Investigations of Chemometric Instrumental Transfer in High Resolution NMR Metabonomic Data Sets

SAND2007-8141C

Todd M. Alam[1], M. Kathleen Alam[2], Sarah K. McIntyre[1], David E. Volk[3], Muniasamy Neerathilingam[3] and Bruce A. Luxon[3]

[1]Department of Electronic and Nanostructured Materials, [2]Energetics Characterization Department,
Sandia National Laboratories, Albuquerque, NM, 87185-0886
[3]Department of Biochemistry and Molecular Biology,
Sealy Center for Structural Biology and Molecular Biophysics, University of Texas Medical Branch
Galveston, TX 77555-1157

NMR spectroscopy continues to be a powerful technique for investigating complex mixtures, including the fields of metabonomics and metabolomics. The increasing complexity of these type of NMR data sets has also resulted in chemometric analysis becoming more common within the NMR community [1]. While the impact of solvent suppression techniques on the variation in high resolution NMR metabonomic spectra has been reported [2], studies comparing different NMR systems are limited. In particular, the transfer of calibration models for select metabolites between different NMR probes, instruments, personnel and extended time periods needs to be addressed.

In this poster we present a detailed analysis of the performance of different instrumental transfer techniques including Direct Standardization (DS), Piece-Wise Direct Standardization (PDS), Orthogonal Signal Correction (OSC) and Generalized Least Squares Weighting (GLSW) on calibration model transfer, along with the impact of spectral preprocessing and deconvolution on the implementation of instrumental transfer. **Figure 1** shows the overlap of 120 ^{1}H NMR spectra obtained from 15 samples of model mixtures of 3 metabolites obtained using either a single pulse 1D or a 1D NOESY sequence, on 2 different probes, and on 2 different instruments (Bruker Avance 600 and a Varian Unity Plus 600). Partial Least Squares (PLS) calibration models were constructed for these samples allowing for the prediction of the individual component concentrations. The transfer of these calibration models between different probes or between different instruments was poor. Original arguments suggested that small variations in line shape or small chemical shift changes were responsible for the failure of these calibrations. PLS analysis following spectral deconvolution and binning utilizing the CHENOMX software suite (Edmonton, Canada) demonstrated that these small spectral variations are NOT responsible for the poor model transfer performance.

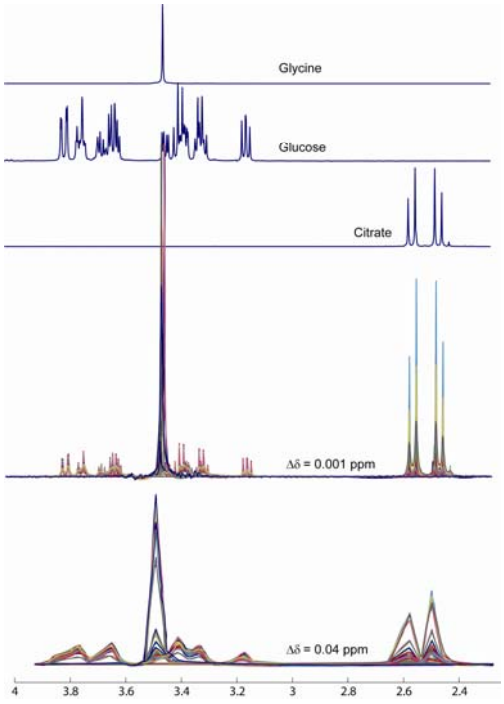

Figure 1: ^{1}H NMR of model mixtures for different instruments and probes and corresponding binning representation.

It is clear that more rigorous instrumental transfer methods are required to overcome these issues. As an example, **Figure 2** shows the significant improvement in the transfer of the glucose concentration calibration model between two different probes using the PDS transfer method, utilizing three standard samples for the standardization transform function determination. The results for the different instrumental configurations using the different transfer methods (DS, PDS, OSC and GLSW) will be presented and discussed.

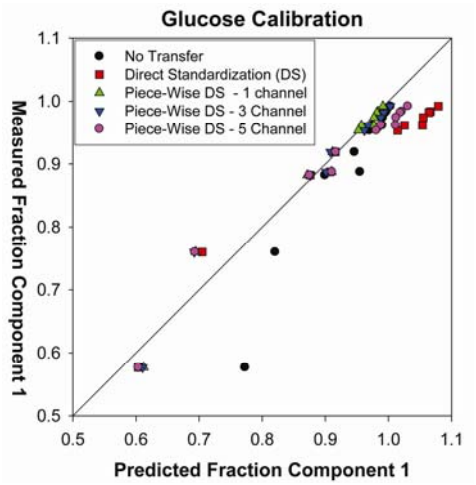

Figure 2: Glucose PDS transfer.

Sandia is a multiprogram laboratory operated by Sandia Corporation, a Lockheed Martin Company, for the United States Department of Energy's National Nuclear Security Administration under Contract DE-AC04-94AL85000. This work was entirely funded by the SNL LDRD program.

References:

[1]. T.M. Alam and M.K. Alam, *Annual Reports NMR Spectroscopy* **2005**, *54*, 42.
[2]. (a) B.C.M. Potts, A.J. Deese, G. J. Stevens, M. D. Reiley, D. G. Robertson, J. Theiss, *J. Pharm. Biomed. Anal.* **2001**, *26*, 463. (b) H. C. Keun, T.M.D. Ebbels, H. Antti, M.E. Bollard, O. Beckonert, G. Schlotterbeck, H. Senn, U. Niederhauser, E. Holmes, J. C. Lindon, J. K. Nicholson, *Chem. Res. Toxicol.* **2002**, *15*, 1380.