EFFECT OF SAMPLING ON THE ESTIMATION OF THE APPARENT COEFFICIENT OF DIFFUSION IN MRI

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ABSTRACT

The Apparent Diffusion Coefficient (ADC) is a quantitative measure derived from MRI that is able to asses the amount of diffusion within living tissues. It is employed to characterize different diseases and to evaluate response to therapy. For ADC estimation, the diffusion signal needs to be sampled using a small number of values, presenting distortions due to the aliasing and windowing effect. In this work we theoretically study these effects and propose some new robust estimators for ADC based on the Fourier Transform of the signal.

Index Terms— ADC, aliasing, MRI, estimation, sampling

1. INTRODUCTION

Diffusion-weighted imaging (DWI) is a magnetic resonance imaging (MRI) technique that provides useful information about the motion of water in biological tissues. Such motion is affected by the internal structure of different tissues and therefore diffusion MRI acquisitions can be used to characterize *in vivo* different properties of such tissues. In the last decade, DWI has shown its enormous potential in brain imaging (in the study of white matter disorders as markers for disease, for instance), as well as in body imaging (e.g., tumor detection, characterization, and assessment of treatment response).

While measures in brain imaging usually have an anisotropic nature (due to the restrictions of neural pathways), in body imaging, tissue characterization commonly follows the assumption of isotropic diffusion. One important measure is the so-called Apparent Diffusion Coefficient (ADC), a measure of the *amount* of water diffusion measured in one particular voxel. The ADC can be estimated from multiple MR images acquired with increasing diffusion-weightings ("b-values", in s/mm^2) [1]. ADC values have shown to be accurate indicators of tumor response to therapy[2], as well as the severity of liver fibrosis and cirrhosis [3].

In order for ADC to become an acceptable quantitative imaging biomarker, it is of paramount importance to provide an accurate estimation of such parameter from the data. Unfortunately, quantitative ADC mapping is affected by multiple artifacts, including motion-related errors [4], image distortions caused by susceptibility, and noise-related effects [5]. Most of the proposed estimation techniques in literature are precisely focused in the reduction of these artifacts. However, there are also other effects that seriously affect the quality of the estimation, such as the number and positions of the samples available. Due to practical restrictions in clinical settings (time, patient motion), only a small number of b values are usually employed. As a consequence, the obtained signal will be affected by aliasing and windowing.

In this work we study the influence of these two issues, sampling and windowing of the diffusion signal, over its Fourier Transform (FT). These effects must be taken into account in order to better understand the sampled signal and thus to improve the estimation of the ADC. We present closed form expressions for the FT of the sampled signal and we use those expressions to derive three different ADC estimators. Those estimators are tested over synthetic and real data. Results here presented can also be easily extrapolated to correct other existing estimation methods.

2. SAMPLING OF THE DIFFUSION SIGNAL

2.1. The diffusion signal

In DWI, the diffusion signal at an individual voxel can be modeled as an exponential decay as [6]:

$$S(b) = S_0 \cdot e^{-b \cdot \mathrm{ADC}}, \tag{1}$$

where S_0 is the signal intensity at $b = 0$ (commonly known as *baseline*), $S(b)$ is the signal intensity at b, and

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ADC is the apparent diffusion coefficient. This equation is also known as the mono-exponential model. Lately, more complex models (such as the bi-exponential) have been proposed in order to cope with the effect of the perfusion over diffusion for low b-values. For the sake of simplicity, in this work we will confine ourselves to the mono-exponential model. Thus, ideally, the ADC can be derived, for any $b > 0$, as $\text{ADC} = b^{-1}\log(S_0/S_1)$. However, in the presence of noise, alternative estimation methods that use more than one single sample are preferred, being dominant those based on least squares (LS) and maximum likelihood [5].

If we normalize eq. (1) by the baseline, we can rewrite it as

$$x(b) = e^{-b\cdot\text{ADC}}\, u(b), \tag{2}$$

where $u(b)$ is the Heaviside step function, and $x(b) = S(b)/S_0$ is the normalized diffusion signal. The continuous Fourier Transform of signal $x(b)$ calculated over the variable b is

$$X(\omega) = \frac{1}{\text{ADC} + j\omega}, \tag{3}$$

and the value for $\omega = 0$ is

$$X(0) = \frac{1}{\text{ADC}}. \tag{4}$$

The FT in this point corresponds with the area of $x(b)$

$$X(0) = \int_{-\infty}^{\infty} x(b)db = \int_{0}^{\infty} e^{-b\cdot\text{ADC}}db = \frac{1}{\text{ADC}}. \tag{5}$$

However, in order to estimate the ADC a sampled version of $x(b)$ must be considered. As a result, the FT of the sampling signal will differ from eq. (5).

2.2. Uniform Sampling

Let us assume that the continuous signal $x(b)$ is uniformly sampled for equally spaced values of variable b, Δb, obtaining the discrete signal $x[n] = x(n\cdot\Delta b)$. Following the traditional sampling theory [7], this can be seen as the product of $x(b)$ with a set of delayed deltas, obtaining a continuous sampled signal, $x_p(b)$:

$$x_p(b) = x(b)\cdot\sum_n \delta(b - n\Delta b),$$

with FT:

$$\begin{aligned} X_p(\omega) &= \frac{1}{2\pi}X(\omega) \circledast \sum_k \delta\left(\omega - k\frac{2\pi}{\Delta b}\right) \\ &= \frac{1}{\Delta b}\sum_{k=-\infty}^{\infty} X(\omega - k\omega_s) \\ &= \frac{1}{\Delta b}\sum_{k=-\infty}^{\infty} \frac{1}{\text{ADC} + j(\omega - k\omega_s)}, \end{aligned} \tag{6}$$

where $\omega_s = \frac{2\pi}{\Delta b}$ is the sampling frequency. Since $x(b)$ is not a band-limited signal, the sampled signal will show aliasing between the replicas of $X(\omega)$. This aliasing will be significant in the case of practical ADC estimation, where only a few samples can be considered. The resulting signal can be easily calculated from eq. (6):

$$X_p(\omega) = \frac{1}{\Delta b}\frac{\pi}{\omega_s}\coth\left((\text{ADC} + j\omega)\frac{\pi}{\omega_s}\right). \tag{7}$$

The FT in the origin will therefore be

$$X_p(0) = \frac{1}{\Delta b}\frac{\pi}{\omega_s}\coth\left(\text{ADC}\frac{\pi}{\omega_s}\right). \tag{8}$$

2.3. Effect of Windowing

When acquiring the different values of the diffusion signal, the effect of the windowing must also be taken into account. The FT calculated in the previous section, see eq. (7), assumes an infinite number of samples, which is not the case in real acquisitions.

Let us assume that the original signal $x(b)$ is limited in b:

$$x(b) = \begin{cases} \exp(-b\cdot\text{ADC}) & 0 \le b \le B_M \\ 0 & b < 0,\ b > B_M \end{cases}$$

with B_M the maximum value considered for b. The FT of the continuos signal now becomes:

$$X(\omega) = \frac{1}{\text{ADC} + j\omega}\left(1 - e^{-B_M(\text{ADC}+j\omega)}\right). \tag{9}$$

whose value for $\omega = 0$ is

$$X(0) = \frac{1}{\text{ADC}}\left(1 - e^{-B_M\cdot\text{ADC}}\right). \tag{10}$$

If we compare these results to those in eq. (5), we can see that the value in the origin of the frequency space has been reduced, precisely due to the windowing of the signal. The wider the signal, the smaller the contribution of B_M. For the range of values employed in practice for ADC estimation, the influence of B_M is noticeable.

If we consider the sampling of the previous section with the windowing, the FT of the sampled signal becomes (after some algebra):

$$\begin{aligned} X_p(\omega) =& \frac{1}{\Delta b}\left(1 - e^{-B_M(\text{ADC}+j\omega)}\right) \\ &\times \frac{\pi}{\omega_s}\coth\left((\text{ADC} + j\omega)\frac{\pi}{\omega_s}\right). \end{aligned} \tag{11}$$

The value in the origin now becomes

$$X_p(0) = \frac{\pi}{\Delta b\cdot\omega_s}\left(1 - e^{-B_M\text{ADC}}\right)\coth\left(\text{ADC}\frac{\pi}{\omega_s}\right). \tag{12}$$

2.4. Fourier Transform of the discrete signal

The previous sections describe the effect of sampling and windowing over the origin of the continuous TF. Alternatively, we can also analyze that value for the discrete signal straight from the samples. Assuming an uniform sampling of the signal $x(b)$, let us refer to the discrete signal as $x[n]$:

$$x[n] = \exp(-n\Delta b \cdot \text{ADC}), \;\; n = 0, \cdots, N-1.$$

The FT of the discrete signal is defined as $X(\Omega) = \sum_n x[n]e^{-j\Omega n}$, so the value in the origin can be calculated as

$$\begin{aligned} X(0) &= \sum_{n=0}^{N-1} x[n] = \sum_{n=0}^{N-1} e^{-n\Delta b \cdot \text{ADC}} \\ &= \frac{1 - e^{-N\Delta b \cdot \text{ADC}}}{1 - e^{-\Delta b \cdot \text{ADC}}} = \frac{1 - e^{-B_M \cdot \text{ADC}}}{1 - e^{-\Delta b \cdot \text{ADC}}}. \end{aligned} \tag{13}$$

Note that we have considered $B_M = N \cdot \Delta b$.

3. APPLICATION TO ADC ESTIMATION

An immediate application of the results in the previous section is the derivation of new estimators for the ADC. The estimators here proposed are directly derived from the previous study. Modifications and corrections of existing estimation methods are also possible.

The center of the Fourier space is the point with higher SNR (because it is the maximum value of the signal) and less affected by aliasing. Thus, any estimator based on that point will likely show interesting robustness properties. In order to estimate the ADC, the area of the signal $x(b)$ must be estimated from the samples. From the sampled signal $x_p(b)$ we define the reconstructed continuous signal as $x_R(b)$ as a low pass filtered interpolation $X_R(\omega) = X_p(\omega) \cdot H(\omega)$, where $H(\omega)$ is a low pass filter with gain Δb at the origin and cut frequency $\omega_s/2$, so that $X_R(0) = \Delta b X_p(0)$ or, equivalently

$$\int_{-\infty}^{\infty} x_R(t)dt = \Delta b X_p(0). \tag{14}$$

In what follows, S_b will denote the area of the signal

$$S_b = \int_{-\infty}^{\infty} x_R(b)db.$$

The easiest way to estimate this area from the samples would be $S_b \approx \sum_k x[k]\Delta b$, although more accurate interpolations, such as splines, can be considered. We next propose different estimators for ADC following the results from the previous section:

Aliasing model: Using the center of the Fourier space of the signal with aliasing, as defined in eq. (8), we can derive an estimator for ADC as:

$$\widehat{\text{ADC}} = \frac{1}{\Delta b} \log\left(\frac{S_b + \Delta b/2}{S_b - \Delta b/2}\right) \tag{15}$$

Aliasing and windowing model: In order to consider both the aliasing and windowing effects, we must use eq. (12). A least square minimization is used:

$$\widehat{\text{ADC}} = \arg\min_y \left[S_b - \left(1 - e^{-B_M y}\right) \frac{\pi}{\omega_s} \coth\left(y\frac{\pi}{\omega_s}\right)\right]^2 \tag{16}$$

Discrete model: Alternatively, we employ the discrete formulation in eq. (13), using a least square minimization:

$$\widehat{\text{ADC}} = \arg\min_y \left[\sum_{n=0}^{N-1} x[n] - \frac{1 - e^{-B_M \cdot y}}{1 - e^{-\Delta b \cdot y}}\right]^2 \tag{17}$$

4. EXPERIMENTS AND RESULTS

For the sake of illustration and validation, a series of experiments will be carried out, using both synthetic and real data. The following implementations of ADC estimators are compared:

Al+T: based on the aliasing model in eq. (15), using trapezoid functions to approximate the integral.

Al+W+T: estimator based on the aliasing+windowing model in eq. (16) using trapezoid functions to approximate the integral.

Al+W+splines: estimator in eq. (16) using splines and 100 points upsampling to approximate the integral.

DS: estimator based on the discrete summation, eq. (17).

DS+splines: estimator based on the discrete summation in eq. (17). The summation of N points is replaced by the summation of 100 points obtained by an upsampling using splines.

LS: Linear Least Squares estimator, as commonly employed in clinical practice.

First, in order to analyze the behavior of the estimators with different parameters, we generate a synthetic 1D signal following eq. (1) normalized to $S_0 = 1$ and ADC$= 10^{-3}$. The signal is corrupted with Rician noise [8] with SNR=10 and SNR=50 in the baseline. Note that there is a great reduction of the SNR

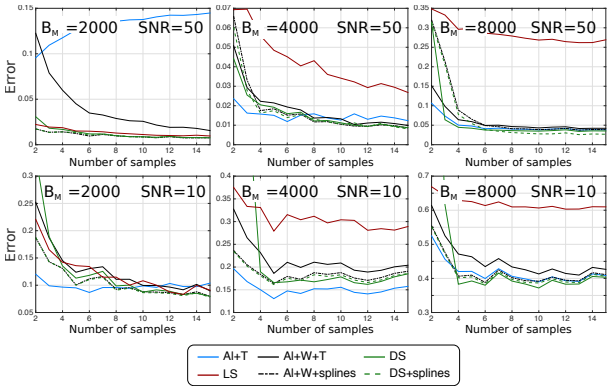

Fig. 1. Synthetic experiment: average error in the estimation of the ADC of the different methods proposed for different SNR, different number of samples (b values) and different maximum value of b, B_M.

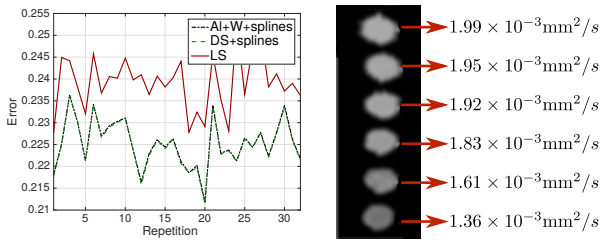

Fig. 2. (Letf) Estimation error over the ADC phantom. (Right) Values of the ADC of the real phantom.

in the diffusion images due to the exponential decay. We define three maximum values of parameter b, $B_M = [2, 4, 8] \cdot 10^3$. For each value we obtain a variable number of samples, from 2 to 15, obtained by uniform sampling. We estimate the ADC for the different configurations and calculate the relative estimation error $\text{Error} = \frac{|\widehat{\text{ADC}} - \text{ADC}|}{\text{ADC}}$. The average for 1000 experiments is depicted in Fig. 1. Note that in most of the cases, the proposed estimators based on DS and Al+W show a very good performance when compared to LS. The methods that use splines for the interpolation are also the ones with the most accurate results. These results are consistent for different number of data points and different SNR values.

Next, the proposed estimators were tested over real MRI data. To that end, a phantom was created consisting of 6 vials with agar-based oil-water emulsions (increasing oil fractions 0-50%), with decreasing ADC (measured experimentally) in the range 2-1.3$\times 10^{-3}$ mm^2/s, see Fig. 2-right. Phantom DWI data were acquired in a 1.5T MRI Scanner (Signa Hdxt, GE Healthcare) with a single-channel head coil, using a diffusion-weighted echo-planar imaging pulse sequence. Acquisition parameters included: b-values 0, 250, 500, 750 and 1000 s/mm^2, slice thickness: 4 mm, axial orientation, no parallel imaging acceleration. 32 repetitions of the same slice were acquired, allowing for a high-quality estimation considered as golden standard. ADC values were estimated for each repetition using the same methods as for the synthetic data, and the estimation errors are shown in Fig. 2-left. Once more, the methods proposed outperform the standard LS estimator in terms of accuracy. Due to the use of splines for interpolation, DS and Al+W show very similar results.

5. CONCLUSIONS

The FT of the mono-exponential diffusion signal when sampled using a limited number of samples has been calculated. Closed-form expressions for the diffusion signal affected by windowing and aliasing are provided, and three new estimators have been derived based on this analysis. Results indicate the proposed estimators to show improved robustness with respect to the commonly employed LS. Although these are preliminary results, they suggest that the proper modeling of the sampled diffusion signal can help increase the accuracy of ADC estimation, and can be easily applied to modify or fine tune other related methods.

6. REFERENCES

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