Average weighted acquisition for faster acquisition of in vivo localized two dimensional correlation spectroscopy of the brain

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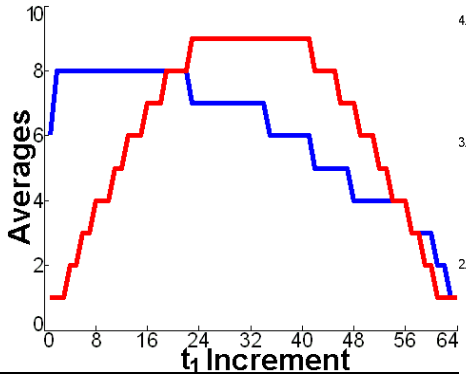
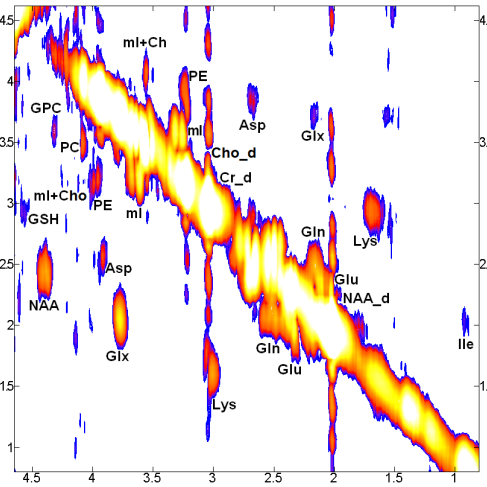
Introduction: Two-dimensional (2D) magnetic resonance spectroscopy (MRS) methods like localized correlated spectroscopy (L-COSY) (1,2) have demonstrated the capacity to uniquely resolve more metabolites than one-dimensional (1D) alternatives. Clinical adoption of these sequences has thus far been limited, however due to the need to acquire multiple t_1 increments, resulting in long scan times. Average-weighting could improve the acquisition efficiency of L-COSY, facilitating faster scans without a commensurate loss of signal quality. Average-weighting matches signal averaging to the signal quality expected from each t_1 increment rather than uniformly averaging each increment equally. These techniques could be made even more versatile for specific applications by optimizing averaging schemes for the expected signal only from particular metabolites. The purpose of this study was to implement average-weighted L-COSY and demonstrate its improved acquisition efficiency and versatility.

Materials & Methods: Average-weighted L-COSY sequences were developed for human brain and a phantom containing sixteen brain metabolites at physiological concentration. Average-weighting schemes were empirically-optimized by analyzing the signal-to-noise ratio (SNR) of each metabolite while sequentially varying the averages of the Δt_1 increments. A separate sequence was developed to selectively-optimize the SNR of the glutathione (GSH) resonance at $[F_2,F_1]$ = 4.55, 2.9 ppm (3) by emphasizing signal averaging of the Δt_1 increments most highly-correlated to the SNR of the GSH peak. Average-weighted L-COSY scan parameters included: TE/TR = 20s/2000ms, 2048 t_2 points, 64 Δt_1 increments of 0.4 ms and corresponding bandwidths of F_2/F_1 = 4000/2500 Hz. Voxels from human studies were 2.5x2.5x2.5 cm^3 (15.6 ml) while those from the phantom were 2.0x2.0x2.0 cm^3 (8.0 ml). All scans were acquired with a 32-channel head coil on a Siemens 7T whole-body MRI scanner. Figure 1 shows the optimized average-weighting schemes for phantom and human brain applications. The average-weighting scheme in brain phantom followed a sine-bell profile, while the scheme optimized for human brain had a profile skewed towards the earlier increments to accommodate the faster T_2* relaxation *in vivo*. Both the human and phantom average-weighting schemes acquired 384 total excitations over the 64 Δt_1 increments, for total scan duration of 12:48. The brain phantom was scanned 10 times with the average-weighted scheme and twice with the GSH-optimized scheme. Each average-weighted scan was followed by a uniformly-averaged L-COSY scan with 512 total excitations and 17:04 duration but otherwise identical parameters for comparison. Three human volunteers were scanned in the occipital lobe using the 12:48 duration average-weighted L-COSY and the 17:04 duration uniformly-averaged sequence. All data were post-processed using a custom MATLAB-based program and signal quantification was performed using volume integrals.



Normalized SNR	Duration	Human (N=3)	Phantom (N=10)
Uniformly Averaged	17:04	1.000	1.000
Average-weighted	**12:48**	**1.003 ± .076**	**1.063 ± .155**
Simulated Uniform	17:04	0.878 ± .072	0.879 ± .040



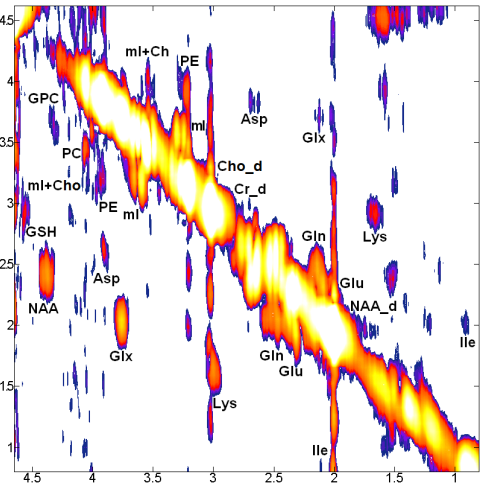


Figure 1 (Top Left): Average-weighting schemes for human (blue) and brain phantom (red). **Table 1 (Left Bottom):** Normalized SNR from uniformly-averaged, average weighted and simulated uniformly-averaged studies in phantom and human brain. **Figure 2 (Middle):** Spectrum from 17:04 duration uniformly-averaged L-COSY scan of normal volunteer (age 32). **Figure 3 (Right):** 12:48 duration average-weighted scan of same voxel as Figure 2.

Results & Discussion: Table 1 shows SNR from 12:48 duration average-weighted scans of human brain and brain phantom normalized to the SNR of the 17:04 duration uniformly-averaged sequence. A third dataset was generated by truncating the final 2 averages of each Δt_1 increment resulting in a simulated uniformly-sampled study with the same total number of excitations as the average-weighted scan. The average-weighted sequence showed higher SNR in human brain (0.3%) and phantom (6.3%) despite a 25% reduction in scan time, and the SNR was 13% and 18% higher, respectively, than the simulated data with an equivalent number of total excitations. Figures 2 and 3 show typical 2D L-COSY spectra generated by the uniformly-averaged and average-weighted sequences, respectively. To test whether the selective emphasis of Δt_1 increments would significantly affect metabolite ratios, the ratio of each quantified peak was compared to the diagonal resonance of creatine at 3.0 ppm. These ratios varied by 8.9% on average between the average-weighted and uniformly-averaged sequences in human brain and 4.5% in phantom studies. This variability in creatine ratios is well within the range of inherent test-retest variation observed in previous reproducibility studies of L-COSY at 3T and 7T. The GSH-optimized sequence yield higher overall GSH peak intensity than either the uniformly-averaged or average-weighted sequences. The integral of the metabolite peak – a proxy for signal intensity – was higher in the GSH-optimized sequence at 5.29 than either the uniformly-averaged (5.12) or average-weighted (4.93) studies. Average-weighting improved the acquisition efficiency of 2D L-COSY at 7T, facilitating reduced scan time while maintaining comparable signal quality. Averaging schemes must be shaped to accommodate the relaxation properties of the scanned metabolites, but could have near-universal application in enhancing the performance of 2D MRS studies. Optimizing averaging schemes to selectively emphasize the sequence for particular metabolites could improve the versatility of L-COSY in specific applications, for example the study of GSH, biomarker for increased oxidative stress commonly studies in neurological dysfunction.

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