

Development of Ultra-High-Throughput NMR Spectroscopic Analysis Utilising Capillary Flow NMR Technology.

Nigel J. C. Bailey¹, Ian R. Marshall¹ and Darryl A. LeBlanc²

1. SCYNEXIS Europe Ltd, Fyfield Business and Research Park, Fyfield Road, Ongar, Essex, CM5 0GS, UK.
2. SCYNEXIS Inc., PO Box 12878, Research Triangle Park, NC 27709, USA.

An ultra-high-throughput method for acquiring NMR spectra is described. By constructing a continuous flow system utilizing an HPLC pump, auto-sampler and a capillary flow NMR probe, it was possible to inject samples into the NMR spectrometer every 30 s using a continuous flow rate of 30 $\mu\text{l}/\text{min}$. ^1H NMR Spectroscopic data were acquired continuously into a pseudo-2D data file, with a **96-well plate completed in less than 50 minutes**. Individual 1D spectra were then extracted from the pseudo-2D file. Spectra (in continuous flow mode) were readily obtained from ca. 3.4 μg of sample, whilst the **LOD was <850 ng**. Reproducibility in terms of peak width, gaps between peaks and integral ratios was observed to be good.

This system offers several advantages over more conventional NMR spectroscopic analyses, notably the limited solvent requirement, high sensitivity, high speed and improved spectral quality as a result of reduced spectral 'dead' regions resulting from residual solvent levels.

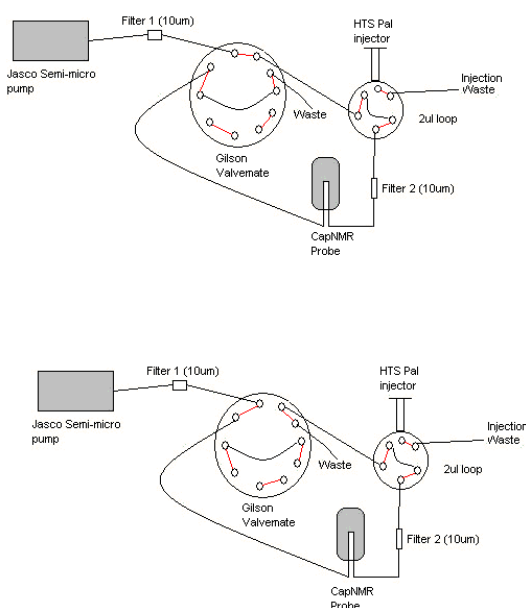


Figure 1: System layout for FI capillary NMR sample introduction. Valve positions indicate method for introducing sample into probe (top) and backflushing to clean the filter (bottom).

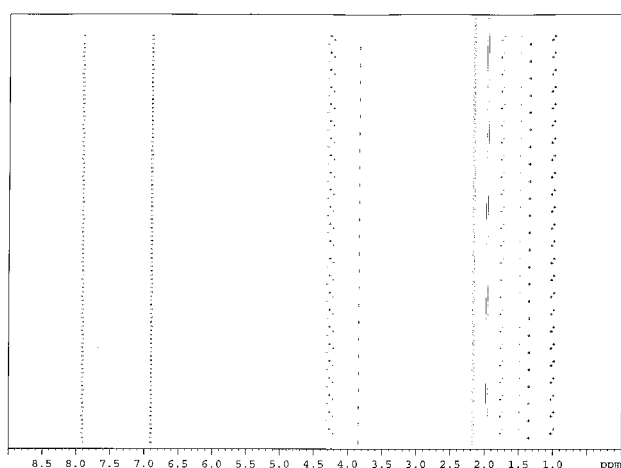


Figure 2: Pseudo 2D plot of continuous flow 500 MHz NMR data showing 96 injections in less than 50 minutes.

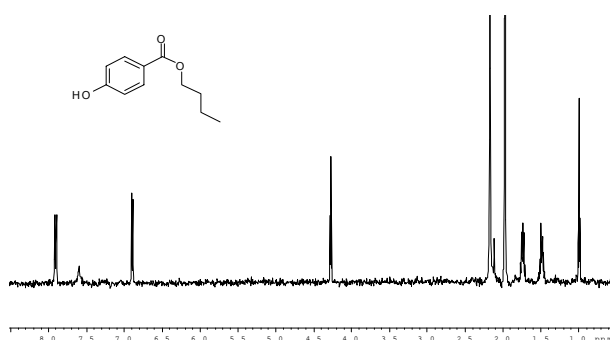


Figure 3. Extracted 1D Spectrum of *p*-hydroxy benzoic acid butyl ester

