Supplementary Text:

Comparison with other correction methods - HCP datasets

Our detection approach identified about 16% of the voxels as having implausible MK values across the HCP datasets. Of these, a much smaller percentage of voxels had negative MK values (0.38%) and negative diffusion tensor eigenvalues (0.11%). Using the proposed MK-curve method, no voxels remained identified as implausible following the correction, although a very small percentage of voxels (less than 0.001%) still had negative MK values and negative diffusion tensor eigenvalues (Supplementary Table S1). Upon inspection, these voxels were at the perimeter of the image, where some background noise voxels entered the brain mask. While all comparison methods reduced the percentage of implausible MK voxels, they did not do it to the same extent as the proposed MK-curve. Specifically, the Gaussian smoothing and the constrained fit approaches were also able to considerably reduce the occurence of negative MK and negative diffusion tensor eigenvalue voxels, and these approaches visually showed large improvements in the number of implausible MK voxels (Figure 7c). However, voxels with apparent implausible MK values remained visible following the correction of both methods. The Gibbs removal and the MMPCA methods reduced the occurrence of voxels with negative MK and negative diffusion tensor eigenvalue, but did not dramatically decreased the occurrence of implausible MK voxels.

Table S1: Mean percentage of voxels with negative MK (NegMK) and negative diffusion tensor imaging eigenvalues (NegDTI) over the entire volume before (original) and after correction across the 10 HCP datasets for each compared method. Of note, since the constrained fit method does not change the dMRI data, we could not calculate the number of detected voxels with implausible MK values following the correction.

	Original (%)	MK-curve (%)	Gaussian smoothing (%)	Constrained fit (%)	Gibbs removal (%)	MMPCA (%)
NegMK	0.384 ± 0.102	< 0.001	0.060 ± 0.030	< 0.001	0.235 ± 0.074	0.269 ± 0.075
NegDTI	0.109 ± 0.039	< 0.001	0.010 ± 0.009	< 0.001	0.061 ± 0.029	0.074 ± 0.032

To further demonstrate the differences between the correction methods, Figure S4 plots the distribution of the MK values (across all subjects) within the detected plausible and implausible MK voxels in the original data, and following each correction method. For visualization purposes, values were trimmed to the range of [-3, 3]. For the voxels detected as implausible (Figure S4 - left), we can observe that the original MK ranged from low or negative values to high positive values, although there were many more low valued voxels than high valued voxels. Following correction using the proposed MK-curve method, most of the corrected MK values were between 0.2 and 2, which resembled the MK range observed in the detected plausible voxels (Figure S4 - right). Following correction, the MK-curve method produced the smallest standard deviation of corrected MK values, which was similar to the standard deviation of MK values observed over the plausible MK voxels. The constrained fit method corrected almost all MK values to be positive; however, most of the corrected values were close to zero, which is still not comparable with the distribution of MK values in plausible voxels. The Gaussian smoothing approach corrected many voxels with implausibly high MK values, but many implausibly low MK values remained. Though the Gibbs removal and MPPCA methods slightly increased the implausibly low MK values (e.g., there were fewer voxels with MK between -3 and -1 compared to the original data), in general they produced the least effective correction results in terms of the large number of negative MK values that remained following the correction.

For the detected plausible voxels (Figure S4 - right), MK values computed from the original dMRI mostly ranged from 0.2 to 2, which are within the physically and/or biologically expected values (Tabesh et al. 2011; Jensen et al. 2005). The MK-curve did not affect plausible voxels, and thus the MK values remained the same after this correction method. The other four methods performed correction on the entire dMRI volume, thus changing the MK values in plausible voxels as well. The Gaussian smoothing maintained a similar MK range and standard deviation as the original MK values, while the other three methods introduced new implausibly low and/or high MK values. For example, the constrained fit method increased the number of voxels with MK values over 3 (for visualization purposes, these values are shown as 3 in the plots), and the Gibbs removal and MPPCA methods outputted corrected voxels with negative MK values where the original values were positive.

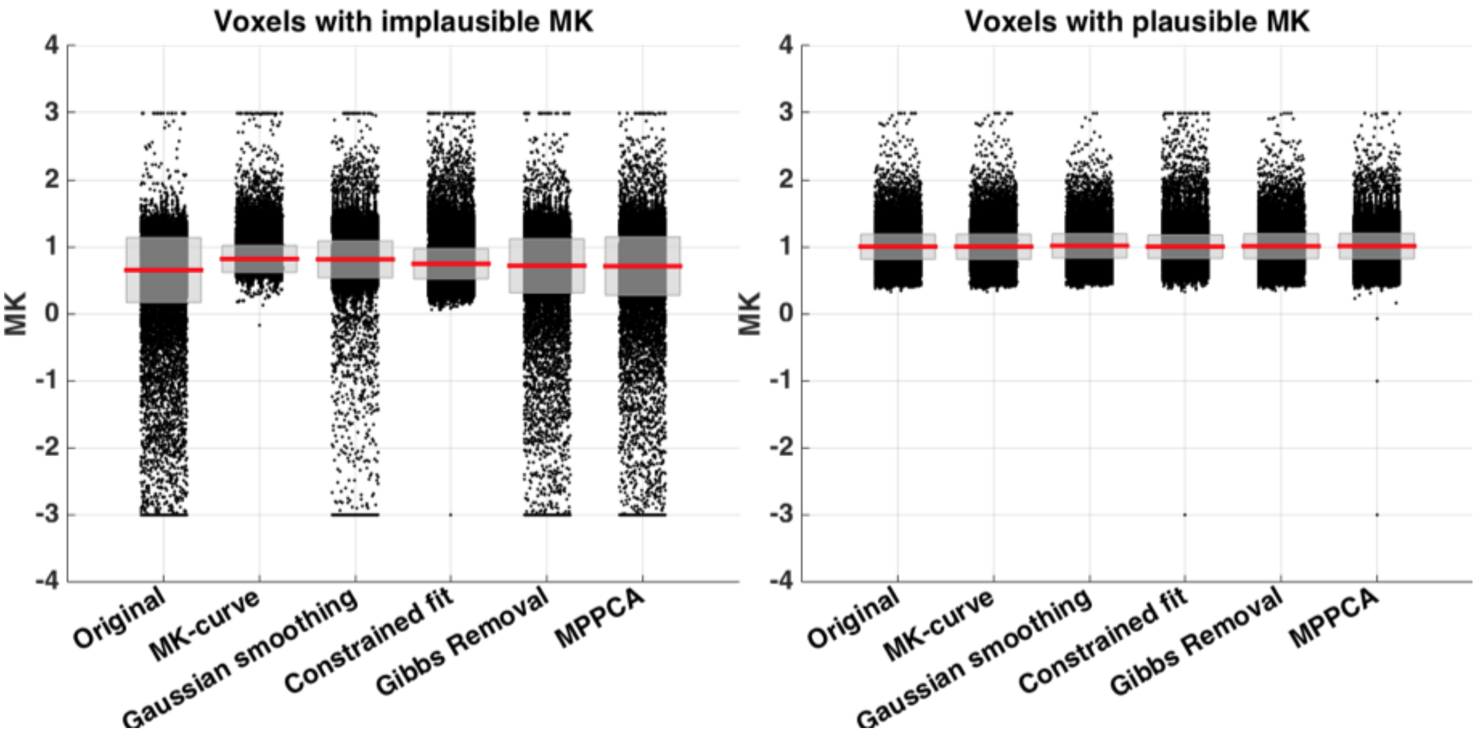

Figure S5. **MK value distribution.** Distribution of MK values across the 10 HCP datasets for the original MK values (before correction) and after application of the correction methods. The plots are separated for voxels that were originally detected as implausible (left plots) and as plausible (right). For the voxels detected as implausible, the proposed MK-curve method mapped most MK values to a range similar to the range of voxels detected as plausible. With other correction methods the MK range in voxels detected as implausible remained having a large range of MK distribution reaching to extremely low and high values. For voxels detected as plausible, the MK-curve method did not affect their MK values, but the compared methods introduced new implausible MK values (e.g. additional negative MK values). The red line and the gray box indicate the mean and the standard deviation of the MK values, respectively. For visualization purposes, MK values are truncated between -3 and 3.