Band 14, 2026, Heft 1

JOHANNES HOFMANN (Hochschule Esslingen)
HANNAH KORN (Hochschule Esslingen)
CLARA WANKMÜLLER (Hochschule Esslingen)
RICHARD BIENER (Hochschule Esslingen)

Bioprocess Digital Twin as Training and Educational Tool

Journal of Technical Education (JOTED)
ISSN 2198-0306
Online unter: http://www.journal-of-technical-education.de

JOHANNES HOFMANN / HANNAH KORN / CLARA WANKMÜLLER / RICHARD BIENER

Bioprocess Digital Twin as Training and Educational Tool

ABSTRACT: Digital twins are a key technology of industry 4.0 and are a powerful tool for operator training simulations (OTS). This work presents a digital twin for a bioprocess. Possible applications in higher education and corresponding learning objectives are presented and discussed. The digital twin is capable of simulating various upstream operation modes (e. g. batch, fed batch, chemostat) and also addresses the issue of automating those processes using sequential function charts (SFC). From a didactic point of view, digital twins have numerous advantages. Students can be introduced to complex issues in a vivid manner. Using a digital twin also reduces the fear of making errors or wrong decisions. Students can freely perform virtual experiments with different parameters and configurations, ultimately leading to a more confident operation of real processes.

Keywords: Digital twin, Operator training simulation, bioprocess, didactic, bioreactor, sequential function chart

Digitaler Zwilling für Bioprozesse als Schulungs- und Ausbildungsinstrument

ZUSAMMENFASSUNG: Digitale Zwillinge sind eine Schlüsseltechnologie der Industrie 4.0 und ein leistungsfähiges Werkzeug für Operator-Training-Simulationen (OTS). In dieser Arbeit wird ein digitaler Zwilling für einen Bioprozess vorgestellt. Es werden Einsatzmöglichkeiten in der Hochschullehre sowie die darauf abgestimmten Lernziele aufgezeigt und diskutiert. Der Digitale Zwilling ist in der Lage, verschiedene Upstream-Betriebsarten (z. B. Batch, Fed-Batch) zu simulieren und diese Prozesse mithilfe von Schrittketten zu automatisieren. Aus didaktischer Sicht bieten Digitale Zwillinge zahlreiche Vorteile. Studierende können auf anschauliche Weise an komplexe Sachverhalte herangeführt werden. Ebenso können Sie selbstständig virtuelle Experimente mit verschiedenen Parametern und Einstellungen durchführen, was letztlich zu mehr Sicherheit im Umgang mit realen Prozessen führt.

Schlüsselwörter: Digitaler Zwilling, Bedienerschulung Simulation, Bioprozess, Didaktik, Bioreaktor, Ablaufsteuerung, Schrittkette

1. Introduction

The digital transformation offers the opportunity to rethink and redesign processes and activities in many areas. Universities are discussing how to integrate digital forms of teaching and learning. Due to the coronavirus pandemic, this topic has particularly gained momentum (Wollersheim et al., 2021). One of those many new digital learning tools are digital twins. Digital twins are virtual representations of physical objects or systems that simulate and analyse their behaviour in real time. They are a key technology of industry 4.0 and play a major role in digital transformation (Javaid et al., 2023). As part of the D³ Project (Digitalisierung Didaktisch Denken) of the University of Applied Sciences Esslingen, which aims to integrate digitalisation into academic education, a digital twin for teaching bioprocess development and automation was developed. In the early 2000s, the digital twin concept was first applied in mechanical engineering (Herwig et al., 2021). However, digital twins are highly dependent on their specific application and level of fidelity, which leads to many definitions and archetypes of the term digital twin (Herwig et al., 2021; Udugama et al., 2021; Van Der Valk et al., 2022).

Operator Training Simulators (OTS) are considered early forms of digital twins, as they are virtual representations of physical systems with an interactive user interface. In the early to mid-1980s, OTSs were employed for the purpose of operator training in the chemical, nuclear and energy industries. In the late 1980s and early 1990s, the implementation of OTSs in the chemical industry evolved from pioneering work to common practice. Their primary purpose is operator training, whereas digital twins are also used for process design and plant performance optimization. Unlike OTS, digital twins are connected to the physical system via data transfer to closely reflect its real-time behaviour, while OTS are updated less frequently and are not necessarily linked to the actual system. Today, digital twins have become a ubiquitous phenomenon within industries characterised by high capital investment, complex operational processes and the potential for significant ramifications in the event of plant or operator failure. OTSs and digital twins are tools that can be used to train future reactor operators and bioprocess engineers in a hands-on manner, without having to carry out the real process. This avoids any disruption to the ongoing production process during training. Those are some of the reasons why the development and use of OTSs and digital twins begin to attract academia interest particularly for bioprocesses development (Herwig et al., 2021).

This article will address the following research questions:

- What are possible applications of OTSs and digital twins in higher education, particularly in the field of biotechnology?
- What learning objectives can be achieved with this tool?

For this purpose, a digital twin of a laboratory bioprocess for the production of biological products was developed. This digital twin enables the behaviour of the bioprocess, including the automation technology, to be described as realistically as possible. The practical application of teaching concepts and learning scenarios based on digital twins in biotechnology education is also demonstrated. The digital twin is characterised by its versatility in terms of deployment scenarios and expansion levels. A basic version of the digital twin is used as an OTS and is capable of simulating various upstream operation modes (e. g. batch, fed batch, chemostat). In addition, a more advanced version can reflect oxygen mass transfer and addresses the issue of automating those processes using sequential function charts (SFC). A third version comprises a fully-functional digital twin, which is connected to a lab-scale bioreactor via an Open Platform Communication (OPC) interface. The latter introduces the possibility of model predictive control, thus enabling participation in current research topics. The emphasis of this work is not only considering technical aspects but also reflecting the use and implementation from a didactic point of view.

2. State of the Art

This chapter examines the state of the art from both a technical and a didactic perspective.

2.1.Configuration of a digital twin / OTS

OTS and digital twins combine process models with a graphical user interface. Process models provide detailed mathematical descriptions of the underlying biological and physico-chemical phenomena and an accurate representation of automation and control actions. While the user interface allows operators to interact with the process. Ideally, the GUI has a similar "look and feel" to that of the plant being modelled. (Isimite et al., 2018).

Other Authors also highlight the advantageous of a GUI that corresponds to the process control system (PCS) on the physical counterpart (Herwig et al., 2021).

Mathematical models employed in the development of digital twins and OTSs are principally categorised as either mechanistic or empirical models. The term "model" is employed to denote a mathematical representation of real-world phenomena or entities (Pavé, 2012). Empirical models use experimental data to explain observed phenomena by fitting the parameters of a function that best describes the data. No attempt is made to account for the underlying biological or chemical phenomena that gave rise to the experimental data (e. g. regression models, neuronal networks) (Isimite et al., 2018). In contrast, mechanistic models are based on first principles and try to explain experimental observations in terms of the underlying biological, chemical and physical mechanisms that occur in the system (e. g. mass balance, energy balance) (Isimite et al., 2018). Mechanistic models can further be divided into structured / unstructured and segregated / unsegregated models. Details can be found elsewhere (Herwig et al., 2025).

2.2. Applications of digital twins and OTSs in the bioprocess industry

According to current research, innovative digital twins can depict biological, physico-chemical and chemical reaction kinetics and account for mechanical and physical properties of reactors and the peripherals. This makes digital twins an ideal tool for fast and cost-driven implementation and optimisation of control and automation strategies. Their use ranges from implementation of conventional controllers (e. g. temperature, dissolved oxygen, etc.) to advanced control strategies and model predictive control thus enabling the development of complete bioprocess control systems (Herwig et al., 2021).

Optimising controllers during production runs is usually extremely difficult, if not impossible, resulting in significant challenges for process engineers. The need for new tools that can overcome these obstacles is therefore enormous. Scenarios in which digital twins could be used for process development include determining the most appropriate controller types and improving controller and overall process performance through the implementation of appropriate control strategies and the automation of processes using sequential function charts (SFCs). An overview of already existing digital twins and OTSs for bioprocesses is given in (Herwig et al., 2021).

2.3. The impact of digital twins and OTSs on education.

Digital twins and OTSs implicitly support multiple learning theories through their capacity to create immersive, interactive environments that overcome traditional limitations of time, space, and resources. Digital twins enable constructivist knowledge building through integration of theoretical knowledge with practical experience. This approach creates opportunities for students to construct understanding through hands-on engagement with virtual models. Digital twins facilitate situated cognition by creating an environment that stimulates students' cognitive interest and encourages learning. In this setting, students can actively explore and absorb new knowledge (Li et al., 2025; Sepasgozar et al., 2024).

Digital twins have unique advantages in creating complex problem-solving situations for inquiry-based learning. The technology enabled students to virtually explore technical phenomena, posing questions and finding answers through digital experimentation. The academic performance of students can be significantly improved (Boltsi et al., 2024; Tao & Xie, 2025).

Digital twins expand traditional simulation learning by combining realistic, risk-free learning environments with real data. They enable the virtual examination of learning scenarios under conditions that would otherwise be inaccessible or dangerous (Ramos & Busboom, 2025; Sparr et al., 2023).

The fast-paced, ever-changing industrial world poses huge challenges for engineering education as it tries to keep up with the pace and continue to provide high quality, flexible and up-to-date learning. Educational process simulators have proven to be an important tool to assist instructors in the classroom and thus help students acquire the knowledge and skills needed in today's industrial world. This is especially true these days, where online courses or labs are an integral part of many curricula (Caño de las Heras et al., 2021a).

Therefore, the educational system and its methods should adapt in order to reflect the new trends and challenges faced by the industry today. To achieve this, the curriculum should be updated so that topics involved in the digitalization of the industry, such as model generation, validation, maintenance, and model-based decision making, have a greater weight (Caño de las Heras et al., 2021a). Digital twins and OTSs with their main application in education don’t need to be cutting edge in respect to fidelity or sophisticated process models. The emphasis should be on teaching the underlying conceptual ideas with a user-friendly design and a seamless integration into Learning Management Systems.

During development, students should be involved in the process as part of a user-centric design. Feedback from students can be gathered in various ways (System usability scale, Likert scale or even discussion groups) (Caño de las Heras et al., 2021a) . Some Authors suggest a systems engineering approach (Isimite et al., 2018). Digital platforms should not forget their educational aim and must be able to motivate and attract the students. In order to increase the pedagogical value and to avoid disengagement of students, some considerations should be made to address a proper learning design. The simulator or digital twin should provide open exploration and ideally enabling the creation of its content (Caño de las Heras et al., 2021a). The learning objectives of a successful simulator or digital twin should follow the revised Bloom’s Taxonomy by Krathwohl and Anderson. This is a two-dimensional framework for learning objectives that integrates a Cognitive Process Dimension (*Remember*, *Understand*, *Apply*, *Analyze*, *Evaluate*, *Create*) with a Knowledge Dimension (Caño de las Heras et al., 2021a; Krathwohl, 2002; Volk, 2020). From the author's point of view, it is desirable to link the learning objectives to the user requirements that are defined early in the conceptual phase.

Another point to consider is how to access transfer of training. The effectiveness of transfer of training has been a concern in a variety of OTS applications (Gerlach et al., 2014). Examples where it is crucial that the effects of virtual training are maintained in real-world scenarios include flight training simulators (Bell & and Waag, 1998; Lee, 2017) and virtual training for surgeons (Seymour et al., 2002). Ismite et al provided an overview of transfer of training methods commonly reported in the academic literature (Isimite et al., 2018).

3. Methods and Setup

A brief description of the setup and methodology used in this work is given in this chapter.

3.1.Configuration of the OTS and digital twin for the bioprocess

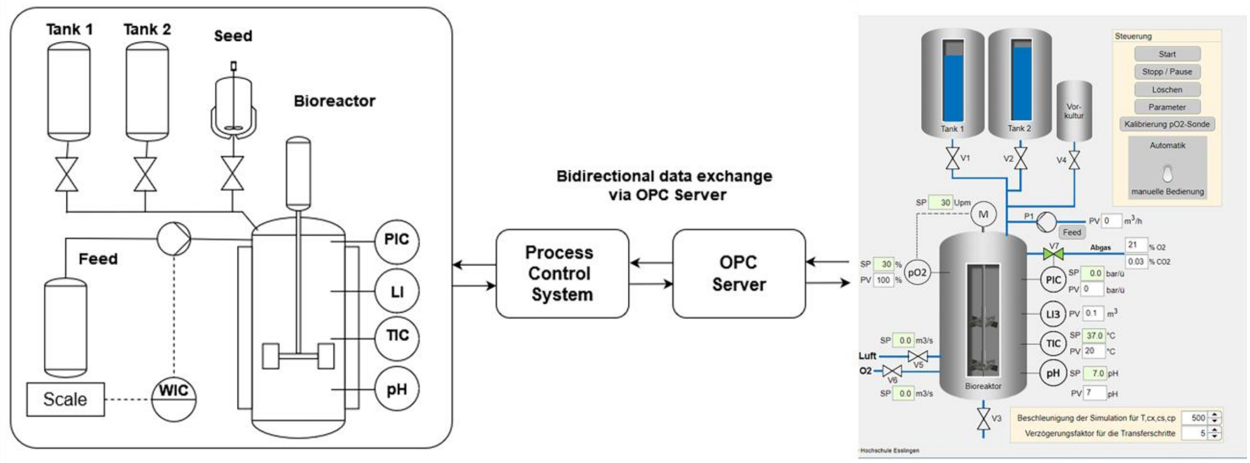

Figure 1: Architecture between digital twin, OPC server and process control system (PCS)

Digital twins and OTS are virtual representations of physical systems. A fully developed digital twin possesses the capability of bidirectional communication. The connection of the digital twin to the bioreactor (Multifors from Infors AG) via an OPC interface is shown schematically in Fig. 1. The digital twin can read various process parameters, including temperature, pH, stirrer speed, gas flow rate, optical density and concentrations of O_2 and CO_2 in the off-gas. In turn, it can adjust process set points or run forecast simulations to predict the behaviour of the process over the next few hours.

During the D^3 project, an OTS was initially developed. This OTS was then gradually transformed into a digital twin by implementing online communication to the real bioprocess via an OPC interface. For use in lecture and lab courses, the OTS was used as a simulation tool only, without the OPC connection to the bioreactor. The reasons for this are two major advantages that result from this setup:

- Better scalability (many students can access the simulation simultaneously).
- Experiments can be simulated much faster than the experiment would take in real time.

Escherichia coli is one of the most important expression systems for recombinant proteins currently in use. This study presents a digital twin /OTS based on a mathematical model describing the growth and product formation behaviour of *E. coli*. The model parameters are adjustable, allowing the user to adapt the model to other microorganisms, such as *Saccharomyces cerevisiae*. For mathematical modelling, an unstructured, unsegregated approach was chosen. Bioprocesses are highly complex and cannot be fully described mechanistically. In order to accurately represent all relevant metabolic pathways, regulatory mechanisms and transport phenomena, a structured mathematical model would be required. In segregated models, cell populations effects must be considered. It is difficult to achieve these aspects in practice without considerable effort and uncertainty. For typical digital twin applications such as monitoring, prediction and control, unstructured models are often more robust, easier to identify and more practical than detailed structured models. Therefore, an unstructured, unsegregated mathematical model is sufficient for a digital twin of bioprocesses. The model parameters were identified using experimental data collected from a number of experiments conducted in the laboratory bioreactor.

The main features of the mathematical model include:

- Specific growth is modelled using Monod kinetics with multiple substrates.
- The influence of temperature and pH on the growth rate is described.
- The model is able to describe overflow metabolism and the associated excretion of acetate.
- Growth inhibition due to the presence of acetate is accounted for in the model.
- The model describes the mass transfer of oxygen from the gas phase into the medium of the bioreactor (oxygen transfer rate).
- It also describes the consumption of oxygen by the cells, known as the oxygen uptake rate.
- Different types of product formation can be modelled, including the induction of gene expression.
- The model has the ability to simulate inhibitory effects caused by product formation.

3.2. Development environment

To avoid dependency on proprietary software the digital twin and the OTS were developed using Matlab App Designer from MathWorks. App Designer is a development environment in Matlab for the development of interactive applications and application layouts. It offers a fully integrated version of the Matlab editor and a comprehensive set of interactive user interface components. Matlab Apps can be compiled as Web Apps and made accessible via Browser. A Matlab Web App Server enables the hosting of Matlab apps and Simulink simulations as interactive web apps that were previously created with the Matlab App Designer. End users can access and run the web apps via a browser without having to install additional software. As part of the D³ project, the IT administration of the University of Applied Sciences Esslingen hosted a Matlab Web App Server. The workflow for developing and hosting Web Apps is shown in Fig. 2.

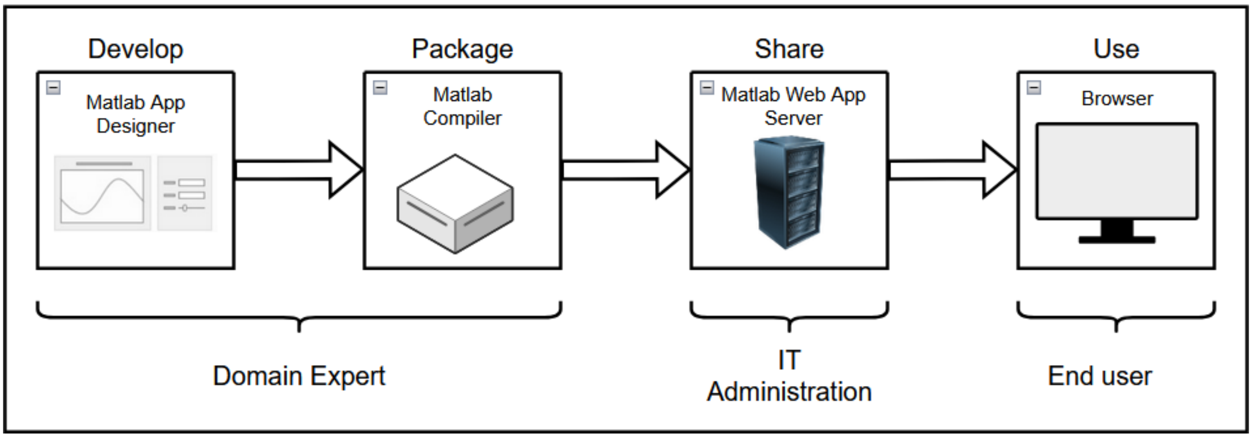

Figure 2: Workflow for providing Matlab Web Apps.

3.3. Didactic design

During the initial conceptual phase, the technical requirements and specifications were defined and the didactic design developed, broadly following the framework proposed by Arnold et al.(Arnold et al., 2018). The digital twin/OTS is integrated as an additional teaching tool in existing modules of the Bachelor's degree programme in Biotechnology to facilitate the acquisition of knowledge and skills by students. The learning objectives that could be effectively supported by the digital twin/OTS were then identified.

Two courses were selected for integrating the OTS into the curriculum: an introductory module (Biochemical Engineering including a lab) and an elective course (Bioprocess Control). During the initial conceptual phase, the module descriptions for both courses were updated in line with the revised Bloom's taxonomy.

The learning objectives were formulated as learning outcomes. Table 1 summarizes the added learning outcomes in module Biochemical Engineering. They target the cognitive process dimensions *remember, understand, apply* and *analyze*. The added learning outcomes for module Bioprocess Control are summarized in Table 2. Here the cognitive process dimensions are *understand, apply, analyze, evaluate* and *create*.

Table 1: Learning outcomes relating to the application of digital twins/OTS in the module "Biochemical Engineering"

Once the module has been successfully completed, the students are able to... • define the concept of a digital twin in the context of biotechnological systems. • perform simulations and analyze the impact of process parameters on microbial growth and product formation.

Table 2: Learning outcomes relating to the application of digital twins/OTS in the module "Bioprocess control"

Once the module has been successfully completed, the students are able to... • understand the concept and applications of digital twins in bioprocess supervision and control. • design and implement a sequential function chart for the automation of a bioprocess using the digital twin and assess its suitability. • check the results of the calculations for their applicability.

- transfer the methods learned and the knowledge acquired to new problems and assess them professionally.

The specified learning objectives and outcomes were then systematically linked to the technical requirements specifications that guided the digital twin's development. In parallel with the technical implementation, the design of the corresponding student assignments took place. Section 4.1 and 4.2 present and discuss the experience gained from applying OTS to the two modules.

3.4. Evaluation

The D³ project has a unique setup that provides a specialized team with background in empirical educational research, didactic, media- and information-technology. This team supports each subproject in updating curricula, carrying out evaluations, and addressing issues concerning didactics and teaching. A cross-project evaluation framework was developed by experts in empirical educational research to ensure a comprehensive assessment of both technical (validation-related) and didactic dimensions. The resulting concept defined seven principal evaluation categories. Based on this framework, each subproject derived its own project-specific evaluation approach. An overview of the main evaluation categories is presented in Table 3.

Given the small number of participating students, conducting statistically valid empirical analyses was not feasible. Therefore, a qualitative evaluation approach based on group discussions was chosen. This method was preferred over questionnaire-based surveys to obtain more in-depth insights into students' experiences and perspectives. In contrast, subprojects with larger participant cohorts employed a quantitative approach using questionnaires and Likert scales. Prior to the discussions, key guiding questions were developed based on the seven main evaluation categories. Complementing the student evaluations, expert interviews were conducted with three subject matter experts. Prior to the interviews, the experts completed the same assignments as the students to enable a direct comparison of perspectives and to assess the assignments technical and didactic adequacy.

During the project only the application of digital twins/OTS in the module "Bioprocess control" was evaluated. The results are discussed in section 4.4. Since the applications in module "Biochemical Engineering" were only recently implemented, it has not yet been possible to carry out an evaluation.

Table 3: Main categories for evaluation

Categories	Examples
Usability	• Intuitive design • Easy to use interface
Conception of teaching and learning units	• Comprehensible assignments • Timeframe for completing the assignments
Use of the digital teaching and learning unit.	• Promoting understanding of the topic • Integration into the course
Self-regulated learning	• Motivation to engage with the content
Research-based learning	• Acquire concrete practical knowledge • experience complex relationships
Learning progress and motivation	• Ability to apply knowledge in practice • Increased motivation to learn

Inclusion and exclusion effects	Have you or other groups of people (e.g. financially disadvantaged people, people with disabilities or people with family responsibilities) experienced any positive or negative effects from the use of the digital teaching and learning unit?

4. Results

In order to address the diverse skill levels of students, digital twins and OTSs with different functionalities have been developed. To minimise overhead and ensure maintainability and future development, a simple yet effective software architecture was developed. This chapter provides a comprehensive overview of the various implementations and use cases of the OTS and digital twin, accompanied by a discussion of the evaluation results.

4.1. Applications of the OTS in module “Biochemical Engineering”

As part of the D^3 project, an OTS-System was first developed. The OTS was deployed as a Matlab Web App and can be accessed via standard web browser. In order to access the web application, it is necessary to have a secure Virtual Private Network connection (VPN). This configuration is used in conjunction with a Moodle online test. Students have to pass the exam in order to participate in the biochemical engineering lab in the 4^{th} semester. The test comprises 15 questions randomly selected from a pool of questions. Two of these questions require students to conduct simulation studies using the OTS. These tasks involve analyzing the impact of overflow metabolism on growth kinetics (see Fig. 3) and calculating the space-time yield from process data of *E. coli* fed-batch cultivations. The underlying biological concepts—such as overflow metabolism—were introduced in lectures during the third semester, providing students with the necessary theoretical foundation before engaging with the simulations.

This test, combined with the embedded simulation of fed-batch cultivation, offers significant didactic advantages. Before performing the actual laboratory experiment—cultivating *E. coli* for recombinant protein production in a bioreactor—students can simulate the bioprocess in the OTS in a time-accelerated manner. While the real fed-batch cultivation in the lab takes approximately two days, the simulation completes the same process in just a few seconds. This enables students to deepen their understanding of the underlying biological principles, practice experimental procedures, and explore different operational strategies in a risk-free environment. In the subsequent laboratory, students carry out the corresponding experiment in a real bioprocess. This allows them to directly apply the knowledge acquired in the OTS simulation to the real process in the sense of a transfer of training. Consequently, the activity supports multiple learning outcomes as outlined in Table 1, addressing key cognitive dimensions *remember*, *understand*, *apply*, and *analyze*.

The following task must be completed using the OTS version of the digital twin.

Examination of overflow metabolism during a fed-batch cultivation of *E.coli*

When a critical specific growth rate μ_{crit} is exceeded, *E. coli* produces acetate as an undesirable by-product. Determine μ_{crit} for fed-batch cultivation of *E. coli*. You can assume that μ_{crit} is in the range between 0.3 and 0.4 h^{-1}.

Procedure:

- Open the OTS version of the digital twin.
- Select "exponential feed" from the feed menu (drop-down).
- In the Feed menu, set a value between 0.3 and 0.4 1/h for the specific growth rate.
- In the Parameter menu, set the values for $Y_{X/S2}$ to 20.
- Make sure that the values for alpha = 0 and beta = 0 are set in the Parameter menu!
- Press the Start button.
- Fill the bioreactor with medium 1 and 2.
- Start the stirrer and the pO_2, pH, and temperature control.
- Wait until the temperature has reached the setpoint of 37°C.
- Calibrate the pO_2 probe.
- Start inoculation by opening valve 4.
- After the end of the batch phase (glucose limitation), start feeding (activate pump).

Observe whether acetate is formed during the fed-batch phase. After the end of the fed-batch phase, press the reset button.
Determine by trial and error the value for μ at which overflow metabolism is activated.

Figure 3: One of the tasks in the biochemical engineering lab entrance test, which must be solved using the OTS.

Since the applications in module "Biochemical Engineering" were only recently implemented, it has not yet been possible to carry out an evaluation. However, our initial experiences in test operations show that students find it easier to deal with the real bioprocess if the process has been simulated beforehand, which is an indication of a successful transfer of training.

Figure 4 shows the user interface of the OTS including the simulation results for the fed-batch cultivation of *E. coli*.

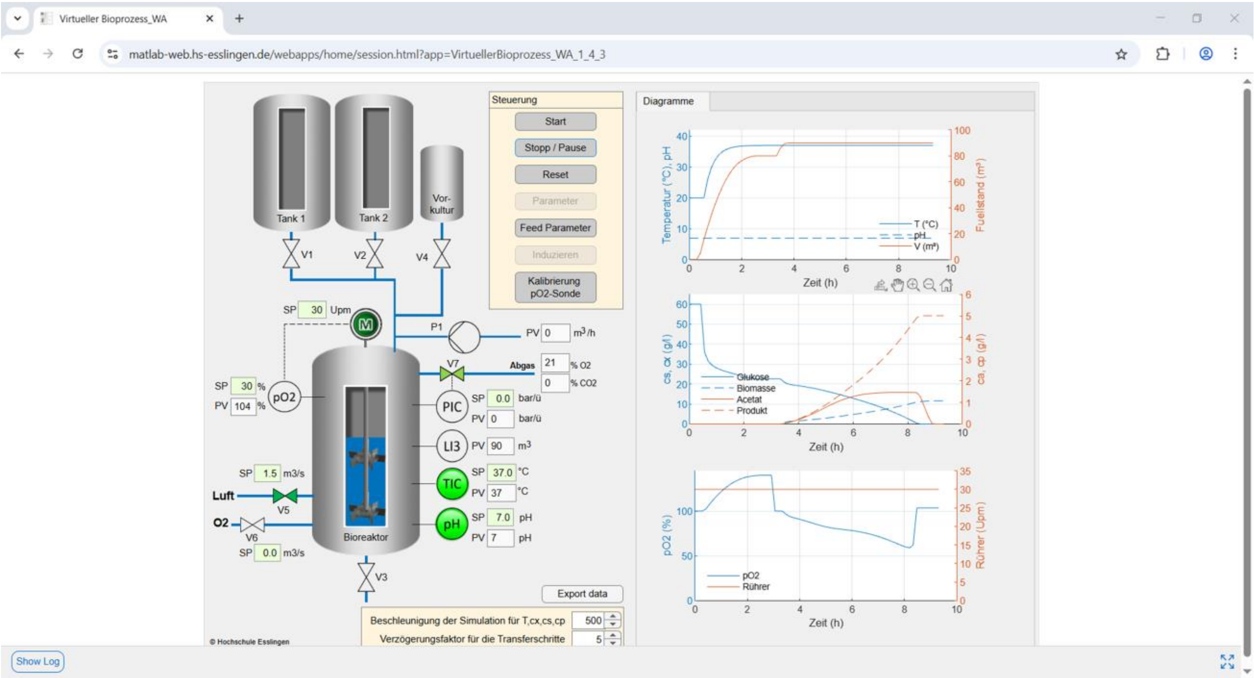

Figure 4: GUI of OTS (Web App). Data showing a cultivation with E.coli that produces acetate as overflow metabolite.

4.2. Applications of the OTS in module “Bioprocess Control”

For the elective course, a standalone OTS application has been developed where students can explore the effects on transport processes, e. g. dissolved oxygen transfer, and likewise automate recipes via sequential function charts using an interface inspired by GRAFCET (Graphe Fonctionnel de Commande Étape/Transition) (*DIN EN 60848*, 2013). GRAFCET is a graphical representation used to design and understand sequential control systems. It is essentially a type of flowchart used to model the behaviour of automation systems, particularly in industrial environments. GRAFCET diagrams consist of steps, transitions and actions that illustrate how a system moves from one state to another based on certain conditions. An example application is the creation of a recipe to automate a bioprocess using sequential function charts (see Fig. 5 and 6). In the elective course "Bioprocess Control" we use the OTS to program sequential function charts. This course takes place during the 6th semester.

As part of their coursework, students must complete a virtual internship with the OTS. A summary of the tasks that must be completed for the assignment is listed here. These tasks target several cognitive processes (*understand, apply, analyze, evaluate* and *create*).

1. Formulate the mass balance equations for the bioreactor. (*Comment: During the 3rd semester the students learnt the principles of mass balancing. The students transfer this knowledge to the bioprocess in the assignment.*)
2. Simulation of basic procedures in the OTS such as filling the bioreactor with the two media tanks and discuss the time courses of glucose concentration. (*Comment: This task is important to familiarize with the features of the OTS.*)
3. Design a recipe for a batch cultivation of *E.coli* in a bioreactor. The initial conditions and objectives of the batch cultivation are specified in the task description. (*Comment: The students learnt during the biochemical engineering lab in the 4th semester how typical recipes look like. They have to transfer this knowledge to the virtual bioprocess in the OTS*).

4. Create and implement a sequential function chart for the recipe and test and analyze the step chain. (*Comment*: *Students must use the OTS-simulation to check whether the specifications from the task have been fulfilled and, if necessary, improve the recipe or the sequential function chart. Accelerating the execution of the process in the OTS allows for quick analysis of the results and enables the execution of several recipe variants in a short time.*)

In order to utilise the OTS for a range of scenarios, it is possible to adjust a variety of model parameters. These include the size of the tank, specific growth rates, decay rates, yields, and different types of feeding strategies. This provides an opportunity for the modelling of diverse expression systems, including *E. coli* and *S. cerevisiae* (baker's yeast). Fig. 7 gives an overview of the modelled process parameters that can be adjusted.

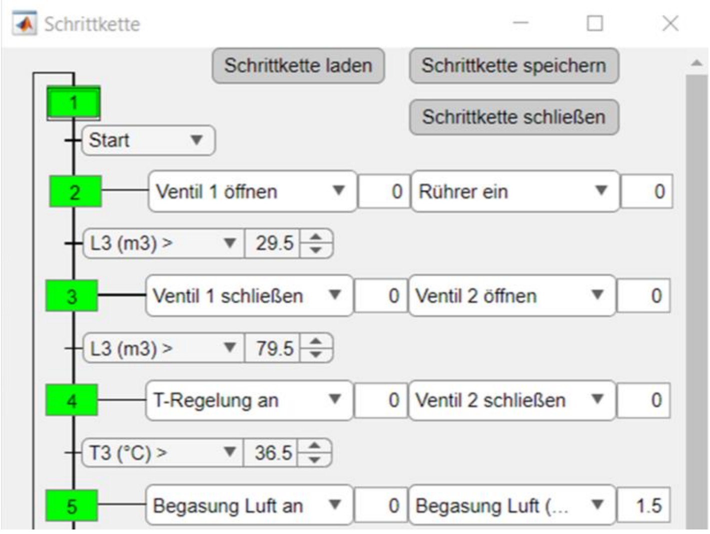

Figure 6: Structure of the GRAFCET inspired sequential function chart

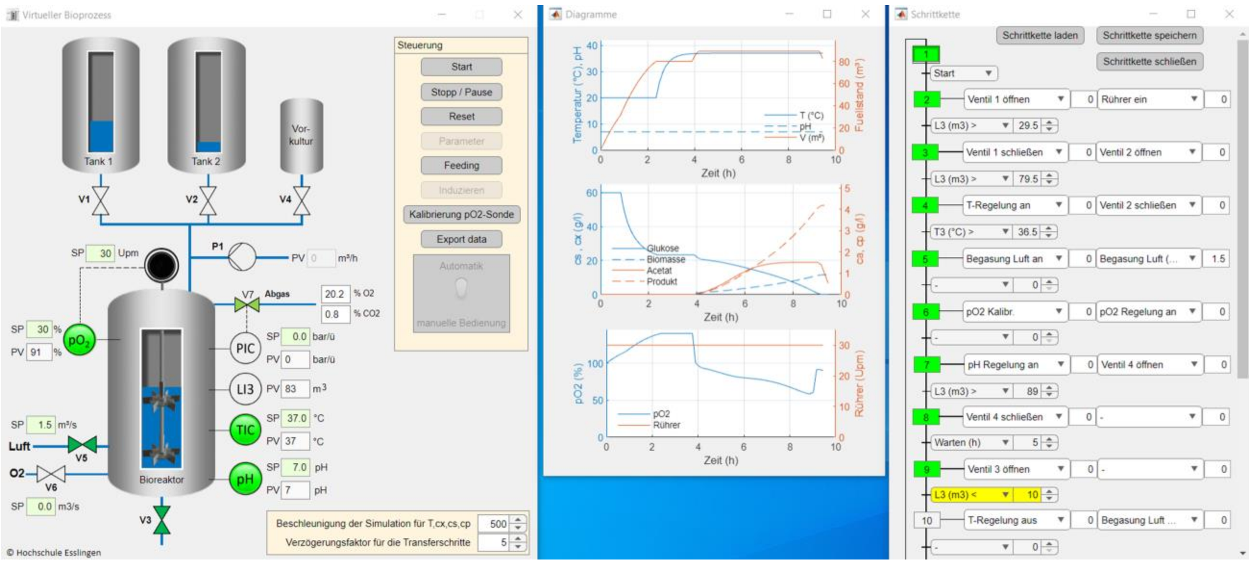

Figure 5: Process automation with sequential function charts

Figure 7: Overview of adjustable model parameters

4.3. Possible real-time applications of the digital twin in education

As illustrated in Fig. 1, the digital twin is connected to a bioreactor (Multifors from Infors HT) via an OPC DA interface. The digital twin has the capability of continuously collecting and processing data from the bioreactor, enabling the simulation to be adapted to the real process data. The following parameters can be collected from the bioreactor during the process: temperature, pH, stirrer speed, gas flow rate, optical density, and concentrations of oxygen (O_2) and carbon dioxide (CO_2) in the off-gas. The digital twin facilitates the adjustment of setpoints, including parameters such as temperature, feed rate, and stirrer speed. This adapted digital twin allows forecast simulations at any time during cultivation. This makes it possible, for example, to determine what effects a change in temperature or feed rate would have on the course of the process. This forecast simulation forms the basis for decisions in the real process, which can lead to optimal behaviour and an optimized product yield. This configuration also facilitates the implementation of model predictive control. Figure 8 shows the GUI of the online application of the digital twin.

From a didactic point of view, this online application is intended for students writing their bachelor's theses or carrying out projects. As previously stated, this configuration is deficient in terms of scalability, meaning that the number of students using this application cannot be increased. The physical bioreactor, which functions as a restrictive component, enables the digital twin to accommodate only one group at a time. A further disadvantage is that the actual bioprocesses are time-consuming, with experiments often taking several days. These challenges have led to the use of the digital twin in an OTS-like way as described in the previous two sub sections.

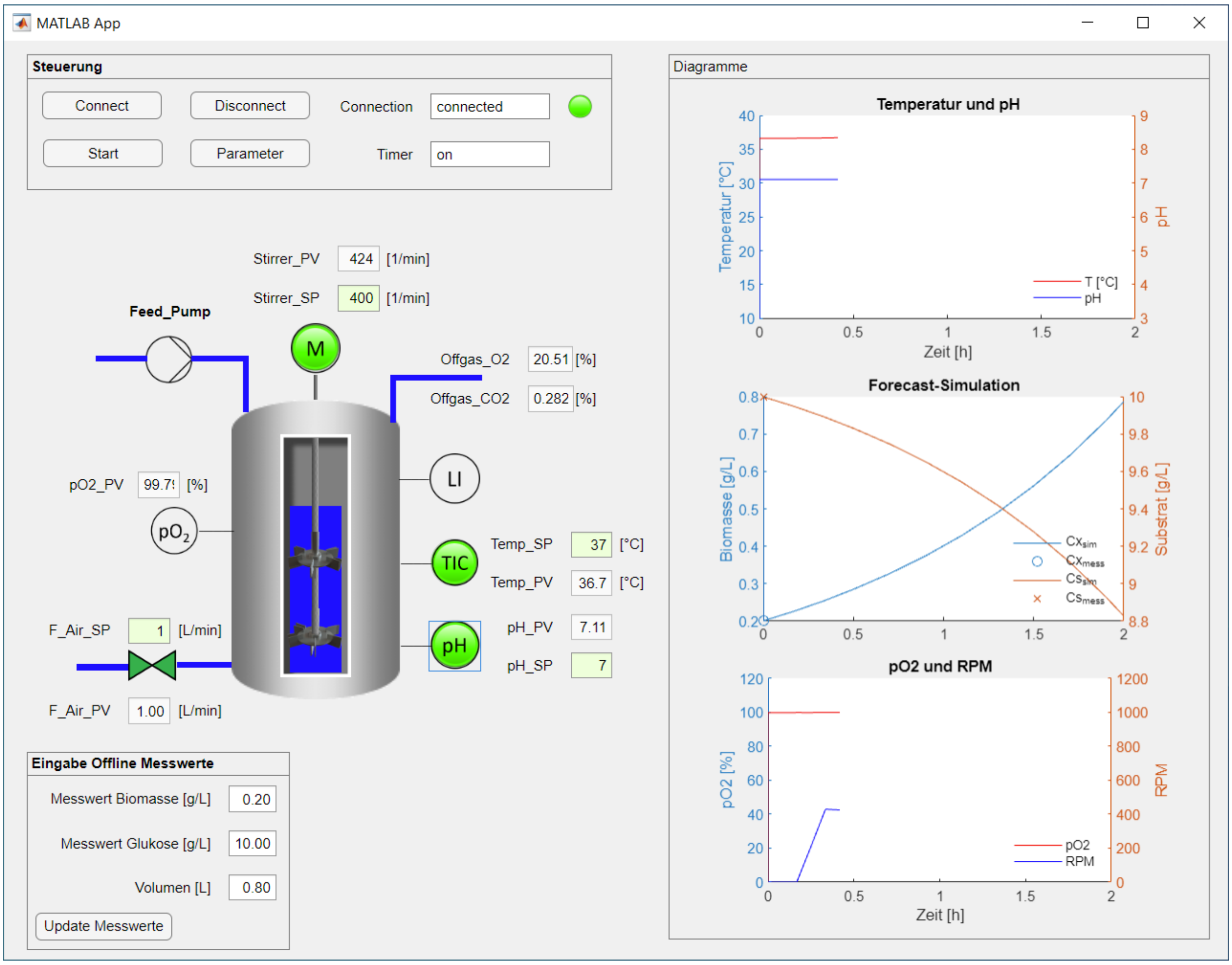

Figure 8: GUI of the online application of the digital twin

4.4. Evaluation of the application of OTS in the module "Bioprocess control"

Two evaluations were carried out during the development phase of the OTS for the application in the elective module "Bioprocess Control". The first evaluation took place at an early stage of the project. As part of the course, students completed the virtual lab using a prototype of the OTS and then evaluated it. This allowed students to be involved in the development of the OTS and provide valuable suggestions for improvement, which were then implemented.

As only five students participated in the elective course, it was not possible to conduct statistically valid empirical analyses. Therefore, a qualitative evaluation approach based on group discussions was chosen.

To ensure outcome-oriented discussions, the sessions were led by a moderator. The discussions were audio-recorded, transcribed, and subsequently analyzed and structured. To derive actionable recommendations, direct quotations were grouped and paraphrased concisely. Table 4 summarizes the findings from one of the evaluations conducted in the elective course. Due to the small number of students, three subject matter experts were also interviewed in addition to the student evaluations. The interviews with these experts were conducted bilaterally without recording, only written notes were taken.

Findings from the evaluations and expert interviews resulted in improvements to usability of the OTS/digital twin and the resolution of performance issues on older computer devices. Furthermore, the design and contents of the student assignments were optimized. Overall, the students gave very positive ratings to the OTS/digital twin and its applications in teaching. Some participants reported that they found the assignment too easy. In the original assignment, the recipe was specified in the task description and only had to be programmed as a sequential function chart. The assignment was then adapted so that students had to design their own recipe as described in section 4.2. Initial results from the current course show that students are able to successfully handle this expansion. Further evaluations are required here.

The evaluation results and our experience in this module show that all of the specified learning objectives could be achieved through the virtual internship setup.

Table 4: Evaluation results

Category	**Subcategory**	**Feedback**
Usability		
	Clear layout of the graphical user interface	The digital twin was well received by the students, and its intuitive and clear usability was highlighted several times. In addition, the digital twin is perceived as very clear and easy to understand.
	Technical implementation	It was requested that the windows adapt to the screen and that the size be adjustable.
		Several students were unable to close a certain window.
		It was requested that a reset only affect the bioreactor and the diagrams, but not the model parameters.
Conception and use		
	Assignment	The task was considered to be very easy to understand.
		The difficulty of the tasks was rated as (too) easy.
		The students estimated that it would take them between two and six hours to complete the assignments, and they considered the workload to be reasonable. They also rated the given timeframe of the assignment positively.
		The students suggested ways to expand the scope of the assignment. (Expand to fed batch operation mode)
		Students see parts of the assignment as an opportunity to review the basics of bioprocess technology, but do not recognize any significant learning effect for themselves. They attribute this to the fact that the tasks are low in difficulty and therefore do not challenge them. One person recognized a learning effect using the sequential function flowchart. Some saw the potential for the digital twin to support the learning process in more difficult tasks, for example, by using it to test assumptions.
Research-based learning		

	Practical relevance to the profession	The students were able to recognize some practical relevance, but had difficulty identifying any concrete added value for their future professional activities.
		The use of digital twins as an innovative and varied method was recognised, and online access was also appreciated.
Learning progress and motivation		
	Joy	The students enjoyed working with the digital twin. They found it to be a welcome change, but not an incentive to explore the further features of the digital twin.
	Increase in motivation	Students may be more motivated by a more complex design of the tasks
Inclusion and exclusion effects		
		The students liked the fact that they could work on assignments remotely.
		The use of the digital twin could disadvantage people who cannot afford a laptop.
		Digital twins cannot replace practical lab courses.
Conclusion		
		Easy to use, fun, effective, clear instructions
		A good addition to the elective course
		Potential to increase level of difficulty

5. Conclusion and Outlook

Digital twins and OTSs offer great didactic potential as a supplement to regular classes and labs. The case study shows the implementation of digital twins and OTSs as learning tools, which can be used in different skill levels and classes. A huge benefit using a digital twin or OTS in bioprocess development is the fact that experiments can be simulated much faster than the experiment would take in real time. Thus, allowing plenty of different virtual experiments in a short time. From a didactic point of view, digital twins / OTSs have numerous advantages. Students can be introduced to complex issues in a vivid manner, encourage them to learn in a playful way, giving them the opportunity to experience a modern way of bioprocess development and optimization. Using a digital twin or OTS also reduces the fear of making errors or wrong decisions. Students can freely perform virtual experiments with different parameters and configurations, ultimately leading to a more confident operation of real processes.

Digital twins and OTSs are powerful teaching tools in biotechnology education, because they can help students develop the skills at all levels of Bloom's revised taxonomy. They can especially help students develop higher-order cognitive skills, which are difficult to develop through lecture-based instruction. These interactive simulation environments not only support the acquisition of foundational knowledge but also actively promote analytical thinking, critical evaluation, and creative problem-solving. By enabling students to safely explore and analyze complex bioprocesses iteratively, digital twins / OTSs facilitate applying theoretical concepts to real-world scenarios. This strengthens learning transfer and prepares students for the demands of modern biotechnological practice.

Recent developments in the field of training simulator design have been marked by a noticeable trend towards the integration of virtual reality technologies in the design of simulators intended for both control room and field operators (Isimite et al., 2018). It is evident that traditional 2D simulators are predominantly used for training control room operators. These simulators are equipped with basic remote communication protocols to facilitate interaction between control room and field operators. 3D emulation of key processing elements in the field can be used to provide virtual reality training for both control room and field operators. Examples of such 3D virtual reality simulators have been reported by several authors (Isimite et al., 2018).

Bibliography

Arnold, P., Kilian, L., Thillosen, A., & Zimmer, G. M. (2018). *Handbuch E-Learning: Lehren und Lernen mit digitalen Medien* (5. Aufl.). utb GmbH. https://doi.org/10.36198/9783838549651

Bell, H. H., & and Waag, W. L. (1998). Evaluating the Effectiveness of Flight Simulators for Training Combat Skills: A Review. *The International Journal of Aviation Psychology*, *8*(3), 223–242. https://doi.org/10.1207/s15327108ijap0803_4

Boltsi, A., Kalovrektis, K., Xenakis, A., Chatzimisios, P., & Chaikalis, C. (2024). Digital Tools, Technologies, and Learning Methodologies for Education 4.0 Frameworks: A STEM Oriented Survey. *IEEE Access*, *12*, 12883–12901. https://doi.org/10.1109/ACCESS.2024.3355282

Caño de las Heras, S., Gargalo, C. L., Weitze, C. L., Mansouri, S. S., Gernaey, K. V., & Krühne, U. (2021a). A framework for the development of Pedagogical Process Simulators (P2Si) using explanatory models and gamification. *Computers & Chemical Engineering*, *151*, 107350. https://doi.org/10.1016/j.compchemeng.2021.107350

DIN EN 60848:2014-12, GRAFCET, Spezifikationssprache für Funktionspläne der Ablaufsteuerung (IEC_60848:2013); Deutsche Fassung EN_60848:2013. (2013). DIN Media GmbH. https://doi.org/10.31030/2248266

Gerlach, I., Brüning, S., Gustavsson, R., Mandenius, C.-F., & Hass, V. C. (2014). Operator training in recombinant protein production using a structured simulator model. *Journal of Biotechnology*, *177*, 53–59. https://doi.org/10.1016/j.jbiotec.2014.02.022

Herwig, C., Pörtner, R., & Möller, J. (Hrsg.). (2021). *Digital Twins: Applications to the Design and Optimization of Bioprocesses* (Bd. 177). Springer International Publishing. https://doi.org/10.1007/978-3-030-71656-1

Herwig, C., Pörtner, R., & Möller, J. (Hrsg.). (2025). *Digitale Zwillinge: Werkzeuge und Konzepte für intelligente Bioproduktion*. Springer Nature Switzerland. https://doi.org/10.1007/978-3-031-75698-6

Isimite, J., Baganz, F., & Hass, V. C. (2018). Operator training simulators for biorefineries: Current position and future directions. *Journal of Chemical Technology & Biotechnology*, *93*(6), 1529–1541. https://doi.org/10.1002/jctb.5583

Javaid, M., Haleem, A., & Suman, R. (2023). Digital Twin applications toward Industry 4.0: A Review. *Cognitive Robotics*, *3*, 71–92. https://doi.org/10.1016/j.cogr.2023.04.003

Krathwohl, D. R. (2002). A Revision of Bloom's Taxonomy: An Overview. *Theory Into Practice*, *41*(4), 212–218. https://doi.org/10.1207/s15430421tip4104_2

Lee, A. T. (2017). *Flight Simulation: Virtual Environments in Aviation*. Routledge. https://doi.org/10.4324/9781315255217

Li, P., Zhang, X., Hu, X., Xu, B., & Zhang, J. (2025). Theoretical model and practical analysis of immersive industrial design education based on virtual reality technology. *International Journal of Technology and Design Education*, *35*(4), 1543–1570. https://doi.org/10.1007/s10798-024-09946-x

Pavé, A. (2012). *Modeling of Living Systems: From Cell to Ecosystem*. John Wiley & Sons.

Ramos, M. P., & Busboom, A. (2025). Integration of Digital Twins with Reinforcement Learning in Industry: A Systematic Review. *2025 IEEE 30th International Conference on Emerging Technologies and Factory Automation (ETFA)*, 1–8. https://doi.org/10.1109/ETFA65518.2025.11205657

Sepasgozar, S. M. E., Khan, A. A., Shirowzhan, S., Romero, J. S. G., Pettit, C., Zhang, C., Oh, J., & Liang, R. (2024). Immersive virtual environments and digital twin applications for education and training: Trends in construction, mining, and urban planning studies. In *Digital Twin Adoption and BIM-GIS Implementation*. Routledge.

Seymour, N. E., Gallagher, A. G., Roman, S. A., O'Brien, M. K., Bansal, V. K., Andersen, D. K., Satava, R. M., Pellegrini, C. A., Sachdeva, A. K., Meakins, J. L., & Blumgart, L. H. (2002). Virtual reality training improves operating room performance results of a randomized, double-blinded study. *Annals of Surgery*, *236*(4), 458–464. Scopus. https://doi.org/10.1097/00000658-200210000-00008

Sparr, K., Steurer, P., Drexel, D., & Hoch, R. (2023). *Using Digital Twins in Learning Factories for Simulation and Optimization* (SSRN Scholarly Paper No. 4469194). Social Science Research Network. https://doi.org/10.2139/ssrn.4469194

Tao, Y., & Xie, A. (2025). Research on the architecture and practice of inquiry learning model integrated with digital twin. *Interactive Learning Environments*, *33*(8), 4976–4989. https://doi.org/10.1080/10494820.2025.2476716

Udugama, I. A., Lopez, P. C., Gargalo, C. L., Li, X., Bayer, C., & Gernaey, K. V. (2021). Digital Twin in biomanufacturing: Challenges and opportunities towards its implementation. *Systems Microbiology and Biomanufacturing*, *1*(3), 257–274. https://doi.org/10.1007/s43393-021-00024-0

Van Der Valk, H., Haße, H., Möller, F., & Otto, B. (2022). Archetypes of Digital Twins. *Business & Information Systems Engineering*, *64*(3), 375–391. https://doi.org/10.1007/s12599-021-00727-7

Volk, B. (2020). Ordnung von Lernzielen – Ordnung des Wissens. Die Bedeutung der Taxonomie von Bloom für die Wissenschaftlichkeit und Praxis der Hochschuldidaktik. In P. Tremp & B. Eugster (Hrsg.), *Klassiker der Hochschuldidaktik? Kartografie einer Landschaft* (S. 219–233). Springer Fachmedien. https://doi.org/10.1007/978-3-658-28124-3_13

Wollersheim, H.-W., Karapanos, M., & Pengel, N. (Hrsg.). (2021). *Bildung in der digitalen Transformation*. Waxmann Verlag GmbH. https://doi.org/10.31244/9783830994565

JOHANNES HOFMANN
Hochschule Esslingen, Fakultät Angewandte Naturwissenschaften, Energie- und Gebäudetechnik
Kanalstraße 33, 73728 Esslingen
Johannes.Hofmann@hs-esslingen.de

Hannah Korn
Hochschule Esslingen, Fakultät Soziale Arbeit, Bildung und Pflege
Kanalstraße 33, 73728 Esslingen
Hannah.Korn@hs-esslingen.de

Clara Wankmüller
Hochschule Esslingen, Fakultät Soziale Arbeit, Bildung und Pflege
Kanalstraße 33, 73728 Esslingen
Clara.Wankmüller@hs-esslingen.de

PROF. DR. RICHARD BIENER
Hochschule Esslingen, Fakultät Angewandte Naturwissenschaften, Energie- und Gebäudetechnik, Bioverfahrenstechnik und Technische Mikrobiologie
Kanalstraße 33, 73728 Esslingen
Richard.Biener@hs-esslingen.de

Zitieren dieses Beitrags:

Hofmann et al. (2026). Bioprocess Digital Twin as Training and Educational Tool. Journal of Technical Education (JOTED), 14(1), 27–44.