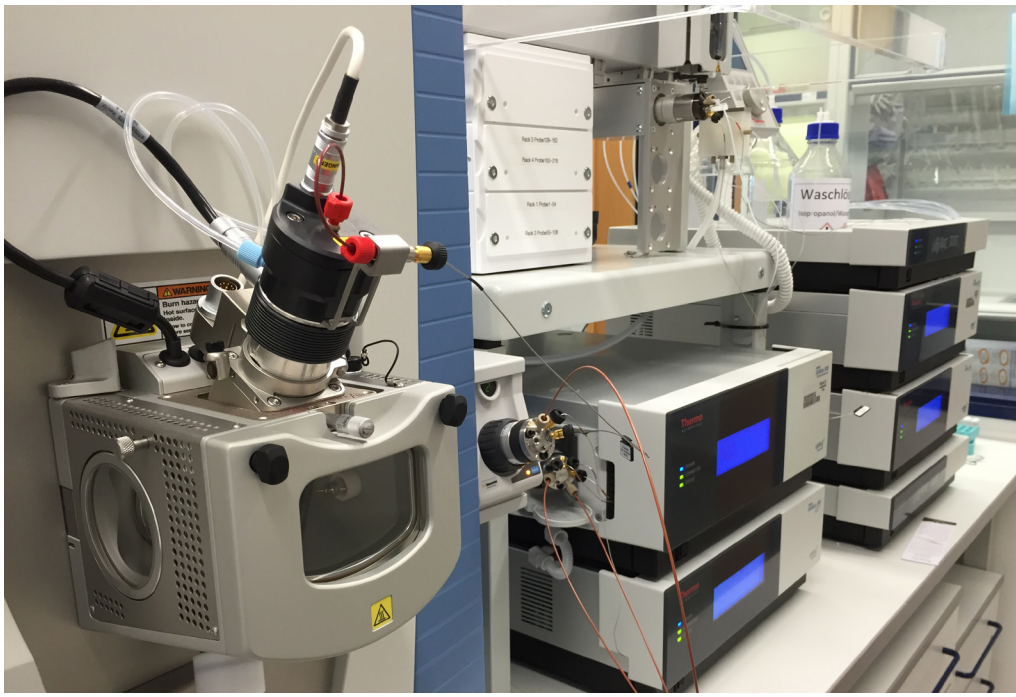
Bayer Pharma AG implements a fully automated interpretation workflow for finding target masses

Introduction

Bayer HealthCare Pharmaceuticals is the pharmaceutical division of Bayer HealthCare AG. The division aims to improve people's quality of life with its products, which are sold in more than 100 countries. To this end, it concentrates on the research and development of innovative drugs and novel therapeutic approaches. At the same time, Bayer HealthCare Pharmaceuticals is constantly improving established products. The division uses the experience it has gained from over a century in the business, concentrating on several major therapeutic groups in which it makes fundamental contributions to medical progress.



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Rene Spang
Head of Laboratory Mass Spectrometry Service
Bayer Pharma AG, Wuppertal, Germany

Rene Spang, Head of Laboratory Mass Spectrometry Service, Bayer Pharma AG in Wuppertal, Germany, has nearly 32 years of experience in the fields of analytical chemistry, chemical synthesis, and optimizing automatic service workflows.

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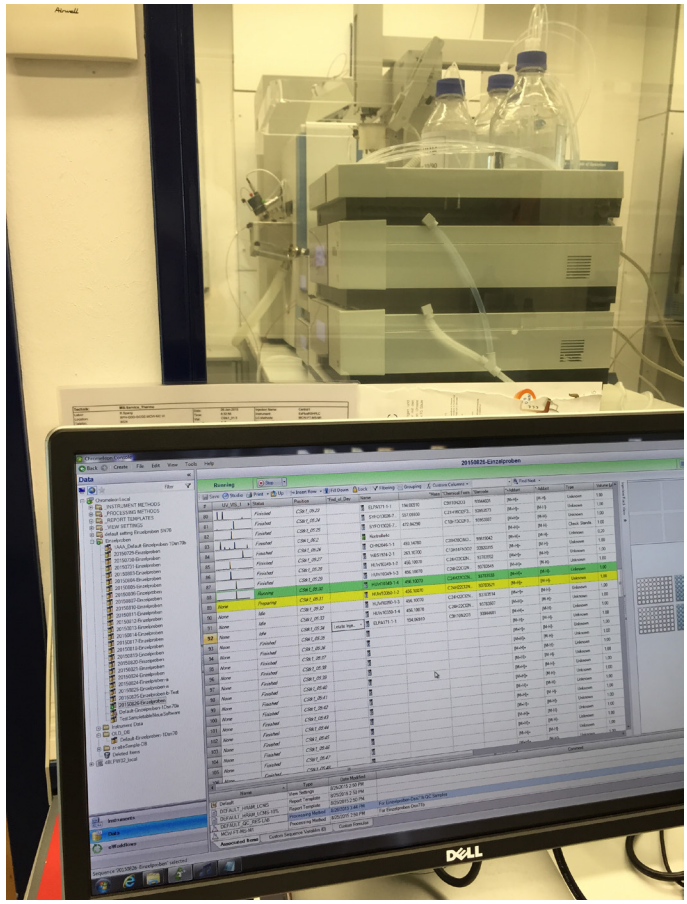

Rene Spang runs a highly automated high-throughput laboratory providing support for the Medicinal Chemistry laboratories with high quality LC-MS and GC-MS information generated using the latest GC, LC, and MS instrument techniques. His laboratory processes more than 1000 samples per day with a fast turnaround.

Background

The Mass Spectrometry Service laboratory originally analyzed samples using a liquid chromatography system with UV and single quadrupole mass spectrometry (LC-UV/MS). However, this system had several drawbacks, particularly around automation of the workflow. It was very restricted in the automatic reporting workflow and used a very labor-intensive process requiring many manual steps to process and report the data. The need for human input meant that analyses could not be performed or evaluated during lunchtimes, evenings, or weekends, significantly limiting laboratory throughput.

With the growing number of samples requiring analysis, Rene was challenged to improve the existing LC-UV/MS system by increasing the quality, reliability, and throughput of results, while simultaneously reducing the entire process turnaround time. Meeting this challenge required new LC-UV/MS instrumentation and software to dramatically improve information quality and workflow automation.

He chose a solution from Thermo Fisher Scientific that included two identical LC-UV/MS systems comprising the Thermo Scientific™ Dionex™ UltiMate™ 3000 RSLC system and the Thermo Scientific™ Exactive™ Plus Orbitrap Mass Spectrometer along with the Thermo Scientific™ Chromeleon™ Chromatography Data System (CDS) software. We spoke to Rene to find out more about his decision process and his experience thus far.

Q: *How did you become interested in the Chromeleon CDS software and the LC-UV/MS solution?*

A: I needed to develop a fully automated interpretation workflow for finding target masses in chemical reactions. I wanted a very robust chromatography [and MS] system with a short runtime and all information within that one run. Previously, we had installed an ion chromatography system with Chromeleon and I found that it gave me a lot of opportunities to develop a customized workflow for my processes. My first contact for this project was at the ASMS [American Society for Mass Spectrometry] conference in the Thermo Scientific booth, where I was able to see the latest LC-MS solutions in combination with Chromeleon. I was impressed with its capabilities.

Q: *Why did you select the Thermo Fisher Scientific solution?*

A: For the software, the main selling point was the reporting tools in Chromeleon. What is important to me is what is important to my customers. They want to see the results of their reactions quickly, in one view. With this system, I can easily create a report that lets them do that. Another big factor in our purchase was the control of both the LC and MS from the same software and the ability to combine the UV and MS data in one report, so I would not have to switch between different software packages for chromatography and mass spectrometry information.

For the hardware, the most important feature was that the mass spectrometer allows the creation of information from both ionization modes in one run. This is possible only with the new Exactive MS, which is important for me as this reduces the analysis time because I have information from both the positive and negative modes in one run. This is not possible with other MS systems such as TOF [time of flight], which needs two separate runs to get the same information. It was also important that I had an accurate mass MS to improve the accuracy of target mass identification.

Q: *What is your experience with the new system?*

A: We have used the system for five months now and it works very well. We run about 140 analyses on each system each day and so far they have worked well. In total, we have analyzed over 9,000 samples so far and in 90% of cases where the target mass was in the reaction, we have found it automatically.

The setup and installation of the systems was very good, we had very good support, and we were able to very quickly learn the software capabilities so, together with the Thermo Fisher Scientific technicians, we could create the application workflow, including the Chromeleon reports. My laboratory technicians were able to quickly gain an understanding of the programming steps in Chromeleon and have found it very easy to use in daily operations. Overall, the performance is good. We have also found that the MS calibration is very stable over a period of weeks.

Q: *How do you use the reporting tools?*

A: The reporting tools in Chromeleon are very good. We have worked with Thermo Fisher Scientific technicians to produce a report that combines the UV and MS data and presents everything my customer needs to see. Chromeleon checks both the positive and negative MS traces for the target mass and will label the peak if a match is found. For each peak where the mass is found, Chromeleon creates a display of the positive and negative MS traces together with the UV spectrum for that peak. For each injection, Chromeleon produces a single-page summary of the hits found and another page for an aligned overlay of the positive and negative MS traces and the UV chromatogram. So now my customers get all the information they need on their sample in just one three-page report.

Chromeleon automatic ally exports these pages to a single PDF report after each analysis. That file is automatically placed into a specific folder based on the detection, or not, of the target mass and the injection type. In this way, injections with hits are separated from those without hits and the QC samples and blanks, making things easier for my technicians.

Q: *Which other features of the software do you use?*

A: Apart from extensive use of the reporting tools, we use SST [System Suitability Tests] and IRC [Intelligent Run Control] to monitor the quality of our QC injections. We check several different aspects of these injections, from UV retention time stability and peak asymmetry [or fronting/tailing factor] to MS mass accuracy. We also use IRC to create an optimum integration path chromatogram from the UV 3D field giving us the maximum response for each peak in the chromatogram.

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We have developed an eWorkflow to allow us to quickly create the daily sequence with the correct methods and injection list. We use the sequence start delay function to enable the system to automatically start up each morning at 6:30 am and run a series of injections to ensure everything is running OK before the technicians arrive. We also use advanced programming to automatically shut the system down at the end of the day, or if there is a problem with the system or a QC standard.

Finally, we use custom variables to allow fast and easy entry of sample metadata using a barcode reader and for selection of different adducts for post-run analysis.

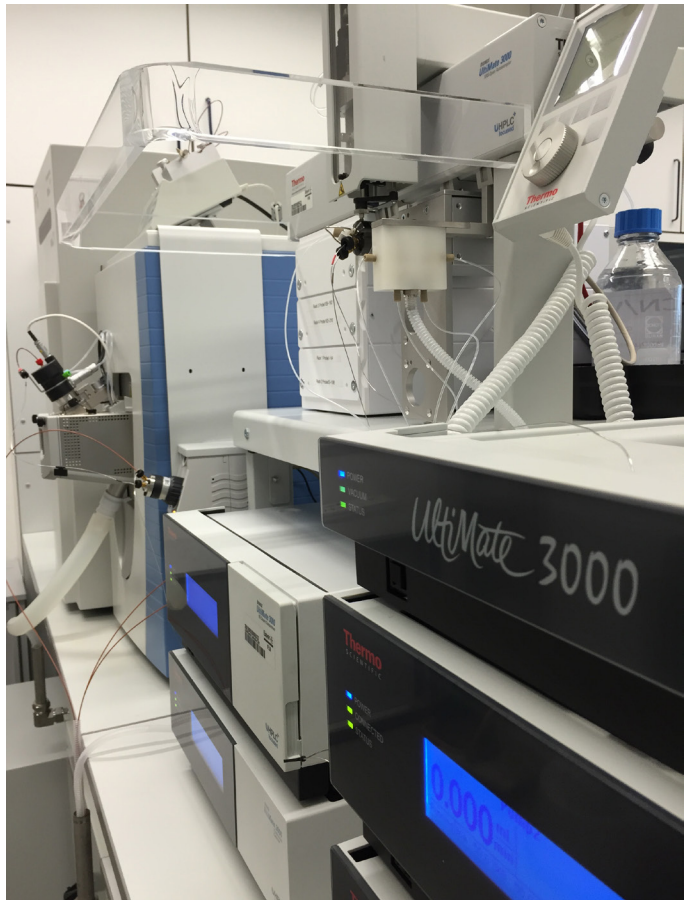
Q: *How well has the new system met the project requirements?*

A: I am very happy with the system and we have created a workflow that is very robust and safe. We now have a fast UHPLC separation that takes just three minutes and we use injection overlap to eliminate any wasted time washing and preparing the autosampler. The MS system is able to switch at a high enough frequency to collect sufficient data [4 Hz with two positive and two negative scans per second] in this run time. The UV and MS data is then automatically analyzed and reported by the Chromeleon software, leaving the analysts to quickly check results. These time savings reduce the total turnaround time for each sample to about 15 minutes from entry to the lab to final result being sent out.

Also, with the fully automated workflow provided by Chromeleon, we are now able to run analyses over lunch, evenings, and weekends, so we can analyze more samples with the same number of technicians.

Q: *Is there anything you particularly like or dislike?*

A: I like the fact that, with the flexibility and capabilities of Chromeleon, we now have the potential to develop new applications in the future. There is nothing that I dislike. Overall, I would have to say that Chromeleon is excellent!



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Find out more at **thermofisher.com/chromeleon**

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