Statistical Methods to Determine the Reliability of in vivo Single Voxel MRS Data

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Introduction

Spectral quality and spectral reliability are closely related, but not identical. Although MRS-signal reliability is an issue of highest importance, its notion received, to the best of the authors' knowledge, no systematic treatment in the *in vivo* MRS-literature in the past. Frequently it remains unclear whether clinical *in vivo* single voxel data MRS data can be trusted, *i.e.*, can be used for diagnostic purposes. In order to make SV-MRS clinically more viable, assessment of spectral reliability of the data should preferably be handled by the MR-scanner system rather than by medical staff. In this contribution, we devise, apply, and test statistical methods for automated data reliability testing. Once the data pass the reliability test, the MRS signal is considered reliable and the variances of the maximum likelihood (ML) estimated parameters approach the Cramér-Rao minimum variance bound (CR-MVB).

Methods

Let $S_m[n]$ be the m-th separately stored response of an M-times repeated single voxel spectroscopy experiment. We assume that this signal can be written as $S_m[n] = S_d[n] + \delta_m[n] + \varepsilon_m[n]$, in which $S_d[n]$ is the deterministic MRS-signal -- by definition equal for each response -- $\varepsilon_m[n]$ is a stochastic signal the electric noise picked up by the coil and the MR acquisition system -- and $\delta_m[n]$ is a second stochastic term which models those signals that cause artifacts, including those from patient motion, RF-signals of non MR origin, scanner instabilities etc. The statistical properties of $\varepsilon_m[n]$ and $\delta_m[n]$ differ. Whereas $\varepsilon_m[n]$ is to a high degree of accuracy of Gaussian nature, the statistic of $\delta_m[n]$ is non-Gaussian, of "heavily-tailed" nature *(1)* , *i.e.*, the tails of the ensuing distribution falls off rather more slowly than that of Gaussian noise, causing artifacts to average out only very slowly. Note that the variance-estimates given by the CR-MVBs, which are frequently used in *in vivo* MRS as an error indicator, are only valid if $\delta_m[n]$ is zero for all m, n. The question of whether our data are reliable, can be translated into the question of whether the noise in the signal $S_m[n]$ as a function of m in the repeated signals is of Gaussian nature. To find out whether the noise is of Gaussian nature, we compute the first four moments about the mean; *i.e.*, the mean (first moment), variance (second moment), skewness (third moment), and kurtosis (fourth moment). For pure Gaussian noise all moments higher than the second moment are zero. Noise is non-Gaussian if moments higher than the second moment differ *significantly* from zero. Since the estimates of the mean[n], variance[n], skewness[n], and kurtosis[n] are stochastic variables themselves, the variance in these moment estimates must be estimated as well in order to judge whether they differ significantly from zero. Simple averaging the skewness and kurtosis over all spectral points n is not correct, since large negative as well as large positive values could average out and thus give a wrong indication of the true spectral reliability. Therefore we introduced the test parameters κ_{mean}, $\kappa_{variance}$, $\kappa_{skewness}$, and $\kappa_{kurtosis}$ defined as the average of |mean[n]|, |variance[n]|, skewness[n]|, and |kurtosis[n]| over an appropriate signal range in time or frequency domain. Additionally, the average coefficient of variance $c_\kappa = 100\sqrt{\kappa_{variance}} / \kappa_{mean}$ over the relevant part of the spectrum was computed.

Results

The upper left spectrum of Fig. 1A shows the conventional ^{1}H mean spectrum of the cortex of a test person who was asked to refrain from any voluntary movements during the measurement. Note that, in contrast to what is expected, the variance-spectrum, displayed on the right hand side of the mean spectrum, is relatively large and has *not* a noisy character. This is due to small involuntary motions and pulsation of the brain. In contrast, the skewness- and kurtosis-spectra below that have a strong noisy character. Figure 1B shows the spectrum of the same localization in the same test person who is asked to make occasionally small voluntary motions. Apart from its amplitude, the conventional mean spectrum strongly resembles the mean of Fig. 1A; its variance-spectrum is substantially larger than that of 1A (especially the range between 1-2 ppm); although still having a noisy character, the skewness- and kurtosis-spectra are the clearest indicators of time variant acquisition conditions, and thus of non-reliability. Table 1 shows the computed κ–values for simulated Gaussian noise with expectation value 0 and variance 1 (1st row), Table II shows the corresponding estimated variances in the values of Table I. Due to the fact that κ–values are computed as the average over normally distributed ***magnitude*** values, its distribution is not normal distributed but has a *folded* normal distribution. Therefore $\kappa_{skewness}$, and $\kappa_{kurtosis}$ are non-zero. The second row of Table 1 shows the computed values of measured scanner noise. By comparing the values of $\kappa_{skewness}$ and $\kappa_{kurtosis}$ *and* their associated variances it is concluded that our scanner noise is indeed of Gaussian nature. The third and fourth row of Table 1 show the κ-values, computed in time domain, of the spectra shown in Fig.1. From the fact that $\kappa_{skewness}$ and $\kappa_{kurtosis}$ of the *in vivo* spectrum without voluntary patient motion does not significantly differ from the values obtained for pure Gaussian noise, we conclude that these data are reliable, and the variances of the maximum likelihood estimated parameters approach the CR-MVB. In contrast, the spectrum of Fig 1B cannot be trusted since $\kappa_{skewness}$ and $\kappa_{kurtosis}$ differ significantly from the normal distribution. Is this case the variances of the ML-estimated parameters do not approach the CR-MVB and the latter cannot be used for error-estimation. Once the reliability test fails, order statistic filtering techniques (ARSOS *(2)*) can be used for signal artifact reduction.

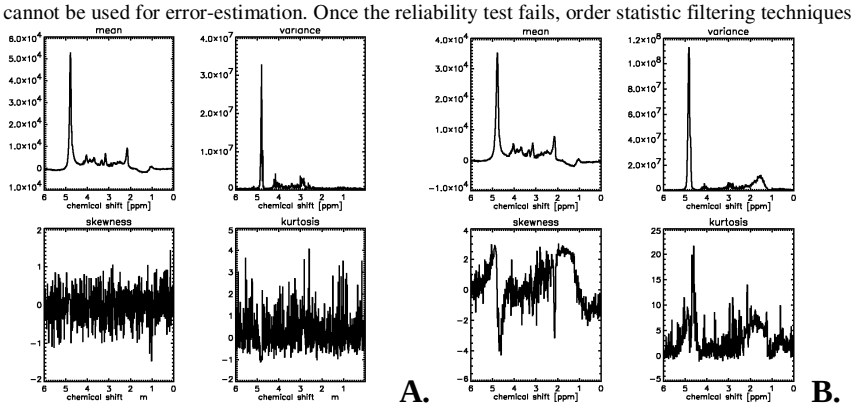

Table I

κ- AND c_κ-VALUES FOR DIFFERENT SIGNAL TYPES

Signal type	κ_{mean}	$\kappa_{variance}$	c_κ (%)	$\kappa_{skewness}$	$\kappa_{kurtosis}$ †
Gaussian‡	0.1418	0.9898	702	0.3272	0.6101
Scanner‡	1.384	91.59	693	0.3409	0.6348
rest#	129.7	823.3	22.1	0.3214	0.6427
moved#	90.40	6161	86.8	1.079	2.883

†'Excess' kurtosis quoted (= kurtosis - 3); ‡noise; #*in vivo* MRS.

Table II

ESTIMATED VARIANCES OF THE κ-PARAMETERS OF TABLE I

Signal type	κ_{mean}	$\kappa_{variance}$	c_κ (%)	$\kappa_{skewness}$	$\kappa_{kurtosis}$ †
Gaussian‡	0.0115	0.0660	N.A.	0.0673	0.4155
Scanner‡	1.204	556.6	N.A.	0.0773	0.4798
rest#	36031.2	323001	N.A.	0.0635	0.3638
moved#	29441.0	$3.776.10^8$	N.A.	0.0769	0.5159

†'Excess' kurtosis quoted (= kurtosis - 3); ‡noise; #*in vivo* MRS.

Figure 1: The first four moments about the mean of a ^{1}H-brain spectrum recorded at 3T of a test person: A. without voluntary motion; B. with voluntary motion.

Conclusion

Automated and user independent statistical methods for testing the *reliability* of *in vivo* MRS signals have been developed and tested, allowing verification of whether the data can be used for diagnostic or scientific purposes. Once the MRS signal passes the reliability test, the variances of the ML-estimated parameters approach the Cramér-Rao minimum variance bound. If the test fails, the CR-MVBs are no appropriate measure of the error in the estimated parameters. In this case the CR-MVB will normally underestimate the error in the parameter estimates. Since the test does not need any user interaction, it is especially suitable for application in a clinical setting.

References

1. R. Brcic, "Some Aspects of Signal Processing in Heavy Tailed Noise", Tech. Report, 2002, Curtin University of Technology, Australia
2. J. Slotboom and D. van Ormondt, "The application of All-Ranks Selection Order Statistic-filtering (ARSOS) in single voxel in vivo MR-spectroscopy", Contrib.#831, ESMRMB, Warsaw, 2006