

# Noise correction for the exact determination of apparent diffusion coefficients at low SNR

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## Abstract

Noise in MR image data increases the mean signal intensity of image regions due to the usually performed magnitude reconstruction. Diffusion-weighted MR imaging (DWI) is especially affected by high noise levels for several reasons, and a decreasing SNR at increasing diffusion weighting causes systematic errors when calculating apparent diffusion coefficients (ADCs). Two different methods are presented to correct biased signal intensities due to the presence of complex noise with (a) a Gaussian intensity distribution and (b) an arbitrary intensity distribution. The performance of the correction schemes is demonstrated by numerical simulations and DWI measurements on two different MR systems with different noise characteristics. These experiments show that noise significantly influences the determination of ADCs. Applying the proposed correction schemes reduced the bias of the determined ADC to less than 10 % of the bias without correction.

## Key words:

Noise correction, Diffusion-weighted imaging, Non-gaussian noise

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## Introduction

In most magnetic resonance imaging (MRI) applications, images are presented as magnitude data. These images are reconstructed from complex data in the time domain as acquired by two-channel quadrature detectors. The reconstruction process typically includes a discrete Fourier transform resulting in complex image data and the subsequent combination of real and imaginary data to a single magnitude image. This last step avoids phase artifacts in the final images (e. g. due to eddy current or susceptibility effects) by deliberately discarding the phase information. However, in the presence of statistical image noise, the calculation of magnitude image data influences the average signal intensity of image regions. This effect can cause considerable numerical bias to the data thereby affecting post-processing of noisy images. This is especially true for the determination of diffusion coefficients, described below, which is very sensitive to the presence of noise.

To study the influence of magnitude reconstruction it is usually assumed that the probability distribution of the noise is Gaussian in the original components of the complex data. Calculating the magnitude data in background regions of images transforms the Gaussian distribution into a Rayleigh distribution. Whereas the Gaussian distribution is symmetric and has an expectation value of zero for the noise intensity, the asymmetrical Rayleigh distribution is non-zero only in the positive range and, hence, the average background intensity is increased from zero to a positive value (1). The quantitative effect of noise on *non-zero* signal intensities has been studied by Henkelman (2) who calculated numerically the change of the signal depending on the noise intensity. The corresponding intensity distribution is the Rician distribution (3); based on the Rician distribution, the signal increase due to noise has been discussed in a paper by Bernstein (4) and intensity correction schemes have been proposed by McGibney et al. (5), Miller et al. (6), and Gudbjartsson et al. (7).

Especially at low signal-to-noise ratios (SNRs) pixel intensities of imaged objects are considerably increased by the magnitude reconstruction. Whereas in most MRI applications these biased signal intensities are either not important for image evaluation or can be avoided by

improving the SNR, this is generally not true for *in vivo* diffusion-weighted MRI (DWI).

If other strategies to improve the SNR are not applicable, e. g. because of hardware constraints, it is at least often possible in conventional imaging to increase the number of excitations  $N_{EX}$  and to average the complex data of multiple acquisitions. The SNR increases proportional to the square root of  $N_{EX}$  and a remaining intensity bias can usually be neglected. However, this strategy is not applicable for *in vivo* DWI because the complex data is typically affected by motion-induced phase shifts. Averaging data with different phases leads to gross image artifacts and partially annihilated image data. Additionally, the acquisition time is considerably prolonged which may be unacceptable for human studies.

Unfortunately, a lower SNR must be expected especially for DWI data compared to most conventional techniques. Long Stejskal-Tanner (or similar) diffusion gradients (8, 9) are inserted into gradient pulse sequences, prolonging the echo time  $T_E$  and decreasing the mean signal intensity if diffusion coefficients are greater than zero. In addition to a decrease of the SNR the latter effect results in a varying SNR and thus *different* noise-induced biases depending on the diffusion weighting. This is a particular problem for a quantitative evaluation of DWI data; the varying bias of intensity causes systematic errors when calculating the apparent diffusion coefficient (ADC) and also influences the determination of anisotropy maps from diffusion tensor data (10, 11).

We present two methods to correct for these systematic errors caused by noise and compare our results with the results of formerly proposed correction schemes (6, 5, 7).

## Theory

As stated above, several papers deal with the influence of normally distributed complex noise on signal intensity when calculating magnitude images. Proposed correction schemes use either approximations (7) or work on power images instead of magnitude images (6, 5).

With modern workstations it has become possible to use an exact correction scheme working on magnitude images, if the underlying noise

has a Gaussian distribution. If the noise distribution is *not* Gaussian and (typically) not even known, an empirical correction algorithm can be used instead.

The general correction scheme, that we propose, is identically set up in both cases. In the given, noisy image, both the mean intensity of the background signal (i. e. of the noise)  $N_{\text{avg}}$  and of the signal intensity to be corrected  $S_{\text{avg}}$  are measured. If the function  $f$  with

$$S_{\text{avg}} = f(S_{\text{org}}, N_{\text{avg}}) \quad [1]$$

is known, the original image intensity  $S_{\text{org}}$  can be calculated using an iterative algorithm for finding the zero  $S = S_{\text{org}}$  of the difference

$$f(S, N_{\text{avg}}) - S_{\text{avg}} \quad [2]$$

as a function of  $S$ . The calculated zero  $S_{\text{org}}$  is then the original signal intensity not biased by noise.

The mean signal intensity  $S_{\text{avg}}$  can be obtained either by averaging over a sufficiently large region of the magnitude image or by averaging a number of independently acquired magnitude images. The latter approach has the advantage that a pixel-by-pixel correction of the image data is possible as required for ADC maps or anisotropy maps, but the acquisition time is prolonged.

## Gaussian Noise

Adding complex Gaussian noise with a variance  $\sigma^2$  to the original signal  $S_{\text{org}}$  leads to the Rician probability distribution  $P(S_{\text{N}}; S_{\text{org}}, \sigma)$  of the signal intensity  $S_{\text{N}}$  with

$$P(S_{\text{N}}; S_{\text{org}}, \sigma) = \frac{S_{\text{N}}}{\sigma^2} \exp\left(-\frac{S_{\text{N}}^2 + S_{\text{org}}^2}{2\sigma^2}\right) I_0\left(\frac{S_{\text{N}} S_{\text{org}}}{\sigma^2}\right) \quad [3]$$

and an average pixel intensity

$$S_{\text{avg}}(S_{\text{org}}, \sigma) = \sigma \sqrt{\frac{\pi}{2}} \exp\left(-\frac{S_{\text{org}}^2}{4\sigma^2}\right) \left[ \left(1 + \frac{S_{\text{org}}^2}{2\sigma^2}\right) I_0\left(\frac{S_{\text{org}}^2}{4\sigma^2}\right) + \frac{S_{\text{org}}^2}{2\sigma^2} I_1\left(\frac{S_{\text{org}}^2}{4\sigma^2}\right) \right], \quad [4]$$

where  $I_0$  and  $I_1$  are the modified Bessel functions of zeroth and first order (4, 3). This function corresponds to the function  $f(S, N_{\text{avg}})$  in Eq. [1]. The

variance  $\sigma^2$  can be calculated from the average background signal intensity  $N_{\text{avg}} = S_{\text{avg}}(0, \sigma) = \sigma \sqrt{\frac{\pi}{2}}$  according to

$$\sigma = \sqrt{\frac{2}{\pi}} N_{\text{avg}}. \quad [5]$$

Miller et al. (6) and McGibney et al. (5) used the properties of power images to perform noise correction. The relation between signal intensity and noise in power images is

$$\langle |S|^2 \rangle = S_{\text{org}}^2 + 2\sigma^2, \quad [6]$$

where  $\langle |S|^2 \rangle$  is the expectation value of the squared intensities and  $\sigma$  the standard deviation of the real part or imaginary part of the noise distribution as used in Eq. [4] and Eq. [5]. Since  $\langle |S|^2 \rangle \neq \langle |S| \rangle^2 = S_{\text{avg}}^2$ , averaged magnitude images cannot be corrected with this scheme. Instead, the image data of all source magnitude images before averaging is required.

Gudbjartsson et al. (7) used the approximation

$$S_{\text{avg}}(S_{\text{org}}, \sigma) \approx \sqrt{S_{\text{org}}^2 + \sigma^2} \quad [7]$$

of Eq. [4] which is valid for high SNR. For low SNR they suggest a correction scheme that is based on the approximation:

$$S_{\text{org}} \approx \sqrt{|S_{\text{avg}}^2 - \sigma^2|}. \quad [8]$$

## Non-Gaussian Noise

If the noise distribution is not Gaussian, the relation between the original signal  $S_{\text{org}}$ , the average of background noise  $N_{\text{avg}}$ , and the signal  $S_{\text{avg}}$  in the magnitude image is in general different from Eq. [4] and not known. However, the relation can be determined empirically by measuring a sufficiently large number of identical complex images of a simple phantom and comparing signal intensities after complex averaging and magnitude averaging. Complex averaging gives a good approximation of the original signal intensity  $S_{\text{org}}$ , whereas the images after magnitude averaging can be used to determine exact values of the background noise  $N_{\text{avg}}$  and the biased signal  $S_{\text{avg}}$ . Under the assumption that the influence of the noise on the signal is independent of the imaged object, this empirical determination has to be done only once for each given MR system.

We assume that the general relation between original signal intensity and signal intensity in the magnitude image is described by

$$S_{\text{avg}} = S_{\text{org}} \cdot \left(1 + g\left(\frac{S_{\text{org}}}{N_{\text{avg}}}\right)\right). \quad [9]$$

Thus,  $f$  from Eq. [1] is given by  $f(S_{\text{org}}, N_{\text{avg}}) = S_{\text{org}} \cdot (1 + g(S_{\text{org}}/N_{\text{avg}}))$ . The function  $g(S_{\text{org}}/N_{\text{avg}})$  depends only on the SNR, i. e.  $S_{\text{org}}/N_{\text{org}}$ , and not on  $S_{\text{org}}$  and  $N_{\text{avg}}$  separately, which would be the most general form. This expresses the plausible assumption, that the ratio  $S_{\text{avg}}/S_{\text{org}}$  is equal at identical SNR independently of  $S_{\text{org}}$ .

To determine  $g$  one has to measure a great number of complex images  $i_{kl}$ , where the index  $l$  describes repetitions of identical acquisitions of a water phantom and  $k$  describes acquisitions with decreasing SNR. (Alternatively, one could use a phantom with areas of different signal intensity to obtain varying SNRs.) From these complex images two averages are calculated:  $c(k)$  is averaged before calculation of magnitude,  $m(k)$  is averaged after calculation of magnitude:

$$c(k) = \left| \sum_l^L i_{kl} \right|, \quad m(k) = \sum_l^L |i_{kl}|. \quad [10]$$

The “complex average” images  $c(k)$  are the reference images that have ideally an arbitrarily high SNR and hence (almost) no biased intensities due to magnitude reconstruction. The “magnitude average” images  $m(k)$  are images that suffer from biased intensities to a varying degree depending on  $k$ , i. e. the SNR.

Two values are calculated from the images  $c(k)$  and  $m(k)$ : the mean signal intensities  $c_S(k)$ ,  $m_S(k)$  and the mean intensities of background noise  $c_N(k)$ ,  $m_N(k)$ . According to Eq. [9] the function  $g(S_{\text{org}}/N_{\text{avg}})$  is given by

$$g\left(\frac{S_{\text{org}}}{N_{\text{avg}}}\right) = g\left(\frac{c_S(k)}{m_N(k)}\right) = \frac{S_{\text{avg}}}{S_{\text{org}}} - 1 = \frac{m_S(k)}{c_S(k)} - 1. \quad [11]$$

If the SNRs of the reference images  $c(k)$  are not sufficiently high, then  $c_S(k)$  does not correspond exactly to  $S_{\text{org}}$  and, therefore, Eq. [11] is not quite correct. Typically, this problem should occur only for reference images with low SNR, i. e. reference images with high values of  $k$ . Thus, we can assume, that the intensities  $c_S(k)$  are correct for  $k \leq k_0$  for an appropriate choice of  $k_0$ .

For  $k > k_0$  the values  $c_S(k)$  can be replaced by corrected values  $\tilde{c}_S(k)$ , that will be a good estimation for the “true”, but unknown intensities  $\hat{c}_S(k)$ . Deriving  $\tilde{c}_S(k)$  from  $c_S(k)$  and  $c_N(k)$  is analogous to calculating  $S_{\text{org}}$  from  $S_{\text{avg}}$  and  $N_{\text{avg}}$ . However, the calculation is simplified with the first-order approximation

$$1 + g\left(\frac{\hat{c}_S(k)}{c_N(k)}\right) \approx 1 + g\left(\frac{c_S(k)}{c_N(k)}\right), \quad [12]$$

so one can determine the corrected values of  $c_S(k)$  from Eq. [9] as

$$\tilde{c}_S(k) = \frac{c_S(k)}{1 + g\left(\frac{c_S(k)}{c_N(k)}\right)}, \quad [13]$$

where  $g(c_S(k)/c_N(k))$  can be interpolated from the already calculated values of  $g$ . Hence,  $k_0$  can be chosen to be the smallest index with  $c_S(k_0)/c_N(k_0) < c_S(1)/m_N(1)$ .

## Materials and Methods

The noise correction scheme was tested with computer simulations and DWI data from two different MRI systems. The simulations were executed using self-written Matlab routines (MathWorks Inc., Natick, Massachusetts, USA); a  $128 \times 128$  matrix with a structured intensity pattern has been superposed by Gaussian noise at 10 simulated  $b$  values (attenuations of intensity), resulting in SNRs between 3.2 and 1.5. 10 magnitude images were averaged for each  $b$  value. We calculated the ADC before and after noise correction using the correction scheme for Gaussian noise, and compared both values with the reference value of the simulation.

DWI experiments were performed on a clinical 1.5 T MRI system (Edge, Marconi Medical Systems, Cleveland, Ohio, USA) with an EPI gradient set (maximum gradient strength 27 mT/m, minimum rise time 375  $\mu$ s) and an experimental 2.35 T imager (Biospec 24/40, Bruker, Ettlingen, Germany) equipped with a special gradient system (inner diameter 12 cm, maximum gradient strength 200 mT/m, minimum rise time 170  $\mu$ s). The clinical system was equipped with a standard quadrature head coil, the experimental system with a homebuilt birdcage coil. Cylindrical water phantoms were used in both cases.

On the clinical system, a diffusion-weighted spin echo EPI sequence with  $T_R$

of 600 ms,  $T_E = 108$  ms, and  $b$  values of 0, 100, 200, ..., 1400 s mm<sup>-2</sup> was used for the DWI measurements. We measured 80 identical frames for each  $b$  value with a FOV of 20 cm, a slice thickness of 2 mm, and matrix size of 81 × 97. The short  $T_R$ , the small slice thickness, and the large  $b$  values were chosen to acquire images with a certain noise level.

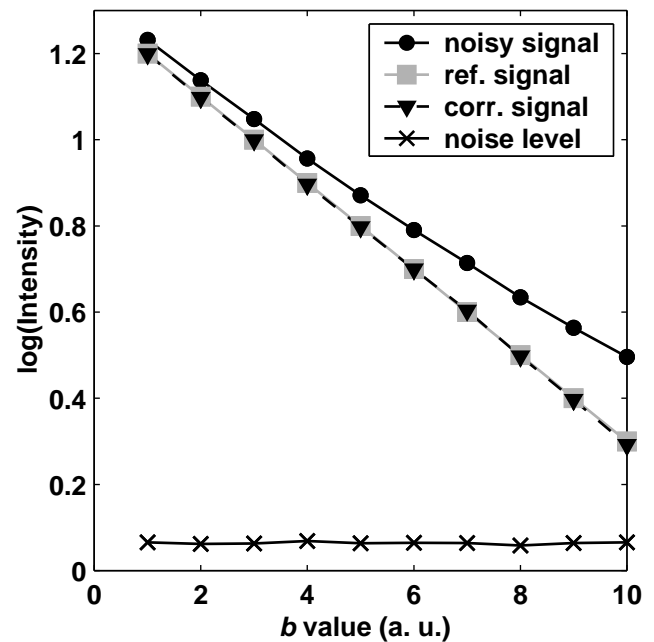
On the experimental system, three sets of images were acquired with different  $T_R$  and  $T_E$  to evaluate the correction scheme for non-Gaussian noise. More than one data set is required to apply this correction scheme since the function  $g$  from Eq. [9] must be determined first, based on a reference measurement. The sequence parameter of these diffusion-weighted spin echo EPI sequences were:  $b = 0, 50, 100, \dots, 1350$  s mm<sup>-2</sup>, slice thickness 2.5 mm, a FOV of 5 cm, and a matrix size of 128 × 64; image acquisition was repeated 30 times. Measurement 1 was performed with  $T_R = 600$  ms and  $T_E = 45$  ms, measurement 2 with  $T_R = 800$  ms and  $T_E = 45$  ms, and measurement 3 with  $T_R = 600$  ms and  $T_E = 60$  ms.

In both cases the complex image data to each  $b$  value were averaged yielding reference images with a very high SNR that we used to calculate reference values of the ADC. Then the magnitude images to each  $b$  value were averaged resulting in noisy images. We compared signal intensities and ADCs calculated of the reference data set and the noisy data set both without and with noise correction for Gaussian noise applied. The data of the experimental system was post-processed additionally with the correction scheme for non-Gaussian noise. Finally, we compared the results of our correction schemes and of the mentioned corrections schemes that were previously proposed (6,5,7).

The SNR was defined as the quotient of the measured mean signal intensity (without correction) and the measured background signal intensity. Thus, the lower limit of the SNR is 1 when the original signal intensity is 0.

## Results

The results of the numerical simulations are shown in Fig. 1. The obvious signal bias caused by complex Gaussian noise added to the image signal in  $k$  space is corrected, reestablishing the



**Figure 1:** Numerical simulation of Gaussian noise and noise correction. The correction scheme for Gaussian noise (based on Eq. [4]) was applied. SNR was between 3.2 and 1.6.

values of the reference signal that were calculated without added noise. The added noise decreased the ADC by 18 % as listed in Table 1.

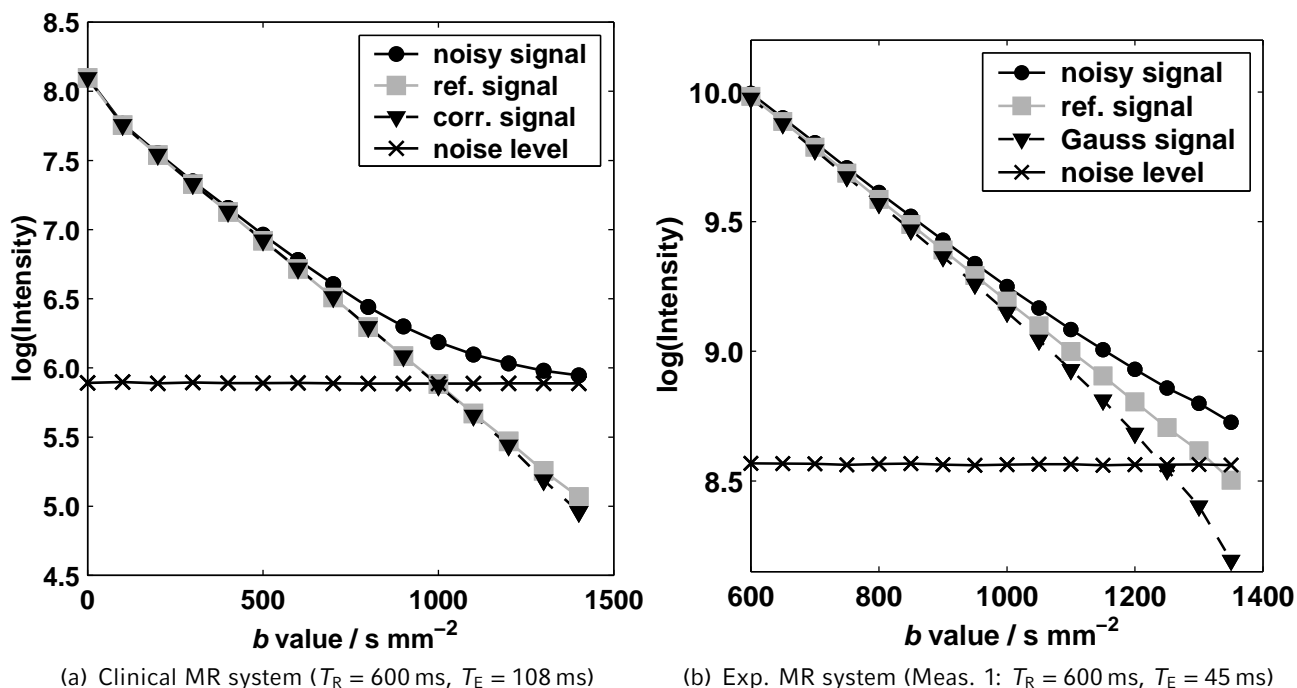
Figure 2 shows the application of the correction scheme for Gaussian noise to image data of two different MR systems. Signal intensities of the clinical system are corrected almost exactly to the calculated reference value, indicating that the image noise of this system can be described by a Gaussian distribution. The ADC deviation is reduced from 27 % to only 2 %. However, applying the same correction scheme to the data of the experimental MR system, signal intensities are clearly over-corrected by a factor of two and the ADC bias changed from -6 % to 7 %. Calculated values of the ADC are given in Table 1.

Figure 3 shows the application of the correction scheme for non-Gaussian noise to image data of the experimental MR system using the data shown in Fig. 2(b) as reference. Although we were using different timing parameters in the three measurements of Fig. 2(b) and Fig. 3, the biased signal intensities are corrected to the reference values with high precision. After correction, the determined ADCs (Table 1) differ only by 0.2 % and 0.1 % from the calculated reference value, whereas the difference is about 5 % without correction.

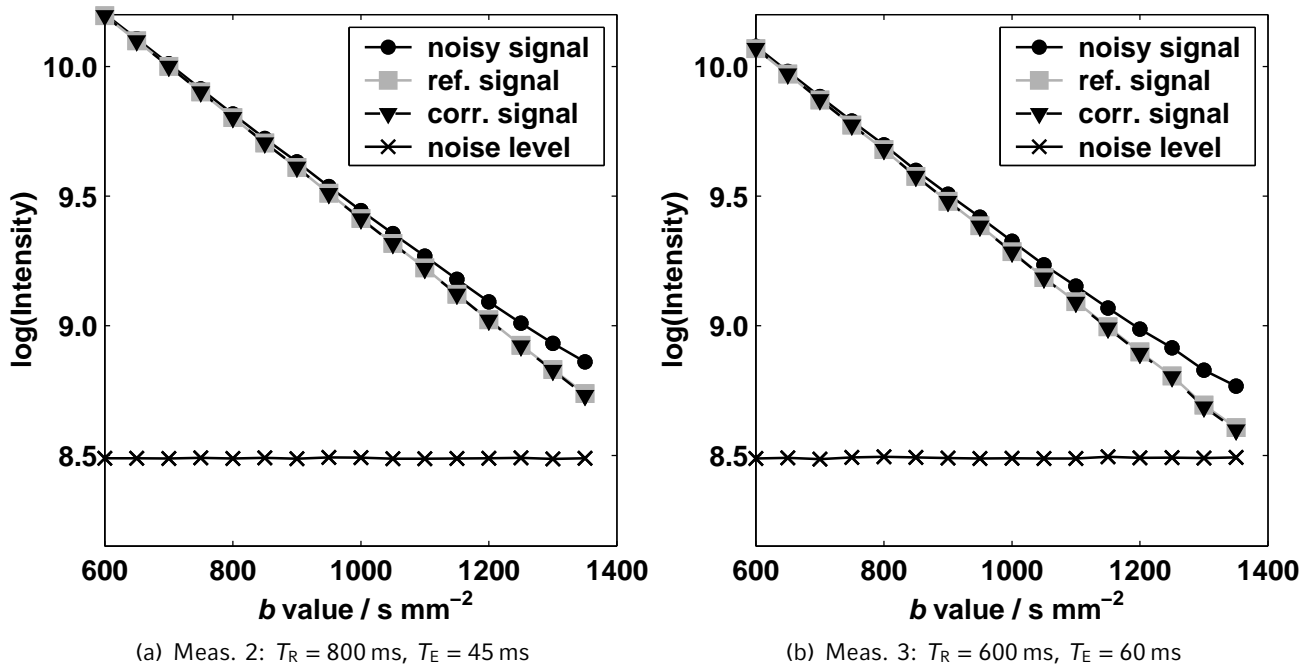
Since the reference values of the ADCs are

**Table 1:** Results of noise correction. ADCs of numerical simulation in arbitrary units, ADCs of MR measurements in  $10^{-3} \text{ mm}^2/\text{s}$ .

		Numerical	Clinical	Exp. Sys.		
		Simulation	System	Meas. 1	Meas. 2	Meas. 3
SNR	max.	3.21	9.11	16.53	20.31	18.22
	min.	1.54	1.06	1.18	1.45	1.32
Reference	ADC	0.100	2.108	2.023	1.984	2.001
Without correction	ADC	0.0820	1.535	1.900	1.916	1.913
	Bias	-18.0 %	-27.2 %	-6.1 %	-3.4 %	-4.4 %
Correction for Gaussian noise	ADC	0.1003	2.159	2.161	2.044	2.087
	Bias	0.3 %	2.4 %	6.8 %	3.0 %	4.3 %
Correction for non-Gauss. noise	ADC	—	—	—	1.987	2.006
	Bias	—	—	—	0.1 %	0.2 %



**Figure 2:** Application of correction scheme for Gaussian noise to data of our clinical MR system (2(a)) and our experimental MR system (2(b)). Only the signal of the clinical system is corrected to the reference value.



**Figure 3:** Application of correction scheme for non-Gaussian noise to data of our experimental MR system.

calculated from the average of the complex images of each series of acquisitions, they differ between the two MR systems due to different room temperatures during imaging and possible deviations of gradient calibration of the two systems. However, that does not influence the accuracy of the results described as bias of those reference values. The linearity of both gradient systems is very high, which is shown by the correlation coefficients of the logarithm of the reference signal intensity and the  $b$  value, that are  $-0.9994$  for the clinical system and  $-0.9991$ ,  $-0.9996$ ,  $-0.9994$  for the three measurements at the experimental system.

Two previously published correction schemes were used for noise correction as well; Table 2 compares the results of those methods with the results of the correction schemes proposed in this paper. The correction scheme working on power images (5, 6) shows good results if the noise is close to Gaussian noise, i. e. in the numerical simulation and with data of our clinical MR system. Applying this correction scheme to image data that is gained by magnitude averaging *before* calculating the power image results in an increased bias of ADC.

The approximative correction (7) corrects the signal changes to a less high degree with remaining ADC biases between 4 % and 13 % in our data sets affected by Gaussian noise and ADC biases of about 2 % in the data sets of our experi-

mental MR system.

## Discussion

If images or image regions with a low or very low SNR occur in DWI, a correction of signal intensities is required for an exact determination of ADCs. To illustrate this: an ADC determination of water (diffusion coefficient  $D \approx 2.0 \cdot 10^{-3} \text{ mm}^2/\text{s}$ ) with  $b$  values of 0 and  $1000 \text{ s}/\text{mm}^2$  has a bias greater than 5 % if the SNR of the measurement is lower than 1.8 at  $b = 1000 \text{ s}/\text{mm}^2$ ; with that noise level the SNR is about 13.3 at  $b = 0$  (Eq. 4). The choice of an appropriate correction scheme depends on the characteristics of noise, on the type of averaging of the acquisitions, and on the lowest SNRs in these images.

If the noise intensity is normally distributed as in our numerical simulations and approximately in images of our clinical MR system, mathematically exact expressions exist that describe the influence of noise on the signal. Using Eq. [4] under these conditions, we corrected the biased ADC and obtained the reference value with very little deviations. We compared two alternative correction schemes and found different disadvantages related to those.

Intensity correction based on power images cannot be used, if the existing image data con-

**Table 2:** Comparison of different noise correction schemes. ADCs of numerical simulation in arbitrary units, ADCs of MR measurements in  $10^{-3} \text{ mm}^2/\text{s}$ .

		Numerical	Clinical	Exp. Sys.		
		Simulation	System	Meas. 1	Meas. 2	Meas. 3
Reference	ADC	0.100	2.108	2.023	1.984	2.001
Proposed correction	ADC	0.1003	2.159	(2.161) <sup>a</sup>	1.987	2.006
	Bias	0.3 %	2.4 %	(6.8 %) <sup>a</sup>	0.1 %	0.2 %
Power corr. $\langle  S ^2 \rangle$ (5,6)	ADC	0.1002	2.164	2.170	2.059	2.101
	Bias	0.2 %	2.7 %	7.6 %	3.8 %	5.0 %
Power corr. $\langle (\overline{ S })^2 \rangle$ (5,6)	ADC	0.1143	2.666 <sup>b</sup>	2.417	2.155	2.240
	Bias	14.3 %	26.5 %	19.5 %	8.6 %	11.9 %
Approximative correction (7)	ADC	0.0957	1.842	2.076	2.019	2.044
	Bias	-4.3 %	-12.6 %	2.6 %	1.8 %	2.1 %

<sup>a</sup> Correction scheme for Gaussian noise used in reference measurement

<sup>b</sup> Signals of the two highest  $b$  values could not be corrected.

sists of averages of magnitude images. Averaging magnitude images is a useful technique to obtain more homogeneous images, which is important for a pixel-by-pixel evaluation, e. g. for generating ADC maps; but in contrast to averaging complex image data the SNR is not improved. However, after having performed averaging of magnitude images the mean value  $\langle (\overline{|S|})^2 \rangle$  is different from the mean value of a true power image  $\langle |S|^2 \rangle$ . Thus, a correction based on power images can be performed only on non-averaged images or on the complete set of images including all repeated acquisitions as separate images, i. e. before magnitude averaging. The latter approach requires the handling of much bigger amounts of data and results in similar results as our correction scheme for Gaussian noise.

The approximative correction proposed by Gudbjartsson turned out to be not sufficient, if the SNR becomes very low. The bias of the ADC was reduced but not as much as with the two other corrections schemes. Advantages of this approach are simple calculation and the ability to deal with averaged magnitude images. However, it is not recommendable with very low SNRs.

We are not aware of any correction schemes that have been previously proposed to correct signal intensities if the distribution of noise intensities is not Gaussian. Our approach resulted in very exact values of the ADC but has the inevitable disadvantage that one reference measurement must be performed for any given MR system. However, this reference measurement

can be used for all further measurements independent of the pulse sequence or the imaged object.

As a consequence of the specific properties of the noise distribution of our experimental MR system, any correction that assumes Gaussian noise over-corrected our data by a factor of two. This property made the approximative correction work incidentally quite well, since the algorithm-specific under-correction and the noise-specific over-correction almost cancelled. However in general, the approximative approach cannot be expected to correct signal intensities biased by non-Gaussian noise.

We were not able to determine the source of the non-Gaussian noise distribution within our experimental MR system. Almost all components of the system from the RF receiving coil over the amplifiers to the analog-to-digital converter contribute to the resulting noise and, thus, make this analysis difficult.

Alternative methods are available to avoid image data without sufficient SNR, e. g. reducing the maximum  $b$  value. This can either be done globally by adjusting the highest  $b$  value to the signal of the image region with the combination of lowest base intensity and highest ADC (12). Or alternatively images with multiple  $b$  values can be acquired and the appropriate maximum  $b$  value to be used for ADC calculation of a certain region or pixel is determined during post-processing; signals belonging to higher  $b$  values are discarded. The first approach has the obvious

disadvantage that a small region of the image determines a parameter that most probably is not well suited for most of the rest of the image. The second approach is disadvantageous in those protocols in which only two  $b$  values are used for ADC determination; more  $b$  values result in a prolongation of acquisition time. Further problems are the choice of an appropriate threshold and the varying number of points that are used for parameter fitting. The latter may cause artifacts since the numerical precision and stability of the fit algorithm usually depends on the number of input data.

In conclusion, our results show that noise can significantly influence the determination of ADCs, which consequently appear systematically decreased. The biased signal intensities can be corrected with one of the two proposed correction schemes, which deal with the two cases of Gaussian and non-Gaussian noise. Especially at very low SNR or non-Gaussian noise these correction schemes work more successfully than formerly proposed strategies.

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