Gaussian Phase Distribution Approximation of the Square Wave Oscillating Gradient Spin-Echo (SWOGSE) Diffusion Signal

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Introduction:
The current work presents analytical formulae for both free and restricted diffusion NMR signal from a square wave oscillating gradient spin-echo (SWOGSE) sequence. Recent work [1] suggests that square wave oscillations provide an optimal probe of small pore sizes. Previous work, e.g. [1], computes the SWOGSE signal for restricted diffusion using the matrix method [2] or a Monte Carlo (MC) simulation [3]. However, both techniques are computationally expensive and impractical for generating parameter maps by model fitting in every voxel of an image. Here we derive analytic formulae using the Gaussian Phase Distribution (GPD) approximation. Others have used this approximation to obtain formulae for pulsed gradient (PGSE) [4,5] and sin/cos wave oscillating gradient (OGSE) [6], but the derivation is more complex for SWOGSE because it lacks continuity. We compare our results with Monte Carlo simulation and show that the approximation is accurate to within a few percent of the signal as well as being several orders of magnitude faster to compute.

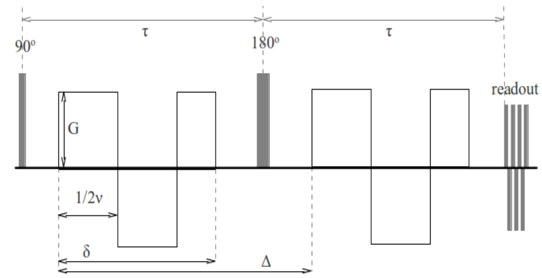


Fig.1: Schematic representation of SWOGSE with ϕ=0

Theory:
The square wave gradient is and is defined by: and is shown schematically in Fig. 1

$$g(t)=\begin{cases} G\cdot(-1)^{\lfloor 2t\nu-\phi/\pi\rfloor} & 0\le t<\delta \\ 0 & \delta\le t<\Delta \\ G\cdot(-1)^{\lfloor 2(t-\Delta)\nu-\phi/\pi\rfloor} & \Delta\le t<\Delta+\delta \end{cases}$$

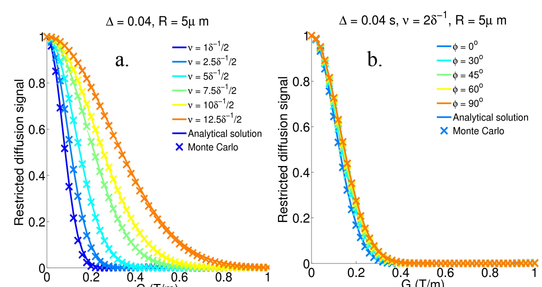
The parameters of the pulse sequence are: the gradient amplitude G, the length of the pulse δ, the diffusion time Δ, the frequency of the square wave ν, and the phase of the square wave ϕ. The general formulae for a gradient with arbitrary frequency and phase are quite lengthy, therefore we give here only the more compact results for the special case when the frequency satisfies the condition $\delta=\frac{N}{2\nu}$, N=1,2,3,..., and the phase is 0. However we use the general formulae for all calculations. The signal attenuation due to free diffusion of water molecules can be written as: $S(2\tau)=\exp(-b\cdot D)$, where 2τ is the echo time, b is the diffusion weighting factor and D is the diffusion coefficient. As described in [4], b can be calculated using a modified form of the Bloch equations: $b=\gamma^2\int_0^{2\tau}\boldsymbol{F}^2(t)dt$, where γ is the gyromagnetic ratio of the hydrogen nuclei and $\boldsymbol{F}(t)=\int_0^t\boldsymbol{g}(t')dt'$ with $\boldsymbol{g}(t)$ the applied field gradient. Therefore, the b-value for SWOGSE is: $b=\frac{G^2\gamma^2\delta}{6\nu^2}+G^2\gamma^2(\Delta-\delta)\left(\delta-\frac{1-(-1)^N+4\delta\nu}{4\nu}\right)^2$.

If diffusion is restricted, the signal echo attenuation β(2τ) can be computed assuming a GPD approximation: $\beta(2\tau)=\frac{\gamma^2}{2}\sum B_n\int_0^{2\tau}dt_1\int_0^{2\tau}dt_2\exp(-\lambda_n D|t_2-t_1|g(t_1)g(t_2))$, where $g(t)$ is the magnitude of the field gradient and B_n and λ_n are geometry dependent functions [5,6]. We solve for the SWOGSE form of $g(t)$ to obtain:

$$\beta(2\tau)=\frac{\gamma^2G^2}{2D^2}\sum_n\frac{B_n}{\lambda_n^2}\left(\frac{(-1)^N e^{-D(\delta+\Delta)\lambda_n}\left((-1)^N e^{D\delta\lambda_n}-1\right)^2\left(e^{D\lambda_n/2\nu}-1\right)^2}{\left(1+e^{D\lambda/2\nu}\right)^2}+2\left(D\delta\lambda_n+N\left(e^{D\lambda_n/2\nu}-1\right)\right)-\frac{2\left(e^{D\lambda_n/2\nu}-1\right)^2}{\left(1+e^{D\lambda_n/2\nu}\right)^2}\left((-1)^N e^{-D\delta\lambda_n}+N\left(e^{-D\lambda_n/2\nu}-1\right)-1\right)\right).$$

Then, the restricted signal is calculated according to $S(2\tau)=\exp(-\beta(2\tau))$.

Results:
We tested the above formulae for free diffusion and restricted diffusion inside a cylinder with radius R when the field gradient is perpendicular to cylinder axis. For a cylinder, the geometric factors are $B_n=\frac{2(R/\mu_n)^2}{\mu_n^2-1}$ and $\lambda_n=\left(\frac{\mu_n}{R}\right)^2$ where μ_n is the n[th] root of the equation $J_1'(\mu)=0$ and J_1 is a Bessel function of first kind [5]. The above expressions can be easily adapted for other geometries (parallel planes, spheres, spherical shells) by using appropriate forms of B_n and λ_n [6]. We implemented the formulae in Matlab and calculated the diffusion signal with δ = 35ms, Δ = 40 ms, and D = $2\cdot 10^{-9}$ m^2/s for the following scenarios:
$R\in[1,2,5,10]\mu$m, $2\nu\in[1,2.5,5,7.5,10,12.5]\delta^{-1}$, $\phi\in[0^o,30^o,45^o,90^o]$, and $G\in[0,0.02,...0.98,1]$T / m
Then we compared the results with the numerical values obtained using the Monte Carlo diffusion simulator in Camino [3]. In all the cases mentioned above, the absolute difference between the analytical values and the simulated ones was smaller than 3% of the signal, which is on a scale from 0 (fully attenuated) to 1 (unattenuated). The diffusion signal inside the cylinder with R = 5 µm is illustrated for different frequencies in Fig.2. a), and for different phases in Fig. 2. b). In these two plots the analytical results are represented with a continuous line, while the values obtained with the MC simulation are depicted with a cross. For the same R, the signal difference between the two methods is shown in Fig. 2.c) for all frequencies and gradient strengths.



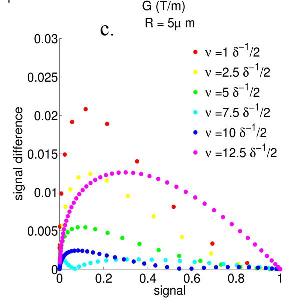


Fig.2: Restricted diffusion signal inside a cylinder with R=5µm as a function of the gradient strength for different frequencies with ϕ=0 (a) and for different phases with ν=2/δ (b).
c) Signal difference between the two curves in (a) as a function of the unweighted signal for all frequencies and gradient strengths.

Discussion:
The plots in Fig.2 a)-c) illustrate that the GPD approximation is suitable for quantifying the diffusion signal given a SWOGSE gradient form. The difference between the analytical results and the simulated values is less than 0.005 for R = 1 & 2 µm and increases with R, but does not exceed 0.03 for R = 10 µm. Largest errors occur for very low frequency (ν = $\delta^{-1}/2$ in Fig.2.c is equivalent to PGSE) or high frequency (ν = 12.5 $\delta^{-1}/2$ in Fig.2. c). The main advantage of having an analytical expression is the reduced computational complexity and running time. In this case the MC simulation took over 10 hours, while the analytical values were computed in less than one tenth of a second, which enables model fitting application, e.g. to generate whole brain parameter maps. As illustrated in Fig.2. a) and c), the diffusion signal as well as the signal difference depend on the frequency of the gradient form, which can be a guideline for choosing the right frequency in an experiment. This method is essential for quantitative diffusion imaging techniques such as ActiveAx[7], using SWOGSE, which enables better sensitivity to the histological range than PGSE[1].

References: [1] Drobnjak JMR10, [2] Callaghan JMR95, [3] Hall TMI09, [4] Price 97, [5] Stepisnik Physica81, [6] Xu MRM09, [7] Alexander08