Simplified mechanistic models for process chromatography of biologics -Yamamoto models for process design, understanding and analysis-

Shuichi Yamamoto

Bio-Process Engineering Laboratory, Yamaguchi University Biomedical Engineering Center (YUBEC), Yamaguchi University, Tokiwadai, Ube, Japan, 755-8611
shuichi@yamaguchi-u.ac.jp

Process-scale chromatography is essential as a unit operation in biopharmaceuticals (biologics) production. As the speed to the clinic is crucial, it is needed to establish rapid and reliable methods for design, operation and validation of the purification process by chromatography.

For this purpose, various high-throughput process design (HTPD) systems have been developed. Most systems use a standard 96-well micro-plate format or the modified version. HTPD may reduce the time and the volume of the sample and the buffer solutions with the aid of design of experiments (DOE).

Another attractive and important way is to use mechanistic chromatography models. Although this approach is not very new, a number of researchers have been investigating this approach recently because of the above-mentioned reasons. Compared with DOE, which is commonly employed especially with high-throughput systems, the mechanistic model approach has several advantages:

- It provides better understanding of the factors affecting the separation
- It allows for extrapolation if governing theories/models are valid
- It enables you to reduce the number of experiments

It is also useful for characterizing the new separation media/format, and understanding the separation mechanism. Continuous processes such as flow-through chromatography and repeated cyclic operations can be designed based on the mechanistic models.

The problems or difficulties of this approach are rather complicated and laborious procedures to determine the parameter values needed for the simulation. Simplified versions of the model are useful not only for prediction of the separation but also for obtaining experimental data quickly, which are needed for the model simulations.

In this lecture I will present simplified models for linear gradient elution chromatography of proteins and other large biological products, and explain how to use such simplified models for process design/optimization/understanding and for bio-recognition study.

References

Yoshimoto, N., Yamamoto, S. (2017) Simplified methods based on mechanistic models for understanding and designing chromatography processes for proteins and other biological products -Yamamoto Models and Yamamoto Approach- in “Preparative chromatography for separation of proteins”, Chapter 4, pp, 111- 157, Wiley, 2017