Mestrelab Research
chemistry software solutions

Case study

Automated qNMR data processing and analysis in the behind-the-scenes of fragment-based drug discovery

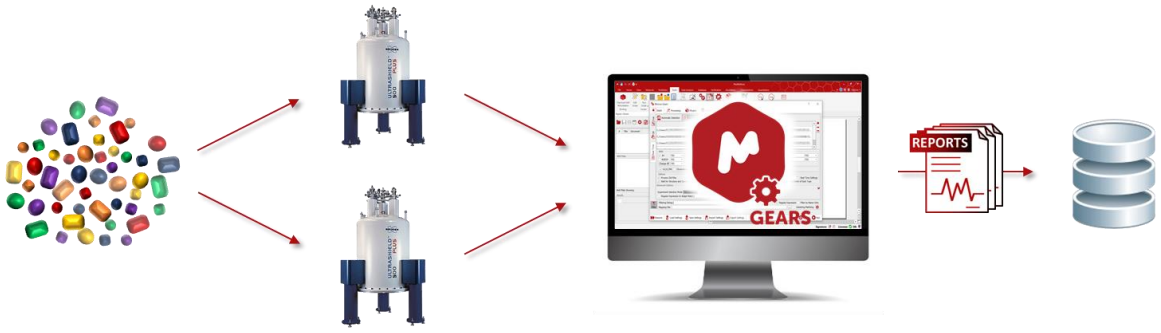
Bringing new drugs into the market is a complex and long process that often requires several years of investigation and considerable human, technological, and economic resources. In the labs of the Cancer Research UK Cancer Therapeutics Unit at The Institute of Cancer Research, London, a Fragment-Based Drug Discovery (FBDD) program has been established for screening and identifying lead compounds with potential therapeutic effects that may serve as starting points for the development of potent drug candidates.

In their primary screening, researchers in the structural chemistry team rely on Nuclear Magnetic Resonance (NMR) spectroscopy to determine the aqueous solubility and curate a 2860-compound library that feeds multiple research projects. Fragment solubility is one of the most challenging factors in the drug discovery and formulation process as it impacts delivery and bioavailability; so, by performing this first screening, weakly soluble fragments (solubility <500uM) are identified and excluded from the following steps. This process involves spectral acquisition on two 500 MHz spectrometers, processing of thousands of datasets, then manual collection and transfer of data for analysis in spreadsheets – an overwhelming and time-consuming task for scientists that marks only the beginning of a longer discovery process.

From manual process to automation

Carrying on with such a colossal project was impossible without automating parts of the workflow: so much data was generated and needed analysis and interpretation. So, in 2018, the **Mnova automation** solution (also known as "Mnova Gears" or simply "Mgears") was adopted by the team to streamline the primary screening steps and improve the workflow efficiency. Mgears is a simple module that can automate complex post-acquisition tasks and alleviate the burden of manual analysis by busy scientists.

For their solubility measurements, an automated qNMR process runs with Mgears and applies a set of parameters and formulas to calculate the fragment concentrations. These analysis settings are defined by expert NMR spectroscopists and implemented as Standard Operating Procedures (SOPs) that can be imported and re-used whenever needed. With this new setup, data proceeding from both spectrometers is captured and processed in batches on a centralized computer, then, compound concentration is calculated within seconds and global reports are automatically generated and saved to an internal ICR database.



Fragment library (2860 fragments) | Spectra acquisition (2x 500 MHz spectrometers) | Automated processing, analysis and reporting | Raw data, results, and reports databasing

Primary screening for aqueous solubility

A time- and resource-efficient screening

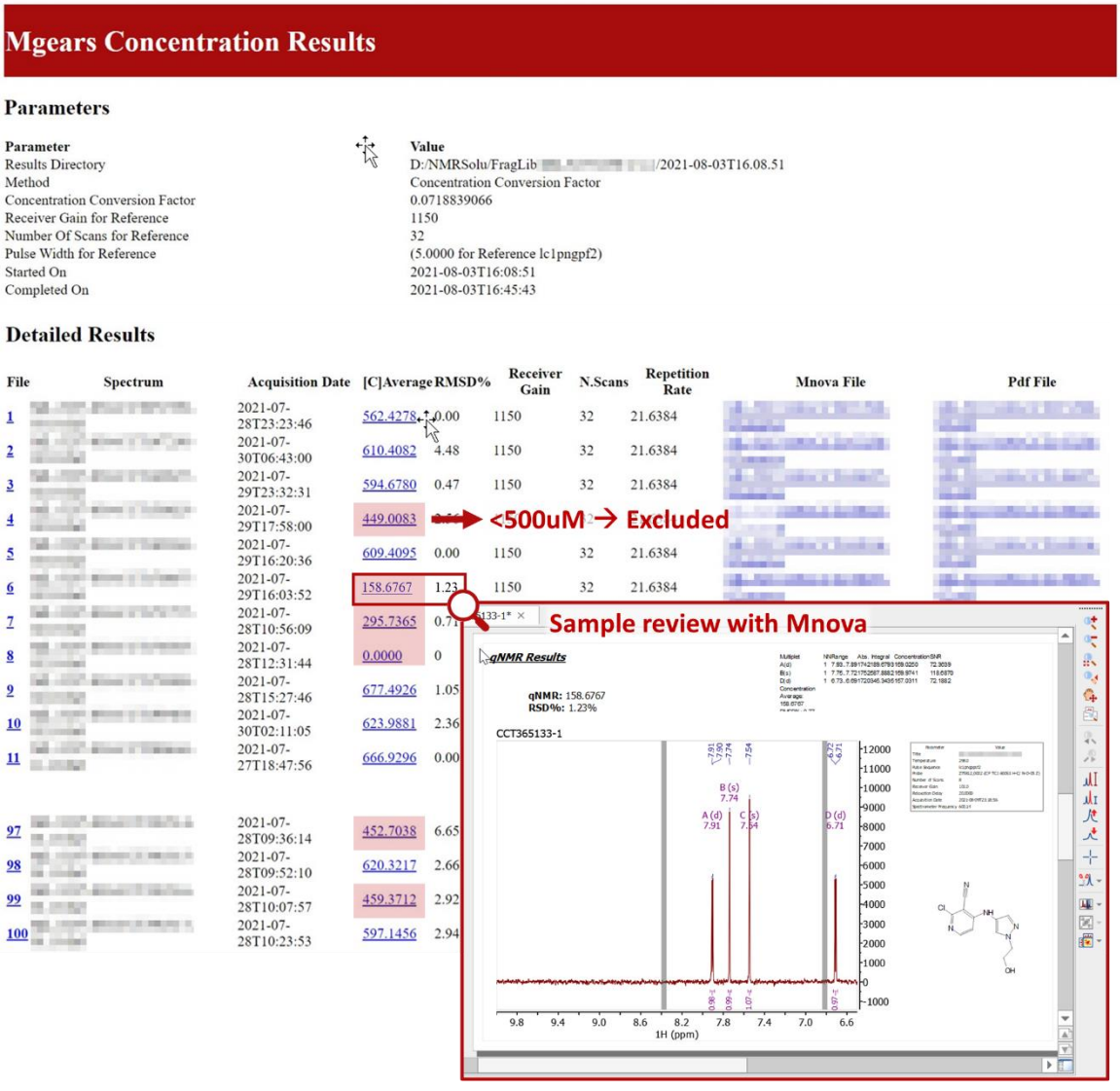
Automating the analysis with Mnova Gears has been a game changer for the team; it has allowed them to upscale the **high-quality processing and analysis capabilities** of Mnova qNMR to increase lab productivity and process robustness.

While 80% of the high-throughput analysis is now done by the automation engine, only minimal user intervention is required for the reviewing of final results. This has reduced by nearly six times the overall time spent on each spectrum which has allowed scientists to focus on more innovative and challenging tasks that are more suited to being performed by a highly trained specialist.

In addition, the output of the automated process is not only more accurate than when it was done manually, but also nicer and more homogeneous, which saved huge time on preparing manual reports, and significantly improved data management practices.

Decision making: quicker and more confident

One of the best things with Mnova Gears, is that the results are saved into a HTML report that can be quickly checked and exported to other report formats. Compounds that are not soluble at 500uM are rapidly spotted and excluded from downstream studies, while inconsistent and problematic results are loaded into Mnova for a closer inspection, explained Maggie Liu, expert NMR Spectroscopist in the structural chemistry team at The Institute of Cancer Research (ICR). The Mgears product comes with a nice and handy result viewer that enables sample revision, edition, and reprocessing when needed. So, it becomes very easy to investigate the reason behind a wrong calculation, to correct the spectrum and to update the result.



Html report showing an overview of the results and including hyperlinks that allow review of individual samples with Mnova

qNMR services within reach of non-experts!

Opening the access to qNMR services to medicinal chemistry teams has definitely been a big and successful change for the institute.

> **Back in 2017, only one project is using qNMR for solubility; since we implemented Mnova automated qNMR in 2018, all our projects are now using the method**
> Maggie Liu, expert NMR Spectroscopist in the structural chemistry team, ICR

NMR experts can configure and save qNMR methods that can be easily imported and re-used at any time, which has enabled them to put SOPs right into the hands of less-experienced NMR users. Thirteen projects have since used these SOPs to measure aqueous solubility of designed drug compounds to check the effectiveness of structure optimization and refine the list of drug candidates. Chemists from different teams run batches of 20-40 compounds once a month and get reliable results that meet research quality standards with a simple button click. This presents a considerable advantage for both experts, who freed more time for other tasks, and non-experts who can now access the service without the need for advanced NMR knowledge, a significant win-win solution.

Committed to improve cancer research and drug development

The ICR has a successful history in drug discovery with twenty clinical candidates discovered since 2005, eleven of which have entered clinical trials, and one has been already approved by FDA for treatment of advanced prostate cancer. Adopting robust software and automated solutions has been a significant measure to leverage innovation at the ICR, giving researchers more time to brainstorm and interact with each other, bringing together multi-disciplinary knowledge, skills, and resources.

At Mestrelab Research we are happy to accompany researchers, scientists, and manufacturers on this exciting drug discovery and development process and offer customizable software solutions for accelerating the transfer of new drugs from bench to bedside. For more information about our solutions, please check our website www.mestrelab.com or contact us on: info@mestrelab.com.

Disclaimer:

The views expressed by Maggie Liu are her own and do not constitute an endorsement from the ICR.

Acknowledgments:

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References:

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