HORIZON 2020

Optimal Decision Making under Uncertainty in Biomanufacturing Operations

Sprawozdania

Informacje na temat projektu

OPTBIOMAN

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Strona internetowa projektu

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Podsumowanie kontekstu i ogólnych celów projektu

Biomanufacturing methods use live systems during the production process, such as, bacteria, viruses, and eukaryotic cells. The use of live systems introduces batch-to-batch variability in terms of yield, quality, cycle times and operating costs. On the other hand, Current Good Manufacturing Practices require achieving strict standards on batch reproducibility, yield and quality. The inherent variability of these processes lead to high risk of rework and/or failure in conforming to these production standards. Capacity limitations and expensive costs associated with labour and materials add another layer of challenges to industry practices. Faced with these challenges, most biomanufacturing companies know that they need to invest early on improving biomanufacturing efficiencies, but they still do not put enough effort on it. Critical assessment of literature and industry feedback indicate that most biomanufacturing companies put significant time and efforts on the underlying biology and chemistry of these processes (cell-level) but often ignore the manufacturing (system-level) dynamics. These include a formal assessment of the financial risks and trade-offs associated with the uncertainty in yield, quality, cycle times and costs in biological decision making.

To address these challenges, an inter-disciplinary modelling and optimization framework is developed to reduce operating costs and improve efficiencies in biomanufacturing operations. Stochastic optimization models are developed to economically optimize biomanufacturing decision under high process variability, failure risks, and expensive operating costs. In contrast to the existing techniques, these new mathematical models link the cell-level dynamics of the biomanufacturing processes (i.e. underlying biology and chemistry) with manufacturing system-level dynamics (i.e. trade-offs in terms of yield, quality and costs). In particular, the research project models and analyses the economics of the upstream fermentation operations and downstream purification operations. First, integrated quality and reliability models are developed to provide fundamental insights for bioreactor harvesting decisions when there is uncertainty in bioreactor’s state information. Next, stochastic optimization models are developed to economically optimize chromatography operating decisions based on yield and quality trade-offs encountered in industry practices. At cell-level, styled probabilistic models are investigated to capture the process variability in terms of yield and quality of both upstream fermentation and downstream chromatography operations. At the manufacturing system-level, Markov decision models that convert these cell-level probabilistic models into cost-optimal operating policies are developed. Novel approximations and heuristics are developed based on the unique features of the problem setting in order to solve large size problems typically encountered in industry practices. Optimal policies are theoretically and numerically analysed for both upstream harvesting and downstream chromatography operating decisions.

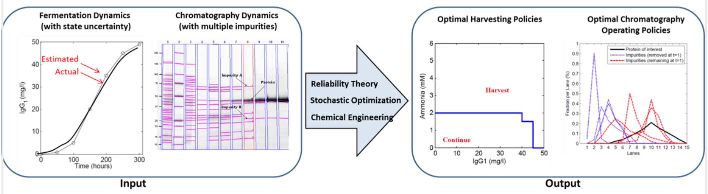
Prace wykonane od początku projektu do końca okresu sprawozdawczego oraz najważniejsze dotychczasowe rezultaty

The project resulted in stochastic optimization models and decision support tools to reduce costs and lead times in biomanufacturing operations. These models were built under two main work packages: The first work package focuses on upstream fermentation operations. A Markov decision model was built to maximize the expected total discounted profit by optimizing the bioreactor harvesting times. The robustness of the optimal harvesting polices were tested through numerical experiments. As a result, several managerial insights were generated for practitioners to better conduct the harvesting decisions under process uncertainty and batch failure risks. The second work package focuses on downstream purification operations. A Markov decision model was built to maximize the expected total discounted profit by optimizing the choice of chromatography technique and pooling windows. The robustness of the optimal policies were tested using a comprehensive set of numerical experiments, and managerial insights were generated for practitioners through case studies. Overall, using real-world case studies from industry, we were able to show that up to 20% improvement in costs and lead times would have been achieved through the application of the analytical models developed in work packages 1 and 2. The project resulted in three peer-reviewed journal publications and two peer-reviewed conference proceedings. In addition, two Master’s thesis were also successfully conducted during the project.

During the project, several dissemination activities were conducted via industry workshops, online platforms, conferences, and working group sessions. For example, research outcomes were presented at several international conferences (i.e. INFORMS Annual Meeting, POMS Conference, EURO, Winter Simulation Conference), and a video was created to disseminate project results. In addition, the project outcomes received several prestigious awards at international platforms (i.e. Winner of the POMS Applied Research Challenge, First Prize in INFORMS TIMES Award). These awards significantly helped to disseminate and also encourage future work.

Innowacyjność oraz oczekiwany potencjalny wpływ (w tym dotychczasowe znaczenie społeczno-gospodarcze i szersze implikacje społeczne projektu)

Case studies reported in our papers (see our articles in Operations Research and MSOM) show that the optimization models developed in this research can significantly reduce lead times and costs in biomanufacturing practice.



A visualization of the interdisciplinary framework for optimizing biomanufacturing operations

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