MODELING THE RESIDENCE TIME DISTRIBUTION OF AN END TO END INTEGRATED BIOMANUFACTURING PROCESS

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Key Words: Numerical simulation, process design, ramp up phase, disturbance propagation

With the advancements in continuous manufacturing focused mainly on the development of individual unit operations, only a few end-to-end integrated continuous bioprocesses (ICB) have been reported. As the scope starts shifting also towards commercial applications, detailed process understanding is required for quality process design, process optimization and developing process control strategies.

We have developed a flexible and modular platform for modeling a residence time distribution (RTD) of an ICB. The platform can be easily modified and extended with new unit operations and additional functionalities. The output model of our platform is capable of describing the RTD in steady-state and rapid ramp up phase. The model also includes description of the mass flow, perturbations in product or buffer species and the propagation of possible disturbances. Furthermore, it is applicable across scales given the different upstream scenarios.

In this presentation our approach towards modeling the RTD will be discussed along with the consideration for a general use-case. The resulting model can serve as a tool for root cause investigations and plays a major role in Quality by Design approaches, process optimization and enabling the implementation of automated process control strategies.
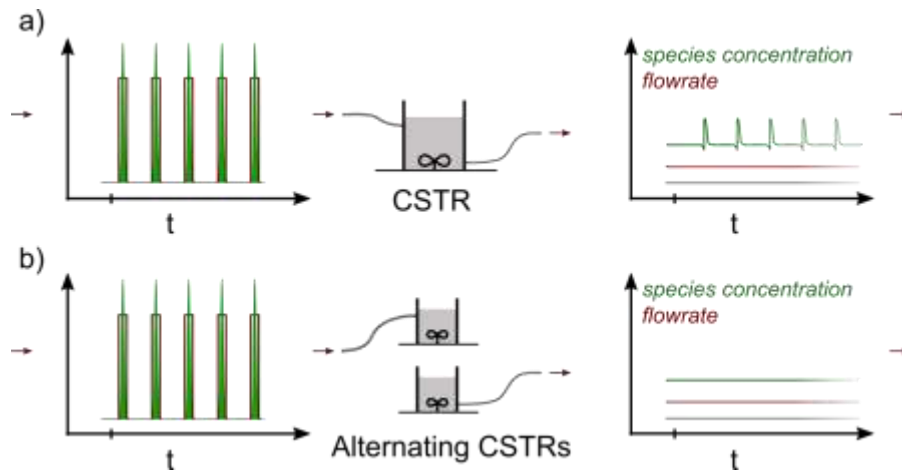

Figure 1 – Semi-continuous unit operations can disrupt the steady flowrate and cause fluctuations in product concentrations. In order to stabilize the flowrate, we can use a CSTR as a surge tank (a). However, during the elution the concentration in CSTR fluctuates. This can be mitigated by using a larger CSTR which would result in broader RTD. The alternative approach with a system of multiple alternating CSTRs (b) overcomes the fluctuations and narrows the RTD, but it increases the complexity of the process. A preferred solution would depend on the operating conditions and the unit operations downstream.