Diffusion Goes Mad Session

Higher Order Diffusion Models and Methods – Going Beyond the Diffusion Tensor

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Diffusion weighted MRI (DWI) has become instrumental in noninvasive characterizations of Central-Nervous-System (CNS) tissues *in vivo*[1,2]. By monitoring micron-scale spin displacements arising from Brownian motions, DWI provides access to dimensions much smaller than the imaging voxel size. The ensuing diffusion-driven contrasts have been harnessed, *inter alia*, for early diagnosis of ischemia[3,4]; for monitoring various CNS pathologies[5]; for studying CNS development[6] and plasticity[7]; and, more recently, even for tracking neural activity *in vivo*[8,9].

It has been long recognized that DWI contrasts vary strongly with the direction of the applied diffusion-sensitizing gradients in white matter (WM)[10,11]. It has been since shown that this diffusion anisotropy can be used to map the orientations of WM fibers *in vivo* and noninvasively[12,13]. To date, the most widely employed model for mapping orientations is the diffusion tensor, which assumes that: (1) a single water reservoir is being interrogated in each voxel; (2) the microstructures comprising the WM fiber are coherently aligned; (3) the fiber's overall structure can be modeled by a single "ellipsoid" conveying the underlying anisotropy and the fiber's respective orientation. To fully characterize the diffusion tensor, several non-collinear measurements using low diffusion weightings are required; the ensuing apparent diffusion coefficients are then transformed to the fiber's principal axis system, from which the rotationally invariant metrics can be extracted[1,2,12-14].

Although highly successful and widely employed, Diffusion Tensor Imaging (DTI) does not take into account the richness of CNS microstructures vis-à-vis their underlying topologies; in some voxels – in particular in those containing crossing fibers and/or other forms of orientational dispersion – the diffusion tensor no long provides an accurate description of the structural morphology. This, in turn, can significantly impact fiber tracking procedures[15]. On the other hand, more elaborate modeling of CNS tissues – and the design of more elaborate methods and acquisition schemes that facilitate the estimation of these higher-order models – could account for some of the CNS's structural diversity, and provide more accurate information on the tissue's microstructure[16].

The aims of this lecture are therefore (i) to explore more advanced diffusion models addressing the possibility of structural heterogeneity still at the low diffusion weighting regime; (ii) to explore higher order diffusion models that require stronger diffusion weighting; (iii) to survey novel diffusion MRI methods departing from the dogma of a single pair of diffusion-sensitizing gradients, and explore their added value in terms of microstructural characterization.

In the first part of the lecture, we shall describe models such as multi-tensor[17] and Ball & Stick[18] and their potential benefits for fiber tracking[15]. We shall then touch upon High Angular Resolution Diffusion Imaging (HARDI) models such as and Persistent-Angular-Structure (PAS)[19] and QBALL[20] MRI, and further discuss measurements of the 3-dimensional propagator via Diffusion Spectrum Imaging (DSI)[21]. In the final part of the lecture, we shall discuss Oscillating-Gradient Spin-Echo (OGSE) approaches[22] for enhancing diffusion MRI's sensitivity towards smaller, more biologically relevant length scales, as well as double-Pulsed-Field-Gradient (dPFG) MRI[23,24] for probing highly disordered systems.

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