

## Contichrom<sup>®</sup> CUBE

A bench top chromatography system for  
batch and continuous processing



# Massive Functionality

## Minimal Footprint



Contichrom CUBE (left) and Contichrom TWIN (right)

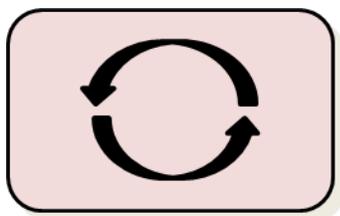
# The Contichrom CUBE System

## Twin-column flexible bench top system

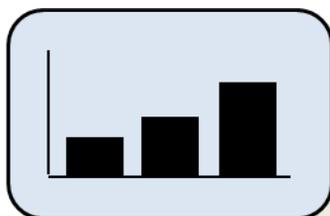
The Contichrom CUBE is a flexible purification system for process development of (bio-)pharmaceuticals such as monoclonal antibodies, peptides and oligonucleotides.

It enables single-column batch and twin-column counter-current processes, such as capture (CaptureSMB®) for monoclonal antibody (mAb) affinity chromatography and MCSGP for peptide. Additionally, the N-Rich process functionality allows the rapid isolation of product-related impurities for CMC development. 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 purification including batch, integrated batch / sequential polishing and continuous countercurrent processes.



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

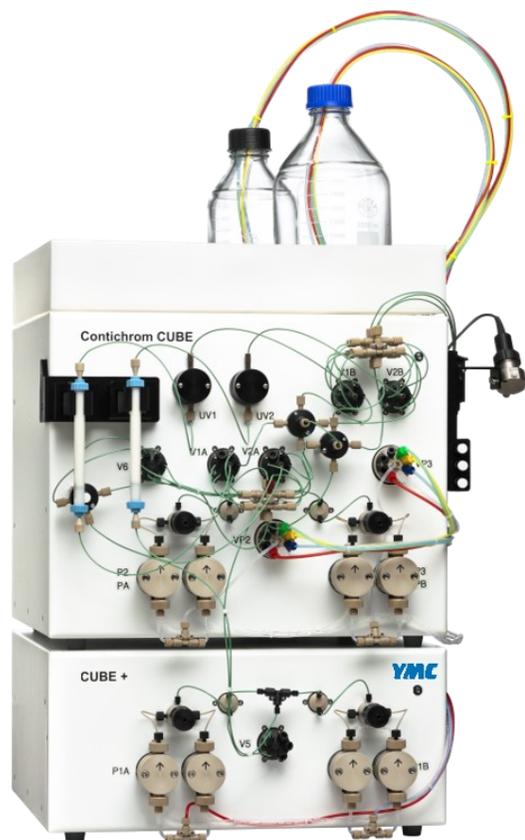


Get 50% more yield with the same target purity and significantly greater throughput.



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

# The Contichrom Platform



The Contichrom CUBE has extended process capabilities for difficult purification challenges. The system consists of the CUBE hardware and PC with batch mode capability, CaptureSMB with AutomAb control, MCSGP with Autopeak control, integrated batch / sequential polishing, buffer dilution and N-Rich.

AutomAb and Autopeak are dynamic process control functions allowing robust operation of the CaptureSMB and MCSGP processes under changing process conditions or feed variations.

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

The CUBE system scales to either the **Contichrom TWIN** CaptureSMB LPLC (photo left below) or the Contichrom TWIN MCSGP HPLC (photo right below).



Both shown are Model 100 of the platform series.

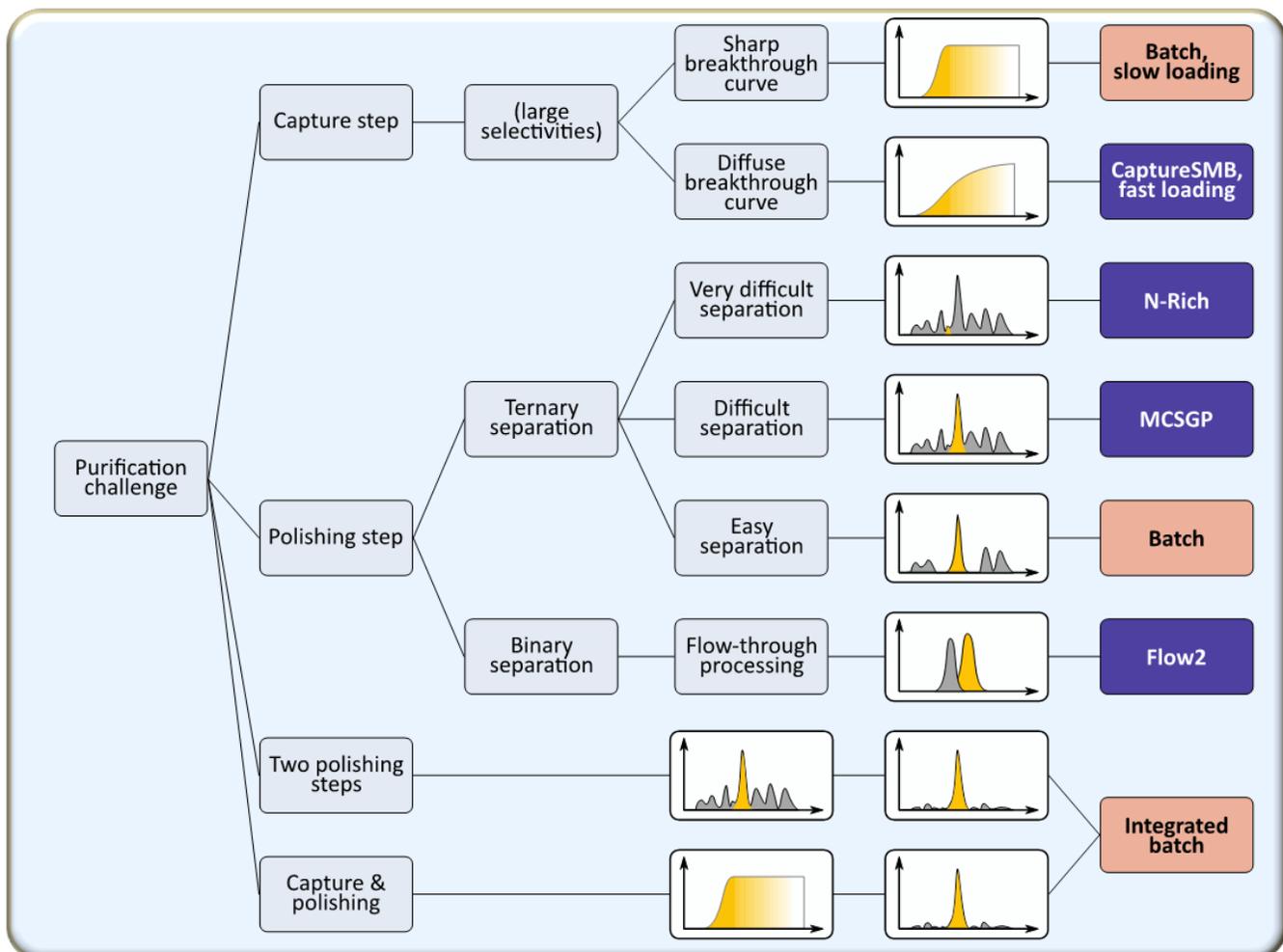
# CUBE Process Capabilities

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**) and the dynamic process control function **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 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. **AutoPeak**, 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

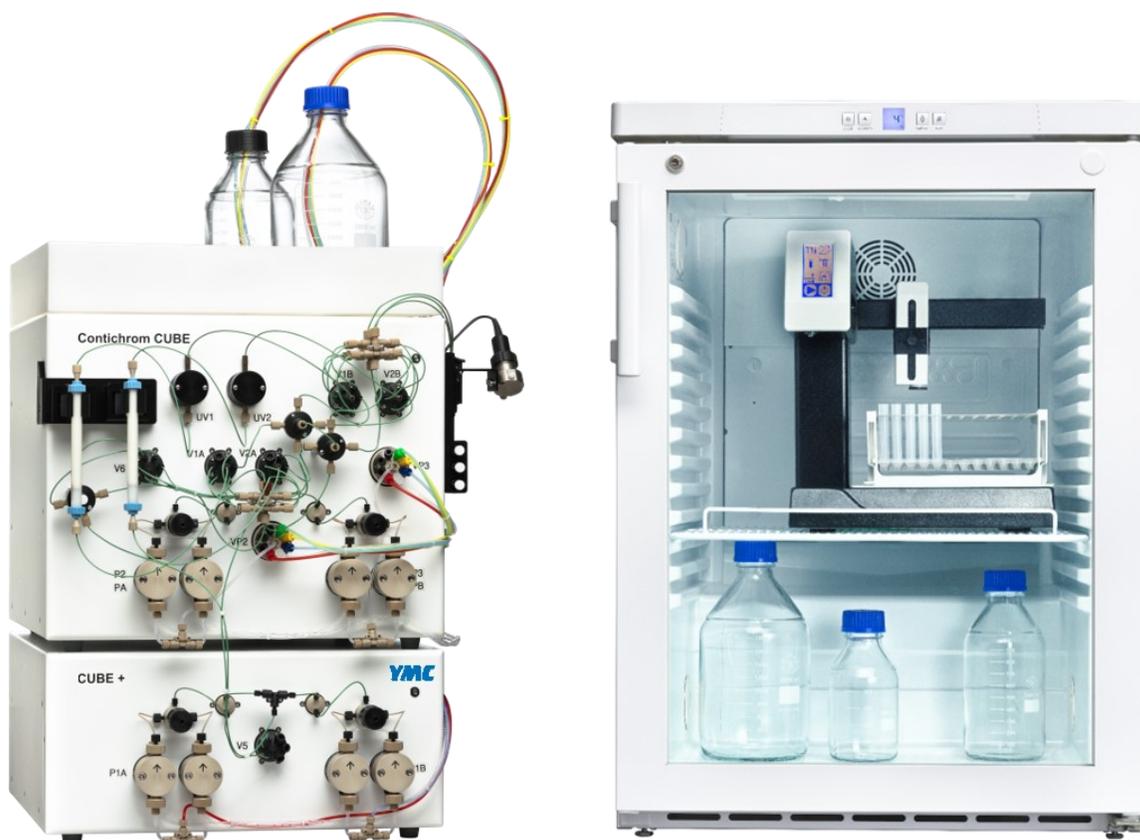
# CUBE System Accessories

## 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.



\* Cooling Cabinet not suited for chromatography using organic solvents

# Contichrom CUBE 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 R-1 and R-2

Several rack types available:

- 50 mL tubes
- 15 mL tubes
- 96-well plates
- 6 mL tube bottles
- More...



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 single variable wavelength detector (190-500 nm)



External variable 4-channel multi-wavelength detector (200-600 nm)

Detectors shown may vary from actual supply

# Process Economics

## CaptureSMB

### ENABLES

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

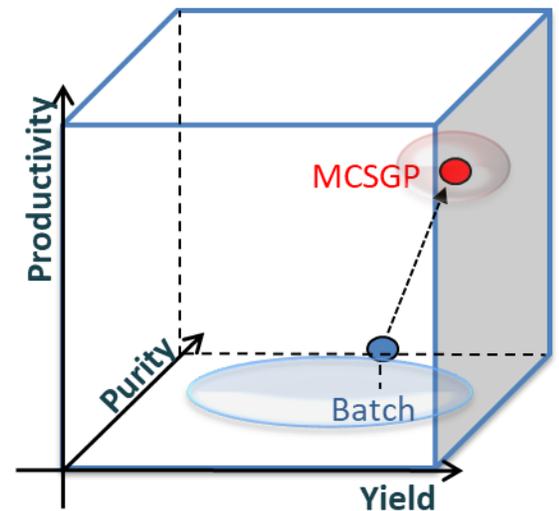
### SAVES

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.

## Integrated batch or 'sequential' 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.

## 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 characterization. With N-Rich, this can be achieved overnight.

# ChromIQ Software

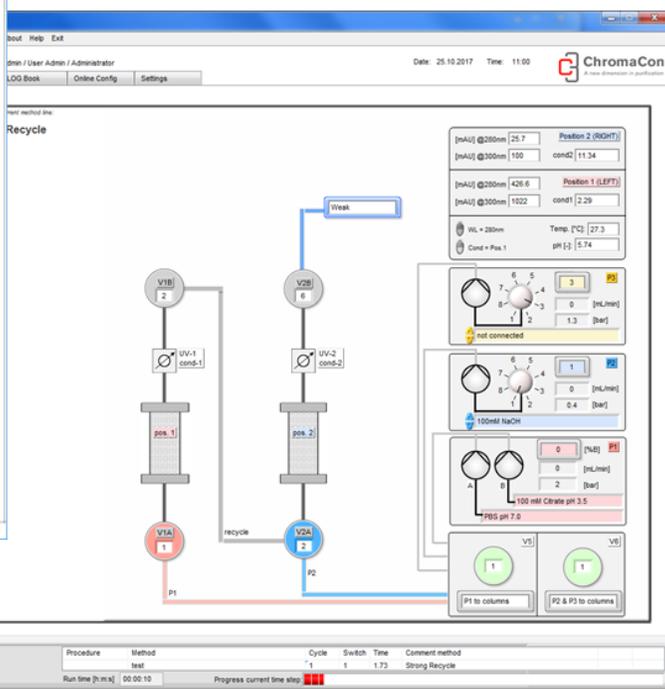
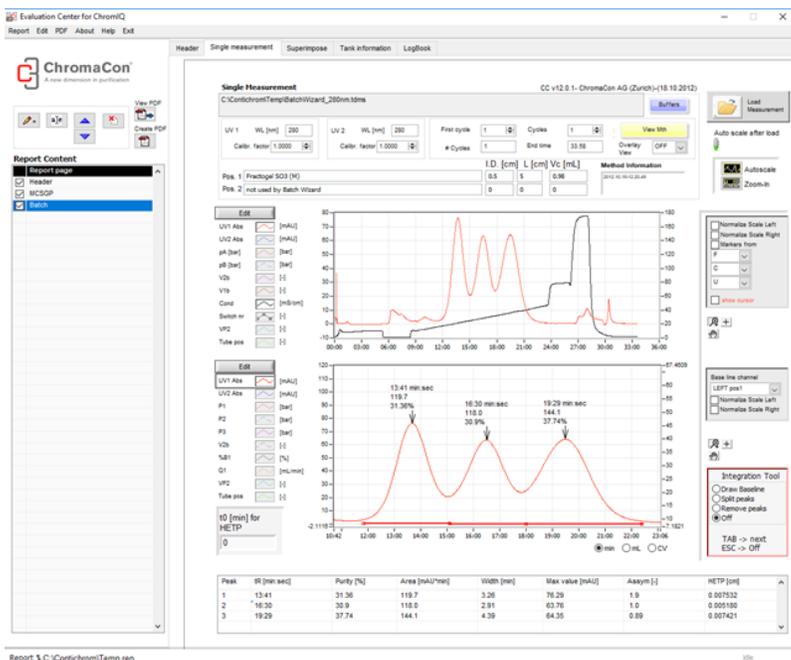
The ChromIQ operating software controls the Contichrom CUBE systems. It supports batch and continuous processes and tools for separation and purification with an intuitive, user-friendly interface.

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 AutoPeak dynamic process control functions.

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



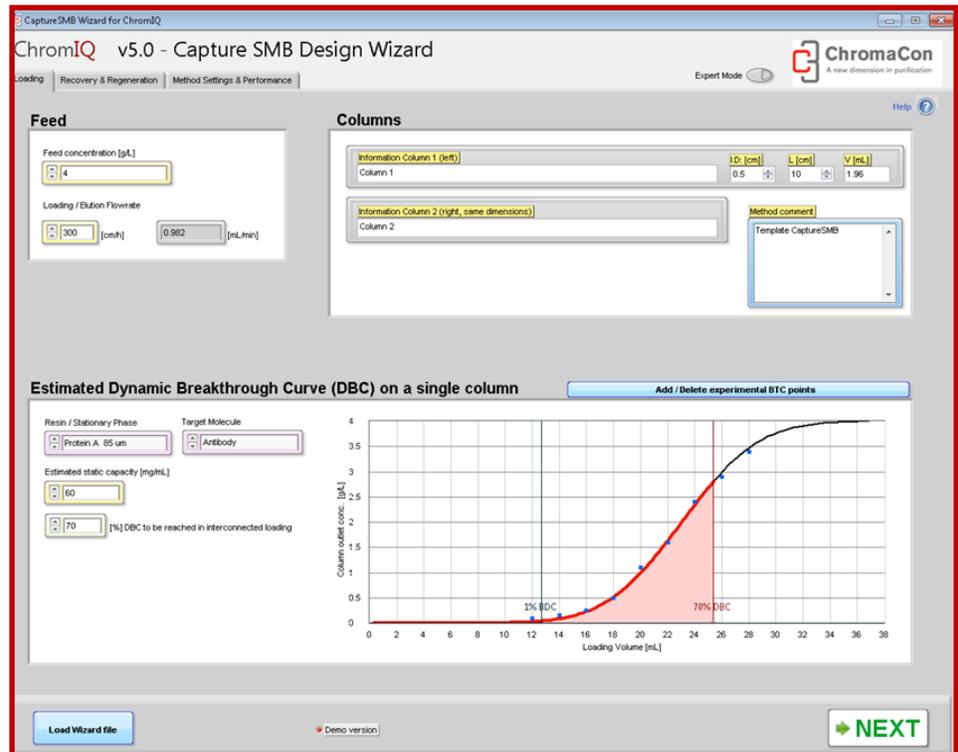
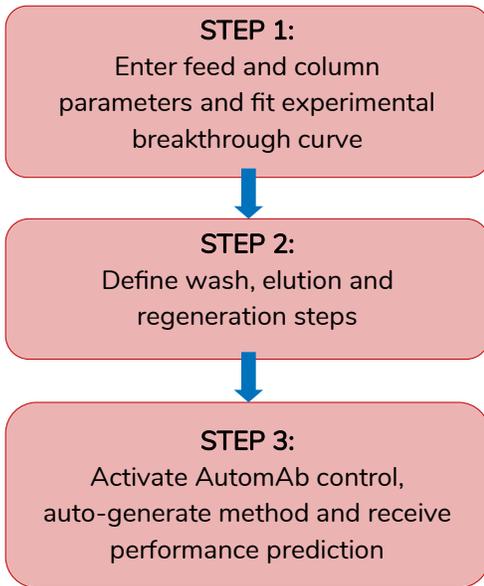
- ◆ Drag-and-drop method creation
- ◆ Wizards for convenient method creation
- ◆ Interactive process picture
- ◆ Single-click evaluation
- ◆ Easy data export (xlsx, csv, jpg)
- ◆ Pre-defined user groups with individual rights management
- ◆ Password protected user comments
- ◆ Logging with time stamp and user-name



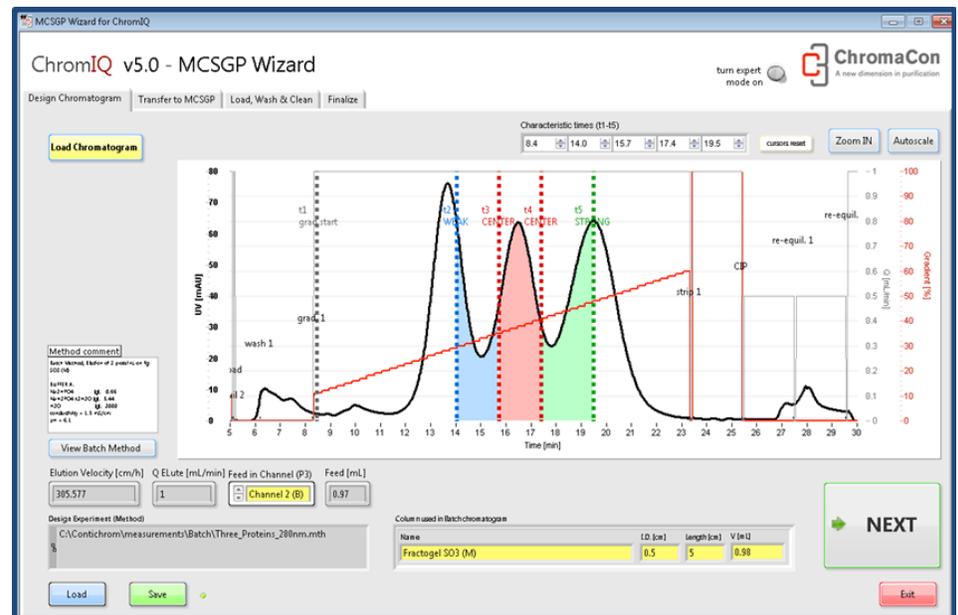
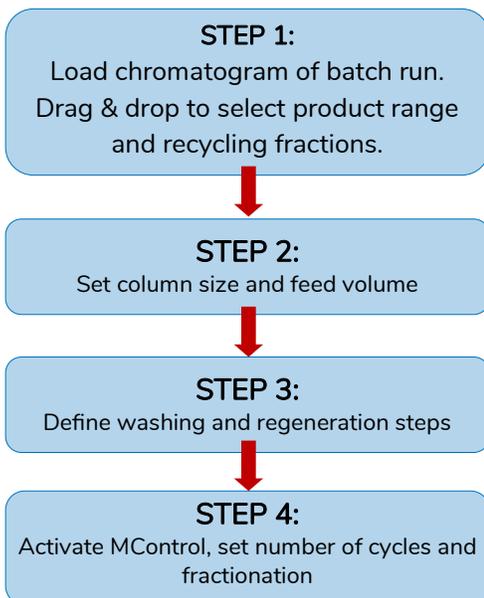
# Process Wizards

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

## CaptureSMB



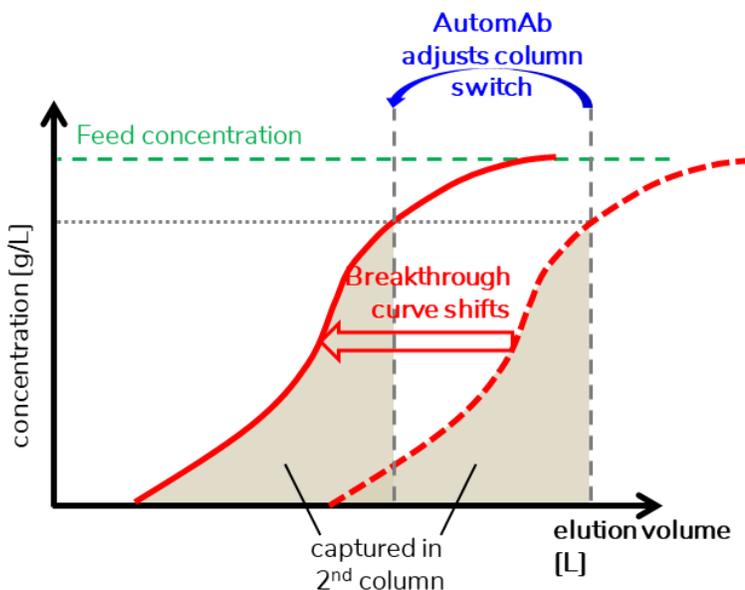
## MCSGP



# 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.

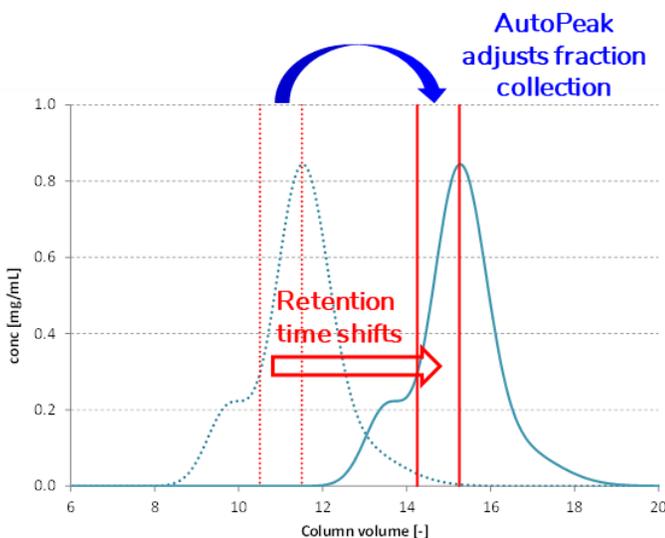


### Advantages of AutomAb

- ◆ 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

## AutoPeak: 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 function 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 AutoPeak

- ◆ AutoPeak 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

# Technical Specifications

## Contichrom CUBE systems

<b>Process capabilities:</b>	Batch (isocratic, gradient), integrated batch, CaptureSMB, MCSGP, N-Rich
<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 (cannot be deleted)</li></ul>
<b>Pressure rating:</b>	100 bar (10 MPa)/ 1450 psi
<b>Flow rate range:</b>	<ul style="list-style-type: none"><li>• 0.1 – 36 mL/min (Contichrom CUBE 30)</li><li>• 0.1 – 100 mL/min (Contichrom CUBE 100)</li></ul>
<b>Buffer selection:</b>	16 Inlets (2 x 8-fold buffer selection valve) 4 Outlets
<b>UV:</b>	2 external UV detectors with 2 variable wavelengths 200-600 nm recorded simultaneously
<b>Conductivity monitoring:</b>	2 Conductivity sensors (1-300 mS/cm)
<b>pH monitoring:</b>	1-14
<b>Pump type:</b>	4 High precision double-piston-pumps with active seal wash
<b>Valves:</b>	4 Reliable multi-position valves
<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 1: 450 mm x 509 mm x 370 mm (20.0" x 17.7" x 14.6") CUBE module 2 : 450 mm x 509 mm x 214 mm (20.0" x 17.7" x 8.4") The CUBE modules are stackable. External detector modules (stackable) each 280 mm x 463 mm x 135 mm (11.0" x 18.2" x 5.3")
<b>Weight:</b>	CUBE module 1 & 2: 17 kg (38 lb)
<b>Materials:</b>	All biocompatible High pressure side capillaries: PEEK Low pressure side tubing: FEP Fittings: PEEK

# GMP Scale-up

## Twin-column process scale

Contichrom® TWIN platform: Best-in-class GMP skids



Contichrom TWIN CaptureSMB 1000 custom unit shown above.

### Example TWIN LPLC product features:

- Ability to run batch, integrated / sequential batch, parallel batch and (continuous) CaptureSMB.
- CIP Option
- Scale-up method conversion
- Allan-Bradley Rockwell or Delta-V operating system
- Compliant with ASME/BPE, GAMP, ASTM, 21CFR part 11
- Integrated Buffer In-line Dilution (BID)
- 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
- Optional single use interface (shown)

Reference papers: Bristol Myers Squibb using Contichrom 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>

TWIN CaptureSMB LPLC	Min L/min	Max L/min	TWIN MCSGP HPLC	System Flow Rate Range (L/min)	Flow Rate Range (L/min) [Recommended]	Column ID Range (cm)
Twin 100	0.004	0.8	100	0.0055 - 0.94	0.01 – 0.67	2.5 - 10
Twin 300	0.02	3.3	300	0.023 – 3.74	0.03 – 3.33	10 -20
Twin 500	0.06	10	500	0.063 – 10.7	0.15 – 8.33	20 - 45

# After-Sales Services

## Training, Maintenance, and Repair

### A reliable and cost-effective service network

Purchasing a CUBE System and operating it are 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 provide on-site and off-site training, webinar-based product support, and 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 us 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 more details, please request a quote from your local YMC representative.

# More YMC Products

## HPLC Columns and Resins

YMC is proud to be a trusted developer and manufacturer of high-quality, reliable, and reproducible resins that are used by chromatographers around the world. Our portfolio contains a wide range of product lines in reversed-phase, normal phase, ion exchange, chiral, and SEC chemistries. YMC media is available in pre-packed columns as well as bulk quantities of packing material, allowing seamless scale-up to preparative applications.

For more information about YMC columns and which products to use with your Contichrom CUBE, ask your YMC representative.



# Contact Information



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

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The YMC logo consists of the letters 'YMC' in a bold, blue, sans-serif font.

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