Tissue-type segmentation using non-negative matrix factorization of multi-shell diffusion-weighted MRI images

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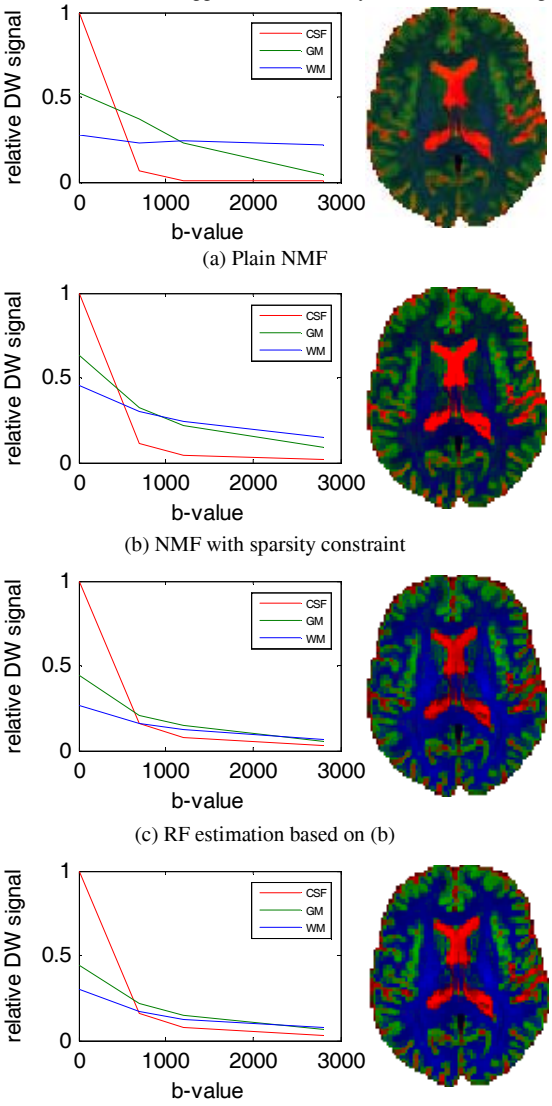
Purpose: Multi-tissue constrained spherical deconvolution (CSD) of multi-shell diffusion-weighted (DW) MRI data is a recently proposed technique that allows simultaneous estimation of the white matter (WM) fiber orientation distribution function (fODF) and the apparent densities of the main tissue types of the brain (cerebrospinal fluid (CSF), gray matter (GM) and WM) [1]. It has been shown that this approach avoids the overestimation of apparent WM density in voxels containing GM and/or CSF, as was the case with single-tissue CSD. In addition, it substantially increases the precision of the fODF fiber orientations and reduces the presence of spurious fODF peaks in voxels containing GM and/or CSF. An important limitation of the current multi-tissue CSD approach is that it relies on the availability of properly aligned anatomical tissue segmentations in order to estimate per-tissue response functions (RFs), which can prove challenging due to EPI distortions. The aim of this work is to develop a reliable tissue-type segmentation method that operates directly on the DW-MRI data and does not rely on the availability of a properly aligned anatomical MRI scan.

Methods: *Acquisition*: DW data were acquired on a 3T scanner, using an 8-channel receiver head coil. Relevant DW-MRI parameters: 5 b=0, 25 b=700, 45 b=1200 and 75 b=2800 s/mm^2 samples; TR/TE=9500/100ms; 2mm isotropic resolution. High-resolution T_1-weighted images (1mm isotropic) were also acquired to aid tissue type identification. *Pre-processing*: DW images were corrected for motion and eddy current distortions [2] and for EPI distortions [3], to ensure proper alignment of the DW images to each other and to the anatomical data. The anatomical image was segmented into four tissue types (CSF, cortical GM (CGM), deep GM (DGM) and WM) as outlined in [4] to serve as a reference. *Tissue identification approaches*: The problem of identifying tissue types from a set of multi-shell DW images can be cast as a non-negative matrix factorization (NMF) problem. NMF is a popular, data-driven multivariate analysis technique which lends itself to finding the hidden constituent parts of the data [5]. Its goal is to approximate a nonnegative matrix $\boldsymbol{V}$ of measurements (m-by-n) by the product of two unknown non-negative matrices: $\boldsymbol{W}$ (m-by-k), also known as the basis matrix, and $\boldsymbol{H}$ (k-by-n), also known as the weight matrix. The rank k of the factorization is generally chosen much smaller than n and m, such that the product $\boldsymbol{WH}$ can be regarded as a compressed representation of the data in $\boldsymbol{V}$. In this particular case, $\boldsymbol{V}$ is simply the matrix containing the raw DW MRI signal, with each row corresponding to a different q-space sample and each column corresponding to a different voxel inside the brain. As our aim is to recover the three main tissue types in the brain, k is set to 3. In general, NMF is not exact and is approximated numerically as: $\min_{\boldsymbol{W},\boldsymbol{H}}\|\boldsymbol{V}-\boldsymbol{WH}\|_2^2$ subject to $w_{i,j} \geq 0$ and $h_{i,j} \geq 0$. After NMF, $\boldsymbol{W}$ would ideally contain 3 tissue specific q-space RF, which can be combined with the weights specified in $\boldsymbol{H}$ to explain the full data set. In addition to the NMF not being exact, the factorization is also not unique. This situation can be improved by imposing additional constraints on the factors. In the case of NMF of multi-shell DW-MRI data, it is sensible to assume that matrix $\boldsymbol{H}$ is sparse, as most brain voxels contain a single tissue type and mixtures should only be found at the tissue interfaces. By including such a sparsity constraint on $\boldsymbol{H}$ we obtain the following minimization objective: $\min_{\boldsymbol{W},\boldsymbol{H}}\|\boldsymbol{V}-\boldsymbol{WH}\|_2^2 + \lambda\sum_{i,j} h_{i,j}$ subject to $w_{i,j} \geq 0$, $h_{i,j} \geq 0$, $\|\boldsymbol{w}_j\|_2 \leq 1$ and $\lambda \geq 0$, where λ is a regularization weight, controlling the strength of the L1 regularization and $\boldsymbol{w}_j$ is the j-th row of $\boldsymbol{W}$. $\|\boldsymbol{w}_j\|_2 \leq 1$ prevents $\boldsymbol{W}$ from becoming arbitrarily large, which would lead to arbitrary small values in $\boldsymbol{H}$, rendering the sparsity constraint ineffective. This approach is also referred to as non-negative sparse coding [6]. Both the general NMF and the non-negative sparse coding problems are solved very efficiently using the approach in [7]. *Response function estimation*: Once the tissues have been segmented using sparse NMF, we select the voxels containing only a single tissue type and average their DW signals to obtain the final multi-shell, multi-tissue RFs. In the case of the WM response, this involves identifying and reorienting single fiber voxels in the WM voxels using either an FA threshold or recursive RF calculation [8].



(a) Plain NMF

(b) NMF with sparsity constraint

(c) RF estimation based on (b)

(d) RF estimation based on anat. segmentation

Fig.1: *Decomposition of* $\boldsymbol{V}$ *(not shown) in* $\boldsymbol{W}$ *(left) and* $\boldsymbol{H}$ *(right). To make inspection easier,* $\boldsymbol{W}$ *is compressed into a 4-by-3 matrix by averaging over each b-value shell.*

Results: With plain NMF (Fig. 1a), good contrast was obtained between CSF voxels and GM/WM voxels, but contrast between GM and WM was suboptimal. By including a sparseness constraint on $\boldsymbol{H}$, GM/WM contrast could be substantially increased, leading to high quality tissue segmentations (Fig. 1b). Selecting the voxels containing only a single tissue type and averaging results in multi-shell, multi-tissue response functions and apparent density maps (Fig. 1c) very similar to those obtained using anatomical segmentation (Fig. 1d). Fig. 2 shows multi-tissue fODFs resulting from the RF estimated in Fig. 1c. The fODFs resulting from Fig. 1d are similar but not shown. Similar results were obtained with different multi-shell acquisitions (results not shown).

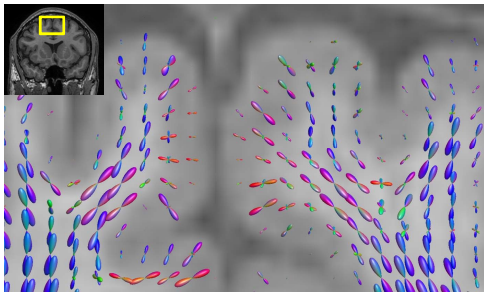


Fig.2: *Multi-tissue CSD fODFs using RF estimated directly from DW data (cfr. fig 1c).*

Discussion: We have introduced a new segmentation approach for multi-shell DW-MRI data based on the principle of NMF. The proposed method provides segmentation of the three main tissue types directly from the raw DW-MRI data, does not use any spatial priors and can be executed for a full brain data set in only a few seconds. In addition, the approach is not specific to brain imaging and can potentially be applied to other multi-shell diffusion MRI data sets. As an example of the usefulness of our approach, we applied it to estimate tissue specific, multi-shell RF for the purpose of multi-tissue CSD. Whereas before, multi-tissue CSD relied on the availability of properly aligned segmentations of anatomical MRI scans to estimate these responses, with our proposed segmentation approach they can be obtained directly from the DW-data.

References: [1] Jeurissen et al., NeuroImage 103:411-426, 2014; [2] Andersson et al., Proc. ISMRM 20:2426, 2012; [3] Andersson et al., NeuroImage 20(2):208-219, 2004; [4] Smith et al., NeuroImage 62(3):1924-1938, 2012; [5] Lee and Seung, Nature 401(6755):788-791, 1999; [6] Hoyer, Proc. IEEE Workshop on Neural networks for signal processing, pp.557-565,2002. [7] Mairal et al., Journal of Machine Learning Research 11:19-60,2010 [8] Tax et al., NeuroImage 86:67-80, 2014.