Highly efficient diffusion exchange spectroscopic imaging for biological applications

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Sensitive to local diffusive properties, diffusion exchange spectroscopy (DEXSY) is a powerful two-dimensional nuclear magnetic resonance (NMR) method for measuring the transport of water directly from one microenvironment to another, allowing for exchange processes between numerous compartments. DEXSY is, however, rarely used, especially when combined with magnetic resonance imaging (MRI) in biological applications, because of its exceptionally long scan time requirements.
Using the marginal distributions constrained optimization (MADCO) framework[1], we present a method to vastly reduce the number of required acquisitions, making DEXSY-MRI feasible for the first time. Experiments are performed on a composite MRI nerve tissue phantom with restricted and free water exchanging compartments. We show that $N=22$ acquisitions were sufficient to accurately determine the exchange spectrum at three mixing times; this number of aquisitions is ~276 times less than what was previously thought to be needed ($N=6075$). The presented framework allows one to add more mixing times at a low data requirement cost (i.e., four acquisitions per additional mixing time). Combined with a fast imaging readout, such as echo planar imaging (EPI), whole human brain imaging using 22 DEXSY acquisitions would take about 22 minutes, which is within the time frame of clinical MRI.
Regarding the diffusion exchange spectrum as a joint probability function and accordingly imposing constraints in the optimization process, provides the opportunity to reliably and feasibly obtain spatially resolved water exchange, as reflected by physical microscopic environments. Cell membrane permeability and active transport processes in healthy and diseased tissue are only partially understood, and currently cannot be directly measured noninvasively and *in vivo*, without imposed restricting assumptions. Fast DEXSY-MRI and NMR can now be beneficial for broad application for heterogeneous materials such as biological tissues, food, plants, and rocks, providing exciting opportunities for investigators in a range of disciplines.

[1]Benjamini D and Basser PJ. Use of marginal distributions constrained optimization (MADCO) for accelerated 2D MRI relaxometry and diffusometry. J Magn Reson, 271:40-45, 2016.