Analysis of the cumulant expansion terms of the diffusion-weighted MRI signal in the human brain

Ezequiel Farrher1, Farida Grinberg1,2, Ivan I. Maximov1, and N. Jon Shah1,2

1INM - 4, Research Centre Jülich GmbH, Jülich, Germany, 2Department of Neurology, RWTH Aachen University, Aachen, Germany

Target audience. This work is devoted to the study of the cumulant expansion of the diffusion-weighted (DW) MRI signal in the human brain. It is of great importance for researchers working in the field of non-Gaussian water diffusion, in particular in Diffusion Kurtosis Imaging (DKI) [1,2].

Purpose. Water diffusion in biological tissue deviates from the Gaussian profile observed in bulk free water due to constraints imposed by the complex cellular microstructure. Deviations of the DW signal from the mono-exponential behaviour become significant at b-values (b) exceeding the range used in conventional human brain DTI (b < 1.0 ms μm^{-2}). The DKI technique was proposed as a model-free approach to quantify these deviations [1,2]. It is based on the cumulant expansion of the DW signal, truncated at second order in b. Thus, the maximum b-value for a DKI analysis must be such that the third and higher expansion orders are still negligible. The maximum b-value in DKI analyses found in the literature falls in the typical range of (2.0 – 3.0) ms μm^{-2} [3-7]. Although some optimization schemes for b-values and gradient directions have been proposed [8], the influence of the b-value fitting range on the cumulant expansion terms of the DW signal has not been yet fully investigated. The aim of this work is to study the dependence of the cumulant expansion terms of the DW MRI signal expanded up to third order in b. This information is relevant for setting the validity of fitting b-value range in DKI. The analysis is done for both numerical simulations and in vivo experiments.

Methods. Synthetic data were simulated using the biexponential model [3,9] as the “ground truth”. In this model the DW signal is given by $S_{\text{biexp}}(b) = f_1 \exp(-bD_0) + (1-f_1) \exp(-bD_1)$, were $D_0$ and $D_1$ denote the diffusivity of the “fast” and “slow” pools, respectively, and $f_1$ is the fraction of the “fast” pool. This model was previously shown to fit the DW signal in the human brain with high accuracy [3,9]. The value of $f_1$ was fixed to 0.65, corresponding to the peak of its distribution in the human brain [3]. Rician noise was added to $S_{\text{exp}}$ according to: $S(b) = \left( \frac{S_{\text{exp}}(b) + N(0,\sigma)}{\|S_{\text{exp}}(b) + N(0,\sigma)\|} \right)^2 + N(0,\sigma^2)$ where $N(0,\sigma)$ is the normal distribution with mean zero and standard deviation $\sigma$. Three values of $SNR \equiv 1/\sigma$ were considered: 20, 60 and 100. The range of b-values was 0 - 10.0 ms μm^{-2}.

Experiments. MRI experiments were performed in a whole-body 3T Siemens Trio scanner (Siemens Medical Systems, Erlangen, Germany) on a healthy volunteer who gave prior written informed consent. A twice-refocused spin-echo EPI sequence with bipolar diffusion gradients was applied using b-values in the range 0 – 50.0 ms μm^{-2}, 6 field gradient directions and voxel-size 2x2x2 mm³.

Results. Figures 1a and 1b show the ratios $[a_2/a_1]$ evaluated from the 2nd order expansion and $[a_3/a_2]$ from the 3rd order expansion in the simulated data for different SNR values. Simulations from two pairs of $(D_0, K_{app})$ are shown: (1.0, 0.5) (solid lines) and (1.0,1.0) (dashed lines). For the in vivo experiments, the histograms of $[a_2/a_1]$ (c) and $[a_3/a_2]$ (d) were evaluated over the four slices for each fitting b-value range and put together into the 3-dimensional surface plot (c,d). Solid and dashed lines show the mean of the corresponding ratio over white matter (WM) and grey matter (GM), respectively. One can see from Figure 1a that the curves of $[a_2/a_1]$ show minima at approximately $b \approx 1.0$ ms μm^{-2}. The same feature, although less pronounced, is observed in the in vivo case. Similarly, the ratio $[a_3/a_2]$ shows minima at approximately $b \approx 3.0$ ms μm^{-2}, in both simulations and experiments.

Discussion. The observed minima of $[a_2/a_1]$ at around $b \approx 1.0$ ms μm^{-2} suggest that the expansion up to 1st order (DTI) is valid in the range $0 – 1.0$ ms μm^{-2}. For $b > 1.0$ ms μm^{-2} the term $a_2$ starts being significant compared to $a_1$, and therefore the 2nd order expansion (DKI) needs to be used to describe the signal. Following the same reasoning, the minima of $[a_2/a_1]$ at roughly $b \approx 3.0$ ms μm^{-2} set the limit for the validity of the 2nd order expansion. For $b > 3.0$ ms μm^{-2} the term $a_2$ starts increasing and therefore the 3rd order expansion term needs to be considered in the analysis. In the case of WM, the minimum is very pronounced, while in GM it is less pronounced and shifted towards larger b-values. In terms of SNR one can see that for lower SNRs the minima are shifted towards larger b-values.

Conclusions. In this study, we have carried out a simple but eloquent analysis of the cumulant expansion terms of the DW MRI signal with the range of fitting b-values. We have proposed an approach to set the limit for the maximum b-value allowed in DKI, in terms of the negligibility of the 3rd order cumulant expansion term. The b-value ranges estimated through this analysis is approximately in agreement with other reports in the literature [8,9]. Our analyses have shown the differences regarding WM and GM. Further quantitative analysis of the expansion terms is currently being carried out in our group.