Biexponential diffusion fit under rician noise assumption

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Introduction: In a free medium diffusion is a gaussian process resulting in an attenuation, S/So, of the NMR signal according to $S = S_0 e^{-bD}$ (where D is the diffusion coefficient and b the diffusion weighting) In biological tissues, however, diffusion becomes a much more complex phenomenon due to effects of restriction, compartmentation, active and passive transport, flow, tortuosity, ... and the above relationship is only a coarse approximation[1]. At low b values (0-200 s/mm^2) flow and IVIM[2] affect this linear behavior, and as we go at higher b values, the nature of the signal decay clearly deviates from the mono-exponential model[3]. For a two compartment no-exchange model the NMR diffusion signal decays as: $S = S_0\left(f_f e^{-bD_f} + (1-f_f)e^{-bD_s}\right)$, where f_f represents the fast diffusion fraction and *Df* and *Ds* the fast and slow diffusion coefficients. As the fast diffusion dominates at early *b*'s, we must probe far into *b* values to retrieve information on the slow diffusion component. However, as we approach noise level, the rician nature of signal distribution in amplitude MR images is more clearly present. Rician distributed noise has a non null mean which introduces a bias in the data that can be seen as a very slow *Ds* diffusion constant. In fast diffusing regions of the brain, all signal may be lost before we attain the highest *b* value. If these final points are to be included in the computation, a gaussian assumption fit will obtain biased results, especially for *Ds* trying to accommodate the noise data. The question is how strong is this bias for current hardware, and whether it is possible to reduce it while still retrieving the maximum possible information of the diffusion decay. We have implemented a rician noise assumption fit, and a noise cut-off criterion. We have obtained that including data below noise level in a gaussian fit gives biased results while a rician based fit resists better to noise contamination. If we implement this noise cut-off in both fits results are similar although gaussian fitted *Ds* are systematically lower than those rician fitted, as expected.

Material and Methods: For gaussian distributed data, the expectation value and the variance of the measured data, correspond to the experimental mean and the square root of the standard deviation. However, for a rician distributed data expectation value only approaches experimental mean at high SNR (~ 6). This introduces a bias in the measured value[4]. We performed two non linear least square fits (Levenberg-Marquardt) based on the minimization of the function $f(x) = \sum (A - E[M])^2$, where *A* is the physical amplitude of the signal (*S*), *M* is it's measured value and *E[M]* the expectation. In the first case, noise contamination was considered to be gaussian and *E[M]* = *M* that corresponds to the maximum likehood estimator. Noise level was taken into account dividing by standard variation inside sum. In the second case, we assumed a rician model for the noise and $E[M] = \sigma\sqrt{\pi/2}\, e^{-A^2/4\sigma^2}\left[(1 + A^2/2\sigma^2)\right] I_0\left(A^2/4\sigma^2\right) + 2I_1\left(A^2/4\sigma^2\right)$ where I_0 and I_1 stand for the zeroth and first order modified Bessel functions of the first kind. This corresponds to a generalized χ^2 and can be used to asses a goodness of fit, or to assess confidence boundaries on fitted parameters.

To test the importance of eliminating high diffusion weighted data from fast diffusion pixels, a non-parametric Wilcoxon test was performed pixel by pixel to asses the *b* value at which the signal ceases to be statistically different from noise[5] and data at superior *b*'s were discarded. Results, with and without, this pre-fit cut-off test are presented.

Acquisitions were performed on a 1.5T (GEMS, USA), with gradients up to 40 mT/m on one volunteer who gave informed written consent. TE = 124 ms, cardiac gating was used (TR =2 RR). Resolution was 1.875 x 1.875 x 5 mm^3 giving a mean SNR of 24. 128 linearly increasing diffusion gradient values were applied (direction XY) and repeated 4 times. Diffusion times δ/Δ = 39/ 46 give a b from 0 to 6800 s/mm^2. Acquisition time was about less than 20 min. Diffusion tensor (b = 1000 s/mm^2 and 55 directions) and T1 weighted SE images were acquired for anatomical reference. Eddy currents could only be corrected between T2 images[6], since much signal is lost on the heavily diffusion weighted images. Long time constant eddy currents were corrected, and the same correction were applied on all diffusion weighted data. Data corresponding to b values 0-200 were discarded to avoid IVIM contamination.

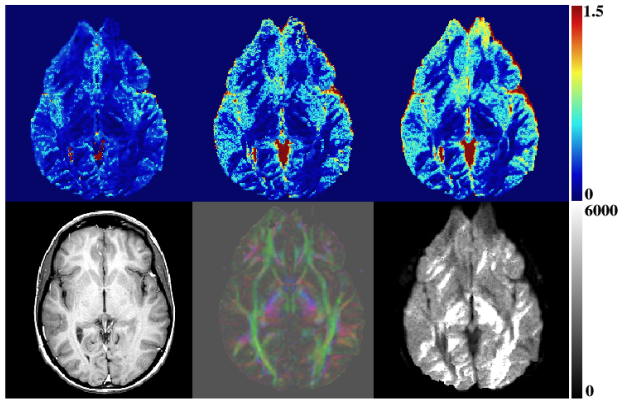

Figure 1: Top: Ds maps: gaussian fit without noise cut-off, gaussian with cut-off and rician without cut-off (10^{-3} mm^2/s and direction XY). Bottom: Anatomy, FA-RGB coded and maxbv, last b value(s/mm^2) where signal is still significantly different from noise.

Results and Discussion: Results for the most sensible of the parameters, *Ds*, are presented in figure 1. Comparing both gaussian fits, with and without cutoff the noise contamination is clearly visible. Fast diffusion regions as cortex or parallel white matter show artificially slower *Ds* when cut-off is not applied. Fitted values coincide only in regions where signal is significant until high *b* values, therefore not polluted by noise. For the rician fit, even if differences between cut-off and no cut-off are slight and drown on noise level, they are also statistically significant although with lower α (data not shown). Rician fit is not completely immune to noise biasing.

Comparing both fits, we can observe that even if rician noise contamination is reduced through the use of a noise cut-off, *Ds* values are still lower for the standard fit (table 1). Differences have been found statistically significant for the ROI shown ($\alpha = 0.01$) and for the whole brain (α = 0.001).

The high values computed for the fast coefficient (for both gaussian and rician fit) may be explained by the fact that at these points signal decays very rapidly and not enough points are fitted to correctly obtain the result.

	Grey Matter			White Matter parallel			White Matter perpendicular		
Fit type	f_f	*Df* 10^{-3} mm^2/s	*Ds* 10^{-3}mm2/s	f_f	*Df* 10^{-3} mm^2/s	*Ds* 10^{-3}mm2/s	f_f	*Df* 10^{-3} mm^2/s	*Ds* 10^{-3}mm2/s
Gauss *no cut-off*	0.71±0.14	1.10±0.23	0.23±0.11	0.81±0.03	1.27±0.08	0.19±0.031	0.74±0.06	1.065±0.19	0179±0.07
Gauss *cut-off*	0.61±0.21	1.20±0.28	0.30±0.17	0.64±0.20	1.79±0.71	0.38±0.20	0.64±0.20	1.79±0.71	0.38±0.12
Rice *no cutoff*	0.61±0.20	1.17±0.23	0.37±0.16	0.73±0.09	1.38±0.28	0.33±0.09	0.68±0.17	1.08±0.19	0.24±0.15

Tab 1: Results are shown for 3 different ROI's in the brain. Error quoted is standard deviation inside ROI. Grey matter was taken from temporal right hemisphere, and parallel and perpendicular white matter are taken from optic radiations in the right and left hemisphere respectively at same height.

Conclusion: Rician distribution of noise in magnitude images introduces bias in fitted parameters for a bi-exponential diffusion analysis. It is possible to avoid some of the major effects of this bias by correctly accounting for the noise distribution, namely by carefully eliminating lost signal data prior to fit. Even though good initial SNR is the best thing in diffusion experiments, use of optimized techniques as presented here can be the next best thing. Correct and solid measumerents are a key issue in the open debate of in *vivo* diffusion MRI interpretation.

References: ***1.*** *Le Bihan, NMR in Biomed, 8:375, 1995* ***2.*** *Le Bihan et al, Radiology 161, 1986* ***3.*** *Clark et al, MRM 44 2000* ***4.*** *Karlsen et al, MRM 41, 1999* ***5.*** *Meca et al, submeeted 12th ISMRM meeting* ***6.*** *Jezzard et al, MRM 39, 1998*