YPSO Ionic®

DESIGN OF A MULTICOLUMN PROCESS FOR mAb CAPTURE

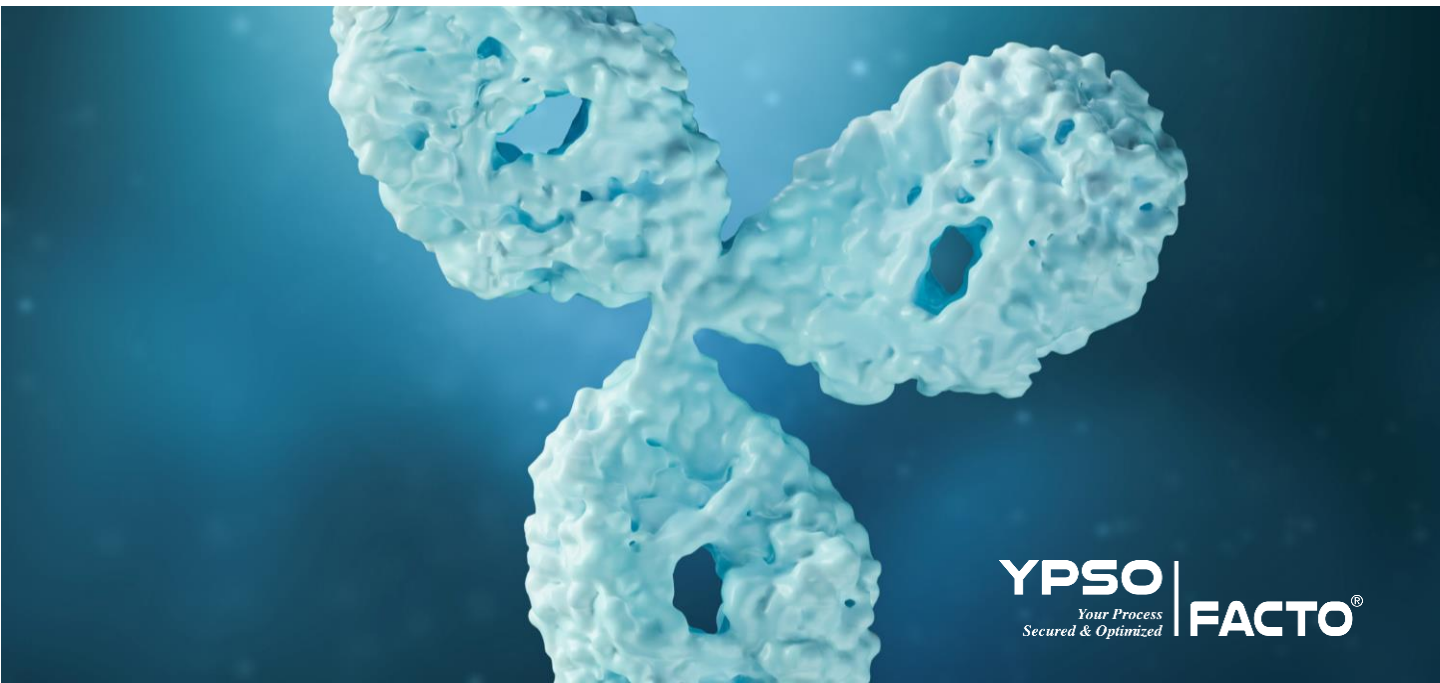
IMPACT OF THE NUMBER OF COLUMNS ON KEY PERFORMANCE INDICATORS

PROCESS: AFFINITY CHROMATOGRAPHY, MULTI COLUMN
PRODUCT: mAb

CHALLENGE

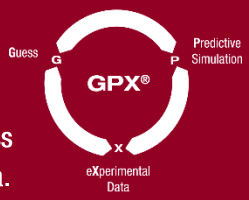
There is an increasing interest in using multicolumn processes for the **capture of monoclonal antibobies** (mAbs) by affinity chromatography. However, selecting and designing the most suitable process is not straightforward. There are indeed a wide range of process configurations, with processes ranging from 1 up to 4 or 5 columns.

In this case study, we use mechanistic simulation as a tool **to rationally compare single-column and multicolumn processes for mAb capture.** We assess the impact of the number of columns on key performance indicators like recovery and productivity.



METHODOLOGY

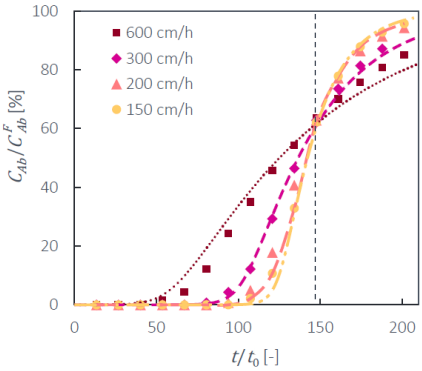
Based on the GPX® Concept: in order to address your challenges, we capitalize on the **Guess ability** of different experts, the possibility of **Predictive simulation** and the use of **eXperimental data.**



❑ Experimental data

Breakthrough curves were measured in the laboratory at different loading flowrates (Hahn et al. (2005), J. Chrom. A, 1093(1-2):98-110).
Chromatographic media: MabSelect Xtra
Column dimensions: 0.5 x 10 cm
Feed concentration: 1 g/L

The average residence time was found to be equal to $t_R = 148t_0$ min



C_{Ab} : mAb concentration
C^F_{Ab} : mAb concentration in the feed
t : time
$t_0 = \frac{\varepsilon_e V_{col}}{Q}$: zero-retention time

❑ Determination of model parameters

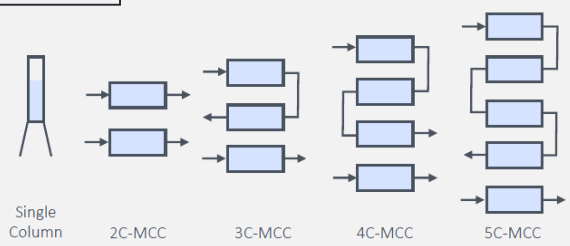
A mixing cell model with a Langmuir adsorption isotherm was used. The kinetics of mass transfer was described in the frame of the Linear Driving Force approximation. The breakthrough curve experiments were used to determine the model parameters.

❑ Process description

The process consists of several successive steps.

- We defined $\boxed{\alpha = \Delta t^R/\Delta t^F}$ as the ratio between the recovery/regeneration time and the feed time
- The feed time was set to the one determined by the equilibrium theory. With the selected operating parameters, this leads to $\boxed{\Delta t^F = 148t_0 \text{ min}}$
- Chromatographic media suppliers typically recommend about 20 CV of different eluents to perform the recovery/regeneration operations (e.g., 5 CV for wash, 5 CV for elution, 5 CV for cleaning, 5 CV for equilibration). Considering a fluid flow rate of 0.5 CV/min, this leads to $\boxed{\Delta t^R = 40 \text{ min}}$

- Different process implementations were considered with a total number of columns n_T from 1 to 5. For multicolumn systems, the number of columns in the loading zone was varied from 1 to 4, while the number of columns in the recovery/regeneration zone was kept constant at 1.



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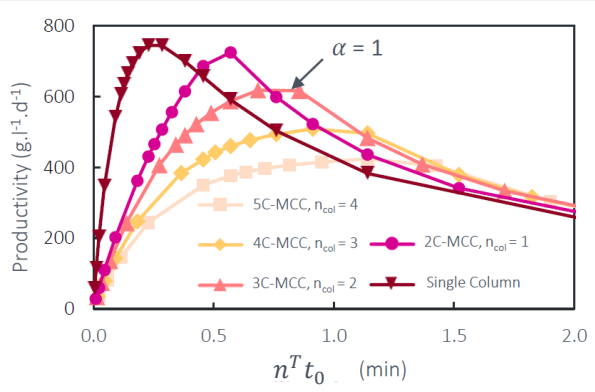
RESULTS

❑ Impact of the column size and flowrate

- Simulations were performed at various zero-retention times t_0, which contain information about the column size and feed flowrate. We have seen that $\Delta t^F = 148 t_0$, so at each t_0 value corresponds a value of the feed time (while Δt^R is kept constant at 40 min).

- It was observed that the maximum of productivity is observed for $\alpha = 1$, i.e., for $\Delta t^R = \Delta t^F$

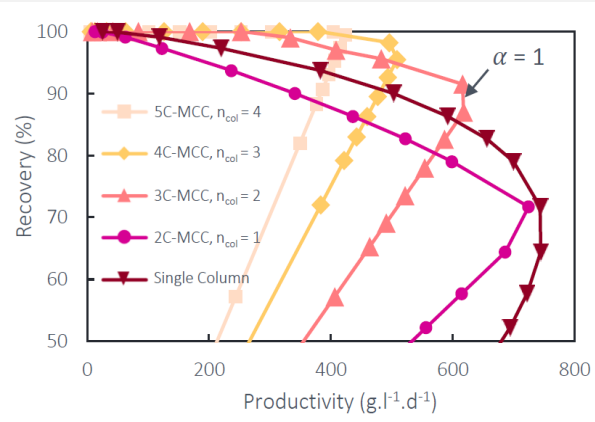


- On the left of the productivity maximum (low $n^T t_0$), the fluid velocity is too high and/or the columns are too short, so that shallow breakthrough curves are obtained. This leads to the loss of large quantities of product, and thus to a low productivity. Besides, $\alpha > 1$, so some idle time is necessary at the end of the load phase, which further decreases the productivity.
- On the right of the productivity maximum (high $n^T t_0$), sharp breakthrough curves are obtained such that the recovery is close to 100%. However, the low fluid velocity and/or long columns result in a low productivity

❑ Selection of the number of columns

- The same data were also plotted in a Recovery vs Productivity plot.
- It was evidenced that there is no "best" process outperforming the others in all cases, but rather a process that is the most suitable for a given objective.

- For instance, if the key target is to reach the maximum productivity, the most suitable process is the single-column process. However, operating the single-column process at the maximum productivity comes at the expense of a low recovery (70%).



- Generally, a constraint is defined on a minimum acceptable yield, and the process with the maximum productivity is selected. In the example under investigation, if a minimum of 90% recovery is targeted, it is found that the most productive process is the 3-column process. But if a recovery of 95% is required, then the 4-column process becomes more productive.

Conclusion

Take home messages

1. There is no “absolute” optimal process. **The optimal process depends on the objectives and constraints!** In particular, it strongly depends on the target recovery and productivity.

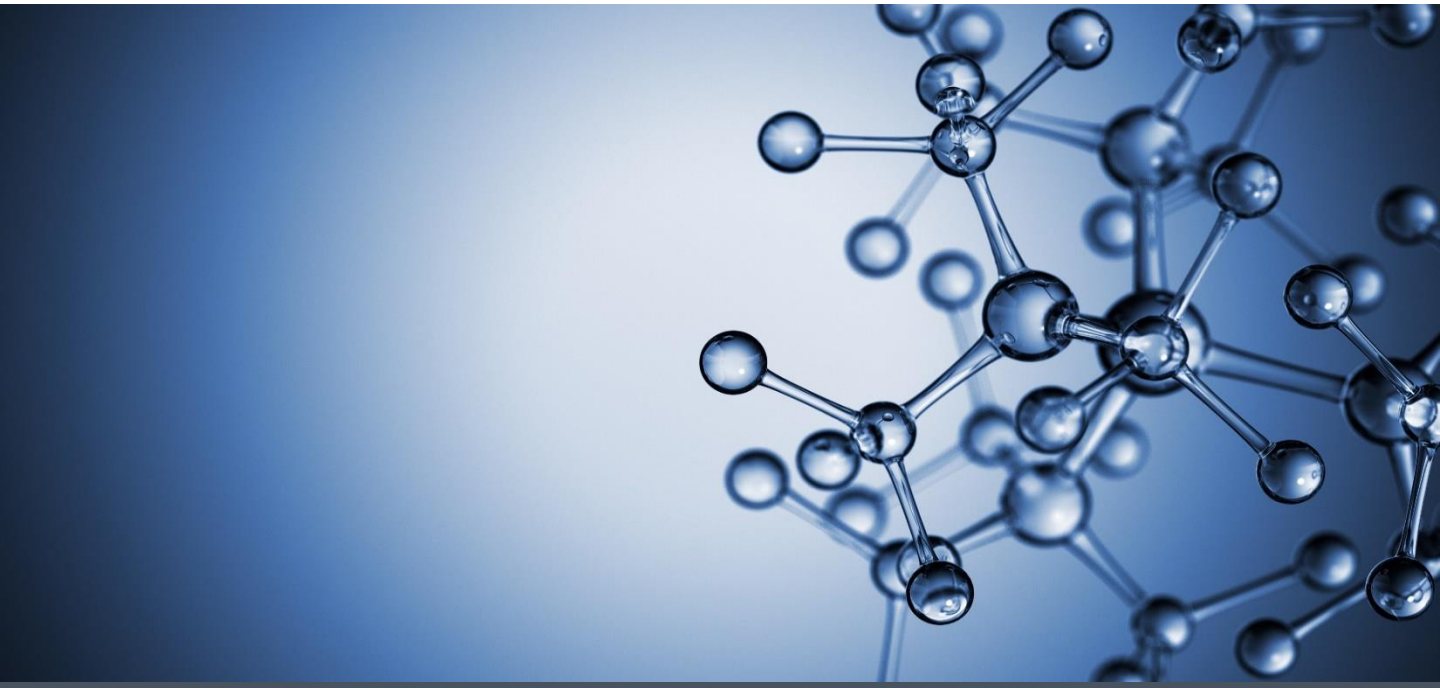
2. Process simulation can be used to screen processes and compare them rationally with a limited experimental burden.

Visit our website and contact us for a demo or more information!

contact@ypso-facto.com

For more details, refer to:

- Pfister et al, J. Chrom. A (2017); 1494:27-39 : https://doi.org/10.1016/j.chroma.2017.02.070
- Pfister et al, Continuous Biopharmaceutical Processes: Chromatography, Bioconjugation, and Protein stability. Cambridge University Press 2018



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