

# Analytical Q-Ball Imaging with Optimal $\lambda$ -Regularization

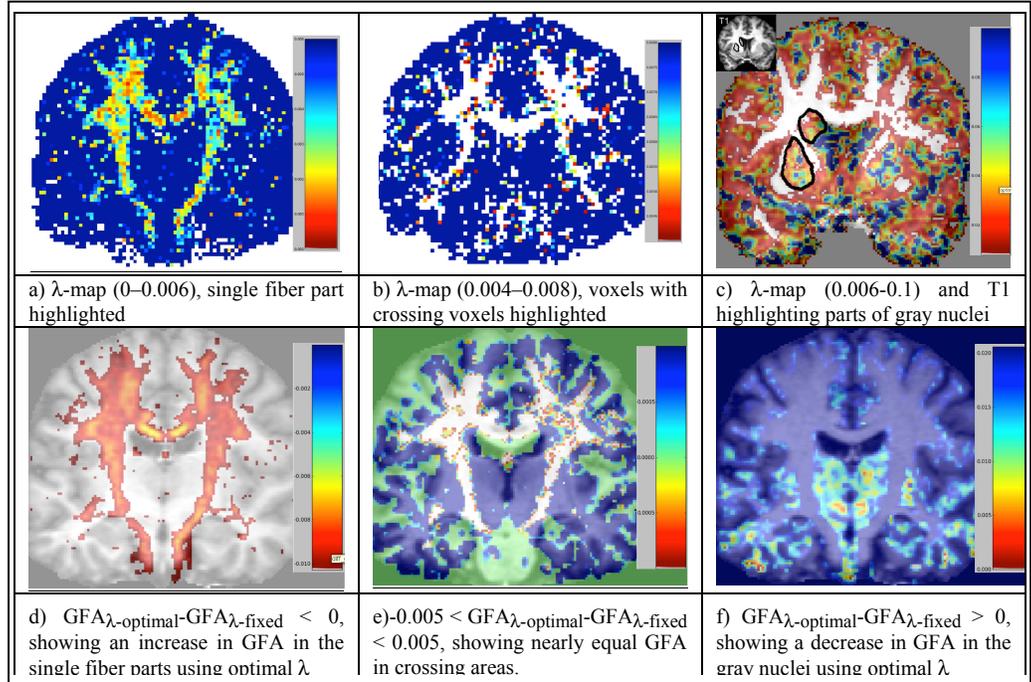
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**INTRODUCTION:** Diffusion MRI is a unique noninvasive imaging technique capable of quantifying and visualizing the angular distribution and the anisotropy of the white matter fibers. Several approaches such as diffusion tensor imaging, q-ball imaging (QBI), spherical deconvolution and many others high angular resolution diffusion imaging (HARDI) have been proposed to describe the angular distribution of the white matter fibers within a voxel. The analytical QBI technique [1] uses a predetermined regularization parameter [2] ( $\lambda = 0.006$ ), which has been well adopted in many clinical studies. Although there are well-known strategies, e.g., the generalized cross-validation (GCV) [3-5] or the L-curve [6], for selecting the optimal regularization parameter  $\lambda$ , the predetermined regularization parameter was adopted for reasons related to practical and computational efficiency based on L-curve simulations [2]. Here, we incorporate the GCV technique into the analytical q-ball formalism. We compare and contrast the fixed  $\lambda$ -regularization parameter ("Fixed  $\lambda$ ") and the automatic GCV-selected optimal  $\lambda$ -regularization ("GCV-based  $\lambda$ "), for estimating diffusion MRI data. We also discuss the potential consequences of our work on quantitative HARDI anisotropy measures and tractography studies.

**METHODS AND RESULTS:** The GCV technique is incorporated into the analytical q-ball formalism by extending the work of [5], using the spherical harmonics (SH) basis. First, the diffusion-weighted (DW) signals are regularized with the "Fixed  $\lambda$ " with  $\lambda = 0.006$  and with optimal "GCV-based  $\lambda$ " found for each voxel, detailed in [9]. Then, the q-ball is estimated via the analytical Funk-Radon transform, detailed in [1]. In this work, we use SH order 6 to reconstruct the q-balls from DW data obtained on a 3T system, with 60 encoding directions, averaged three times per direction, seven  $b = 0$  images,  $b = 1000$  s/mm<sup>2</sup>, 72 slices with isotropic 1.7 mm

resolution, 128x128 image matrix, TE = 100 ms, and TR = 12s [8]. The Gaussian noise standard deviation of this dataset was estimated to be approximately 5.07, as determined through the automatic method PIESNO [9]. The underlying SNR of a representative region-of-interest (ROI) of a T2 image was about 25.7 [10]. The value of SNR was adopted into our simulation study, described below. Fig.1 shows the optimal  $\lambda$ -map as determined by the GCV-based technique. The colormap is different for each subfigure. The  $\lambda$ -map shows that the values of the optimal  $\lambda$  is spatially and anatomically dependent, and not equal to  $\lambda = 0.006$  everywhere.  $\lambda = 0.006$  is a good trade-off between smoothness and angular resolution of q-balls with crossing fibers [2]. This is confirmed in 2-crossing regions (Fig1b) with values approximately equal to 0.006. However, the fixed  $\lambda$  is overestimated for single fiber parts (Fig.1a) and underestimated for more complex fiber parts (Fig.1c). This is reflected by an increase of generalized fractional anisotropy (GFA) [7] in single fiber parts and a GFA decrease in complex regions (Fig1d-f) using optimal  $\lambda$ . To study the dependence of  $\lambda$  on the fiber



configuration, a multi-tensor simulation was set up with three distinct fiber configurations, (1, 2 and 3 orthogonal crossing fibers), to test the statistical performance of QBI. Two quantitative measures were used in this study—the relative error in estimating the GFA and the dispersion of fiber directions. In quantifying the dispersion of fiber directions, we use the mean squared error in degrees between the ground truth fiber directions and the estimated fiber directions from the q-ball maxima. In Fig.2, we first note that, as the fiber configuration is more complex (from 1 to 3 fibers), the relative GFA error is considerably reduced using optimal GCV-based  $\lambda$  (blue curves). We also note that the fiber dispersion experiment reveals very similar behavior between the Fixed- $\lambda$  and the optimal GCV-based  $\lambda$  regularization.

**DISCUSSION AND CONCLUSION:** In this work, we have presented the analytical QBI with optimal GCV-based regularization. The method is the optimal extension of analytical q-ball imaging with fixed regularization  $\lambda = 0.006$  [1]. We have shown two important results. 1) GFA seems indicative of shape variation in QBI and GCV-based  $\lambda$  shows a distinct advantage when the underlying structure is complex and in single fiber parts of real data. Hence, this suggests that optimal GCV-based  $\lambda$  is important for anisotropy measure studies using HARDI. 2) The Fixed- $\lambda$  and GCV-based  $\lambda$  are comparable when looking at the dispersion of q-ball maxima. This is reassuring and suggests that tractography results from the two approaches will produce similar results. This can be explained by the intrinsic smoothness of the QBI technique and the fact that Funk-Radon transform is robust to noise because it performs DW signal averaging, i.e., the integral along the great circle. This similarity between the q-ball directions from Fixed- $\lambda$  and GCV-based  $\lambda$  will most likely be different when a sharper reconstruction technique is employed. Although we have focused on QBI, the optimal GCV regularization can be applied to any method using a SH estimation of the DW signal (e.g. high order tensor [6], spherical deconvolution [4], diffusion orientation transform [11], exact QBI [12,13,14]).

**REFERENCES:** [1] Descoteaux et al MRM 2007. [2] Descoteaux et al MRM 2006. [3] Craven and Wahba Numer. Math. 1979. [4] Sakaie et al NeuroImage 2006. [5] Koay et al JMR (197) 2009. [6] Hansen, WIT Press 2001. [7] Tuch MRM 2004. [8] Anwander et al Cere Cortex 2007. [9] Koay et al JMR (199) 2009. [10] Koay et al JMR 2006. [11] Özarslan et al NeuroImage 2006. [12] Canales-Rodriguez et al MRM 2009, [13] Aganj et al ISBI 2009, [14] Tristan-Vega et al MICCAI 2009.

# of fibers	Relative error in estimating the GFA	Dispersions in the maxima of the q-ball ODF	
		GCV-based $\lambda$	Fixed $\lambda$
1		$0.93^\circ \pm 0.78^\circ$	$0.83^\circ \pm 0.67^\circ$
2		$1.92^\circ \pm 2.9^\circ$	$1.78^\circ \pm 2.89^\circ$
3		$2.01^\circ \pm 3.6^\circ$	$1.94^\circ \pm 3.6^\circ$