

How can flexibility
and process economics
be combined
in one LC system?



Contichrom®

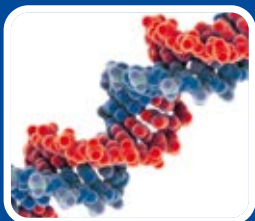
Preparative liquid chromatography

Contichrom®
lab equipment
for superior
LC purification



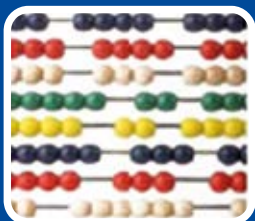
Which aspects are important for a purification system?

Introducing the flexible Contichrom® lab (all-in-one) process capability.



Flexibility

- Contichrom® allows developing all downstream process modes (batch, SMB, CaptureSMB, multi-column, MCSGP) with one single piece of equipment and easy process conversion



Process economics

- The MCSGP process increases both purity and yield by 50 % compared to the corresponding batch process
- Contichrom® allows rapid automated process-development



Scalability

- Contichrom® allows retention of the developed product profile, yield and purity specifications upon upscaling

Contichrom® lab is a preparative liquid chromatography system designed for discovery, process development and scale-up, offering great flexibility in process choices. With Contichrom® lab, all process modes (batch, SMB, CaptureSMB, MCSGP, multi-column) can be performed with a single equipment and control software. The Contichrom® control software has been developed to enable the conversion of batch to multi-column processes using a method wizard and to allow the fast development of scalable processes, omitting extensive screening steps.

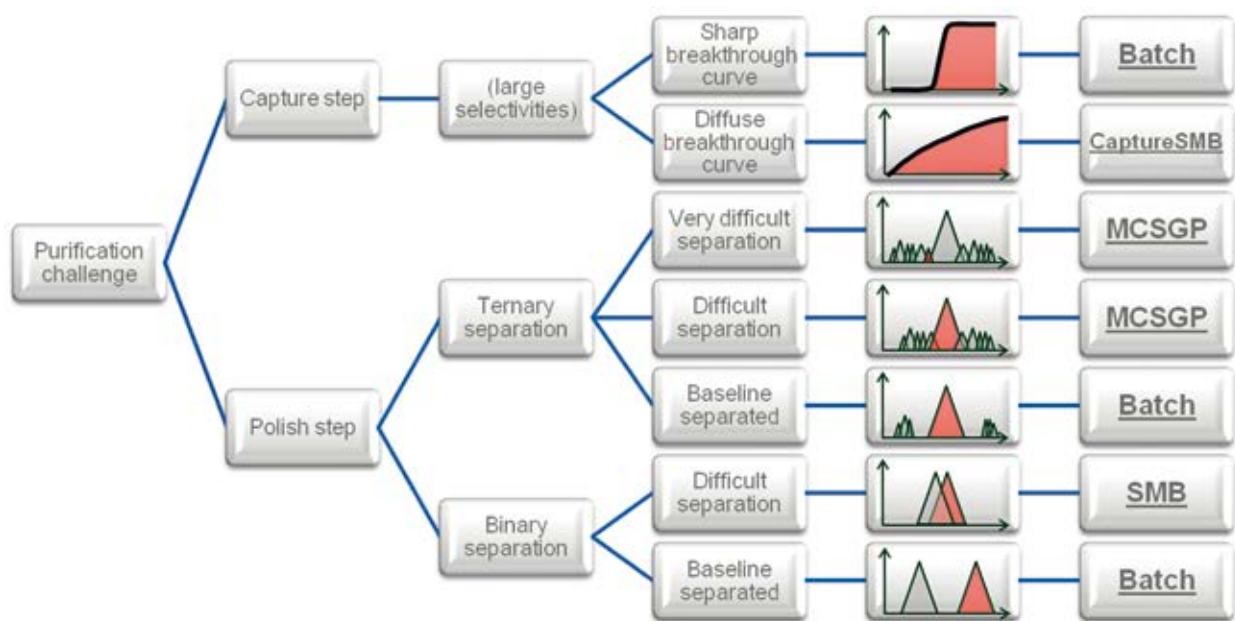
The Contichrom® lab adds another dimension to process chromatography, as it allows development of processes based on the MCSGP (**M**ulti-column **C**ountercurrent **S**olvent **G**radient **P**urification) principle which is much more efficient than a batch process.

All standard media (Ion exchange, mixed-mode, HIC, RP, SEC, Affinity) can be used as well as all standard organic solvents and aqueous buffers.



Which processes can your purification system operate?

Flexibility in process development means that based on the purification challenge the best process is chosen with respect to ease, development time and costs.



For affinity capture with low dynamic binding capacity having a broad breakthrough curve, CaptureSMB is superior to batch. For simple ternary separations, batch processes are the best options if product (red) and impurity (grey) are well separated. However for difficult ternary separations of overlapping impurities, the MCSGP process is superior. The isolation of product-related impurities for pre-clinical and toxicological assessments, normally a tedious task, is easy using the MCSGP process (far left). With Contichrom® lab equipment all processes as shown above can be performed.

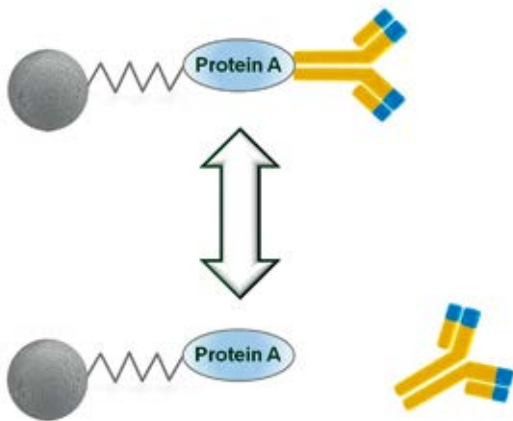


Contichrom® lab equipment allows development of a simple batch process first and then automatic switching to an MCSGP process, providing superior process economics.

How can affinity capture be faster and more cost effective?

Using CaptureSMB®, a twin column cyclic process, with Contichrom® equipment instead of a single column process for Protein A capture steps has significant advantages:

- Higher loading velocities shortening the transit time for the capture step by 50 %
- Due to faster processing, preservation of protein integrity
- Optimal use of Protein A resin capacity leading to a resin cost saving of 50 %
- Annual Protein-A resin cost savings in production scale of several Mio USD
- Easy and robust twin-column equipment design and software wizard



Application Areas

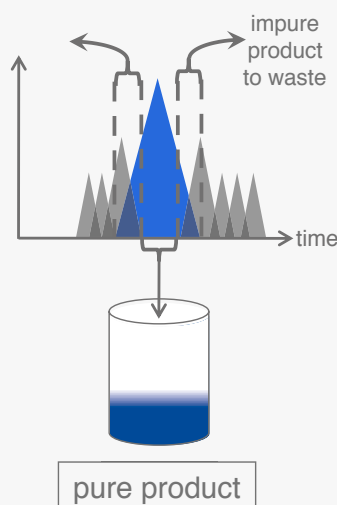
- Fast capture of monoclonal antibodies
- Capture of proteins to customized ligands (chemical and biological)
- Capture of therapeutic compounds from fractionated blood plasma
- Capture of API from natural extracts

How can purity and yield be optimized simultaneously?

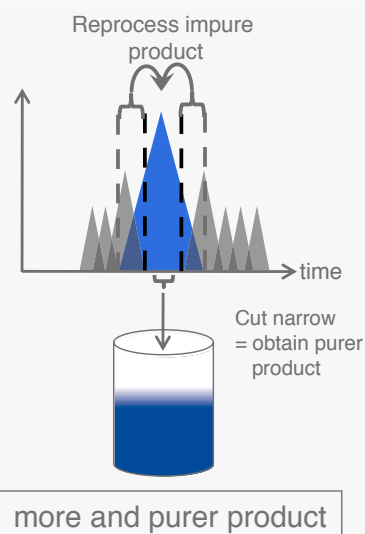
The MCSGP process operates with twin columns instead of one column, whereby the impure side fractions containing product are recycled internally, extracting all product and thereby increasing both yield and purity. The MCSGP process mode is typically operated with the same transit time as a batch chromatography step.

A batch derived from a MCSGP process has the same «batch definition» as one from a normal single column batch process. It is a specific quantity of material or API processed in one process or series of processes so that it could be expected to be homogenous.

Conventional batch chromatography



ChromaCon's internal recycling chromatography (MCSGP)



Application Areas

- Discovery: isolation of leads
- Process development: purification of proteins, synthetic peptides
- Purification of oligonucleotides
- Isolation of product-related impurities
- Purification of conjugates and PEGylated proteins
- Purification of small molecules and natural products

How can impurities be isolated more efficiently?

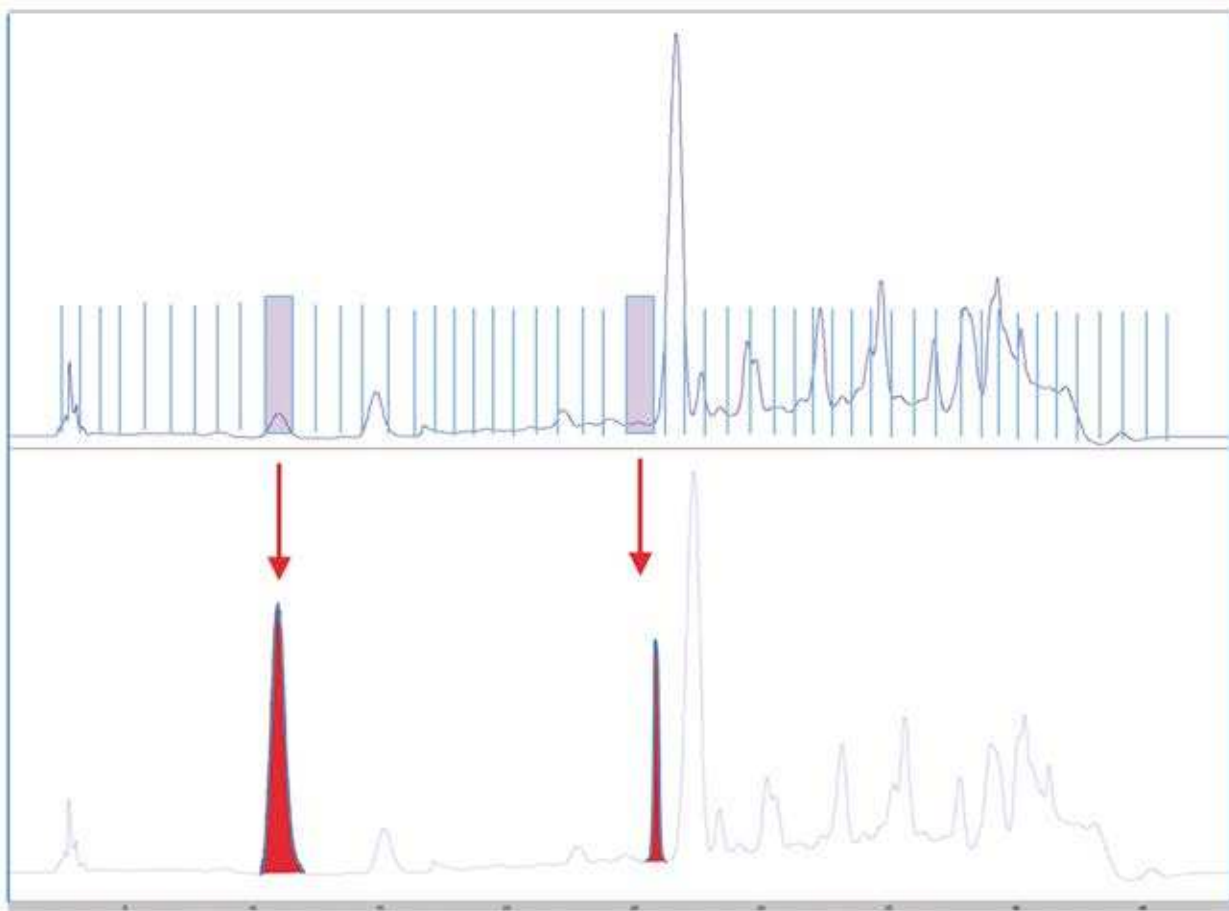
Applications in Discovery and in the isolation of product-related impurities:

The Problem:

- Discovery: In shotgun proteomics (bottom-up), due to the complexity of the samples, extensive front-end separation is essential to alleviate the problem of peptide undersampling, to maximize protein identifications and to tackle the vast dynamic range.
- Related impurities: Isolation of product-related impurities is normally a tedious task requiring several hundred injections to isolate sufficient material for pre-clinical and toxicological studies.

The Solution:

- The MCSGP process allows selective enrichment of a defined region of the chromatogram (red)
- The enriched fraction can be isolated for functional characterization or analyzed directly on-line using mass spectrometry analysis



Selectively enriched fractions

Does your system provide automated process development?

Contichrom® lab equipment and software have been designed to be very user-friendly. The control software helps the user to easily navigate and manage process setup, execution, and reporting.

Fast and automated process development

- Wizards with graphical user interface for easy method programming
- Automated conversion from batch to MCSGP process
- Extensive library of pre-defined methods for all standard operations

Easy to operate

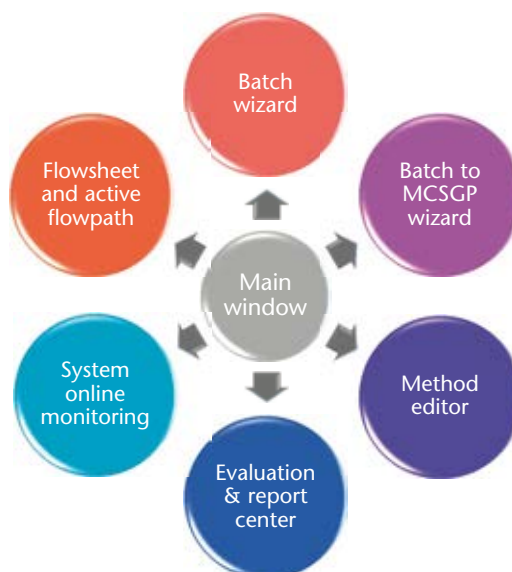
- Intuitive software for operation of batch and MCSGP
- Active flow path highlighted in flowsheet
- Pause/continue functionality, even for continuous chromatographic operations

Integrated evaluation and reporting

- Detailed evaluation capabilities with standardized PDF reports
- Data export functions

Full data security and traceability

- Full audit trail and change control
- User management hierarchy provides high operational and data security
- FDA 21 CFR Part 11 compliant



How can you switch to a superior process?

The Contichrom® wizard allows switching a batch process to a superior MCSGP process in just three steps:

Step 1: Firstly, a non-optimized batch process is developed, the product peak is identified and the batch chromatogram is stored in the database. For conversion of a batch to an MCSGP process, the respective batch chromatogram is retrieved.

Step 2: Using the Contichrom® software wizard, the borders of the product peak (red) are defined by simply dragging bars to define the boundaries. The narrower the boundaries are defined, the purer the isolated product. Then the boundaries of the recycling fractions (blue) are set by dragging another set of bars and the start and end points are defined.

Step 3: Pressing the software wizard button will automatically convert batch process into an MCSGP process.

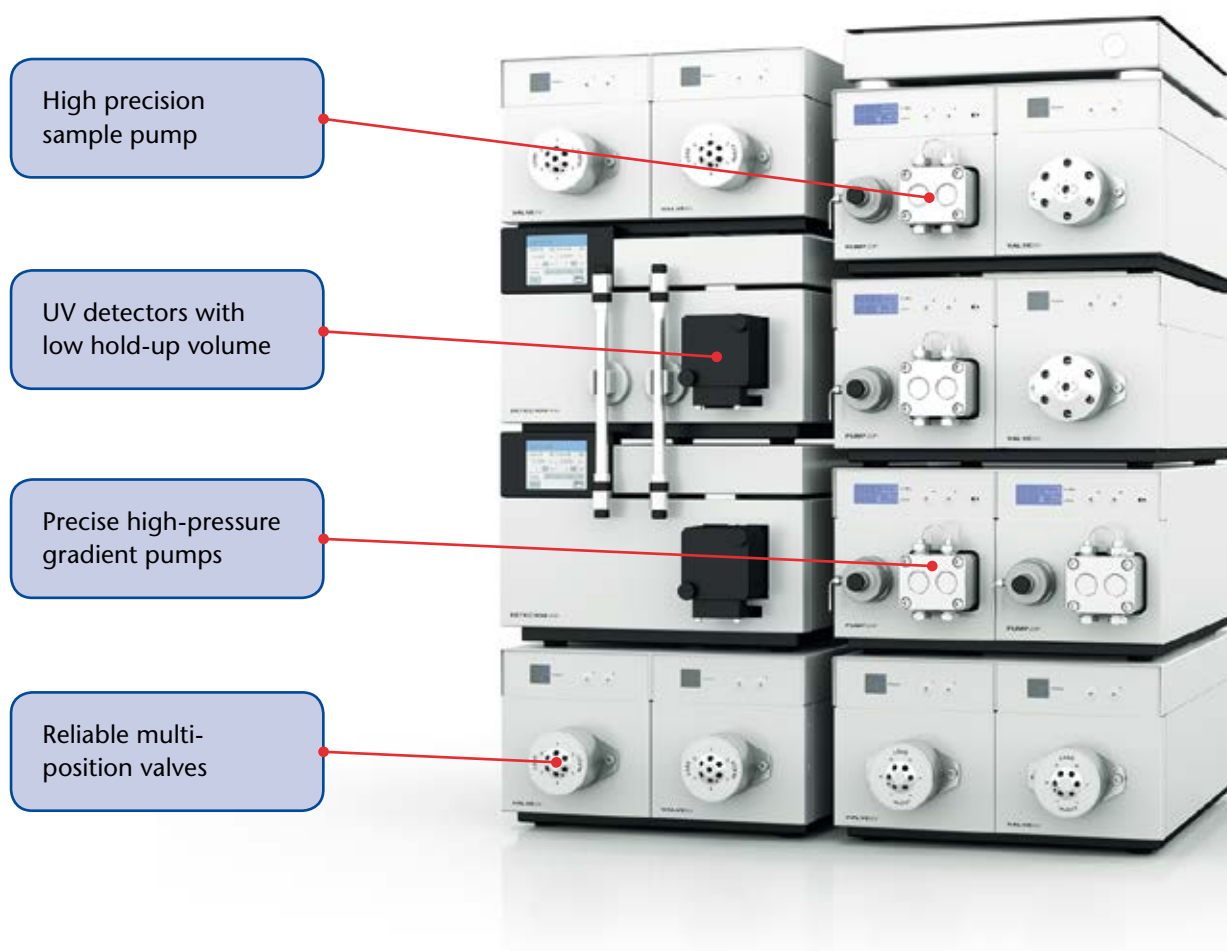
The screenshot displays the 'Contichrom® MCSGP-Wizard' software interface. The main window shows a chromatogram with a red line indicating the product peak and blue shaded areas representing recycling fractions. The interface includes several panels: 'MCSGP Operating Parameters' on the left, 'Fractogel SCS (M)' on the right, and a 'gradient mode' section at the bottom right. A 'Write Method' button is visible at the bottom center. Three callout boxes provide instructions for the conversion steps:

- Step 1:** retrieve chosen chromatogram of batch run from database (points to the 'Fractogel SCS (M)' panel)
- Step 2:** interactive definition of product range (red) and recycling fractions (blue): pull bars to define boundaries (dotted lines) (points to the chromatogram)
- Step 3:** press button to convert batch to MCSGP process (points to the 'Write Method' button)

How do you combine multi-functionality with a small footprint?

Application fields:

- **Process development:** facilitated through flexibility in choosing the right process for a given process challenge
- **Isolation of product-related impurities:** the tedious task of isolating product-related impurities for pre-clinical/toxicological characterization is considerably facilitated using Contichrom® with MCSGP mode
- **Preparative product purification:** The Contichrom® lab is available in two versions with two different pumps:
 - Contichrom® lab-10: 0.01–10 mL/min for up to 20 g product/day
 - Contichrom® prep-100: 1–100 mL/min for up to 200 g product/day



The Contichrom® purification system requires less space than most preparative HPLC systems.

Multi-functionality with a small footprint

- Contichrom® is a preparative liquid chromatography system intended for process screening and development.
- Instead of time-consuming Design of Experiments (DoE) for establishing optimized starting conditions, Contichrom® offers a software wizard tool to easily convert a basic batch process to a superior MCSGP process, thus reducing development time for robust and economic processes considerably.
- The Contichrom® operating software provides pre-defined methods for standard batch operations and for an intuitive user-friendly operation and data security, being compliant to 21 CFR part 11 requirements.
- The Contichrom® lab has a modular design where parts can be easily accessed and replaced. It has an interactive instrument display and many functionalities, such as a pause / continue functionality. A large buffer storage area on top of the instrument provides sufficient space for continuous process modes.
- The system and sample pumps are based on high quality KNAUER BlueShadow® pump technology, ensuring reproducible flow rates at both low and high pressures.
- The system is suitable for low, medium and high pressure and is solvent resistant and biocompatible, offering functionality for small molecule and macromolecule preparative purifications.
- The Contichrom® system is scalable to pilot and process scale. At up-scaling, the product profile is retained.
- The Contichrom® system is particularly suitable for PAT in line with QbD.



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Technical specifications

Main system components:

- System configuration: 2-column setup
- 1 x binary high pressure gradient pump
- 2 x isocratic pumps, 2 x UV detectors
- 6 x 6-way 7-port valves, 2 x 2-way 6-port valves
- 1 x degasser, 1x pH/conductivity sensor
- 1 x computer / monitor / keyboard / mouse
- 1 x Contichrom® operating software
- 1 x ethernet switch

Maximum system pressure:

100 bar

Pump description:

- double piston pump
- biocompatible, titanium inlays
- active piston seal wash
- flow rate:
 - Contichrom® lab-10: 0.01–10 mL/min
 - Contichrom® prep-100: 1–100 mL/min
- maximum delivery pressure: 100 bar
- gradient capability

UV detector description:

- spectrophotometer for routine HPLC and other flow-through detection tasks
- wavelength range 190–750 nm
- light source: deuterium lamp

Degasser description (lab-10):

- 4-channel degasser module
- degassing by gas permeation through Teflon® AF amorphous fluoropolymer membrane

Valve description:

- electrical valve drive
- LED display
- PEEK body, TEFZEL seal

pH / conductivity sensor description:

- Conductivity 0–500 mS/cm
- pH measurements 0–14
- temperature sensor

Materials:

- all biocompatible
- tubing: PEEK
 - Contichrom® lab-10: 0.5 mm i.d.
 - Contichrom® prep-100: 1.0 mm i.d.

Fraction collector (optional):

- Fraction collector FOXY R1 ISCO with integrated diverter valve
- Fraction capacity from 36–144 tubes, 0.2 mL–50 mL per fraction
- biocompatible and can be used in cold rooms

Purified product output capacity:

- Contichrom® lab-10: up to 20 g/day
- Contichrom® prep-100: up to 200 g/day

Operation:

- room temperature
- cold room (4 °C) compatible

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Operating software features

Software description:

- Contichrom® operating software (in English) including manual.
- Integrated, intuitive software for operation and evaluation of batch and continuous chromatography.
- Wizard allows easy programming of methods including MCSGP.
- Run log stores all information for each experiment.
- Easy-to-use graphical user interface for method programming. Advanced users can access program detailed settings.
- Unique pause/continue functionality, even for continuous chromatographic operations.
- User management gives high operational and data security.
- Provides all tools for FDA 21 CFR Part 11 compliance.

Pre-defined user groups

- Administrators
- R&D-, production-users

Rights management

- Each group has defined rights as set by the administrator
- User accounts are password protected

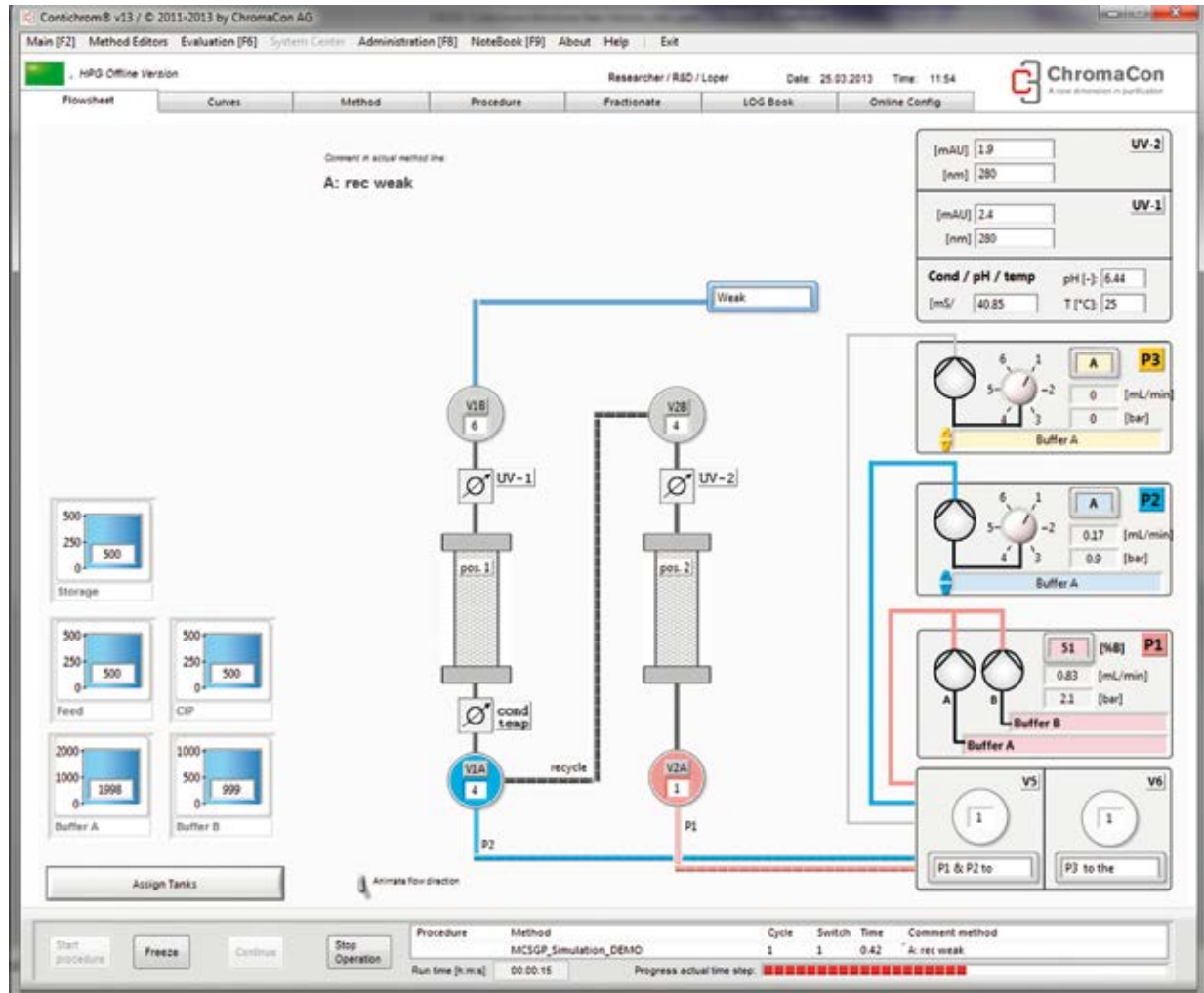
Logging

- All user/hardware activities are logged with time stamp and user name

Electronic signature

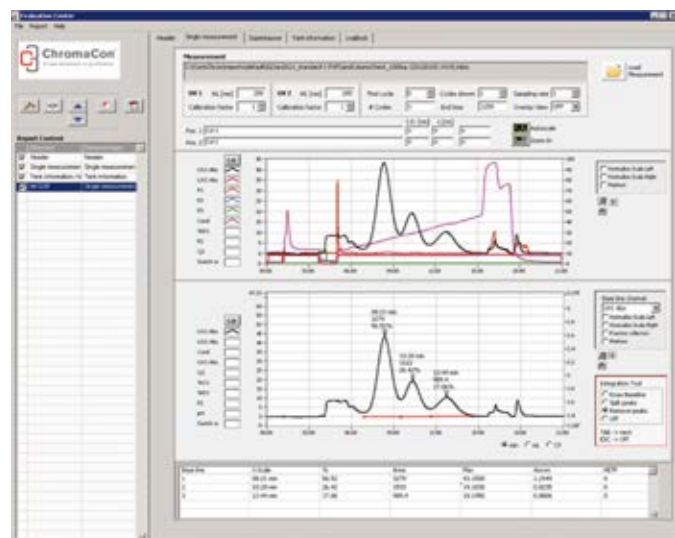
- A checksum of the log & measurement file is computed and saved together with the files in order to create an electronic signature

Operating software: main window: status & flowsheet tab



Main-Flowsheet Tab

- active connections are highlighted
- display of status/measurement of
 - valve position
 - pump parameters
 - UV signals/settings
 - conductivity
 - pH/temperature
 - tank levels
- run time information
 - method in operation
 - duration of time step



When will you start to implement all these advantages?



Please contact us ...

... for an offer, technical information and support,
after-sales service, shipping information:



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