



The unique **automated sampling and sample processing system** for on-line analytics in up- and downstream bioprocesses.

Numera enables high-frequency sampling of small volumes and leads to precise and reliable results around the clock. In combination with our Software Lucullus PIMS, it covers the entire workflow from process planning, automated sample processing, data recording to online data analysis and advanced process control.

Sampling

Biomass-containing samples are drawn automatically from stainless steel and benchtop glass bioreactors maintaining their sterility. Volumes up to 2 ml are drawn with minimum sample loss. Using **Multi-plexer Modules**, up to 16 bioreactors or downstream devices are coupled independently, each connected with a sample line of up to 10 m length. The sampling frequency lies between 6 and 15 minutes only, depending on sample processing steps.

Sample processing

With the **Dilution Module**, biomass-containing samples are precisely diluted over a wide range. The simultaneous addition of reagents is used to perform protein precipitation, product extraction or staining reactions. The biomass-containing samples are filtrated with a unique **Filtration Module** with maximum sample yield. Cross-contamination is prevented by using a new filter section for each sample. The variety of available filter membranes allows to meet specific requirements, regarding cell-densities and the organism used.

Sample storage

Samples are collected and stored in cooled conditions in the Sample Collector. The size of the **Sample Collector** can be adapted to specific needs based on different volumes, numbers and types of vials. It performs additional liquid handling steps, if needed. Each vial is labeled with a unique barcode and sample ID for distinctive identification in subsequent analytics.

On-line analytics

The samples are automatically transferred to various directly coupled analytical devices. Analysis is started through remote control and results are collected from our software **Lucullus PIMS**. Cell-containing samples are passed to cell analyzers or flow cytometers. Filtrated samples are directly injected in an HPLC or transferred to enzymatic bio analyzers.

Application experience

In cooperation with the Vienna University of Technology and the Zurich University of Applied Sciences, a multitude of applications have been tested. Specific application notes are available on our website. Numera is currently used in a wide range of bioprocesses in industry and academia, including:



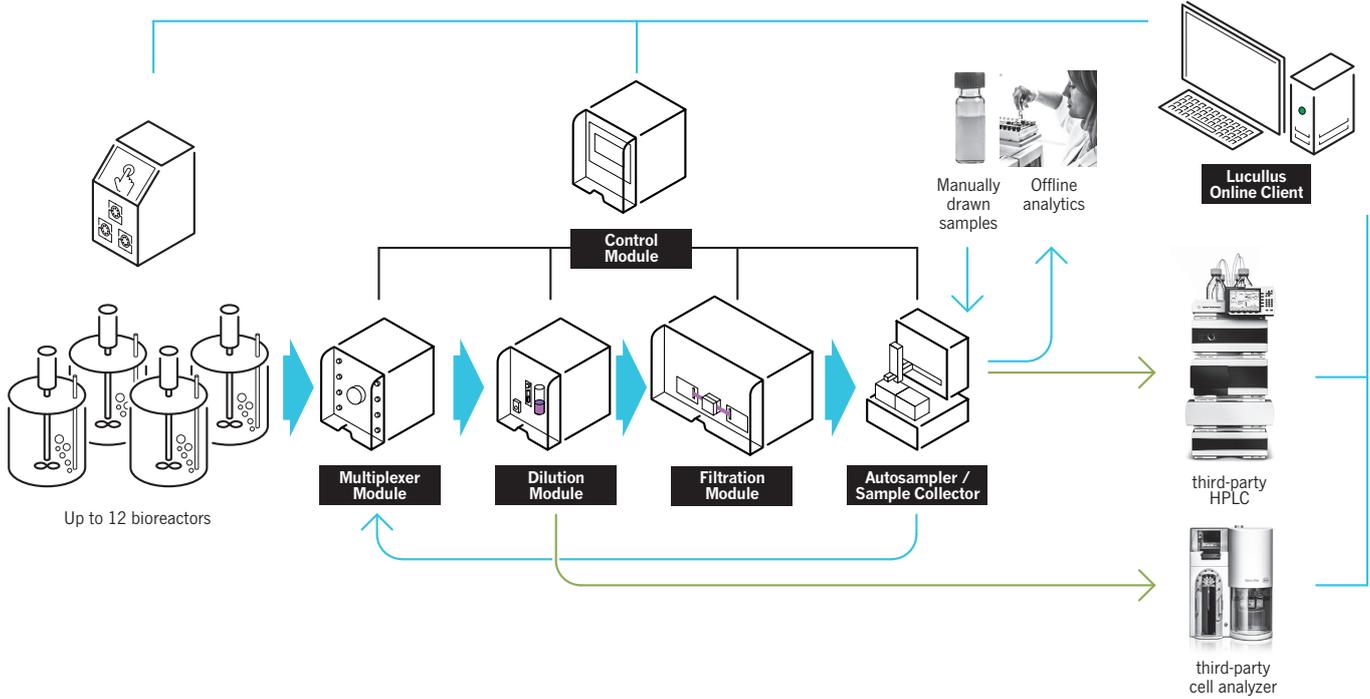
Analytes

Proteins, Antibodies (IgG)
Carbon hydrates (Glucose, Lactose, Lactate, Glycerol, ...)
Vitamins (B2, Niacinamide, Folic Acid...)
Amino Acids (Glutamine, Glutamate, Asparagin, ...)
Cell count, viability
Nitrate, Phosphate

Organisms

Mammalian cells (CHO)
Escherichia coli
Pichia pastoris
Lactobacillus
Bacillus subtilis
Microalgae

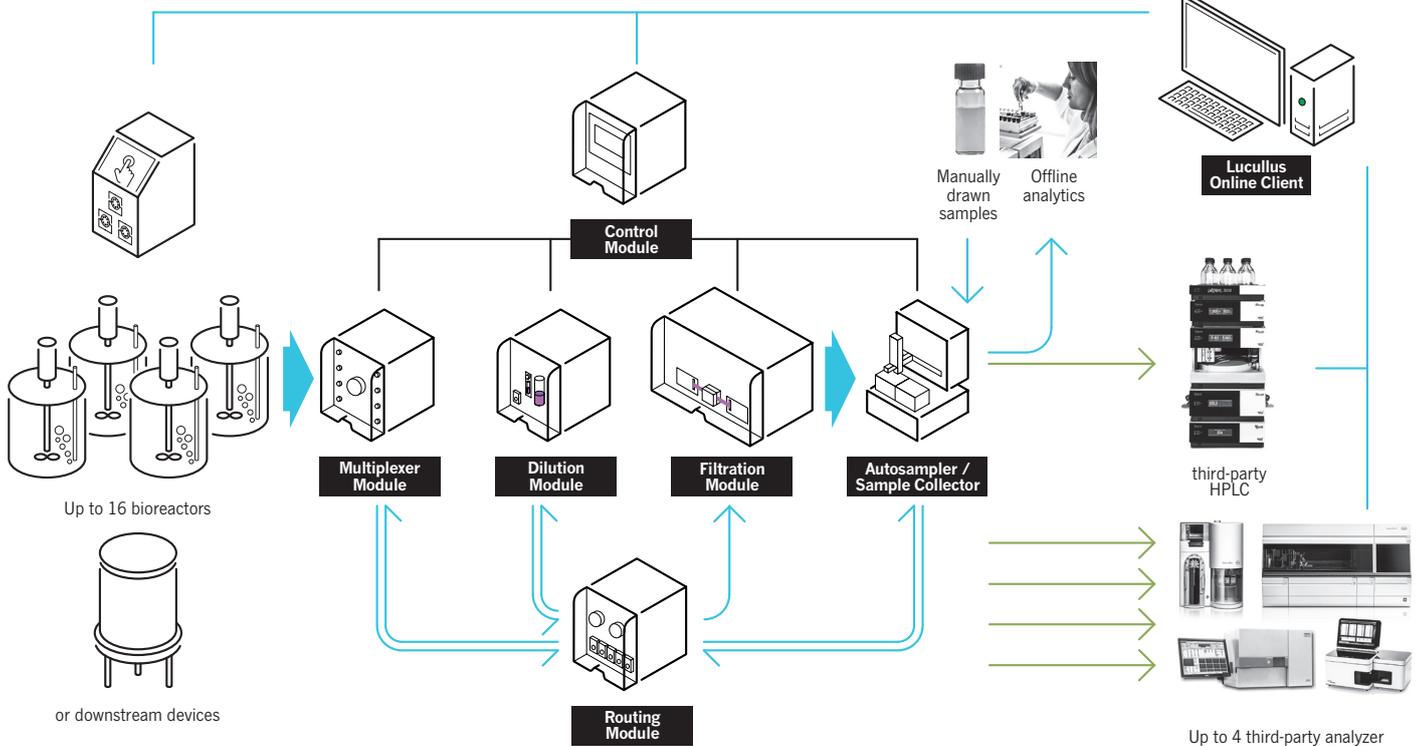
Standard setup



The standard setup with up to 3 Multiplexer Modules allows you to couple up to 12 bioreactors. Samples are processed using the Dilution Module and Filtration Module. Biomass-containing samples are transferred to cell analyzers with or without previous dilution. The Sample Collector stores filtrated

samples and directly injects or transfers them to an HPLC system (e.g. Agilent 1200 series or Thermo Scientific™ UltiMate™ 3000). Manually taken samples can be added to the Sample Collector and be automatically processed by Numera and analyzers.

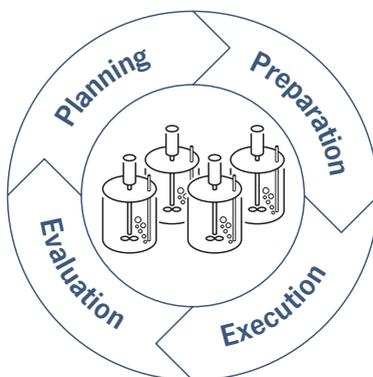
Advanced setup



The advanced setup integrates up to 16 bioreactors or downstream devices, up to 4 different third-party analyzers and HPLC. The Routing Module adds extra flexibility. It allows fast

and direct transfer of biomass-containing samples to analytical devices or storage in the Sample Collector. For every single analyzer sample processing is individually customized.

Lucullus Process Information Management System is a well-established database application to collect and organize bioprocess related data from various devices and vendors. It provides efficient enterprise-wide bioprocess control and data management – from the very idea to the final report.



Lucullus is much more than a simple data recorder. It guides you through systematic planning of process groups (e.g. based on DoE), following equipment allocation, process scheduling, control recipes and media assignment. During the planning phase, sampling of your bioreactors can be scheduled with different frequencies and analytical methods. You can directly export your sample list and print labels for the vials.

During the process, Lucullus collects data from bioreactor control units, additional devices such as scales or sensors and all online or offline coupled analyzers. Data is presented together with meta data, user interactions and parameters in a clear form, which enables direct process comparisons even with historical data.

Online-calculations allow the conversion of data into relevant information. This information can be used to control your process through control recipes (step chains) and implemented controllers.

Data evaluation with Lucullus PIMS helps you extract relevant information and add it to a configured report, using graphical and tabular presentation formats. Data exchange to Microsoft® Excel, MatLab® or other third-party software is also supported.

Advanced bioprocess development



This figure shows some examples of possible connected third-party devices.

Lucullus supports various communication protocols, such as ASCII, OPC, TCP/IP ASTM, Modbus, and proprietary protocols. Therefore, it's possible to collect data from different sources and even to remotely control connected devices using specific commands. In combination with Numera, this allows a **unique and totally integrated solution for automated sampling, on-line analytics and process control.**

Furthermore, the availability of online measurements and real-time data enables new pathways in developing bioprocesses using advanced control strategies: Controlling of substrate concentrations, monitoring product quality, soft-sensor-based feedback-control, event-based triggering of process steps and much more. Our specialists will gladly help you realize your specific application.



Low-volume and high-frequency sampling

Monitoring of multiple bioprocesses with high-frequency and fully automated sampling around the clock

Numera typically draws biomass-containing samples from 200 µl up to 2 ml. The blow-back option guarantees minimized samples loss in the sample line – regardless of its length. Therefore, Numera is useful in combination with small reactors starting at 0.25 L working volume and allows high-frequency sampling, drawing only minimal volumes from the reactor.

Precise sample preparation

Significant and reliable data with Swiss precision technology

All active and passive components used in our modules are designed for an overall precision of ≤ 2% SD with maximum accuracy. This provides a substantial gain of information from all subsequent online and offline analytics and represents a significant advantage over manual sample processing.

Membrane filtration

Consistent cell removal and maximum sample yield with high cell densities

The unique membrane filtration procedure with filters from Pall® is designed for fast and effective cell removal even at high cell concentrations of up to 200 g/l CDW without clogging. The high-quality membranes provide complete removal of fine particles, cells, bacteria, and fungi and extremely low protein binding capacity minimizing the likelihood of target analyte binding. A new filter for every sample avoids cross-contamination.

Integration in Lucullus PIMS

From planning to evaluation: a unique solution from a single provider

Numera is fully integrated in the Lucullus Process Information Management Software. Lucullus covers the complete upstream processing workflow and provides automated online calculations, process evaluation and advanced process control strategies. Communication with all bioprocess related devices, e.g. control units, scales, pumps, sensors and analyzers of various vendors is available.

On-line analytics

The following devices are supported for on-line analytics in combination with Numera:

HPLC	UltiMate™ 3000 HPLC (Thermo Scientific™) 1200 Series (Agilent Technologies)	Chromeleon OpenLAB CDS ChemStation Edition
CELL ANALYZER	Cedex HiRes (Roche Diagnostics) ViCell (Beckmann Coulter)	Cedex Remote Control Software ViCell Remote Control Software
BIO ANALYZER	Cedex Bio HT (Roche Diagnostics) Nova Bioprofile FLEX (Nova Biomedical)	Host interface OPC connection
FLOW CYTOMETER	Cube 8 (Sysmex) CytoSense (CytoBuoy)	In preparation CytoUSB and CytoClus

Support for further devices is under development and will be available soon. For more information, please check the device list on our website www.numera-pat.com. We will gladly establish a solution for the device you are using. Contact us for more information.

**Numera and Lucullus:
a unique all-in-one solution from a single provider**

www.numera-pat.com

Sample

Automated high-frequency low-volume sampling of biomass-containing samples around the clock.

Measure

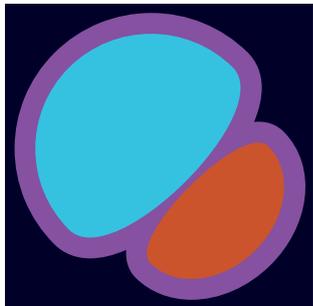
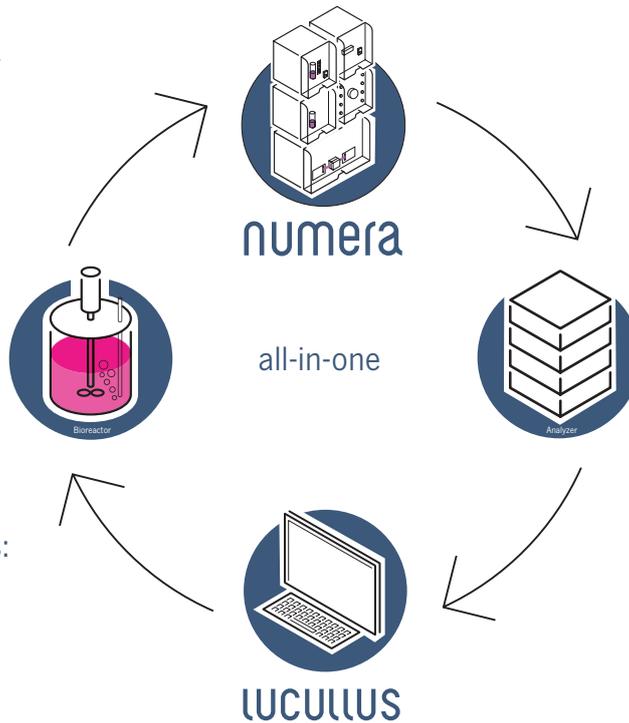
Versatile high-precision sample preparation and filtration. Online measuring with various analytical devices.

Control

Advanced control strategies: Event-based triggering, feedback-control loops, soft-sensors and much more.

Monitor

Automated data import, conversion, and verification for real-time process evaluation and comparison.



securecell

Our Vision

Building on more than 25 years of experience in on-line analytics, information processing and automation technology, we aim to be the trusted technology provider for optimized bioprocessing workflows through automated sampling and process information management.

Who we are

Securecell emerged in 2009 from the company Biospectra, founded as a spin-off from the ETH Zürich in 1992. Ever since, development of online analytic solutions for bioprocess applications has been one of our focus areas. Our urge to deliver the best solutions for our customers' specific needs makes us relentless in optimizing and developing new technologies for more efficiency in bioprocessing.

CONTACT

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