

OPTIMISED METHODOLOGY FOR ^1H NMR LIPIDOMICS OF SERUM

Tuulia Tynkynen¹, Reino Laatikainen¹, Taru Tukiainen², Ville-Petteri Mäkinen^{2,3,4},
Per-Henrik Groop^{3,4}, Kimmo Kaski², Olli Gröhn⁵, Merja Hallikainen⁶, Hilikka Soininen⁷, Tuula Pirttilä⁷,
Mika Ala-Korpela^{2,3,4} and Pasi Soininen¹

¹ Laboratory of Chemistry, Department of Biosciences, University of Kuopio, Finland

² Computational Medicine Research Group, Department of Biomedical Engineering and Computational Science, Helsinki University of Technology, Finland

³ Folkhälsan Institute of Genetics, Folkhälsan Research Center, Biomedicum Helsinki, Finland

⁴ Division of Nephrology, Department of Medicine, Helsinki University Central Hospital, Finland

⁵ A. I. Virtanen Institute for Molecular Sciences, University of Kuopio, Finland

⁶ Brain Research Unit, Mediteknia, University of Kuopio, Finland

⁷ Department of Clinical Science, Neurology Unit, University of Kuopio and Kuopio University Hospital, Finland

*Correspondence to pasi.soininen@uku.fi :: <http://www.computationalmedicine.fi/>

Many diseases, for example, diabetes, dementias, and atherothrombosis [1], involve alterations in lipid metabolism. Proton NMR spectroscopy offers a way to study lipid composition of body fluids since functional groups of lipid compounds resonate at their characteristic region, and thus, allows their recognition from the spectrum. Sophisticated analysis,

however, is the key for reliable data and extensive molecular coverage. Here we focus on the optimisation of the ^1H NMR lipidomics approach for metabonomics use. We also present some of the lipid descriptors available and discuss the suitability of this approach for clinical metabonomics.

Sample preparation and acquisition

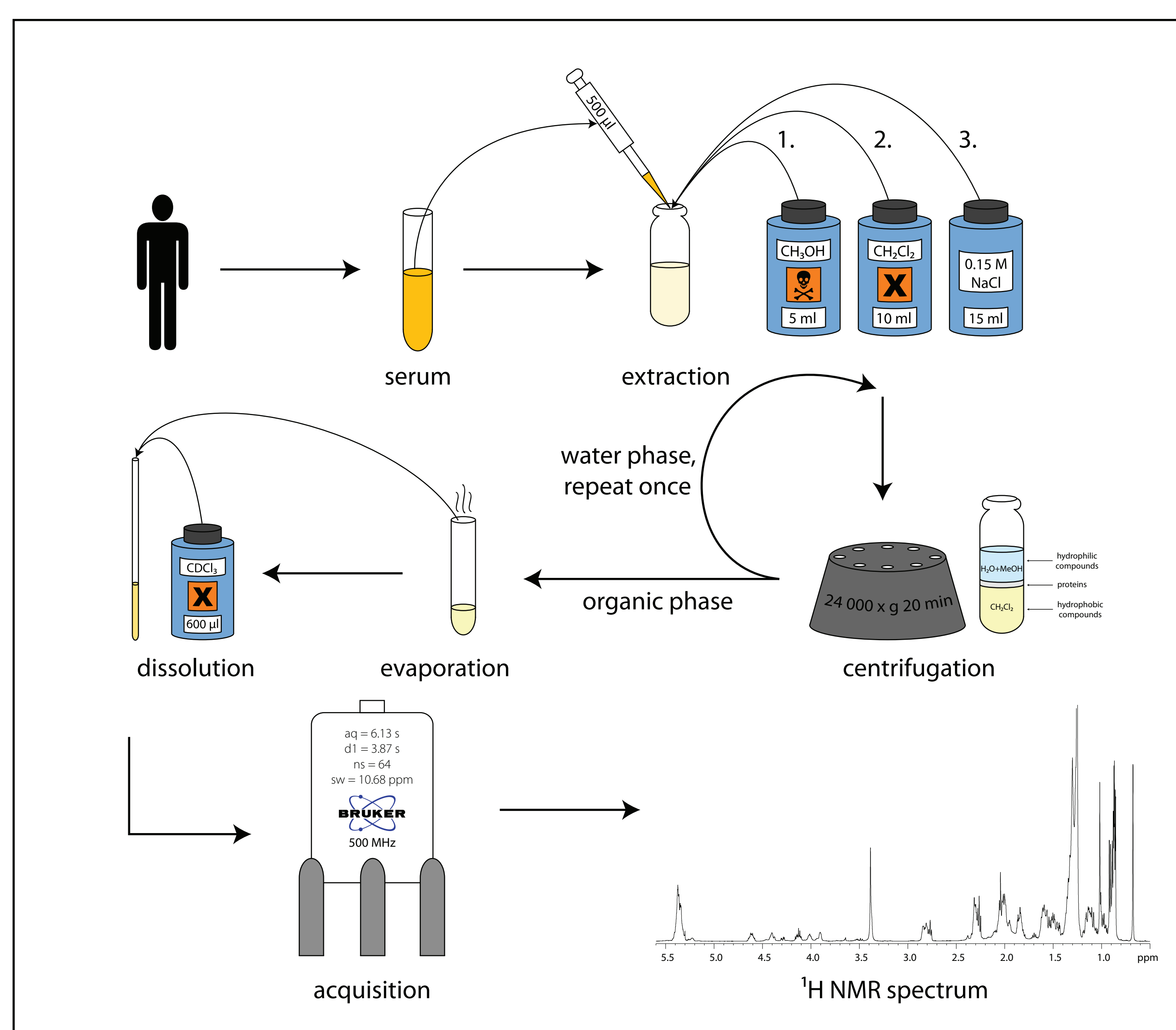


Figure 1. Extraction and acquisition protocols for serum lipids.

Fitting strategy

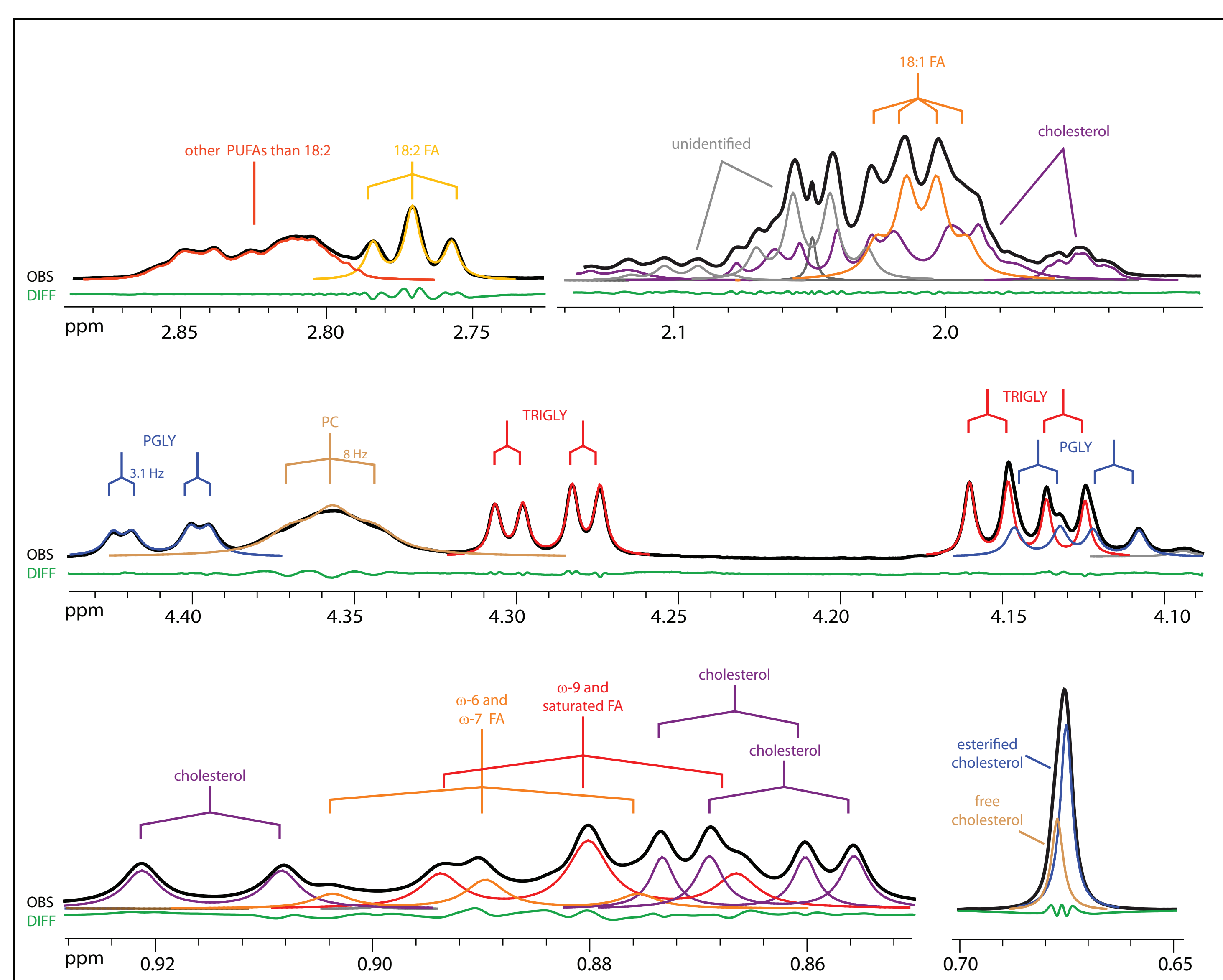


Figure 2. Different parts of the spectra of extracted serum samples with lines from deconvolution analysis. Black line represents the observed spectrum (OBS), and the coloured lines represent the fitted signals. The green line at the bottom represents the difference (DIFF) between the observed spectrum and the fitted signals. The line fitting was performed using the constrained total-line-shape fitting protocol of the PERCH NMR Software [2]. Chemical shift and coupling constant constraints for the fitting were obtained from the analyses of particular lipid components' NMR spectra. The coupling trees above the spectra illustrate the multiplet structure constraints used for the fitting.

Results

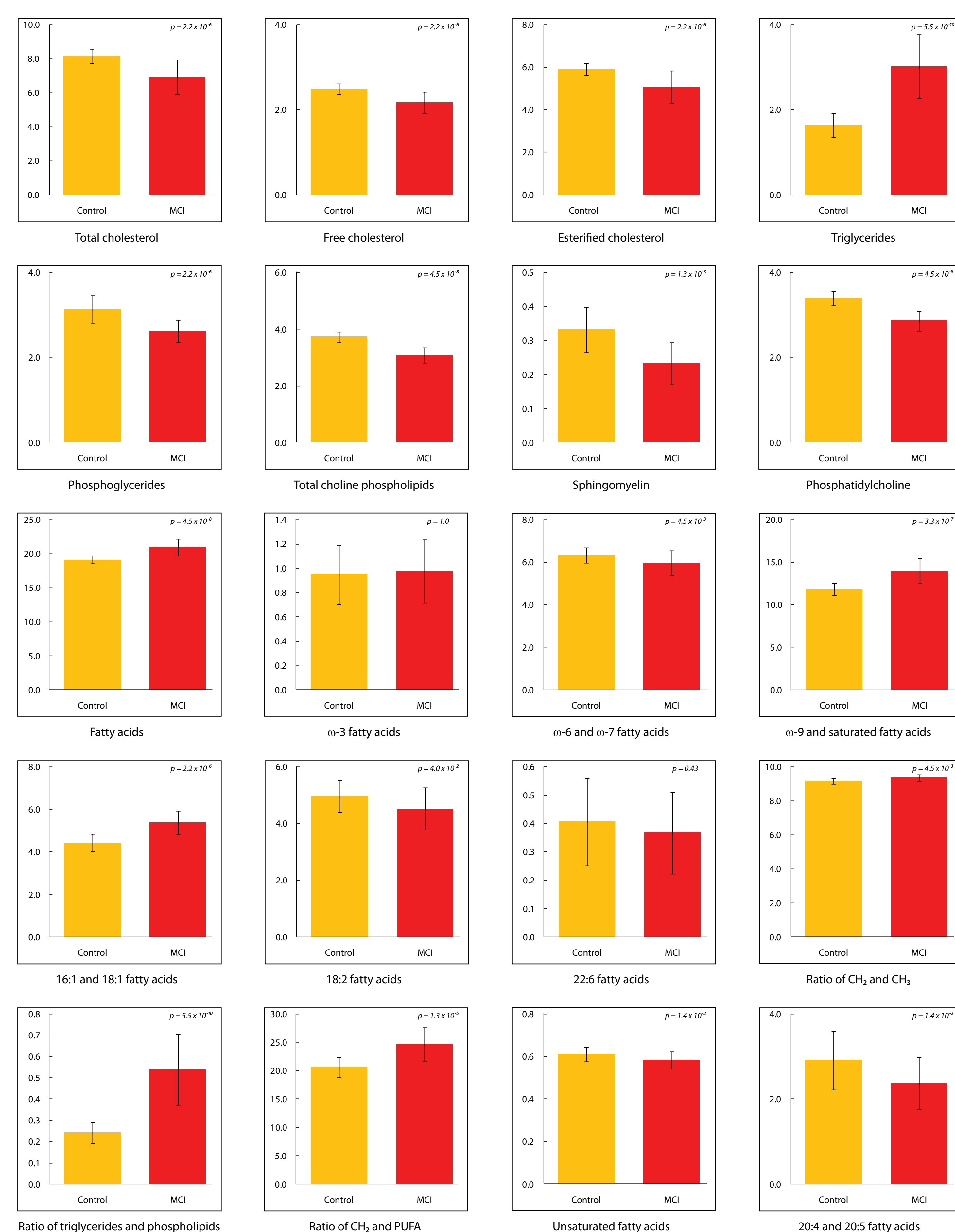


Figure 3. Averages, standard deviations and p -values of selected lipid descriptors defined from extracted serum samples of 20 controls and 20 MCI patients. The p -values were determined using Kolmogorov-Smirnov method.

Conclusions

In this poster, a protocol for lipid extraction and quantification based on ^1H NMR spectroscopy and constrained total-line-shape fitting was presented. The presented methodology was applied for over 500 serum samples from two different clinical studies related to mild cognitive impairment (MCI) and type 1 diabetes. The identified lipid descriptors available are likely to provide important extra information for metabonomics studies and disease risk assessment. Altogether, 26 physiologically relevant lipid descriptors could be determined, and it was shown (Figure 3) that the levels of several lipid descriptors are different among MCI patients and controls. The results from the ongoing clinical metabonomics applications will be reported elsewhere.

[1] Mäkinen, VP; Soininen, P; Forsblom, C; Parkkonen, M; Ingman, P; Kaski, K; Groop, PH; Ala-Korpela, M. Mol. Syst. Biol. 2008, 4, 167.

[2] Soininen, P; Haara, J; Vepsäläinen, J; Niemitz, M; Laatikainen, R. Anal. Chim. Acta. 2005, 542, 178.