

Miniaturizing separation science

The development and characterization of new chromatography media is both complex and time consuming. At Merck KGaA in Darmstadt, Germany, the implementation of automated miniature column chromatography protocols has helped to improve throughput and reduce the amount of material required, allowing more measurements to be performed in less time.

Protein purification is a crucial step in the production of biopharmaceuticals, and is frequently performed using chromatographic processes. To help biotech companies accelerate their product development, manufacturers are continually striving to develop new chromatography media, screening prototype resins with novel functionalities and improved performance to extend their product portfolio.

The Chromatography R&D and Manufacturing Science and Technology (MSAT) groups of Merck's life science business are both engaged in the development of specialist chromatographic media – such as Fractogel®, Eshmuno® and ProSep® – for the effective and efficient purification of biomolecules, as well as the creation of supporting resin performance application data. The groups actively support the company's worldwide customer base through a network of scientists and engineers, as well as 10 M Lab™ collaboration centers located across the globe. The M Lab collaboration centers in Europe, Asia, and the US are equipped with similar liquid handling platforms configured for miniature column chromatography, ensuring that customers receive the same level of support regardless of location, as well as simplifying method transfer between sites for flexible allocation of resources. Peter Menstell, Applications Engineer from the Chromatography R&D group, explained: "When a new resin is under development, a variety of experiments

must be performed to characterize the different candidates, including the determination of selectivity, and static and dynamic binding capacities. The dynamic binding capacity is determined under flow conditions, and was previously carried out using standard 1, 5 or 10 ml lab-scale columns. However, a large amount of feed material was required for each column, and evaluation of all the different candidates was very time consuming. We needed to reduce the feed amount and perform more measurements in less time, and this led us towards miniature column chromatography."

André Kiesewetter, an MSAT Applications Engineer, takes up the story: "We decided to upgrade our in-house robotic capabilities to include state-of-the-art automated miniature column chromatography using Atoll RoboColumns®, a proven, user-friendly technology that can be easily implemented on a liquid handling platform. We compared various workstations, eventually deciding that the close collaboration between Atoll and Tecan – and the popularity of the technology – made the combination of RoboColumns and the Freedom EVO® workstation the ideal solution for both resin and application development assays. We can also take advantage of the system's liquid handling capabilities to perform dilutions and other sample preparation steps in our workflows."

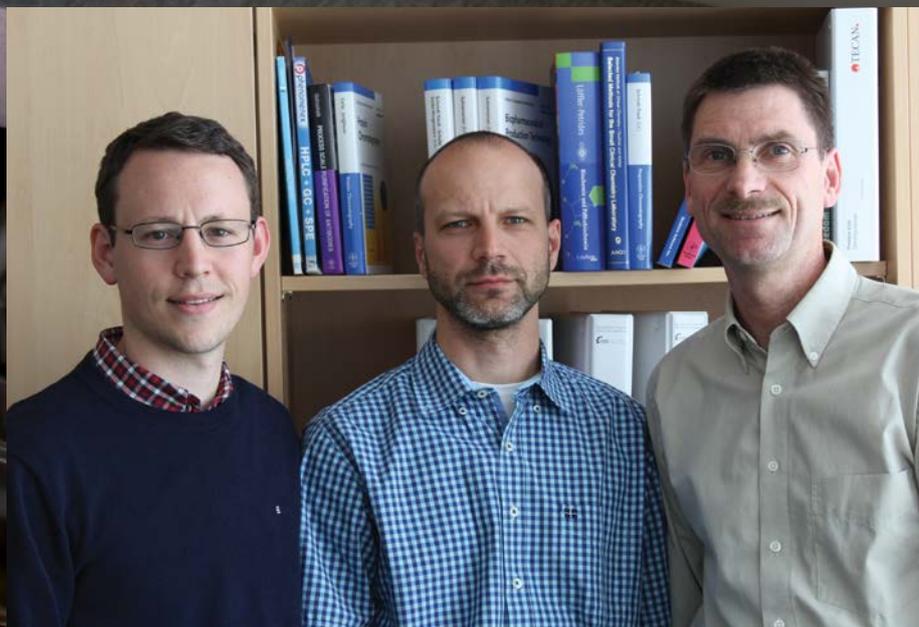
André continued: "We ran the first trials after just a few weeks of protocol

development, and within six months had successfully developed and validated our automated miniature column chromatography method. We can screen eight columns in parallel, completing dynamic binding capacity determinations and resin selectivity measurements in three to six hours, depending on the operating parameters, compared to over 24 hours for sequential testing on a conventional system. We use 5- to 10-fold less feed material, and the labor intensity is reduced, freeing up more time for us to perform other valuable tasks."

Senior Applications Engineer Andreas Stein added: "We received valuable support from Tecan during the implementation period, and also benefitted from the availability of an application note describing the optimum performance settings for automated miniature column chromatography. Programming the workstation is easy to learn, and the integration between Freedom EVOware® and other programs, such as visual basic scripts, is a huge advantage; a system with an open program is much more flexible."

"Automated high throughput experiments generate many samples for analysis, which could potentially create a bottleneck. Now that the miniature column chromatography application is running really well, our aim is to go a step further and automate the analytics, establishing a fully integrated workflow to alleviate any possible hold-ups," concluded Andreas.

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From left to right, Peter Menstell, André Kiesewetter and Andreas Stein

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