Bayer Crop Science Boosts Agricultural Innovation with Cutting-Edge Waters Cyclic Ion Mobility Instrument

The Crop Science Division of Bayer AG addresses the challenges facing the global food system through innovative agricultural research and development using the Waters SELECT SERIES Cyclic IMS instrument

Technology: Waters™ SELECT SERIES™ Cyclic IMS™, UNIFI™ Scientific Information System

CROP SCIENCE AT BAYER AG

An international enterprise with core competencies in the life science fields of healthcare and nutrition, Bayer AG designs products and services to help people and the planet thrive by supporting efforts to master the major challenges presented by a growing and aging global population. In fiscal year 2020, Bayer employed around 100,000 people, had sales of €41.4 billion, and spent €4.9 billion on R&D.

For more than a century, the company has worked to solve some of the toughest problems in farming. Bayer invests heavily to shape agriculture through breakthrough innovation for the benefit of farmers, consumers, and the planet. With 40,000 dedicated employees in its Crop Science Division, the company's agricultural research capabilities include biology, biotechnology, chemistry, and data science. By harnessing new developments in these areas, Bayer Crop Science Division focuses on:

- Growing more crops per acre
- Reducing the environmental impact of farming
- Enabling smarter decision making to make farming more efficient.

Nine employees in the Mass Spectrometry and PC Data Screening Laboratory for the Bayer Crop Science Division at Monheim am Rhein, Germany, use advanced analytical chemistry tools to break new ground in agricultural research.



The Waters Wilmslow team invited Dr. Glaubitz (left) and his colleagues to the demo lab in 2019 to see the SELECT SERIES Cyclic IMS system.

WORKING WITH WATERS

In 2019, Dr. Johannes Glaubitz, Lab Leader, and his colleagues from Bayer Crop Science were invited to visit the Waters demo lab in Wilmslow, UK, to see the SELECT SERIES Cyclic IMS instrument and allow them to explore the feasibility of the instrument for their unmet needs.

Dr. Glaubitz recognized the potential of the instrument to help Bayer researchers develop safe and effective crop treatments. The laboratory already had a Waters SYNAPT™ mass spectrometer and MassLynx™ software, as well as a long-standing relationship with the Waters support team.

Dr. Glaubitz describes the team's focus:

"Our mass spectrometry (MS) laboratory research focuses on structure elucidation using MS, as well as liquid chromatography coupled with MS (LC-MS) for early research and early biology trials. Our work looks at how compounds are distributed within the plant or target, and which metabolites are forming there. We do a lot of fast screening measurements to get an overview on the behavior of a compound, and then we do a deep dive analysis when we want to look more closely at specific ones. Our overarching goal is to develop new agrochemicals to improve farming practices."

To conduct this research, the team continuously looks for new analytical technology and tools capable of helping Bayer scientists drive innovation and help farmers. That led to the company's investment in the Waters SELECT SERIES Cyclic IMS instrument in 2020.

INNOVATIONS IN CROP SCIENCE

In the face of an ever-changing climate, a growing population and limited resources, Bayer is looking closely at how to grow more healthy, safe, and affordable food in a sustainable way.

The Crop Science Division of the company works towards developing agricultural innovations that shape what's possible for farmers, consumers, and the planet. To do this, Bayer invests more in research and development than any other company in the industry. Bayer employees are encouraged to think creatively about agricultural innovation. They rely on science and data, but they also use their own ingenuity to drive new ideas forward.

The team at the Mass Spectrometry and PC Data Screening Laboratory works with advanced analytical technologies to research and develop small molecules. Dr. Glaubitz describes how the laboratory uses its research capabilities in biotechnology, crop protection, and data science to deliver tailored solutions to farmers faster:

"We look closely at evolving technologies to see how they could benefit our research. Our team always focuses on the future of instrumentation, and the solutions we choose need to be capable of a broad range of analysis. We cannot rely on a specific technique. You never know what comes next, especially in early research for crop protection and pharma products. We need to be agile."

The Crop Science Division researchers saw an opportunity when they learned about new instrumentation from Waters that offered higher ion mobility resolution (the ability to separate ions based on their gas phase conformation) and novel IMS^n capability. Mr. Jürgen Lukas, Senior Lab Scientist at Bayer Crop Science, felt that the improved ion mobility performance coupled with MS provided an interesting approach to push the boundaries of MS in the laboratory's work in crop science, as well as to solve some challenges.

WORKING WITH WATERS

Dr. Glaubitz describes the Bayer team's thought process before purchasing the instrument in 2020:

"We have a strong, reciprocal relationship with Waters and work very closely with the support team in Germany. When we buy a new system, it's a three-fold decision. We buy the instrument, we buy the service, and we buy the software. Our previous experience played a large part, because we have had good service from Waters, and we knew they build very robust instruments. We also needed an instrument with high resolution that was superior to what we had previously, while also providing good sensitivity. We looked at other vendors, but we chose the SELECT SERIES Cyclic IMS because it had the superior ion mobility (IM) capabilities, mass resolution, and high sensitivity we needed."



Dr. Glaubitz and his team use the SELECT SERIES Cyclic IMS to achieve higher performance for their routine MS analysis.

"We were having trouble identifying very low levels of metabolites, and we tried to compensate by raising the concentration in the samples. Of course, that approach has downsides regarding the biological activity and biological linearity, because not every sample is linear. We've also had samples overstress the system, which didn't respond in a realistic way. That's not what we want in our research. The need for higher resolution to work with the complexity of our samples was another driver for our interest in the SELECT SERIES Cyclic IMS. Sometimes we couldn't get the results we needed on certain compounds. Additionally, our laboratory has so much throughput that we wanted to lower the concentration in our samples because the lower you get, the less maintenance the instrument needs afterwards."

The lab's SYNAPT instrument was due for replacement and Dr. Glaubitz and his team needed to find a new instrument for the same routine, high throughput analysis. The laboratory team evaluated solutions from multiple vendors, including the Thermo Scientific Orbitrap mass analyzer, which doesn't offer IMS. However, having attended the 2019 demo day in Wilmslow, Dr. Glaubitz saw the potential of the SELECT SERIES Cyclic IMS technology before the instrument was even officially launched.

> " At the time, the instrument didn't even have a housing around it. But the technology was very cool, and we could see the value. That spawned discussions with Waters about its use for routine applications, which was something they hadn't fully considered at the time. We saw the potential, and we wanted to work with Waters as they developed the technology, so it could address the challenges we saw in our laboratory."
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> DR. JOHANNES GLAUBITZ
> *Lab Leader*

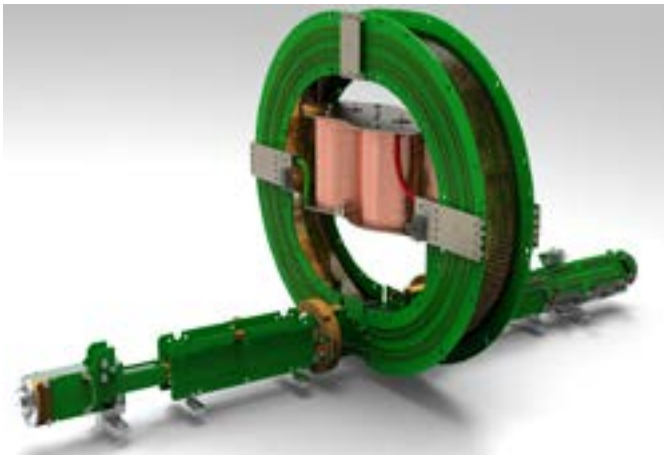
The two teams began to collaborate to determine how this evolving technology could achieve the high throughput needed. The Bayer Crop Science team worked closely with Waters to outline their needs, and eventually purchased and installed the SELECT SERIES Cyclic IMS in spring 2020.

WATERS SELECT SERIES CYCLIC IMS INSTRUMENTATION

IMS separates ions on the basis of their size, shape, charge and mass. It can be employed as a standalone technique, or it can be coupled to MS, supplying an extra dimension of resolution that provides information about the three-dimensional structure of an ion, as well as increasing peak capacity and confidence in compound characterization. IMS-MS also offers significant utility in the analysis of isomeric species, where different structures are reflected by differences in collision cross sections (CCS).

The newly developed cyclic ion mobility technology from Waters has a unique circular path, which enables the user to define the path length by simply performing multi-pass experiments. Ions of a given mobility range can be selected and passed around the device as many times as necessary, allowing the researcher to "zoom in" on analytes of interest.

As a result, the SELECT SERIES Cyclic IMS instrument provides advanced characterization whereby ions are selected by their ion mobility and subsequently reinjected with collision-induced dissociation to provide unique IMS^n data. This revolutionary instrumentation combines cyclic ion mobility capability with the latest time-of-flight (TOF) MS technology, providing mass resolution that ensures the visibility of more detail in a sample than ever before.



The cyclic ion mobility technology allows users to define path length by performing multi-pass experiments, which offers higher resolution than MS alone.

In addition to the novel Cyclic IMS technology, the instrument also includes many new technologies that enhance the sensitivity, mass resolution and dynamic range of the system, including:

1. The latest generation of StepWave™ ion transfer optics that increases transmission of small, labile compounds.
2. Post-mobility ion optics that maintain the fidelity of the ion mobility separation whilst simultaneously conditioning the ion beam for best time-of-flight (TOF) MS performance. Also provides collision induced dissociation capability, enabling post-ion mobility fragmentation experiments.
3. A new TOF design that enhances both the sensitivity and resolution.
4. A dual-gain detection system that increases the dynamic range provided by the system and enables ion mobility to be used for the most challenging analytical problems.[1]

The Mass Spectrometry and PC Data Screening Laboratory researchers were early adopters of the Waters SELECT SERIES Cyclic IMS, which already has provided significant benefits and fulfilled the requirements of continuing the high throughput usage experienced with the SYNAPT. While its use was delayed because of COVID-19 restrictions, the team quickly discovered the benefits of the technology once they could return to the laboratory in May 2020; processing over 20,000 samples in a three-month period.

The Bayer team uses Waters UNIFI Scientific Information System for processing, visualization and reporting of the SELECT SERIES Cyclic IMS data. UNIFI's data mining and comparison capabilities enhanced the researchers' ability to understand results, as well as aggregate and manage data.

Mr. Lukas explains the impact on the team's work:

"We've achieved a good balance in performance with the SELECT SERIES Cyclic IMS and UNIFI software. Our main work is high-throughput assays, so a quick cycle time is important because we must be as fast as possible. The system is very robust, and our downtime has clearly improved, so that makes our customers happy. Now we're running x10 diluted samples, which is great. And the ability to lower the amount of sample needed for the analysis offers other benefits because we can save a portion of a sample for future tests, if needed, which saves our customers a lot of time and effort. And the time and cost of maintenance for the SELECT SERIES Cyclic IMS looks good too."

A UNIQUE COLLABORATION

When the Bayer team began looking closely at the SELECT SERIES Cyclic IMS, their plans were outside of the scope of the Waters team's focus during the development process for the technology. Because the instrument was so new, that presented an opportunity for Waters to see how the system performed in situations they hadn't tested – giving them valuable input on the instrument's performance.

> " We're using the Waters SELECT SERIES Cyclic IMS in routine high throughput applications, and we're making the instrument a workhorse in the lab. It's good to see how well it's working now, because the initial focus was more on research applications. Just one year later, we have the Cyclic IMS doing everything we need it for, and we're continuing to work with Waters on other things, like data management and providing feedback, to ensure continued evolution of the software."
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> MR. JÜRGEN LUKAS
> *Senior Lab Scientist*

This collaboration also helped Waters personnel see the greater potential of the SELECT SERIES Cyclic IMS instrument, and it led to a lot of interaction between the Bayer lab team and the Waters development team that took the technology in new directions. There was a learning curve to ensure the SELECT SERIES Cyclic IMS could be tailored to suit Bayer's needs, however this process has helped both companies push the capabilities of the technology in new ways.

" A small group of people from both companies met regularly to go through the different topics and work towards improvements. We don't normally test new instruments like this, so it was fun to have the latest technology and see how it could help us. There was a lot of back and forth. Waters learned about what we wanted and how we wanted the instrument to work. We got a deeper understanding of the development process. We wanted to get the best use out of the technology for our research, and Waters benefited from understanding how their customers could use the instrument in other ways than they initially projected."

MR. JÜRGEN LUKAS
Senior Lab Scientist

NEXT STEPS

Dr. Glaubitz believes the SELECT SERIES Cyclic IMS instrument's capabilities have the potential to significantly advance the possibilities for his team's research and in agricultural innovation. Having seen the reliability and the improvements in sensitivity and mass resolution that the instrument offers as a routine analysis tool for metabolite identification, the Mass Spectrometry and PC Data Screening Laboratory researchers are continuing the process of integrating the SELECT SERIES Cyclic IMS into the laboratory's workflows and making tweaks with Waters on the instrument control software.

In addition to the cutting-edge technology, the Bayer team credits continuous support from Waters as a key factor in navigating these new possibilities.

" We need to enlarge our footprint regarding metabolite searches and identification, because that's a clear demand from our customers. That's not an easy task. But the support from Waters on the technical side will help us get there. At the same time, they'll learn from our perspective as we work towards these bigger goals."

DR. JOHANNES GLAUBITZ
Lab Leader

Additionally, the laboratory's team is diving further into the IM capabilities of the SELECT SERIES Cyclic IMS that make it ideal for use in cutting-edge crop science research. Dr. Glaubitz anticipates huge leaps in the team's research as they harness IMS technology for their work. He explains:

"Ion mobility will help us further by providing more efficient answers, while also maintaining the quality level that we need. We're looking for proof of concept that IM performs well for our daily workflows, and we're working to determine the gain in additional efficiency and insight into our samples. The technique is really promising."

References

1. Giles, K.; Ujma, J.; Wildgoose, J.; Pringle, S.; Richardson, K.; Langridge, D.; Green, M. A Cyclic Ion Mobility Mass Spectrometry System. *Analytical Chemistry*, **2019**, 91, 13, 8564–8573 https://doi.org/10.1021/acs.analchem.9b01838

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