**Benefits of Using Macrokinetic Bioreactor Models in Rigorous Flowsheet Simulators**

Jan C. Schöneberger1\*, Armin Fricke1, M. Nicolas Cruz Bournazou2

*1 Chemstations Europe GmbH, Berlin, Germany; 2 Department of Chemistry and Applied Biosciences, ETH Zürich, Swizerland*

*\*Corresponding author: js@chemstations.eu*

**Highlights**

* Simulation of coupled up- and downstream processes
* Rigorous First-Principal modelling of biotechnological processes
* Economic analysis and optimization of complete biotechnological processes

**1. Introduction**

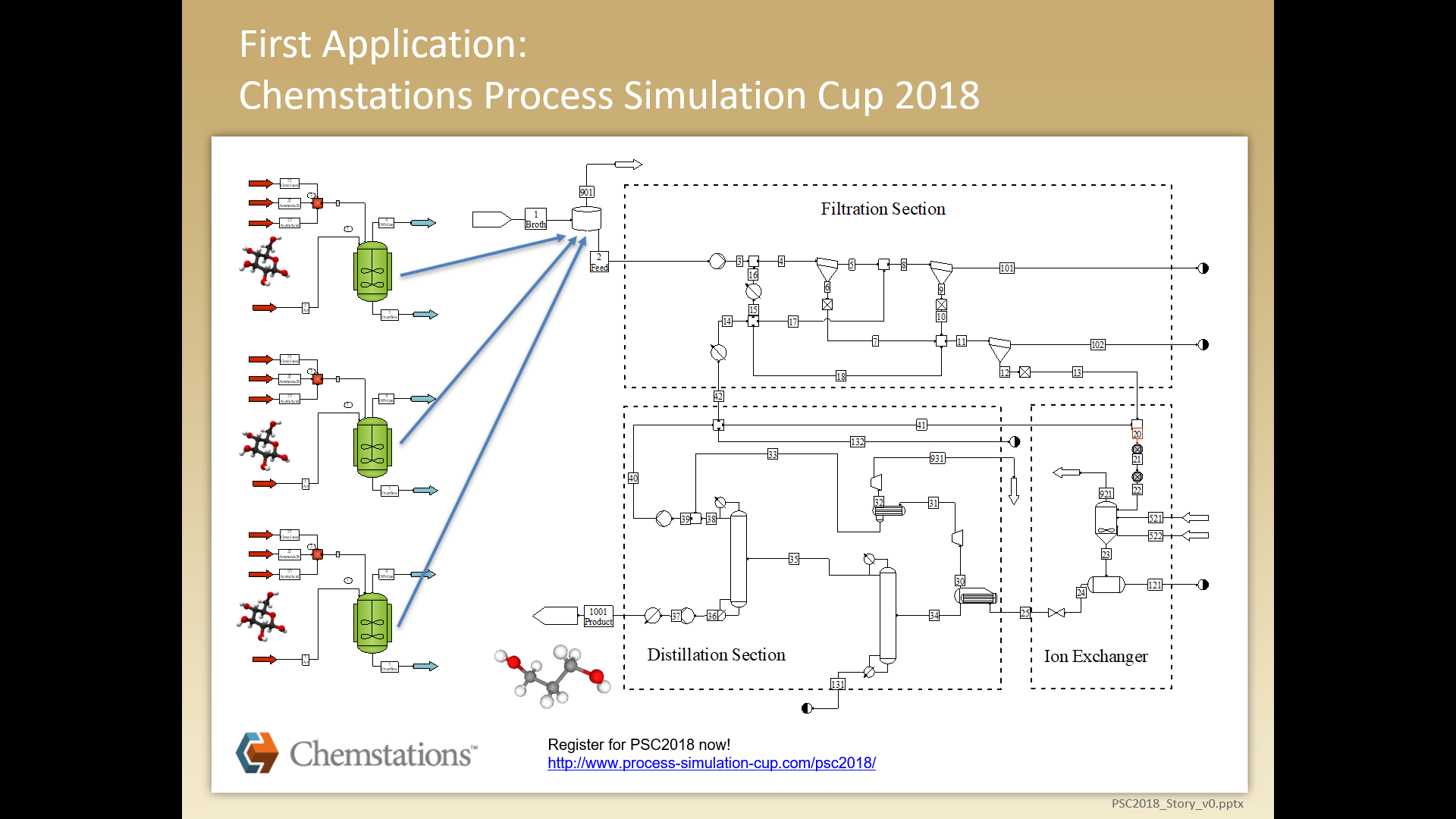
The number of biotechnological processes that are realized in large-scale dimensions is steadily increasing. In addition to food technology applications such as breweries or biofuel applications like biogas and bioethanol plants, biorefineries for the production of basic and specialty chemicals are becoming more important. In classical EPC business, flowsheet simulators are used to solve the mass and energy balances of the processes taking into account the laws of thermodynamics. The results from the simulation form the basis for equipment dimensioning and plant wide process optimization.

The apparatus models used in biotechnology differ from the apparatus models used in classical chemical processes. Reactors or fermenters in biotechnological processes are often operated discontinuously. Downstream processes can be operated batch wise, but depending on the amount of product, a continuous process is often the more economical solution.

In the modeling of bioreactors, the high number and complexity of biochemical intracellular reactions makes it difficult to accurately describe the dynamic behavior of the reactor. In addition, the properties of the microorganisms are subject to constant change. Macrokinetic models can be used to describe these reactions at least for a certain time period or a specific state of the bacteria’s life cycle. However, these models commonly need to be adjusted and model parameters must be updated regularly.

**2. Methods**

In this work two approaches are presented for including macrokinetic models in a flowsheet simulator, a mass-balance based approach and a mole-balance based approach. The different simulation results of these approaches are discussed in detail by means of a simple example from Fogler [1]. The mole-balanced approach is then applied to an Escherichia coli based production process for 1,3-Propanediol (PDO). Therefore, a more complex macrokinetic is used, similar to the one published by Anane et al. [2]. The PDO process is modelled in CHEMCAD as a combination of four batch fermenters and a continuous downstream process with filtration section, ion exchanger, and distillation section. The flowsheet is depicted in Figure 1.



**Figure 1.** Simulation flowsheet of a bacteria based PDO production process.

**3. Results and discussion**

The simulation of the complete production chain from cane juice to PDO allows a detailed estimation of the operational expenditures (OPEX), considering the costs of the feed (cane juice, ammonia, and acetic acid), the utilities (electricity, steam, and cooling water), chemicals (caustic soda and sulfuric acid), and the revenues gained with the produced PDO as a function of the final product quality. Such calculations enable an economic optimization of the production process.

The maximization of the PDO plant’s benefit was the task of the Process Simulation Cup 2018 [3], where students from all over the world were allowed to change predefined design variables. Table 1 shows the development of the calculated profit by enabling over the one year’s runtime of the cup the design variables of the different sections.

**Table 1.**  Achieved profit of the PDO plant during the different stages of the PSC2018.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Initial Solution | Optimization of the distillation section | Optimization of the distillation section and the recycle flows | Optimization of the substrate flows with fixed downstream | Optimization of the substrate flows + air flow with fixed downstream | Optimization of the coupled process |
| -387 $/h | 191 $/h | 422 $/h | 695 $/h | 1.192 $/h | 1.408 $/h |

**4. Conclusions**

The results given it Table 1 demonstrate impressively, how the usage of microkinetic bioreactor models in rigorous flowsheet simulators help to find optimal or at least improved operation parameters for biorefineries.

**References**

1. H.S. Fogler, Elements of Chemical Reaction Engineering, 5th Edition, Prentice Hall, 2016
2. E. Anane, D. Lopez, P. Neubauer, M.N. Cruz, Biochemical Engineering Journal 125 (2017) 23–30
3. www. process-simulation-cup.com\psc2018 (Last called 03.01.2019)