

# **Industrial Applications of the Internet of Things**

Gerta Kapllani<sup>(⊠)</sup>

WBW Wirtschafts-und Betriebswissenschaften, Montanuniversität, 8700 Leoben, Austria

**Abstract.** In the age of Industry 4.0, a substantial concern for modern manufacturing organizations in optimizing production processes under an Internet of Things (IoT) framework is noted. Moreover, given the significant volume of production, energy efficiency is an inevitable issue. To a great extent, improving production performance depends on the development of new technologies. As a result, this research targets to conduct a research review for the implementation of industry 4.0 technologies in continuous manufacturing. While there is a significant amount of research on batch manufacturing and industry 4.0, continuous manufacturing is less addressed in these scientific works. In an attempt to fill this gap, we try to understand the transition from batch processing manufacturing to continuous processing manufacturing within certain industries, emphasizing the benefits of industry 4.0 relevant to the industry and sustainability. Another crucial part of this study is identifying open issues and challenges of industry 4.0 infrastructure in continuous manufacturing. For such reason, we developed two research questions that we will try to answer during this work. The first one is which are the technologies being implemented as part of industry 4.0 in continuous manufacturing and the second one, does the implementation of such technologies in continuous manufacturing led to energy efficiency improvement.

**Keywords:** Continuous process · Energy efficiency · Industry 4.0 · Research review · Continuous manufacturing

## **1 Introduction**

With the increasing development of new technology solutions through the internet of things, big data and data mining there is a need to dig deeper into the interdisciplinary areas of manufacturing cooperation with these advanced technological solutions. Internet of Things (IoT) is identified as an emerging technology used in the manufacturing domain in monitoring and controlling processes and operations [\[1\]](#page-8-0). Different studies emphasize the relationship of industry 4.0 with manufacturing in general without concretely studying continuous manufacturing [\[2\]](#page-9-0). While there is a significant amount of research on batch manufacturing and industry 4.0, continuous manufacturing is less addressed in these scientific works. In an attempt to fill this gap, we try to understand the transition from batch processing manufacturing to continuous processing manufacturing within certain industries, emphasizing the benefits of industry 4.0 relevant to the industry and sustainability. Another crucial part of this study is identifying open issues and challenges of industry 4.0 infrastructure in continuous manufacturing. However, these last years have noticed considerable extension in the application of advanced analytics through IoT in continuous process manufacturing. In addition to that, in many manufacturing industries, there is an increasing awareness of energy savings and energy efficiency considered green manufacturing [\[3,](#page-9-1) [4\]](#page-9-2). Also, manufacturers are aiming at identifying best practices that lead to less and less energy consumption. Many industries have traditionally operated in batch mode. Recently can be noticed an increasing trend for switching from batch operations to continuous operations, especially in the pharmaceutical manufacturing which is considerably gaining momentum. Continuous manufacturing in pharmaceutical industry has been researched for more than two decades. Moreover, Muzzio at Rutgers University started the first research program for continuous manufacturing of pharmaceuticals in the early 1990s. However, the concept of continuous processing has been introduced in different industries such as oil, paper, fertilizers, foods, automotive, etc. On the other side, continuous manufacturing in the pharmaceutical industry's first publication by Imperial Chemical Industries (ICI) made headlines in 1984. Academia and industry are cooperating closely in the matter to outline insights output that can revolutionize the manufacturing production environment. The main contribution of this paper is to identify and categorize current practices and technologies of industry 4.0 implemented in continuous manufacturing industries. Moreover, another focus is trying to address sustainability in terms of energy efficiency in matter in continuous industrial production. For such reason, we developed two research questions that we will try to answer during this work. The first one is which are the technologies being implemented as part of industry 4.0 in continuous manufacturing and the second one, does the implementation of such technologies in continuous manufacturing led to energy efficiency improvement.

## **2 Methods**

"The systematic literature review in this paper is conducted through mixed methods proposed by PRISMA statement and guidelines advocated by Webster and Watson 2002 [\[5\]](#page-9-3)". As result, the review process consists of three main phases: the planning phase, the acting phase, and reporting of results. In the planning phase is discussed the planning part of conducting a review focusing on the available literature, in the acting phase are being discussed the actual steps to conduct the review and in the reporting of results part are included in the results, discussion, and conclusion this study.

We developed a query to search in our database of choice Scopus which provides indexed only peer-reviewed reputable journals [\[6\]](#page-9-4). Due to the diversity of content in technical areas we started our query using "continuous manufacturing", "production continuous manufacturing", "Industry 4.0". Due to the low number of papers identified and for the sake of the robustness of the search we extended our search in areas we were concerned about such as "continuous process\*", "continuous manufacturing system", "data-driven", "industrial big data", "analytics", integrating digital environment with the production environment. We build the query employing Boolean operators OR, AND and wild cards with respective variations of keywords:

*Query defined*:

(("continuous manufacturing" OR "production continuous manufacturing" OR "continuous process\*" OR "continuous manufacturing system") AND ("data driven" OR "industry 4.0" OR "industrial big data" OR "analytics")).

To conduct a qualitative review in this paper we adopt the PRISMA methodology. Using the query defined we searched the literature in the scientific database Scopus. The review is entirely on the research objectives introduced in the above section. Hence articles that did not address those objectives are not considered for further review. The initial total number of the identified records is 1949. Only English-written papers were selected. After limiting the query to all open access papers, the number of retrieved studies was further reduced to 629. Moving forward, a careful title-abstract-keyword screening was made conforming to our research scope that aims to cover industrial applications of the Internet of Things in continuous manufacturing. There were 603 articles excluded at this step. The majority is not focused on continuous manufacturing, not covering technologies implemented, not focused on industrial application, or repeated theoretical cycles on the topic. In the last step, the full-text paper is studied with a thorough assessment resulting in 26 articles. The detailed schema is in Fig. [1.](#page-3-0)

We also followed some quality assessment review for the screened articles an approach based on the Kitchenham SLR model.

**QA1.** Are the goals and objectives of each article clearly stated?

**QA2**. Is the methodology and scope of the article clearly defined?

**QA3**. Does the research have an industrial application?

**QA4**. Does the article comply and answers our pre-defined research questions in our study?

This quality assessment is a sort of customized protocol that helped us to enforce the PRISMA methodology findings. It is worth mentioning that the excluded papers in Fig. [1](#page-3-0) did not fulfill the QA mentioned above. All questions should be answered in the paper's literature otherwise the paper is not valid for further review. The final papers taken into consideration did answer all these questions in their literature and have major contributions on this work.

### **3 Results**

In the majority of the studies process analytical technology (PAT) is highlighted as a rapidly evolving technology for process industries. Beside that Digital Twin, Quality-by-Design (QbD), Data Mining and Machine Learning implemented through the Internet of things are considered innovative technologies. Although, the integration of one or more technology can be translated as a very challenging task due to implementation. Extensive research is conducted in the pharmaceutical industry as a form of continuous manufacturing. Other industries studied are steel, energy, pulp and paper, automotive, chemical, agrochemical, and biopharmaceutical. The research tries to emphasize the advantages of continuous manufacturing over batch manufacturing in terms of economic, energy efficiency, energy costs, scale-up flexibility, failures, and environmental load.



**Fig. 1** PRISMA guideline literature review

## <span id="page-3-0"></span>**3.1 Process Analytical Technology (PAT)**

This technology is gaining momentum in many industries, especially in pharmaceutical one [\[7](#page-9-5)[–14\]](#page-9-6). One aspect of including PAT in Freeze-drying manufacturing can provide additional information on the Critical Process Parameters (CPPs) and Critical Quality Attributes (CQAs) during biopharmaceutical processing. It is proven that this technology reduces time, operational costs, and energy consumption. However, is stated that besides many benefits of using this technology, feasibility at commercial sale requires further exploration [\[9\]](#page-9-7). PAT plays a crucial role in continuous flow processing providing real-time monitoring and analysis for a range of applications within the pharmaceutical industry. Continuous manufacturing processes ensure safety and quality of a product. This paper has demonstrated the synergy between different PAT tools, their predictive power to detect and monitor process deviations [\[15\]](#page-9-8). The paper "Pat for continuous chromatography integrated into continuous manufacturing of biologics towards autonomous operation" [\[13\]](#page-9-9) is proven potential for inline measurement. It proposes a reliable inline

PAT concept for the simultaneous monitoring of different product components after chromatography. Moreover, is highlighted that Biologic manufacturing moves toward high-throughput continuous process alternatives. It is suggested for standard batch chromatography or integrated counter-current chromatography (iCCC), an inline measurement of multiple components (e.g., the main component and side components) would be promising to simplify process control. PAT technology has been integrated with emerging technologies such as machine learning attempting to give promising insights. This paper aims to assess the potential of ANNs within the PAT concept to aid the modernization of pharmaceutical manufacturing [\[7\]](#page-9-5). It concludes that real-time application for PAT is still scarce. Possible future direction and research gaps as the real-time training capabilities of NNs for continually increasing volume of data should be further studied, as well as the role of time-series ANNs could be investigated in much more detail.

#### **3.2 Data Mining**

The paper "Challenges and opportunities in modelling wet granulation in the pharmaceutical industry—A critical review" has been discussed how data-driven models based on neural networks have been indicated to be used for application in continuous granulation with great accuracy compared to other approaches, which can also be implemented for process control. This data-driven modelling can play an important role in future process design, optimization, and control of pharmaceutical wet granulation processes [\[16\]](#page-9-10). Different studies rely on data mining techniques mostly in continuous production in the pharmaceutical industry. Many challenges need to be addressed in the industrial environment such as scaling, high data volume, data security, and the risk of using Blackbox models. Many industries are focused in applying analytics and automation to their production environment. For that purpose, different data mining techniques are performed and evaluated in an industrial context solving complex challenges. Nowadays the overall trend is comparing classical machine learning algorithms with ensemble methods. In this paper in the steel industry, they experimented with different techniques for fault detection and diagnosis. The result of their study is that machine learning methods can be used and applied to the steel manufacturing process which relies on monitoring strategies such as fault detection to reduce the number of errors that can lead to huge losses. Future research needs to evaluate techniques for fault diagnostics in real time using predictive maintenance. Future research is crucial as sensors record huge amounts of data that need Big Data Analytics to help with analysis for better decision-making. The real-time manufacturing process is compromised due to a lack of proper monitoring techniques for identifying faults [\[17\]](#page-9-11).

#### **3.3 Digital Twin and Quality-by-Design**

Most of the studies identify digital twins and quality by design as correlated terms which represent powerful emerging technologies, especially in the pharmaceutical context. "Quality-by-Design (QbD) is demanded by regulatory authorities in biopharmaceutical production. Within the QbD frame advanced process control (APC), facilitated through process analytical technology (PAT) and digital twins (DT), plays an increasingly important role as it can help to assure to stay within the predefined proven acceptable range (PAR). This ensures high product quality, minimizes failure and is an important step towards a real-time-release testing (RTRT) that could help to accelerate the timeto-market of drug substances [\[18\]](#page-9-12)". Several recent studies tend to present a thorough description of the digital twin development for a continuous pharmaceutical by the Process Analytical Technologies (PAT) and Quality by Design (QbD) guidelines emphasizing that reduced material costs and limited development timeframe manifest the digital twin an efficient tool in technological development [\[19](#page-9-13)[–22\]](#page-10-0). Future research is needed to address the integration of Digital Twin technology in a data-driven environment which has its complex challenges presented in the above section.

<span id="page-5-0"></span>Below we give a summary of our final customized dataset (Table [1\)](#page-5-0).

| Title  | Technology   | References |
|--|--|------------|
| Application of artificial neural networks in the<br>process analytical technology of pharmaceutical<br>manufacturing-a review  | Neural Network + PAT   | [7]        |
| Improving the load flexibility of industrial air<br>separation units using a pressure-driven digital twin  | ASU (air separation units)   | $[15]$     |
| Simulation for predictive maintenance using<br>weighted training algorithms in machine learning  | Data mining  | [23]       |
| Digital twin for HIV-Gag VLP production in<br>HEK293 cells   | DigitalTwin, PAT, QbD  | [8]        |
| Digital twins for scFv production in Escherichia coli  | Quality-by-Design (QbD), digital twin, pat                                       | [18]       |
| Challenges and opportunities in modelling wet<br>granulation in pharmaceutical industry-a critical<br>review   | Data mining  | [16]       |
| A data mining approach for continuous battery cell<br>manufacturing processes from development towards<br>production   | Datadriven, data mining  | $[24]$     |
| Investigating the trade-off between design and<br>operational flexibility in continuous manufacturing of<br>pharmaceutical tablets: a case study of the fluid bed<br>dryer | Datamining, blackbox model   | $[25]$     |
| A review on data-driven process monitoring methods:<br>characterization and mining of industrial data  | Fault detection and diagnosis (FDD), data-driven<br>process monitoringtechnology | $[26]$     |
| Digital twin of low dosage continuous powder<br>blending-artificial neural networks and residence<br>time distribution models  | ANN, DigitalTwin, PAT, QbD   | $[19]$     |
| Innovative drying technologies for<br>biopharmaceuticals   | PAT  | [9]        |
| Energy strategies in the pulp and paper industry in<br>Sweden: Interactions between efficient resource<br>utilisation and increased product diversification                | Energy management systems  | [27]       |
| Optimally managing chemical plant operations: an<br>example oriented by industry 4.0 paradigms   | RTO system(digital twin, industry 4.0)   | $[28]$     |

**Table 1** Summary results according to final studies

(*continued*)



#### **Table 1** (*continued*)

Below we are presenting the Ishikawa diagram of cause-effect for the transition from batch to continuous that we have customized based on our needs on the literature we have taken into consideration. It is considered a powerful tool for brainstorming and generating new ideas for a problem. It is widely believed that identifying the causes of a problem leads to potential solution.

Concretely while studying the literature, it is noted that the transition from batch to continuous manufacturing has many advantages but also brings on the table many challenges. An attempt of ours is to display our main findings in the cause-effect diagram in Fig. [2.](#page-7-0) In terms of resources, the most challenges identified are lack of continuous manufacturing expert's domain, lack of motivation, management, and human errors. For advantages and challenges from a technical point of view, the digitalization process is crucial for production using real-time analytics, PAT technology, internet of things with a huge techno-economic impact. Data mining can enable accurate insights with data modelling but comes with many challenges of handling high volume and variety of data.

The transition process is recognized as very important the quality assurance component. Last but not least, continuous manufacturing using IoT identified energy usage and foot print reduction as two leading goals in terms of energy efficiency.

## **4 Discussion**

Nowadays still most manufacturers rely on batch production. The reasons are different, but mostly due to the historical prevalence of batch operations, and a lack of motivation to make changes to operating practices because of the minimal cost of production relative to the profit margins expected in these industries. Much of the resistance to change arises from the fear of the impact on product quality.

Many researchers studied batch processing or batch production systems. In their study, the authors combined different techniques such as OEE analysis, Internet of Things (IoT), and cyber-physical production system (CPPSs) that lead to energy savings. They focused on the process cycle time and energy consumption in the batch production. Another crucial component to achieving overall productivity in the batch process is production scheduling. It plays a huge role in heat integration and represents a tool that could help to reduce energy consumption in batch processing. The manufacturing industry has been one of the biggest energy consumers.

As a consequence, energy efficiency has become a very significant factor for manufacturing enterprises to reduce energy consumption for minimizing costs and environmental impact, finding new solutions to produce "more with less". The main findings of this study are that energy efficiency has to be defined separately for each manufacturing level, and process-level energy efficiency is successfully defined for all manufacturing processes. Energy efficiency at the production line and factory levels can be significantly improved with better scheduling and the inclusion of shutdown or eco-modes in the work



<span id="page-7-0"></span>**Fig. 2** Ishikawa diagram cause-effect-problem

planning of the machines. However, the main industry that has mostly switched from batch processing to continuous one is the pharmaceutical industry. Another interesting article [\[33\]](#page-10-13) that writes about the transition from batches to continuous and generally for continuous processing or continuous manufacturing, presents some interesting questions such as how to ensure quality and regulatory compliance. How to maintain consistent process control and quality when there are no checkpoints between batches?

To answer this question is needed real-time monitoring and advanced analytics are. Another article [\[10\]](#page-9-15) in support of the transition from batches to continuous manufacturing in the pharmaceutical industry, confirms that the continuation of production means companies can minimize waste and energy usage, reduce changeover costs, and better monitor drug quality on a continuously through data analytics and real-time checks. Moreover, US Federal Drug Administration (FDA) confirms this switch due to flexibility, the positive effects on the production side, and the minimization of human errors. On the other side is pointed out many risks that come with the implementation of continuous production. In the end, they come up with a case study; the global Biotech company that leverages real-time monitoring and advanced data analytics through automation excellence to achieve continuous manufacturing in a new digital manufacturing facility. Internet of things (IoT), predictive technologies are said to rely on one common core: process analytical technology (PAT). In continuous manufacturing environments, many industries (mostly pharmaceutical) are relying on in-line PAT.) However, this study has supported the idea that pharmaceutical continuous manufacturing does not yet coordinate with PAT technology in terms of control framework. Further research and collaboration from academia and industry is more than needed and praised regarding the matter of discussion.

### **5 Conclusion**

Reviewing the recent literature, the following has been noticed:

Only a small number of papers present energy efficiency in continuous manufacturing through the internet of things (IoT). Their research is mostly focused on footprint reduction and energy usage in cycle times. There are many challenges in the implementation of continuous manufacturing and also from the transition between batch and continuous manufacturing which are also discussed in the Ishikawa diagram, most of which are related to digitalization, automation, lack of expert domain, human errors, and lack of motivation.

The biggest part of the research emphasizes PAT technology in the pharmaceutical industry. More research is needed in the implementation of continuous manufacturing in other industries besides pharmaceutical industry.

#### **References**

<span id="page-8-0"></span>1. Papakostas, N., O'Connor, J., Byrne, G.: Internet of Things Technologies in manufacturing: [application areas, challenges and outlook \(2016\).](https://doi.org/10.1109/i-Society.2016.7854194) https://doi.org/10.1109/i-Society.2016.785 4194

- <span id="page-9-0"></span>2. Zhang, Y., Ma, S., Yang, H., Lv, J., Liu, Y.: A big data driven analytical framework for [energy-intensive manufacturing industries. J. Clean. Prod.](https://doi.org/10.1016/j.jclepro.2018.06.170) **197**, 57–72 (2018). https://doi.org/ 10.1016/j.jclepro.2018.06.170
- <span id="page-9-1"></span>3. Chavan, R., Thipparaboina, R., Yadav, B., Shastri, N.: Continuous manufacturing of co[crystals: challenges and prospects. Drug Deliv. Transl. Res.](https://doi.org/10.1007/s13346-018-0479-7) **8** (2018). https://doi.org/10.1007/ s13346-018-0479-7
- <span id="page-9-2"></span>4. Fore, S., Mbohwa, C.: Greening manufacturing practices in a continuous process industry: case study of a cement manufacturing company. J. Eng. Des. Technol. **13**, 94–122 (2015). <https://doi.org/10.1108/JEDT-04-2014-0019>
- <span id="page-9-3"></span>5. Page, M.J., et al.: The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ **n71** (2021). <https://doi.org/10.1136/bmj.n71>
- <span id="page-9-4"></span>6. Elsevier | An Information Analytics Business. [https://www.elsevier.com/.](https://www.elsevier.com/) Accessed 03 Oct 2022
- <span id="page-9-5"></span>7. Nagy, B., Galata, D.L., Farkas, A., Nagy, Z.K.: Application of artificial neural networks in the process analytical technology of pharmaceutical manufacturing—a review. AAPS J. **24**(4) (2022). <https://doi.org/10.1208/s12248-022-00706-0>
- <span id="page-9-14"></span>8. Hengelbrock, A., et al.: Digital twin for HIV-Gag VLP production in HEK293 cells. Processes **10**(5) (2022). <https://doi.org/10.3390/pr10050866>
- <span id="page-9-7"></span>9. Sharma, A., Khamar, D., Cullen, S., Hayden, A., Hughes, H.: Innovative drying technologies [for biopharmaceuticals. Int. J. Pharm.](https://doi.org/10.1016/j.ijpharm.2021.121115) **609** (2021). https://doi.org/10.1016/j.ijpharm.2021. 121115
- <span id="page-9-15"></span>10. Domokos, A., Nagy, B., Szilágyi, B., Marosi, G., Nagy, Z.K.: Integrated continuous pharma[ceutical technologies—a review. Org. Process Res. Dev.](https://doi.org/10.1021/acs.oprd.0c00504) **25**(4), 721–739 (2021). https://doi. org/10.1021/acs.oprd.0c00504
- <span id="page-9-16"></span>11. Ley, S.V., Chen, Y., Robinson, A., Otter, B., Godineau, E., Battilocchio, C.: A comment on continuous flow technologies within the agrochemical industry. Org. Process Res. Dev. **25**(4), 713–720 (2021). <https://doi.org/10.1021/acs.oprd.0c00534>
- <span id="page-9-17"></span>12. Sagmeister, P., et al.: Advanced real-time process analytics for multistep synthesis in contin[uous flow\\*\\*. Angew. Chem. Int. Ed.](https://doi.org/10.1002/anie.202016007) **60**(15), 8139–8148 (2021). https://doi.org/10.1002/anie. 202016007
- <span id="page-9-9"></span>13. Vetter, F.L., Zobel-Roos, S., Strube, J.: Pat for continuous chromatography integrated into continuous manufacturing of biologics towards autonomous operation. Processes **9**(3) (2021). <https://doi.org/10.3390/pr9030472>
- <span id="page-9-6"></span>14. Maruthamuthu, M.K., Rudge, S.R., Ardekani, A.M., Ladisch, M.R., Verma, M.S.: Process analytical technologies and data analytics for the manufacture of monoclonal antibodies. Trends Biotechnol. **38**(10), 1169–1186 (2020). <https://doi.org/10.1016/j.tibtech.2020.07.004>
- <span id="page-9-8"></span>15. Kender, R., et al.: Improving the load flexibility of industrial air separation units using a [pressure-driven digital twin. AIChE J.](https://doi.org/10.1002/aic.17692) **68**(7), e17692 (2022). https://doi.org/10.1002/aic. 17692
- <span id="page-9-10"></span>16. Singh, M., Shirazian, S., Ranade, V., Walker, G.M., Kumar, A.: Challenges and opportunities in modelling wet granulation in pharmaceutical industry—a critical review. Powder Technol. **403** (2022). <https://doi.org/10.1016/j.powtec.2022.117380>
- <span id="page-9-11"></span>17. Nkonyana, T., Sun, Y., Twala, B., Dogo, E.: Performance evaluation of data mining techniques in steel manufacturing industry **35**, 623–628 (2019). [https://doi.org/10.1016/j.promfg.2019.](https://doi.org/10.1016/j.promfg.2019.06.004) 06.004
- <span id="page-9-12"></span>18. Helgers, H., Hengelbrock, A., Schmidt, A., Vetter, F.L., Juckers, A., Strube, J.: Digital twins for scFv production in *Escherichia coli*. Processes **10**(5) (2022). [https://doi.org/10.3390/pr1](https://doi.org/10.3390/pr10050809) 0050809
- <span id="page-9-13"></span>19. Beke, Á.K., Gyürkés, M., Nagy, Z.K., Marosi, G., Farkas, A.: Digital twin of low dosage continuous powder blending—artificial neural networks and residence time distribution models. Eur. J. Pharm. Biopharm. **169**, 64–77 (2021). <https://doi.org/10.1016/j.ejpb.2021.09.006>
- <span id="page-10-0"></span>20. Schmidt, A., et al.: Process analytical technology as key-enabler for digital twins in continuous [biomanufacturing. J. Chem. Technol. Biotechnol.](https://doi.org/10.1002/jctb.7008) **97**(9), 2336–2346 (2022). https://doi.org/ 10.1002/jctb.7008
- <span id="page-10-9"></span>21. Chen, Y., Yang, O., Sampat, C., Bhalode, P., Ramachandran, R., Ierapetritou, M.: Digital twins in pharmaceutical and biopharmaceutical manufacturing: a literature review. Processes **8**(9) (2020). <https://doi.org/10.3390/pr8091088>
- <span id="page-10-12"></span>22. Zobel-Roos, S., et al. (2019). Accelerating biologics manufacturing by modeling or: Is approval under the QbD and PAT approaches demanded by authorities acceptable without a digital-twin? Processes **7**(2) (2019). <https://doi.org/10.3390/pr7020094>
- <span id="page-10-1"></span>23. Jittawiriyanukoon, C., Srisarkun, V.: Simulation for predictive maintenance using weighted training algorithms in machine learning. Int. J. Electr. Comput. Eng. **12**(3), 2839–2846 (2022). <https://doi.org/10.11591/ijece.v12i3.pp2839-2846>
- <span id="page-10-2"></span>24. Rohkohl, E., Schönemann, M., Bodrov, Y., Herrmann, C.: A data mining approach for continuous battery cell manufacturing processes from development towards production. Adv. Ind. Manuf. Eng. **4** (2022). <https://doi.org/10.1016/j.aime.2022.100078>
- <span id="page-10-3"></span>25. Jiang, S.-L., Papageorgiou, L.G., Bogle, I.D.L., Charitopoulos, V.M.: Investigating the tradeoff between design and operational flexibility in continuous manufacturing of pharmaceutical [tablets: a case study of the fluid bed dryer. Processes](https://doi.org/10.3390/pr10030454) **10**(3) (2022). https://doi.org/10.3390/ pr10030454
- <span id="page-10-4"></span>26. Ji, C., Sun, W.: A review on data-driven process monitoring methods: characterization and mining of industrial data. Processes **10**(2) (2022). <https://doi.org/10.3390/pr10020335>
- <span id="page-10-5"></span>27. Johansson, M.T., Broberg, S., Ottosson, M.: Energy strategies in the pulp and paper industry in Sweden: Interactions between efficient resource utilisation and increased product diversification. J. Clean. Prod. **311** (2021). <https://doi.org/10.1016/j.jclepro.2021.127681>
- <span id="page-10-6"></span>28. Vaccari, M., et al.: Optimally managing chemical plant operations: an example oriented by [industry 4.0 paradigms. Ind. Eng. Chem. Res.](https://doi.org/10.1021/acs.iecr.1c00209) **60**(21), 7853–7867 (2021). https://doi.org/10. 1021/acs.iecr.1c00209
- <span id="page-10-7"></span>29. Kumar, A., Udugama, I.A., Gargalo, C.L., Gernaey, K.V.: Why is batch processing still dominating the biologics landscape? Towards an integrated continuous bioprocessing alternative. Processes **8**(12), 1–19 (2020). <https://doi.org/10.3390/pr8121641>
- <span id="page-10-8"></span>30. Narciso, D.A.C., Martins, F.G.: Application of machine learning tools for energy efficiency in industry: a review. Energy Rep. **6**, 1181–1199 (2020). [https://doi.org/10.1016/j.egyr.2020.](https://doi.org/10.1016/j.egyr.2020.04.035) 04.035
- <span id="page-10-10"></span>31. Savoska, S., Ristevski, B.: Towards implementation of big data concepts in a pharmaceutical company. Open Comput. Sci. **10**(1), 343–356 (2020). [https://doi.org/10.1515/comp-2020-](https://doi.org/10.1515/comp-2020-0201) 0201
- <span id="page-10-11"></span>32. Shen, K., David, J., De Pessemier, T., Martens, L., Joseph, W.: An efficient genetic method for multi-objective continuous production scheduling in Industrial Internet of Things **2019**, 1119–1126 (2019). <https://doi.org/10.1109/ETFA.2019.8869049>
- <span id="page-10-13"></span>33. From batch to continuous tablet manufacturing: a control perspective—ScienceDirect. https:// [www.sciencedirect.com/science/article/pii/S2405896321017213. Accessed 04 Oct 2022](https://www.sciencedirect.com/science/article/pii/S2405896321017213)