



**BioSC<sup>®</sup>**

## Sequential MultiColumn Chromatography

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Adebiotech, 29th October 2013

Rousset Fabien Ph.D.

Head of Biopharma technologies

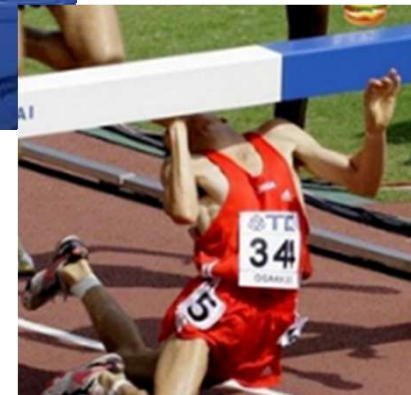
## Novasep's proven expertise

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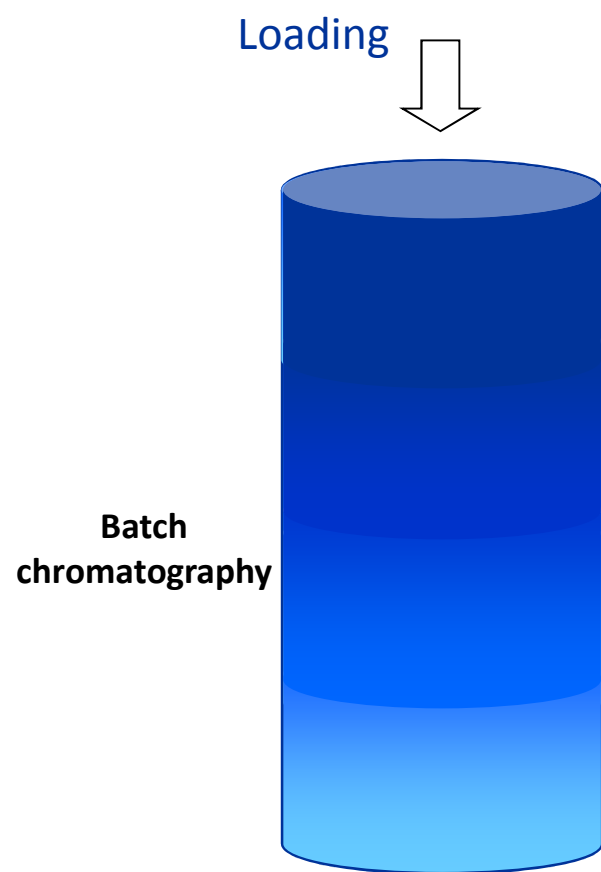
- Pioneer in 1990's of separation of optical isomers
- Since 1990, Novasep has developed simulation software and proprietary chromatography technologies (Varicol®...)
- Numerous APIs were purified using continuous chromatography technologies
- 3 Novasep sites are using FDA-inspected SMB systems
- ...and 15 APIs are produced at commercial scale (Pfizer, UCB, Cephalon, Lundbeck...)
- Novasep centers of expertise for continuous chromatography: US (Boothwin), EU (Pompey, Pompey & Chasse sur Rhône) and Asia (Shanghai)

→ ***Novasep are now applying this proven expertise in cGMP continuous chromatography to the BioPharma industry, bringing dramatic cost reductions and process efficiency.***

Will it worth a trial?



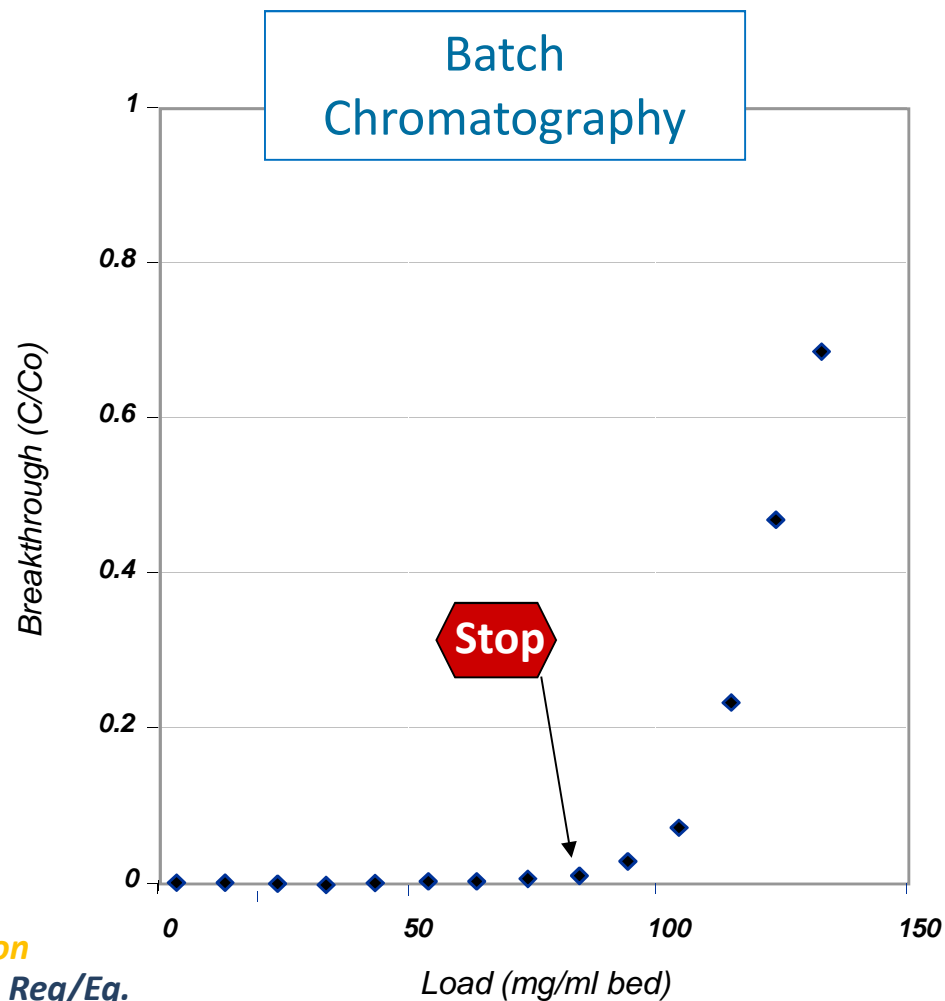
*How far a Sequential Multi-Column Chromatography (SMCC) process from a batch process is?*



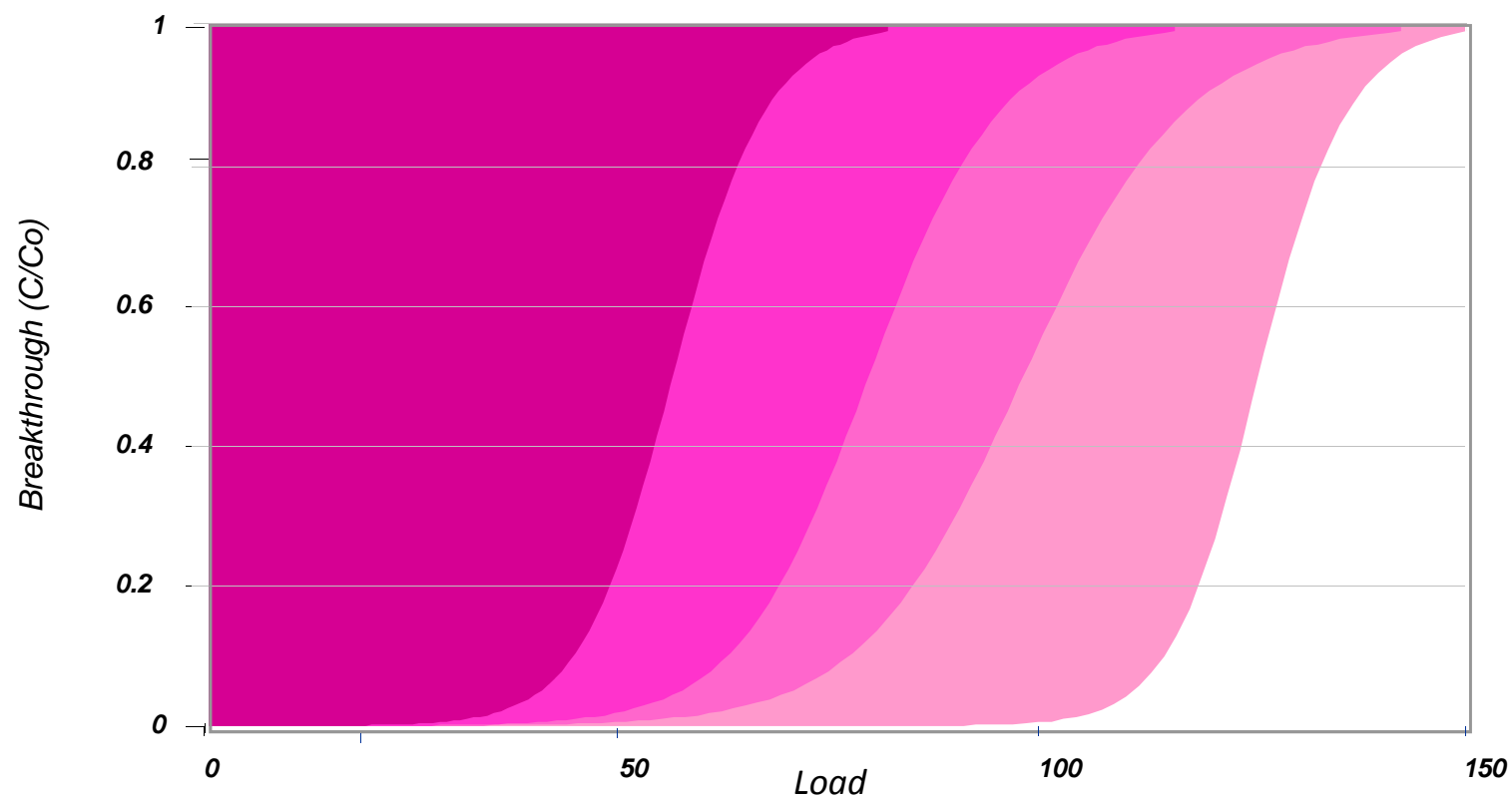
Resin is **NOT** used at its maximum capacity

Wash Elution Reg/Eq.

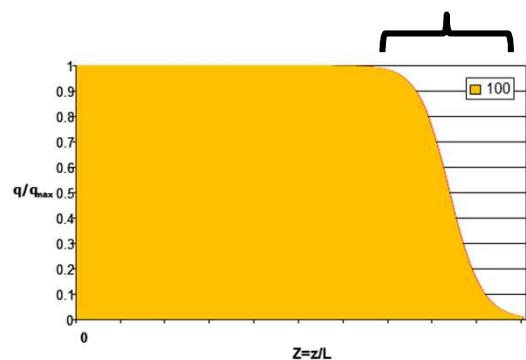
  



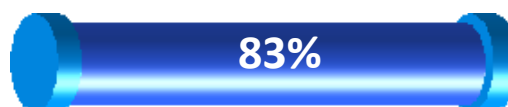
- With increasing velocities, leaking occurs sooner



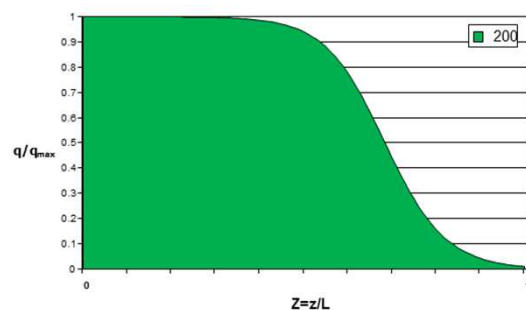
## SMCC with BioSC®



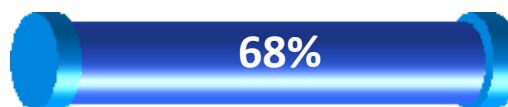
*Single batch @ 100cm/h*



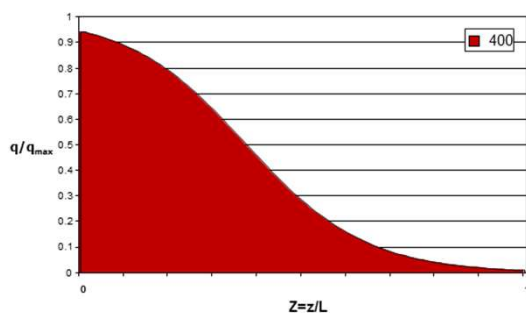
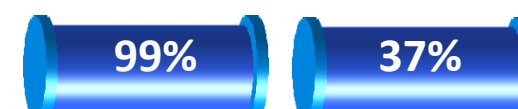
*SMCC with 2 columns*



*Single batch @ 200cm/h*



*SMCC with 2 columns*

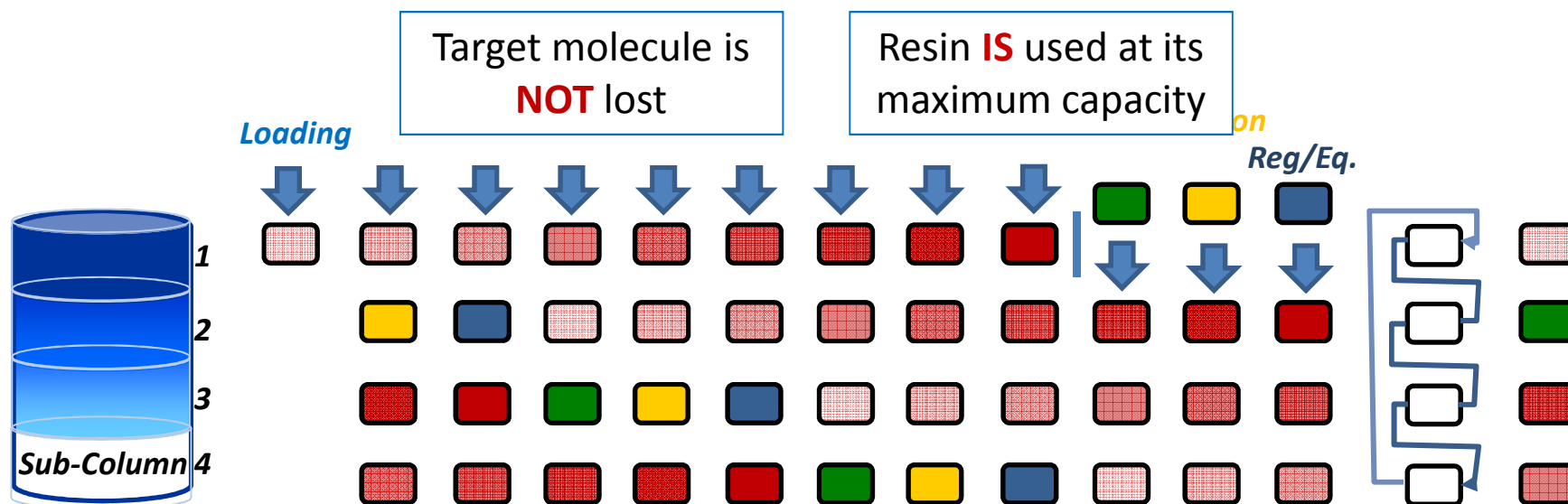


*Single batch @ 400cm/h*



*SMCC with 3 columns*

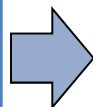




Start of  
production  
1<sup>st</sup> cycle



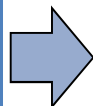
Batch Affinity  
Chromatography



**Compromise to be found:**

Thermodynamics “DBC” vs Kinetics “Flow Rate”

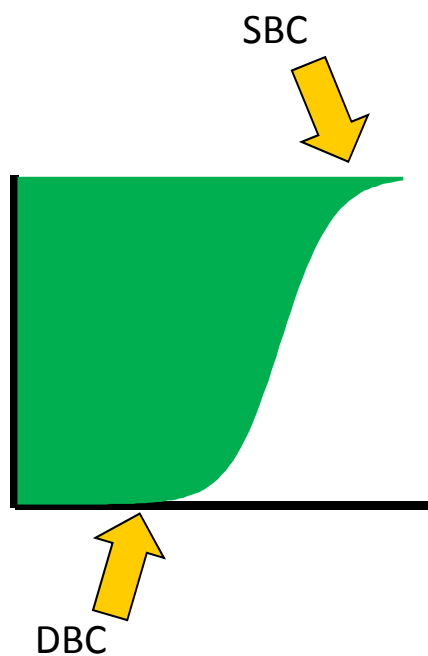
SMCC/BioSC®  
Affinity  
Chromatography



**Kinetics is not a limitation anymore:**

“SBC” & high Flow Rate for max of productivity

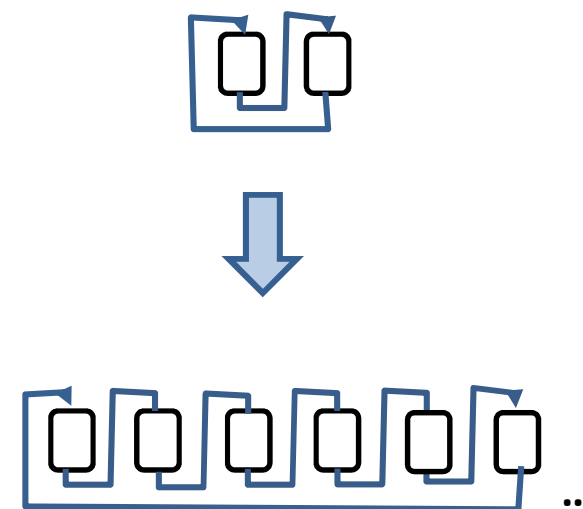
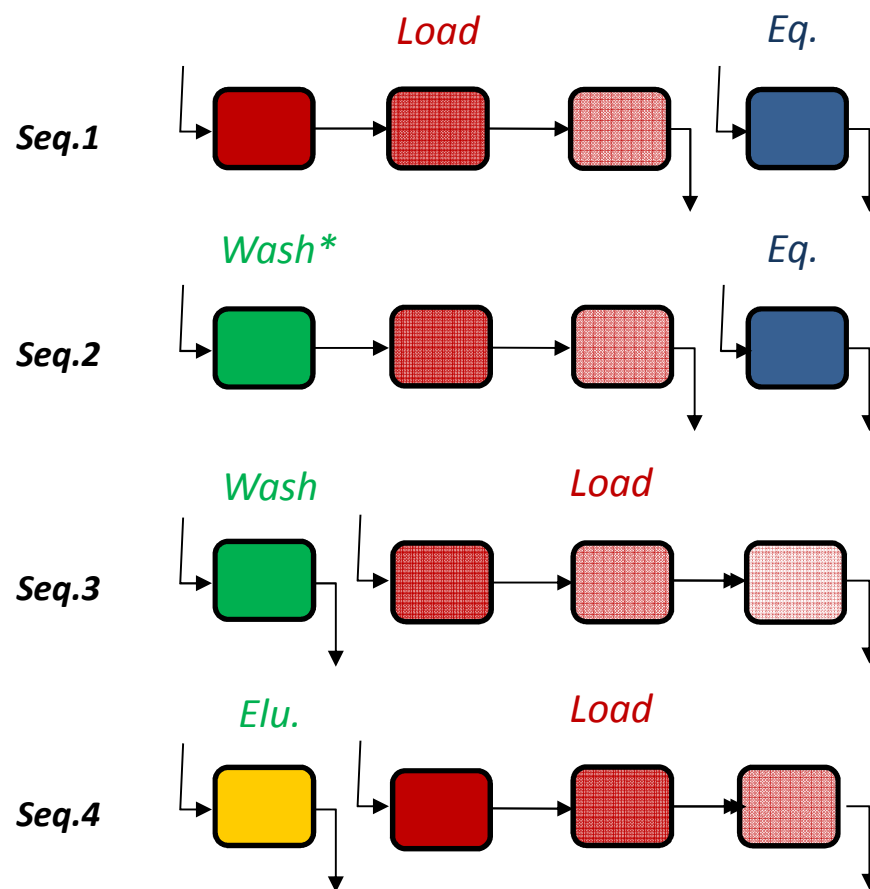
## SMCC with BioSC®



	Resin (L)	Time Prod. (hr)	Productivity (gr/L/day)	Buffer cons. (L/gr)
SMCC	51	4.5	1568	0.28
	23	10.1	1572	0.28
Batch	196	6.1	268	0.76
	78	12.8	342	0.57

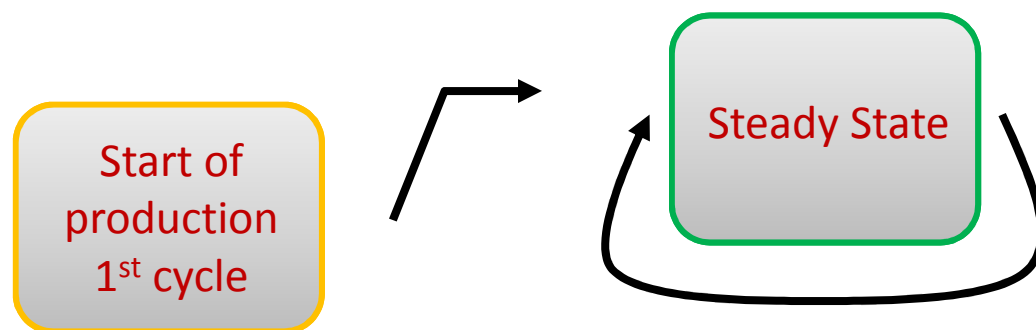
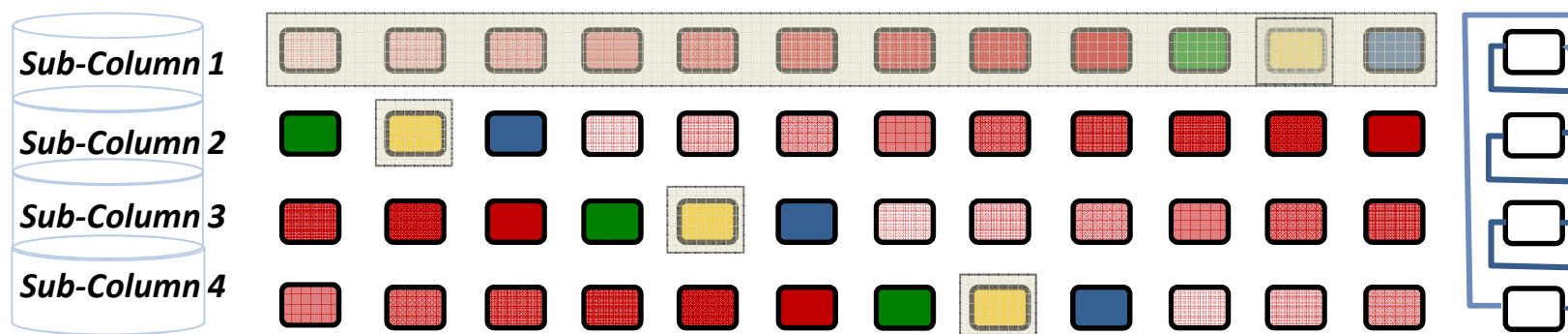


## Patent EP2040811



- SMCC on 2 to 6 columns:
- Minimize the loss during wash
- Optimize sequence vs FR & wash
- Discontinuity enables max productivity

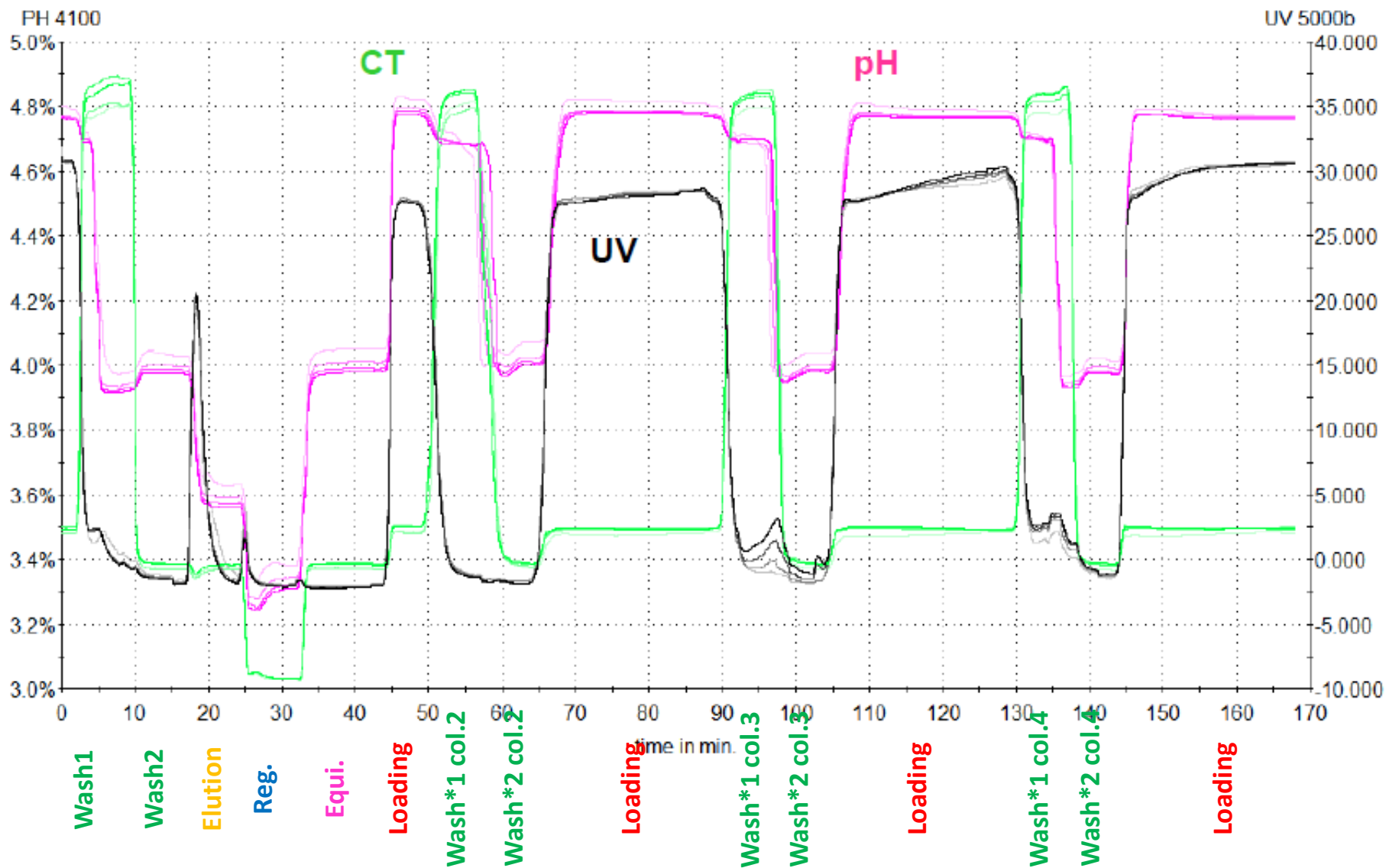
**Patent US 8,216,475**  
**(Adv. Control Syst.)**



In Process Monitoring:

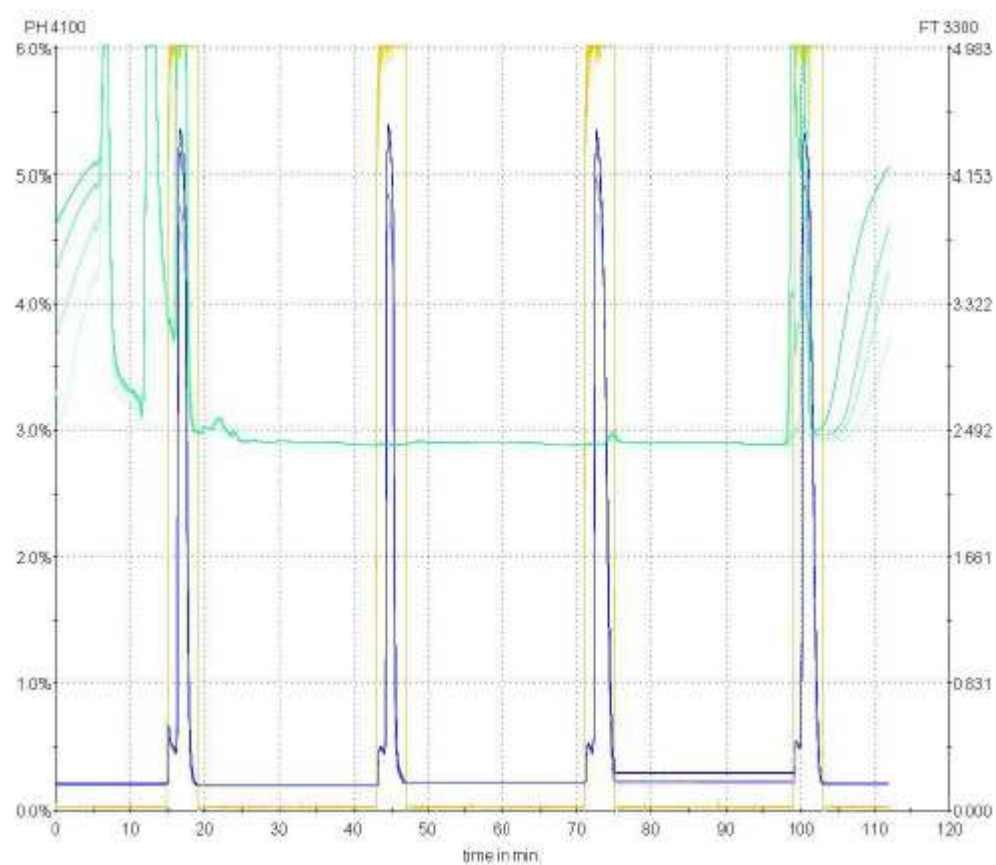
- pH
- Cond
- UV...

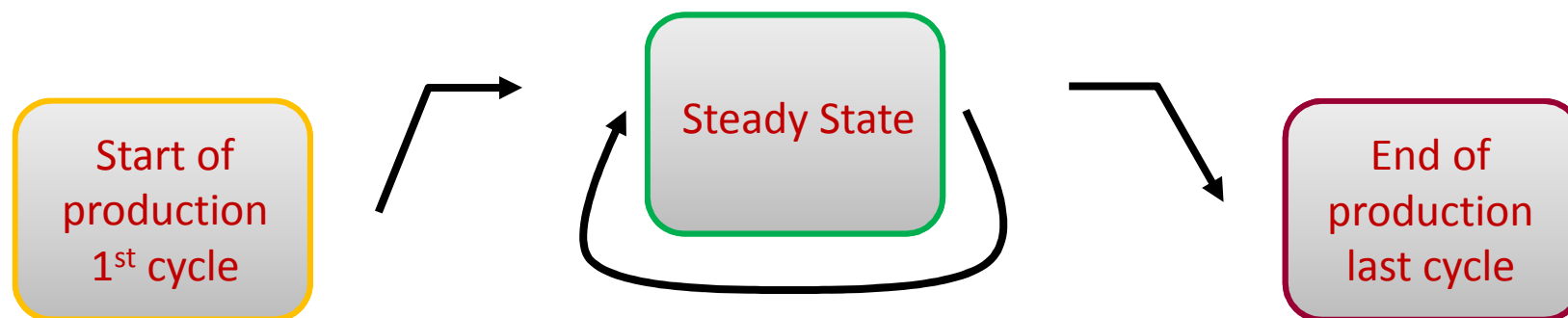
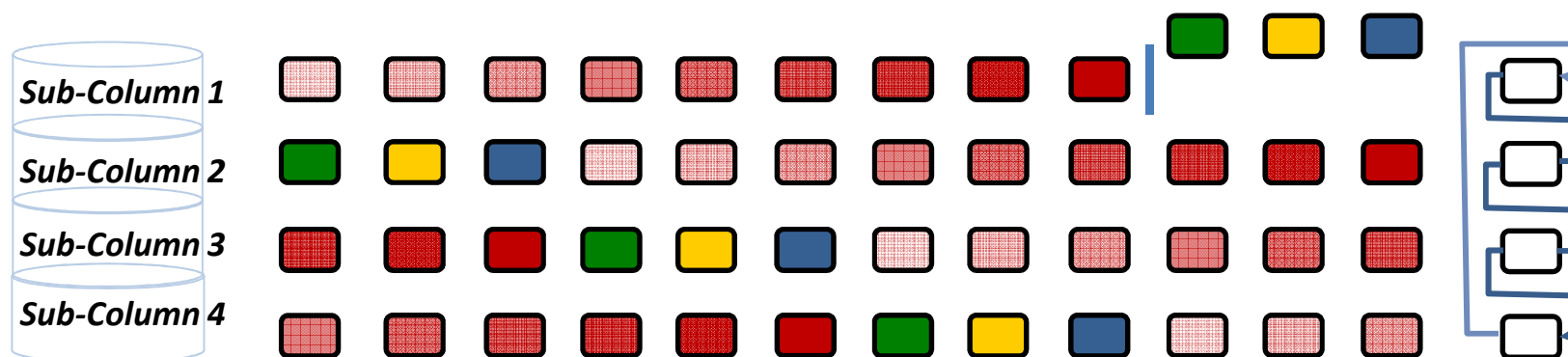
## SMCC with BioSC® (On Line Monitoring)



## SMCC with BioSC® (On Line Monitoring)

- From cycle to cycle and from column to column, the BioSC® shows excellent robustness

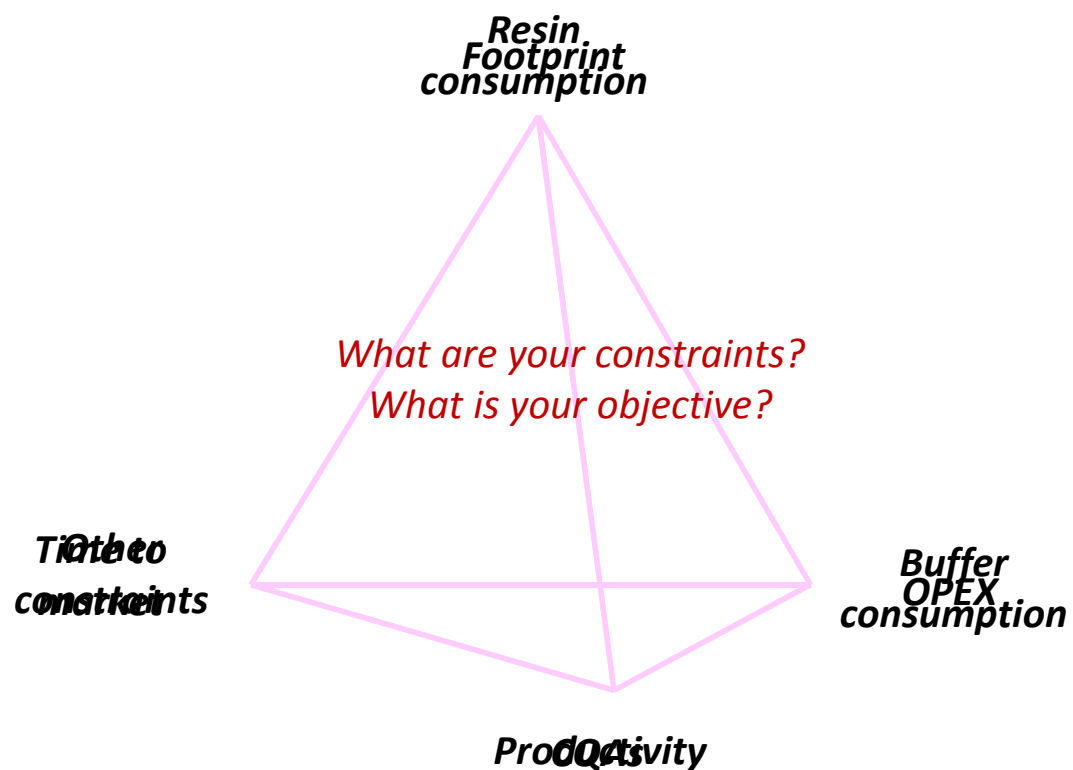




Pre-loading, conditioning, Cleaning in place, steady state and end of production are sequences that can be put in series

*How to define a SMCC sequence?*





## Valuable technology for...

- Affinity, IEX, HIC, *by maximizing resin utilization*
- mAbs, blood proteins, vaccines *by protecting target molecules*
- Perfusion, Fed-batch/ batch *by streamlining all processes*



### Unique solution when OPEX/CAPEX must be driven down

- Optimize COGs (resin and buffers) and Labor time
- Reduce footprint (for multi-products facility...)
- with no change of process parameters (Branded and Biogenerics/Biosimilars)
- ***Optimal solution for low titers / large volumes***

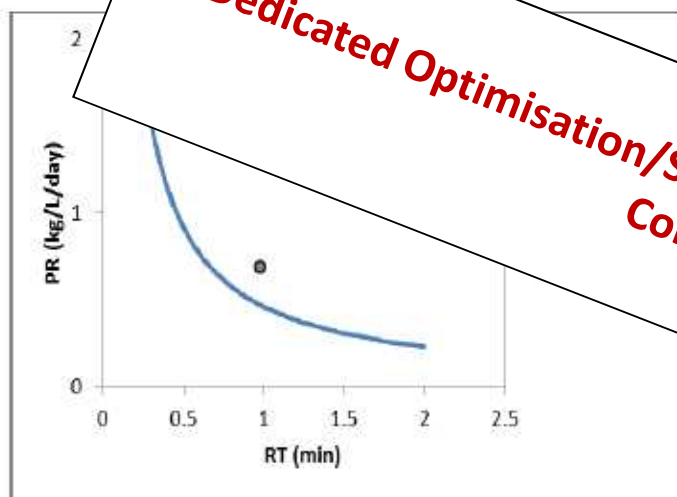


BioSC® helps to optimize processes as

- *Number of simultaneous steps can be greater than 3*
- *Can operate with only 2 columns*
- *Enables to rehabilitate old slow processes requesting more than 4 columns*
- *Enabled by dedicated simulation/optimization software*



## Estimated BioSC performance B



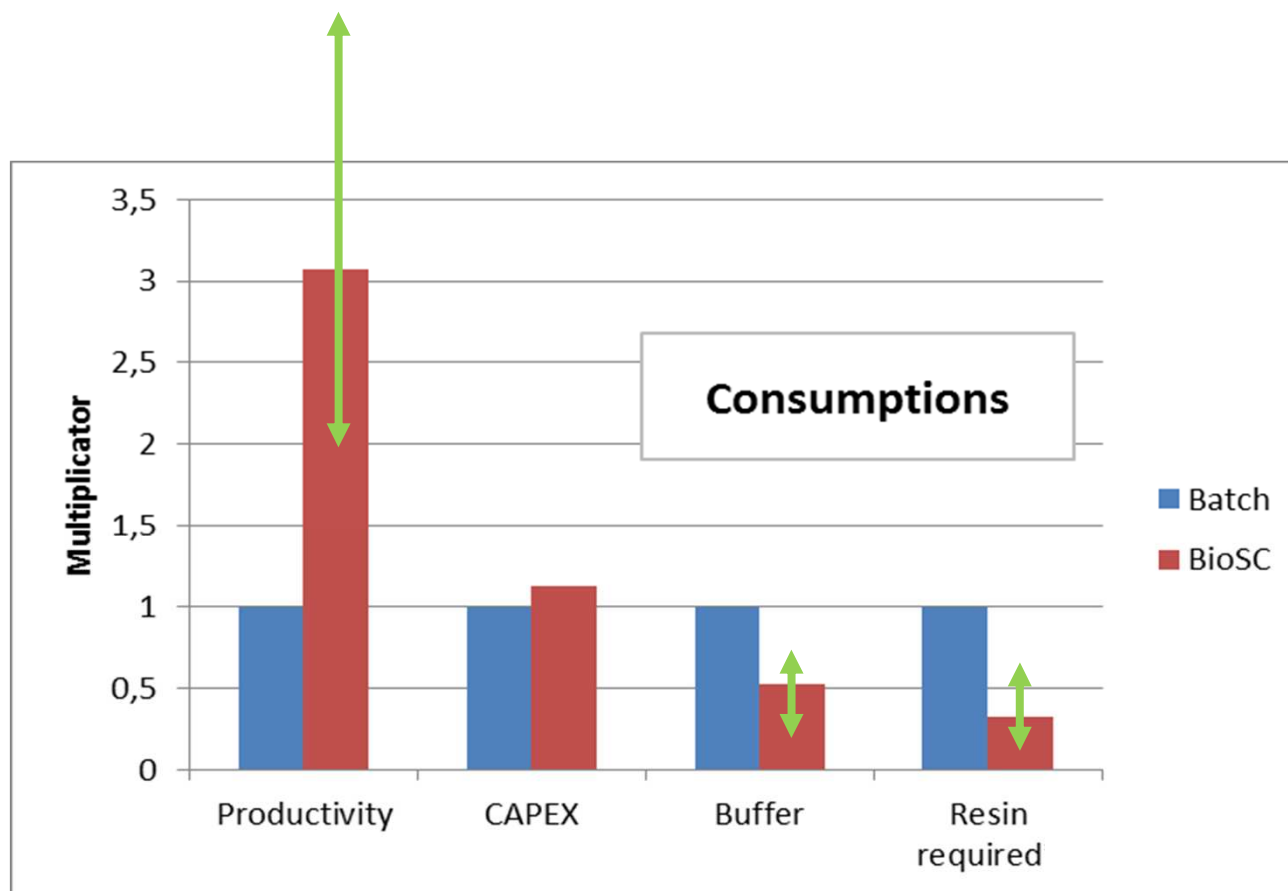
Resin = AbSolute High Cap  
Titre = 0.65 g/L hlgG

Reference batch  
2 fold

**Dedicated Optimisation/Simulation Software for BioSC®:**  
**ColHelp®**

Process	Ncol	RT* (min)	Productivity, PR (kg/L/day)	Buffer consumption, BC (L/g)
Batch B	1	1	0.69	0.63
BioSC B	2	0.3	1.53	0.65

- *Amgen, IBC Seattle March 2011*
- *Seattle Genetics, BPI Providence Oct.2012*
- *Bayer Technology Services, BPI Boston Sept.2013*
- In all studies, HCP clearance, purity, yield, DNA removal, proA leaching remains similar comparing SMCC to batch process
- Some questions remain to be addressed as process validation, viral clearance, resin lifetime.



## BioSC® Product line



Standard Features	Production		
	S	M	L
Number of Modules	2 to 6		
Pre-filtration	< 0.01	0.1	5
Typical Flow Rate (L/h)	5 to 16	25 to 50	5 to 150
Standard Max Operating Pressure (bar)	1	1-20	150
Dimensions WxHxD (cm)	6	6	6
Weight (kg)	70x100x60	200x100x100	200x200x100
	150	200	700

**Modularity is offered for the design of your BioSC®**



*"If I have seen further it is by standing on the shoulders of giants"*  
*Isaac NEWTON.*



Thank you for your attention!

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## Productivity Comparison

### SMCC

(Steady State)

# columns	cmH	cmID	L resin	Loading (g/Lr)	Cycle time (min)	# cycles	Production time (hrs)	Productivity g/Lr	Productivity g/Lr/day	L buffer / g product
4	8	45	51	59	54	4	4.5	294	1568	0.28
4	8	30	23	59	54	11	10.1	662	1572	0.28

### Batch

# columns	cmH	cmID	L resin	Loading (g/Lr)	Cycle time (min)	# cycles	Production time (hrs)	Productivity g/Lr	Productivity g/Lr/day	L buffer / g product
1	25	100	196	36	122	3	6.1	76	268	0.76
1	25	63	78	36	128	6	12.8	192	342	0.57

Productivity		
SMCC Steady Steate	SMCC 5 cycles	Batch
1568 g/l.day ( x 5.8 )	1306 g/l.day ( x 4.8 )	268 g/l.day

Buffer		
SMCC Steady Steate	SMCC 5 cycles	Batch
0.28 L/g ( / 2 or - 50 %)	0.44 L/g ( / 1.3 or - 23% )	0.57 L/g

- The current SMCC productivity numbers (g/Lr/day and g/Lr) are for steady-state mode
  - Start-up and end of production sequences decrease productivity due to lower loading during initial loop and elution of all columns during final loop
- Delivers significant economy of scale
  - ~5-6 Fold increase in productivity
  - ~1.3-2 Fold reduction in water usage
    - Positively impacts facility CapEx, foot print, utilities, tanks, etc.
  - Increase in process speed

(0.2 g<sub>mAb</sub>/L)

Run #	mAb load (g/L)	V(load) cm/h	V(other) cm/h	Yield cm/h	Purity (SEC) %	HCP ppm/IgG	Protein-A ppm/IgG
1	30	300	212	92.07	97.27	23	2.0
2	30	450	212	88.27	97.18	31	1.5
7	46	450	450	90.87	97.31	22	0.5
8	57	450	450	88.86	97.35	23	1.1
9	64	450	450	98.13	97.44	11	1.1

- BioSC can easily adsorb process variations without CQAs and process efficiency impacts
- The full utilization of the resin does not lead to process characteristics decrease