



# The Contichrom<sup>®</sup> CUBE FPLC Systems

Twin-Column  
Protein Purification Systems  
for Batch and Continuous Processing

# The Contichrom CUBE Platform

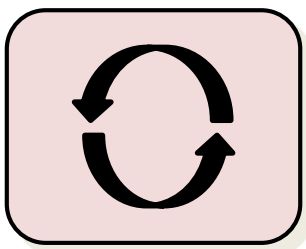
## Twin-Column Preparative FPLC System

The **Contichrom CUBE** and **CUBE Combined** are flexible modular purification systems for process development of biopharmaceuticals such as monoclonal antibodies.

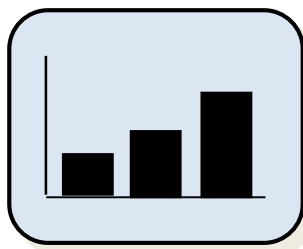
- ❑ The **Contichrom CUBE** enables single-column batch and twin-column counter-current capture (CaptureSMB®) processes, typically used for monoclonal antibody (mAb) purification. The CUBE system can be upgraded to the CUBE Combined system with an additional CUBE+ hardware module and software upgrade.
- ❑ The **Contichrom CUBE Combined** enables single-column batch and several continuous processes, including counter-current capture and polishing. It is an all-in-one process tool for challenging purification tasks for all proteins. The N-Rich process functionality allows the rapid isolation of product-related impurities for CMC development of Biologics.

The systems are offered with pump flow rates of up to 36 mL/min or 100 mL/min.

The unique twin column operational design and software offer several process choices for optimal separation and purification of proteins and oligonucleotides, including batch, integrated batch and continuous countercurrent processes.



**Run batch, integrated batch and continuous processes with ChromIQ automation software.**



**Get 50% more yield with the same target purity and significantly greater throughput.**



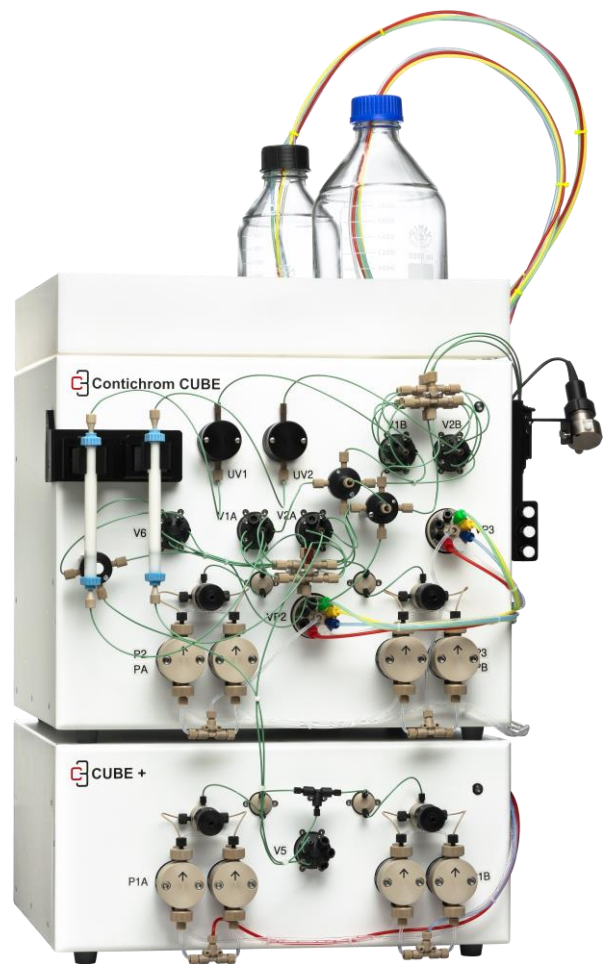
**Counter-current processes save significantly operating costs, including Protein A resin.**

# The CUBE Systems



The **CUBE** has both batch and CaptureSMB (optimized 2C-PCC) process capabilities for mAb Protein A capture. For smooth operation of continuous processes, the AutomAb dynamic process control function keeps the CaptureSMB process at an optimum.

An ideal tool for protein purification and specifically for monoclonal antibodies.



The **CUBE Combined** has extended process capabilities for difficult purification challenges. The system consists of the CUBE and an additional CUBE+ module. The extension adds continuous polishing capabilities such as MCSGP and N-Rich.

MCSGP is supported by MControl, a dynamic process control function keeping the MCSGP process always at an optimum.

The systems are delivered ready-to-use with fully mounted tubing and pre-delivery IQ/OQ testing.

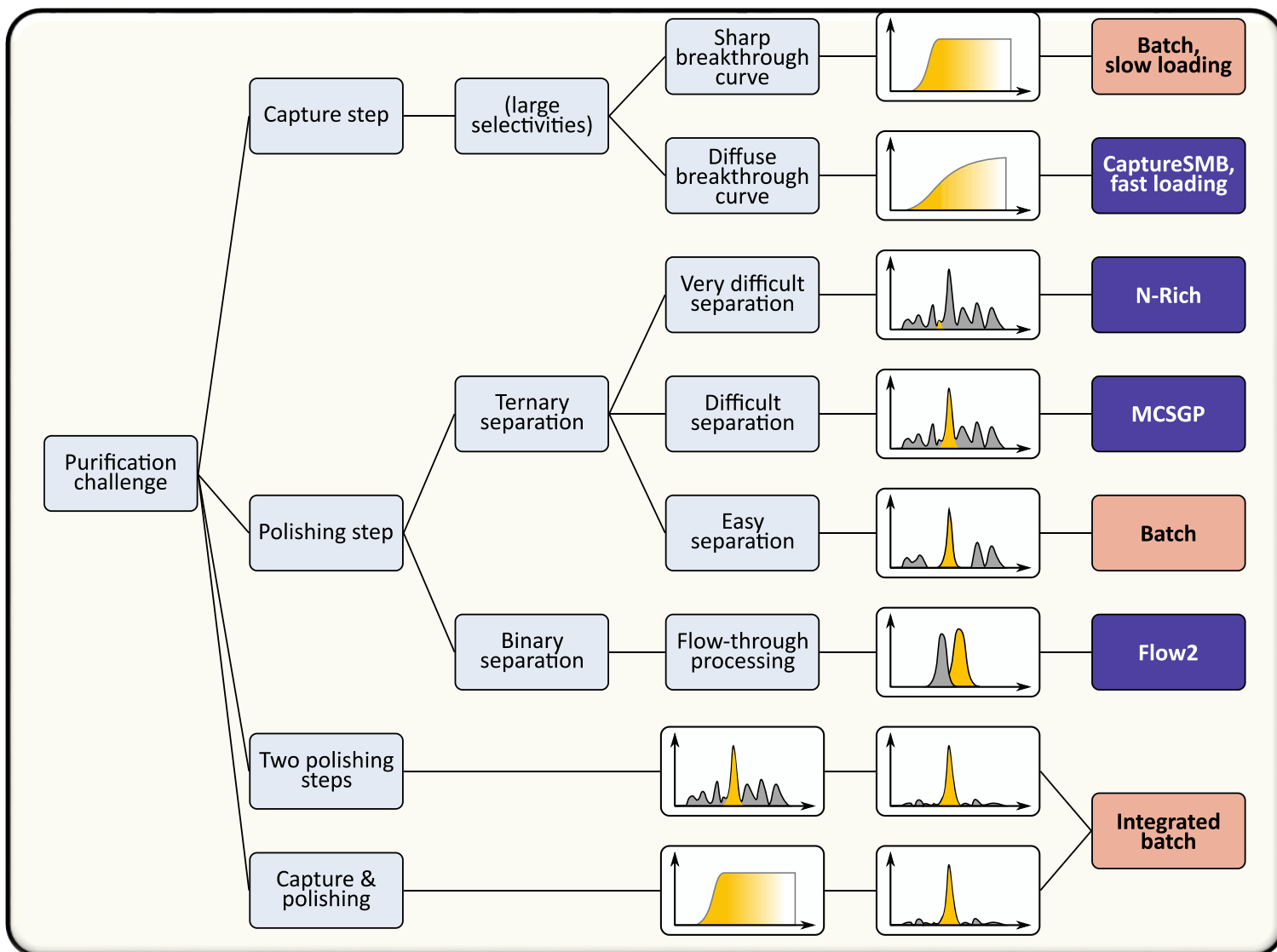
# CUBE Process Capabilities

The Contichrom CUBE has batch process capabilities like conventional FPLC systems. Additionally, enhanced continuous process capabilities offer increased performance gains (productivity, yield and throughput).

Twin column capture applications (**CaptureSMB** / optimized 2C-PCC) and the software tool (AutomAb) are useful for automated optimization of the mAb capture process. Twin column capture processes will result in significant cost-of-goods savings at GMP scale-up.

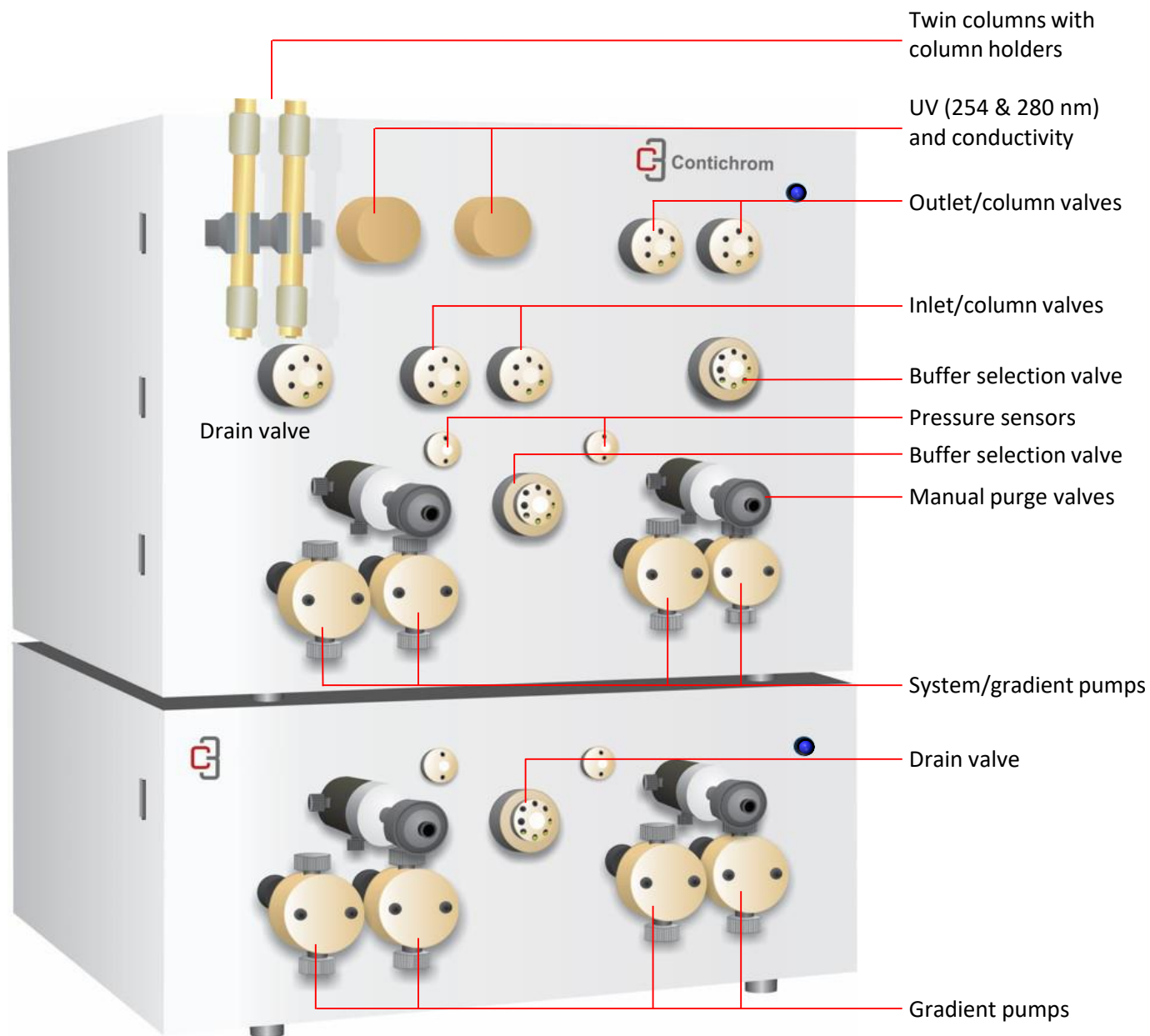
The Contichrom CUBE Combined adds additional twin-column/membrane process capabilities for polishing applications:

- **MCSGP: Multi-column Counter-current Solvent Gradient Purification.** A powerful gradient elution process that increases yield by up to 80% while maintaining target purity. MControl, a dynamic process control tool, keeps the MCSGP process at an optimal operating mode.
- **N-Rich:** a process for enriching and isolating minor components from complex mixtures – an ideal tool for fast isolation of product-related impurities for pre-clinical testing.



Flow-2 process is not yet available as a ChromIQ Software wizard

# Powerful Functionalities



- compact benchtop design
- large buffer tray
- clear easy-to-access interface
- high visibility tubing inlets and outlets
- flexible tubing connections
- high performance pumps (36 or 100 mL/min)
- easy-mount clip-in column supports
- 2 long life LED UV detectors each at 254 nm and 280 nm
- easy plug-in CUBE and CUBE+ installation
- pH detector
- 2 conductivity flow cells
- laptop and desktop computer options

# CUBE System Accessories

## Benchtop Cooling Cabinet

### Preserving Product Integrity During Purification

Cooling of product feed and of fractions is important for preserving product integrity. We offer a compact cooling chamber that fits on a lab bench and can accommodate a fraction collector (Foxy R-1), feed bottles and also columns allowing for preparative runs under cooled conditions.

Additional useful accessories include a sample loop system for feed loading, an external valve with an injection loop and a stable, re-usable transport box.



# CUBE System Accessories

## Enhancing System Performance and Convenience

Additional accessories include two external multi-wavelength detectors (190-500 nm), a sample loop system for feed loading, an optional external loading valve with sample injection loops of 500  $\mu$ L up to 20 mL, a screening valve for column screening addressing up to 6 columns and re-usable transport boxes.



Fraction collectors Foxy R-1 and R-2



Valve system with 6 positions for column screening



Injection valve system with injection loops of 500  $\mu$ L up to 20 mL allowing to apply different sample volumes



Preparative flow cells in PEEK or steel



External variable wavelength detector (190-500 nm)



External variable multi-wavelength detector (190-700 nm)

# Process Economics

## Integrated batch chromatography

The twin-column setup allows to run two consecutive process steps in an integrated way, using in-line dilution between the first and second process step, eliminating intermediate hold steps.

## CaptureSMB (optimized 2C-PCC)

### ENABLES

Two-fold faster processing of feed streams preserving product integrity; higher project turnover.

### SAVES

30% CAPEX, 30-60% OPEX, 40-60% Protein A consumption, 40-60% buffer consumption.

## MCSGP

### ENABLES

Isolation of pure components from complex mixtures; 50-90% more yield and higher purity; up to 10x faster processing than batch.

### SAVES

Up to 30% CAPEX, 50% OPEX, 70% buffer consumption.

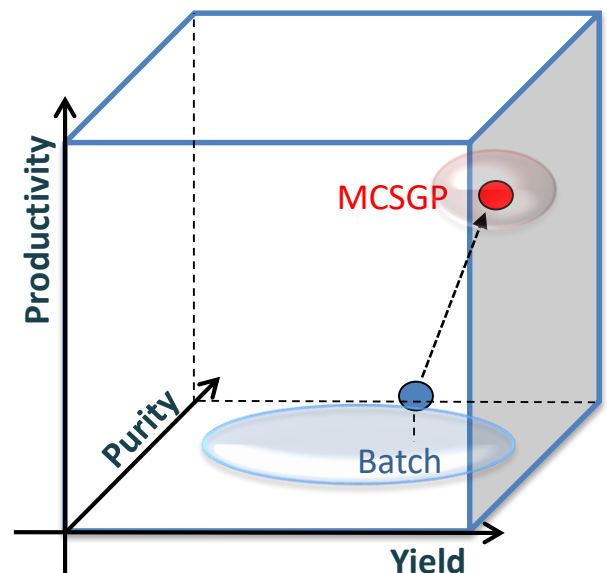
## N-Rich

### ENABLES

The enrichment of a minor components while simultaneously depleting the large excess of interfering product. It is particularly useful for isolation of product-related impurities.

### SAVES

Tedious repetitive analytical separations taking weeks to isolate the compound of interest. With batch processes, up to several hundred analytical injections are needed to isolate sufficient amounts for further characterizations. With N-Rich, this can be achieved overnight.



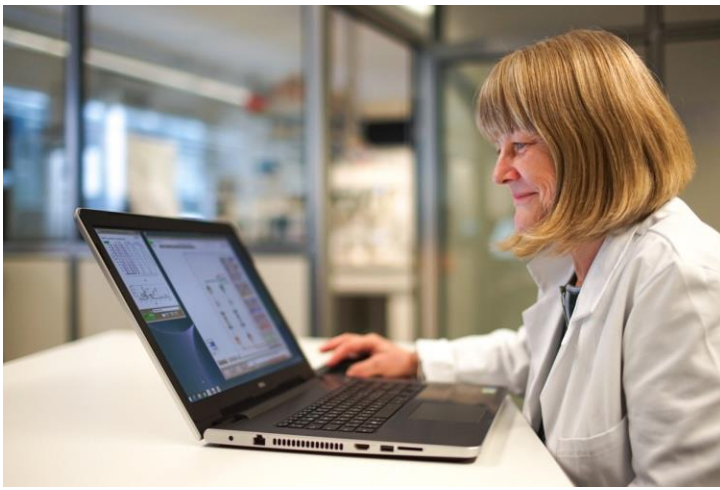


# ChromIQ Software

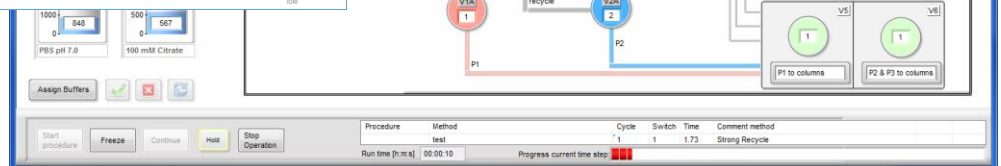
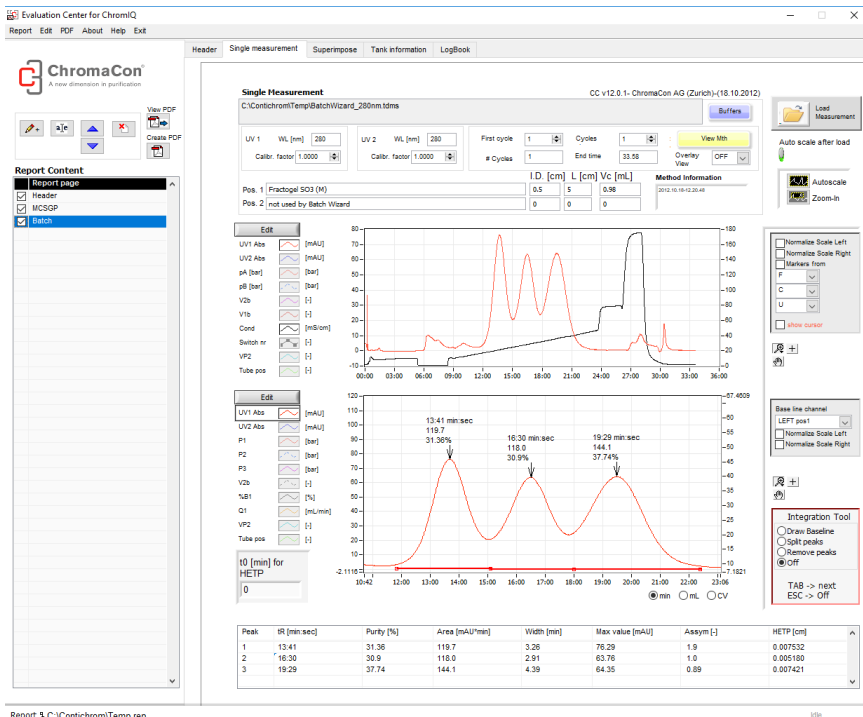
The ChromIQ operating software controls the Contichrom CUBE systems. It supports batch and continuous processes and tools for separation and purification with an intuitive, user-friendly interface.

ChromIQ has easy step-by-step wizards to help you design batch chromatography runs and to convert them to more efficient Contichrom Processes. ChromIQ also includes the AutomAb and MControl dynamic process controllers.

ChromIQ includes a number of features that are particularly helpful for continuous processes such as a buffer management system and cycle overlay display options.



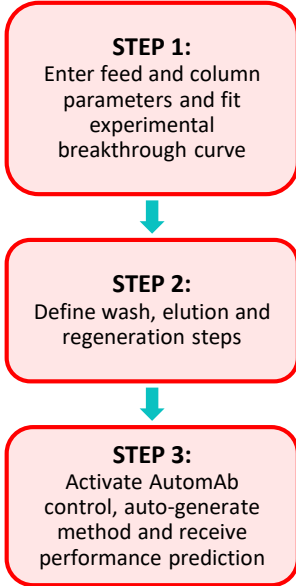
- ✓ Drag-and-drop method creation
- ✓ Wizards for convenient method creation
- ✓ Interactive process picture
- ✓ Single-click evaluation
- ✓ Easy data export (xlsx, csv, jpg)
- ✓ Pre-defined user groups with individual rights management
- ✓ Password protected user accounts
- ✓ Logging with time stamp and user name
- ✓ Electronic signature with check-sum of log and measurement files



# Process Wizard Examples

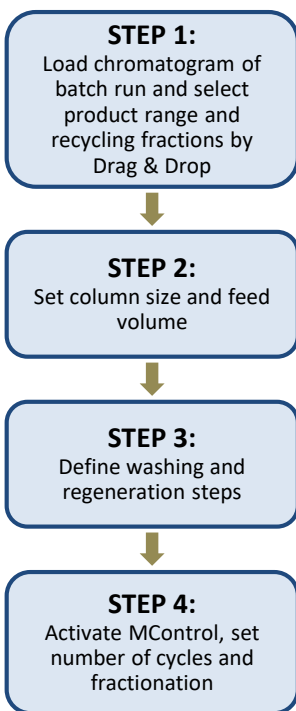
Load the process wizards from the ChromIQ Software for easy design of processes.

## CaptureSMB



The screenshot shows the 'Capture SMB Design Wizard' interface. It includes sections for 'Feed' (Feed concentration: 4 g/L, Loading/Elution Flowrate: 300 cm/h, 0.982 mL/min) and 'Columns' (Information Column 1 (left) and Information Column 2 (right, same dimensions)). A graph displays the 'Estimated Dynamic Breakthrough Curve (DBC) on a single column' with 'Column outlet conc. [g/L]' on the y-axis and 'Loading Volume [mL]' on the x-axis. The graph shows a curve with a shaded area under it, indicating the DBC. A '1% DBC' point is marked at approximately 12 mL, and a '70% DBC' point is marked at approximately 24 mL. The interface also includes a 'Method comment' field with 'Template CaptureSMB' and a 'NEXT' button.

## MCSGP

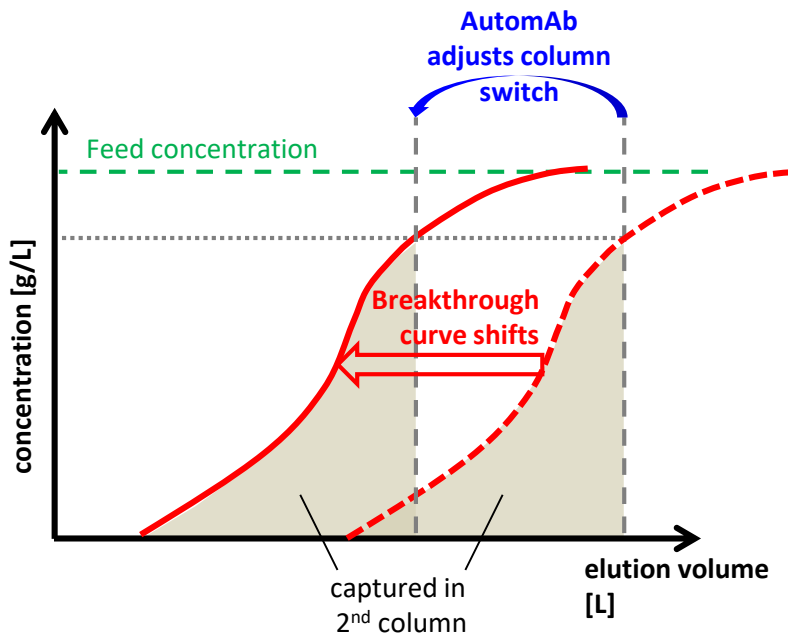


The screenshot shows the 'MCSGP Wizard' interface. It includes a 'Load Chromatogram' button and a graph displaying 'UV [mAU]' on the y-axis and 'Time [min]' on the x-axis. The graph shows a chromatogram with several peaks and a red dashed line representing a breakthrough curve. The interface also includes a 'Method comment' field with 'Batch Method, Elution of 3 proteins on IgG S03 (M)' and a 'NEXT' button. The bottom section shows 'Elution Velocity [cm/h]' (305.577), 'Q Elute [mL/min]' (1), and 'Feed [mL]' (0.97). A table lists 'Column used in Batch chromatogram' with columns for Name, ID, Length, and V. The table contains one entry: 'Fractogel S03 (M)' with ID 0.5, Length 5, and V 0.98.

# Dynamic Process Control

## AutomAb: Dynamic CaptureSMB process control

AutomAb is a tool that automatically optimizes the CaptureSMB process in terms of resin capacity utilization, throughput, and ensuring steady product quality. AutomAb controls the process and maintains optimal process performance effectively offsetting process changes such as feed titer variations and column aging.

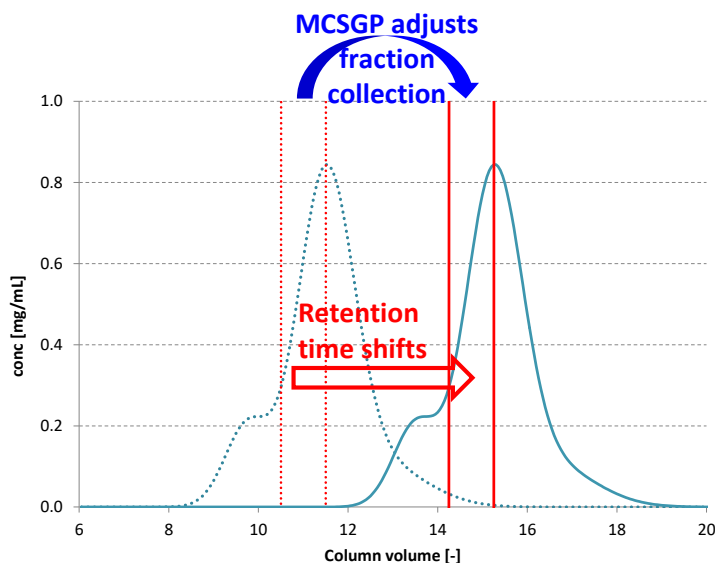


### Advantages of AutomAb

- works with minimum process knowledge
- runs fully automatically without intervention
- works with low and high feed titers
- works without feed signal measurement
- works with “dirty” feeds with a high impurity signal and low product feed concentrations
- works without detector calibration

## MControl: Dynamic MCSGP process control

The outcome of chromatographic runs can be influenced by various parameters such as temperature, buffer quality, conductivity, pH and quality of the stationary phase (bed height, resin aging, packing variation) leading to variability. To counteract such effects, we have developed a control algorithm allowing to keep the MCSGP runs always at an optimum by compensating for variations. The resulting MCSGP process is very robust and will run at an optimum without sacrificing productivity.



### Advantages of MControl

MControl compensates for peak shifts by adjusting the fractionation start

- Always the same product in same fraction
- Always the same product quality
- Perfect control of cyclic continuous processes

# GMP Scale-Up

## Twin-column pilot-process scale

EcoPrime® Twin: Best-in-class GMP skids





### Product features

- Integrated Buffer Inline Dilution (BID)
- Ability to run batch, integrated batch, parallel batch and CaptureSMB. MCSGP will be available soon
- CIP & SIP
- Drain & blow dry
- Custom designed set up
- Scale-up method conversion
- Allan-Bradley Rockwell or Delta-V operating system
- Compliant with GMP, GAMP, ASTM, 21CFR part 11
- All wetted parts cleanable
- Flow accuracy: better than 0.5% variation.
- Gradient accuracy: better than 0.5% variation
- Pressure rating: 7.5 bar (108 psi)
- Flow path: 316L stainless steel

EcoPrime® is a trademark of YMC and YMC Process Technology Ltd. System quotes can be obtained under [www.ymcpt.com](http://www.ymcpt.com) or [sales@ymcpt.com](mailto:sales@ymcpt.com).

Type	Min L/min	Max L/min
EcoPrime Twin 100	0.004	0.6
EcoPrime Twin 250	0.02	2.4
EcoPrime Twin 500	0.06	9
EcoPrime Twin 1000	0.12	18

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Bristol Myers Squibb using EcoPrime Twin GMP scale-up system and performing process simulation and process validation:

James Angelo et al., (April 2018). Scale-Up of Twin-Column Periodic Counter-Current Chromatography for MAb Purification, *BioProcess International*.

Daniel Baur et. Al., (2018). Model assisted process characterization and validation for a continuous two-column protein A capture process. *Biotechnology and Bioengineering*. Advance online publication. <https://doi.org/10.1002/bit.26849>

# Technical Specifications

## Contichrom CUBE & CUBE Combined Systems

<b>Process capabilities:</b>	Batch (isocratic, gradient), integrated batch, CaptureSMB, MCSGP, N-Rich, Flow-2
<b>Operating software:</b>	User-friendly operating software with step-by-step wizards to help you to design batch chromatography runs and to convert them into more efficient Contichrom processes, such as MCSGP and N-Rich. ChromIQ also includes dynamic process controllers AutomAb and MControl.
<b>Software compliance:</b>	ChromIQ software with essential elements of 21CFR Part 11 compliance: <ul style="list-style-type: none"><li>• Pre-defined user groups, administrators, R&amp;D and production users</li><li>• Rights management for individual user groups</li><li>• User accounts are password protected</li><li>• Logging with time stamp and user name (non-deletable)</li><li>• Electronic signature with checksum of log and measurement files</li></ul>
<b>Pressure rating:</b>	50 bar (5 MPa)/ 725 psi
<b>Flow rate range:</b>	<ul style="list-style-type: none"><li>• 0.1 – 36 mL/min (Contichrom CUBE &amp; CUBE Combined 30)</li><li>• 0.1 – 100 mL/min (Contichrom CUBE &amp; CUBE Combined 100)</li></ul>
<b>Buffer selection:</b>	16 Inlets (2 x 8-fold buffer selection valve) 4 Outlets
<b>UV, fixed wavelength:</b>	2 Long lifetime LED UV detectors, each 254 & 280 nm recording simultaneously
<b>Conductivity monitoring:</b>	2 Conductivity sensors (1-300 mS/cm)
<b>pH monitoring</b>	1-14
<b>Pump type</b>	High precision double-piston-pumps with active seal wash 2 Pumps (CUBE), 4 pumps (CUBE Combined)
<b>Valves:</b>	4 Reliable multi-position valves 1 Automated drain valve (CUBE), 2 automated drain valves (CUBE combined)
<b>Computer hardware:</b>	Stand-alone laptop computer (Windows, 64 bit, full HD resolution, 1920 x 1080 or higher) with ChromIQ software
<b>Other:</b>	Cold room compatible Large buffer tray Portable & compact Runs resins and membrane stationary phases
<b>Dimensions:</b>	CUBE module: 450 mm x 509 mm x 370 mm (20.0" x 17.7" x 14.6") CUBE+ module: 450 mm x 509 mm x 214 mm (20.0" x 17.7" x 8.43") The modules are stackable.
<b>Weight:</b>	CUBE module: 30 kg (67 lb) CUBE+ module: 17 kg (38 lb)
<b>Materials:</b>	All biocompatible High pressure side capillaries: PEEK Low pressure side tubing: PTFE Fittings: PEEK

# After Sales Services

## Training, Maintenance, and Repair

### A reliable and cost-effective service network

Purchasing an FPLC System and operating it is only part of a customer's value proposition. After sales support such as Preventive Maintenance (PM) and total life cycle costs are an important consideration in a system's procurement evaluation.

We offer PM, repair and system validation and qualification support including IQ-OQ and a generic PQ testing scheme. We also offer an annual Software PM package.

We perform on-site and off-site training, webinar-based product support and we organize annual workshops on continuous chromatographic purification.

Our system is designed to have very low maintenance costs: only wear parts from pumps and valves need to be exchanged occasionally in an easy way without disassembling the system.

We offer continued support through remote control system access allowing to guide the user in using the system beyond the initial training.



We offer comprehensive and cost-effective Preventive Maintenance and Repair Service packages.

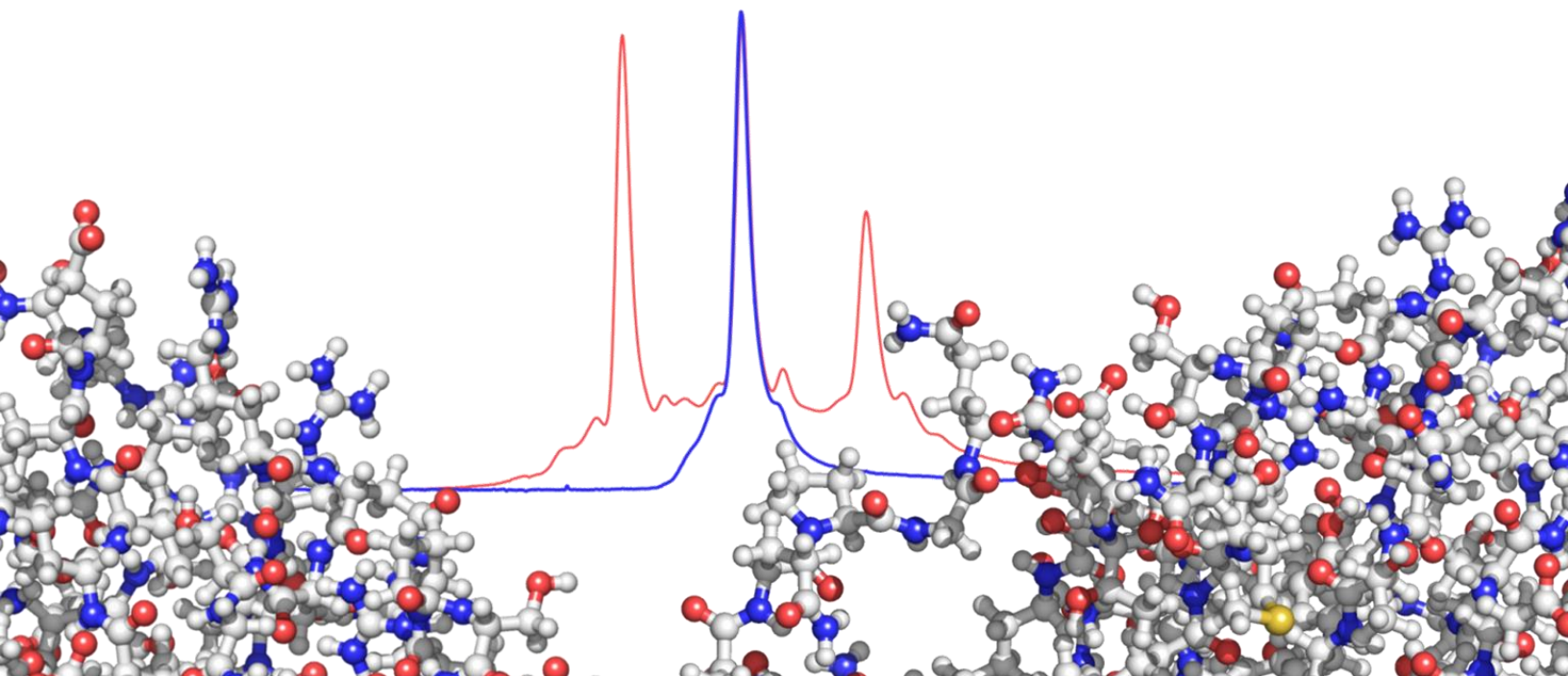
Worldwide Preventive Maintenance and Repair Service packages. On-site and off-site service with fast turnaround times.

**For details please require a quote at your local ChromaCon representative.**

# Selected Publications

1. J. Angelo, J. Pagano, T. Müller-Späth, K. Mihlbachler, S. Chollangi, X. Xu, S. Ghose, and Z. J. Li, "Scale-Up of Twin-Column Periodic Counter-Current Chromatography for MAb Purification," *BioProcess Int.* **16** (4), 28-37 (2018).
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3. D.J. Karst, F. Steinebach and M. Morbidelli, "Continuous integrated manufacturing of therapeutic proteins," *Curr. Opin. Biotechnol.* **53**, 76–84 (2018).
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8. M. Angarita, D. Baur, T. Muller-Spath, R. Lievrouw, G. Lissens, and M. Morbidelli, "Twin-column CaptureSMB: a novel cyclic process for protein A affinity chromatography," *J. Chromatogr. A* **1389**, 85–95 (2015).
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15. T. Müller-Späth, L. Aumann, G. Ströhlein, H. Kornmann, P. Valax, L. Delegrange, E. Charbaut, G. Baer, A. Lamproye, M. Jöhnck, M. Schulte, and M. Morbidelli, "Two step capture and purification of IgG<sub>2</sub> using multicolumn countercurrent solvent gradient purification (MCSGP)," *Biotechnol. Bioeng.* **107**, 974–984 (2010).
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17. T. Müller-Späth, L. Aumann, L. Melter, G. Ströhlein, and M. Morbidelli, "Chromatographic separation of three monoclonal antibody variants using multicolumn countercurrent solvent gradient purification (MCSGP)," *Biotechnol. Bioeng.* **100**, 1166–1177 (2008).

# Contact



Contact us now to find out how you can solve your separation challenges more easily

Your contact at ChromaCon:

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Web: [www.chromacon.com](http://www.chromacon.com)

Your local representative:



SWISS  
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