On the Influence of the Temporal Gradient Profile on the Apparent Diffusion Coefficient in the Motional Narrowing Regime in Closed Geometries

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$$ADC = -\ln\left(1 - q^2 \mathrm{E}\{\phi^2\}/2\right)/b \quad (1)$$

$$\mathrm{E}\{\phi^2/2\} = \sum_{m=1}^{\infty} B_{0,m} B_{m,0} \langle \exp(-p(t_2 - t_1)\lambda_m)\rangle_2 \quad (2)$$

$$B_{m,m'} = \int_V dr^3 u_m^*(\vec{r}) u_m(\vec{r}) B(\vec{r}) \quad (3)$$

$$\langle h(t_1, t_2)\rangle_2 = \int_0^1 dt_1 \int_{t_1}^1 dt_2 f(t_1) f(t_2) h(t_1, t_2) \quad (4)$$

$$p = D_0 T / L^2 \qquad q = \gamma G T$$

Introduction

The time dependent diffusion constant D is an important marker for tissue integrity. In principle, magnetic resonance diffusion weighted imaging allows the measurement of D, but thereto infinite narrow diffusion gradients are required. Experimentally, this is rarely applicable. Thus, instead of D, the so called apparent diffusion coefficient (ADC) is usually measured. The ADC is determined by both, the diffusion process and the profile of the diffusion gradients [1]. In the slow diffusion limit, the influence of the temporal gradient profile may be determined elegantly using a formal series expansion. However, in the motional narrowing regime, such a series expansion is not possible. The aim of this work was therefore to develop a more direct technique to determine the influence of the gradient shape on the ADC in the motional narrowing regime for closed geometries.

Theory

We use the multiple correlation function technique [1] and follow the notation of [2]. Be λ_m and $u_m(\boldsymbol{r})$ eigenvalues and eigenfunctions of the Laplace operator satisfying the boundary conditions of the confining geometry. T is the diffusion time, L the typical length scale (e.g. the radius of a cylinder) and ϕ is the phase that a random walker acquires due to the diffusion gradients. The ADC is then determined by the expectation value of ϕ^2 (eq. 1). This second moment can be calculated explicitly by eq. 2, which consists of two separate parts: one describing the geometry ($B_{0,m}\, B_{m,0}$) and one describing the gradient scheme ($\langle\rangle_2$). The exponential function in eq. 2 may expanded in a series for small p (then the summation over $B_{0,m}$ can be carried out), but not for large p (=long times).

Methods

To solve the double integral of eq. 2 we employ subsequent partial integrations, where the exponential $\exp(pt\lambda)$ is always integrated and the gradient temporal profile *f(t)* is differentiated. Theoretical results are validated numerically using the Matrix simulation approach of [1].

Results

If *f(t)* is differentiable, the final result is:

$$\langle \exp(-p(t_2 - t_1)\lambda)\rangle_2 = \sum_{n=0} \frac{1}{(p\lambda)^{n+1}} \int_0^1 dt_1 f(t_1) f^{(n)}(t_1) - \sum_{n,m=0} \frac{(-1)^m}{(p\lambda)^{n+m+2}} f^{(n)}(1)\left(f^{(m)}(1) - f^{(m)}(0)\exp(-p\lambda)\right) \quad (5)$$

Thus, the correction terms are determined be the derivatives of *f(t)*. Unfortunately, many important temporal profiles, like the Stejskal-Tanner profile, are not differentiable. In that case, the integration must be performed stepwise. Then, each non-differentiable point contributes with the following terms:

$$\sum_{n,m} (p\lambda)^{-n-m-2}(-1)^m \left(f^{(n)}(t_+) - f^{(n)}(t_-)\right) f^{(m)}(t_-) + \text{terms that decay with } \exp(-p\lambda\Delta T) \quad (6)$$

Here, t_+ and t_- are the time points infinitesimally before and after the non-differentiable point, ΔT is the time between two non-differentiable points. The first correction term of order p^{-2} is thus determined only by the "jump" points of the temporal profile:

$$\left(-f^2(1)/2 - f^2(0)/2 + \left(f(t_+) - f(t_-)\right) f(t_-)\right)\lambda^{-2} p^{-2} \quad (7)$$

In many cases when the direct integration $\langle\rangle_2$ can not be performed, eq. 5 is applicable or can used for numerical integration. E.g. $f(t) = \tanh(a(t - 1/2))/\tanh(a/2)$ is a good model to investigate the transition from differentiable to non-differentiable temporal profiles but the direct integration can not be performed analytically. Using eq. 5, one finds the leading terms

$$\frac{-a^{-1} + \tanh^{-1}(a)}{\tanh(a)} \lambda^{-1} p^{-1} - \lambda^{-2} p^{-2} - \frac{8a}{3}\tan(a)\lambda^{-3} p^{-3} + O\left(p^{-4}\right) \quad (8)$$

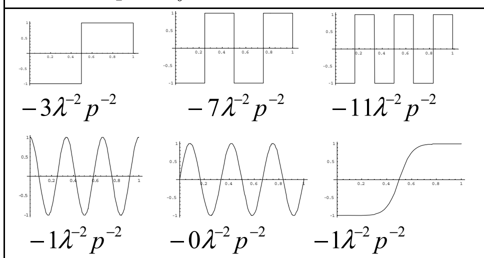

Fig.1: Temporal gradient profiles *f(t)*: Stejskal-Tanner with 1, 2 and 3 oscillations, cosine, sine, tanh. The first correction terms for the second moment in the motional narrowing regime are only dependent on the "jump" points of the temporal gradient profile, according to eq. 7.

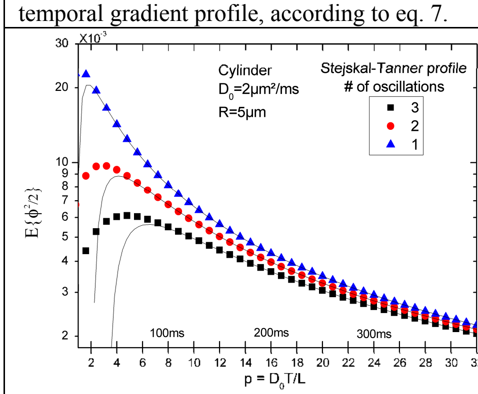

Fig.2: Second moment in dependence of normalized diffusion time. Numerical simulations (dots) correspond well to eq. 7 (drawn through line). More oscillations require larger p for the motional narrowing regime to be valid since the exponential terms in eq. 6 decay slower (ΔT is smaller).

Discussion

The presented approach allows the straightforward computation of the correction terms for a much greater set of temporal profiles than the previous direct integration method. 2nd and higher derivatives of a unitstep function correspond to derivatives of the Dirac delta function, which results in the jump points playing a crucial role for the correction terms of non-differential profiles: Performing the integration over a derivative of a delta function yields derivatives of *f(t)*. However it is important that the integral over a unitstep function multiplied by the delta function is ill defined. This must be circumvented by integrating stepwise. The employed formalism is very adequate for closed geometries like a cylinder or a sphere. While these may be considered valid model geometries for e.g. axons or spherical cells if the random walkers do not leave the cell, the inclusion of extra-cellular water in the formalism is not straightforward. E.g. a proper definition of the length scale *L* may be problematic. Also, the leading correction term does scale as $p^{-3/2}$, not as p^{-2} like for open geometries [3]. The most important application of the proposed partial integration technique may be the investigation of higher moments, where the direct integration is cumbersome, and it could thus shed light onto what kurtosis imaging is actually measuring [4].

References: [1]Barzykin JMR 139;1999 [2] Grebenkov. Rev. Mod. Phys. 79;2007 [3]de Swiet et al. J. Chem. Phys. 104;1996 [4] Jensen et al. MRM 53;2005