TOSOH

Octave™ Multi-Column Chromatography

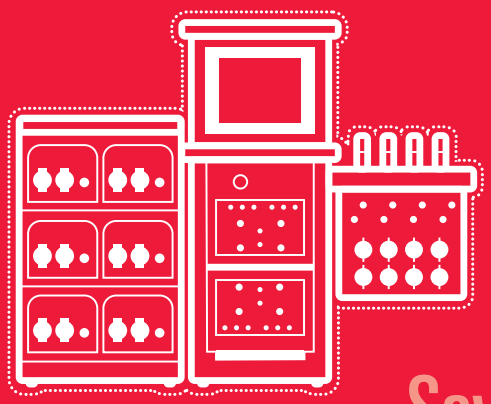
A holistic solution for process intensification

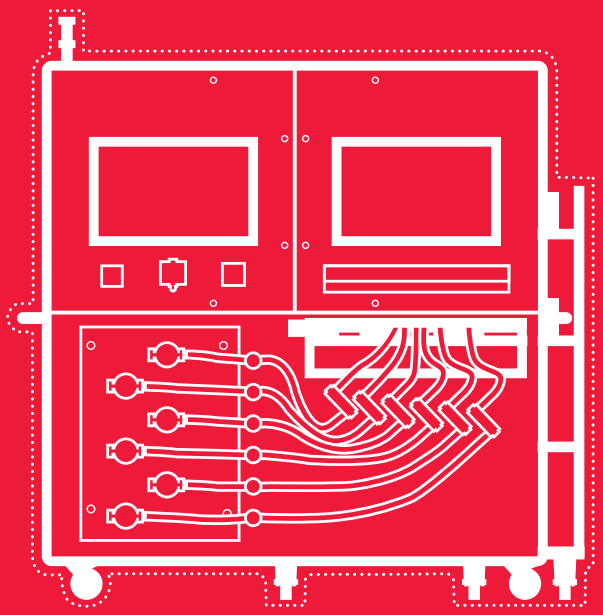
Method Development

Octave PRO

Production

Octave BIO





MCC

Reduce Operating Costs

Save Time

Increase Productivity

Scalability

SkillPak

Bioprocessing

Flexibility

Experts in Chromatography

TOSOH BIOSCIENCE

TOSOH BIOSCIENCE

TOSOH

Process intensification – The paradigm shift in process chromatography

Despite advances in the processing and manufacturing of biological therapeutics, downstream purification (DSP) of molecules is still a time, resource, and cost intensive procedure. Furthermore, advancements in upstream production have exacerbated the bottlenecks of current DSP processes.

The default approach to DSP is to sequentially process liquids batchwise via disjointed unit operations (e.g. filter and liquid chromatography systems). Chromatography steps often contribute most to time, resource, and cost inefficiencies, where large columns and large volumes of expensive affinity resin are operated at long residence times and used to purify comparably small volumes of product. This lack of productivity can be overcome using novel approaches, namely multi-column chromatography (MCC), which offers the following benefits over batch chromatography.

While the adjacent small molecule pharmaceutical industry already benefits from introducing continuous chromatography (e.g. enantiomer production) the biologics industry is just now adapting the MCC technique for intensifying purification. Seeking highly efficient purification to address resource and throughput concerns, industry leaders and visionaries are already adapting MCC to accommodate fast growing and agile biopharma market trends. This is strongly supported by regulatory bodies like the FDA, who identified the benefits of transitioning to continuous downstream processing (Guideline ICH Q13).

Transition to MCC

Batch Processing

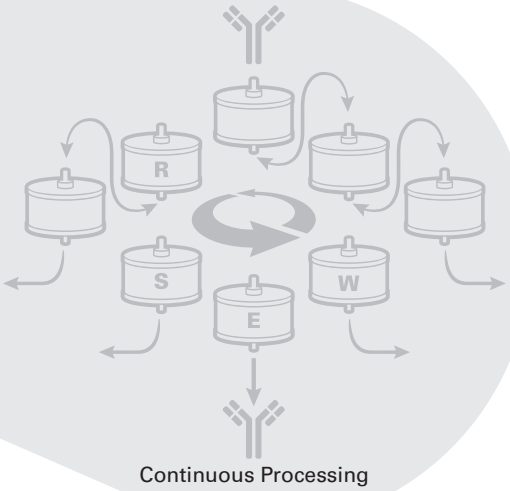
Up to 90% resin savings
due to higher productivity

Up to 40% solvent savings
due to better utilization of the column bed

Up to 5 x smaller footprint
due to smaller buffer vessels, columns, and instrumentation

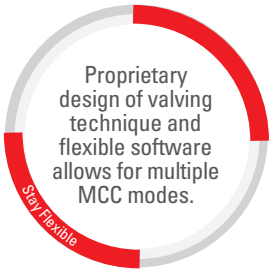
Seamless scale-up
(mg- to kg-range of purified product)
due to common system architecture and software and prepacked column availability

End-of-lifetime usage of resin batch
rapid cycling on smaller columns



Continuous Processing

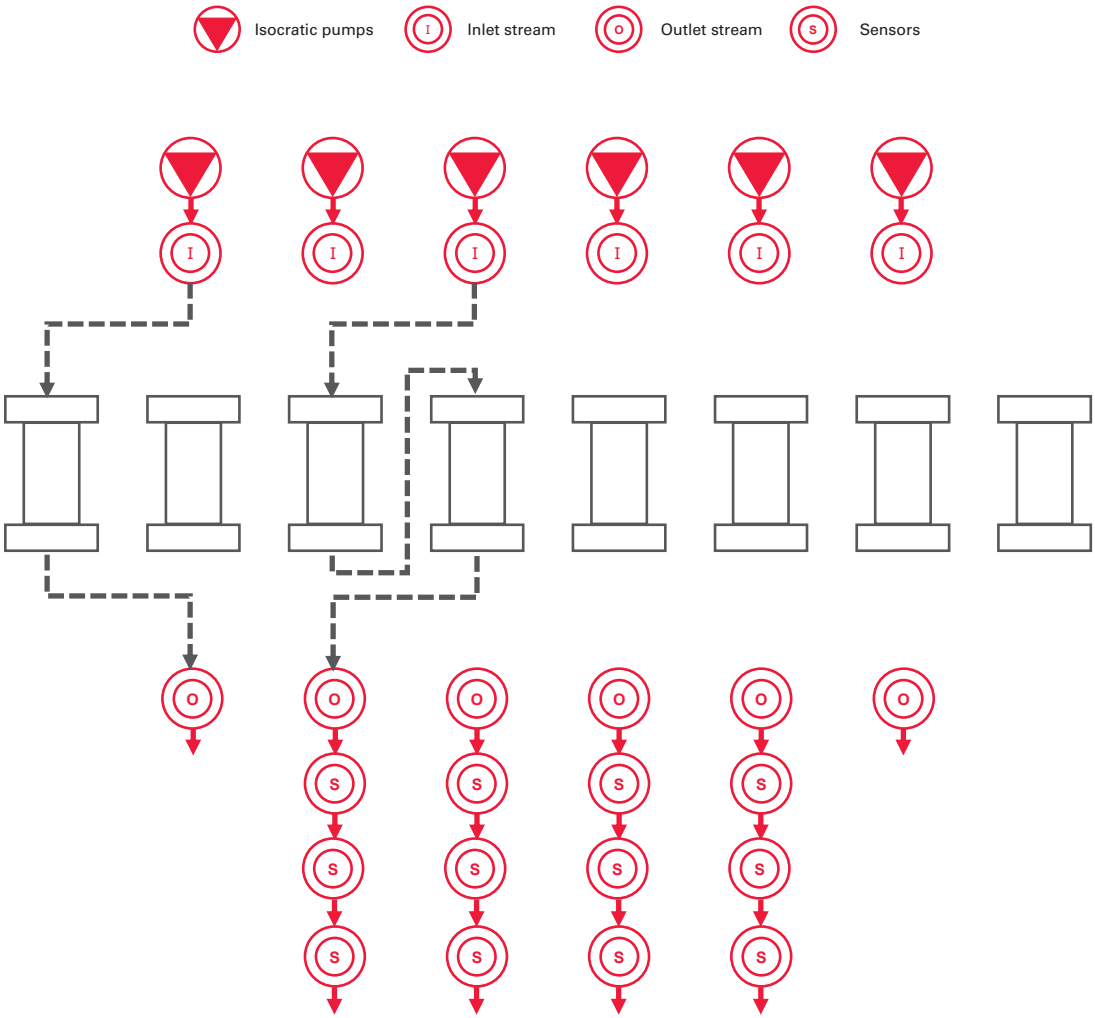
Working principle of MCC in bioprocess



Multi-column chromatography is a bioprocessing technique which uses a set of small process columns to continuously load and process material and generate purified product with comparable yield and product quality under high-throughput conditions. Typically, these MCC columns have a shorter bed height, and enable processing at faster flow rates to achieve greater efficiencies. To better utilize the capacity of each column, especially at these faster flow rates, two to three interconnected columns are typically loaded in-series.

Our MCC instuments are comprised of a set of isocratic pumps; a valve manifold with six inlets, six outlets, and eight column positions; and a set of sensors to monitor the process streams. These hardware components are controlled by software that operates the pumps and valves directing inlet streams to the appropriate columns while monitoring the separation parameters and process stream outputs. Our Octave BIO and Octave PRO systems are both based on this same architecture to make processes scalable. At any given time, columns are undergoing different process steps, and the valve block technology simplifies and coordinates the simultaneous sets of operations.

Moreover, this can be changed during the run – by doing so the columns can be attributed to different solvent streams in a cyclic manner – the famous simulated moving bed.

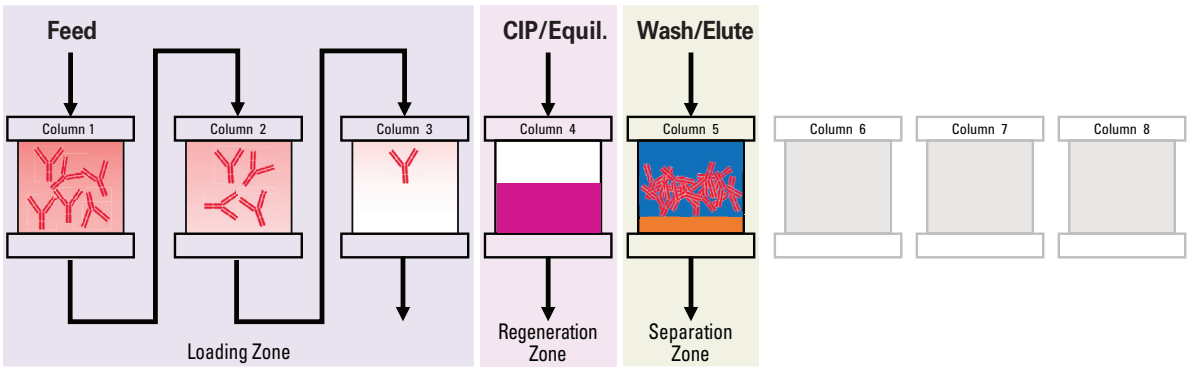


Purification of biomolecules via capture chromatography

Typical implementations of MCC in bioprocessing are for affinity steps with a bind and elute mode of operation (step mode) to purify antibodies, recombinant proteins, or peptides.

The five steps of affinity chromatography (feed, wash, elute, clean, and equilibrate) are conducted with the column set as follows: Every moment three columns are being loaded (loading zone), all residual steps are conducted simultaneously on the remaining columns (Separation and Regeneration Zones).

Depending on the process parameters (capacity, max. flow rate, number of washing steps, titer etc.) the number of columns utilized for your process may vary. That's why our systems can accommodate up to 8 columns.

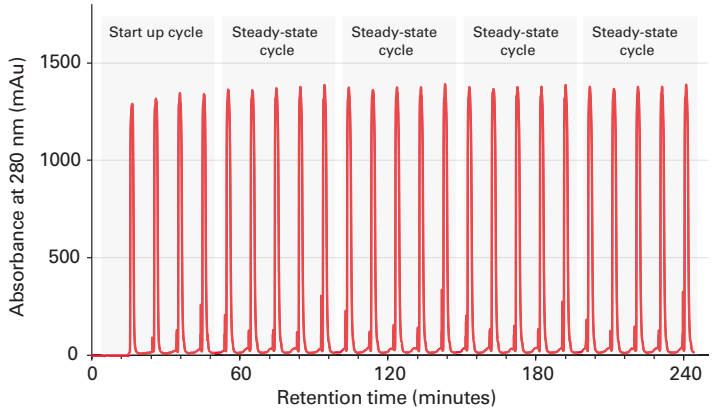


Within one cycle, all columns undergo a consistent and complete chromatography process.

Stay Flexible

During a run, live chromatograms are viewable from zones of interest.

The chromatogram shown illustrates the purification of mAbs from a clarified cell culture supernatant. Direct comparison of process performance using a column with equal total resin volume operated in batch mode reveals productivity gain of ~ 300% for the transition to MCC underlining the potential of continuous biochromatography for time and costs savings.



Column set: 5× SkillPak™ BIO AF-rProtein A HC-650F, 0.8 cm ID × 2 cm length each
Sample load: 85% of static binding capacity, 463 mL feed stock solution processed in total
Process liquids: Feed (3.4 g Adalimumab/L from clarified Chinese hamster ovary cell culture supernatant), Wash (100 mmol/L NaP pH 7.0), Elution (100 mmol/L NaAc pH 3.0), CIP (200 mmol/L NaOH), Equilibration (100 mmol/L NaP pH 7.0)

Mode	Column volume (mL)	Cycle time (min)	Residence time (min)	Recovery (%)	Load level (mg prod/mL resin)	Buffer consumption (mL buffer/mg prod)	Productivity (mg Prod/(mL resin*h)
Batch	1 × 5	160	5.00	97.9	48	0.64	17.5
MCC	5 × 1	49	0.50	97.1	63	0.44	71.1

+300%

TOSOH

Process Development

Octave BIO

No compromises!
Octave BIO offers these modes:

- Step mode
- Isocratic mode
- Batch mode
- Gradient mode
- Parallel LC mode

Want to learn more?
Visit our website.

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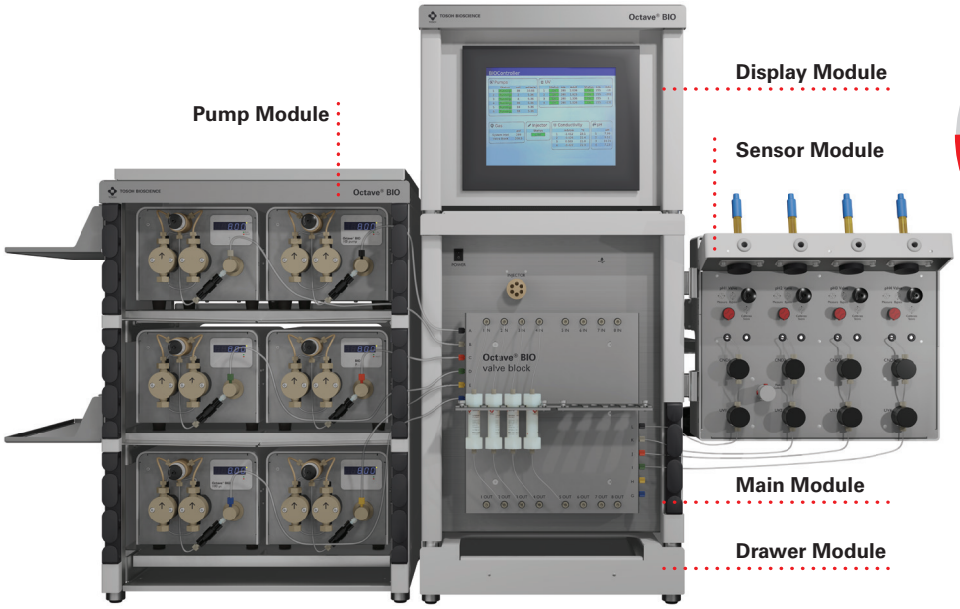


The most flexible development system for your journey to MCC.

Stay Flexible

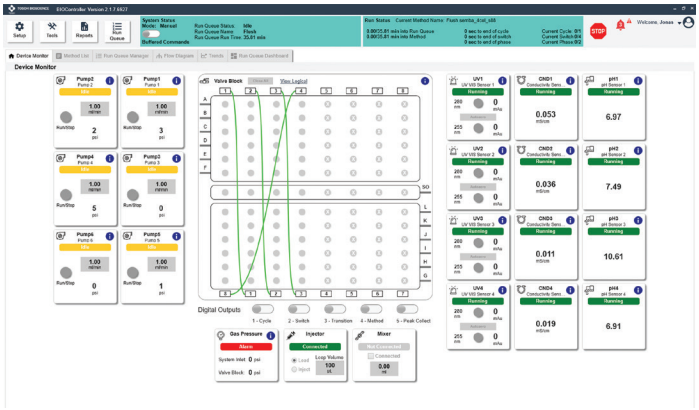
The Octave BIO from Tosoh Bioscience is the most comprehensive and versatile multi-column chromatography (MCC) system for process development and proof of concept. The unique modular and bio-compatible design is tailored to enable both; highly versatile step-mode bioprocessing of small and large proteins as well as established, isocratic SMB applications.

The system flow path features PEEK tubing and a biocompatible valve block design that allows for the connection of 1 to 8 columns to accommodate increasingly intensified upstream titers, while reducing the clutter of rotary valves and external tubing. The system features six independently driven pumps that are each assigned to a process fluid, with each pump being user-replaceable among four sizes to cover a wide range of process scales. Built-in UV, conductivity, pH detectors enable complete process monitoring, while added features like the onboard sample injector, mixer, and gradient capability enable process development experiments as well.

The Octave BIO is the system to begin your process intensification journey, with tools and software to ease the transition.

The BIOController™ system control software provides a clean, user-friendly interface to execute and monitor your MCC process. This Windows™ compatible application features an intuitive, user-friendly interface that allows rapid mastery of its powerful functionality.

Methods are written with the PROComposer™ application and transferred into BIOController's Run Queue. The methods can be used with a variety of column sizes that match the capabilities of the Octave BIO because BIOController adjusts the time, volume and flow rate parameters based on the column dimensions and scaling selection entered in the Run Queue Manager. Each method is repeated within the sequence for a defined number of cycles, indefinitely or for a set time period.



	Pump Module
6	Octave BIO pumps
	Valve Module
1	Valve Block
1	Sample Injector
	Drawer Module
1	Reservoir Tray
	Display Module
1	System Status Display
	Sensor Module
4	Dual-channel UV Sensors
4	Conductivity Sensor
4	pH Sensors
1	Peak Collect Valve
	User Interface, Software and Support
1	Windows™ 10 computer with monitor, keyboard and mouse
	PROComposer MethodWizard process design tool
	PROComposer method authoring software
	BIOController system control software

Specifications for the Octave BIO	
Dimensions (W/D/H)	137 × 51 × 98 cm
Weight	171 kg
Power requirements	100-120/220-240 VAC, 50/60 Hz
Valve pressure	At least 2 bar above process pressure
Flow rate range	up to 300 mL/min (2.4 mm valve block)
Inlets	6
Outlets	6
Columns	1-8
Maximum operating pressure	270 psi (18.6 bar)
UV sensors	4, LED, dual wavelenghts (255 & 280 nm)
Conductivity sensors	4, range 0-200 mS/cm
pH sensors	4, range pH 0-14
Modes	Step, batch, gradient, parallel, SMB

Ordering Information: Octave BIO

Part #	Description
MCC Benchtop	
0041100	Octave BIO Benchtop System 12 mL/min
0041101	Octave BIO Benchtop System 36 mL/min
0041102	Octave BIO Benchtop System 100 mL/min
0041103	Octave BIO Benchtop System 300 mL/min
MCC Benchtop Components	
0041107	Octave 12 mL/min pump
0041108	Octave 36 mL/min pump
0041109	Octave 100 mL/min pump
0041110	Octave 300 mL/min pump
0041104	Octave BIO 1 mm valve block
0041105	Octave BIO 1.6 mm valve block
0041106	Octave BIO 2.4 mm valve block

Front

Back

TOSOH

Production

Octave PRO

Everything under control.
Octave PRO provides:

- Single-use flow path design
- Repeatable, method-based operation
- GMP-ready
- Process data access

Want to learn more?
Visit our website.

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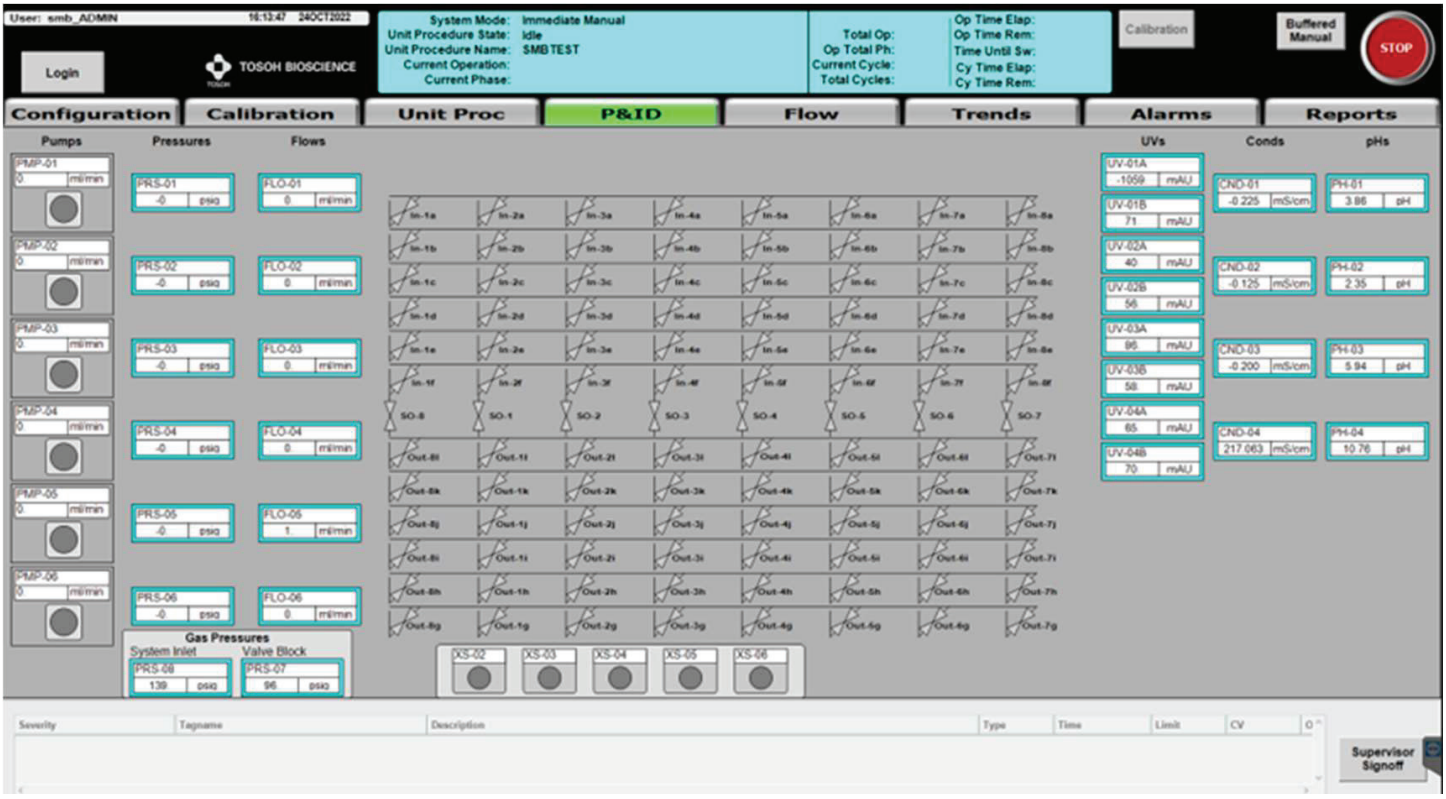
The Octave PRO from Tosoh Bioscience is a comprehensive multi-column chromatography (MCC) system for clinical production under GMP conditions. The system not only unlocks resin savings, buffer savings, and other tangible benefits that MCC can provide it will also make space available on your manufacturing site due to its small footprint design.

The system flow path features all bio-compatible tubing and valve block that allows for the connection of 1 to 8 columns to accommodate increasingly intensified upstream titers, while reducing the clutter of rotary valves and external tubing. The system features six independently driven pumps that are each assigned to a process fluid, with each pump being single-use. Built-in UV, conductivity, pH detectors enable complete process monitoring.

The Octave PRO is operated with GMP-compliant software. PROController™ system control software provides a clean, user-friendly interface to execute and monitor your MCC process. With the PROComposer method authoring software you are GMP-ready to seamlessly run methods developed on the Octave BIO and linearly scale to the Octave PRO system.



Overview and Comparison

	Octave BIO	Octave PRO
Project support	Development, Pre-clinical	Clinical, Commercial
Form factor	Bench top, portable	Skid, portable
Column capacity	1–8	1–8
Valve block	User-interchangeable; 3 channel diameters	Single use (SU)
Pumps	6	6; SU heads
Pump flow max.	12, 36, 100, 300 mL/min	2.5 L/min
Method software	PROComposer	PROComposer
Control software	BIOController	PROController
Data integrity	For Process Development	Ready for 21 CFR part 11 compliance
Bioreactor Size	Up to 150 L	Up to 2000 L
Processing Scale	Up to 500 g	Up to 20 kg

Specifications for the Octave PRO

System Architecture

Description	Specifications
Dimensions (W / D / H)	213 / 115 / 219 cm, (198 cm without alarm tower)
Weight	450 kg
Operating flow rate	1 – 150 L/hr (2.5 L/min)
Maximum operating pressure	6 bar (87 psi)
Valve Pressure	8 bar (116 psi)
Gas inlet pressure	9 bar (130 psi)
Column Positions/Connections	1 to 8 columns, ¾ in. sanitary clamps
Valve block	1 single-use assembly containing 104 pneumatic two-way valves
Inlet number	6
Outlet number	6
Pumps	6; 4-piston-diaphragm pump, flow rate ranges 1-150 L/h
Flowmeters	6; 1 after each pump, flow rate ranges 0.01-8 L/min
Pressure sensors	6; 1 after each pump, measuring range 1-10 bar
Outlet sensors	4 assignable single-use combination UV/conductivity/pH
UV sensors	UV 280 nm & 305 nm
Conductivity sensors	CND range 0–850 mS/cm
pH sensors	pH range 0-14

Single-Use Flowkit

Item	Description
Inlet Connections	6 Aseptiquik® G
Outlet Connection	6 Aseptiquik® G
Pumps	6 Quattroflow® EZ-Set Pump Chamber quaternary diaphragm single-use heads
Pressure sensors	6 single-use gauge tees (TS1, 1 after each pump)
Flow sensors	6 single-use; ultrasonic (1 after each pump)

Single-Use Materials of Construction

Component	Wetted Materials
Pump head	polypropylene (PP), thermoplastic elastomer (TPE), ethylene propylene diene monomer (EPDM)
Pressure adapter	PP, TPE
Flow sensor	PP
Valve block assembly	USP class VI compliant polyetherimide (PEI), polyvinylidene fluoride (PVDF), polyfluoroalkoxy (PFA)
Optical/conductivity/pH flow cell	quartz (UV-transparent), EPDM, stainless steel 1.4435 (SS 316L), polyphenylsulfone (PPSU)
Fittings	PEEK, platinum cured silicone, PP
Tubing	¼ in. ID polybraided platinum cured silicone, pump inlet is weldable ¼ in. ID Advantaflex biopharmaceutical grade thermoplastic elastomer (TPE)
Gamma irradiation dose	25-40 kGy

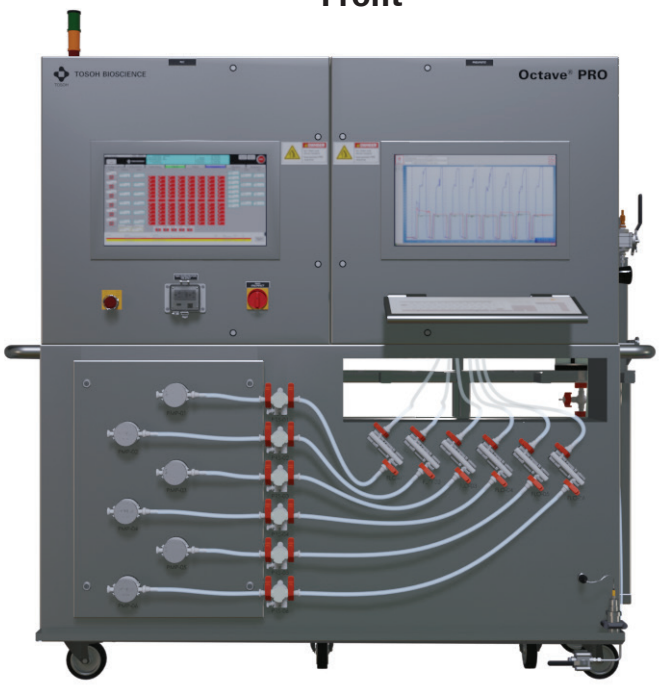
Electrical Requirements

Parameter	North America	EMEA
Voltage	120V; 1 phase	220-240V; 1 phase
Amps	30A	15A
Frequency	60 Hz	50 Hz
Number of Cords	1	1
Type of Plug	NEMA L5-30P, with ground	Must meet local code, with ground

Ordering Information: Octave PRO

P/N	Description
0041200	Octave PRO US, Octave PRO GMP ready multi-column chromatography skid for US region.
0041201	Octave PRO EU, Octave PRO GMP ready multi-column chromatography skid for EU region.
0041202	Octave PRO SU Flowkit, Full single-use flowkit for the Octave PRO.

Front



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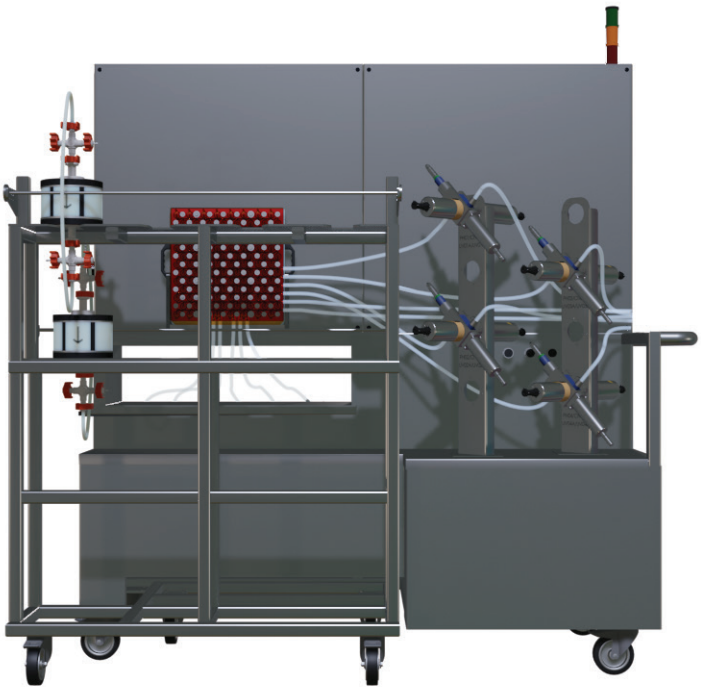

TOSOH

Process Intensification

A holistic MCC solution! Complementing our Octave systems:

- SkillPak pre-packed columns
- Best-in-class TOYOPEARL® affinity resins
- PROComposer Method Wizard
- PROComposer Method Creator
- Service & Support

Want to learn more? Visit our website.

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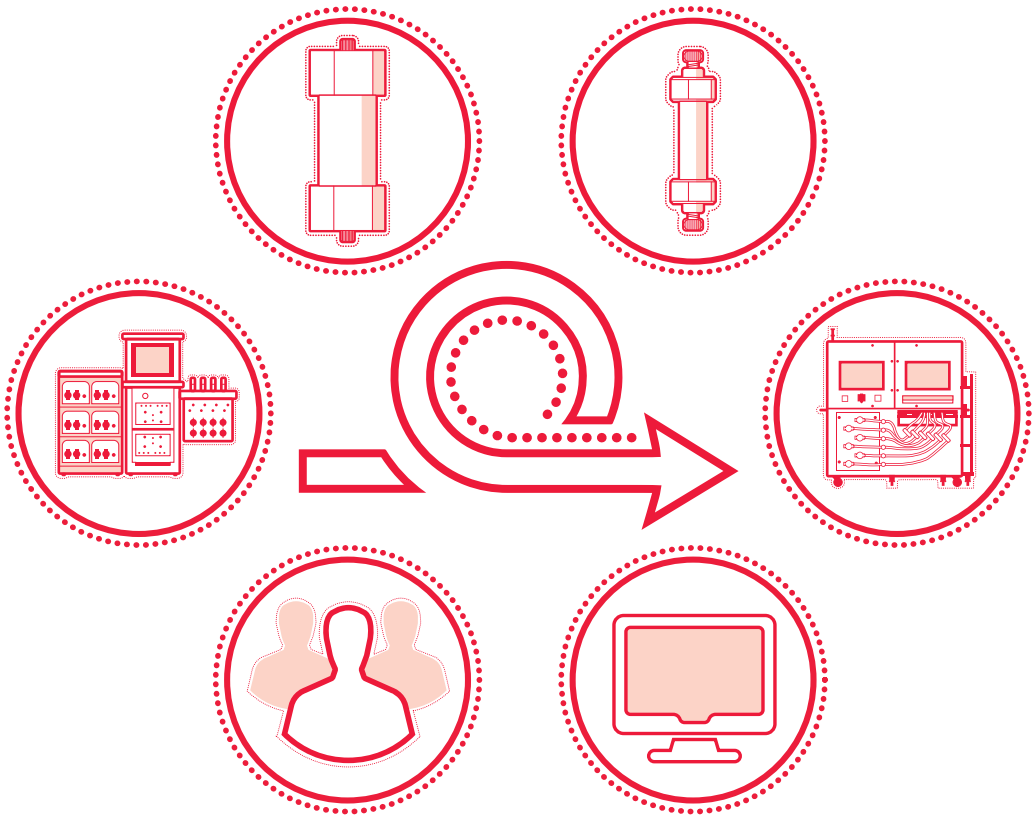
How to intensify your process – Tosoh's holistic MCC solution

By default, process development for traditional chromatography steps is done at the bench scale to minimize the necessary investment. To realize a large-scale purification, column dimensions and respective LC systems are scaled-up to the intended product throughput, but this is done only after the requisite bench scale development.

Transferring processes to multi-column chromatography uses a similar approach in that intensification of batch processes with MCC is typically done at the bench scale. For this transition, Tosoh Bioscience provides both the versatile Octave BIO hardware to accommodate a wide range of process conditions, flexible software tools needed for the method development and method generation of an MCC process, as well as MCC optimized SkillPak BIO columns for method development and testing. SkillPak BIO columns come with both outstanding attributes (packing quality, stability and reproducibility) and a wide range of dimensions to enable its customers a seamless process development.

Scale up is executed after a proof of concept has been achieved of a well-defined MCC process with evident benefits. To address these needs, Tosoh Bioscience provides the GMP-ready Octave PRO solution, unified software tools for easy method scale-up, and the SkillPak PRO line of columns, which feature the same MCC attributes as the SkillPak BIO columns, in a scaled up, MCC optimized format.



SkillPak pre-packed columns

SkillPak are chromatography columns pre-packed with TOYOPEARL, TSKgel, or Ca^{++}Pure-HA process chromatography media. These columns have been designed to develop and scale-up purification processes for biomolecules, such as monoclonal antibodies, proteins, and oligonucleotides.

Whether you are screening resins, developing a purification process, working on the scale-up conditions of your batch or MCC process, or moving to manufacture under GMP conditions – the SkillPak columns are ready to use upon receipt. They offer ideal flow characteristics and reliable and reproducible performances for industrial downstream processing. Choose from these variants:

SkillPak for batch process development

SkillPak MAX for GMP production with batch mode

SkillPak BIO for MCC process development

SkillPak PRO for GMP production with MCC mode

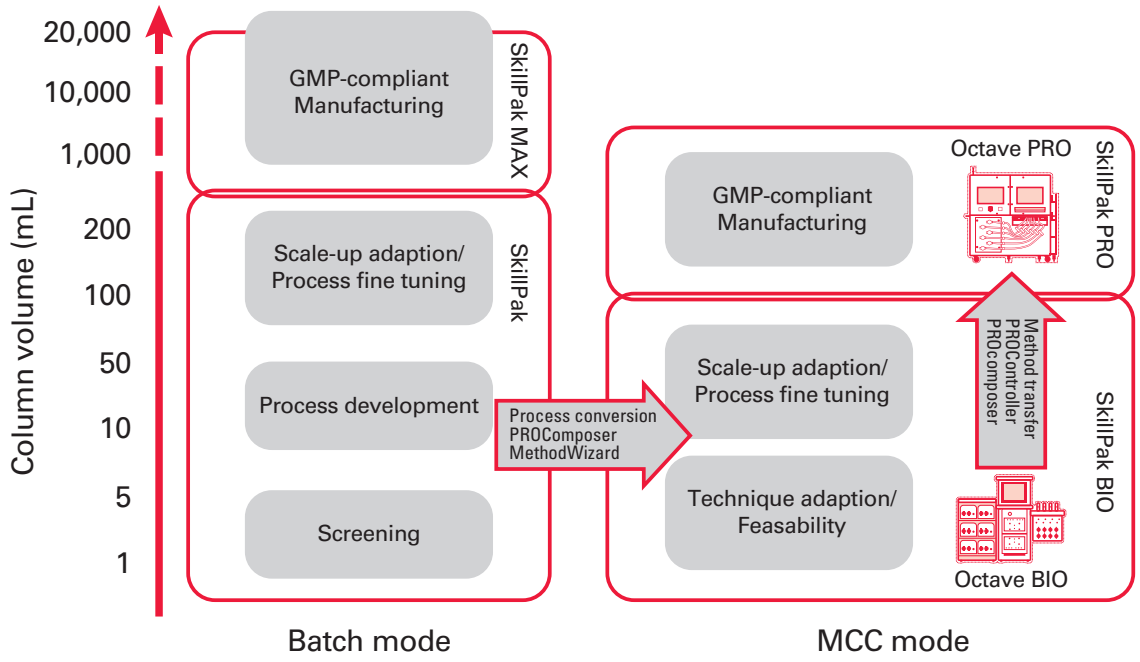
Among those four options, SkillPak BIO and SkillPak PRO hardware have been developed specifically to deliver the best experience and optimized process performance for multi-column chromatography applications.

SkillPak PRO column dimensions and use cases

Step	Dimensions	Volume	Flow rate at 0.5 min residence time
Process fine-tuning/ Manufacturing	8.0 cm ID × 5.1 cm	256 mL	512 mL/min
	14.0 cm ID × 5.1 cm	785 mL	1570 mL/min
	20.0 cm ID × 5.1 cm	1600 mL	3200 mL/min

SkillPak BIO column dimensions and use cases

Step	Dimensions	Volume	Flow rate at 0.5 min residence time
Screening/ Process development	0.8 cm ID × 2.0 cm	1 mL	2 mL/min
	1.6 cm ID × 2.5 cm	5 mL	10 mL/min
Technique adaptation/ Scale-up	1.6 cm ID × 5.1 cm	10 mL	20 mL/min
	2.5 cm ID × 5.1 cm	25 mL	50 mL/min
	5.0 cm ID × 5.1 cm	100 mL	200 mL/min



Available resins for SkillPak BIO and SkillPak PRO columns

Resin name	Application mode	Recommended for purifying...
TOYOPEARL AF-rProtein A HC-650F	Capture via Protein A	Monoclonal Antibodies
TOYOPEARL AF-rProtein L-650F	Capture via Protein L	Antibody Fragments
TOYOPEARL NH_2-750F	Polish via Anion exchange	Antibodies, antibody fragments, and other biomolecules
TOYOPEARL Sulfate-650F	Polish via Cation exchange	Antibodies, antibody fragments, and other biomolecules
TOYOPEARL GigaCap S-650S	Polish via (strong) Anion exchange	Viruses and vaccines, and other biomolecules
TOYOPEARL SuperQ-650S	High throughput capture, intermediate purification, and polishing via (strong) Anion exchange	Therapeutic nucleic acids

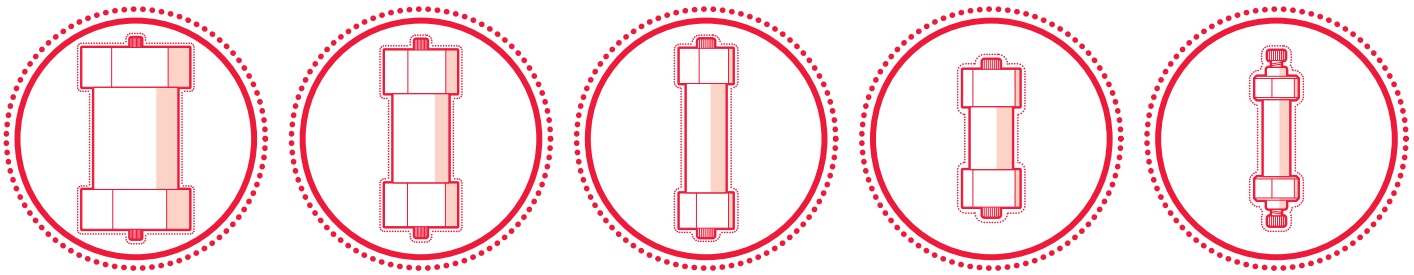
Please see our SkillPak brochure or website for ordering information.

Best-In-Class TOYOPEARL affinity resins

For multi-column chromatography, affinity chromatography processes present the most evident benefits from process intensification. As a result, another key component of Tosoh's comprehensive process intensification suite are TOYOPEARL best-in-class affinity resins, particularly TOYOPEARL AF-rProtein A HC-650F.

TOYOPEARL AF-rProtein A HC-650F is a high capacity Protein A resin for monoclonal antibody purification. The multi-point attachment between the ligand and base matrix results in excellent base stability for up to 200 CIP cycles with 0.1 mol/L NaOH. Achievement of high linear velocities at relatively low pressure enables high throughput processing at moderate pressure limitations. Improved mass transfer characteristics allow it to maintain a larger percent of its capacity at lower residence times relative to agarose base stable resins. Good pressure-flow characteristics and kinetics contribute to maintaining good capacity, particularly at low residence times.

Extended lifetime and caustic stability, relatively low pressure operation at high linear velocities, and good capacity at low residence times are all traits that make TOYOPEARL AF-rProtein A HC-650F a good fit for multi-column chromatography operation, where processes experience high capacity, and low residence time operation, with increased cycling for processing and cleaning.



Ease of process conversion and method transfer

Our unified PROComposer method-generating software package runs with any Windows-based PC and guides you from method development and proof of concept through to scale-up of highly efficient MCC processes.

The PROComposer Method Wizard simplifies conversion of batch to MCC methods. The Wizard provides tools to determine MCC process parameters, model a specific method, and compare batch and MCC process performance.

Moreover, methods developed with the Wizard saves methods in a format that can be opened, saved, and edited in the Tosoh Bioscience PROComposer Method Creator, which in turn can run on any Octave MCC system. As an added feature, batch methods can also be saved and edited in PROComposer format for running in single column mode.

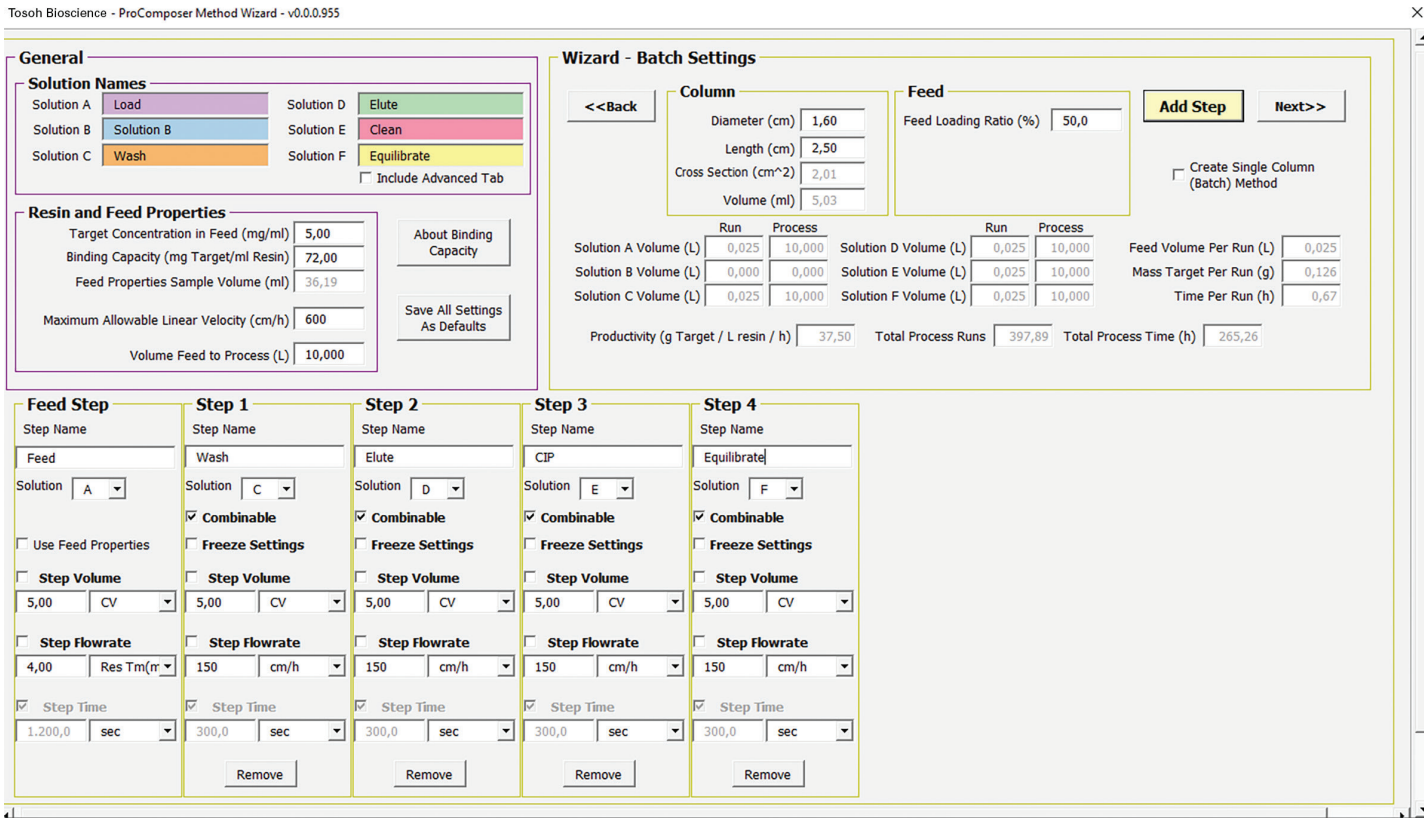
Parameter input for PROComposer Method Wizard

How to use the PROComposer Method Wizard

The Wizard is very easy to use. Simply enter the known parameters and protocol steps for your batch process, select the column size, number of columns in the loading zone and desired feed loading ratio for the MCC process, and the Wizard recommends the number of columns for MCC and compares the critical parameters of both processes.

How to adjust your process with PROComposer Method Wizard

Adjust column size, resin capacity, residence time, and maximum allowable flow velocity to optimize productivity, buffer usage, and/or process time.

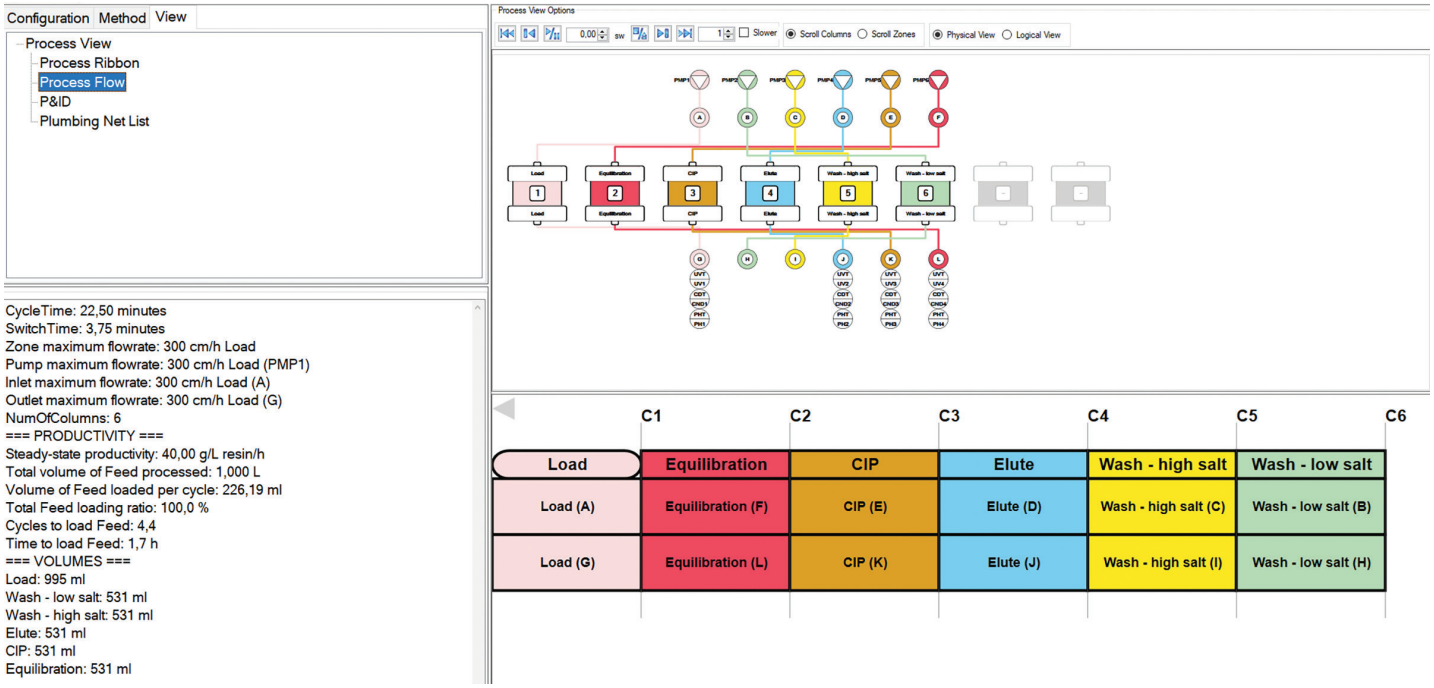


Method visualization of PROComposer Method Creator

The PROComposer Method Creator is used to create or edit multi-column chromatography and single column methods. The method files created with PROComposer on a Windows PC are transferred to the Octave BIO and Octave PRO Chromatography Systems for execution.

Methods created with PROComposer can be run with a variety of column sizes matched with our MCC systems (especially among the SkillPak BIO and PRO product lines). The systems scale pump flow rates based on the column dimensions entered into the BIOController (Octave BIO) or PROController (Octave PRO) user interface.

Tosoh Bioscience provides all equipment and knowledge necessary to transfer your batch method to a continuous one. With our outstandingly flexible systems you will be able to adopt to a variety of purification methods and translate them to highly-efficient, GMP-compliant manufacturing of biomolecules. Contact us to learn more about our MCC solutions.



For applications with our holistic MCC solution, visit our website for more information.

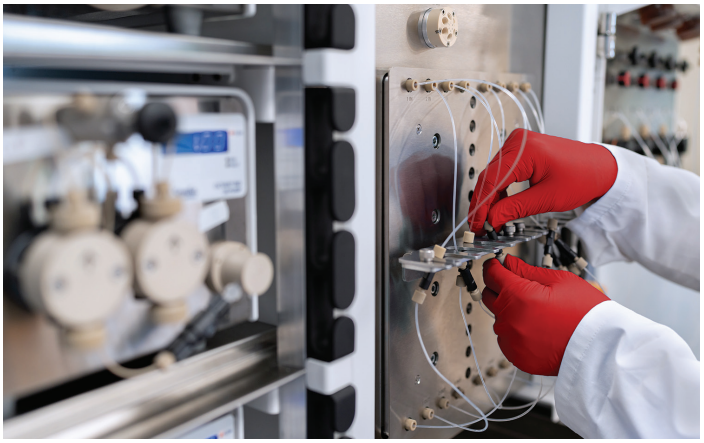
Services

Tosoh Bioscience is a globally operating company with locations around the world. Local service technicians are committed to provide the best quality support and service.

Our highest goal is to make your work with our systems and consumables as productive as possible. Therefore, regional service hotlines operated by Tosoh Bioscience staff with decades of chromatography experience enable fast response to any hurdles you might face.

Our service portfolio for MCC includes:

- Installation, familiarization, and training
- Maintenance
- Qualification (IQ, OQ, FAT, SAT)
- Repair on-site
- Extended warranty
- User education classes and visits
- Service agreements



Tiered Support Agreements*

Level	Gold	Silver	Bronze
Prolonged warrenty status	Included	-	-
Preventive maintenance (annual visit)	Included	Included	Included
Additional discounts on	Consumable parts, Multiple planned PM visits, user education	Warranty parts, Consumable parts, Multiple planned PM visits, user education	Multiple planned PM visits
Non-scheduled service technical mission	Included	Included	-
Response time	Onsite response within 5 business days, Same/next business day remote support	Onsite response within 10 business days, Same/next business day remote support	Same/next business day remote support

* Regional variances in services may exist and services are subject to change. Please contact your distributor for precise service information.

Please visit our website to connect with your regional sales, service, and support contacts.

In the Americas:
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