237e Aqueous Two-Phase Extraction – a Case Study in Process Analysis and Control

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Bioseparation involves a series of separation steps that focus on the purification and downstream processing of biological molecules. These products include therapeutic proteins, diagnostic and added-value products from agriculture. The development of efficient separation techniques has become imperative because of the advances in genetic engineering technology that enables large-scale production of recombinant proteins. Ready access to purified proteins is also mandatory for theoretical studies as well as for practical biotechnological use. However, the extraction of protein is expensive and might account for 50% or more of the total production cost. This work focuses on the analysis of continuous Aqueous Two-Phase Systems (ATPS) and uses tools learned in process dynamics and control classes. Aqueous two-phase systems have been used, extensively, in the separation and purification of biomolecules in pharmaceutical research. The main advantages of these types of extraction processes are their biocompatibility, ease of scale-up, and low operation costs. Furthermore, these methods are approved by regulatory agencies. Compared to current separation methods, ATPS are versatile and can be designed for enzyme extraction and purification based on size, molecular mass, conformation, charge and/or hydrophobicity. Two-phase systems have been investigated extensively to describe the mechanisms responsible for phase separation. These theoretical studies help in understanding the factors influencing protein partitioning. The derived models provide invaluable tools for scale-up purposes and further system optimization and control. However, process scale-up offers unique challenges, such as meeting production requirements in the presence of disturbances and decreasing downtime, that are not addressed in current modeling frameworks. The dynamic behavior of these systems has to be investigated and understood to enhance plant-wide control of continuous ATPS and to assess safety and environmental risks at the earliest possible design stage. Starting from simple mass balances, we were able to derive a mathematical model that fully describes steady-state and transient behaviors of single-stage continuous aqueous two-phase systems. The example is instructive because it challenges assumptions often made in the analysis of processes studied in introductory course in process control. Simulation results are presented and clearly show how step changes in the inlet flow rate affect the dynamic behavior of the system.