Filtered multi-tensor tractography using free water estimation

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Introduction: Diffusion Weighted Imaging (DWI) enables neuroscientists to determine how neural fibers originating from one region connect to other regions. We introduce a method for tracing fibers that takes into account free water by extending the existing framework of Malcolm et al. [1], which performs multi-tensor tractography within an unscented Kalman filter (UKF) framework. This approach provides an inherent regularization of the tracts, since each estimate is guided by those previous, in addition to the observed local signal. The proposed UKF method also provides an estimate of the confidence in the estimation at each step, as given by the covariance matrix. In this work, the signal model is augmented by an additional weighted term for the isotropic diffusion component of free water, and the Kalman filter is modified to enforce constraints on the weights. The proposed method including the free-water term can be very useful in tracing fibers through edema or lesions, where traditional tractography algorithms fail.

Methods: In diffusion weighted imaging the signal is partly due to the diffusion of water along axonal fibers, and partly to free water, which shows isotropic diffusion with an apparent diffusion coefficient of about $d_A = 3 \cdot 10^{-3} mm^2/s$ at body temperature [2]. We model the signal $s = [s_1,...,s_n]^T$ as a weighted mixture of three Gaussian tensors $s_i = s_0(0.5w\exp(-bu_i^T D_1 u_i) + 0.5w\exp(-bu_i^T D_2 u_i) + (1-w)\exp(-bu_i^T D_{iso} u_i))$ where s_0 is a baseline signal intensity, b is an acquisition-specific constant, u_i is the i-th gradient direction, w is a weight term, and D_1, D_2 and D_{iso} are diffusion tensor matrices. The tensors D_1, D_2 represent the contribution of the fiber to the signal. In this study we assume the shape of the fiber tensors to be ellipsoidal, i.e. there is one dominant diffusion direction m with eigenvalue λ_1 and the remaining orthonormal directions have equal eigenvalues $\lambda_2 = \lambda_3$. Hence, the tensors can be written as $D = \lambda_1 mm^T + \lambda_2(pp^T + qq^T)$ with m, q, p forming an orthonormal basis aligned to the principal diffusion direction m. The tensor D_{iso} models the contribution of free water and therefore can be written as a diagonal matrix with d_A as diagonal elements. Notice that the term $(1-w)$ in the model equation represents the fraction of free water. At each step of the tractography we examine the measured signal, estimate the underlying model parameters using a state-space filter to match the signal, and propagate forward in the principal direction of diffusion m. Since the signal reconstruction is non-linear, we employ an unscented Kalman filter to perform the estimation, which uses a deterministic sampling technique to pick a set of sample points based on the current covariance P_t and mean x_t of the state. These sample points are then propagated through the signal model from which a new estimate is recovered. We assume identity dynamics for the transition function since the fiber configuration does not change drastically from one point to the next. The state is represented as $x = [m_1, \lambda_{11}, \lambda_{12}, m_2, \lambda_{21}, \lambda_{22}, w]^T$. To guarantee that the tensors don't become degenerate and that the weight of each diffusion term stays positive we constrain the state to have positive eigenvalues and a bounded weight ($w \geq 0$ and $w \leq 1$). This means, for each iteration where at least one of the requirements is broken, we wish to find the state $\hat{x}$ closet to the unconstrained state x, which still obeys the constraints. Using P_t as weighting matrix, this becomes the quadratic programming problem: $\min_{\hat{x}}(x-\hat{x})^T P_j^{-1}(x-\hat{x})$ subject to $D\hat{x} \leq d$, where D and d are constructed to match the above constraints [3]. We iterate through this loop until the model appears isotropic.

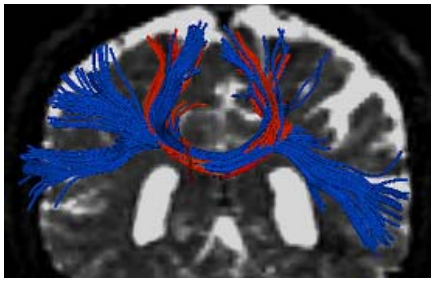

Figure 1: Transcallosal fibers traced by the Levenberg-Marquard solver (red), and the proposed method (blue).

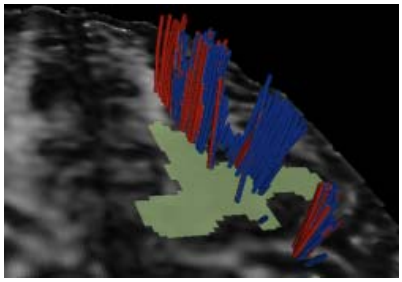

Figure 2: Corticospinal tract traced using the new method (blue), and the original method (red) through the edema (green)

Experiments: We tested our approach on two human brain scans: a healthy subject, and a subject with a tumor in the parietal lobe surrounded by a large volume edema. First, we traced out the lateral transcallosal fibers in the healthy subject using the newly proposed method. For comparison we used the same three-tensor model with free water from above, but estimated the model parameters using a Levenberg-Marquardt nonlinear least-squares solver. In the subject with the tumor, we traced the fibers of the corticospinal tract, which run through the region affected by the tumor, using the new method, and the original algorithm by Malcolm et al., without free water. Lastly, we derived a free water map from the full brain tractography of the healthy subject and examined it for anatomical correctness.

Results: Fig. 1 contrasts the results of tracing the transcollosal fibers using the proposed free-water based method, and the Levenberg-Marquard solver. It can be seen that the new method produces a more complete tract reconstruction. Fig. 2 shows the results of tracing the corticospinal tract through the region affected by the tumor. In virtue of the free water term, the new method is able to trace some fibers in the region of the edema that the original method misses. Moreover, for this case, the new method has a lower signal reconstruction error, with a mean squared error of 3.63%, compared to the original method (4.37%). Finally, the free water map matches the anatomical expectations. For example, as can be seen in Fig. 3, the fraction of free water is higher around the ventricles and cortical areas.

Figure 2: Transversal plane of the free water map. Darker shades correspond to more free water.

References: [1] Malcolm, J.G., Shenton, M.E., Rathi, Y.: Filtered Multi-tensor Tractography. IEEE Trans. On Medical Imaging 29, 2010. [2] Pasternak, O., Sochen, N., Gur, Y., Intrator, N., Assaf, Y.: Free Water Elimination and Mapping from Diffusion MRI, Magnetic Resonance in Medicine, 2009. [3] Malcolm J.G., Shenton M.E., Rathi Y., Two-Tensor Tractography Using a Constrained Filter, Medical Image Computing and Computer-assisted Intervention, 2009