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The effects of basis sets on magnetic resonance spectroscopy quantification for stock PRESS sequences, a simulation study

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Synopsis

Realistic synthetic PRESS spectra were generated for three different echo times for each of the three major vendors. These spectra were then fit to the matched basis set (i.e., the basis set used to generate it), as well as the mismatched basis sets at the same echo time from other vendors, and the matched basis set but with the hard pulse approximation, to investigate how sensitive resulting quantification is to basis sets. It was found that the concentration for low-concentration metabolites is highly susceptible to small changes in basis sets (e.g., GABA varied by 115 ± 188%).

Introduction

Point resolved spectroscopy[1] is the most commonly used magnetic resonance spectroscopy sequence, and the major vendors' implementations differ in the shape of the RF pulses[2] with the refocusing pulses being of particular importance for resulting spectral shapes as well as their exact timings (i.e., TE1/TE2). For example, the General Electric (GE) utilizes 137° Shinnar-Le Roux pulses[3] (the 137° enables shorter pulses at the cost of $\sin\left(\frac{137}{180}\pi\right)^4 \approx 0.75$ factor in signal decrease) for refocusing pulses, while Siemens uses 180° Mao pulses[4]. As such, the spectral shape for J-coupled metabolites acquired across different platforms at the same echo time will vary. Although it has previously been shown that this can result in substantially different spectral shapes obtained from the different vendor implementations at the same echo time[2] the effects on quantification with realistic spectra have yet to be investigated. Realistic synthetic spectra were generated for three different echo times for each of the three major vendors: Siemens, GE and Philips. These synthetic spectra were fit to the matched basis set (i.e., the basis set used to generate it), a basis set using the matched timings and flip angles but with the hard pulse approximation, as well as the mismatched basis sets at the same echo time from the two other vendors to investigate how sensitive resulting quantification is to small changes in basis sets. It was shown with realistic synthetic data in both metabolite concentrations and spectral appearance, where the ground truth is known, that the concentration for low-concentration metabolites is highly susceptible to small changes in basis sets.

Methods

Synthesis of Spectra

Spectra were simulated for each of the three vendors and three echo times (30/80/144 ms) using exact timings and shaped RF specific to the vendor and echo time in MARSS[7]. The vendor basis sets were simulated with 128^3 spatial points to appropriately model the transition bands[2], and the hard pulse basis set was generated by only using a single spatial point for each of the three vendors. Spectra were synthesized at each TE similar to what has previously been performed[8,9]. This was achieved by exponentially line broadening each of the simulated 18 metabolites by $\frac{1}{\pi T_2^m}$, where T_2^m is the transverse relaxation constant for each of the individual metabolites, then broadening by a Gaussian linewidth of 8 Hz[2] to resemble the effect of field inhomogeneities (NAA fullwidth at half maximum of 6.2 Hz), which reflects a good linewidth in the occipital cortex at 3T[10]. These broadened simulated spectra were then scaled by their respective concentration[11], and multiplied by the appropriate scaling factors derived from analytical solutions to the Bloch equation for each echo time and metabolite to incorporate realistic T_1 and T_2 relaxation[12–16]. The macromolecule signal was approximated as the sum of 10 individual Lorentzian resonances with measured concentration and T_2 values[17].

Quantification of Spectra

Spectra were simulated for a TE = 30 ms (general-purpose short echo spectroscopy), TE = 80 ms (for glutamate detection[5]) and TE = 144 ms (for lactate detection[6]) for each of the three major vendors. At each individual echo time the synthesized spectra were then fit via linear combination modelling (LCM) in INSPECTOR[18,19] to each of the four basis sets. The relative errors, $RE_m^{B_v(TE)}(TE)$ for each of the metabolites and macromolecules calculated using each vendor basis set were then calculated via

$$RE_m^{B_v(TE)}(TE) = \frac{C_m^{B_v(TE)}(TE) - C_m^T}{C_m^T} \cdot 100\%$$

where $C_m^{B_v(TE)}$ is the concentration extracted from the LCM fit at each of the three echo times using the basis set $B_v(TE)$ and C_m^T represents the ground truth concentrations known a priori and hence are irrespective of echo time.

Results and Discussion

At each simulated echo time, small but noticeable differences between the three vendors were observed (Figure 1). Perfect fits were acquired in the case when the basis set matched the synthesized data, resulting in accurate quantification, i.e. 0% error, as expected. Spectra were noise free so that the measured relative errors can be directly attributed to imperfect fits. Fits obtained with the other basis sets, for instance, in vivo Siemens spectrum analyzed with GE basis set, had noticeable small but non-zero residuals (the three synthesized GE spectra are shown in Figure 2, with results for Siemens and Philips being similar but not shown). Despite all fits having relatively small residuals the concentration of all low-concentration metabolites for all echo times varied substantially from the known ground truth when suboptimal basis sets were employed for all three echo times (Tables 3-5). Longer echo times exacerbated these issues, which is expected as all TE = 0 ms spectra would be identical. The large relative errors despite adequate fits are a result of overlapping metabolites masquerading for one another. These results are consistent with previous results demonstrating that fit quality alone cannot validate a model[20].

Conclusions

Basis sets which do not use the experimentally realistic shaped RF pulses and timings, or basis sets which employ the hard pulse approximation, can appear to produce adequate quality fits, however the concentration of critical metabolites derived through linear combination modeling can vary substantially from the ground truth. The only remedy are basis sets that match the experimental reality as closely as possible.

Acknowledgements

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Figures

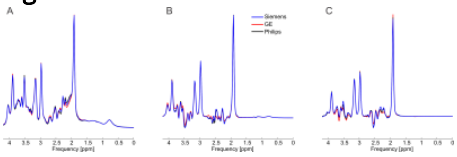

Figure 1: The synthesized spectra for TE = 30 ms, A, TE = 80 ms, B, and TE = 144 ms, C, across the three different vendor implementations of PRESS with blue depicting the Siemens implementation, red depicting the GE implementation and black depicting the Philips implementation. Spectra have been normalized to account for differences in voxel profile due to different pulses (i.e., different transition widths).

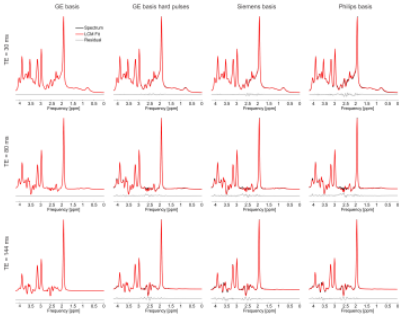

Figure 2: The synthesized GE spectra at the three different echo times along with the fits for the four different basis sets. The synthesized spectra are given in black, the fit in red and the residual in grey. Perfect fits can be observed with the GE basis, as expected, since these particular spectra were synthesized from the GE basis, while non-perfect fits were obtained with the other three basis sets. Similar results were obtained for the synthesized Philips and Siemens spectra (results not shown).

	GE spectrum			Siemens spectrum			Philips spectrum		
Metabolite	GE basis hard pulses	Siemens basis	Philips basis	Siemens basis hard pulses	GE basis	Philips basis	Philips basis hard pulses	GE basis	Siemens basis
Asc	138.1	88.2	53.8	79.2	-37.8	31.3	116.2	54.7	95.7
Asp	19.8	36.0	37.9	38.2	-54.0	11.5	6.0	-59.9	-12.4
Cho	31.3	35.2	-18.0	83.1	8.4	-49.2	3.8	8.3	19.8
Cr	8.5	3.5	-0.1	6.2	-10.3	-1.7	9.6	-18.6	-6.4
GABA	-39.4	34.6	156.7	-95	0.1	114.9	-100	-7.8	-41.6
GPC	4.0	-1.9	27.9	-11.9	-28.1	39.2	27.2	-47.6	-33.7
GSH	-3.2	-24.7	-69.4	31.4	51.9	-63.0	24.1	105.3	64.3
Glc	-57.6	13.4	110.6	-26.8	38.2	85.9	65.0	-69.6	-100
Gln	-16.8	91.9	152.3	-45.3	-5.6	103	-54.1	-10.6	-23.8
Glu	2.9	-27.6	-51.9	6.1	5.7	-28.3	8.3	10.3	9.5
Gly	121.6	94.7	389.3	36.5	-3.2	359.4	584.7	145.6	232.9
Lac	6.5	-5.1	-23.0	26.7	15.7	-14.1	56.1	46.8	29.9
NAA	3.7	-0.2	11.6	-1.5	-7.0	11.6	-0.2	-16.5	-16.0
NAAG	14.8	0.3	-50.3	33.8	36.2	-54.6	48.8	79.5	75.7
PE	-50.2	-4.8	58.8	-63.7	26.9	52.1	14.7	23.3	-6.9
Tau	23.1	-14.2	-55.0	7.4	-4.4	-41.6	-13.3	34.5	57.6
mI	-1.5	-8.0	-27.0	-4.9	-1.8	-22.6	-12.8	5.8	3.0
sI	-48.1	-32.4	-69.8	-32.6	72.1	-55.3	1.8	102.1	8.8
MM	3.5	0.5	0.4	1.6	-3.9	-1.1	8.7	-8.4	-4.8
Cho + GPC	13.1	10.5	12.6	19.7	-15.9	9.8	19.4	-29	-15.9
Glu + Gln	-1	-4.1	-11.7	-4.0	3.5	-2.4	-4.0	6.2	3.0
mI + Gly	7.7	-0.4	4.1	-1.8	-1.9	6.0	31.9	16.3	20.2
NAA + NAAG	5.1	-0.1	3.5	3.1	-1.3	3.0	6.2	-4.0	-4.1

Table 1: The relative errors (%) for each of the metabolites and macromolecules for TE = 30 ms spectra. Large relative errors are incurred for all low-concentration metabolites, indicating a high sensitivity to perturbations in the basis set.

	GE spectrum			Siemens spectrum			Philips spectrum		
Metabolite	GE basis hard pulses	Siemens basis	Philips basis	Siemens basis hard pulses	GE basis	Philips basis	Philips basis hard pulses	GE basis	Siemens basis
Asc	17.1	99.0	-62.3	106.1	-1.5	19.2	335.8	15.3	301.2
Asp	85.9	183.4	4.8	170.8	-100	-57.5	182.3	-100.0	32.9
Cho	10.6	-56.2	-17.4	-79.6	91.0	74.9	-86.4	-1.9	-6.0
Cr	0.3	-1	-0.3	1.6	-1.6	-0.9	3.5	-1.8	-2.2
GABA	221.0	-38.5	16.3	-31.7	123.3	128.5	-31.6	44.1	-85.5
GPC	-9.8	12.3	-2.0	63.5	-25.6	-33.7	64.4	12.5	-0.2
GSH	91.1	107.4	87.0	17.6	-10.7	-19.1	21.2	1.1	58.3
Glc	21.2	124.6	116.1	102.8	53.4	-7.4	67.0	87.5	90.9
Gln	232.0	-10.1	54.5	-30.0	157.5	9.1	-30.1	130.7	-36.3
Glu	140.4	72.5	95.8	29.1	-43.7	34.7	32.0	-52.5	-35.1
Gly	225.6	428.6	440.6	364.5	-79.0	67.1	112.7	-100.0	-68.6
Lac	-75.7	-60.5	-65.6	-64.7	102.5	-33.6	-64.8	219.0	-13.5
NAA	-6.3	-24.3	-12.2	-11.7	-1.7	6.7	-13.5	-9.6	-14.3
NAAG	107.4	242.4	117.2	158.7	-3.0	-73.7	221.3	86.4	172.9
PE	-36.7	28.9	12.1	111.0	-100.0	-67.2	12.9	-100.0	90.9
Tau	-22.2	-74.8	-40.5	173.9	506.6	46.2	45.3	356.4	-61.8
mI	-4.6	-12.2	1.3	8.3	-14.9	-1.1	18.8	-14.8	-3.8
sI	67.5	-8.5	24.5	217.2	-93.5	47.6	25.4	-81.7	-23.6
MM	49.6	34.6	29.0	69.8	-7.5	14.1	84.7	-31.0	-15.0
Cho + GPC	-3.0	-10.5	-7.1	15.8	13.3	2.5	14.1	7.7	-2.1
Glu + Gln	158.5	56.2	87.7	17.4	-4.1	29.7	19.8	-16.5	-35.4
mI + Gly	12.6	20.7	34.1	34.9	-19.6	3.9	25.8	-21.2	-8.6
NAA + NAAG	8.6	10.5	4.7	10.6	-1.9	-3.8	17.1	2.9	10.2

Table 2: The relative errors (%) for each of the metabolites and macromolecules for TE = 80 ms spectra. Large relative errors are incurred for all low-concentration metabolites, indicating a high sensitivity to perturbations in the basis set.

	GE spectrum			Siemens spectrum			Philips spectrum		
Metabolite	GE basis hard pulses	Siemens basis	Philips basis	Siemens basis hard pulses	GE basis	Philips basis	Philips basis hard pulses	GE basis	Siemens basis
Asc	332.4	116.3	312.5	25.1	24.0	37.6	103.3	-64.3	5.7
Asp	394.5	-31.8	-100.0	211.9	-65.8	3.4	193.1	-51.0	16.5
Cho	45.9	-40.3	-88.8	44.0	-65.2	50.8	98.1	-92.4	-84.8
Cr	6.5	-7.2	-9.1	3.6	-2.4	0.4	6.0	-2.6	-3.2
GABA	193.0	13.7	132.2	-40.7	137.1	-4.6	-12.1	186.0	67.5
GPC	-7.7	27.0	47.5	-15.1	39.7	-29.5	-38.8	63.9	47.7
GSH	167.4	4.9	38.2	-54.5	-100.0	-87.0	127.4	-93.0	171.7
Glc	147.0	52.4	15.9	-100.0	696.3	-35.3	-89.9	874.5	-35.1
Gln	126.8	106.8	-38.7	38.9	301.1	217.6	-79.2	183.4	-100.0
Glu	-17.7	-79.5	-38.2	-16.2	43.0	18.1	-6.9	0.8	-30.3
Gly	221.2	169.8	27.7	192.2	711.8	552.3	268.9	284.9	130.6
Lac	-51.1	-100.0	-67.0	-72.1	55.5	-23.4	-16.7	100.8	-46.2
NAA	-15.4	-20.7	-15.8	-18.8	2.6	2.5	-23.7	2.8	-3.8
NAAG	296.5	363.8	223.3	346.2	-71.2	-40.3	493.1	-75.7	51.1
PE	340.4	463.4	148.6	334.2	242.8	-100.0	-60.1	342.6	111.7
Tau	55.2	-61.0	-53.6	-2.2	148.8	87.7	22.5	4.1	-30.6
mI	20.4	-53.0	-20.2	0.8	28.2	-3.6	20.1	9.7	-35.8
sI	69.6	-30.4	6.3	20.2	-51.4	-69.0	35.0	-46.9	-43.6
MM	-44.2	12.4	-10.7	-14.1	-63.9	-35.0	-3.9	-24.7	-6.3
Cho + GPC	10.2	4.5	2.1	4.6	4.8	-2.8	6.8	11.8	3.5
Glu + Gln	10.8	-42.8	-38.3	-5.4	93.8	57.3	-21.1	36.8	-44.1
mI + Gly	35.4	-36.4	-16.6	15.1	79.3	37.9	38.7	30.3	-23.3
NAA + NAAG	25.2	29.4	15.4	28.8	-7.1	-3.1	43.7	-7.5	3.3

Table 3: The relative errors (%) for each of the metabolites and macromolecules for TE = 144 ms spectra. Large relative errors are incurred for all low-concentration metabolites, indicating a high sensitivity to perturbations in the basis set.