# Automated parallel chromatography in 96 array format

Purification of therapeutic products is a major cost factor in pharmaceutical manufacturing. Development of the purification process imposes a major bottleneck in drug production, because the various purification parameters need to be experimentally optimized for each protein-based pharmaceutical product before entering full-scale production.

Application of high throughput technologies to chromatographic purification can greatly benefit process development by enabling parallel screening of the various parameters and giving rapid and reliable results. A miniaturized format would reduce the consumption of valuable samples as well as reagents and chromatographic resins.

Automated parallel chromatography enables various protein purification applications, including:

- expression screening to select clones with best recombinant protein expression, or cell culture screening, for mAb selection;
- condition screening to determine optimum purification conditions;
- resin screening to test different resins in parallel;
- method development to optimize gradient elution, for transfer to large scale purification;
- sample conditioning/purification/concentration for downstream applications like protein crystallography or MS analysis;
- process analytics for bioreactor monitoring, to determine the optimal harvesting point.

The Freedom EVO® liquid handling workstation, together with Atoll's 96-array MediaScout® RoboColumn system, enables fully automated parallel column chromatography of up to eight columns, removing all manual steps from column equilibration to column regeneration, and even detection. MediaScout RoboColumns feature individual mini columns arranged on a 96-well format base plate, with each column sealing to a fixed tip of the liquid handling (LiHa) arm through a pressure tight inlet (patents pending). MediaScout RoboColumns are compression prepacked with any commercially available process separation resin in the volume range from 50 to 600 µl, and bed heights from 2.5 to 30 mm.

The Freedom EVO platform in protein chromatography configuration features a robotic manipulator (RoMa) arm that handles the MediaScout RoboColumns by its base plate, and a Te-Chrom™ holder to position the base plate securely during chromatography. Through the eight fixed metal tips on the LiHa arm, the workstation provides accurate and precise flow rates down to 16.2 cm/h, and is able to achieve fractions as small as 25 µl and simulate concentration gradients by using incremental buffer conditions. Eluted liquid can be collected in standard 96-array plates, and an optional Te-Stack™ allows fraction collection by sliding the collection plate by one row between each fraction. Analysis of the fractions can be automated with an optional reader, such as the Tecan Infinite® M200, to yield chromatographic results from the data points obtained.

The system offers a powerful new tool for fully automated high throughput process development, by allowing valid chromatographic conditions to be used without the need for sophisticated LC systems.

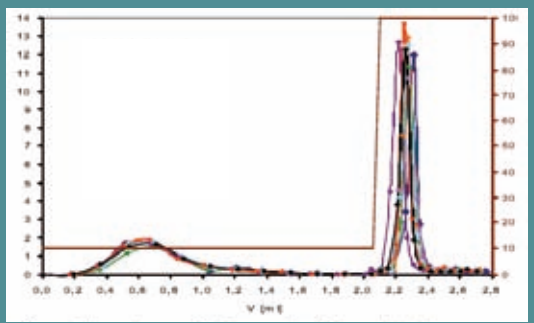
*MediaScout is a registered trademark of Atoll, GmbH. ProSep is a registered trademark of Millipore Corporation.*

*Toyopearl is a registered trademark of Tosoh Corporation.*

For more information about Tecan's automated parallel chromatography, visit **www.tecan.com/proteinchromatography**

**High reproducibility low volume column chromatography**

Simultaneous automated step-gradient elution for the separation of two proteins (1 mg/ml each of lysozyme and cytochrome c) on cation exchange resin (Toyopearl® SP-650S) was performed in eight 200 µl MediaScout RoboColumns on a Freedom EVO workstation. The resulting eight elution profiles were superimposed to show the excellent reproducibility.



**Rapid sample preparation for in-process monitoring**

A sample from each of eight parallel fermentation reactors was applied to eight MediaScout RoboColumns with cation exchange resin (ProSep® vA Ultra). The columns were rinsed and the antibodies were rapidly eluted, neutralized and analyzed by high performance cation exchange chromatography. The normally time-consuming sample preparation step was shortened by nearly one order of magnitude.