AUTOMATION OF PRODUCTION PLANNING ENHANCED BY AI

THE NEXT LEVEL FOR PHARMA COMPANIES

01 Introduction

Due to the relative abundance of data and increasing processing power, the decrease in costs for artificial intelligence (AI) is rendering the introduction of AI to areas of complex algorithmic problem-solving feasible and economically viable. This paper proposes a practical approach to enhancing existent, advanced production planning applications in the pharmaceutical industry and demonstrates how the "AI journey" can safely be embarked upon in critical business processes, such as pharmaceutical production.

Specifics of planning pharmaceutical production generate a viable use case for AI

Taking the path to continuous improvement is easier said than done. Manufacturers face increasing variability coupled with increased product and supply-chain complexity.

Figure 1 shows the number of new, active pharmaceutical ingredients in the pharmaceutical industry and indicates the increasing complexity. Drivers for this evolution are, for example, faster development cycles due to the application of big data analysis and machine learning, novel technologies like cell and gene therapy, and the increasing importance of personalized medicine [1].

In 2005 personalized medicine contributed only 5 percent to all FDA approvals, while this share increased to 27 percent in 2016 (statista.com). Consequently, almost all of the top 50 pharma companies have increased their number of stock keeping units (SKUs) since 2013, as shown in figure 2.

The impact of ever-increasing variability and complexity is often a degradation in delivery performance, which results in larger inventories, rising fulfillment costs, and poor utilization of labor and equipment. Figure 2 shows that inventories grew in 20 of the 50 top pharmaceutical companies.

In environments like the pharmaceutical industry where variation and complexity must be juggled with stable or even increasing levels of quality, confusion reigns supreme and firefighting in production processes is the norm. Profits erode as manufacturers employ more staff to manage frequently occurring exceptional circumstances, pay additional freight fees at a premium to overcome material deficiencies, and pay overtime premiums to get orders back on track. This leads to a situation in which any improvement is neutralized by increasing complexity and, in the end, stagnating margins [2].

However, 10 of the top 50 pharmaceutical companies are masters of complexity. They have managed to reduce their inventories while increasing their SKUs. So the question is: how does one become a master of complexity?

In the recent past, Porsche Consulting has proposed eight practices to achieve leading-edge pharma operations [2]. Practice number eight involved accelerating industry 4.0 rollout and choosing use cases with high business impact that are also feasible. One of these use cases would be an AI-enhanced planning system.

Turning our view to the underlying information technology at the heart of the matter. Software manufacturers are already promising to provide assistance through production scheduling systems such as SAP's Production Planning and Detailed Scheduling (PP/DS), AspenOne's Plant Scheduler, and Oracle's JD Edwards APS Production Scheduling, to name but a few. All of these so-called advanced planning solutions employ mathematical optimization models in order to provide a means to plan a production schedule as a dynamic process while incorporating various constraints, especially regarding capacity, directly into the planning process [3].

In the pharmaceutical planning environment, a number of modelling options must be provided that enable the bill of materials (BOM) and recipes necessary for large-scale production of pharmaceuticals to be represented with the utmost precision. These include detailed shift plans, alternative resources, relationships, recursive BOMs, and joint production. To generate the best possible production plan, the production planner should therefore be provided with "intelligent" planning tools. Examples of such tools are customer-specific heuristics, genetic optimization, dynamic and fixed pegging, dynamic setup times, and the representation of comprehensive order networks.

The representation of quality control activities in the pharmaceutical industry is a significant challenge for software developers and application architects. Although modelling quality-control activities at similar levels of detail is achievable in most cases, it is rarely possible to plan quality control, let alone integrate production and quality control planning. Although times during production are planned and recorded to the minute, no order-specific data is found in most quality control tools. Instead, sequence-concentrated planning and fixed buffer times are used. Having optimized production with innovative planning concepts and more efficient

planning tools, working with fixed buffer times for quality control is an economic cataclysm and a general obstruction for the entire supply chain.

Clearly, at an organizational level, the major challenges in production planning in the industrial manufacture of pharmaceuticals can be summarized as follows:

1. Increasing product variety and its knock-on effects cause higher demands on production planning software.
2. Special requirements for modelling planning inputs due to the inherent complexities of pharmaceutical production processes.
3. Order-specific planning of quality control activities is an integral part of the entire production planning process.

Sorting through the AI hype: Finding an effective and practical approach to embarking on the AI journey

Artificial intelligence is one of the main drivers of the digital revolution. It is already changing the way organizations act and make decisions, and it is helping companies to manage faster and more efficiently. A very important aspect of the use of AI is to relate the quest for more efficiency to the actual possibilities.

With recent advances in AI it only seems pertinent to examine the application of AI technology in order to alleviate the challenges in pharmaceutical production planning. In doing so, it is important to sort through the hype, to separate fact from fiction, from not only a technological perspective, but also considering the approach and methodology.

In the specific case of pharmaceutical production planning, AI will be a direct part of the value chain and thus strongly integrated into the product. It is therefore important not to treat AI as a black box, but rather to fully understand the output generated and furthermore understand how to influence the generated production plan with appropriate input.

This article demonstrates a novel approach to combining existent planning systems, including onboard optimizers, with custom AI technology to produce an economically viable production planning system as applied to the specific challenges of the pharmaceutical industry.

Number of new Active Pharmaceutical Ingredients (APIs)

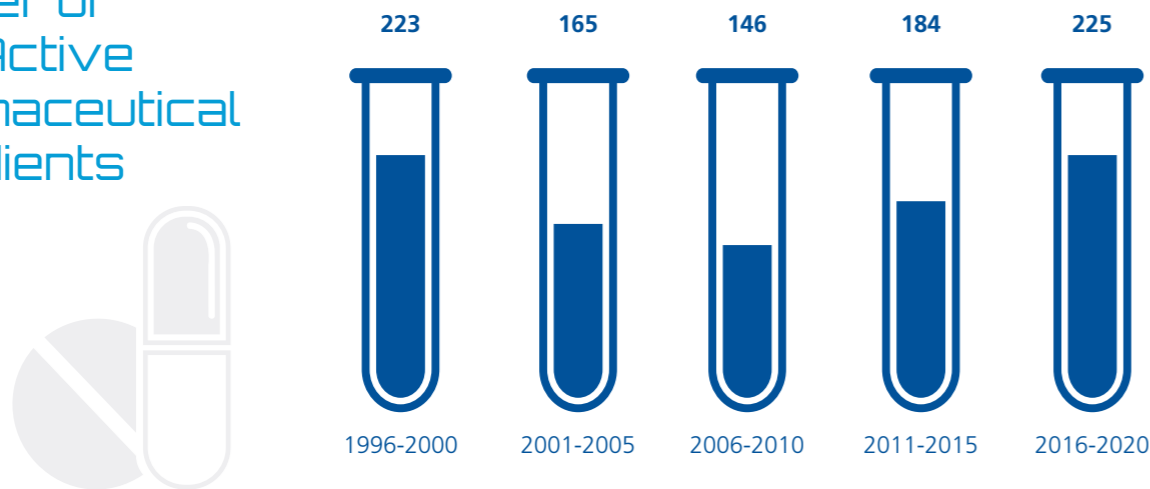| 223	165	146	184	225
1996-2000	2001-2005	2006-2010	2011-2015	2016-2020

Figure 1. Increasing complexity in pharmaceutical industry as shown by increasing number of new APIs (Source: Statista.com)

Ø -0.6 %

High >

Growth performer

Complexity masters

SKUs
Increase
since
2013

Ø 50 %

Follower

Inventory performer

< Low

< Increasing inventories

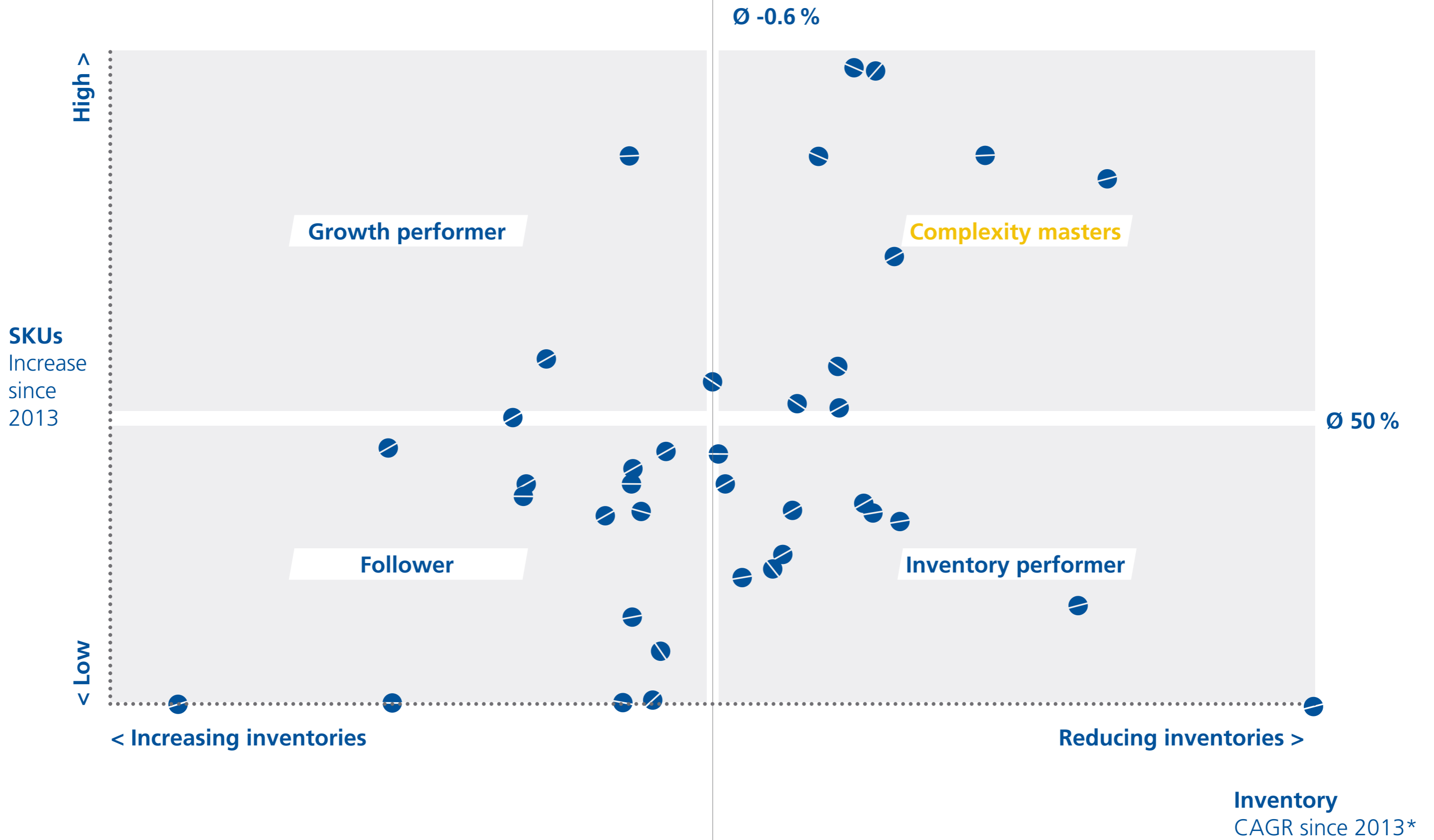**Reducing inventories >**

Inventory
CAGR since 2013*

Figure 2. Change in stock keeping units (SKUs) and Inventory of top 50 pharma companies, revenue based (Source: Porsche Consulting research, 2019)

02

Production planning as key success factor for efficient production

Lack of quality in planning and scheduling can reduce productivity by 5 percent, as measured in Overall Equipment Effectiveness (OEE) (Porsche Consulting project experience). Inventories are often increased to improve supply reliability and uphold stable production. Excellent planning and scheduling is thus a significant competitive advantage. From an operational/practical standpoint, achieving excellent planning and scheduling presents pharmaceutical companies with five major challenges:

1. Intra-day adjustments in the production sequence
Short-term re-sequencing within a frozen zone results in less adherence to the original production plan. Production is frequently asked to adjust to changes in demand. To achieve this flexibility, the inventory is increased, thereby causing high levels of throughput times.

2. Unclear effect of breakdowns on delivery times
Compared to other industries, pharmaceutical companies have low OEE, especially in packaging. High product variability and low batch volumes contribute to this. However, equipment breakdowns or reduced efficiency due to small stoppages are also contributing factors to a low OEE. Lead times therefore become ambiguous, resulting in reduced delivery performance and low customer satisfaction.

3. Reduced OEE due to non-optimal setup sequence
The pharmaceutical industry is marked by enormous variability in changeover times, especially in packaging. If you are switching from one product to another, which is the same drug but with a different number of tablets per box, a partial changeover is sufficient. Under most other circumstances, however, a full changeover is required. By following a specific production sequence, the OEE can be improved by 5 percent (Porsche Consulting project experience). More focus on meeting delivery requirements (challenge 1) results in less focus on the right production sequence.

4. Lack of integration among interface areas
Several interfaces have to be considered in the pharmaceutical value stream, such as from bulk to packaging and from packaging to quality control. Planning and scheduling should consider the complete value stream and thereby optimize the inventory at the interfaces. The interface to quality control is especially challenging, as capacities in quality control are not reflected by most planning and scheduling tools.

5. Daily firefighting activities
Daily challenges — such as absent employees, equipment breakdown (challenge 2), lack of material — need to be addressed. This can be quite laborious, as it often involves adjusting the production schedule. For example, if employees are absent due to illness, the scheduler needs to find the replacements with the proper set of skills . The scheduling will eventually need to be adjusted, as some equipment might have to be shut down, at least partially. The challenge is to find the best solution with the lowest negative effect on OEE and delivery performance, whilst maintaining optimal costs. This is very complex and can take a significant number of working hours, resulting in high labor costs.

03

Target picture of an ideal production planning system enhanced by AI

The challenges described in section 2 serve as input for the functional specification of an optimal production planning environment, which may be broken down further by regarding various planning horizons within the production planning process. Figure 3 shows a comparison of production planning approaches across short and long-term planning horizons.

Our experience shows that much of today's production planning becomes an increasingly manual task with decreasing planning horizon. This stands to reason, since the criticality of changes made to the production schedule in the short-term increases whilst requiring the integration of a much greater number of variables. Traditionally, computers would not have been entrusted with tasks at this level of required intelligence, and indeed, standard procedural implementations of the logic required to perform alterations to a production schedule within the frozen zone would be neither reliable nor economically viable. However, as is currently observable in many other business scenarios, the introduction of AI into the context of short-term production planning becomes a game changer.

In the vast majority of today's production planning processes, detailed scheduling relies on manual shift planning for each production area on a day-by-day basis. Tomorrow's fully automated scheduling systems, however, will utilize AI to incorporate short-term events that generate revised production schedules at equipment and worker level in real time. A look at the different planning horizons in Figure 3 makes clear that the benefits of integrating AI into the planning process increase, the closer one gets to commencing production. When dealing with short-term adjustments within the frozen zone due to sudden staffing shortages or reduced machine capacities, an appropriately trained AI-based system can be particularly helpful by suggesting staffing and parameters for the on-board optimizer. This is regarded as an optimal solution to the problem, since similar patterns are known from previous situations.

One of the major challenges to the operation of mission-critical

AI applications is transparency in dealing with the inner workings of the AI model. Despite the existence of methods to understand "black-box predictions" [4], their complexity makes a more practical approach essential. Modern planning schedulers allow interfacing to their optimization algorithms, such that a "layered AI" approach may be implemented where a layer of custom AI influences the operation of the optimization core (figure 4). The inner workings of the AI thus becomes more transparent and maintainable. By definition, an onboard generic optimization algorithm may already be classed as AI. The proposed custom AI wrapper, however, is a machine-learning algorithm whose accuracy will improve with time.

In this layered setup, exchange between the generic algorithm and AI wrapper utilizes three methods:

1. Optimized planning parameterization

Weighting of planning criteria is a major factor that influences optimization accuracy and performance. The AI wrapper actively modifies and sets these planning criteria, thereby greatly optimizing the accuracy and performance of the APS genetic algorithm.

By using the various data sources, including a manufacturing execution system and Enterprise Resource-Planning (ERP) systems, the AI wrap-
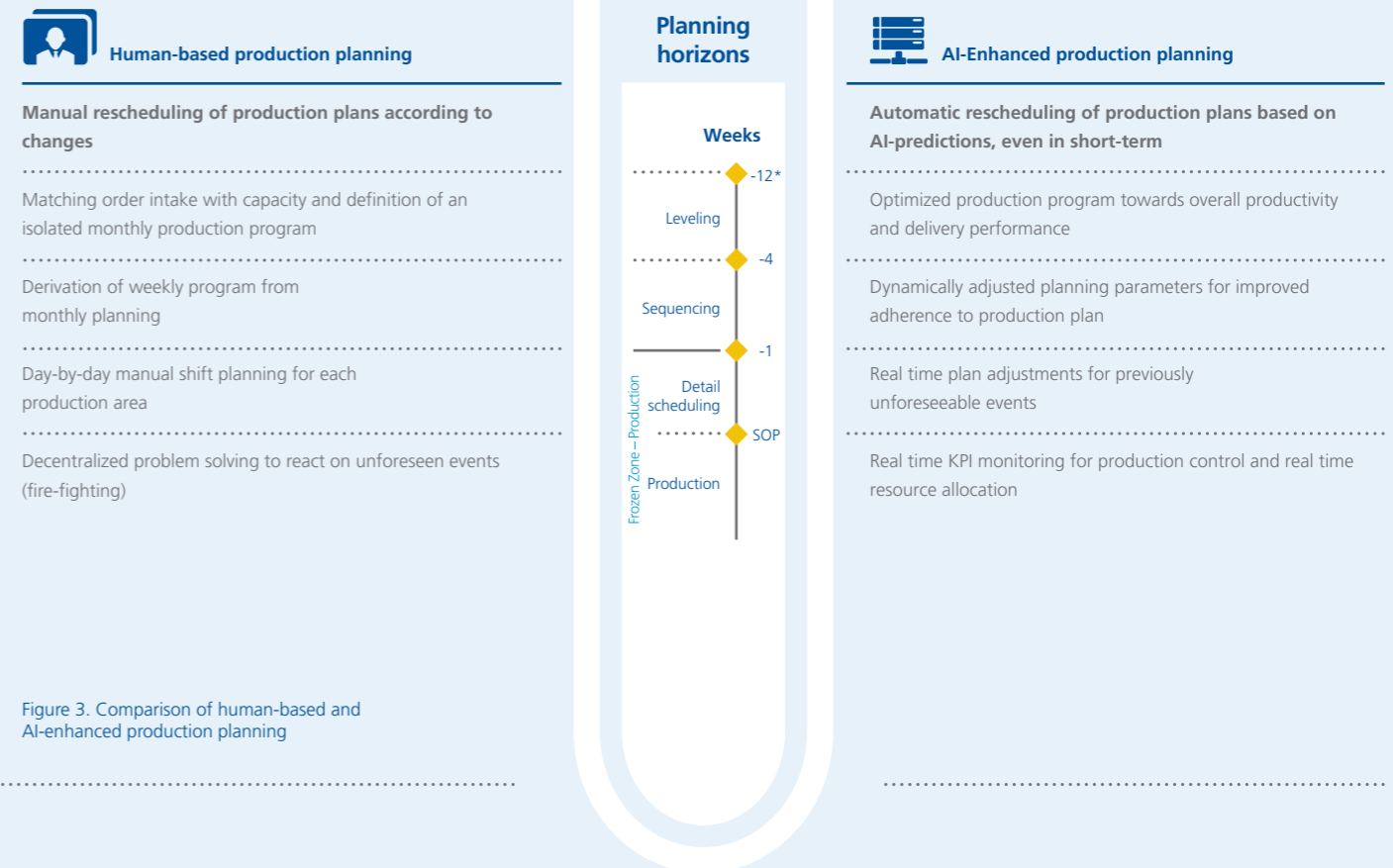

Human-based production planning

Manual rescheduling of production plans according to changes

Matching order intake with capacity and definition of an isolated monthly production program

Derivation of weekly program from monthly planning

Day-by-day manual shift planning for each production area

Decentralized problem solving to react on unforeseen events (fire-fighting)

Planning horizons

Weeks

-12*

Leveling

-4

Sequencing

-1

Detail scheduling

SOP

Frozen Zone – Production

Production

AI-Enhanced production planning

Automatic rescheduling of production plans based on AI-predictions, even in short-term

Optimized production program towards overall productivity and delivery performance

Dynamically adjusted planning parameters for improved adherence to production plan

Real time plan adjustments for previously unforeseeable events

Real time KPI monitoring for production control and real time resource allocation

Figure 3. Comparison of human-based and AI-enhanced production planning

01
Optimized Planning Parameterization
Table interface

02
Production Abstraction
Function interface

03
Actual activity duration utilization
Function interface

AI-Wrapper
Custom AI-functionality layer
ORACLE · python · jupyter

Generic Algorithm (Optimization Core)
Standard APS-Optimization functionality
SAP · aspentech · ORACLE JD Edwards
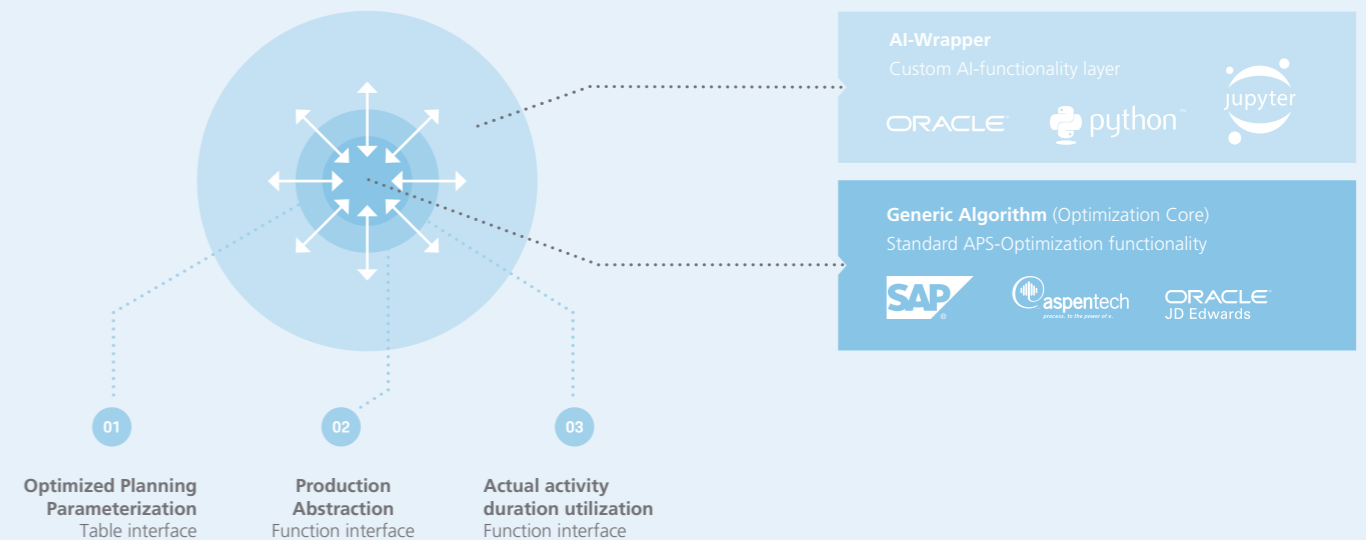
Figure 4. Interaction of APS optimizer and AI wrapper

Activity network based on alternative production

Total Costs

15 → 20 → 35

10

15

10 → 25 → 10

Simplified activity network substituted by AI-Engine

10 → 25 → 15
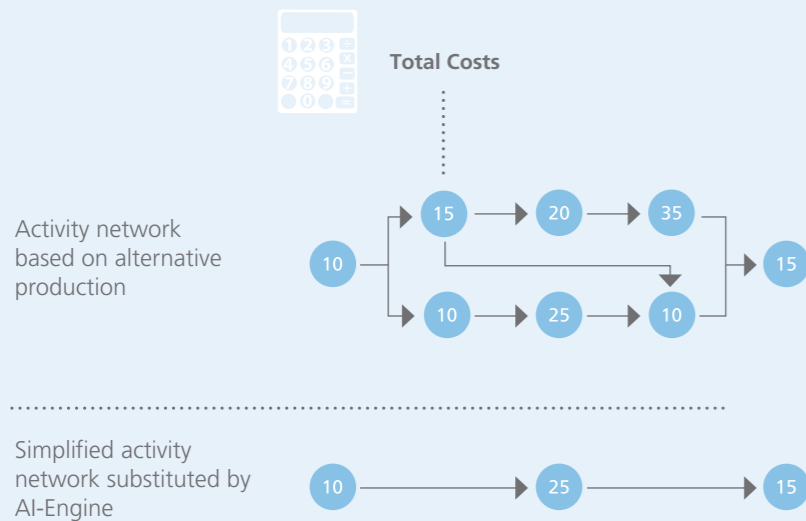
Figure 5. An example of production sequence abstraction

Activity times

30 · · · · · Quality Control

200 · · · · · Sec. Packaging

120 · · · · · Prim. Packaging

60 · · · · · Pressing

Regular activity times of production routing in backorder-situation

Planned time: 410 min

Activity times

24 · · · · · Quality Control

146 · · · · · Sec. Packaging

101 · · · · · Prim. Packaging

47 · · · · · Pressing

AI-Optimized parameter-Set for short-term Planning Rus to clear backorder-situation

NEW production time: 318 min
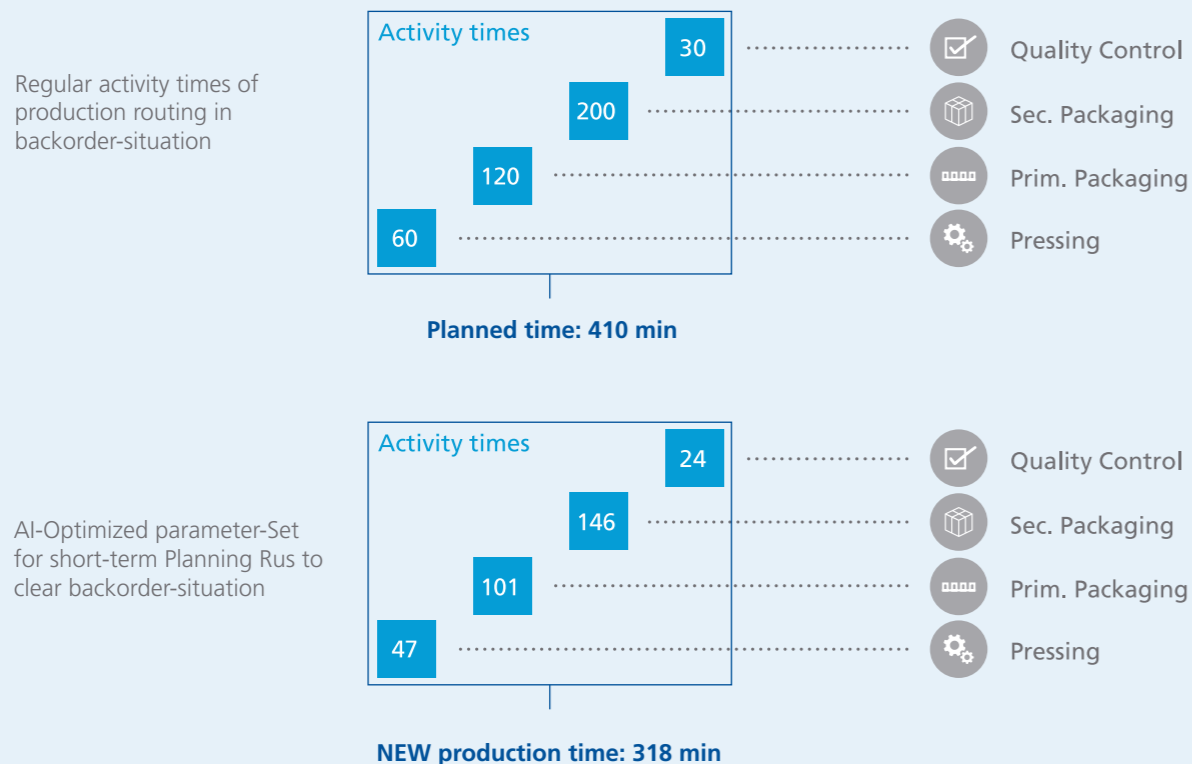
Figure 6. An example of Actual Activity Duration Utilization

per is trained (under supervision) to identify the optimal planning parameters for the APS optimizer under any given circumstance in which a planning run is to be carried out. The AI wrapper will therefore use historic scenarios to produce a set of planning criteria to maximize the performance of APS optimization and its results.

2. Production sequence abstraction

Optimization performance in all APS systems is heavily dependent on the complexity of activity networks (production schedules) and the optimization cost of individual activities within networks.

Complex networks with many redundant and/or obsolete activities, are often processed by the optimizer. This has a detrimental effect on optimization performance. An example could be a specific drug that had to be processed by a certain machine for secondary packaging after blistering; the blistering and the secondary packaging can be treated as one activity.

The AI wrapper is trained to locate these redundancies and make suitable substitutions, thereby significantly reducing the optimization overhead and increasing optimization performance (fig. 5).

3. Actual activity duration utilization

Optimizers traditionally use various forms of master data, such as activity durations, to generate an optimized production schedule. In the case of activity durations, however, these sources of information are particularly theoretical, and deviations (positive or negative) in actual activity durations cannot be taken into consideration, leading to inefficiencies. For example, if certain activities were known to be performed faster under specific circumstances, the optimizer could schedule more activities in the same amount of time (fig. 6).

Actual activity duration utilization does exactly this by allowing the actual activity times identified by the AI wrapper to be utilized by the APS optimizer, rather than theoretical activity durations as maintained in the master data.

In figure 6, the exemplary pharmaceutical production line from tablet pressing to quality control indicates a planned duration of 410 minutes. The actual production time the AI wrapper would utilize is 22 percent faster.

We expect the number/types of interactions between the custom AI layer and standard APS optimization algorithm to increase as we gain experience in the practical usage of AI-enhanced production planning systems.

REACHING THE NEXT LEVEL:

AI use cases are the key to reaching the next level of margin increase in the pharmaceutical industry.

04

Playbook: How to establish an advanced production planning concept

Installing an AI-based planning system should start by thoroughly understanding the business and the needs of the organization (initiation and analysis). Three steps are required to achieve this. First, the as-is planning process needs to be mapped, including existing roles and interfaces. The process will have to be optimized before starting the digitization. The general rule is: "Do not digitize bad processes!" Second, the IT landscape is mapped, including available data. Third, the target is concretized. This includes defining the relevant KPI objectives and success criteria. This ensures that resources are allocated to the use cases with the highest business impact.

Once the business objectives are clear and the facts for the solution development are known, the scenario building and implementation can begin. We propose a combination of SCUM, as typical for software projects, and the MHP-specific CRISP AI to develop the AI portion of the project (fig. 7). Essential for project delivery using the SCRUM methodology is dividing the final product into viable subproducts that can be completed in two-week sprints. Each sprint, which is AI-focused, follows the six steps of CRISP AI:

1. **Business understanding**
2. **Data understanding**
3. **Data preparation**
4. **Modelling**
5. **Evaluation**
6. **Build and integration**

The CRISP AI methodology provides a structured approach to planning an end-to-end AI project. It is a robust and well-proven methodology by MHP, derived from the well-known CRISP DM (data mining) methodology. The benefit of CRISP AI is the clear focus on the production of a viable end-to-end product, as opposed to a stand-alone algorithmic solution to a data sci-

ence problem. For sustainable implementation, it is important to train key stakeholders in the utilization of the software tool. Best practice is to directly involve them in the sprints during development. These key stakeholders become the digital production planners in the organization. They are also the experts for potentially scaling the approach.
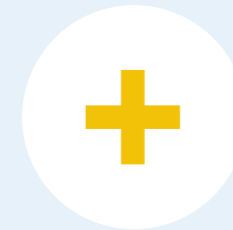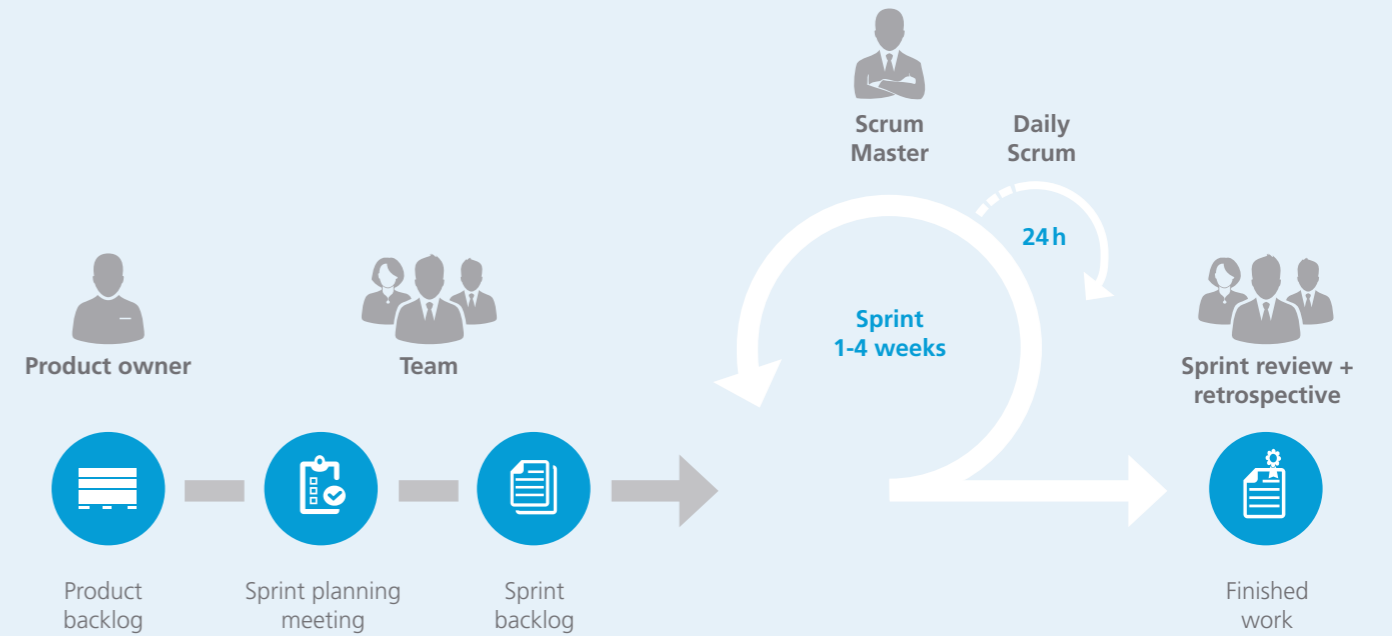
Figure 7. Exemplary project sketch with applied SCRUM and CRISP AI

05

Outlook: Closing the loop

Artificial intelligence in production planning offers a variety of possibilities for advanced optimization and automation of planning processes. However, this is just the beginning.

If one also considers the inbound side — that is, the side before production — problems and challenges can be identified even earlier and solutions found much more effectively. For example, an additional integrated supplier risk management [5] can identify raw material and component bottlenecks, including possible effects on production, at an early stage and propose solutions by means of AI.

Integration of the logistics' outbound side in the systemic loop enables even greater potential. For example, decisions can be made to solve production bottlenecks in the area of not only production but also logistics. By use of AI-technology, logistics and transport service providers can be integrated at an early stage to take into account restrictions and bottlenecks on the production side.

With complete integration of production as well as inbound and outbound logistics, artificial intelligence can be transformed from a mere IT tool that provides valuable functionality for individual business areas to the orchestrator of end-to-end value chain management — with transparency and solution competence across a company's entire value chain network.

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