



Contichrom[®] Discovery

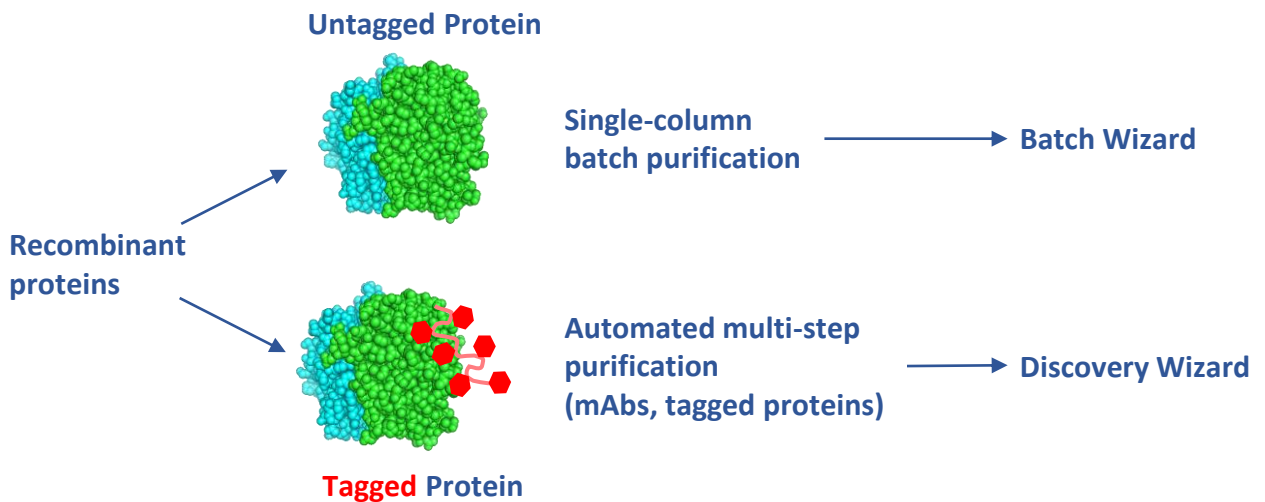
An Automated Batch and Multi-Dimensional
FPLC Protein Purification System

Contichrom[®] Discovery

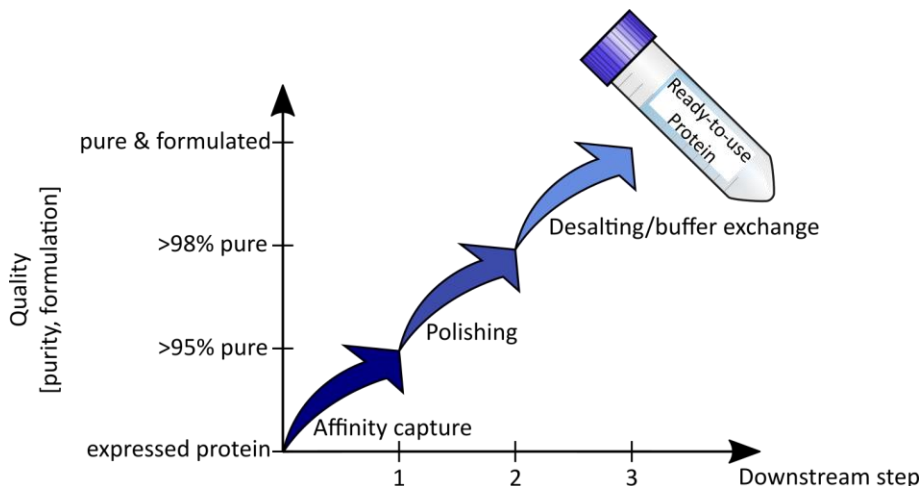
Availability of pure proteins in quantities of tens of milligrams is a prerequisite for many life science applications such as for assay development and structural studies.

The **Contichrom Discovery** is an easy-to-operate preparative FPLC protein purification system offering an expandable library of single-column batch and automated multi-step purification protocols for antibodies and tagged proteins.

For the latter, protein purification protocols are sequentially coupled and highly automated to add convenience, reproducibility and speed. Automated multi-step purification protocols are particularly useful for classes of proteins, such as antibodies and tagged proteins where a standard multi-step protocol can be established minimizing manual intervention.



Discovery Wizard: One Process with up to Three Chromatography Steps



Automated Purification

Multiple fixed and customized recipes with many integrated process choices

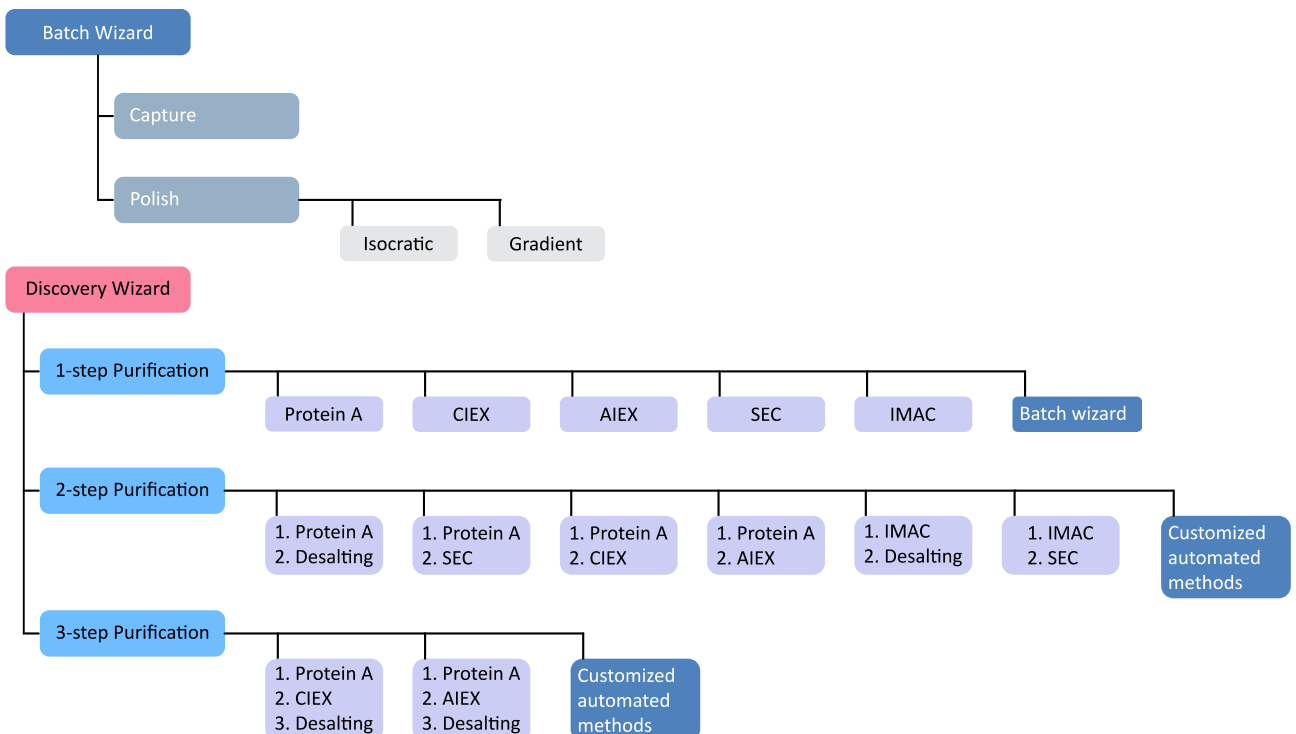
The Contichrom Discovery system and its operating software ChromIQ offers batch functionality as well as automated multi-step processing functionality for purification of proteins and oligonucleotides. These include automated capture steps for monoclonal antibodies (mAbs) or tagged proteins, for example His-tags or Fc-tags, as well as orthogonal connected second polishing steps, for example size exclusion chromatography (SEC) or ion exchange chromatography (IEX) and further desalting / buffer exchange steps.

The Batch wizard functionality of the ChromIQ software provides easy design and operation of all single column processes with isocratic and gradient mode.

The Discovery wizard provides a library of automated 1-, 2- and 3-step purification recipes. Some suitable resin consumables are provided with the system as a purification kit.

Customization: you can customize purification steps and connect them to extend the given recipe library or to design new purification sequences from scratch.

High Throughput: With additional hardware upgrades you can get unattended high throughput purification capabilities of up to 18 samples with a 3-step purification protocol.



Speed – Flexibility – Convenience

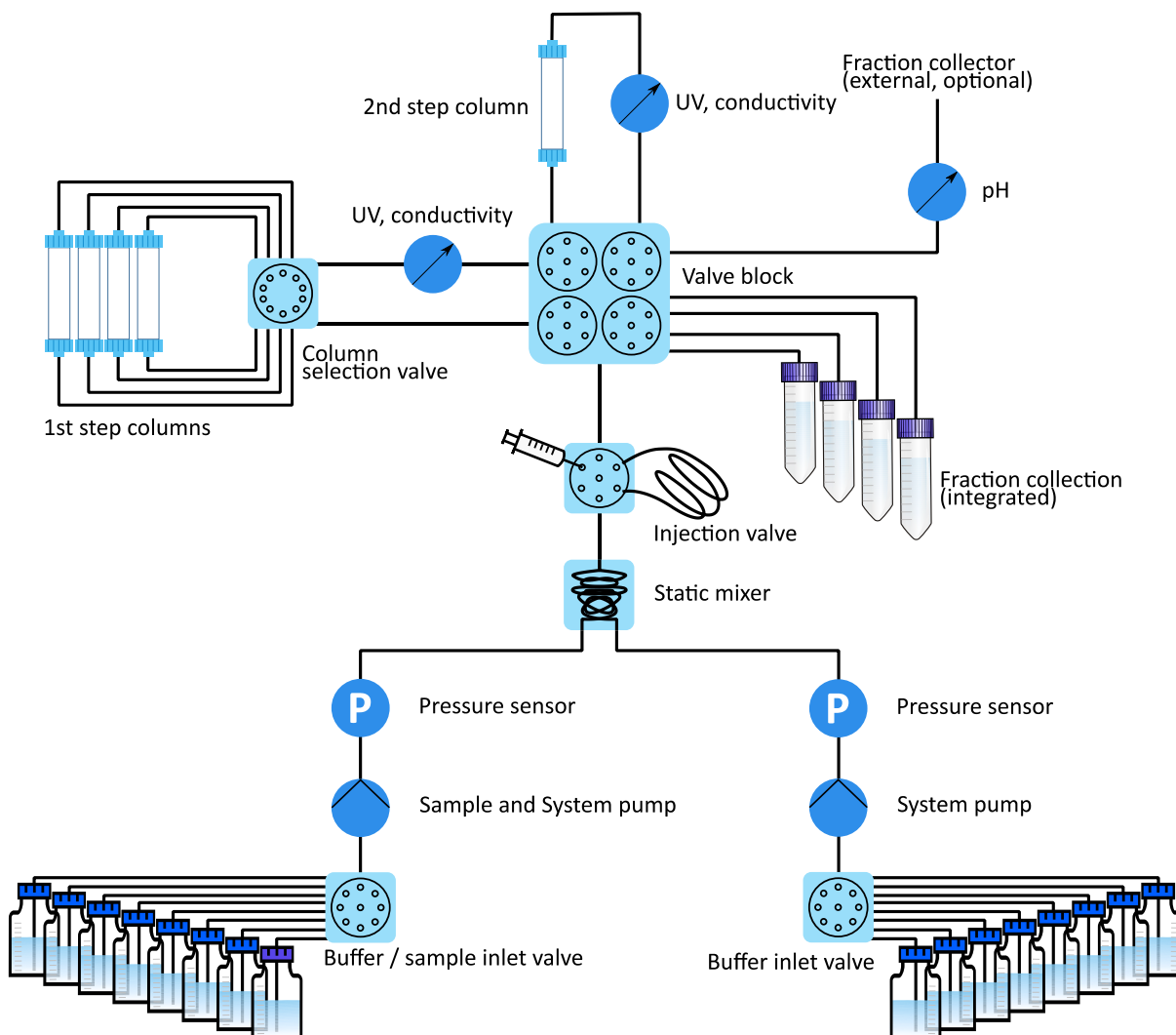
The Contichrom Discovery system has been designed for **speed**, **flexibility** and **convenience**.

Speed is provided through the unidirectional design of connected purification steps with in-line dilution, avoiding any holding steps in loops. Uniquely, the eluates from one process step are not stored in intermediate loops but the different process steps are fully integrated and streamlined providing an unparalleled fast processing.

Flexibility is provided through the possibility to either use fixed recipes or preparing

customized purification trains using the Discovery Wizard and by extending the purification train even further using normal single-column batch chromatography with the Batch Wizard. With accessory valves and a software upgrade, automated high throughput purification of multiple samples can be performed.

Convenience is provided through a high level of automation, the user-friendliness of the ChromIQ software and the seamless interplay of the system, the recipes and the pre-packed columns/consumables.



Schematic overview of the setup of the Contichrom Discovery.














Speed And Yield

The **Contichrom Discovery** system with its automated purification protocols and pre-packed columns have been designed for having the choice of obtaining either fast processing (loading protocol 1) or high load (loading protocol 2). Fast processing is obtained by limiting the load quantity to 10 mg of protein. High load is obtained by doubling the loading quantity and reducing the flowrate.

The pre-optimized multi-step protocols all start with an affinity capture step, followed by

desalting or a polishing step and a subsequent optional desalting step. Typically, 10-20 mg of protein can be recovered per run, depending on the molecular weight and whether a high throughput or a high yield protocol is chosen. Purification protocols and a choice of recommended pre-packed columns provide convenience and flexibility.

Different purification protocols and different sample loads require different process times, as shown in the table below.

| | Multi-step protocols | | | | | |
|----------------------|---|--|---|--|---|---|
| | A | B | C | D | E | F |
| Step 1 |  IMAC |  IMAC |  Protein A |  Protein A |  Protein A |  Protein A |
| Step 2 |  Size Exclusion |  Desalting |  Size Exclusion |  Desalting |  CIEX or AIEX |  CIEX or AIEX |
| Step 3 | | | | | |  Desalting |
| min/sample for 10 mg | 100* | 38 | 90 | 34 | 60 | 74 |
| min/sample for 20 mg | 100* | 38 | 106 | 50 | 76 | 90 |

Loading protocol 1: consists of a loading speed of 600 cm/h and a loading volume of 10 mL.

Loading protocol 2: consists of a loading speed of 300 cm/h and a loading volume of 20 mL.

*Loading speed not limiting.

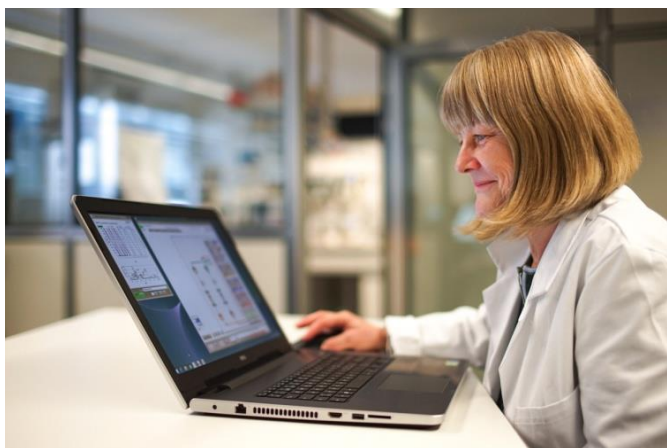
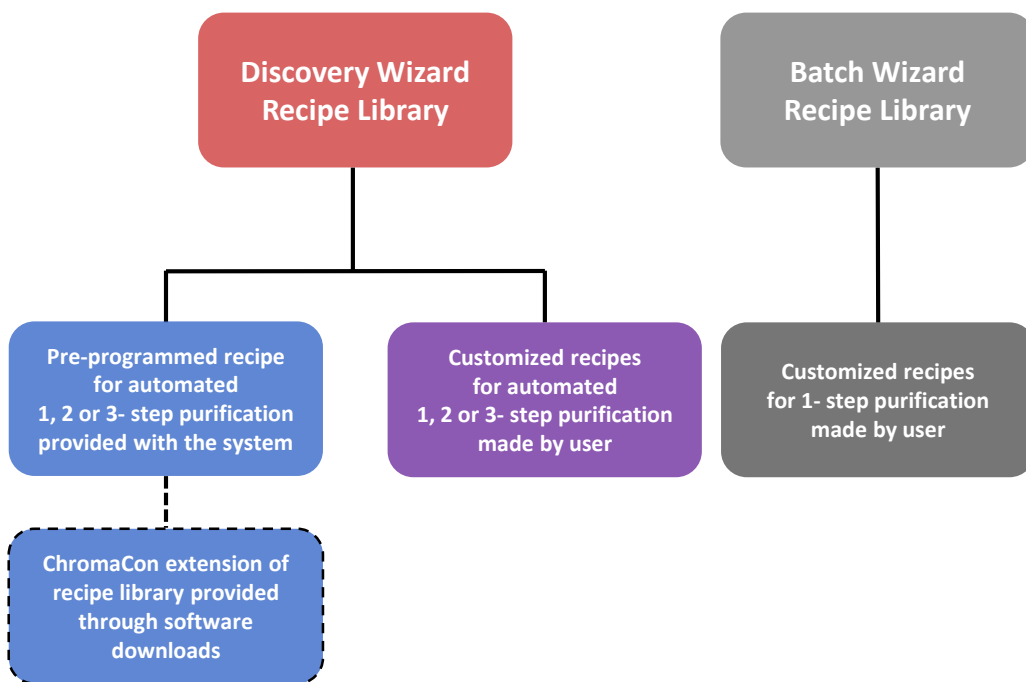
ChromIQ Software

The ChromIQ operating software supports two different wizards enabling an intuitive, user-friendly operation for batch and automated multi-step connected batch processes.

The **Batch Wizard** helps to design single-column chromatography runs in both isocratic and gradient mode. The **Discovery Wizard** supports pre-defined automated recipes for one, two- or three step integrated chromatography. The recipe libraries of both Wizards can be extended with own,

customized recipes and with additional recipes from ChromaCon.

ChromIQ includes a number of features that are particularly helpful for automated processes, such as a buffer management system showing the recipes for buffer preparation, the number of runs that can be performed with the remaining buffer volumes, and a pressure watchdog preventing the system from running dry.

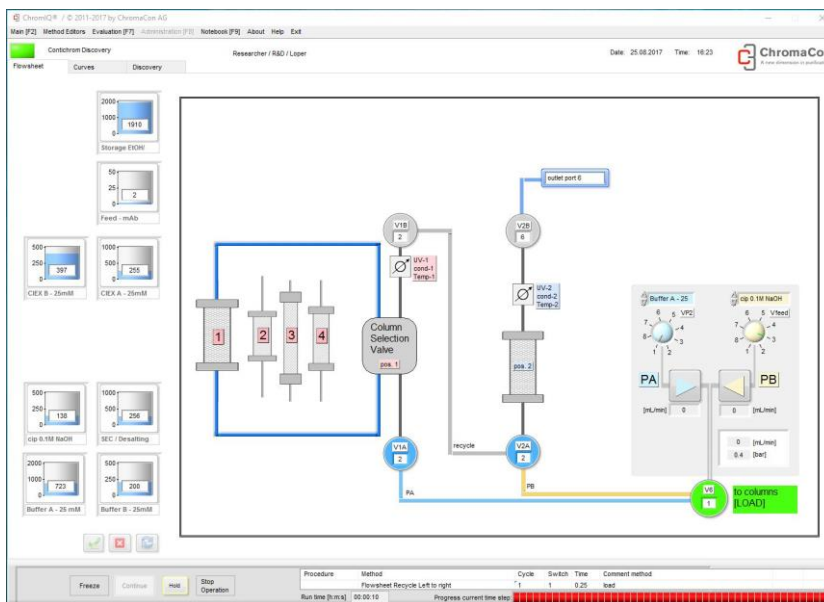


- ✓ Optimized standard methods for 1-, 2-, and 3-step processes
- ✓ Interactive process picture
- ✓ Single-click evaluation
- ✓ Easy data export (xlsx, csv, bmp, eps, emf)
- ✓ Pre-defined user groups with individual rights management
- ✓ Password protected user accounts
- ✓ Logging with time stamp and user name
- ✓ Electronic signature with checksum of log and measurement files

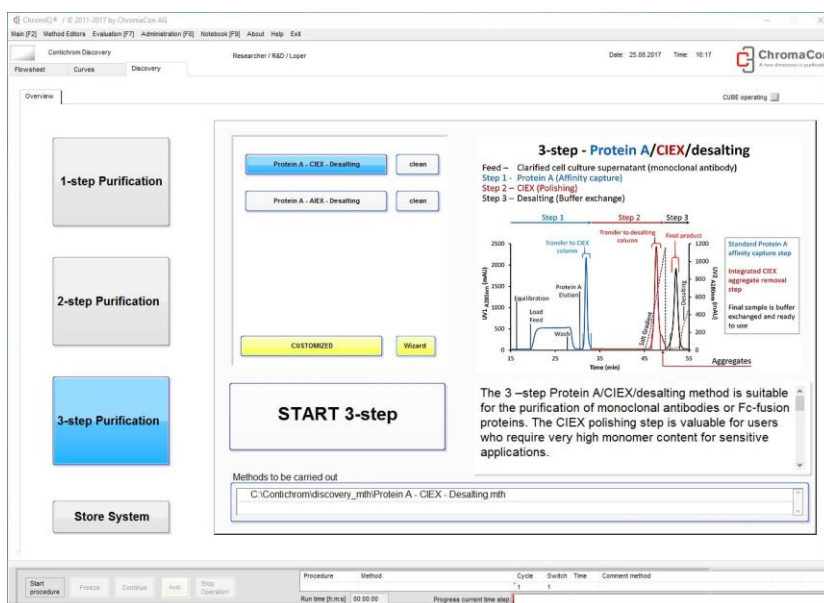
ChromIQ Software

The ChromIQ user interface for multi-dimensional purification is easy to use. It provides all necessary information where it is needed – and only when it is needed. The Discovery Wizard helps choosing the right pre-

optimized process for typical purification challenges. During the run, the current status of the system and of the processes are displayed.



An animated flow-sheet provides real-time information on the system status and process. The buffer management status (displayed on the left) shows remaining buffer volumes in real-time.



Discovery Wizard for 3-step purification. Pre-optimized protocols can be chosen. Basic information on the processes is displayed directly inside the software (displayed on the right).

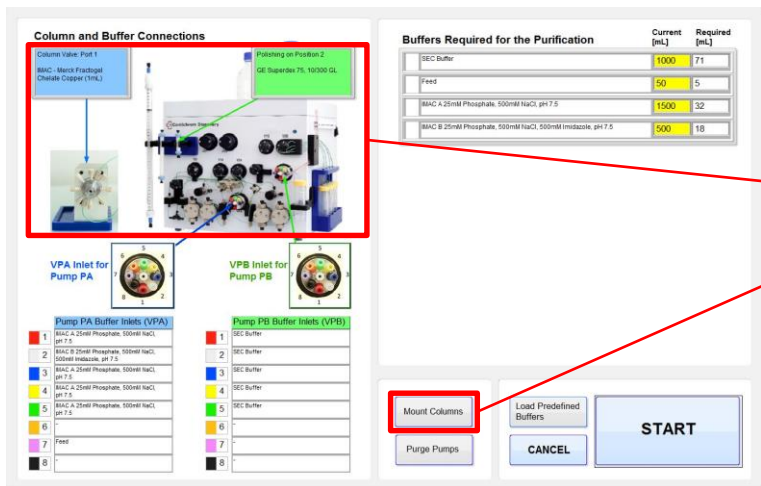
Walkthrough Example: 2-step IMAC-SEC



1. The entry page shows options for 1-, 2- or 3-step purifications and a button to prepare the system for storage. Click the “2-step Purification” button, which will turn blue.



2. The middle column shows the different purification sequence options and also the possibility to run custom 2-step processes. Click the “IMAC-SEC” button which will turn blue. Now general information on IMAC/SEC processes is displayed on the right. Next, press “START 2-step”.



3. After entering the project and sample names, this screen with information for getting the system ready to run is displayed. The picture shows where to mount which column. The “Mount Column” button shows detailed information and allows to flush the column with buffer for pre-equilibration.

Walkthrough Example: 2-step IMAC-SEC

Column and Buffer Connections

Column Valve: Port 1
MAC - Macro Fractional Celsis Copper (10L)

Positioning on Position 2
GE Superdex 75, 10/300 GL

VPA Inlet for Pump PA

VPB Inlet for Pump PB

Buffers Required for the Purification

| | Current [mL] | Required [mL] |
|---|--------------|---------------|
| SEC Buffer | 1000 | 71 |
| Feed | 50 | 5 |
| MAC A 20mM Phosphate, 500mM NaCl, pH 7.5 | 1500 | 32 |
| MAC B 20mM Phosphate, 500mM NaCl, 500mM Imidazole, pH 7.5 | 500 | 18 |

Pump PA Buffer Inlets (VPA)

| | |
|---|---|
| 1 | MAC A 20mM Phosphate, 500mM NaCl, pH 7.5 |
| 2 | MAC B 20mM Phosphate, 500mM NaCl, 500mM Imidazole, pH 7.5 |
| 3 | MAC A 20mM Phosphate, 500mM NaCl, pH 7.5 |
| 4 | MAC A 20mM Phosphate, 500mM NaCl, pH 7.5 |
| 5 | MAC A 20mM Phosphate, 500mM NaCl, pH 7.5 |
| 6 | SEC Buffer |
| 7 | Feed |
| 8 | SEC Buffer |

Pump PB Buffer Inlets (VPB)

| | |
|---|------------|
| 1 | SEC Buffer |
| 2 | SEC Buffer |
| 3 | SEC Buffer |
| 4 | SEC Buffer |
| 5 | SEC Buffer |
| 6 | SEC Buffer |
| 7 | SEC Buffer |
| 8 | SEC Buffer |

Buttons: Mount Columns, Load Predefined Buffers, Purge Pumps, CANCEL, START

4. The right table shows the required buffers for the selected purification method. Current and required buffer volumes are displayed. The table on the bottom left shows the connection between the color-coded buffer inlet tubes and the buffer tanks.

Column and Buffer Connections

Column Valve: Port 1
MAC - Macro Fractional Celsis Copper (10L)

Positioning on Position 2
GE Superdex 75, 10/300 GL

VPA Inlet for Pump PA

VPB Inlet for Pump PB

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Pump PA Buffer Inlets (VPA)

| | |
|---|---|
| 1 | MAC A 20mM Phosphate, 500mM NaCl, pH 7.5 |
| 2 | MAC B 20mM Phosphate, 500mM NaCl, 500mM Imidazole, pH 7.5 |
| 3 | MAC A 20mM Phosphate, 500mM NaCl, pH 7.5 |
| 4 | MAC A 20mM Phosphate, 500mM NaCl, pH 7.5 |
| 5 | MAC A 20mM Phosphate, 500mM NaCl, pH 7.5 |
| 6 | SEC Buffer |
| 7 | Feed |
| 8 | SEC Buffer |

Pump PB Buffer Inlets (VPB)

| | |
|---|------------|
| 1 | SEC Buffer |
| 2 | SEC Buffer |
| 3 | SEC Buffer |
| 4 | SEC Buffer |
| 5 | SEC Buffer |
| 6 | SEC Buffer |
| 7 | SEC Buffer |
| 8 | SEC Buffer |

Buttons: Mount Columns, Load Predefined Buffers, Purge Pumps, CANCEL, START

5. After all buffers have been filled and connected, the pumps can be purged to make sure that they contain the right buffers. The system is then ready and the "START" button can be pressed.

Did you check:

- Buffer Volumes ?
- Pump inlet connections ?
- Columns and Column positions ?

Buttons: go BACK and check, START the Run

6. The Software reminds you once more of the critical steps for preparing the purification run. Now you can "START the Run" to automatically purify your protein.

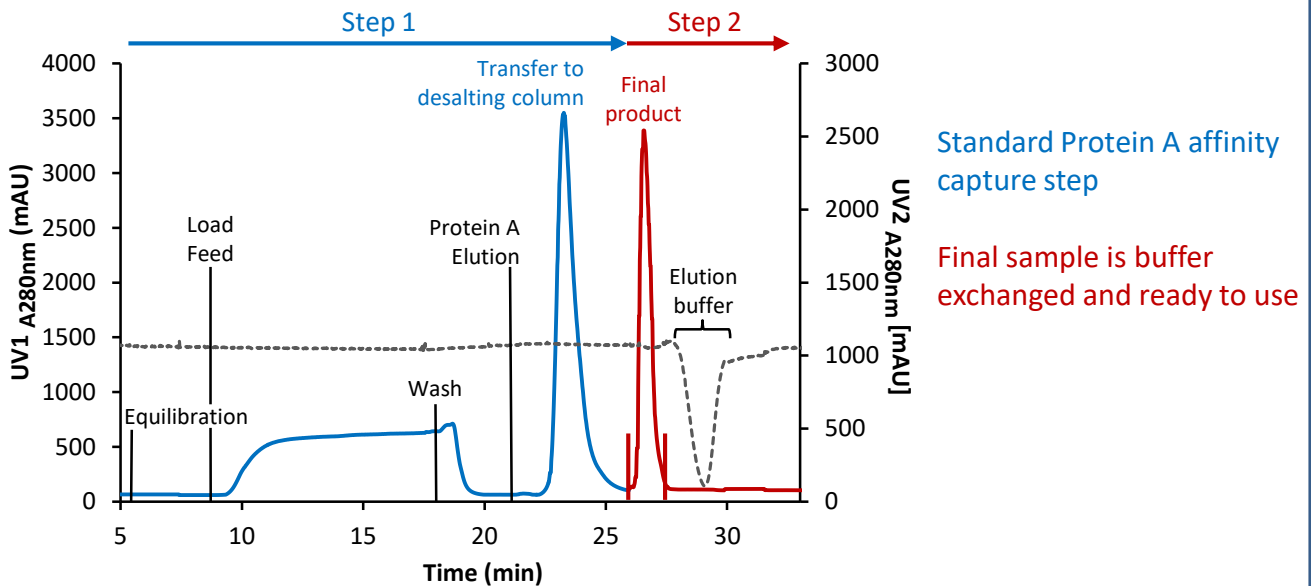
Application Examples

2-step purification of a monoclonal antibody Protein A / Desalting

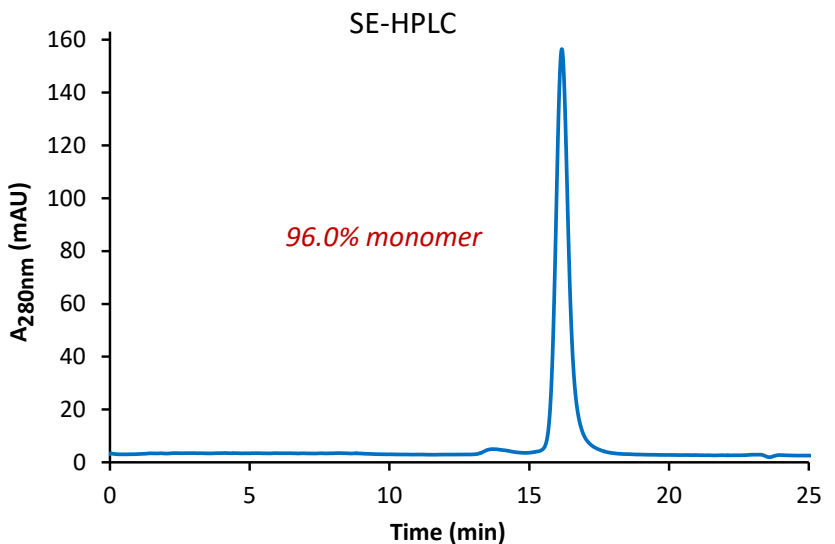
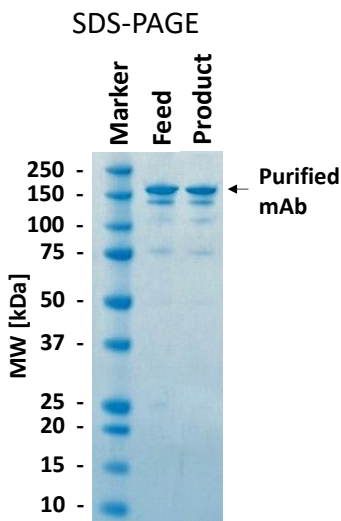
Conditions

Feed: 10 mL clarified cell culture supernatant (monoclonal antibody), 1 mg/mL
Step 1: Protein A (Affinity capture)
Step 2: Desalting (Buffer exchange)

Run



Results



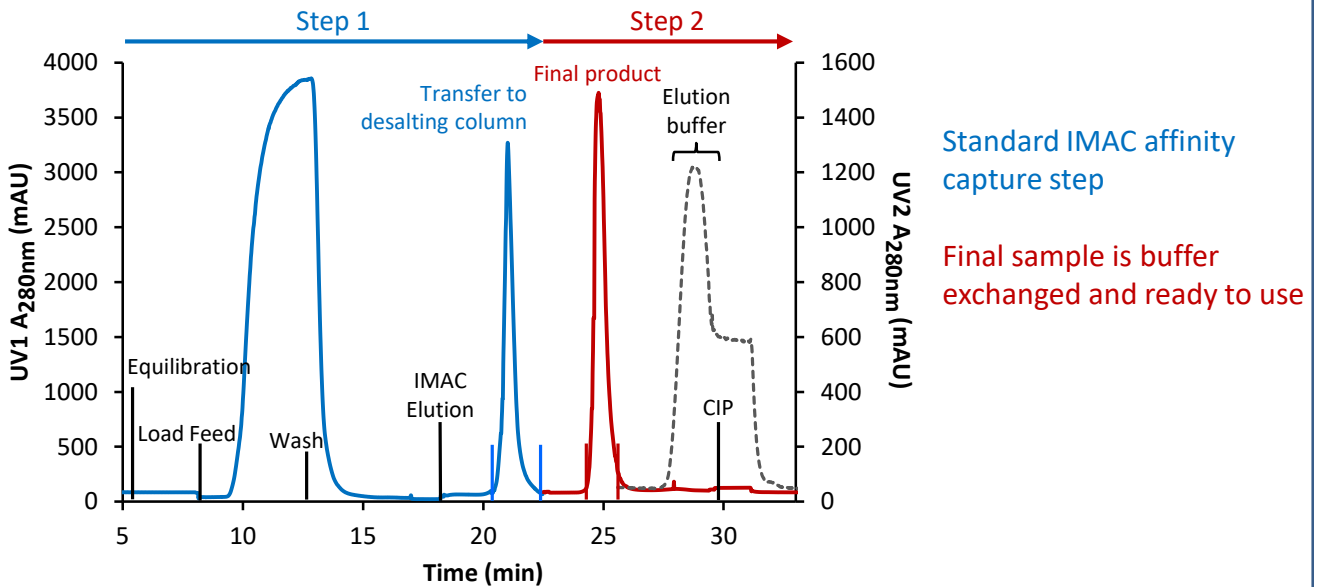
Application Examples

2-step purification of a His-tagged protein IMAC / Desalting

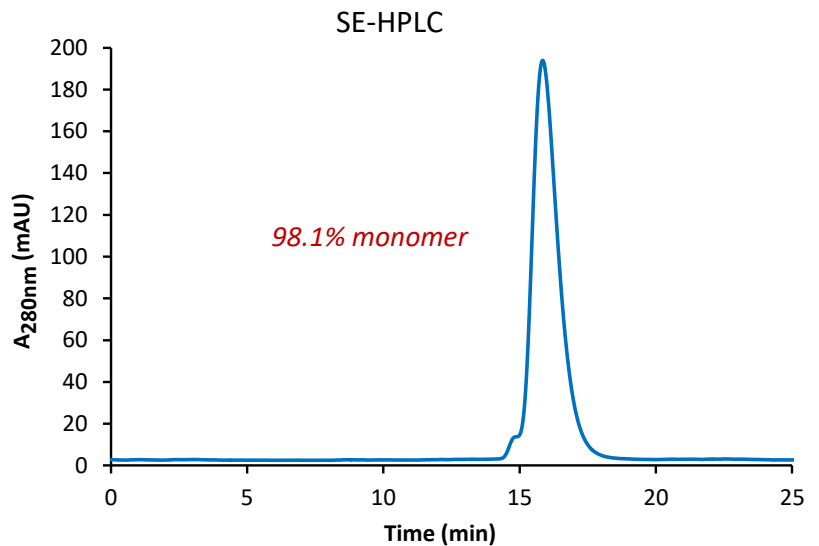
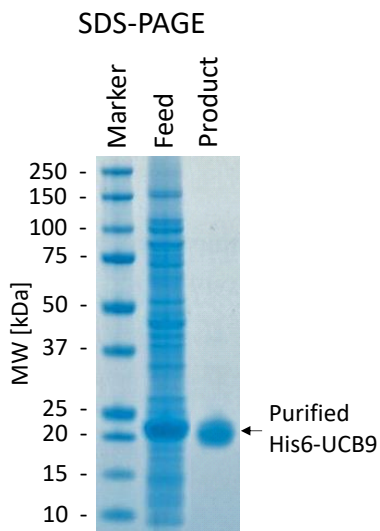
Conditions

Feed: 5 mL, E. coli BL21(DE3) cell lysate, 0.5 mg/mL
Step 1: IMAC (Affinity capture)
Step 2: Desalting (Buffer exchange)

Run



Results

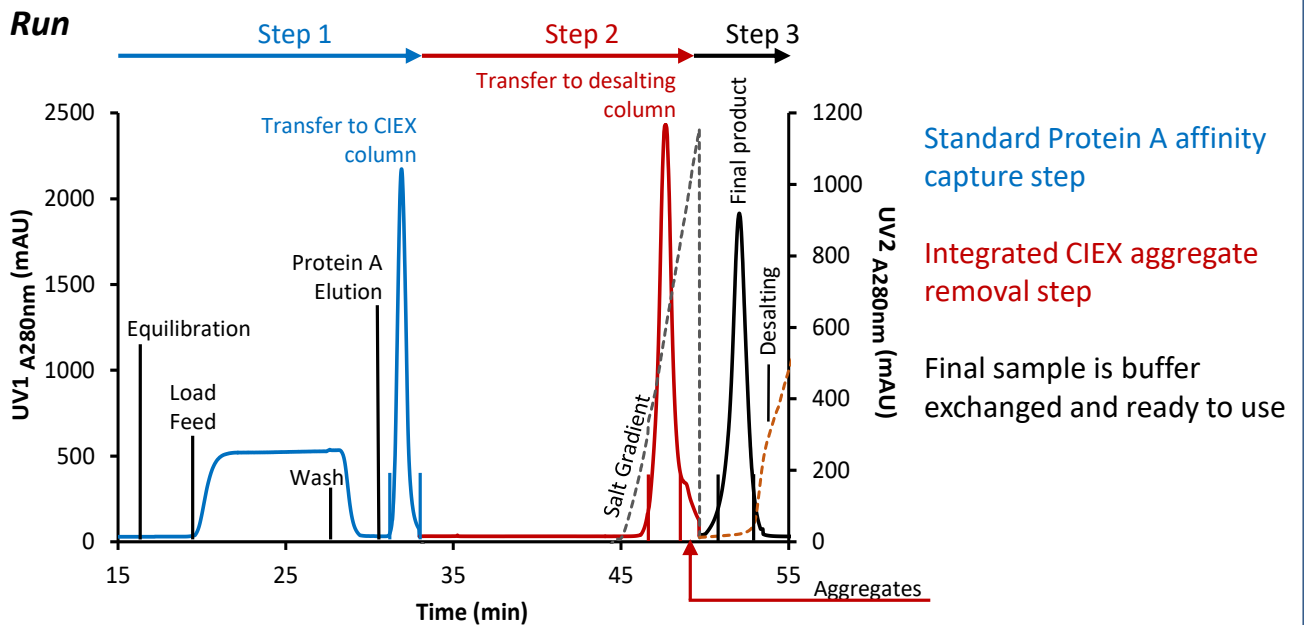


Application Examples

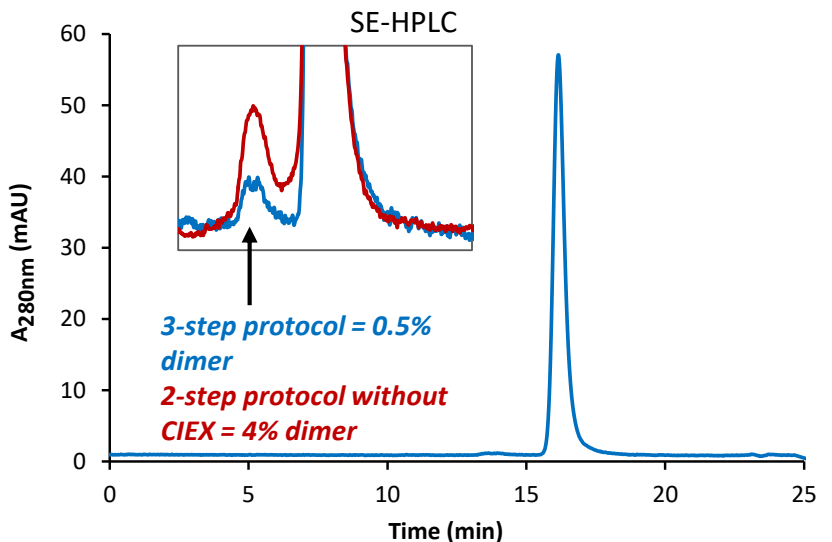
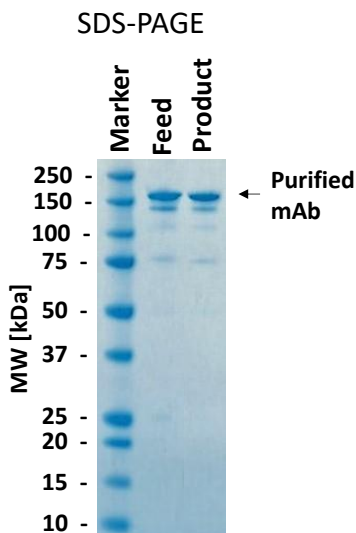
3-step purification of a monoclonal antibody Protein A / CIEX / Desalting

Conditions

Feed: 10 mL clarified cell culture supernatant (monoclonal antibody), 1 mg/mL
Step 1: Protein A (Affinity capture)
Step 2: CIEX (Polishing)
Step 3: Desalting (Buffer exchange)



Results

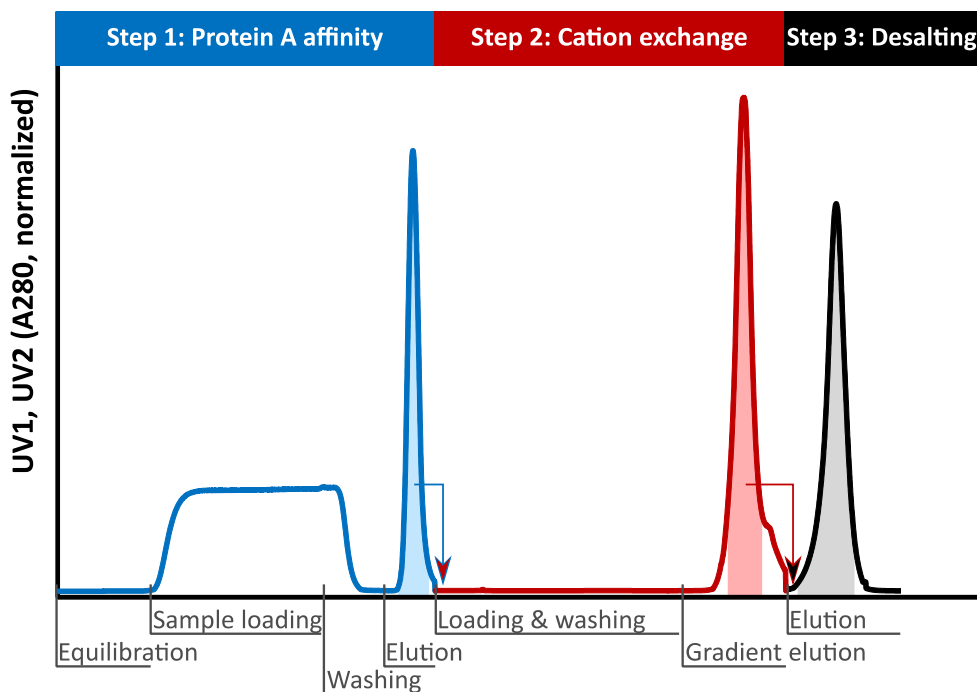


Unattended High Throughput Purification

The **Contichrom Discovery** HT system with additional external loading valves can be used for unattended, high-throughput purification of monoclonal antibodies or other protein samples using a multi-step purification protocol with up to 18 sample loads. The purification protocols are integrated without intermediate loop storage of eluates, thus providing short processing times for multi-step purification protocols. If the second process

step requires a different buffer composition than the eluent of the first step, inline-dilution can be used.

High throughput purification applications are particularly useful for screening of monoclonal antibody variants from different clonal expression variants or for screening of protein mutants.



Chromatogram of an unattended and automated 3-step purification of a 10 mL monoclonal antibody (mAb) feed volume. Total run time: 74 min including cleaning.

| | Activity | Number of purified mAbs | System run time |
|---------------------------------|--|-------------------------|-----------------|
| Working day | 3-step purifications incl. overnight purifications incl. column washes | 19 | 24 h |
| Working week (Monday-Friday) | | 91 | 112 h |

Up to 91 protein samples can be purified per week with a 3-step purification protocol with 10 mg of protein obtained per run.

System Accessories

Adding convenience & value: Accessories include a sample loop system for feed loading, an external valve with an injection loop and a stable, re-usable transport box.



Fraction collectors Foxy R-1 and R-2



Re-usable system transport box



High-Throughput sample valve system for loading up to 9 samples



Sample loading loop kit
500 μ L up to 20 mL

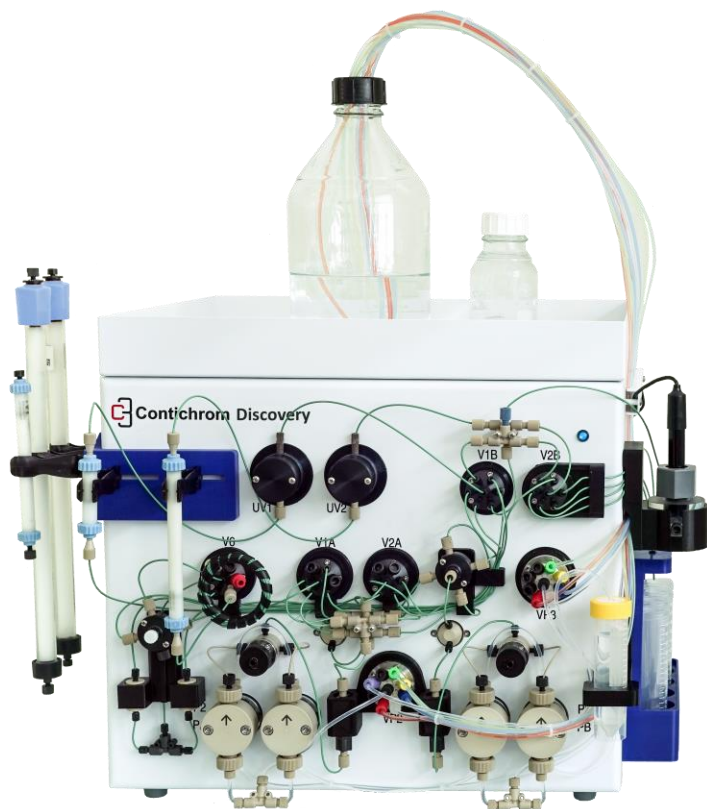


External variable wavelength detector
(190-900nm)

System Accessories

Cooling of product feed and of fractions is important for preserving product integrity. A compact cooling cabinet that fits on a lab bench and can accommodate a fraction collector (Foxy R-1) and feed bottles is available.

For unattended high-throughput purification the feed samples and the sample loading valves (up to 9 samples per valve, total max. of 18) can be placed in the cooling chamber as well.



Who uses the Contichrom Discovery?

Bio/Pharmaceutical companies

- High-throughput purification of mAbs and tagged proteins with a SEC polish step
- Conventional batch purification of proteins
- Process development for therapeutic proteins

Research institutions

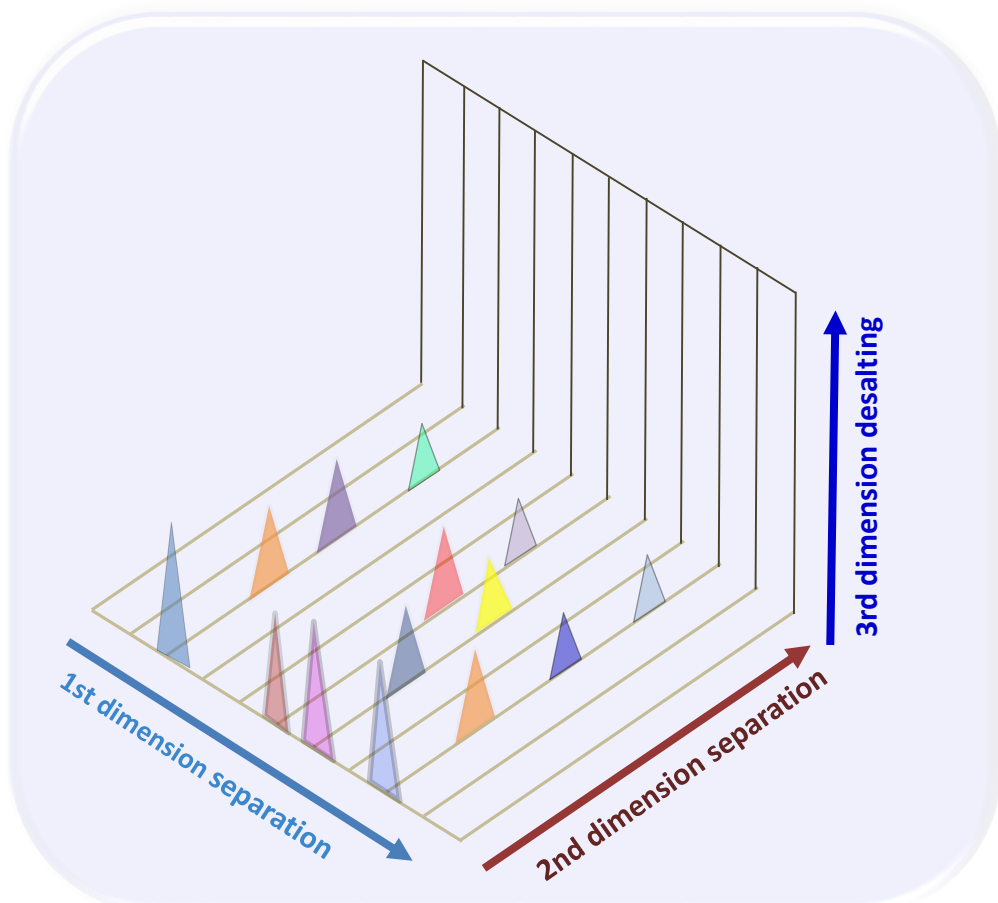
- Biomarker discovery, target identification, protein-based assays
- Fast production of biological targets without need for manual optimization of purification protocols

CDMOs and CROs producing Biologics

- Process development of Biologics
- Production of recombinant proteins for pre-clinical research

Universities and colleges

- Protein purification for non-protein experts
- Unlock new research opportunities as high quality protein targets become affordable and easily accessible
- Production of biological targets using tagged proteins
- Protein purification for protein crystallographers



Installation & After Sales Services

All systems are pre-tested to verify the high level of quality. The system is delivered pre-assembled. Installation is done with an automated installation qualification and operation qualification (IQ-OQ) protocol that re-checks the system and generates a test summary. The Contichrom Discovery is then ready for use; the Discovery kit contains a full set of pre-packed columns suitable for the multi-step purification method recipes.

We offer on-site and off-site training, webinar-based product support and we organize workshops on continuous chromatographic purification. Finally, you can always call us or our local partners for troubleshooting.

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 training. We also offer free ChromIQ software upgrades.

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. The UV detectors have a long lifetime and lamp changes are feasible. We recommend to exchange the wear & tear parts every 6 months (heavy use) or every 12 months (regular use). We provide instructions how to do this but you are also welcome to get help from our PM partners.



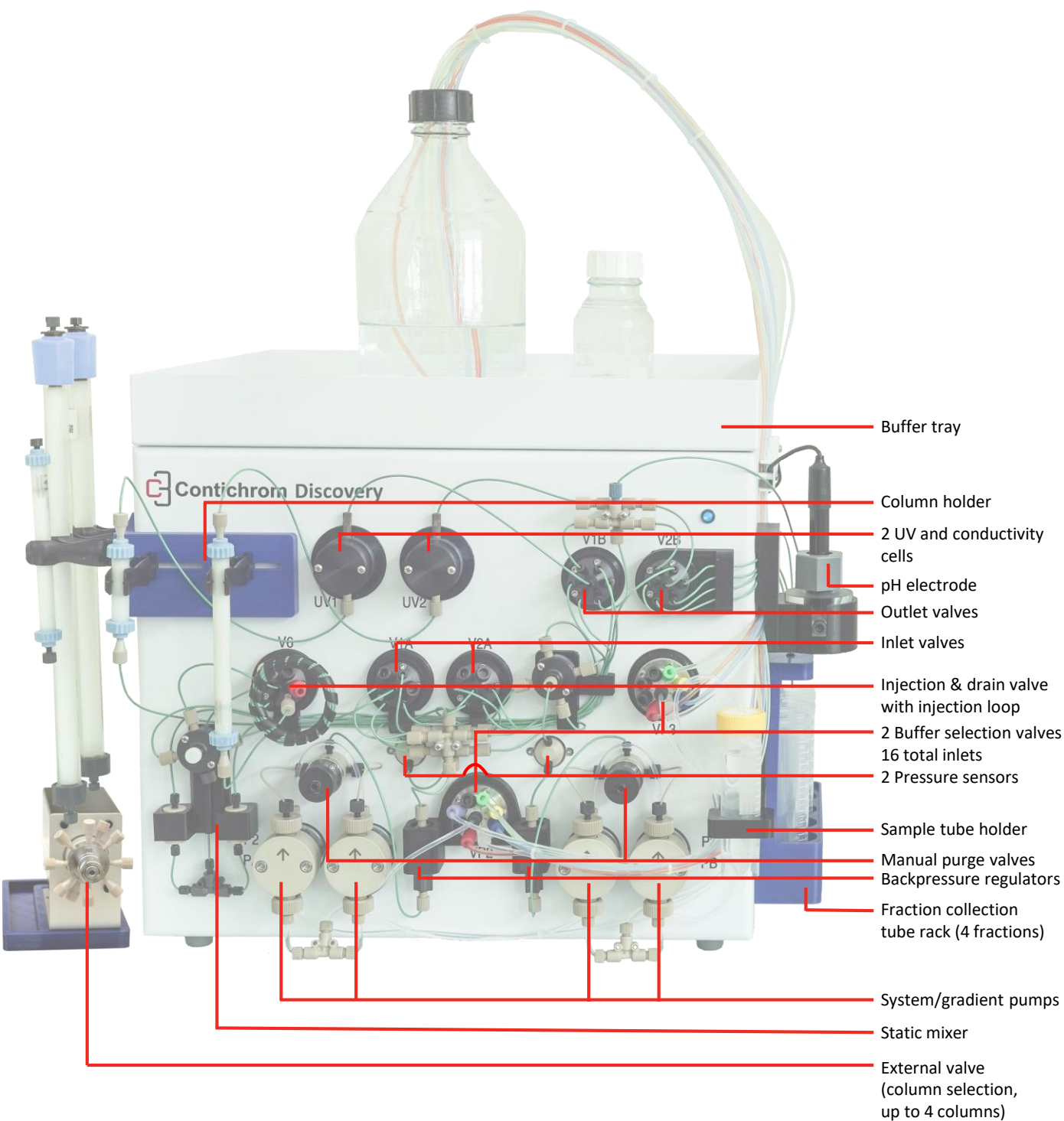
We offer comprehensive and cost-effective Preventive Maintenance and Repair Service packages.



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

For details please ask for a quote at your local ChromaCon representative.

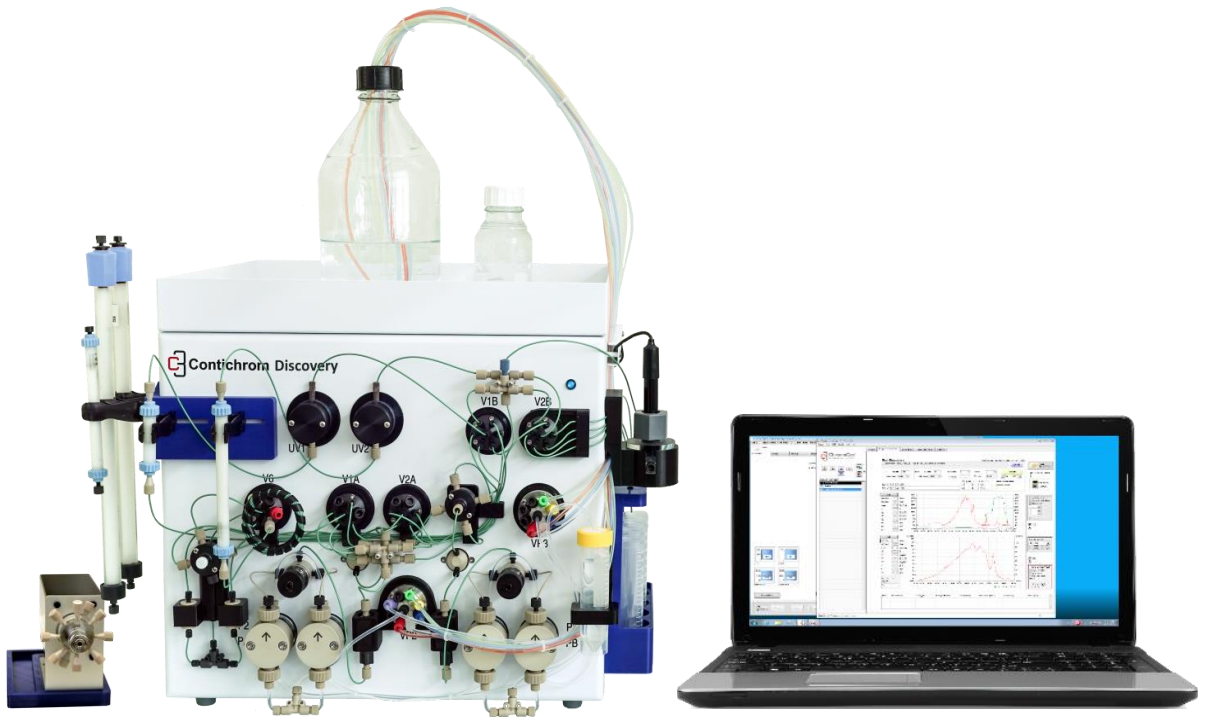
Contichrom® Discovery Functions



Technical Specifications

| | |
|--|---|
| Process capabilities | Batch Wizard (isocratic, step, gradient elution), Discovery Wizard for automated 2- or 3-step purification. Upgradable for high-throughput purification with additional external valves for sample loading. |
| Operating software | ChromIQ is a user-friendly operating software with step-by-step wizards to guide the design and automatically run single column and multi-dimensional batch chromatography runs. |
| Software compliance | The software contains essential elements of 21CFR Part 11 compliance: <ul style="list-style-type: none">• Pre-defined user groups, administrators, R&D and production users• Rights management for individual user groups• User accounts are password protected• Logging with time stamp and user name (non-deletable)• Electronic signature with checksum of log and measurement files |
| Pump type | 2 High precision double-piston pumps with active seal wash |
| Pressure | Rating: 50 bar (5 MPa) / 725 psi Sensors: 2, after each pump |
| Flow rate range | 0.1 – 36 mL/min |
| Buffer selection | 16 Inlets (2 x 8-fold buffer selection valve) 5 Outlets |
| UV, fixed wavelength | 2 Long lifetime LED UV detectors, each with 260 & 280 nm recorded simultaneously |
| Conductivity monitoring | 2 Conductivity sensors (1-300 mS/cm) |
| pH monitoring | 1-14 |
| Valves | 6 Multi-position valves 1 Automated drain & injection valve 1 External column selection valve |
| Mixer | Static mixer with non-return valve 0.1-36 mL/min |
| Sample loading | Sample pump for drawing samples from bottles or vials. Multiple automatic injections possible. Injection valve for injection loop loading. Injection loops (500 µL-20 mL) for syringe injections available as accessories. |
| Buffer management | For monitoring buffer tank levels. Pressure drop watchdog to prevent system from running dry. |
| Fraction collection | Built-in: collection of 4 fractions; external fraction collector optional. |
| Computer hardware | Stand-alone laptop computer (Windows, 64 bit, full HD resolution (1920 x 1080) or higher) with ChromIQ software |
| Other | Cold room compatible Large buffer tray Portable & compact Runs resins and membrane stationary phases. A starter kit of suitable pre-packed columns are included. |
| Dimensions (width x depth x height) | 515 mm x 450 mm x 380 mm (20.3" x 17.7" x 15.0") |
| Weight | 30 kg (67 lb) |
| Materials | <ul style="list-style-type: none">• All wetted parts are biocompatible• High pressure side capillaries: PEEK• Low pressure side tubing: PET• Fittings: PEEK |
| Upgrade capabilities | For high-throughput purification with additional external valves for sample loading |

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

Your local representative:



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