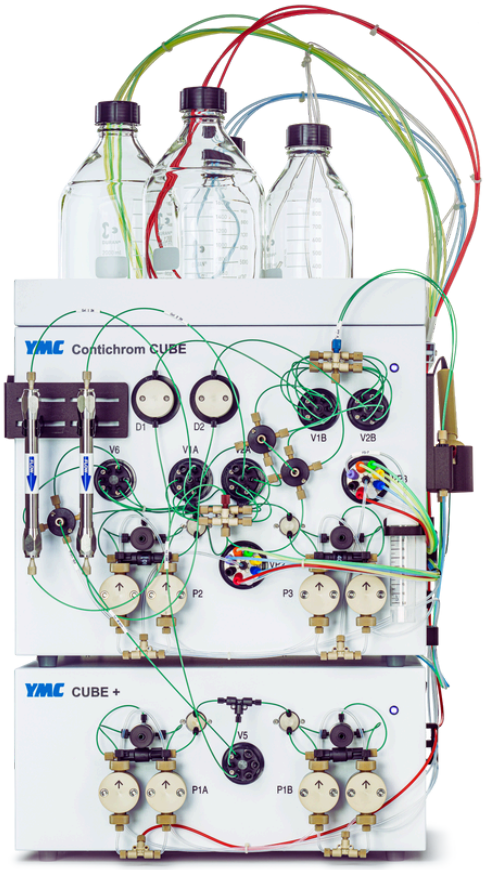
Contichrom® CUBE

Advanced System for Batch, 2D/3D Integrated Batch, and Continuous Chromatography



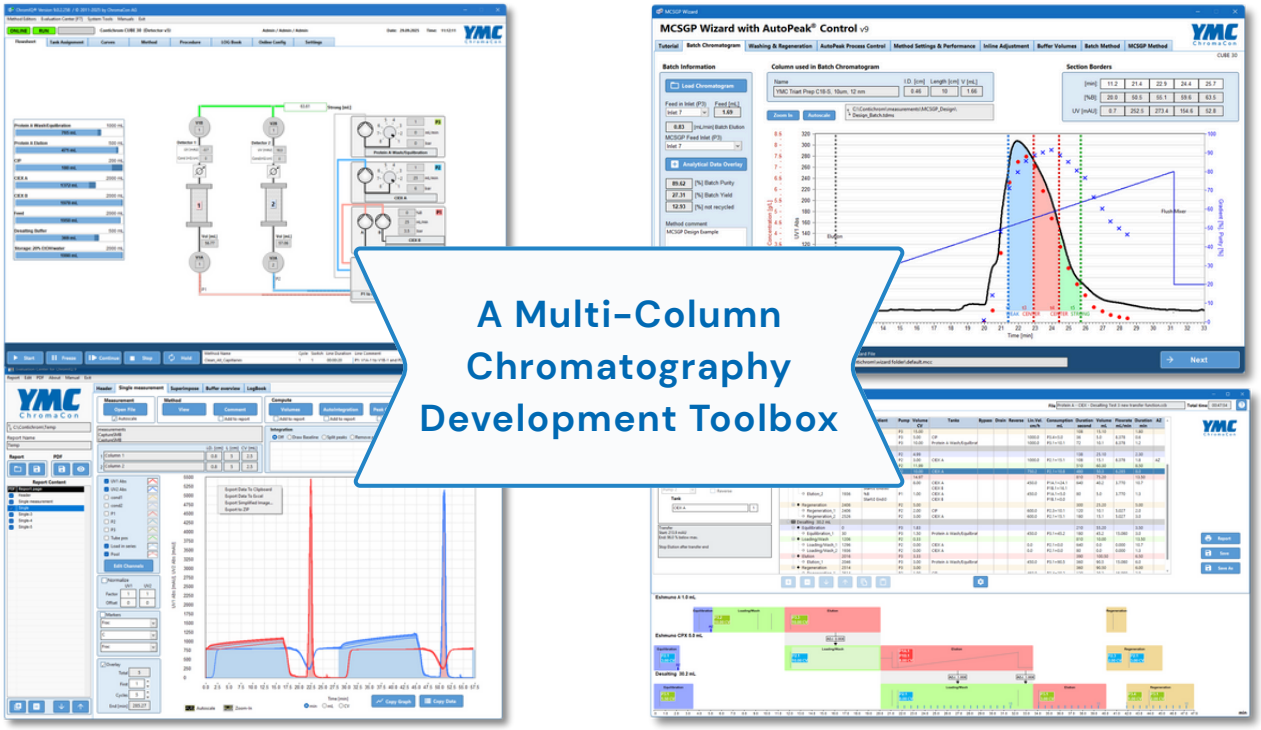
Next Generation Purification and Process Development

Rapidly develop robust and economical purification processes with the Contichrom® CUBE, a versatile and scalable Fast Protein Liquid Chromatography (FPLC) system. The hardware and software are built for multi-column functionality out of the box, which is key to quickly implementing 2D/3D integrated batch and advanced twin-column continuous chromatography processes like MCSGP with AutoPeak®.

Thanks to the system's robust 100-bar design, higher flow rates and better resolution can be obtained. This design easily accommodates modern, high-performance resins (with particle sizes down to 10 µm) across all common chemistries: Protein A/L/G, IEX, RP (C-18, C-8, C-4), MMC, HIC, IMAC, and SEC. The system is therefore ideally positioned for the preparative-scale purification of challenging biotherapeutics, including monoclonal antibodies (mAbs), ADCs, AAVs, proteins, peptides, and oligonucleotides.

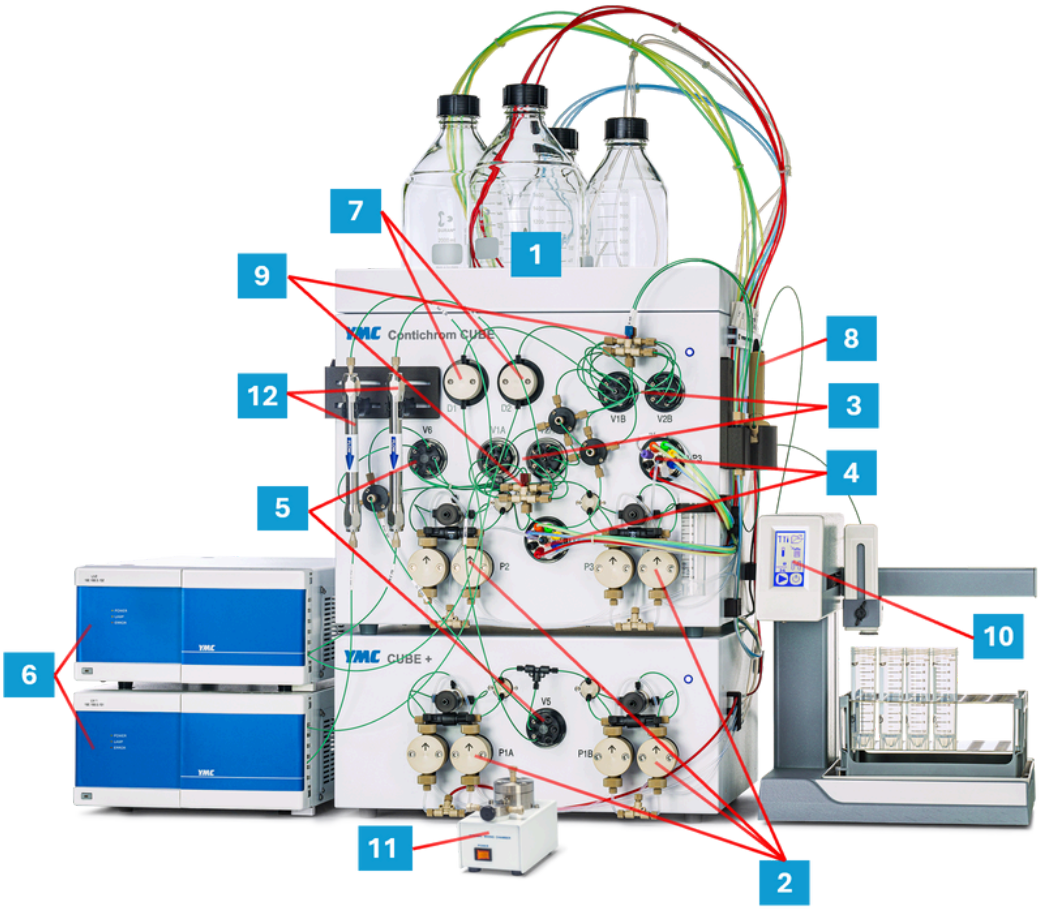
ChromIQ® 9 Software Suite

The ChromIQ 9 suite features a collection of intuitive, wizard-driven modules, each tailored to a specific purification challenge — from standard batch chromatography, 2D/3D integrated batch chromatography, as well as advanced, continuous capture and polishing — all accessible from a single, centralized interface.



Contichrom® CUBE: Hardware Overview

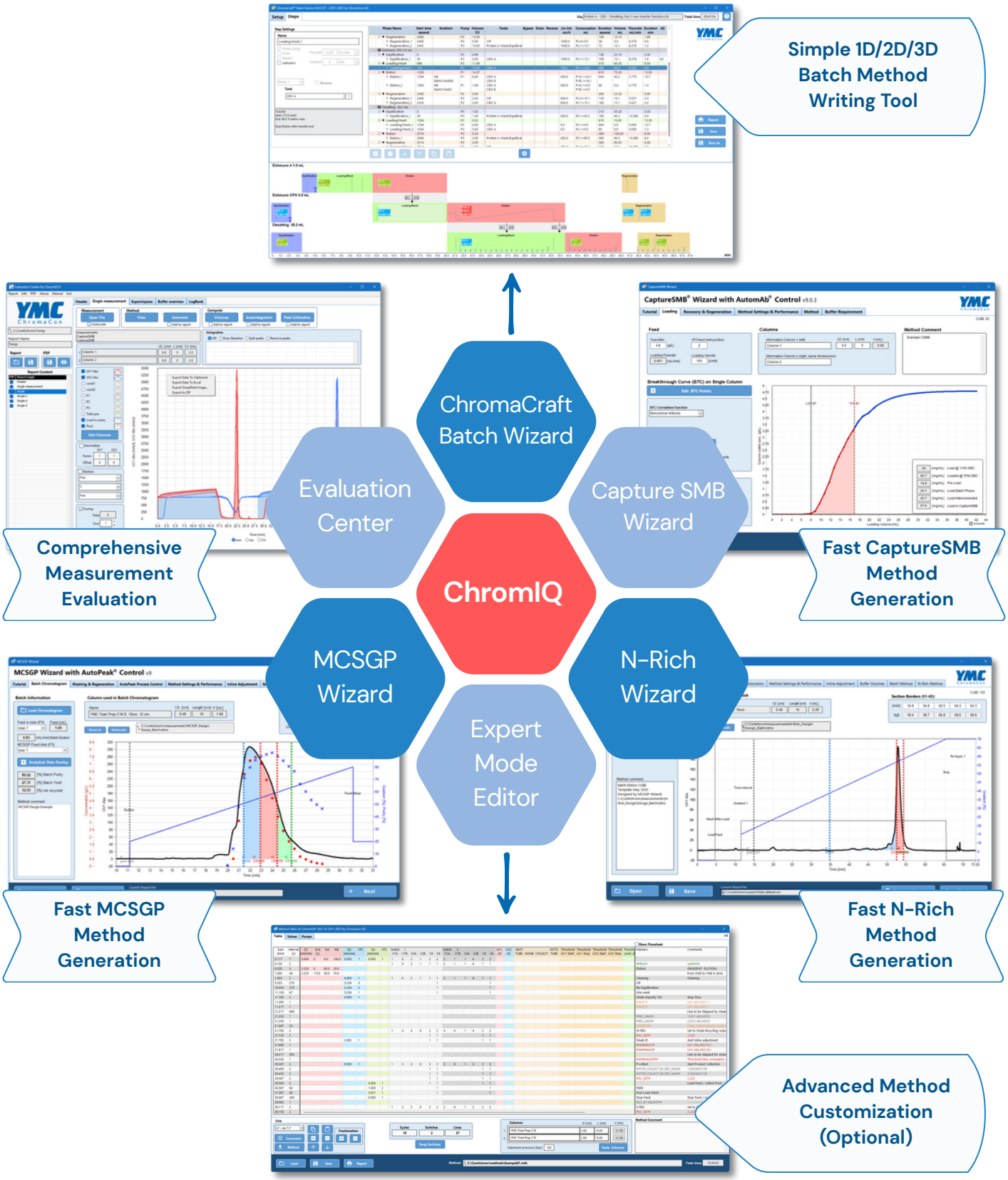
The Contichrom® CUBE system is built on a foundation of robust, high-performance hardware components, engineered for reliability and flexibility. The standard base configuration enables a wide range of applications, from basic batch chromatography to the most advanced continuous processes.



1. **Compact modular system (100 bar):** Large buffer tray
2. **Pumps (x4):** 2 Gradient pumps, 1 Feed pump & 1 Wash pump (36 & 100 mL/min options)
3. **Column selection valves (x4):** Provides inlets and outlets for 2 columns
4. **Buffer selection valves (x2):** Connected to Feed & Wash pumps (8 inlets each)
5. **Drain valves (x2):** Allows rapid purging of all pumps
6. **UV-Vis Detectors (x2):** External, variable 4-channel multi-wavelength (200-600 nm)
7. **Conductivity sensors (x2):** Internal, temperature-compensated monitoring (0–250 mS/cm)
8. **pH sensor:** pH range 1–14
9. **Flow path:** Tubing and fittings are selected to ensure biocompatibility and high-pressure performance
10. **Fraction collector:** High-capacity R1 (single rack) and R2 (dual rack) options
11. **Dynamic mixer:** Ensures homogeneous mixing for reproducible gradients
12. **Recommended Column ID:** Contichrom CUBE 30 = 0.5 - 2.7 cm
    Contichrom CUBE 100 = 0.8 - 5.0 cm

ChromIQ 9: Software Suite Overview

ChromIQ 9 is a versatile and comprehensive software suite that facilitates all aspects of single and multi-column process development, from method design to data analysis.



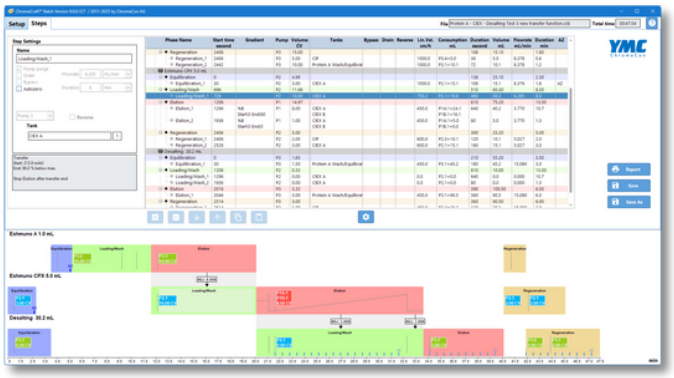
ChromIQ 9: Visually Aided Method Design

ChromaCraft enables easy Batch & 2D/3D Integrated Batch design

STEP 1:
Choose process type and define buffer setup

STEP 2:
Enter column and step parameters into table

STEP 3:
Set product transfer and fractionation triggers, auto-generate method

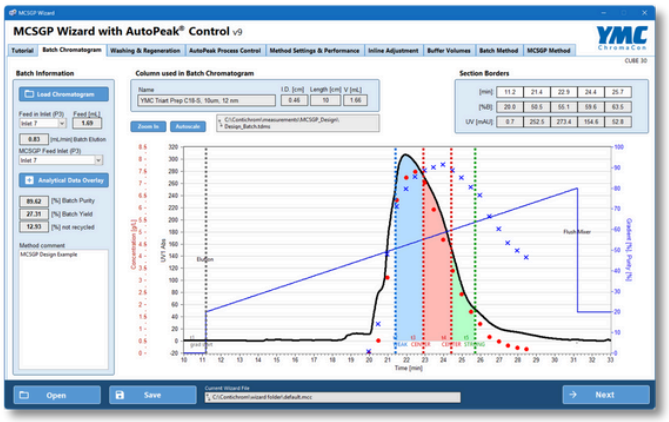


MCSGP Wizard for easy Batch to MCSGP method transfer and process performance prediction

STEP 1:
Load batch run chromatogram and define product and recycling phases by Drag & Drop

STEP 2:
Define washing and regeneration steps, activate AutoPeak

STEP 3:
Set number of cycles, receive performance prediction and auto-generate methods

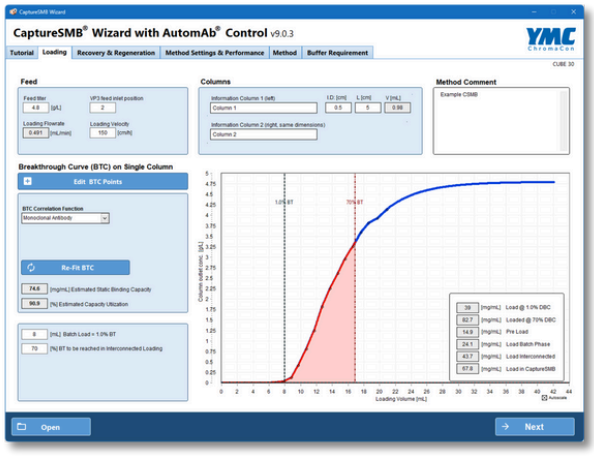


CaptureSMB Wizard for easy CaptureSMB method creation and process performance prediction

STEP 1:
Enter feed and column parameters and fit experimental breakthrough curve

STEP 2:
Define washing and regeneration steps, activate AutomAb

STEP 3:
Set number of cycles, receive performance prediction and auto-generate methods

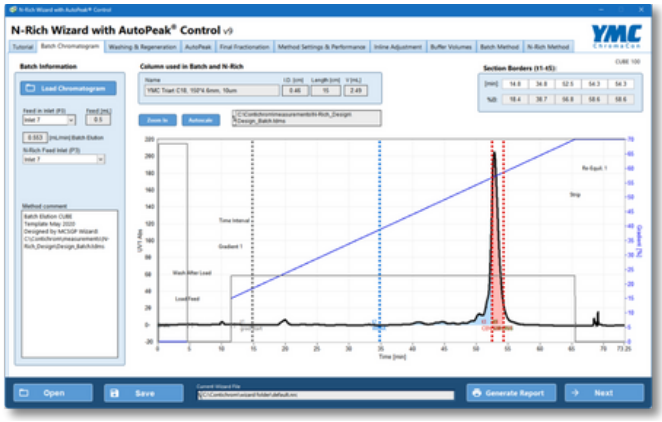


N-Rich Wizard for easy Batch to N-Rich method conversion

STEP 1:
Load batch run chromatogram and define enrichment zones by Drag & Drop

STEP 2:
Define washing and regeneration steps, activate AutoPeak

STEP 3:
Set number of enrichment cycles, define final elution protocol and fractionation scheme, auto-generate methods



ChromIQ 9: Software Modules

Software Module	Primary Function	Key Features & Benefits
ChromIQ 9 Operating Software	Direct hardware control, method execution, and real-time monitoring for the complete chromatographic purification workflow.	Access all software modules and documentation, setup user-rights management, change the hardware configuration and settings, configure the buffer management system, run a method or a multi-method procedure, access dynamic flow-sheet, customize and view real-time data/signals, apply on-the-fly method changes, view the log book.
ChromaCraft™ Batch	Easy-to-use method editor for creating standard single-column and complex multi-column batch chromatography methods.	Features a dynamic, chronological Gantt Chart that provides instant, visual feedback for easy method building. Includes a dedicated **Product Transfer Window** for setting UV transfer criteria and in-line dilution parameters between integrated purification steps.
CaptureSMB® Wizard	Wizard for designing twin-column continuous capture chromatography procceses.	Requires input of a single batch breakthrough curve; interface analyses curve to automatically set process parameters; includes **AutomAb®**, a dynamic control system that uses real-time UV to trigger phase switches, ensuring consistent loading despite feed titer variations.
MCSGP Wizard	Wizard for designing twin-column continuous polishing processes.	Method design is based on visually defining elution zones (early/late eluting side-fraction recycle, product collection) on a batch chromatogram using drag-and-drop lines; uses **AutoPeak®** dynamic control to align collection with the peak using real-time UV triggers, adapting to retention time shifts.
N-Rich® Wizard	Wizard for setting up automated, twin-column cyclic processes to enrich and isolate low-abundance impurities.	Design uses the visual, drag-and-drop interface to define the main product depletion zone and the target compound recycle zones; automated recycling achieves on-column accumulation of target compounds before a final elution.
Evaluation Center	Integrated module for comprehensive analysis, visualization, and compilation of all continuous and batch run data.	Evaluation Center has unique tools for analyzing continuous chromatography runs including one-click **Cycle Overlay** to visually confirm cyclic steady state; and **Auto Integration** to quantify and monitor the evolution of process phases; export professional, structured PDF reports directly or export data to Excel for analysis.
Method Editor (Expert Mode)	Expert-level, timetable-based interface for precise, line-by-line programming of all hardware commands and conditional logic.	Provides complete, granular control for advanced users; enables fine-tuning of methods generated by the wizards and creation of highly customized protocols.
OPC UA Interface	Connectivity function to integrate the system with external interfaces.	Supports the OPC UA communication protocol for seamless data exchange.

Contichrom®: Overview of Process Capabilities

While the Contichrom CUBE can easily execute standard single-column batch capture & gradient polishing purification methods, the core innovation of the Contichrom CUBE system lies in its ability to run integrated & multi-column continuous processes with integrated dynamic process control (AutoPeak and AutomAb). This technology moves beyond the limitations of sequential batch chromatography, enabling interconnected, continuous operations that **fundamentally improve process economics and efficiency**.

MCSGP with AutoPeak®

Continuous polishing chromatography with automated side-cut recycling

Oligonucleotides Peptides **mAbs** Recombinant proteins **AAV** mRNA **Vaccines** Blood plasma proteins

CaptureSMB with AutomAb®

Continuous capture chromatography for maximum resin utilization

mAbs Bi-specifics **mRNA** Vaccines **Recombinant proteins** Blood plasma proteins

N-Rich with AutoPeak®

Automated enrichment and purification of impurities from complex matrices

Impurity isolation from: Oligonucleotides **Peptides** mAbs **Recombinant proteins** AAV **mRNA**

2D/3D Integrated Batch

Integrate multiple orthogonal purification steps on one system

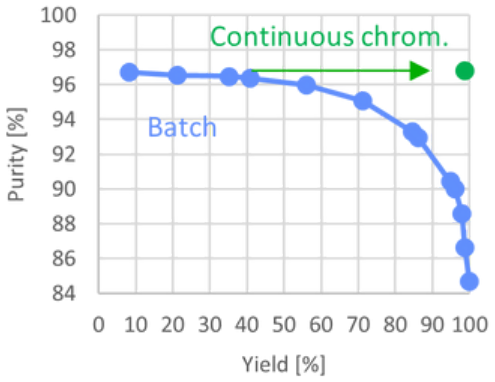
Oligonucleotides Peptides **mAbs** Recombinant proteins **AAV** mRNA **Vaccines** Blood plasma proteins

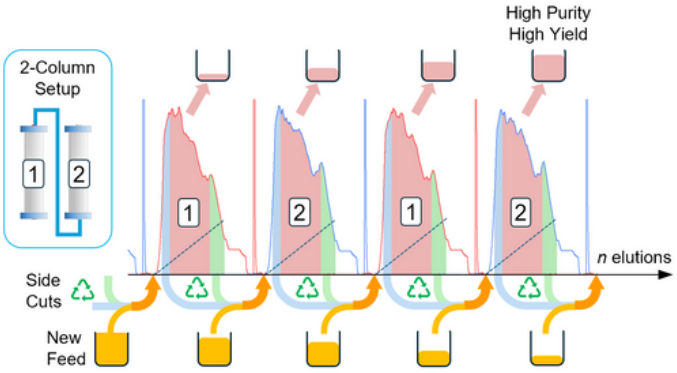
MCSGP with AutoPeak® Dynamic Control

Eliminating the Purity-Yield Trade-off

THE CHALLENGE: Conventional single-column batch chromatography for polishing steps (for complex APIs like oligos and peptides) is limited by an inherent purity-yield trade-off. Achieving high purity requires discarding low-purity side-fractions, leading to significant product loss or demanding costly external re-chromatography, which drives up Cost of Goods (CoG).

THE SOLUTION: MCSGP with AutoPeak is a continuous polishing technology utilizing a twin-column system. MCSGP maximizes both yield and purity simultaneously by internally recycling low-purity side cuts, providing exceptional process robustness and eliminating re-chromatography.





How MCSGP works

MCSGP is a cyclic process that alternates ("switches") between two twin-columns. Each switch consists of a complete elution of one column, while the second column is cleaned and loaded:

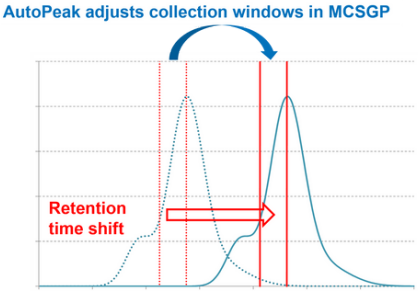
Interconnected phases: Low-purity side-cuts eluting from Column 1 are transferred with in-line dilution buffer to ensure re-adsorption of the valuable product on the downstream column.

Parallel Phase: Column 1 elutes and high-purity center-cut product is collected while Column 2 is simultaneously loaded with new crude feed.

At the end of a switch, the columns switch positions, and the purification process repeats without interruption, maximizing recovery and minimizing waste.

AutoPeak® Control for MCSGP

To ensure consistent high purity and yield despite batch-to-batch variations, AutoPeak uses in-line sensors (UV and conductivity) to monitor the elution profile in real-time. The system dynamically adjusts chromatographic phase boundaries (e.g., product collection start/stop) to compensate for retention time shifts, column aging, bed-height differences, or feed variability, enabling robust, continuous runs with minimal supervision.



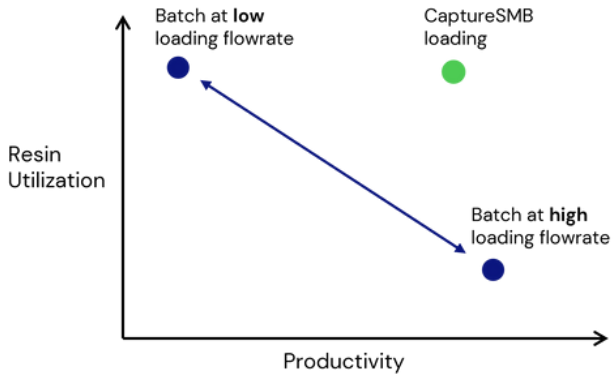
MCSGP Features	Operational Benefit	Quantified Result	Conventional Batch Limitation
• **Multi-column Countercurrent Principle**	Eliminates the purity-yield trade-off. Achieves high yield and high purity simultaneously.	**10% to 50% absolute increase in product yield**	Requires conservative center-cut fractionation, leading to product loss or external reprocessing.
• **Internal Product Recycling with In-line Dilution**	Eliminates the costly re-chromatography steps. Reduces analytical/QC burden.	**Re-chromatography is eliminated. Up to 5x higher throughput for equivalent product output.**	Requires pooling, storage, and re-running of low-purity side-cuts from multiple batches.
• **AutoPeak Dynamic Process Control**	Ensures process robustness and consistent output quality by adapting to process drift.	**Enables extended, automated 24/7 operation.**	Product pools are identified post-chromatography and after significant analytical testing
• **Parallel Operation and Smaller Columns**	Boosts throughput and reduces equipment and buffer costs (CAPEX/OPEX).	**Allows for smaller column dimensions and utilizes parallel processing to eliminate column idle time.**	Restricted by long, sequential cycle times and requires large columns to handle batch volumes.

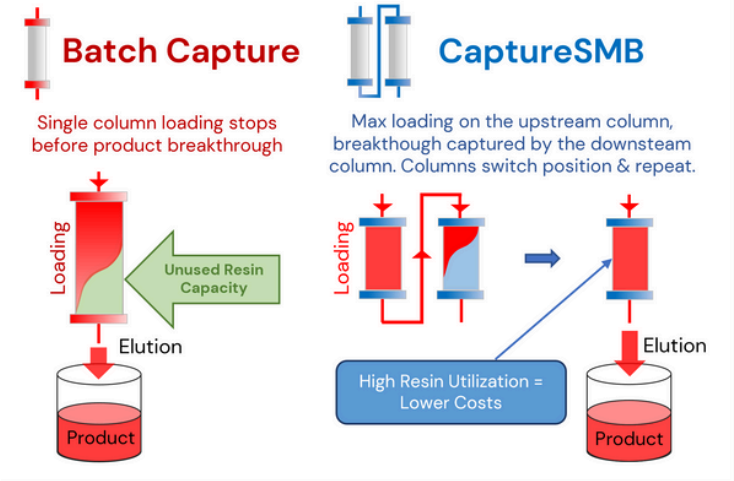
CaptureSMB with AutomAb® Dynamic Control

Driving 2-4x Productivity in Bioprocessing

THE CHALLENGE: Conventional batch chromatography, especially the initial Protein A capture for Monoclonal Antibodies (mAbs), is inherently inefficient. Columns are large and expensive due to low resin utilization (typically 50-70% DBC) and long idle times, driving up costs and process time.

THE SOLUTION: CaptureSMB is a paradigm shift to continuous capture, utilizing two columns in a countercurrent fashion. This process has two types of phases; parallel phases and interconnected phases, together they provide significant performance advantages over batch capture methods, maximizing resin utilization, shrinking column size, and dramatically boosting overall throughput.



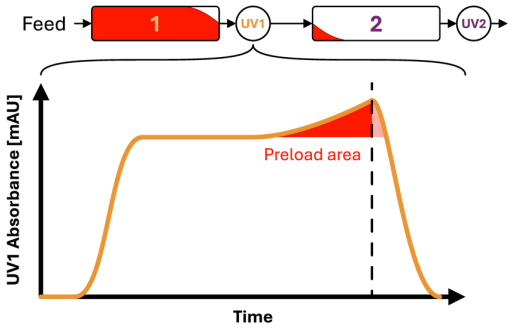


How CaptureSMB Works

CaptureSMB uses a 2-column setup operating in a continuous, cyclical manner. During the interconnected phase, as one upstream affinity capture column becomes saturated, the feed is automatically switched to the next column. The saturated column proceeds through the remaining steps (wash, elution, regeneration, re-equilibration) in parallel. Once finished, columns switch position. This coordinated, continuous loading and parallel processing results in maximum resin utilization, reduced buffer usage, and decoupled operation, streamlining the entire manufacturing train.

AutomAb® Control for CaptureSMB

To ensure optimal loading despite batch-to-batch variations in feed titer or product quality, AutomAb control utilizes a pair of in-line UV sensors, located at the column exit, to monitor the breakthrough curve in real-time. The system dynamically adjusts the inter-connected loading duration based on these real-time measurements, ensuring mAb that load duration responds to column aging and feed titer variations over time.



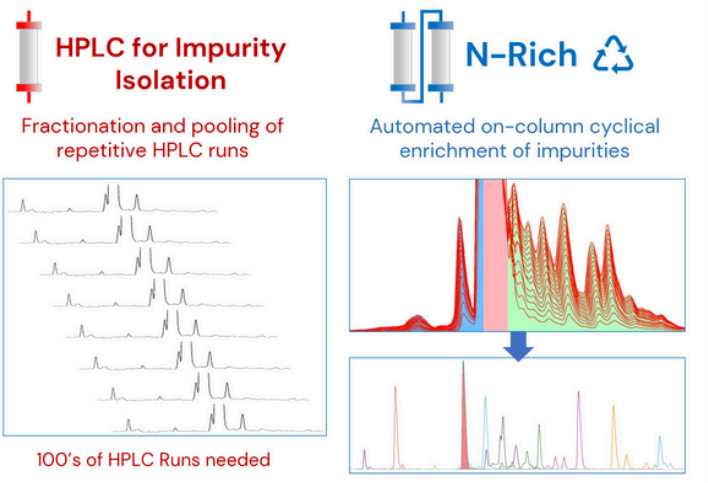
CaptureSMB Features	Operational Benefit	Quantified Result	Conventional Batch Limitation
• **Periodic Countercurrent Operation (PCC)**	Maximizes resin utilization (safely load beyond breakthrough).	**20% to 50% reduction in resin volume**	Only utilizes 50–70% Resin Binding Capacity.
• **AutomAb dynamic process control**	Ensures process robustness and consistent output quality.	**Avoids yield loss by dynamically adjusting to feed titer variability**	Requires conservative timing, reducing overall efficiency.
• **Continuous loading & parallel processing**	Boosts throughput. Eliminates column idle time.	**2x to 4x higher productivity**	Restricted by long, sequential cycle times.
• **Smaller column dimensions**	Reduces equipment and buffer costs (CAPEX/OPEX).	**Up to 50% reduction in buffer consumption**	Requires large columns and high-volume buffer tanks.

N-Rich: Automated Compound Enrichment

Solving the Bottleneck of Impurity Isolation

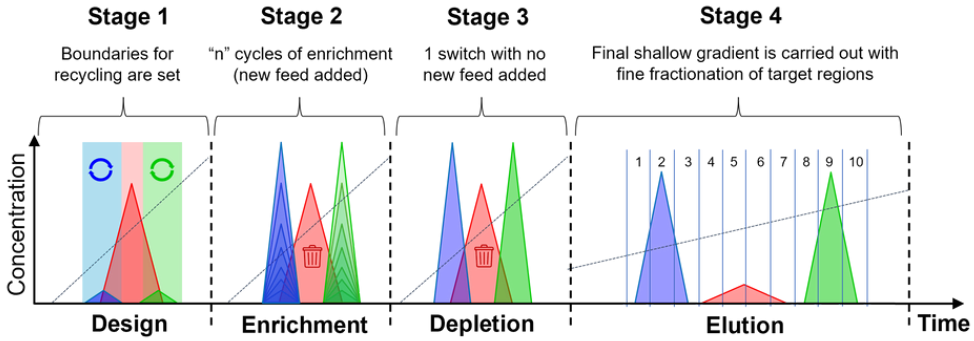
THE CHALLENGE: High-value therapeutic drug development (Peptides, Oligonucleotides, Proteins, mAbs) requires the identification and characterization of low-abundance impurities or variants (ICH guidelines). Obtaining the necessary milligram quantities of these minor compounds requires highly repetitive, low-productivity analytical HPLC runs that can take weeks or months of continuous operation, creating a critical bottleneck.

THE SOLUTION: N-Rich is a cyclic/continuous twin-column chromatography process designed to automatically enrich the target compounds (impurities or variants) on-column from cycle-to-cycle. This process enables the fast isolation of milligram quantities, utilizing cost-effective semi-preparative media while achieving high-resolution results.



How N-Rich Works

N-Rich is composed of three distinct phases; enrichment, depletion, and elution. During enrichment, target is accumulated and concentrated (see blue and green peaks below) while non-target material is depleted and removed (red). To achieve this, the process uses two columns, switching their positions to ensure the target compound is continuously recycled onto the second column with in-line dilution to enable re-adsorption, while any unwanted components are directed to waste. Fresh feed is added each cycle to ensure a steady supply of target compound for enrichment.



N-Rich Features	Operational Benefit	Quantified Result*	Conventional Batch Limitation
• **On-Column Cyclic Enrichment & Accumulation**	Isolates milligram-scale minor compounds. Eliminates hundreds of analytical runs and pooling.	**Up to 80x faster processing (peptide). Time cut from 32 days to 3 days (mAb).**	Time-consuming pooling from hundreds/thousands of HPLC runs. Low total mass recovery.
• **Two-Column Continuous Operation with In-Line Dilution**	Enables high-resolution purification using cost-effective semi-prep media via displacement effects.	**11x purity improvement over semi-prep batch. Fractions elute at a higher concentration (reduces up-concentration).**	Insufficient resolution on cost-effective semi-prep resins.
• **Targeted/Broad Enrichment Strategy**	Flexible design for single co-eluting impurities or broad spectrum enrichment.	**Achieved 88% purity on critical co-eluting impurity. Up to 70x reduction in solvent consumption.**	Isolation limited by co-elution properties. High solvent cost and waste.
• **UV-Based Dynamic Process Control (AutoPeak)**	Ensures robust, unattended operation by compensating for retention time shifts.	**Unattended operation for multiple cycles/days. Consistent purity from run to run.**	Requires constant monitoring and manual fraction cut adjustments.

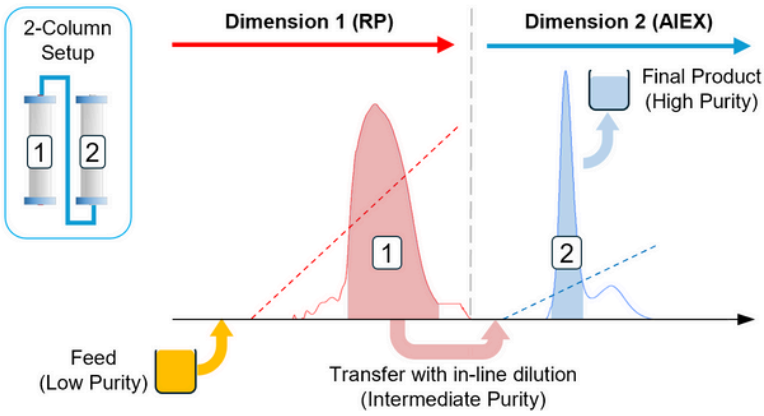
**Enrichment and purification of peptide impurities using twin-column continuous chromatography, Journal of Chromatography A, Volume 1667, 2022*

Contichrom®: Batch/2D/3D Capabilities

2D Integrated Chromatography for TIDES

Beyond fully continuous processes, the twin-column setup is ideal for performing 2D integrated batch chromatography. This powerful capability allows for the direct coupling of two different chromatography steps (e.g., Dimension 1 = Reversed Phase polishing (RP), Dimension 2 = AIEX polishing) into a single, automated process. The product-containing eluate from the first column is directly transferred to the second column (see diagram), with inline dilution to ensure optimal binding conditions. This eliminates the need for intermediate hold tanks, manual handling, and associated quality control, significantly reducing process time and facility footprint.

2-Step: 2x Gradient Polishing



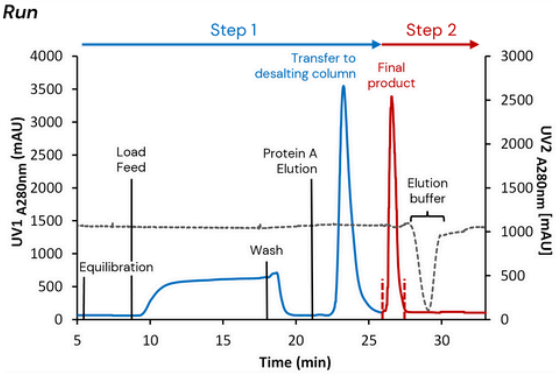
2D/3D Integrated Chromatography for mAbs/Proteins

2-Step: Protein A Capture + Desalting

Conditions

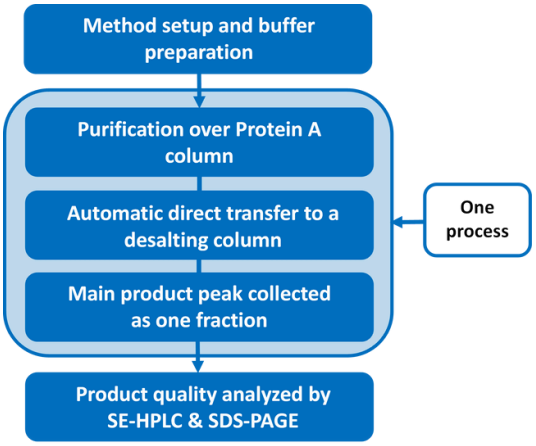
Feed: Cell culture supernatant (monoclonal antibody)
Step 1: Protein A (Affinity capture)
Step 2: Desalting (Buffer exchange)

Run

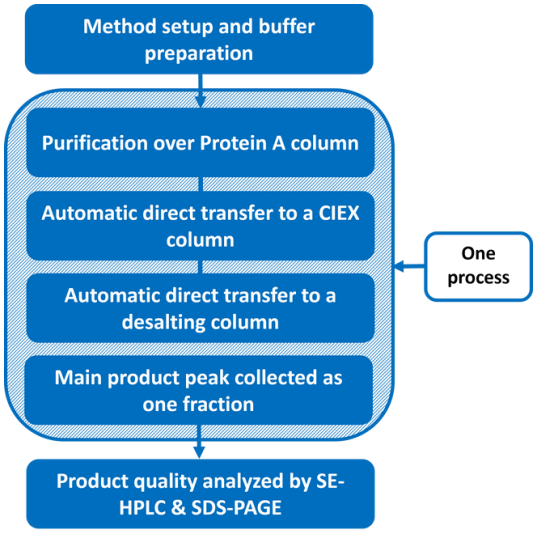


Standard Protein A affinity capture step

Final sample is buffer exchanged and ready to use



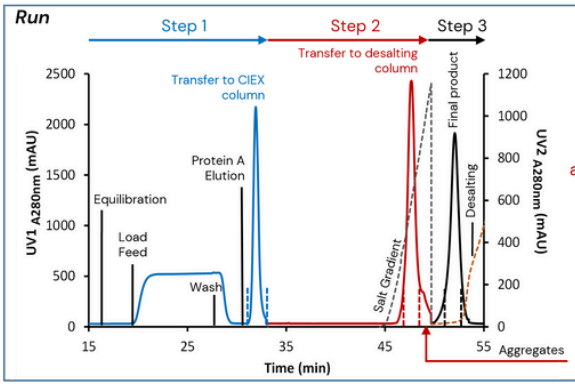
3-Step: Protein A Capture + CIEX Polishing + Desalting



Conditions

Feed: Cell culture supernatant (monoclonal antibody)
Step 1: Protein A (Affinity capture)
Step 2: CIEX (Polishing)
Step 3: Desalting (Buffer exchange)

Run



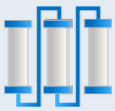
Standard Protein A affinity capture step

Integrated CIEX aggregate removal step

Final sample is buffer exchanged and ready to use

Contichrom®: Batch/2D/3D Capabilities

The Contichrom CUBE + ChromaCraft Batch method creation tool unlocks the possibility to create a wide variety batch and integrated batch purification processes customized to your specific purification needs. The table below is a summary of possible purification types that can be executed along with a description of the supported accessories required for the job (For accessories see page 18).

Dimensions	1st Step	2nd Step	3rd Step	Required Accessory Hardware
 **Batch**	Isocratic *Affinity chromatography (Protein A, Protein L, His-Tag) Size Exclusion Chromatography Desalting*			No additional hardware required (Column Bypass Valves are very useful for all applications)
	Gradient *IEX, RP, Mixed Mode*			
 **2D Batch* (Integrated)**	Isocratic *Affinity chromatography (Protein A, Protein L, His-Tag)*	Isocratic *Size Exclusion Chromatography, Desalting*		
	Isocratic *Affinity chromatography (Protein A, Protein L, His-Tag)*	Gradient *IEX, RP, Mixed Mode*		
	Gradient *IEX, RP, Mixed Mode*	Gradient *IEX, RP, Mixed Mode*		Buffer Selection Valve Kit for Gradient Pump 1A & 1B Column Bypass Valve Kit
 **3D Batch (Integrated)**	Isocratic *Affinity chromatography (Protein A, Protein L, His-Tag)*	Gradient *IEX, RP, Mixed Mode*	Isocratic *Size Exclusion Chromatography, Desalting*	Buffer Selection Valve Kit for Gradient Pump 1A & 1B Column Bypass Valve Kit Column Selection Valve Kit
	Isocratic *Affinity chromatography (Protein A, Protein L, His-Tag)*	Gradient *IEX, RP, Mixed Mode*	Gradient *IEX, RP, Mixed Mode*	
	Gradient *IEX, RP, Mixed Mode*	Gradient *IEX, RP, Mixed Mode*	Isocratic *Size Exclusion Chromatography, Desalting*	

*Alternating batch is also supported in the ChromaCraft Batch Editor

Contichrom®: Summary of Technology Advantages

MCSGP with AutoPeak®

Continuous polishing chromatography with automated side-cut recycling

- Increase yield at target purity
- Eliminate re-chromatography
- Reduce QC burden
- Increase project throughput
- 24/7 continuous manufacturing
- Dynamic process control

- Significantly Reduce PMI

Oligonucleotides Peptides **mAbs**
Recombinant proteins **AAV** mRNA
Vaccines Blood plasma

CaptureSMB with AutomAb®

Continuous capture chromatography for maximum resin utilization

- Increase resin capacity utilization
- Decrease buffer consumption
- Increase productivity
- Decrease manufacturing footprint
- Dynamic loading control
- 24/7 continuous manufacturing

- Reduced Cost of Goods (CoGs)

mAbs Bi-specifics **mRNA** Vaccines
Recombinant proteins Blood plasma

N-Rich with AutoPeak®

Automated enrichment and purification of impurities from complex matrices

- Automated on-column enrichment
- Analytical purity, semi-preparative scale
- Increase sample concentration
- Fewer fractions for pooling
- Less up-concentration needed

- Reduced solvent consumption

Impurity isolation from:
Oligonucleotides **Peptides** mAbs
Recombinant proteins AAV **mRNA**

2D/3D Integrated Batch

Integrate multiple orthogonal purification steps on one system

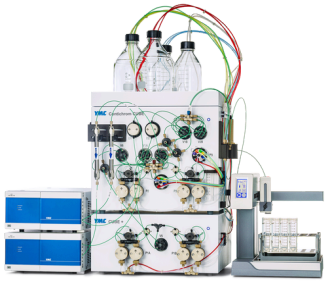
- Link multiple purification steps
- Automated, end-to-end purification e.g. Capture > Polishing > Desalting
- Seamless, rapid processing
- Single product pools
- Eliminate all manual steps between purifications
- Reduced consumables usage

Oligonucleotides Peptides **mAbs**
Recombinant proteins **AAV** mRNA
Vaccines Blood plasma

Contichrom®: A Scalable Purification Platform

Processes developed on the Contichrom CUBE scale easily to the Contichrom PILOT 300X, Contichrom TWIN LPLC or the Contichrom TWIN HPLC. Visit our website for more information about our production-scale systems.

Contichrom CUBE (Development)



100 mL/min, 100 Bar

Contichrom PILOT 300X (Small-Scale Production)

300 mL/min, 100 Bar

Contichrom TWIN LPLC / HPLC (Large-Scale Production)

1 - 40 L/min
20 Bar & 100 Bar
(Customizable)

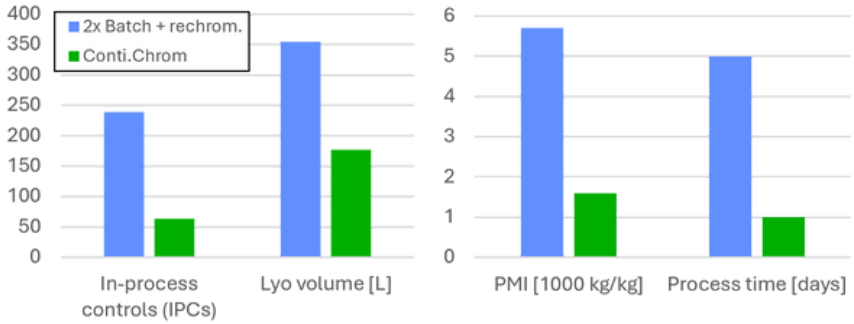
Industrial Validation for Peptides: Saving 80% of time and 100s of IPC analyses

Leading CDMO Bachem adopted process-scale MCSGP for tides manufacturing, confirming the technology's viability for high-volume commercial production under GMP.

Continuous Chrom. Advantages:

- Processing time reduced 80%
- Lyophillization-volume cut by 50%
- Solvents/buffers cut by 70%
- IPCs cut by 75-95%
- Re-chromatography eliminated

Source: Case Study: Reducing Solvent Consumption for large-scale peptide API manufacturing
https://www.bachem.com/knowledge-center/white-papers/



Contichrom® CUBE: Hardware Components

System Overview

The Contichrom CUBE system consists of two stackable modules: the lower CUBE+ module and the upper CUBE module. In addition, external UV detectors, a fraction collector, and an operating PC are typically supplied as standard. Excluding the PC, the system requires total space of **120 cm (W) x 70 cm (D)**, making it suitable for placement on a standard lab bench or in a cold room (4°C) for work with thermally sensitive molecules. The front of the unit provides clear access to the wetted flow path components, including pumps, valves, and detector connections, simplifying user interaction and maintenance. A large, integrated buffer tray on top of the CUBE module provides ample storage for mobile phase containers.

High-Precision Pumps with Pressure Sensors

The system is equipped with four high-precision, dual-piston pumps that are the engine of its versatile fluidic capabilities. These pumps are designed for high flow rate accuracy and the low pulsation required for high-performance liquid chromatography.

- **Pump Configuration:** Pumps **P1A** and **P1B**, located in the CUBE+ module, are joined on the high-pressure side to function as a binary gradient pump, enabling the generation of precise linear gradients. Pumps **P2** and **P3**, located in the CUBE module, operate as independent isocratic pumps. Each is equipped with an 8-inlet buffer selection valve, allowing for automated switching between up to 16 different buffers or samples across the two pumps.

- **High-Pressure Operation:** All pumps are rated for a maximum system pressure of **100 bar (10 MPa / 1450 psi)**. This high-pressure capability is essential for use with modern, small-particle-size chromatography resins that provide superior resolution but generate higher backpressures.

- **Flow Rate Range:**
- **CUBE 30**: 0.1 - 36 mL/min
- **CUBE 100:** 0.5 - 100 mL/min
- **Flow Rate Accuracy:** ±2%
- **Flow Rate Precision:** 0.5% RSD

- **Active Seal Wash:** Each pump incorporates an active, self-flushing seal wash feature. This continuous washing of the piston surface with a user-supplied solution (e.g., 20% isopropanol) prevents the precipitation of buffer salts behind the high-pressure seal, a common cause of premature seal failure. This feature significantly enhances the longevity and reliability of the pumps, especially during long, continuous runs with high-salt buffers.

- **Pressure Sensors:** 4x integrated pressure transducers for system and column pressure monitoring

- **Wetted Materials:** The pump fluid path is designed for biocompatibility and chemical resistance, with wetted materials including PEEK, Synthetic Ruby, Sapphire, Zirconia, UHMWPE, and FFKM.

Valve System

A network of six reliable, electrically actuated multi-position rotary valves and two automated drain valves forms the core of the system's fluidic control. This valve arrangement acts as the system's central "traffic controller," enabling the sophisticated, automated switching sequences required for the CaptureSMB, MCSGP, and N-Rich processes.

- **Column Valves:** Four central column valves (V1A, V1B, V2A, V2B) precisely direct flow to, from, and between the two column positions, enabling all single-column and interconnected twin-column operations.

- **Buffer Selection Valves:** Two 8-port valves (VP2, VP3) on the suction side of pumps P2 and P3 allow for automated selection from a wide range of buffers and samples.

- **Drain Valves:** Two automated drain valves (V5, V6) facilitate rapid priming of buffer lines and pumps at high flow rates, directing flow to waste without pressurizing the main system.

- **Wetted Materials:** The valves are designed for biocompatibility and chemical resistance, with wetted material made mainly from PEEK.

Contichrom® CUBE: Hardware Components

To provide comprehensive real-time monitoring of the purification process, the Contichrom CUBE system is equipped with a full suite of detectors. The placement of detectors at the outlet of each column is critical for the dynamic control of twin-column processes.

Multi-wavelength UV Detectors

UV-Vis Detectors: The standard configuration includes two external, variable 4-channel multi-wavelength UV-Vis detectors, with one detector positioned at the outlet of each column.

- **Technology:** Diode Array Detector (DAD)
- **Wavelength Range:** 200–600 nm
- **Channels:** Up to 4 wavelengths can be monitored simultaneously per detector.
- **Light Source:** Long-life deuterium lamp.
- **Optical Path Length:** A standard 0.5 mm path length flow cell is included to provide a wide linear range (0–1000 mAU), preventing detector saturation at high product concentrations. The cells are easily exchangeable for other path lengths.
- **Wetted Materials:** PEEK, Fused Silica, PTFE, Stainless Steel.

Conductivity Sensors

Two internal, temperature-compensated conductivity sensors are located after each UV detector, providing accurate gradient monitoring with a measurement range of 0–250 mS/cm.

Flow Path

All tubing and fittings in the flow path are selected to ensure biocompatibility and high-pressure performance.

- **High-Pressure Tubing (Post-Pump):**
- CUBE 30: PEEK, 1/16" OD, 0.03" (0.75 mm) ID
- CUBE 100: PEEK, 1/16" OD, 0.04" (1.0 mm) ID
- **Low-Pressure Tubing (Pre-Pump):**
- FEP, 1/8" OD, 1/16" (1.55 mm) ID

pH Sensor

An external pH sensor (range 1–14) is typically placed in the product outlet line for in-line pH measurement. The pH flow cell is rated to 7 bar (0.7 MPa).

Fraction Collector

The system supports the high-capacity Foxy R1 (single rack) and Foxy R2 (dual rack) fraction collectors, enabling fully automated, walk-away operation.

- **Capacity:** A wide variety of racks are available to accommodate virtually any collection vessel, including 15 mL and 50 mL centrifuge tubes, 1.5 mL microcentrifuge tubes, and 96-well deep-well or microplates.

- **Contamination Prevention:** A diverter valve with a contained flow path and drip tray with a secondary drain prevents spillage and cross-contamination during tube changes.

Dynamic Mixer

To ensure homogeneous mixing for reproducible gradients, a dynamic mixer is installed after the gradient pumps (P1A/P1B). This is especially critical for reversed-phase applications or when using difficult-to-mix solvents.

- **Design:** The preparative-scale mixer combines a lower chamber with a magnetic stirrer for rapid, dynamic mixing and an optional upper chamber for additional mixing. The mixer also dampens pulsation and ensures a smooth UV baseline in sensitive applications.
- **Volume:** 1.1 mL, or 5.9 mL when upper chamber is installed.
- **Wetted Materials:** Stainless steel is standard, with titanium or PEEK available for biocompatible applications.

Recommended Column ID

- Contichrom CUBE 30 = 0.5 - 2.7 cm
- Contichrom CUBE 100 = 0.8 - 5.0 cm

Contichrom® CUBE: Standard Specification

Category	Parameter	Specification
System	Control System	ChromIQ operating software on an external PC
	Maximum System Pressure	100 bar (10 MPa, 1450 psi)
	Dimensions (W x H x D)	CUBE/CUBE+ Modules (stacked): 45 x 59 x 46 cm, 2x UV Detectors (Stacked): 28 x 27 x 47 cm
	Weight	CUBE Module: 30 kg, CUBE+ Module: 17 kg, 2x UV Detectors: 7.5 kg each
	Power Supply	100-240 V (AC)
	Environmental Conditions	Operating Temperature: +4°C to +30°C (Cold room compatible) Relative Humidity: 20-80%, non-condensing
Pumps	Pump Type	4x High-precision dual-piston pumps with active seal wash - 1x Binary gradient pump (P1A/P1B) - 2x Isocratic pumps (P2, P3)
	Flow Rate Range	**CUBE 30:** 0.1 - 36 mL/min **CUBE 100:** 0.5 - 100 mL/min
	Flow Rate Accuracy	**CUBE 30:** ±2% (above 0.8 mL/min) **CUBE 100:** ±2% (above 2.0 mL/min)
	Flow Rate Precision	0.5% RSD
	Pulsation	**CUBE 30:** < 2% (at 1 mL/min, 50 bar) **CUBE 100:** < 4% (at 50 mL/min, 17 bar)
	Wetted Materials	PEEK, Synthetic Ruby, Sapphire, Zirconia, UHMWPE, FFKM, PFA, ETFE
Valves	Valve System	6x Electrically actuated multi-position valves 2x Automated drain valves
	Buffer/Sample Inlets	Binary Pump (A/B): 2 Isocratic Pumps (P2, P3): 16 (2x 8-port valves)
	Wetted Materials	PEEK, PPS, PTFE composite, PAEK, PAEK/PTFE
Detectors & Sensors	UV-Vis Detectors (x2)	Type: Variable 4-channel Diode Array Detector (DAD) Wavelength Range: 200–600 nm Light Source: Deuterium lamp Optical Path Length: 0.5 mm (standard, exchangeable) Linear Range: 0–1000 mAU Wetted Materials: PEEK, Quartz, PTFE, Stainless Steel
	Conductivity Sensors (x2)	Range: 0–250 mS/cm Features: Integrated temperature compensation Wetted Materials: Titanium, PEEK
	pH Sensor (x1)	Type: External probe with flow cell Range: 1–14 Max Pressure: 7 bar (0.7 MPa, 100 psi) Wetted Materials: PEEK, glass
	Pressure Sensors	4x integrated pressure transducers for system and column pressure monitoring

Contichrom® CUBE: Standard Specification

Category	Parameter	Specification
Flow Path & Mixer	High-Pressure Tubing	Material: PEEK, 1/16" OD Inner Diameter (ID): **– CUBE 30:** 0.03" (0.75 mm) **– CUBE 100:** 0.04" (1.0 mm)
	Low-Pressure Tubing	Material: FEP, 1/8" OD, 1/16" ID
	Dynamic Mixer	Type: Chamber with magnetic stirrer Volume: 1.1 mL (standard); 5.9 mL (with optional upper chamber) Wetted Materials: Stainless Steel (standard); PEEK, Titanium (optional)
	Outlets	4 product outlets, 4 waste outlets
Fraction Collector	Supported Models	Teledyne ISCO Foxy R1 (1 rack) or Foxy R2 (2 racks)
	Fraction Capacity	Supports all standard formats, including 96-deep-well plates, 15 mL and 50 mL tubes
	Features	RFID rack recognition (Foxy R2), integrated diverter valve with drip tray to prevent cross-contamination
Operation	Recommended Column ID	**CUBE 30:** 0.5 – 2.7 cm **CUBE 100:** 0.8 – 5.0 cm
	Process Capabilities	- Single & alternating batch chromatography - Integrated batch chromatography with inline dilution - CaptureSMB (continuous capture) - MCSGP (continuous polishing) - N-Rich (impurity enrichment)
Operating Software	Software Name	ChromIQ® Software Suite
	Method Design	**– ChromaCraft™:** Wizard for batch & integrated 2D batch process design **– Process Wizards:** Simplified, step-by-step method creation tools for CaptureSMB, MCSGP, N-Rich
	Dynamic Process Control	**– AutomAb®:** Dynamically adjusts loading time in CaptureSMB based on real-time UV breakthrough **– AutoPeak®:** Dynamically adjusts fraction collection windows in MCSGP and N-Rich based on real-time UV triggers
	Data Evaluation & Integrity	- Evaluation Center: For analysis, peak integration, and cycle overlays - Reporting: Export to PDF, CSV, or image files - Traceability: Full, unalterable logbook of all system events and user actions - Security: Multi-level user rights management and data integrity checksums
	Connectivity	OPC UA compatible (optional license required)

Contichrom® CUBE: Optional Hardware Accessories

Multiple external hardware options are supported in ChromIQ 9 and their functionality is also fully integrated into the ChromaCraft Batch editor as standard.

Expansion Option	Part	Details
Buffer Selection Valve Kit for Gradient Pump 1A & 1B (Includes 2 valves)		**1D Batch:** Eluent screening valve for gradient optimization **2D/3D Integrated batch:** Enables gradient + gradient double polishing (*This kit requires the "Column Bypass Valve Kit"*)
Column Bypass Valve Kit (Includes 2 valves)		**2D/3D Integrated batch:** Quickly flush or sanitize the system without dismounting the columns. Allows multiple methods in series without long cleaning steps in-between
Column Selection Valve Kit - Left position only (Includes 1 Valve)		**1D Batch:** Allows column screening for 3 additional columns (5 total) **3D Integrated Batch:** Enables 3-step methods
Injection Valve Kit (Includes 1 Valve)		For injecting small sample volumes (Column tests/ Small scale purification of precious sample)
Valve for Outlet In-Line Adjustment (VOILA) (Includes 1 Valve)		This valve option stabilizes sensitive products before collection by applying in-line adjustment at the system outlet to modify product concentration, pH or other parameters
Column Ovens (x2), Heating and Cooling		Temperature range: 5-85° Celsius (Heating and cooling). Max flow rate: **5 mL/min**. Max column dimensions: 30 cm length, 1 cm ID
Column Heater (2 position) + Column Jackets		Temperature range : Up to 80° Celsius (no cooling). Max flow rate: **100 mL/min.** Max column dimensions: Any length, 3 cm ID
CUBE Accessories Storage and Drainage Rack (*Coming 2026*)		This custom designed organizational unit keeps your workspace tidy. Includes expansion space for accessories, additional bottle storage capacity, and a drainage system for leaks and spillages
Cold Cabinet for Foxy R1 Fraction Collector (*Not suitable for organic solvents*)		W/D/H: 60, 61, 85 cm Gross capacity: 140 L Gross weight: 48 kg Spark resistant Buffer & feed bottles cooling inside Accurate temperature setting between +2°C and +40°C Visual and audible door and temperature alarm Self closing door glass door

Contichrom® - Summary of Key Benefits

With twin-column technology, Contichrom systems are designed to deliver significant improvements over standard purification processes. As a development system, the Contichrom CUBE is comprehensive both in its hardware specification and software capabilities, enabling users to design methods for even the most challenging problems.

Flexible Process Capabilities: The Contichrom CUBE is built for versatile purification, performing standard single-column batch chromatography, integrated 2D & 3D batch processes, and continuous processes like CaptureSMB (for capture) and MCSGP (for polishing). This single, compact benchtop unit allows researchers to quickly select and optimize the ideal strategy for any molecule or objective.

A Single, Integrated Software Ecosystem: ChromIQ 9 is the comprehensive chromatography development platform that provides a unified environment for method creation, control, and reporting. The suite features intuitive, wizard-driven modules—tailored for every challenge from standard batch to continuous processing—all managed from a single, centralized interface, eliminating the complexity of managing disparate software.

Seamless Scalability for Manufacturing: All methods developed on the laboratory-scale Contichrom CUBE are directly and reliably scalable to the Contichrom PILOT or Contichrom TWIN manufacturing systems (LPLC and HPLC). This ensures a smooth, predictable, and compliant technology transfer for production under GMP.

Enhanced Process Automation & Robustness: Contichrom systems are uniquely equipped with our patented dynamic process control technology (AutoPeak® & AutomAb®). This provides a purification platform optimized for automation and robustness, enabling the development of fully continuous 24/7 purification processes.

Dramatically Improve Sustainability and Process Economics: Continuous processes significantly improve the Process Mass Intensity (PMI) and lower the overall cost of goods. MCSGP increases yield and enables upstream synthesis downscaling, while CaptureSMB maximizes resin utilization and reduces buffer consumption, allowing for a more sustainable operation.

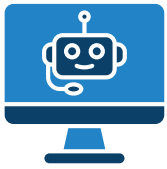
Maximize Productivity and Throughput: Continuous capture and polishing methods maximize output from expensive chromatography equipment and resins. This dramatically increases the productivity and helps to minimize the operational footprint required for a process.

Eliminate Re-Chromatography and Reduce QC Burden: By achieving target purity with maximized yield, MCSGP eliminates the need to rework or re-process side-fractions. This significantly simplifies manufacturing by reducing intermediate handling, storage, and the analytical QC burden typically associated with batch processes.

Service and Support

To ensure maximum uptime and performance, a full range of service and support options is available. We offer:

- Preventative Maintenance Services (on-site): Annual subscriptions including discounts based on contract duration and number of systems
- Ad hoc repair and maintenance services (on-site)
- Real-time technical support by phone, e-mail or through remote access, providing thorough guidance beyond the initial installation and training
- Customized workshops, on-site or off-site (CaptureSMB, MCSGP, N-Rich, Integrated-Batch or other topics).
- Support services for process development and scale-up
- Process modelling services
- Annual scheduled workshops on continuous chromatography purifications



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

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

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