

PRODUCTION SIMULATION: MOVING TOWARDS A ROBUST PRODUCTION PROCESS

As we strive towards an efficient and robust production process, questions regarding achievable production capacity, utilization of equipment, and possible optimization arise. These questions can be answered by taking a holistic approach towards the entire production process. The creation of batch plans, the identification of bottlenecks, as well as the analysis of media consumption and equipment occupancy are made possible by using INOSIM software. ZETA integrates production simulations into the engineering process, providing significant added value for both the design and engineering of planned processes as well as the analysis and optimization of existing process plants.

Simulating the production process

A production simulation is an event-driven material flow simulation. This means that material flows, mass balances, resource utilization, capacities, and timing sequences in the production facility operations are depicted in the simulation. It is important to make appropriate assumptions and work on specific questions.

Application areas for production simulations

During **process planning**, production simulations are a tool to clarify questions concerning equipment occupancy, setup times, shift schedules and media consumption over time, as well as to determine theoretical process capacities. In the context of **plant development**, simulation supports the dimensioning of process equipment and pipelines.

ZETA experts use the INOSIM software in all phases of the project. The software acts as both a valuable engineering tool and a comprehensive tool for production planning. A virtual image of the production processes – a digital twin – is created throughout the project from initial estimates to minute-by-minute resolution of production. Thus, warehouse capacities, personnel requirements, and possible shift schedules are known long before commissioning. In addition, a virtual operation of production highlights any automation challenges at an early stage, paving the way for efficient production planning.

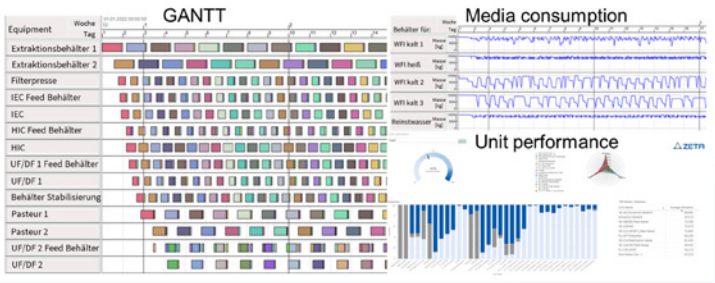

Figure 1: The simulation links process recipes and equipment, and provides a time-resolved picture of production in the form of an equipment utilization plan (Gantt chart) and diagrams showing the temporal consumption of media. Interpreted by experts, these results are valuable when making fact-based decisions.

"Even a small number of components which are all simple in themselves, can result in complex system behavior when combined," explains Roland Maichin, Corporate Head of Project Development at ZETA. Maichin emphasizes the advantages that simulation offers in engineering, stating that "An intuitive assessment of potentials, bottlenecks, and the capacities you need in terms of auxiliary

materials and resources is not possible without a high degree of uncertainty. Process simulation offers the possibility to develop in a more targeted way and to identify future challenges in operation at an early stage of system planning."

Furthermore, production simulations are used to optimize the operation of existing plants with a variety of objectives, such as boosting productivity, improving robustness and increasing capacity utilization. To this end, the actual state of production is first mapped, whereby relevant influencing variables remain parameterizable to ensure flexibility. With the help of various empirical, mathematical and stochastic methods, production behavior can then be tested and evaluated in different scenarios. This makes it possible to identify the best operating modes for the operator.

Common scenarios include start-up scenarios, shut-down scenarios, product changes, or failed buffer preparations. Favorable time windows for maintenance are always of great interest. Personnel planning also plays a central role, with the key question being how much personnel are available for specific tasks.

Modular simulation setup

The simulation architecture is built in layers, in the core of which lies the main process (see figure 2). Theoretical process capacity derives from simulating this core process – independent of any equipment limitations of the plant – and critical process steps are identified. For each layer, questions relating to feasibility, capacities, batch sizes, robustness and flexibility for adaptations and any optimization can be clarified. Given that all these questions can also be answered regarding product changes is not least an advantage for the operators of multipurpose systems.

ZETA Best Practice: The customer benefits from the use of INOSIM software

ZETA has successfully implemented a number of simulation projects, some of which are currently underway or in planning. A key advantage of production simulations is that they provide an in-depth understanding of the system. The added value that is subsequently created for the customer often manifests itself in significant operating and investment cost savings, as the following best-practice examples illustrate.

A CAPEX reduction of over four million euros was achieved in a greenfield project in Hungary. The focus here lay on the existing concept design for a multi-product plant for vaccine production. The aim was to review the existing concept and, if necessary, adjust the number and the size of the equipment required to achieve the specified production capacity. Capacity limits were determined, and the production routine was optimized. The ZETA team's approach was to map the production of all the contract manufacturer's 25 products, and to consider scenarios for equipment failures. The challenge here was the variability of the production sequence. The results of the analyses showed that the required capacity could be achieved with less equipment than originally assumed. A simplified production strategy meant that two containers and a CIP skid could be omitted, all without changing the main processes.

A simulation project involving the integration of a new production line into the site of a blood plasma processing company resulted in savings of more than five million euros. ZETA provided the concept design and carried out simulation studies. In the brownfield environment, the available space for the plant was limited and existing media systems had to be utilized in the most efficient way. Regarding a particular WFI tank, the question arose as to whether its capacity was sufficient to supply the new line. A bottleneck analysis was carried out, and then ZETA developed and optimized the concepts for the provision of buffers, WFI supply and cleaning (CIP). Thanks to ZETA's integrated planning approach, it was possible to design the new production line despite spatial limitations. Specifically, a buffer tank, a CIP skid and a WFI tank were dispensed within this project. The customer also benefited from the development of a strategy to simplify the handling of buffer solutions. Again, the main process remained unchanged.

The following impressive, best-practice example describes a simulation that started during the commissioning of a system for fractionating blood plasma. It became apparent that a skid could not utilize its predicted capacity because of bottlenecks

caused by split transfer lines used for certain media. At first glance, the solution consisted of an extensive mechanical expansion of the transfer systems – with numerous pipelines and valves required for this, changes to the automation system, loss of production due to a longer shutdown, and qualification steps to be carried out again. With the help of a simulation model of this system, the ZETA team discovered that there was a much simpler solution to achieve the production target. ZETA's experts were able to develop production scenarios that required only minimal changes: a single additional transfer line and a few adaptations to the software and the production processes saved the plant operator over ten million euros.

These successful projects that ZETA carried out in close cooperation with the respective customers clearly demonstrate that integrating production simulations into engineering processes can fulfill customer requirements to their greatest satisfaction. The greater the complexity in the operation of the respective plants, the more customers benefit from this technology, as essential questions about the operation of the plant are clarified in advance and the desire for a robust process is met in the best possible way.

Load-based engineering – shaping a sustainable future

ZETA is valued for its holistic approach and its comprehensive view of production systems and their infrastructure. The company places particular emphasis on cleanroom and building technology. A dedicated business line supports customers in achieving their decarbonization and sustainability goals. Here, the potential of production simulation has long been recognized. Hans Eder, Associate Director of the ZETA Sustainable Energy Solutions business line, illustrates his vision with an example: "Ventilation systems for cleanrooms are usually greatly oversized in relation to the actual particle load. This naturally leads to high energy consumption. However, how many particle emissions there actually are, depends largely on the number of people present in the cleanroom. Production simulations are used to show how many people are required for each process step in the

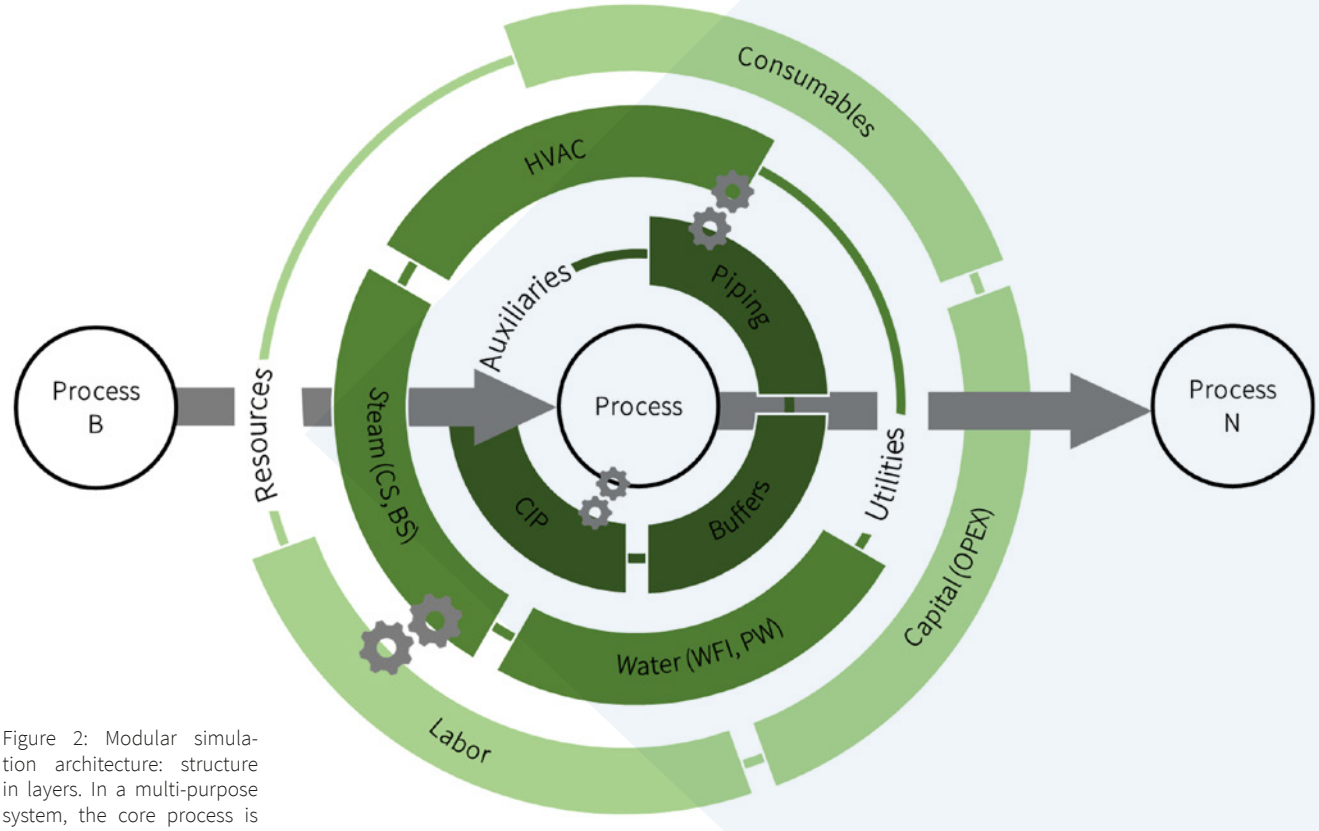

Figure 2: Modular simulation architecture: structure in layers. In a multi-purpose system, the core process is changed.

cleanroom. Depending on the number of staff, the ventilation system can be regulated downwards without exceeding the critical particle count in the cleanroom." Hans Eder sees a further possibility for saving energy in the heating and cooling processes: "Here, simulations could be used to determine the actual demand and possibly reduce it by adapting the production processes."

Online production monitoring

A promising future topic is real-time production monitoring, in which simulations run continuously in the background while a plant is in operation and decisions can be made based on predictive production data. All data from the IT/OT systems must be integrated so that the simulation software INOSIM Foresight can access it: real-time production data, data from the respective batch systems and from the process control systems, or EMS data. This poses challenges in the field of automation technology that can only be overcome with cross-disciplinary expertise.

At ZETA, the close interlocking and integration of process technology, engineering, digitalization, and automation is lived practice. Together with its subsidiary SIGMA Process & Automation GmbH, ZETA has set itself the goal of developing the potential of production simulation and driving it towards online production monitoring.

Clear added value through production simulation

Whether production simulations are used for plant development, process planning, optimization, or production planning, the advantages are always clear: complex systems can be understood much better and different scenarios can be examined in a virtual environment. This allows fact-based decisions to be made and risks to be reduced. Design accuracy is also improved. These advantages result in significant cost savings.In the basic design phase, the process is defined and established further. Changes in the early engineering phases are possible, either by value engineering or as process adaptations or optimizations. In the detail design phase, the point has come when facility design changes are becoming expensive and time critical. It must be kept in mind that every major change in the later engineering phases will have an influence on the course of the project.

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ABOUT ZETA

The ZETA Group, with 1.400 highly qualified employees and 28 subsidiaries worldwide, specializes in the design, manufacturing, automation, digitalization and qualification of customized biopharmaceutical facilities for aseptic process solutions. ZETA acts as a one-stop shop, combining plant engineering with HVAC, cleanroom and BMS/EMS design.

Biopharmaceutical active ingredients, such as anti-cancer drugs, insulin, vaccines and infusions are produced in these highly complex, "tailor-made" facilities. ZETA supports its customers along the entire drug development and manufacturing pathway with sophisticated solutions from laboratory to industrial production scale. Through its Smart Engineering Services, ZETA creates digital twins of process plants and has thus established itself as a market leader for digital solutions in the pharmaceutical and biotech industry.