Hybrid modeling for the simulation of chromatography processes

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Abstract

Ion-exchange chromatography is frequently employed as a polishing step to remove both aggregates and light impurities in the purification of monoclonal antibodies (mAb) within the biopharmaceutical industry (Grönberg, 2018). Mechanistic models of increasing complexity have been proposed to predict and simulate elution profiles under varying conditions such as column dimensions, load ratio, and flow rate. However, the development of these models is challenging due to the complex adsorption mechanism of the salt-dependent interactions between proteins and resin (Wang et al., 2016). As a result, these models are generally inaccurate in fully describing the underlying physical phenomena, leading to plant-model mismatch issues (Meneghetti et al., 2014).

Black-box models can serve as an alternative, but they often suffer from poor generalization and interpretability. To address these limitations, hybrid models can be developed, combining the strengths of both approaches. Hybrid models utilize process data while maintaining a degree of physical understanding, thereby enhancing both predictive accuracy and interpretability (Sansana et al., 2021).

In this work, we aim at setting up a procedure to guide the development of hybrid models for chromatography simulation, based on available experimental data. We employ the General Rate Model coupled with the Langmuir adsorption isotherm as our mechanistic model. We test various hybrid structures and data-driven strategies.

Results indicate that, while the hybrid model consistently outperforms the purely mechanistic model, the limited availability of data remains a critical issue affecting the applicability of hybrid models. However, preliminary tests show that data augmentation techniques can improve the model performance, and therefore appear to be a promising strategy to enhance the predictive capability of hybrid models.

Keywords: hybrid modeling, ion-exchange chromatography, pharmaceutical manufacturing,

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