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DTU Department of Chemical and Biochemical Engineering

Potential of predictive model-based dissolved oxygen control for intermittent fed-batch processes

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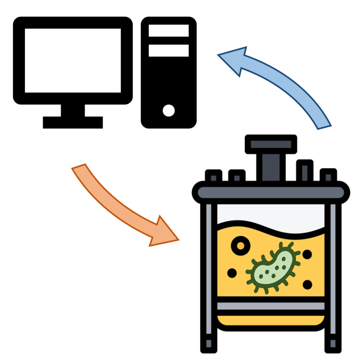
Motivation

The level of dissolved oxygen (DO) in a bioreactor is essential for the cultivation of microorganisms[a]. Traditional control strategies acting on the stirrer speed and aeration rate usually struggle with the dynamic nature of the system[b]. Their purely reactive algorithms especially show their limitations when challenged with abrupt changes in nutrient additions. The resulting drops in DO can negatively influence the cells metabolism and physiological state[c].

Model predictive control (MPC) algorithms present promising alternatives for such intermittent feeding profiles. Applied to high-throughput small scale multi-reactor systems they can avoid oxygen limitations during the cultivation and enable optimal process conditions.



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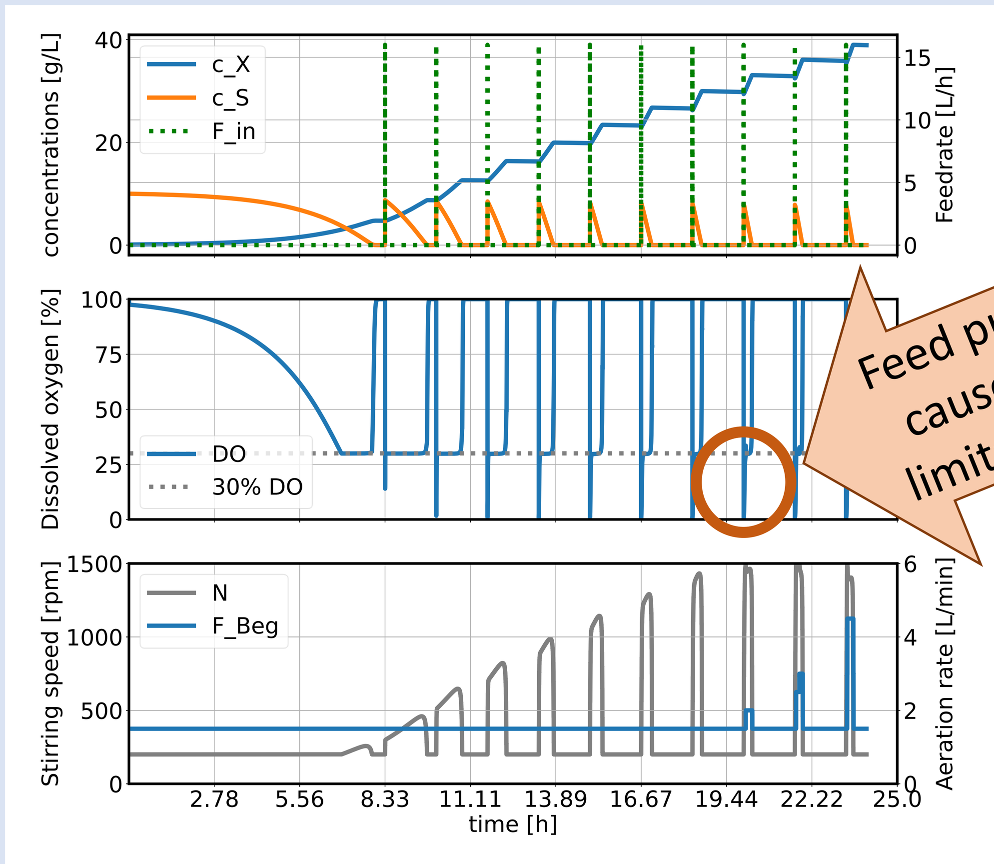
Traditional PID control

Simple and proven control algorithm, but the bioprocess system dynamics make tuning non-trivial. Risk of non-optimal process conditions when challenged with pulsed substrate addition.



Setup of a process model

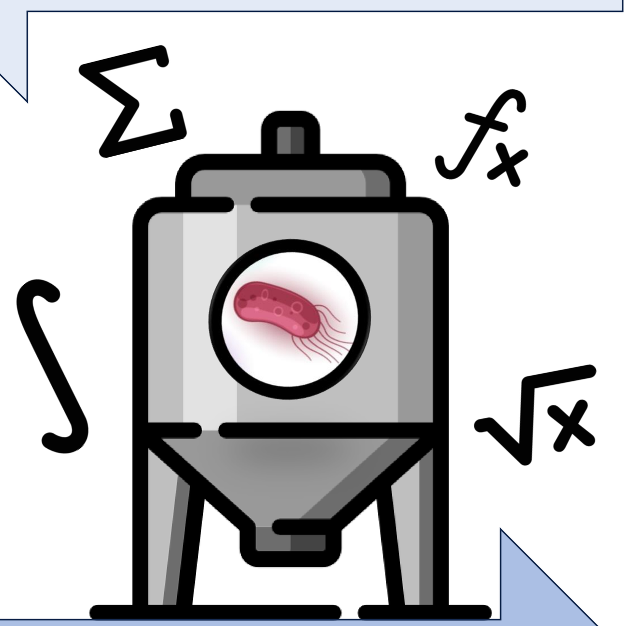
Combination of simple mass and elemental balances to create a mechanistic model of the fed-batch process with a focus on cell physiology.

$$\frac{d}{dt}\begin{bmatrix} c_{O2} \\ c_X \\ c_S \\ V_R \end{bmatrix} = \begin{bmatrix} k_L a \cdot (c_{O2,eq} - c_{O2}) - q_S \cdot c_X \cdot Y_{O2/S} \\ \left((q_S - q_m) \cdot Y_{X/S} - \frac{F_{in}}{V_R} \right) \cdot c_X \\ (c_{S,in} - c_S) \cdot \frac{F_{in}}{V_R} - q_S \cdot c_X \\ F_{in} \end{bmatrix}$$

In order to describe the non-linear nature of the cell metabolism and the liquid-gas a Monod-type kinetic and the Van't Riet equation are introduced.

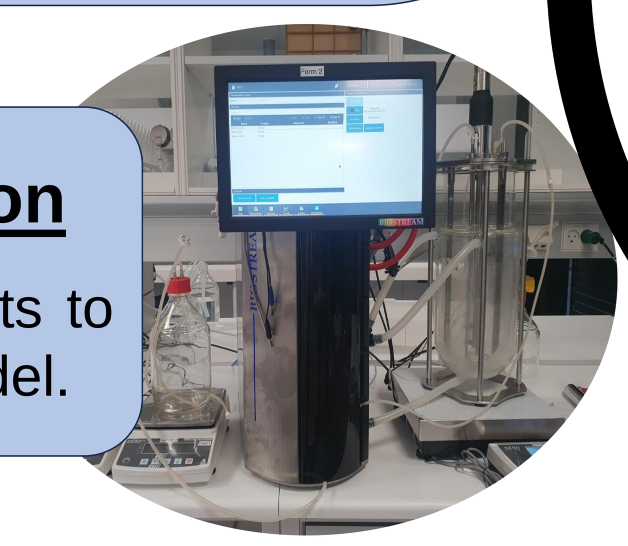
$$q_S = q_{S,max} \cdot \frac{c_S}{c_S + K_S} \cdot \frac{c_{O2}}{c_{O2} + K_{O2}}$$

$$k_L a = k \cdot N^{\alpha_1} \cdot D^{\alpha_2} \cdot \left(\frac{F_{air}}{A} \right)^{\beta}$$

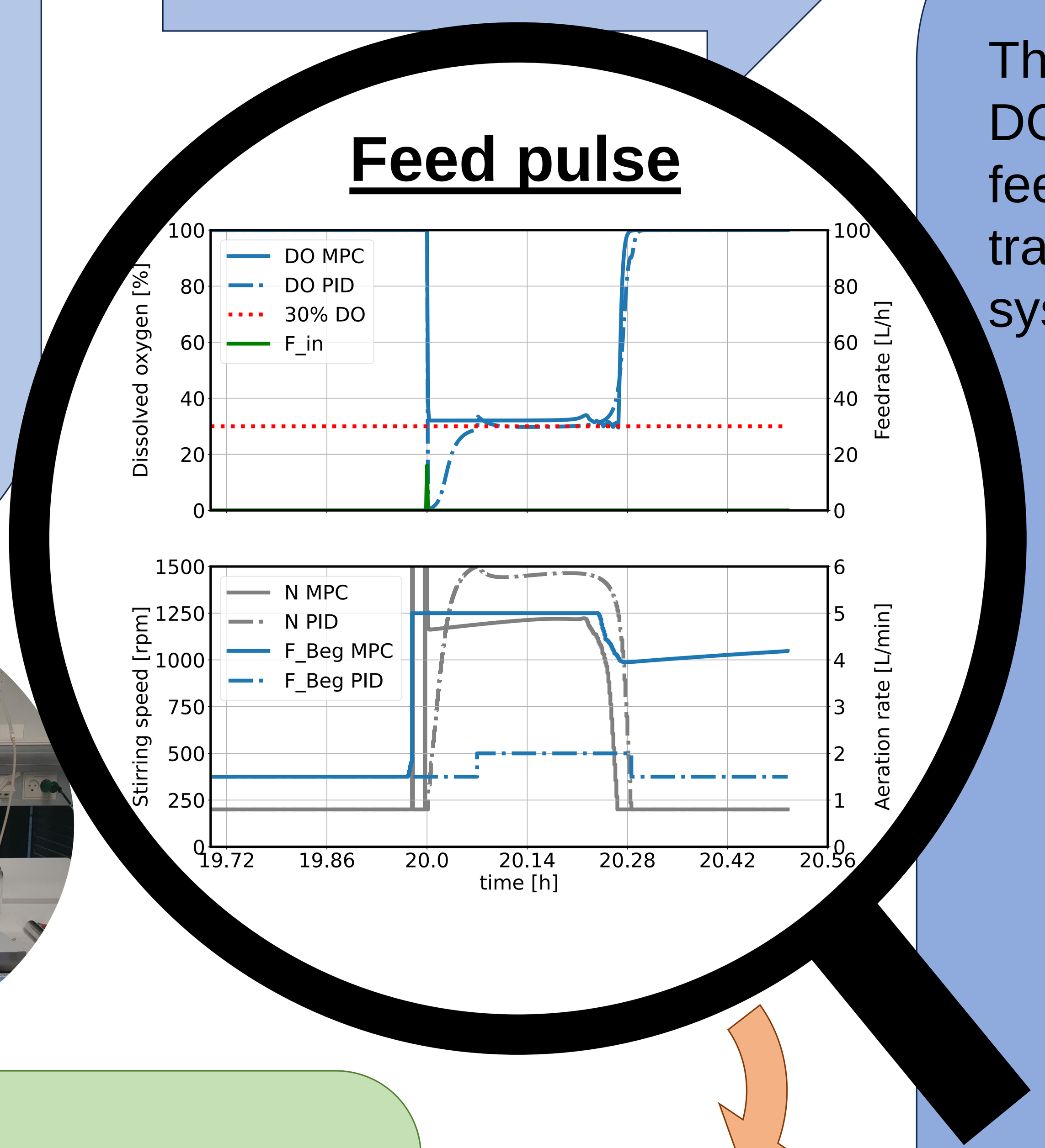


Parameterization

Lab scale experiments to parameterize the model.

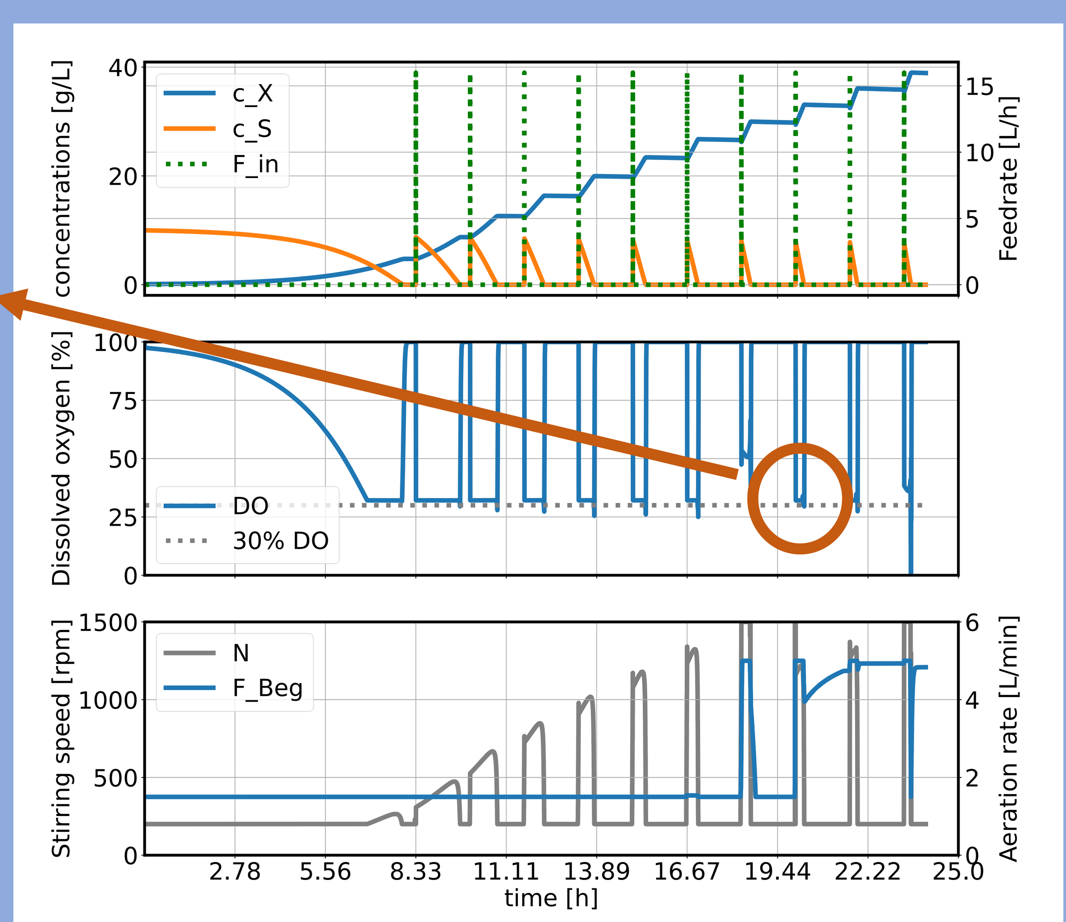


Feed pulse

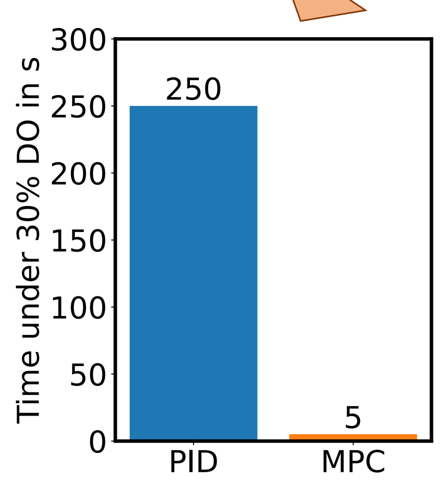


Applied & Parameterized MPC

The parameterized and tuned MPC minimizes DO limitations by considering the known feeding profile, calculating the optimal input trajectory and predicting the reaction of the system.



The direct comparison to the PID controller shows a minimal time spent underneath the set threshold of 30% DO with similar control action. The negative impact of temporal oxygen limitation can therefore by significantly reduced.



Conclusion & Outlook

- Predictive action of MPC avoids DO limitations for intermittent feeding profile *in-silico*
- Test performance with different types of noise
- Application of controller to lab-scale experiments

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b. Cardello, R.J., San, K., 1988. The design of controllers for batch bioreactors. Biotech & Bioengineering 32, 519–526.
c. Kim, J.W., Krausch, N., Aizpuru, J., Barz, T., Lucia, S., Neubauer, P., Cruz Bournazou, M.N., 2023. Model predictive control and moving horizon estimation for adaptive optimal bolus feeding in high-throughput cultivation of E. coli. Computers & Chemical Engineering 172.

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