

# Optimized Measurement of Anomalous Diffusion

J. P. HALDAR<sup>1</sup>, Q. GAO<sup>2</sup>, X. J. ZHOU<sup>2,3</sup>, AND Z-P. LIANG<sup>1</sup>

<sup>1</sup>BECKMAN INSTITUTE, ELECTRICAL AND COMPUTER ENGINEERING, UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN, URBANA, IL, UNITED STATES, <sup>2</sup>CENTER FOR MR RESEARCH, UNIVERSITY OF ILLINOIS MEDICAL CENTER, CHICAGO, IL, UNITED STATES, <sup>3</sup>RADIOLOGY, NEUROSURGERY, AND BIOENGINEERING, UNIVERSITY OF ILLINOIS AT CHICAGO, CHICAGO, IL, UNITED STATES

## INTRODUCTION

Several groups have recently proposed the use of the Kohlrausch-Williams-Watts (KWW) stretched-exponential function to model the diffusion attenuation curves observed in biological tissues [1-4]. The KWW function is given by  $M_0 \exp[-(bD)^\alpha]$ , where the free parameters of the model are the *anomalous exponent  $\alpha$* , the *apparent diffusion coefficient  $D$* , and the *unweighted signal intensity  $M_0$* . The KWW model has the flexibility to accurately model multi-exponential decays, and the anomalous exponent offers a novel source of contrast associated with the structural complexity of the diffusion environment. Noise contamination is a significant limitation of high  $b$ -value diffusion weighted (DW) imaging experiments, and is of particular concern when estimating parameters of complicated functions like the KWW model. We propose to address the noise issue using two techniques. First, we optimize the choice of experimental  $b$ -values using the Cramér-Rao bound (CRB) [5]. Second, we mitigate the effects of noise by using a previously proposed statistical joint-reconstruction algorithm [6,7].

## THEORY

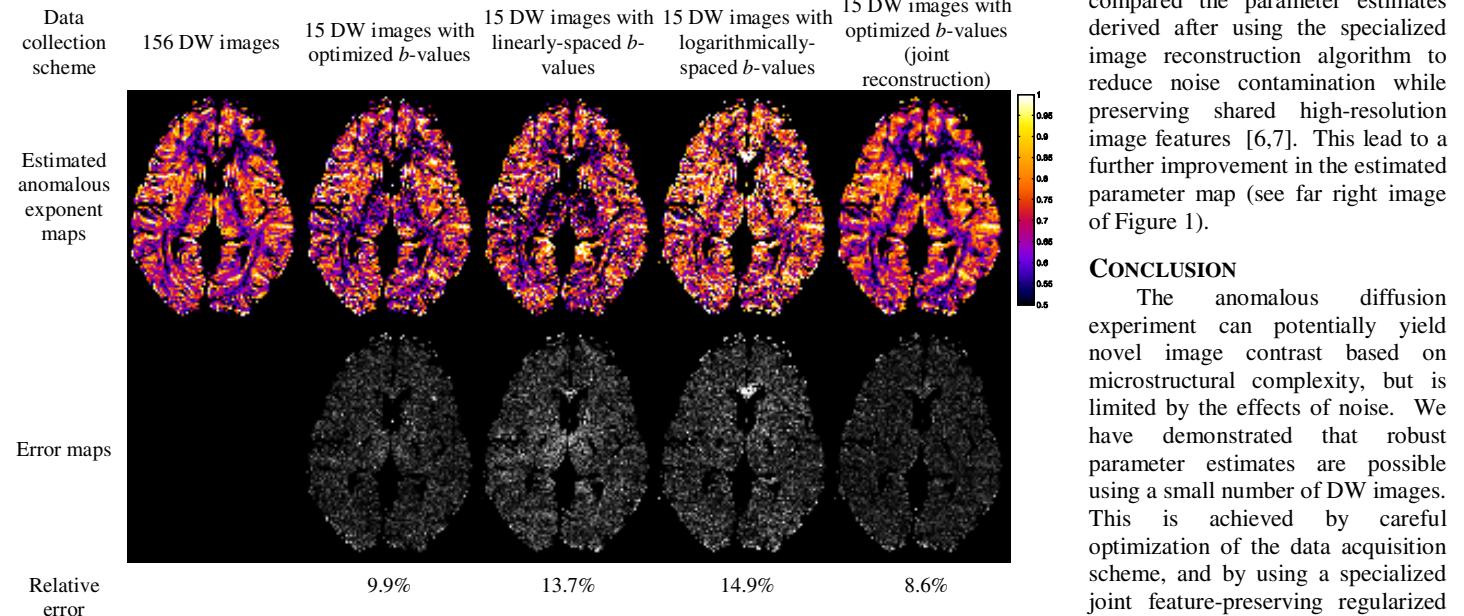
The CRB is a theoretical bound on the variance of any unbiased parameter estimate [5], and can be used to compare the SNR-efficiency of different experiments. We calculated the CRB for the KWW model, and used it to compare the different  $b$ -value sampling schemes listed in Table 1. Linearly- and logarithmically-spaced schemes have been previously used in the literature [1-4]. We found that linearly-spaced  $b$ -values are slightly superior to logarithmic spacing for diffusion parameters found in the normal human brain. We also used a stochastic descent algorithm to minimize the CRB over the typical range of diffusion parameters, yielding an optimized sampling scheme which improves the achievable SNR-efficiency of the experiment by more than a factor of 2 compared to linear and logarithmic schemes.

**Table 1.** Different  $b$ -value sampling schemes (units of  $\text{s/mm}^2$ ) that were compared

Linear Sampling	30	385	740	1095	1450	1805	2160	2515	2870	3225	3580	3935	4290	4645	5000
Logarithmic Sampling	30	43	62	90	129	186	269	387	558	804	1159	1671	2407	3469	5000
Optimized Sampling	30	30	30	430	430	480	480	480	2090	2190	5000	5000	5000	5000	5000

## METHODS AND RESULTS

The CRB results were evaluated using simulated and experimental data. In the experiment, a total of 156 DW human brain images were acquired from the same healthy subject at 3T using a customized single-shot EPI sequence, and nonlinear least-squares d KWW parameter estimates were derived from the full dataset using the VARPRO algorithm [8]. The KWW parameters were then estimated using subsets of the data corresponding to the three previously described  $b$ -value sampling schemes. The quality of the estimated anomalous exponent maps was compared to the gold standard map derived from the full set of 156 images. The results are shown in Figure 1; as expected, the linearly-spaced sampling scheme outperformed the logarithmically-spaced scheme, while the optimized scheme was significantly more accurate than either of the others. We also



**Figure 1.** Experimental results comparing different  $b$ -value sampling schemes and different reconstruction techniques.

## REFERENCES

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