Extracting a biomarker for the mean cross-sectional area from the ODF

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Introduction:

Finding new biomarkers related to the microstructure of white matter (WM) is an active area of research in the MRI community [1]. As opposed to the usual MRI markers such as fractional anisotropy (FA), these biomarkers provide a closer insight on the tissue structure. We introduce a new microstructure based biomarker that is related to the axon diameter distribution (ADD) and can be obtained with a q-space imaging [2] technique like DSI [3] or MAP [4]. This feature is related with the nature and purpose of WM paths in both normal and pathological conditions [5], and is obtained from the Orientation Distribution Function (ODF) [6] as twice its maximum value. We show that this value is related with the mean cross-sectional area (MCSA) of an ensemble of parallel axons. The same geometric feature was proposed in [4] as a scalar index of microstructure, but was not related to the ODF. In this work we give the formal relation between this microstructure feature and the ODF, and validate it using state-of-the-art numerical simulations.

Methods:

In anisotropic WM voxels where the underlying tissue is made of aligned axons, the angle of the ODF maxima coincides with the axon orientation. In [4] it was proved, under the hypothesis that the gradient pulses (δ) are infinitely small and we are under the long diffusion time regime ($\Delta \gg \delta$), that the integral of the q-space attenuation over the plane perpendicular to a fiber path is equal to the reciprocal of the MCSA of the ADD. Using the central section theorem of the 3D Fourier transform, in [7] it was proved that this integral is equivalent to twice the amplitude of the ODF in the direction normal to the plane. Combining both results, we obtain the relation between the MCSA and the ODF amplitude.

To validate this relationship, we generate synthetic diffusion data using Monte-Carlo simulations with Camino [8]. In the simulations, WM is a 3D environment called substrate, formed by randomly placed parallel cylinders. A total of 22 different substrates were considered, each one containing 10,000 cylinders whose diameter are randomly taken from a Gamma distribution that approximates the ADDs observed in histology data [9]. A DSI acquisition protocol was used to sample 515 q-space points in a cubic fashion with q-values ranging between 0 and 432 1/mm with δ=1ms, Δ=100ms and TE=.101ms. To ensure convergence, we set a large number of particles (3,000,000). To be consistent with our model, we only consider the signal produced by the intra-axonal space. Some of the substrates simulated with Camino and their corresponding ADDs are visualized in Figures 1 and 2. In the histograms, the solid line represents the analytic Gamma distribution as a function of axon radius (r), while the bars represent the simulated radii distribution.

Results:

Figure 3 shows the known versus the estimated MCSA in μm^2 (denoted as) for 22 substrates. The MCSA was estimated as twice the amplitude of the ODF, calculated as in [6]. The estimated values correlate well with the known values, but are slightly overestimated. This can be attributed to the truncation of the q-space by the sampling scheme, causing an underestimation of the q-space plane integral, and opposite for the MCSA.

Conclusions:

We introduced an easy to calculate biomarker that can characterize the axon diameter distribution and can be obtained from any QSI acquisition as the ODF amplitude. We validate the assumptions by means of Monte-Carlo simulations of WM-like environments. Validations on real data are to come.

Modeling and Analysis Methods:

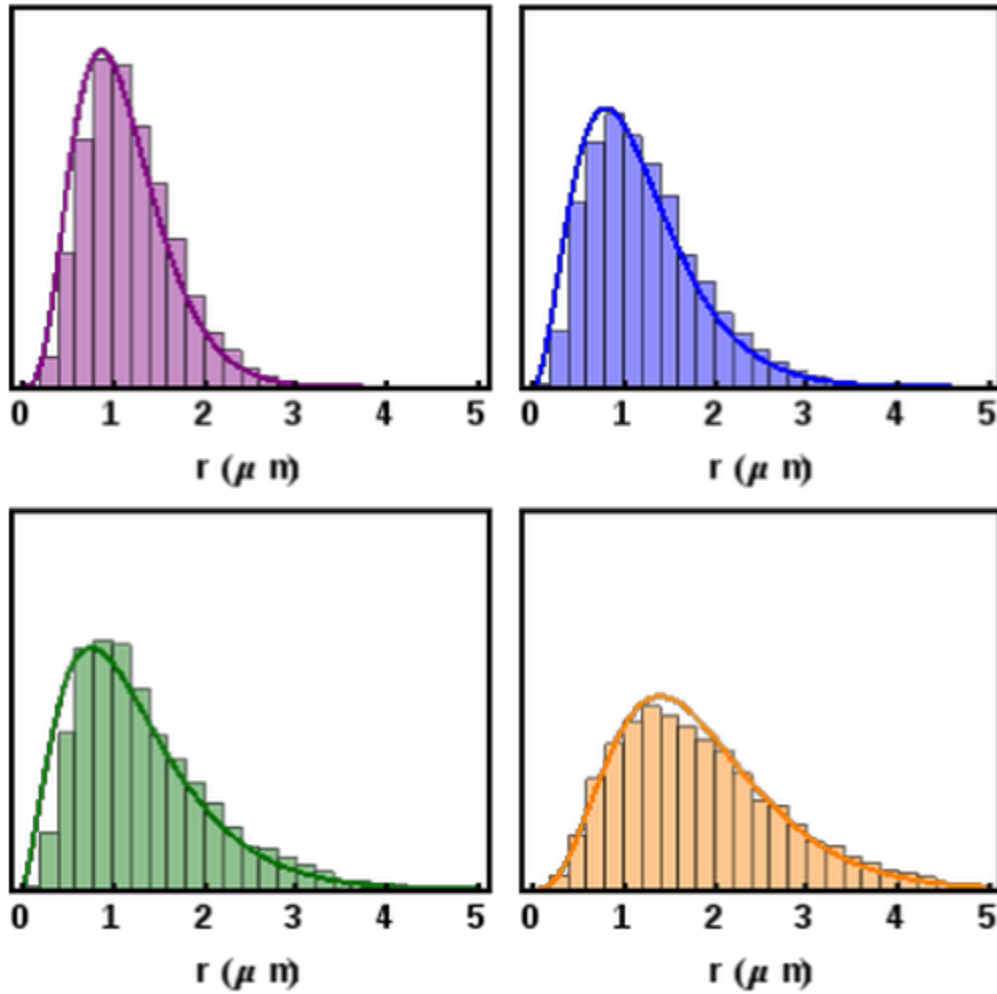Diffusion MRI Modeling and Analysis

Figure 2. Analytical and simulated Gamma distributions as a function of radius.
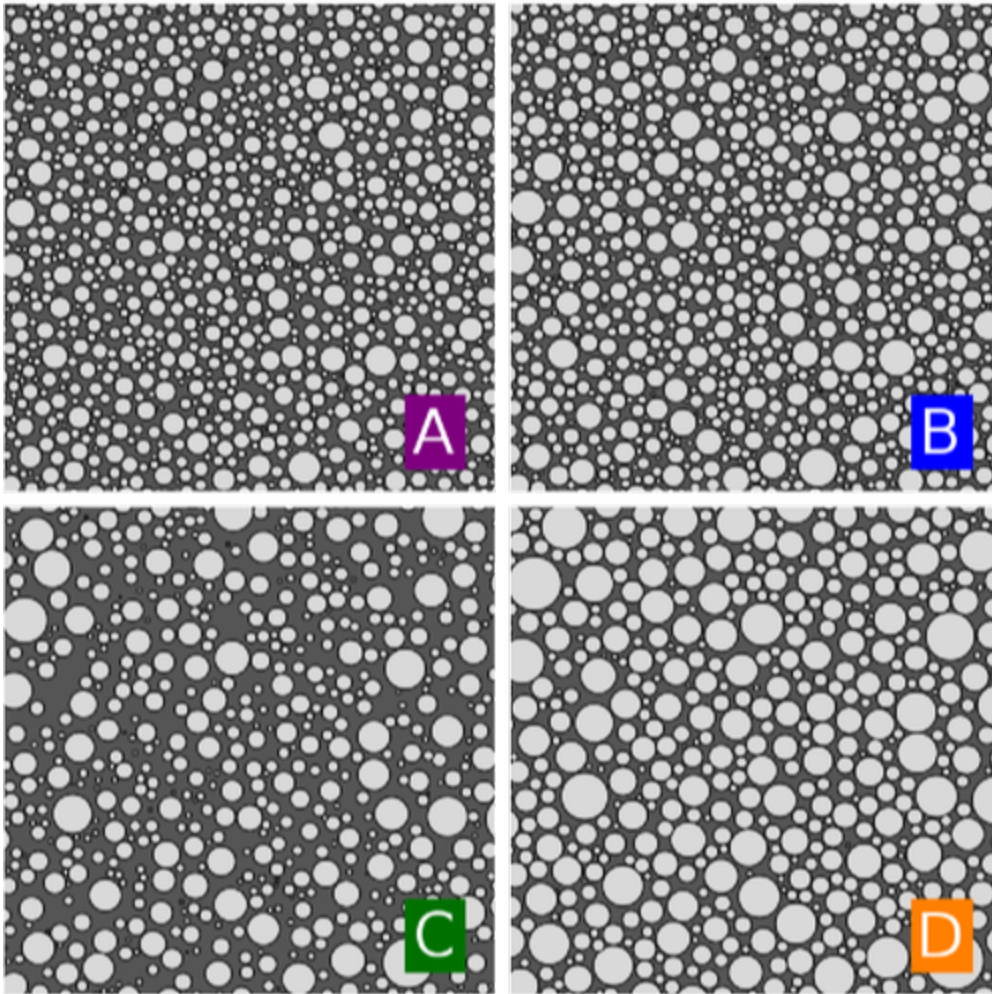
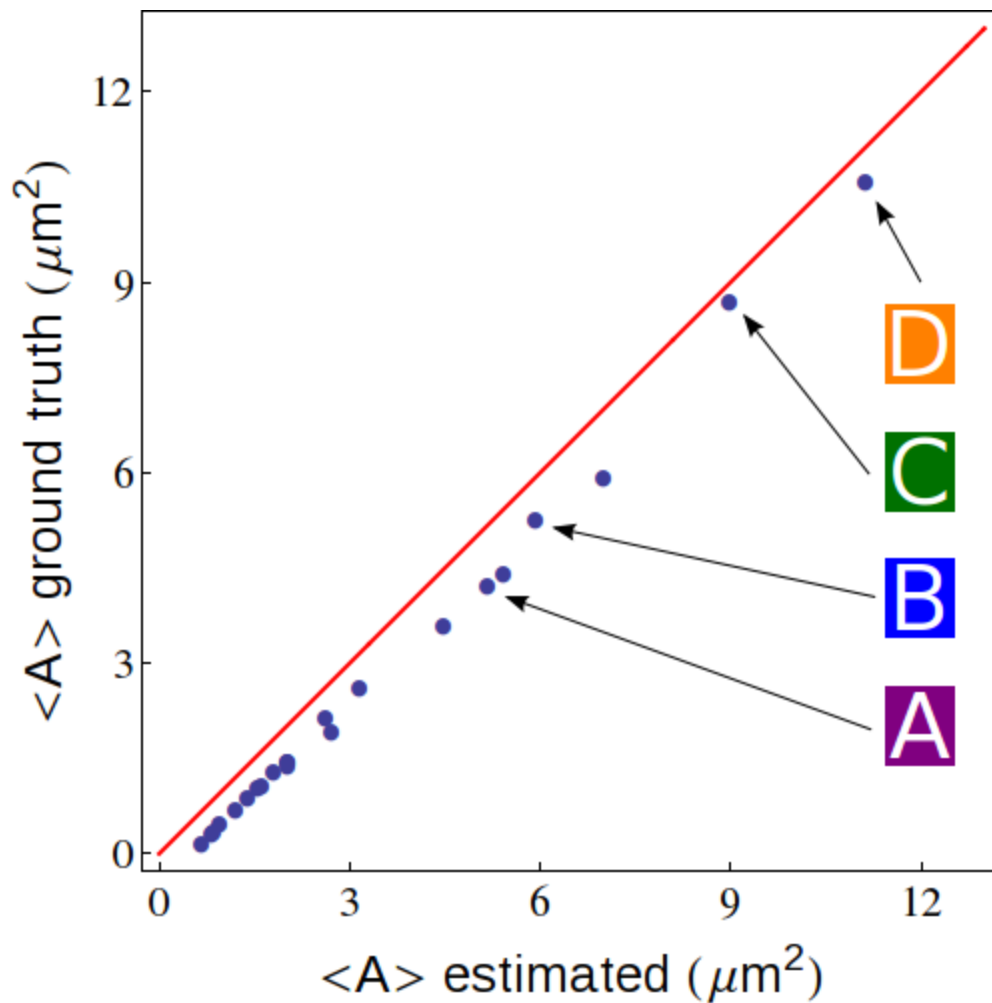Figure 1. Cross-section of simulated radii distributions

Figure 3. Comparison of known versus estimated
mean cross-sectional area for 22 distributions.

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