IDP:

Stochastic optimization of Biopharmaceutical operations control policies using a Markov decision process model

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Topic:

Biopharmaceuticals are pharmaceutical drugs derived from biological sources used for therapeutic or diagnostic purposes. They possess a particularly high efficacy and efficiency in treating complex health conditions, like cancer, inflammatory diseases or metabolic disorders.

The primary biological production process is structured into two main stages: The upstream process contains all production steps related to the cultivation of the living organisms, while the downstream process comprises the separation and purification of the target molecule. Subsequently the purified active pharmaceutical ingredient (API), obtained from the primary biological production process, is formulated into its final dosage form, e.g. a syringe, during the secondary pharmaceutical production.

This IDP focuses on the integrated up- and downstream operations of the biopharmaceutical manufacturing. Due to the use of living cells in the production process, one has to deal with process-inherent operational uncertainties relating to the process stage’s times and yields. Operational decisions made in the upstream part, subject to uncertainties, have an impact on the downstream operations thereafter. Neglecting this impact can lead to sub-optimal decisions made for the upstream operations.

In 1996 Schmidt defined a stochastic optimization model using a Markov decision process (MDP). He specifically addressed the shortcomings in production control of the bioreactor seed train by defining a discrete set of bioreactor states and determining the
ideal control policy to maximize the overall productivity of the system. By defining the problem as a MDP he considered intrinsic operational uncertainties of the process, like batch failures. Nevertheless Schmidt (1996) significantly simplified the bioreactor states as well as neglected the impact of upstream decisions on the downstream operations. Also, MDP actions are not linked to bioreactor control variables.

The objective of this IDP is thus to design of a stochastic optimization model representing bioreactor state and control variables in a MDP framework to find the optimal control policy for the integrated up- and downstream operations to maximize overall long-term system productivity.

Tasks:

Your task will be to:

1. Identify relevant state and control variables for the integrated Biopharma operation.
2. Conduct a literature review on stochastic optimization models applying MDP/ADP to the optimization of control policies, in particular to biotechnological production.
3. Develop a stochastic optimization model using the MDP framework integrating identified state and control variables.
4. Implement the mathematical model in an appropriate modelling environment, e.g. Python.
5. Perform a numerical study and derive general insights on the optimal process control of bioreactor seed train operations.

Prerequisites:

You should be familiar with stochastic optimization, in particular Markov decision processes (MDP) and approximate dynamic programming (ADP). Any additional insights to the process
industry or biopharmaceutical industry, specifically the production process are a plus but not required.

**References:**

