SUCCESS STORY

CHASE
Chemical Systems Engineering

Programme: COMET – Competence Centers for Excellent Technologies

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Digital twin device BioMaRe ("Biomasserechner") running on FESTO hardware (© CHASE)

BUILDING A DIGITAL TWIN FOR INDUSTRIAL BIOPROCESSES

MONITORING & CONTROL OF BIOREACTOR FERMENTATION PROCESSES IN A REAL-TIME ENVIRONMENT

In 2004, the food and drug administration (FDA) published a guidance for innovative pharmaceutical development, manufacturing and quality assurance called PAT. These guidelines aimed to emphasize the transition of the biopharmaceutical sector from an extensive product testing during manufacturing to a quality by design approach (QbD) based on process understanding. A key enabler to meet the regulatory specifications is mathematical modeling of the underlying process mechanics. Mechanistic models serve as great tools for monitoring and control, enhanced process design, system analysis and knowledge sharing. Based on those models, digital twins can be developed that represent the physical plant in real-time and can be used to guide decision making throughout the process. In the project BioTwinKit between CHASE and FESTO, a digital twin based on mechanistic models was developed and deployed as a prototype on hardware components provided by FESTO. The device was equipped with a graphical user interface to interact with the digital twin. Several case study experiments using *Escherichia coli* have been conducted with the soft sensor. Cell growth, substrate uptake rate, biomass yield coefficients and product formation rates were calculated based on simple, readily available measurements such as feeding rates and off-gas composition. The mechanistic model incorporated the reactor mass balances described by a system of first order ordinary differential equations as well as the elemental balances for carbon and degree of reduction. We showed that the biomass and substrate estimates were more accurate using the mechanistic model based

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soft sensor compared to pure elemental balancing. Moreover, the application range could be extended to non-substrate limited growth. To close the loop between monitoring (soft sensing) and model- based control, we developed a model predictive controller (MPC) to control the behaviour of the bioprocess based on the soft sensor estimates. We believe that this approach enables knowledge-based bioprocessing utilizing modern model-based tools for prediction and real-time process control.

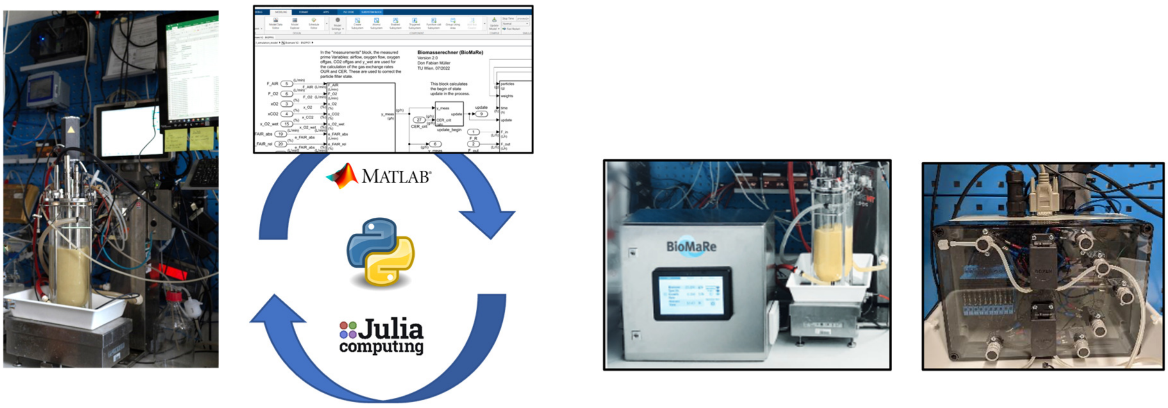

Figure 1: The physical bioreactor cultivation process (left) was incorporated in a real-time online environment and connected to external devices (PLCs, autosampler…) for optimal process monitoring and control. Algorithms were developed using the programming languages MATLAB, Python and Julia.

Project coordination (Story)
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