Diffusion Goes Mad Session

Advanced Models - Ball & Stick, Multi-Tensor, PASMRI & Etc…

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Diffusion Magnetic Resonance (MR) methodologies have been long recognized for their ability to non-invasively interrogate dimensions which are much smaller than the imaging voxel size[1,2]. This unique capability is now harnessed for a myriad of applications, including, *inter-alia*, the early detection of ischemia[3] onset, monitoring the progression of pathophysiological processes[4], resolving the orientation of White Matter (WM) fibers[5,6], following brain plasticity[7], and, more recently, even studying the functional properties of Central-Nervous-System (CNS) tissues[8].

The diffusion process is probed in MR by the application of diffusion-sensitizing gradients[9], and the ensuing signal decay reflects the displacement of protons within the tissue. However, as most biological tissues are heterogeneous, the information available will depend on the diffusion regime which is being probed (e.g., on how the b-values are chosen[6]); furthermore, adequate models need to be devised in order to extract meaningful microstructural information from the ensuing signal decay. Perhaps the most familiar, and certainly the most widely employed diffusion methodology to date is the Diffusion-Tensor-Imaging (DTI) approach[6], which entails diffusion measurements at rather low b-values in a set of non-collinear directions; the diffusivities obtained in each direction are in turn transformed to rotationally invariant metrics of the diffusion tensor – which in turn are used to map the orientation of WM fibers.

The diffusion tensor model, although highly successful in many instances, assumes a-priori that a single water reservoir is being interrogated in each voxel, and that the tissue structure can be modeled by a single "ellipsoid" which reports on the anisotropy and direction of the compartment. Although DTI is highly useful in many cases, these assumptions are somewhat simplistic given the structural richness of most CNS tissues vis-à-vis their highly complex underlying topology (consider for example even the simplest case where fibers are crossing within a single voxel), and the non-specificity of water to any particular tissue "component" (axonal, intra- or extra-cellular, myelin water, etc.). In attempting to access further information on the tissue architecture, we must impose more elaborate diffusion models on the diffusion-driven signal decay, which account for such compartments, and which would thus be able to resolve richer information on the tissue microstructure[10].

Alternatively, one may employ different diffusion-weighting mechanisms, where the underlying physics may offer increased sensitivity to certain microstructural properties; Just two examples include the Oscillating-Gradient-Spin-Echo (OGSE) approach[11-13], which provides access to short effective diffusion periods and thus can probe smaller length scales, or double-Pulsed-Field-Gradient (d-PFG) MR approaches[14-

[20], which can convey the apparent eccentricity even when anisotropic compartments are completely randomly oriented.

The aims of this educational lecture, which will be aimed at a broad audience interested in advanced diffusion MR models and methods, are threefold:

(1) To explore several prominent more advanced models of diffusion in the CNS (still in the low b-value regime), which address the possibility of obtaining information on different tissue components/compartments within a given voxel[10,21-24].

(2) To describe several higher order models[25-28], some of which require high b-value measurements, and mainly address the issue of crossing fibers within a single voxel.

(3) To briefly outline a few diffusion MR methods that exploit non-Gaussian diffusion[16,29-33] as the source of contrast, and describe their potential for uncovering microstructure in the CNS.

In the first part of the lecture, we shall depart from the more conventional diffusion tensor notation, and describe more elaborate models such as the Persistent Angular Structure (PAS) MRI, the Ball & Stick model, and several other models for characterizing tissue components, and show how they can be used to resolve new information which is either obscure in DTI or, in fact inherently unavailable in such an analysis[10]. In the second part of the lecture, we shall touch upon High-Angular-Resolution-Diffusion-Imaging (HARDI) method and show that they can be used to resolve underlying tissue structure[11-14]. Finally, in the last part of the lecture, we shall briefly describe diffusion methodologies that are slightly less model-dependent such as the Oscillating Gradients Spin Echo (OGSE)[11,34], the double-Pulsed-Field-Gradient (d-PFG) MR method[35,36], and Diffusion Kurtosis Imaging (DKI)[37-39], and show that they can resolve unique microstructural information in tissues.

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