner, J.E., Stejskal, E.O.: *J. Chem. Phys.* **49**: 1768-1777, 1968. (5) Cohen, Y., Assaf, Y.; *NMR biomed.* **15**: 516-542, 2002. (6) Frøhlich A.F., *et. al.; App. Magn. Reson.* **29:** 123-137, 2005.