



METABOLOMICS

Advances in Quantitative NMR-based Metabolomics

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Innovation with Integrity



Analytical Performance and New Technologies

Metabolomics plays a crucial role in understanding health, disease and personalized medicine. In this contribution, we delve into two key aspects: a detailed assessment of the analytical performance in NMR metabolomics of human serum and the exciting prospects offered by the Fourier 80 benchtop NMR system.

Methods

Pooled human serum and plasma for reproducibility studies were obtained from commercial providers. Single donor samples for modelling on the Fourier 80 were collected in the US, Spain and Australia under IRB approval. Human serum and plasma specimen were mixed in equal parts with 75 mM sodium phosphate buffer in H₂O/D₂O (80/20) containing TSP (trimethylsilyl propionate) as internal reference and NaN₃ to prevent bacterial growth. NMR data were acquired using the Bruker IVDr platform at 600 MHz and the Bruker Fourier 80 benchtop system.

In both cases, a 1D-NOESY pulse sequence was employed for efficient water suppression. All experiments were run in full automation. Quantitative calibration was achieved by using an external reference in combination with the PULCON principle. Data for deriving benchtop NMR PLS models were recorded in cooperation with CiC Biogune (Bilbao, Spain) and the Australian National Phenome Center (Murdoch, Australia).

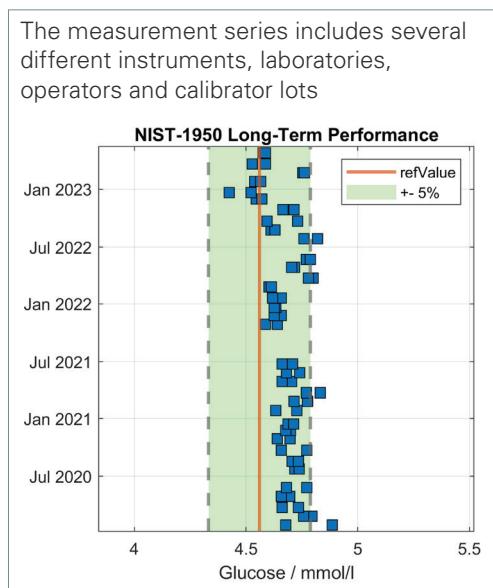


Figure 2: Long-term reproducibility of the IVDr platform using the NIST-1950 material

High-field NMR Performance (Avice IVDr platform 600MHz)

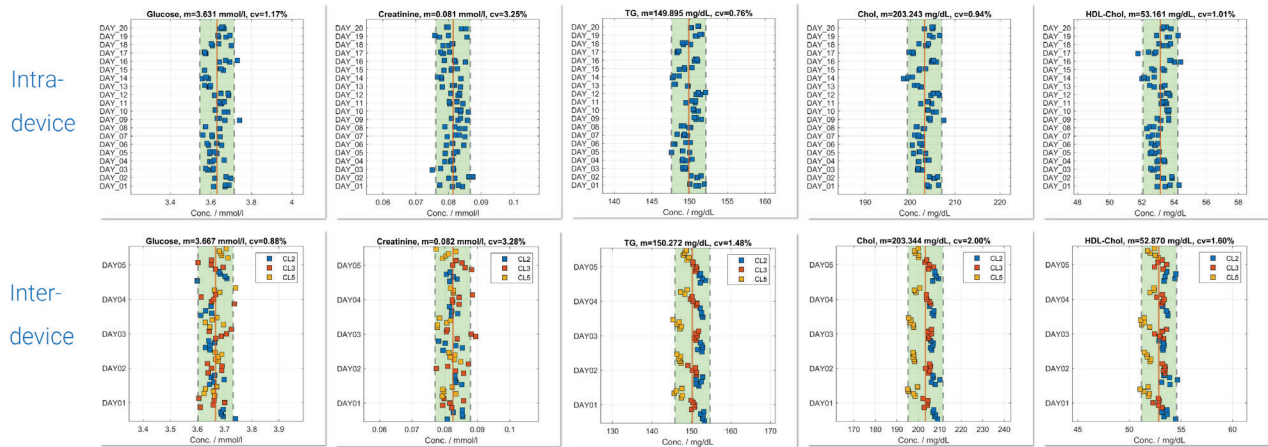


Figure 1: Intra- and inter-device precision on a standardized NMR platform (Avice IVDr platform). Each data point represents an individual aliquot of pooled human serum. Color-coding of data points indicates different instruments.

Benchtop NMR Performance (80 MHz)

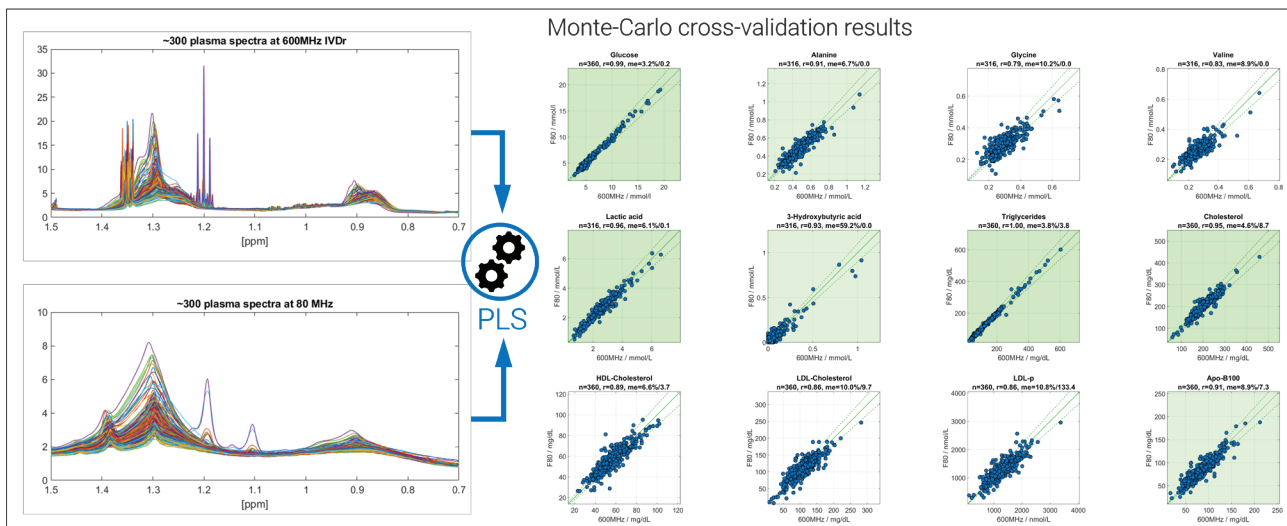


Figure 3: NMR quantification in human serum on the Fourier 80 via partial least squares (PLS) regression. Green background color indicates a correlation coefficient of > 0.9. Total experiment time was 4 mins on the Avice IVDr platform and 15 mins on the F80 platform



Sample	Parameter	Value	Reference
NIST-1950	Glucose	4.54 mM	4.56 mM
NIST-1950	Alanine	0.33 mM	0.30 mM
NIST-1950	Glycine	0.28 mM	0.25 mM
NIST-1950	Valine	0.19 mM	0.18 mM
NIST-1951_vl 2	Valine	137 mg/dl	145 mg/dl
NIST-1951_vl 2	Cholesterol	241 mg/dl	245 mg/dl

Tab. 1: Fourier 80 performance on NIST reference samples

Spectral overlay of replicate measurements of pooled human serum pool (N=10)

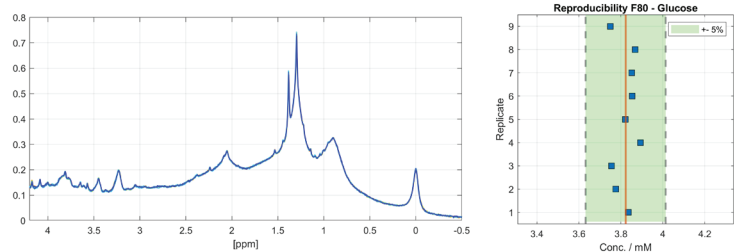


Figure 4: Reproducibility on the Fourier 80

Results

Reproducibility Assessment: An extensive evaluation of reproducibility within and across devices was conducted using the Bruker IVDr NMR platform, encompassing 160 analytes—41 metabolites, 114 lipoprotein parameters, and 5 inflammation markers.

An inter-device imprecision of less than 5% was observed for 101 analytes, a cv value of less than 10% was observed for 131 analytes.

The IVDr platform’s long-term reliability was affirmed through consistent measurements of the NIST 1950 reference material over several years.

Fourier 80 Benchtop NMR System: The F80 was demonstrated to be an effective tool for quantifying metabolites and lipoproteins in human biological fluids. A PLS model, trained with data from three laboratories and approximately 300 samples, showed high correlation coefficients, with 46 parameters exceeding 0.9 and 82 parameters above 0.8, underscoring the instrument’s reproducibility and precision

- Standardized protocols ensure highly reproducible results between instruments and laboratories
- Methods are transferable from high-field to benchtop NMR platforms, which have lower sensitivity but are smaller, more affordable and require less maintenance

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