ÄKTAprocess

PROCESS CHROMATOGRAPHY

ÄKTAprocess™ is an automated liquid chromatography system built for process scale-up and large-scale biopharmaceutical manufacturing (Fig 1). The proven design has been verified during development and can be user-configured to meet specific process demands. ÄKTAprocess is the obvious choice of system to use when scaling up processes developed on smaller ÄKTAexplorer™ and ÄKTApilot™ systems.

- Versatile user-configuration with UNICORN™ control
- Post-purchase configuration increasing usability and lifespan
- Traceable USP Class VI materials
- Intelligent packing of AxiChrom™ columns
- Full regulatory documentation and services

Versatile user-configuration

ÄKTAprocess is a versatile platform providing thousands of configuration possibilities (Fig 2). The system is available in three flow rate ranges that extend up to 1800 l/h for large volume manufacturing. The compact design with a built-in computer allows the system to fit neatly into a plant with a minimum of clutter.

ÄKTAprocess can be constructed in either electropolished stainless steel or polypropylene depending on your process conditions and plant requirements. Stainless steel systems are recommended for use in applications where salt concentrations are low and pH is above 5. Polypropylene systems have high quality, corrosion resistant polypropylene pumps to make your process more secure. This type of system is recommended for applications with low pH and high salt concentrations, such as in the production of monoclonal antibodies.

ÄKTAprocess systems can be configured to develop gradients at any flow rate with feedback loop technology. This ensures thorough mixing of liquids/solvents without air bubbles so that even challenging gradients can be created with 2% accuracy (Fig 3).

Fig 1. The ÄKTAprocess system features versatile user-configuration possibilities.

The built-in computer with UNICORN software allows stand-alone operation or integration into any plant-wide control system. Additional configurations include, for example, the choice of extra inlets and outlets, the type and quantity of selected monitors, and isocratic versus gradient functionality.

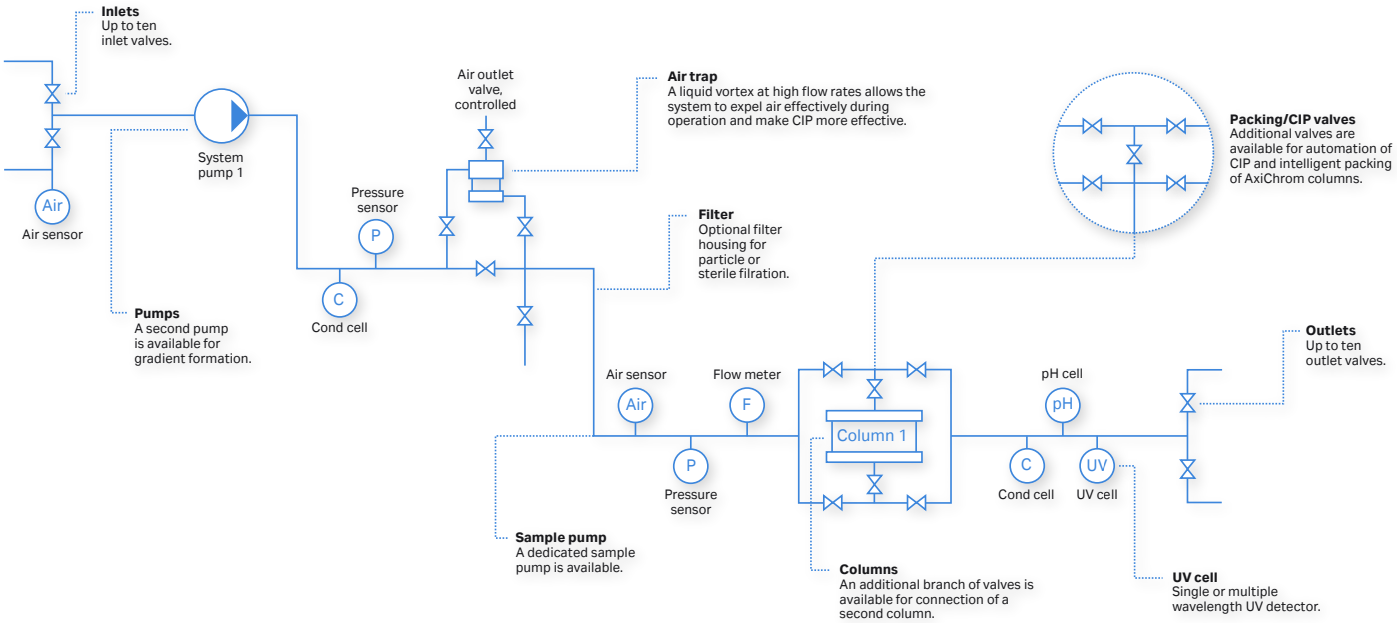

Fig 2. The liquid flow path.

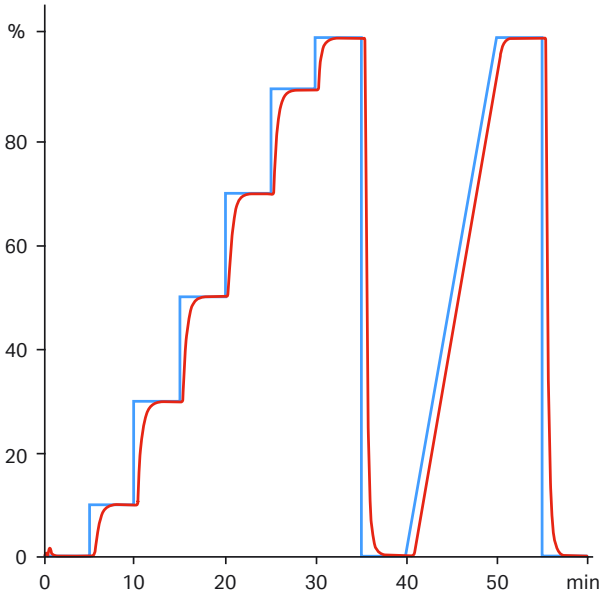

Fig 3. Chromatograms from ÄKTAprocess showing the programmed and resulting step gradient (left) and linear gradient (right).

Post-installation modification increasing usability and lifespan

Owing to the flexibility of the design, post-installation changes to ÄKTAprocess such as the addition of valves, filters, and pumps are possible. This allows a system to be reassigned to another process with different requirements, thereby increasing the versatility and working time of ÄKTAprocess. Upgrades may also be applied to increase the lifespan of ÄKTAprocess, which also protects its investment value.

Sanitary design

ÄKTAprocess has a number of features that make sanitization with 1 M sodium hydroxide simple and effective. Sanitization is the use of a chemical agent to reduce a microbial population to an acceptable, predetermined level.

UNICORN allows automation of cleaning-in-place (CIP) and a new type of air trap makes CIP more efficient. All wetted parts can be changed to prevent cross-contamination when the system is used for campaigning.

In a sanitization study the system was subjected to high level of microbial challenge organisms (1×10^6 Colony Forming Units CFU/ml). The yeast, *Pichia pastoris*, was used for antimicrobial testing. The results show that the method is sanitized effectively and that the numbers of viable organisms were efficiency reduced.

Validatable control with UNICORN software

UNICORN software is a single familiar interface for both chromatography and membrane separations that provides efficient control of process, flexible method programming, extensive data evaluation, and powerful reporting functionality.

Improved and cost-effective process security is now provided as a standard. The system control unit, CU 960, allows process operation even if communication with system computer and UNICORN is lost either physically or due to operating system faults.

Wizards have been incorporated for straightforward setting of parameters used in intelligent packing of AxiChrom Columns. Scouting for method development and peak comparison provides a high degree of efficiency in pharmaceutical production as well as process scale-up and scale-down work.

UNICORN has undergone an independent audit and is designed as a validatable control package in FDA 21 CFR part 11 and GMP compliant environments. The electronic signature and record system uses a dual password confirmation, documenting locking scheme, and traceable audit log. For integration purposes, UNICORN communicates with control systems within the plant via OLE for Process Control (OPC). OPC supports application area such as data access for real time values and security control to protect sensitive information.

Reproducible results with scalability

Now, with ÄKTAprocess, the ÄKTA platform enters production scale chromatography. ÄKTAexplorer and ÄKTApilot systems are the first choice for research, small scale production, and rapid process development. Since all ÄKTA systems use the same UNICORN control software, methods can be quickly scaled-up and transferred to ÄKTAprocess for use in full GMP production.

To illustrate scalability, BSA was captured by SP Sepharose™ Fast Flow in AxiChrom 50 mm, 100 mm, and 400 mm columns that were connected to ÄKTAexplorer 100, ÄKTApilot, and ÄKTAprocess systems, respectively. AxiChrom columns have axial compression packing, and uniform flow and distribution through the bed ensure excellent results. Figure 4 shows the result – a perfect 64-fold scale-up on three AxiChrom columns connected to three different ÄKTA systems.

SP Sepharose Fast Flow

Columns:	AxiChrom 50, AxiChrom 100, and AxiChrom 400
Sample:	7.5 mg BSA and 2.5 mg Lactoferrin per ml 50 mM acetic acid, pH 4.5
Buffer A:	50 mM acetic acid, pH 4.5
Buffer B:	50 mM acetic acid and 1 M NaCl, pH 4.5
Elution:	0–100% Buffer B

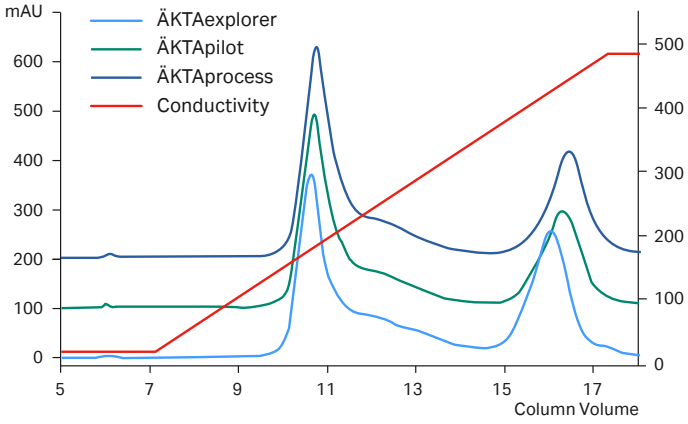

Fig 4. 64-fold scale-up with BSA and Lactoferrin using ÄKTAexplorer 100 and AxiChrom 50, ÄKTApilot and AxiChrom 100, ÄKTAprocess and AxiChrom 400, respectively.

Intelligent packing of AxiChrom columns

ÄKTAprocess has been developed to perform intelligent packing of AxiChrom columns. In addition to saving time, intelligent packing ensures consistent reproducibility of results with scalability, whether upscaling or downscaling, throughout the AxiChrom column family. Intelligent packing utilizes axial compression for packing of the media, and even contained-filling of production size AxiChrom columns. Parameters used in the intelligent packing procedure are set using a wizard in UNICORN software. UNICORN controls the packing and testing, with continual monitoring of the pressure to detect when the bed is settled, through to final compression of the bed.

Full regulatory documentation and services

Process safety is an integral part of ÄKTAprocess. We provide documentation to show that the materials used to build the system are all USP Class VI and are traceable back to their original production batches.

Regulatory authorities expect manufacturers of pharmaceuticals to qualify equipment before use in production. Fast Trak Validation™ offers a comprehensive range of specialist services to support the development and production of biopharmaceuticals. Validation documentation can be ordered for the ÄKTAprocess systems, such as Installation and Operation Qualification (IQ/OQ) documentation, which is subject to inspection by regulatory authorities. In addition to producing the documentation, Cytiva also offers its expertise to perform the actual qualification of the system on-site.

Fast Trak Validation also offers Standard Operating Procedures (SOPs) that describe how to use and maintain ÄKTAprocess during regular operation. SOPs can be specifically written for systems controlled by UNICORN software while other SOPs are required for procedures used in Good Manufacturing Practice (GMP) environments.

System specifications

Piping diameter	System flow rate
6 mm i.d. PP*	4–180 l/h
3/8" o.d. (7.7 mm i.d.) SS†	4–180 l/h
10 mm i.d. PP	15–600 l/h
1/2" o.d. (9.4 mm i.d.) SS	15–600 l/h
1" o.d. (20.4 mm i.d.) PP	45–1800 l/h
1" o.d. (22.1 mm i.d.) SS	45–1800 l/h
UV wavelength range	Single (280 nm) or multiple wavelengths
pH range	0–14 (spec. valid between 2 and 12)
Conductivity range	1 mS/cm to 200 mS/cm
Ingress protection	NEMA 4X / IP 56 electrical cabinet
Electrical standards	UL 508A, EN 61010-1
Tubing size	
PP	6 mm, 10 mm, and 1"
SS	3/8", 1/2", and 1"
Skid size (W × D × H)	
6 mm, 10 mm, 3/8", and 1/2"	850 mm × 1205 mm × 1670 mm (D = 1750 mm if including monitor and keyboard)
1" PP and SS	1050 mm × 1730 mm × 1900 mm
	(D = 2275 if including monitor and keyboard)

* PP = polypropylene
† SS = 316 L stainless steel

Operating pressure and temperature

PP (6 mm, 10 mm, and 1")	6 bar (max 40°C)
SS (3/8" and 1/2")	10 bar (max 40°C)
SS (1")	6 bar (max 40°C)
Surrounding temperature	2–26°C
Applied solutions	PP systems: 4–60°C (max 3 bar at 40–60°C)
Applied solutions	SS systems: 4–80°C (max 3 bar at 40–60°C and max 1 bar at 60–80°C)

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CY13469-07Aug20-DF

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