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# Production and Maintenance Planning Optimisation in Biopharmaceutical Processes under Performance Decay using a Continuous-time Formulation: a Multi-objective Approach

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## HIGHLIGHTS

- A novel planning formulation for biochemical processes under performance decay is proposed.
- The model addresses the main production and maintenance constraints to solve planning problems.
- The model performance is compared to a literature industrial-based example.
- Results highlights the advantage of a continuous single time-grid formulation.
- A multi-objective approach discusses the assessment of tactical operational decisions.

## ABSTRACT

This work addresses the optimal planning of biopharmaceutical continuous manufacturing processes under performance decay, modelling its operational constraints in a mixed integer linear programming (MILP) model, based on a Resource Task Network (RTN) continuous single-time grid formulation. The model assesses the manufacturing constraints for the determination of the production schedule while defining the appropriate maintenance planning timing in downstream units to assure optimal process performance. An improved model approach is discussed and compared with the application results to literature-based industrial cases. In order to evaluate different solutions towards the multiple decision maker's strategic and operational objectives, the definition of the Pareto sets for three bi-objective analyses is performed with the augmented  $\epsilon$ -constraint method, using the profit

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