Transforming Downstream Processing through Multi-Column Chromatography

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Bioprocess Group

ISPE Boston Area Chapter
"Continuous Manufacturing of Biopharmaceutical"
Takeda Pharmaceuticals
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LEWA Nikkiso America, Inc.

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– Engineering
– Fabrication

LEWA GmbH
Headquarters
Industrial Division
– Sales
– Engineering
– Pump production
– Fabrication

LEWA China
– Sales
– Engineering
– Pump production
– Fabrication

Nikkiso Co., Ltd.
Group Headquarters

LEWA-Nikkiso America, Inc.
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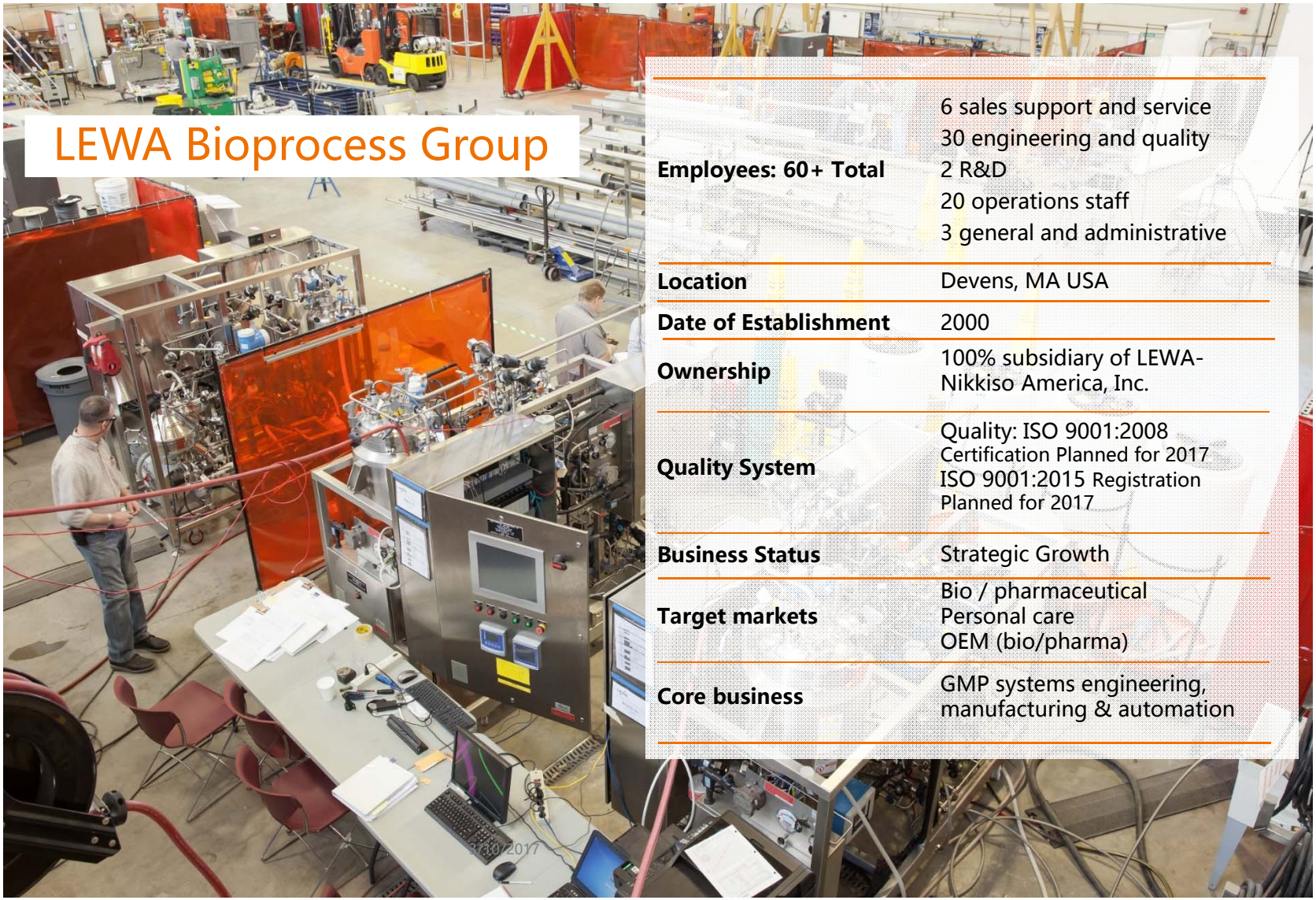
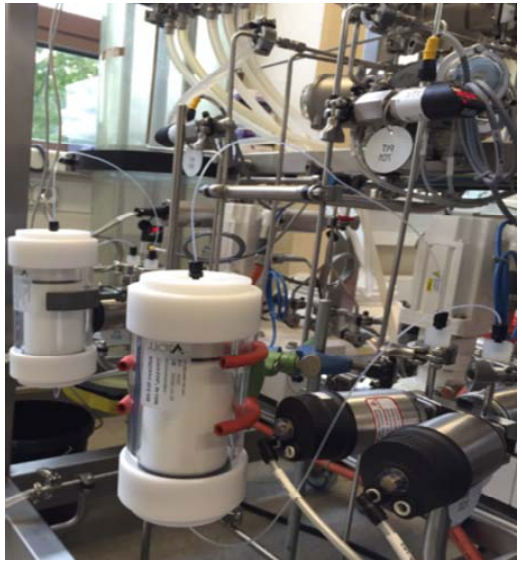
LEWA Bioprocess Group



Employees: 60+ Total	6 sales support and service 30 engineering and quality 2 R&D 20 operations staff 3 general and administrative
Location	Devens, MA USA
Date of Establishment	2000
Ownership	100% subsidiary of LEWA-Nikkiso America, Inc.
Quality System	Quality: ISO 9001:2008 Certification Planned for 2017 ISO 9001:2015 Registration Planned for 2017
Business Status	Strategic Growth
Target markets	Bio / pharmaceutical Personal care OEM (bio/pharma)
Core business	GMP systems engineering, manufacturing & automation

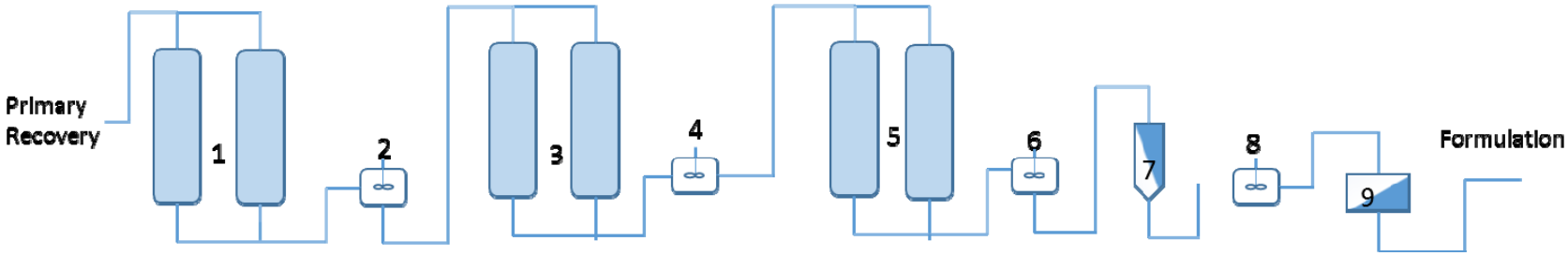
Agenda

- Introduction to Multi-Column Chromatography and its implementation in the DSP
- Batch vs Continuous
- System Design
- Process Design
- Verification



Introduction to Multi-column Chromatography and its implementation

Paradigm shift to integrated continuous DSP platform in biopharmaceutical manufacturing, in particular by implementing continuous multi-column chromatography steps

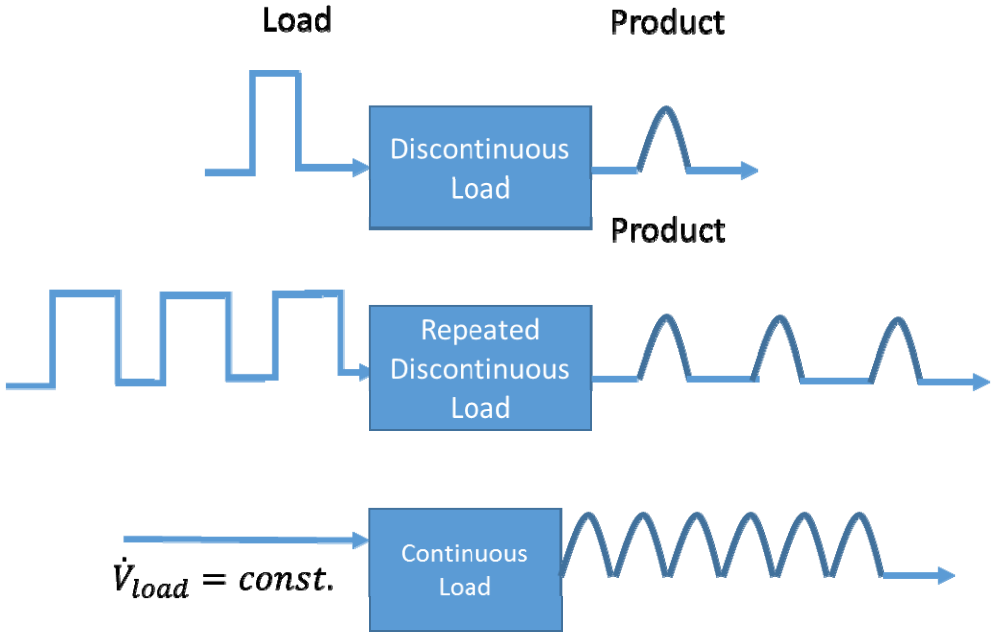


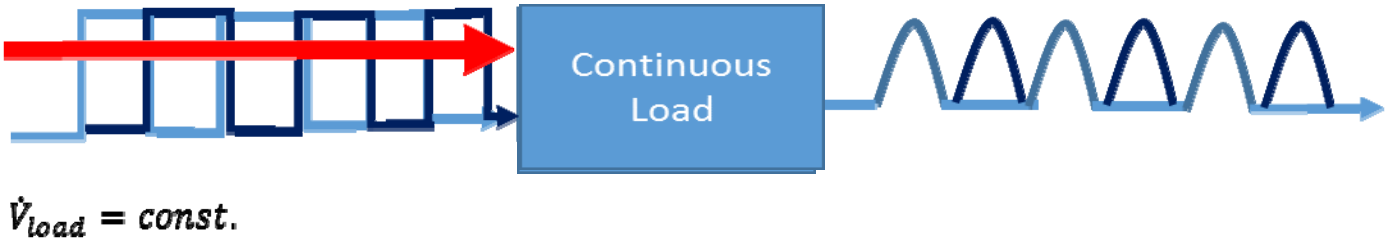
Drivers

- Breaking the ”bottleneck” in DSP due to increased upstream titers
- Enabling higher productivity in multicomponent facilities, especially of CMOs
- Introducing **biosimilar/biobetter** **cost effective**
- Call of the FDA to implement continuous processes
- Allowing cost-effective, robust and sustainable processes with reduced risks

Batch vs Continuous

Definition:
chemical engineering (type of operation)
and
chromatography (type of load)

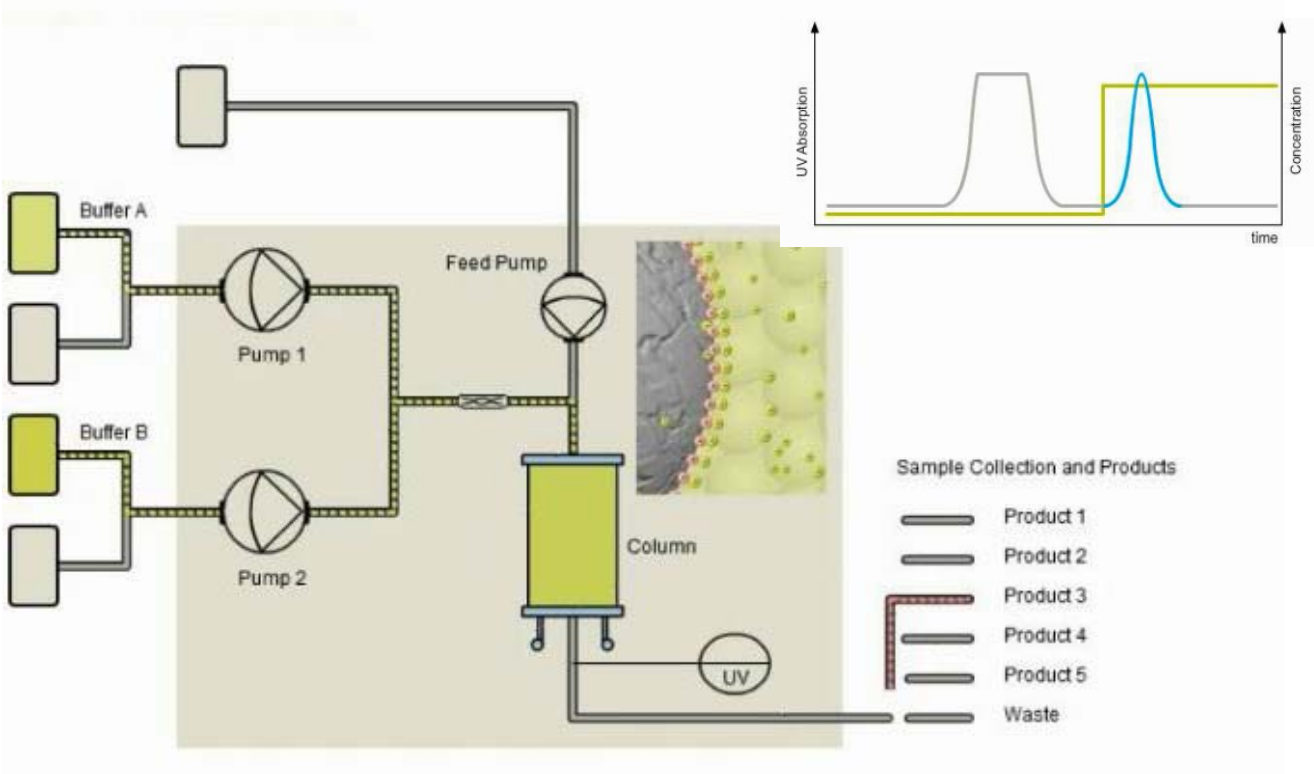


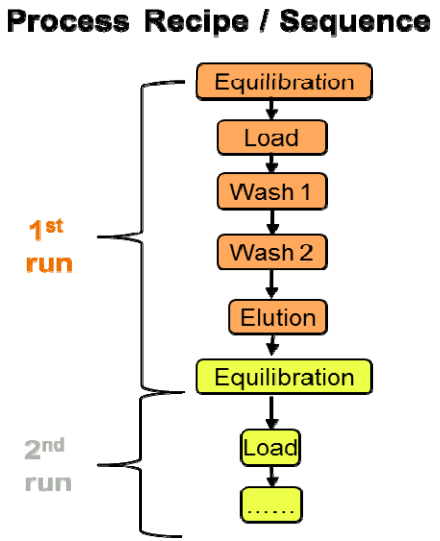


Regulatory meaning: **Charge** or **Lot** which is an amount collected in period of time with consistent characteristic

Transforming DSP through Multi-Column Chromatography

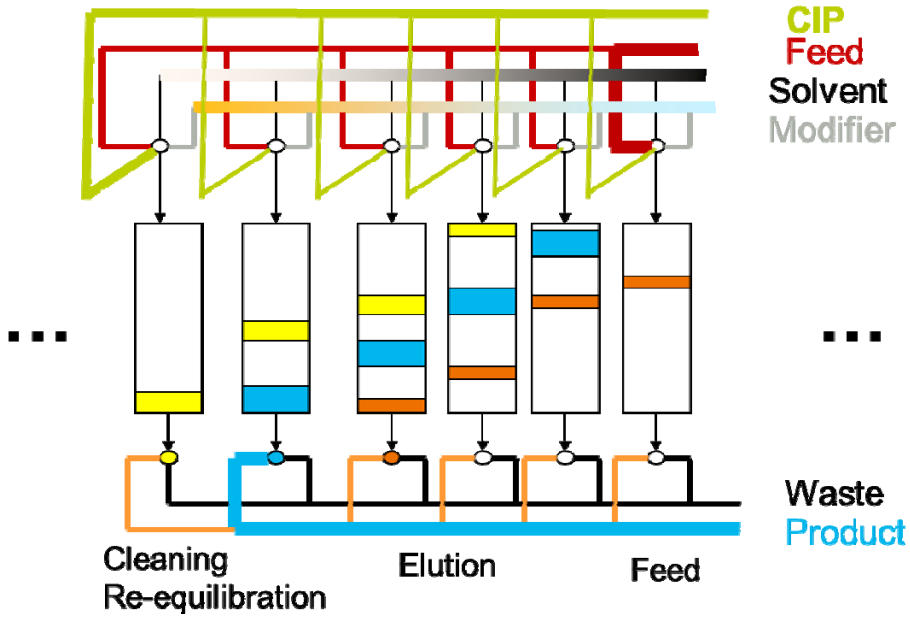
Batch Chromatography

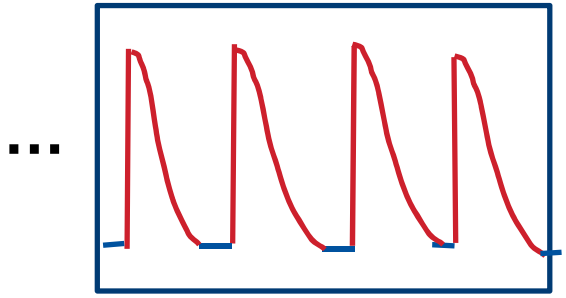




Multi-Column Continuous Chromatography

using parallel or sequential connected columns





Feed continuously.

Operating parameters controlled at “steady state”.

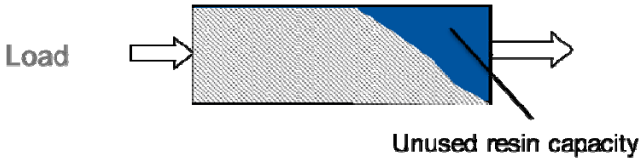
Variability in feed characteristics and processing conditions
→ product variability.

Cyclic product collections with variable composition

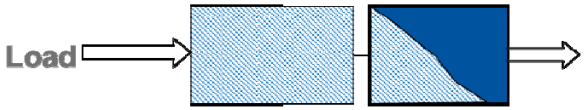
Transforming DSP through Multi-Column Chromatography

Transition from Traditional to Continuous Batch

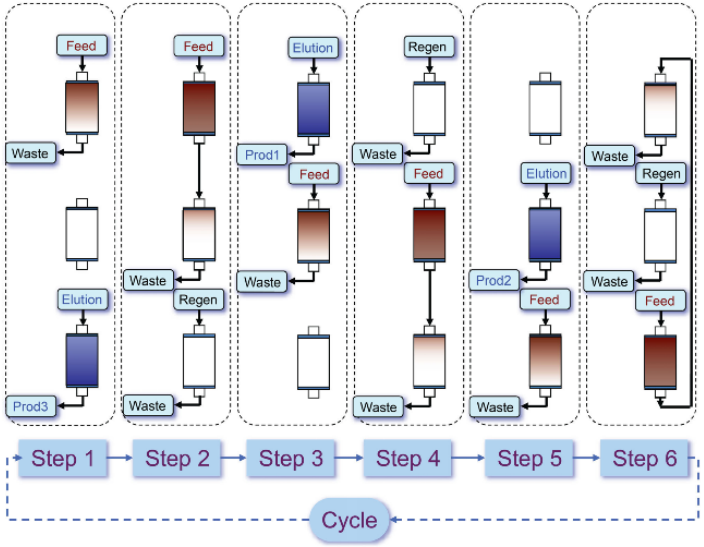
Single column
batch chromatography



Two zone batch
chromatography



3 or 4 -PCC by GE



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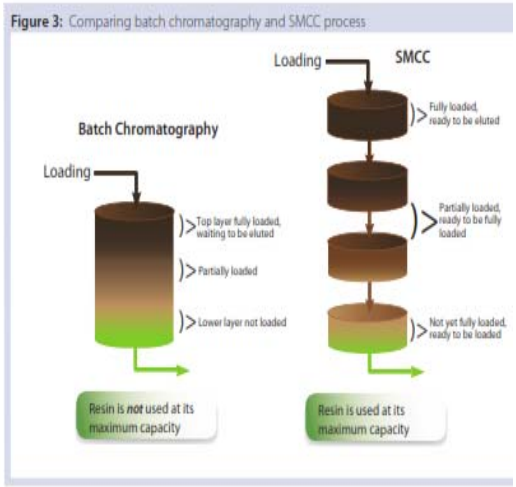
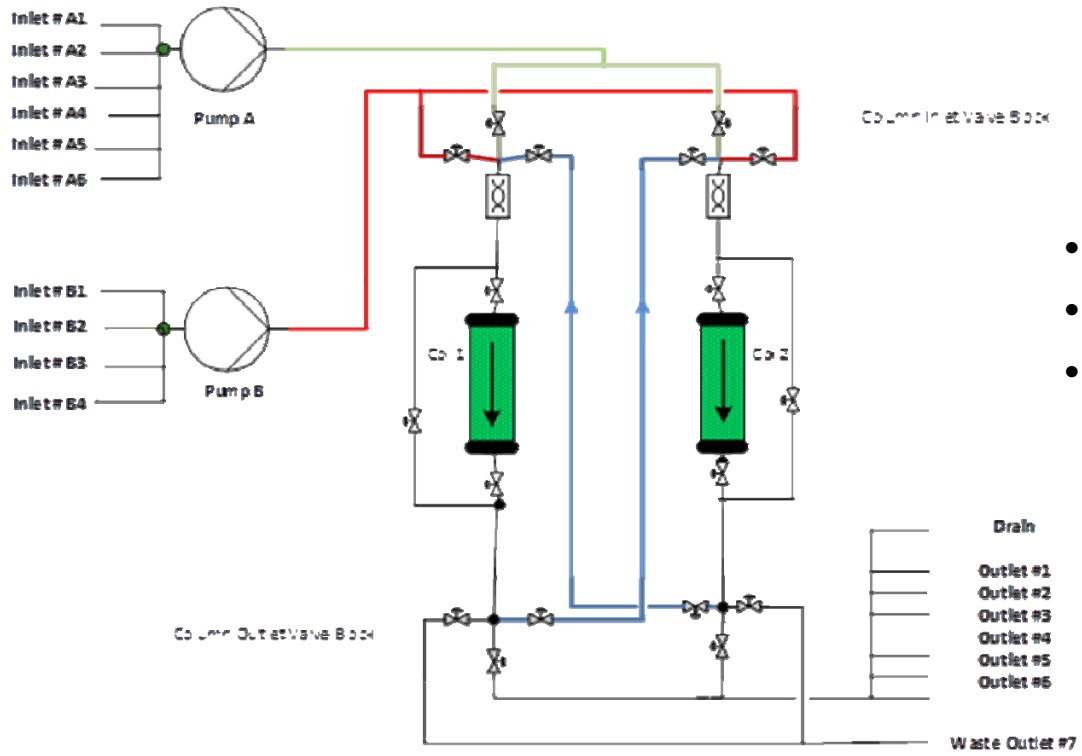
SMCC by NovaSep



CaptureSMB by ChromaCon

www.chromacon.com

Technical challenges – Simple Equipment Design



- Symmetric design
- Minimum hold-up volume
- Optimal piping design to avoid excess pressure drops

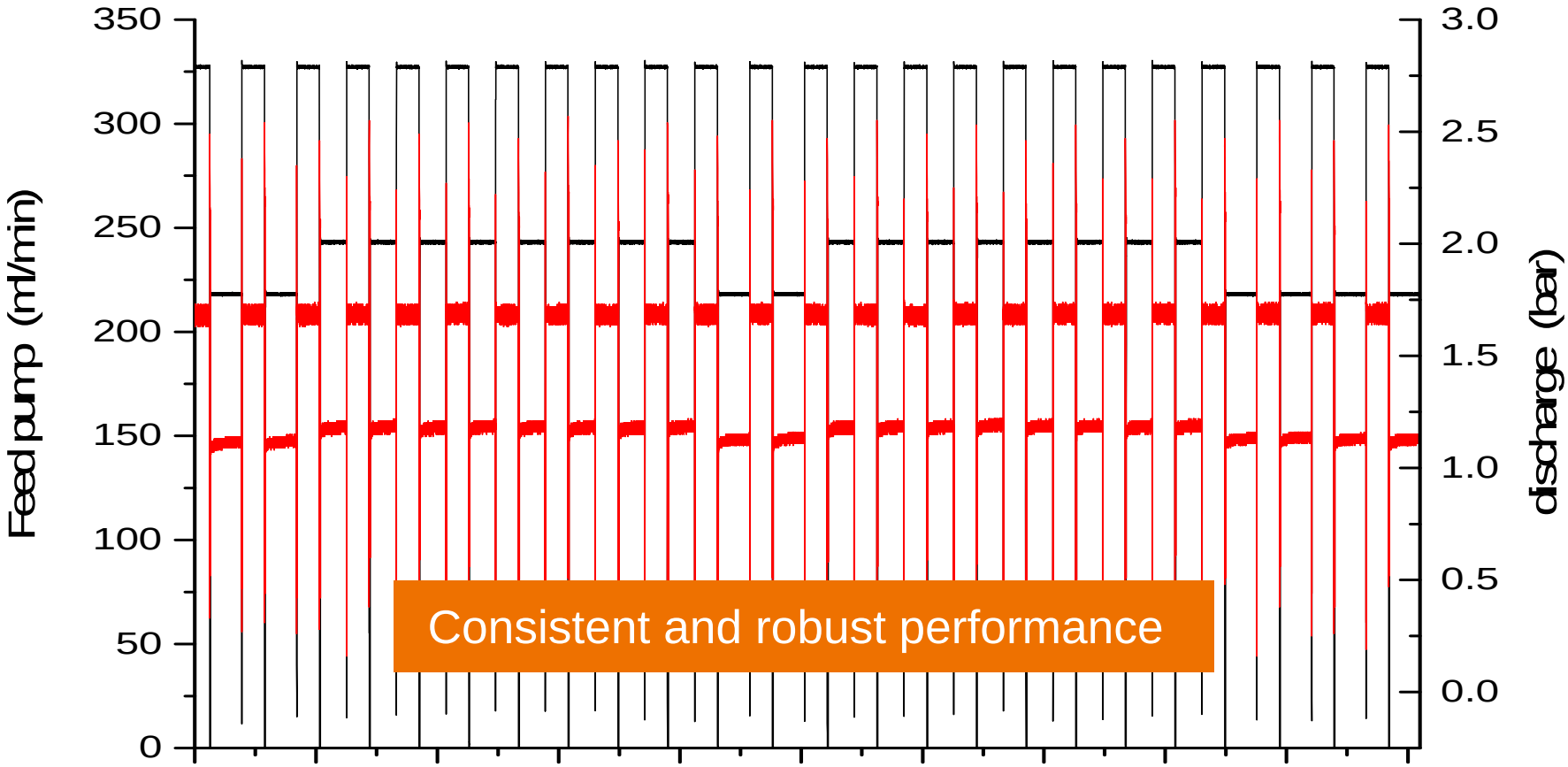
More robust operations with less risks due simplicity in process and equipment.

Fewer hardware components (pumps, valves, piping) → less risk for breakdown

Lower CapEx investment and footprint !

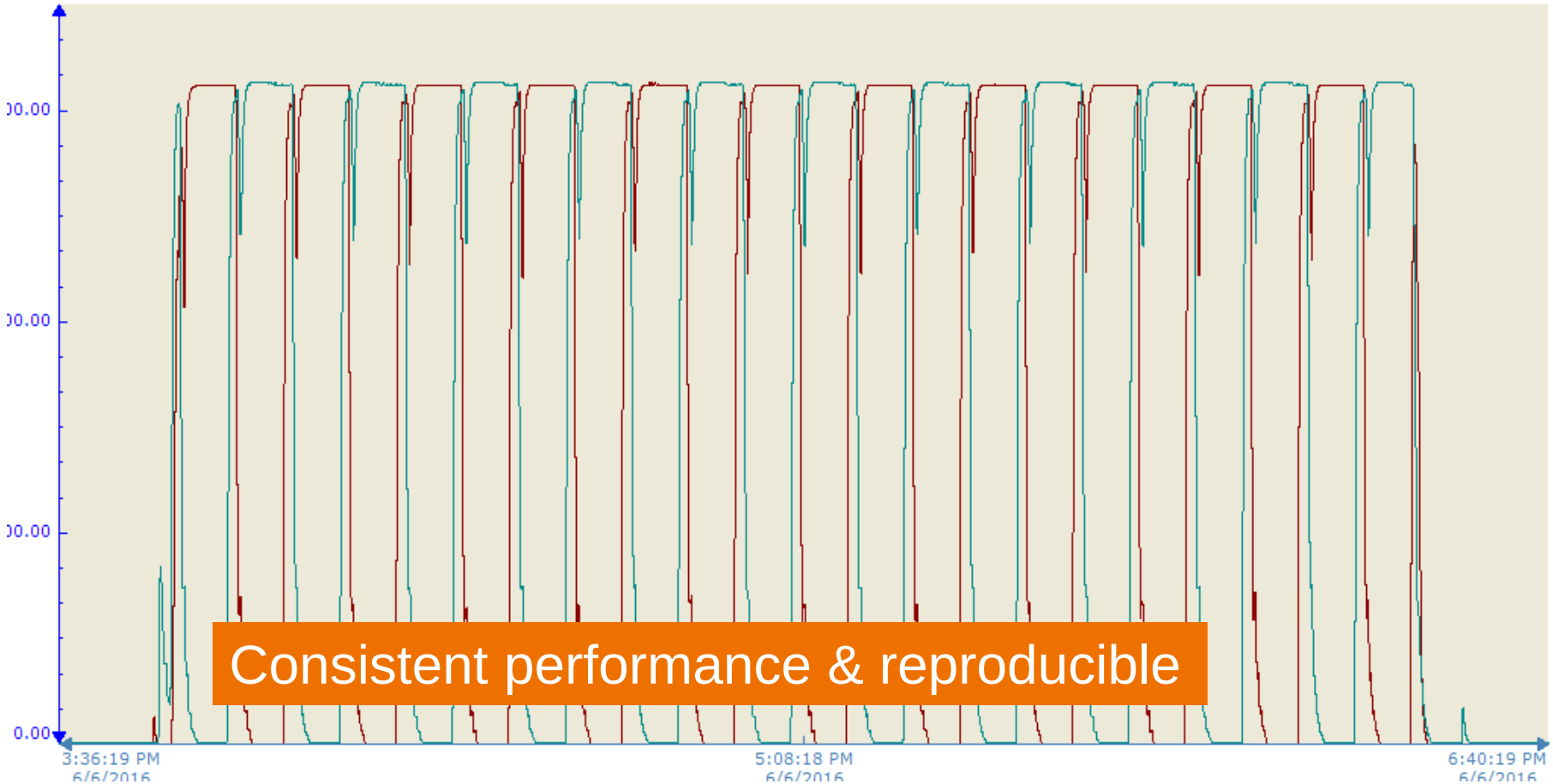
Long-term study over 210 loads (13 days)

monitoring feed flow rate and pump discharge pressure - here last 24 hours



Long-Term Study – Buffer Delivery

monitoring only conductivity at the outlet of both columns



Process Design and Performance – Platform Process

Traditional Capture

Titer 1 g/L and Load 40 g/L_{resin}
Column 20 x 25 cm / 7.85 L

	CV	linear cm/h	run time min
Column Equilibration	5	250	18
post wash 1	3	250	18
post wash 2*	2	250	12
Regen*	3	250	18

product per load [g]	298
productivity [kg/L/d]	0.100
buffer per load [L]	149
buffer/product [L/kg]	526

Continuous Capture

Titer 1 g/L and Load 50 g/L_{resin}
Two columns 10 x 10 cm / 1.6 L $_{total}$
Linear velocity 250 cm/h

	CV
Load Start-Up	15
Load Connected	26.72
Load Parallel	21.88
Parallel *	20
Elution	3
Post-Wash1	2
Process cycle [h]	4

product per cycle [g]	84
productivity [kg/L/d]	0.323
buffer per cycle [L]	31.7
buffer/product [L/kg]	380

Triple productivity → **67 %** less resin or in current setting **80,000** USD
Reduction in buffer consumption by ca. **30%**

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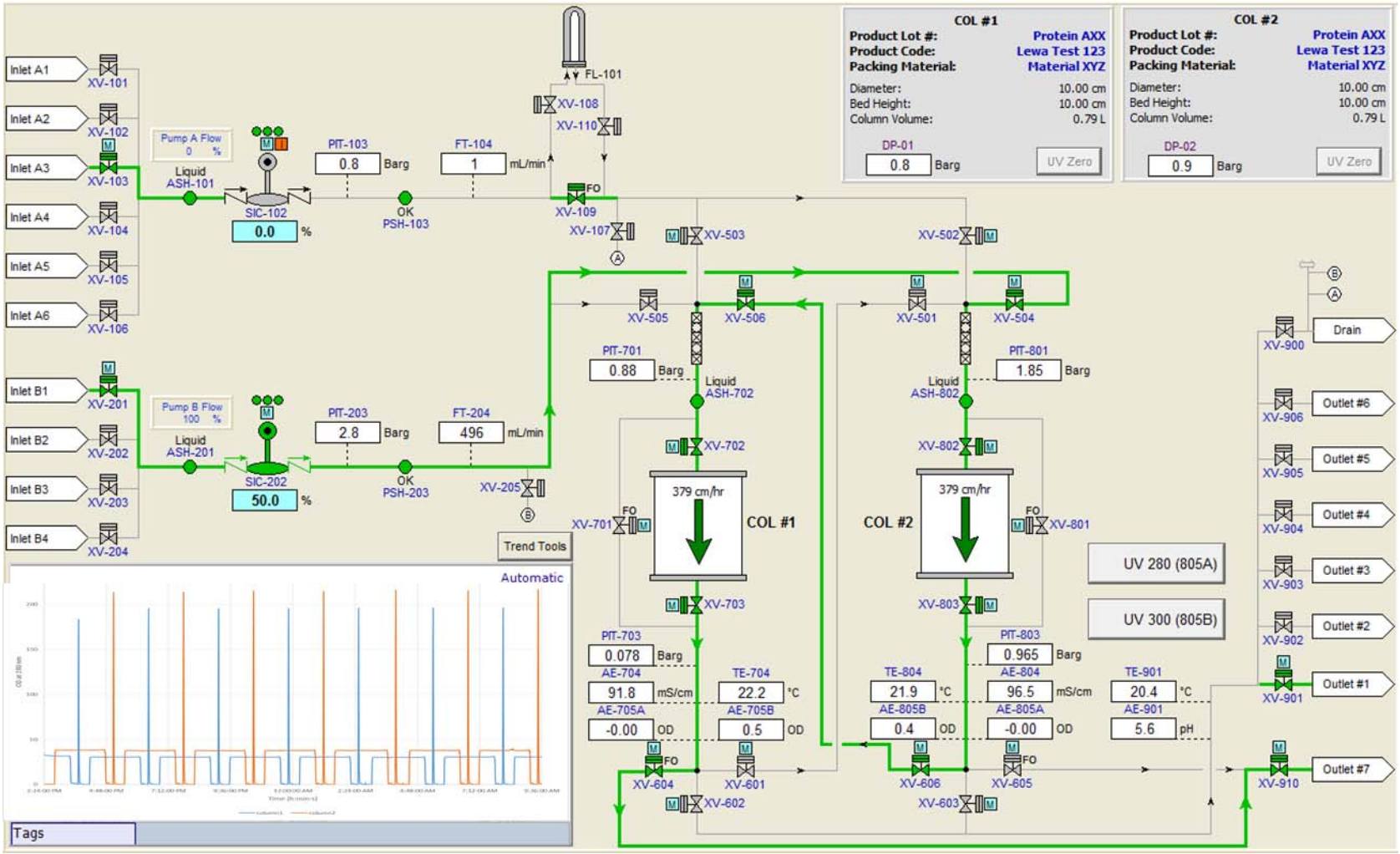

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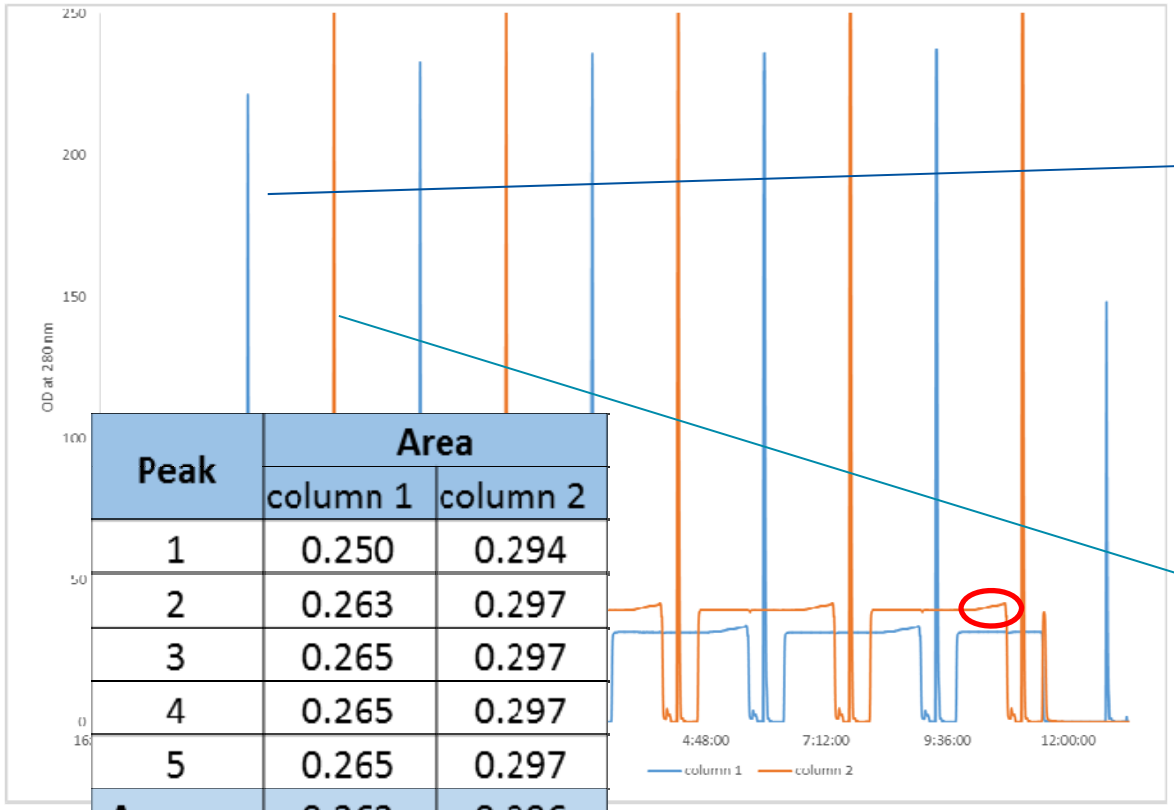
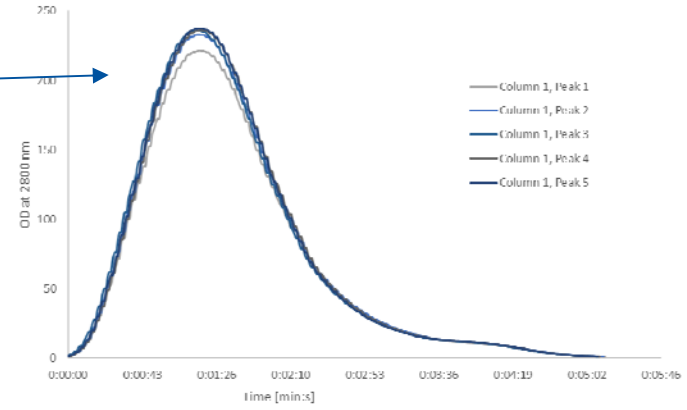
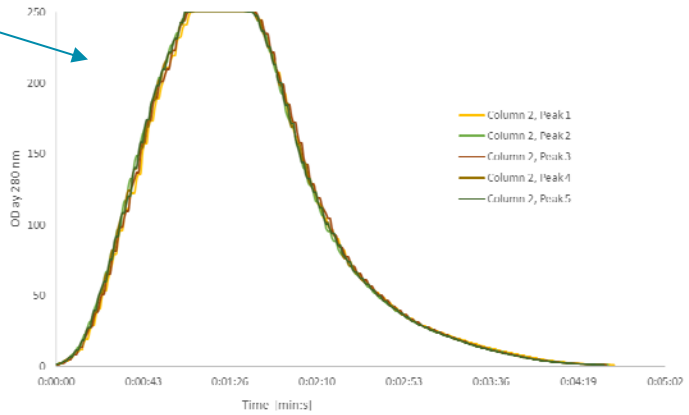


Peak	Area	
	column 1	column 2
1	0.250	0.294
2	0.263	0.297
3	0.265	0.297
4	0.265	0.297
5	0.265	0.297
Average	0.262	0.296
SD	0.0064	0.0014





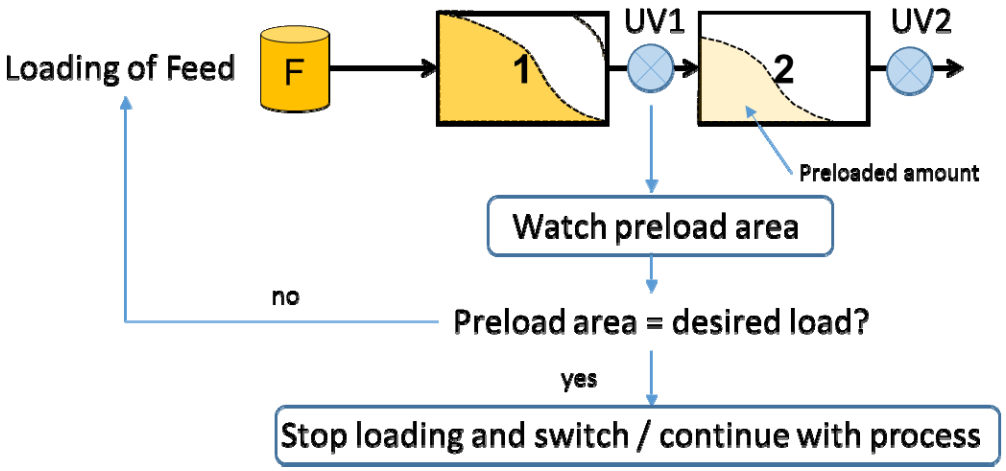
Dynamic Control Strategies to accommodate Process Variabilities

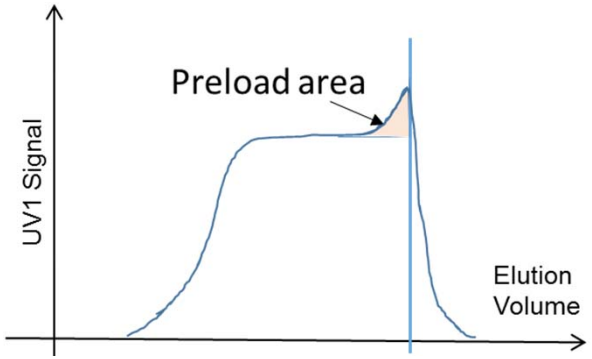
Incoming feed titer variability from upstream cell-culture

Reduction of Protein A binding capacity due to exposure to caustics

Goal: Constant feed flow to minimize the need of surge tanks

Constant load and optimal performance of Protein A Column





Questions?

For further information, please contact
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