Information-Theoretic Analysis of Brain White Matter Fiber Orientation Distribution Functions

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Objective: High angular resolution diffusion imaging (HARDI) is a variant of conventional MRI that uses multiple radially-distributed gradients to encode directional profiles and orientations of water diffusion. Diffusivity profiles can be resolved more clearly than conventional diffusion tensor imaging (DTI) in brain regions where fiber tracts cross, providing more accurate information for fiber-tracking (tractography), disease detection, and analysis of anatomical connectivity.

We evaluate a new information-theoretic metric, the symmetric Kullback-Leibler divergence (sKL-divergence), for measuring differences between diffusivity profiles in HARDI. We compute sKL-divergence from spherical harmonic expansions of the orientation-dependent diffusion functions (ODFs). We show that sKL-divergence is more robust than standard inner product measures for detecting small rotational deviations between HARDI data, at various diffusion weights and noise levels, making it an attractive measure for HARDI registration.

Kullback-Leibler Divergence of Two Diffusivity Functions: In HARDI, the signal attenuation in a specific direction, $g(\theta,\phi)$, is given by the Stejskal-Tanner equation

$$S(g) = S_0 \exp(-bD(g))$$

b is the diffusion weighting factor and D is the scalar diffusivity (apparent diffusion coefficient). Inspired by [1], we model the diffusivity function as a probability density function (pdf), by normalizing its integral over the spherical angle Ω to 1:

$$p(\theta,\phi) = D(\theta,\phi)\big/ gtr(D),$$

$$gtr(D) = \int_\Omega D(\theta,\phi)\,d\Omega,$$

For two diffusivity functions D_p and D_q, we define the symmetric KL-divergence based on the corresponding pdfs $p(\theta,\phi)$ *and* $q(\theta,\phi)$*:*

$$sKL(p,q) = \frac{1}{2}\left\{ \begin{aligned} &\frac{1}{gtr(D_p)}\left[\int_\Omega D_p \log(D_p)\,d\Omega - \int_\Omega D_p \log(D_q)\,d\Omega\right] \\ &+\frac{1}{gtr(D_q)}\left[\int_\Omega D_q \log(D_q)\,d\Omega - \int_\Omega D_q \log(D_p)\,d\Omega\right] \end{aligned} \right\}$$

Direct estimation of sKL in the above equation is computationally expensive, but is faster if we expand the diffusivity functions $D(\theta,\phi)$ as a spherical harmonic (SH) series:

$$sKL(p,q) = \frac{1}{2}\left\{ \begin{aligned} &\frac{1}{c_{00}^p} \sum_{l=0,even}^{\infty} \sum_{m=-l}^{l} \left[c_{lm}^p d_{lm}^p - c_{lm}^p d_{lm}^q\right] \\ &+\frac{1}{c_{00}^q} \sum_{l=0,even}^{\infty} \sum_{m=-l}^{l} \left[c_{lm}^q d_{lm}^q - c_{lm}^q d_{lm}^p\right] \end{aligned} \right\}$$

Here $D_j = \sum_{l=0,even}^{\infty} \sum_{m=-l}^{l} c_{lm}^j Y_{lm}$, $\log(D_j) = \sum_{l=0,even}^{\infty} \sum_{m=-l}^{l} d_{lm}^j Y_{lm}$, and $j \in \{p, q\}$.

Reorientation of Diffusivity Functions: We adopt the "Preservation of Principal Directions (PPD)" method, which preserves the shape of the diffusivity function along the local principal fiber orientation. Here we propose a fast algorithm to determine the principal direction of the diffusivity function, based on the principal component analysis (PCA) of its shape. At each direction sampled by the diffusion gradient $g(\theta_i, \phi_i)$, $0 \le i < n_s$, we define a point with distance to the origin $d_i = D(\theta_i, \phi_i)\, g(\theta_i, \phi_i) = (d_{i0}, d_{i1}, d_{i2})$, where the last term is the Cartesian coordinates of d_i. The mean and the covariance matrices, μ and Σ, of the point set $\{d_i\}$ are given by

$$\mu_j = \frac{1}{n_s}\sum_{i=0}^{n_s-1} d_{ij};\ \Sigma_{ij} = \frac{1}{n_s}\sum_{k=0}^{n_s-1}(d_{ki}-\mu_i)(d_{kj}-\mu_j),\ 0 \le i,j < 3.$$

The principal direction of the diffusivity function is determined by the first eigenvector of Σ. The rotation matrix R, which adjusts the direction of the diffusivity function, is then obtained using the PPD procedure, and the new gradient directions $g(\theta_i',\phi_i') = R \cdot g(\theta_i,\phi_i)$

The values of the reoriented diffusivity functions D' in the original directions (θ_i, ϕ_i) can be computed from the SH series, as the basis functions Y_{lm} are continuous and defined at all spherical angles:

$$D'(\theta_i,\phi_i) = D(\theta_i - \Delta\theta_i, \phi_i - \Delta\phi_i) = \sum_{l=0,even}^{\infty} \sum_{m=-l}^{l} c_{lm} Y_{lm}(\theta_i - \Delta\theta_i, \phi_i - \Delta\phi_i)$$

Experiments and Results:

Synthetic examples. We constructed a two-fiber diffusivity function using two orthogonal Gaussian tensors, T_0 and T_1, with typical eigenvalues for white-matter (WM) fibers. We set $T_0 = diag(200, 200, 1700) \times 10^{-6}$ (mm²/s); T_1 was obtained by rotating T_0 90 degrees around the y-axis. We also generated an isotropic gray-matter (GM) diffusivity function by setting $T_{iso} = diag(700, 700, 700) \times 10^{-6}$ (mm²/s). Then the diffusivity function D is given by

$$D = -\frac{1}{b}\sum_{i=0}^{n-1} p_i \exp(-b g^T T_i g)$$

where n is the number of fibers. $p_0 = p_1 = 0.5$ for two-fiber structures and $p_0 = 1$ for the isotropic diffusivity function. Different b values (500, 1500, 3000) s/mm² were tested. The order of the SH series (l_m) was set to 8.

HARDI data. The HARDI data was acquired from a healthy 22-year-old man on a 4T Bruker Medspec MRI scanner using an optimized diffusion tensor sequence. Imaging parameters were: 21 axial slices (5 mm thick), FOV = 24 cm, TR/TE 6090/104.5 ms, 0.5 mm gap, with a 128×100 acquisition matrix and 30 images acquired at each location: 3 low ($b = 0$) and 27 high diffusion-weighted images in which the encoding gradient vectors were uniformly radially distributed in space ($b = 1100$ s/mm²). The reconstruction matrix was 128×128, yielding a 1.875×1.875 mm² in-plane resolution. The total scan time was 3.09 minutes. We set $l_m = 4$ for the spherical harmonic analysis.

Fig. 1 shows the principal directions determined from HARDI by the PCA method. **Fig. 2** compares the fiber directions when the HARDI data was rotated by 60 degrees around the inferior-superior axis passing through its center of mass, with and without reorientation of the diffusivity functions. **Fig. 3** shows that direct interpolation of the MR signals results in the least swelling, or loss of anisotropy, in the diffusivity function. Linear interpolation using log(D) performs better than D in terms of degrading the signal geometry. Computing log(D) may therefore be an acceptable alternative to computing S. **Fig. 4** shows that at different noise levels, the sKL cost function detects angular discrepancies in diffusivity functions more sensitively than the inner product with/without the $l = 0$ term, in low b-settings. sKL is also still comparable in performance with the inner product without $l = 0$ term, at a high b-value.

We further compared the three cost functions, which were summed over all voxels, in the 3D HARDI data. Two identical HARDI data was initially overlapped (rotation angle = 0 degree), and then one image was rotated (with diffusivity functions reoriented) up to ±20 degrees, with sKL and inner products (with/without $l = 0$ term) computed at every two degrees. **Fig. 5** shows that sKL has very sharp gradient near the optimal solution, and is sensitive enough to detect 2-degree deviation of the images. The symmetric KL-divergence is therefore a good candidate cost function for registration of HARDI, which we expect to evaluate in the near future.

Reference:
Ozarslan, E., B.C. Vemuri, and T.H. Mareci. Magn Reson Med, 2005. 53(4): p. 866-76.

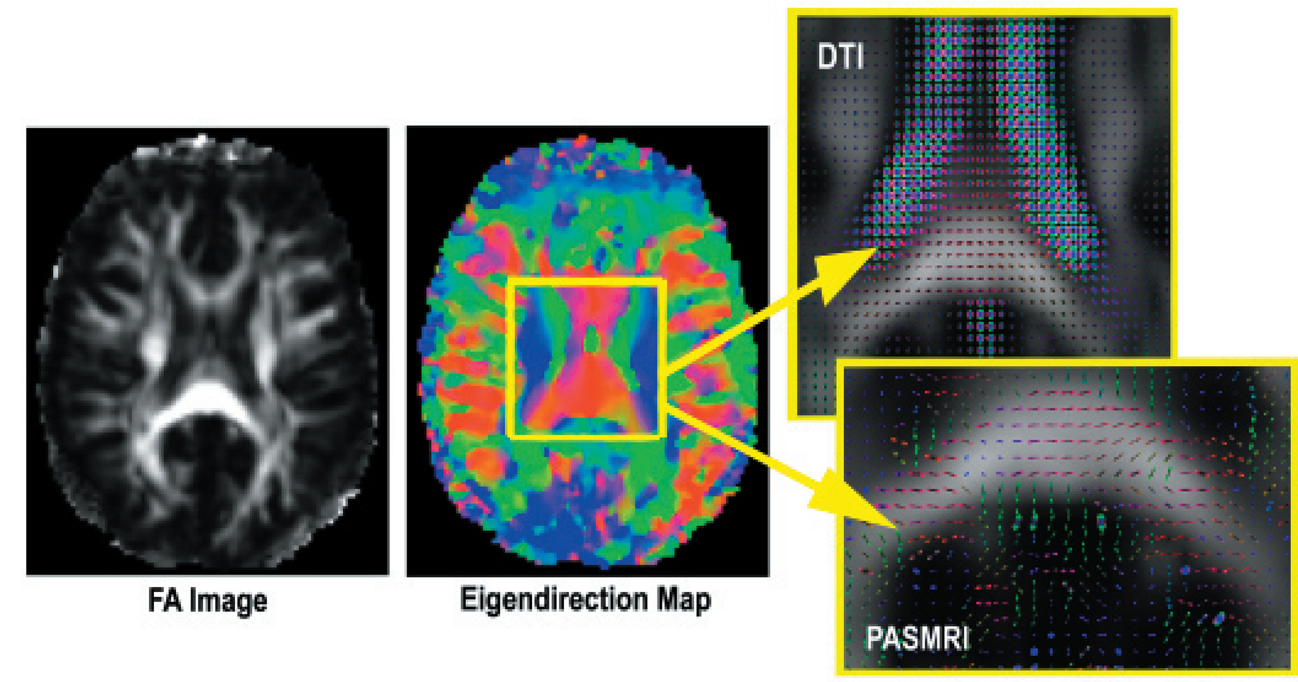

Fig. 1. The eigendirection map for the HARDI data, determined using the PCA method. Fibers with right-left orientation are shown in red, anterior-posterior in green, and inferior-superior in blue. The eigendirections correctly depict the orientations of major WM fiber structures, and are compatible with the tensor glyphs and persistent angular structures (PAS) computed using the visualization software "Camino".

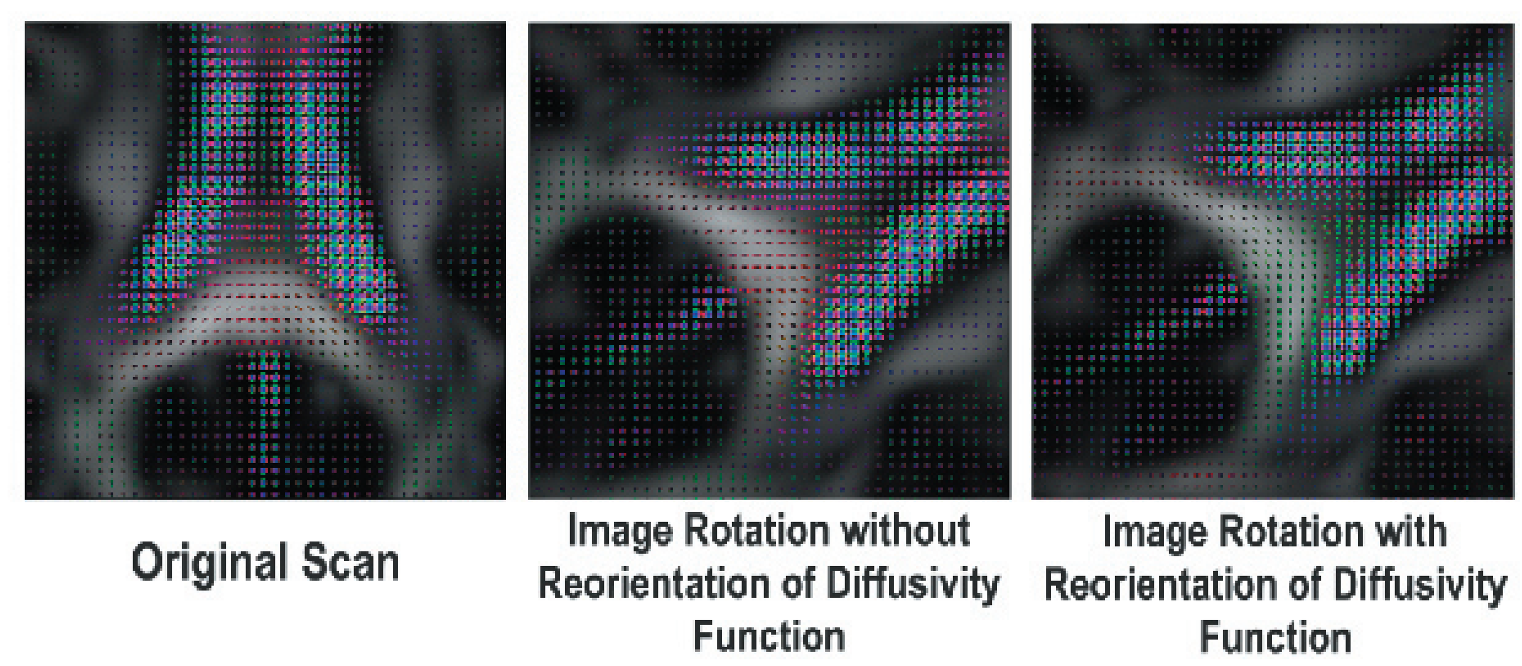

Fig. 2. The orientation-dependent diffusivity functions in the splenium of the corpus callosum are no longer consistent with the known directions of the underlying WM fibers when the image voxels are simply resampled to new locations by rotation but without reorientation of diffusivity functions. The PPD procedure corrects this, and the diffusivity functions remain aligned with the WM fibers that they represent.

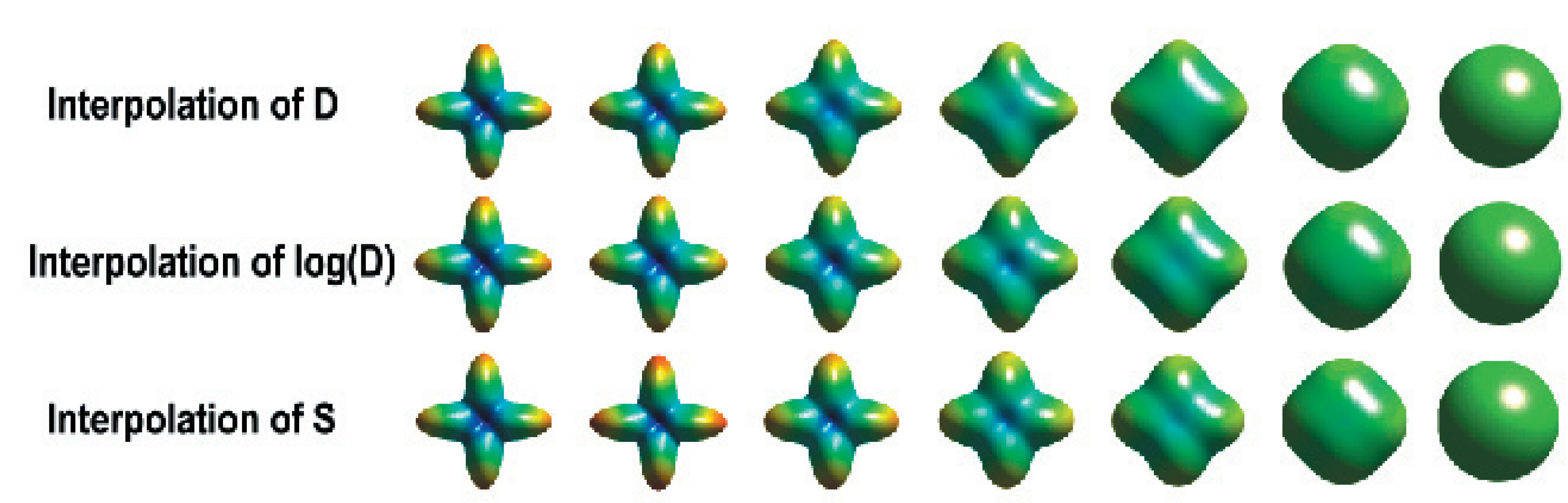

Fig. 3. shows diffusivity functions at intermediate positions x = 0.1, 0.3, .. 0.9, obtained by linear interpolation of the diffusivity function D, log(D), and MR signals S in each gradient direction, when the two-fiber synthetic function was placed at x = 0, and the isotropic one at x = 1. Interpolation using the MR signal S best preserves the anisotropy of the diffusivity function.

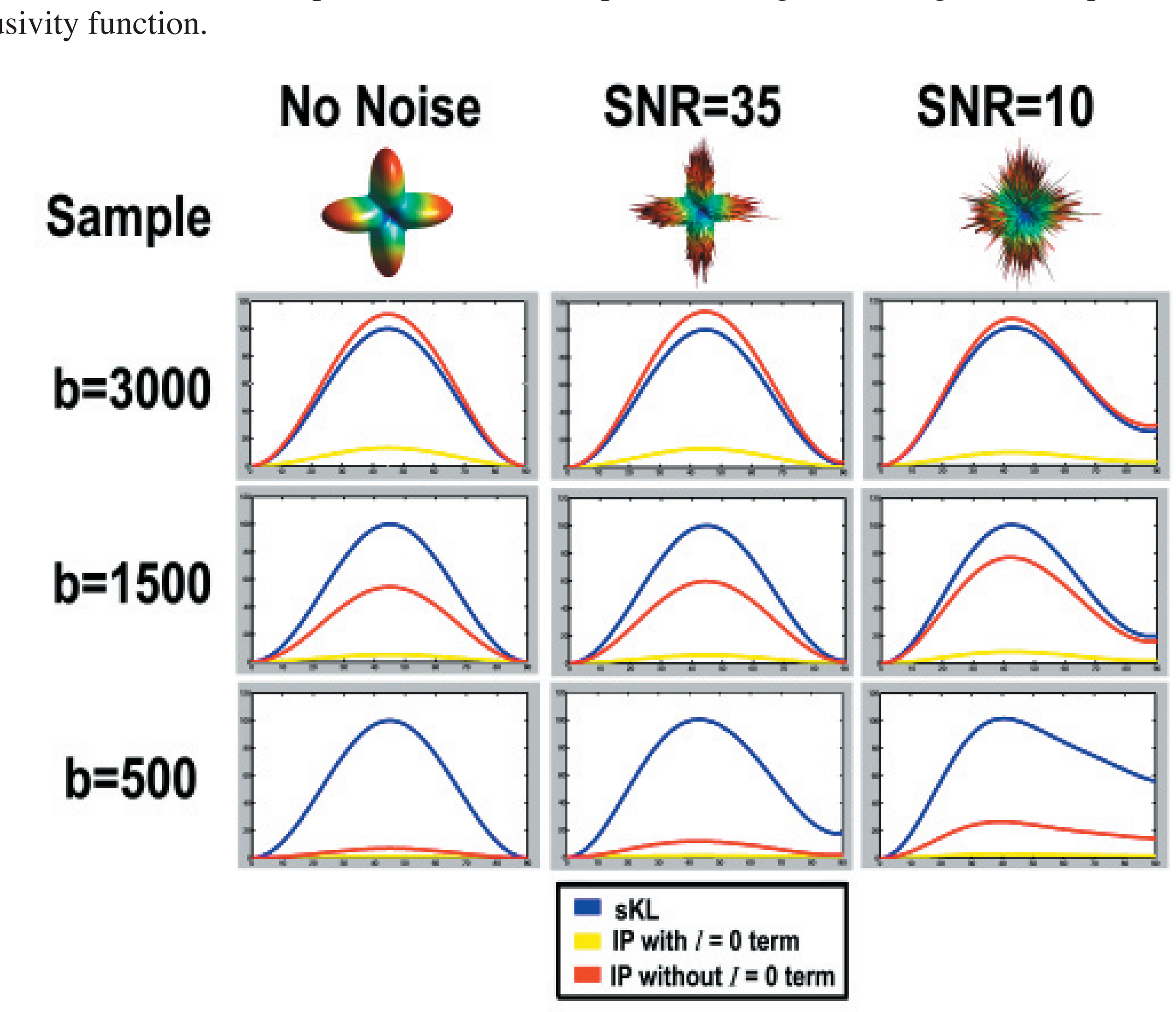

Fig. 4. Two identical synthetic diffusivity samples (no noise or with Rician noise added) were initially overlapped and rotated by $\varphi = 0$ to 90°. We compared the differences between the rotated and non-rotated samples with the symmetric KL-divergence (sKL) and inner product (IP) with/without $l = 0$ term. In noise-free samples, $\varphi = 45°$ gives the maximum sKL and minimum IP values. To facilitate comparisons, sKL and IP values have been normalized such that the normalized sKL(φ) = 100 × sKL(φ)/sKL(φ = 45°), and normalized IP(φ) = 100 × [1 − IP(φ)/IP(φ = 0°)].

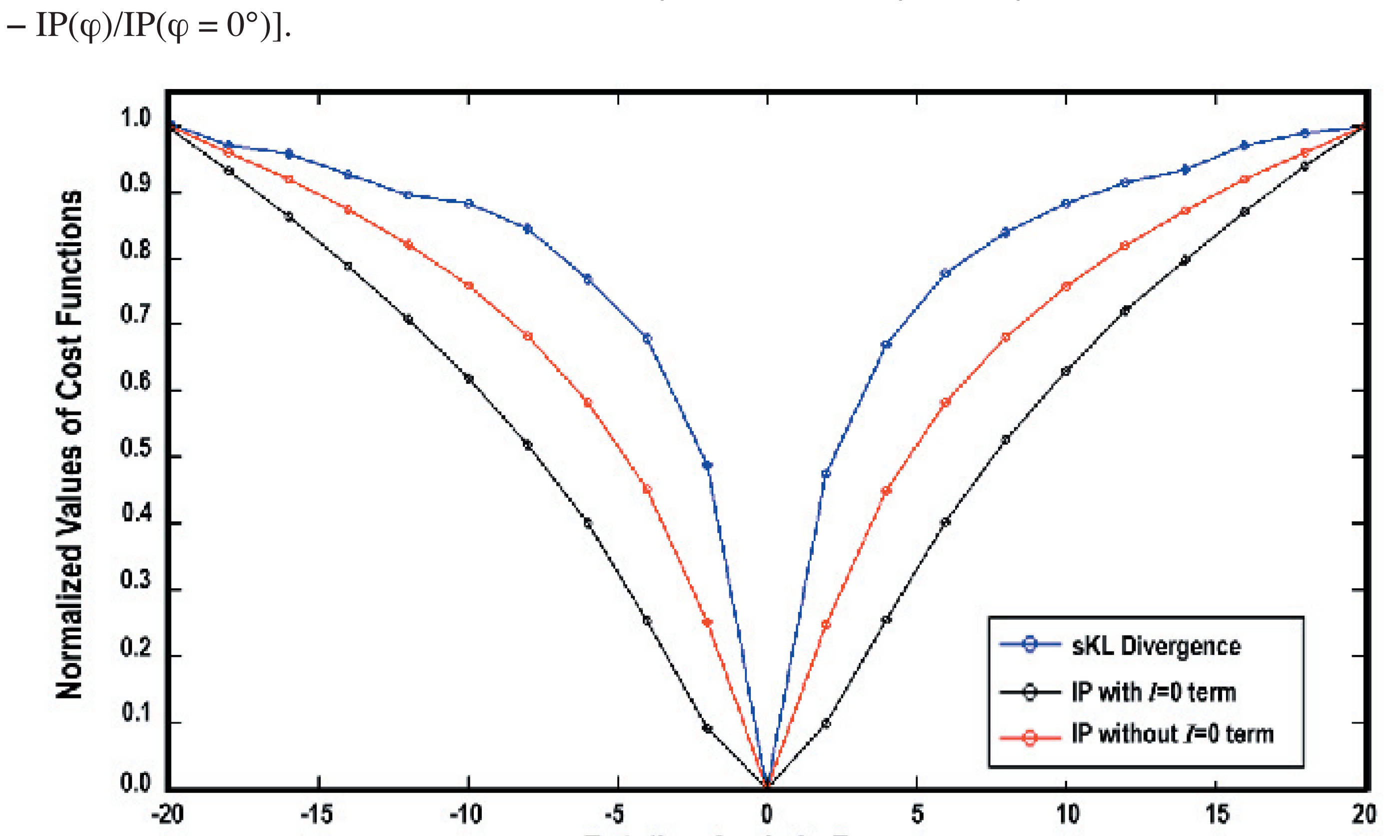

Fig. 5. Comparisons of the changes in symmetric KL-divergence (sKL) and inner product (IP) (with/without $l = 0$ term) at different rotation angles φ (from -20° to +20°, in increments of 2°) for two identical HARDI diffusion profiles. sKL and IP values have been normalized, with normalized $f(\varphi) = \mathrm{abs}[(f(\varphi) - f(\varphi = 0°))/(f(\varphi = 20°) - f(\varphi = 0°))]$. The angular profile of sKL is very sharp, and can detect rotational deviations of the image, with a magnitude as small as 2°.