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Technical Paper

Digital twin-enabled automated anomaly detection and bottleneck identification in complex manufacturing systems using a multi-agent approach

Christina Latsou *, Maryam Farsi, John Ahmet Erkoyuncu

Centre for Digital Engineering and Manufacturing, Cranfield University, Cranfield MK43 0AL, UK

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ABSTRACT

Digital twin (DT) models are increasingly being used to improve the performance of complex manufacturing systems. In this context, DTs automatically enabling anomaly detection, such as increase in orders, and bottleneck identification, such as shortage of products, can significantly enhance decision-making to mitigate the consequences of the identified bottlenecks. The existing literature has mainly focused on implementing top-down approaches for analysing the bottlenecks without considering the emergent behaviour of micro-level agents, including inventory levels and human resources, and their impact on the macro-level system's performance. In order to handle the aforementioned challenges, this paper extends the current literature by proposing a novel DT integrated in a multi-agent cyber physical system (CPS) for detecting anomalies in sensor data, while identifying and removing bottlenecks that emerge during the operation of complex manufacturing systems. An extended 5 C CPS architecture, using multi-agent approach, is implemented to allow DT integration. The agent-based simulation technique enables capturing the probabilistic variability, and aggregate parallelism and dynamism of parallel dynamic interactions within the DT-CPS. A new single agent at the exo-level of the multi-level agent-based modelling structure, called the 'monitoring agent', is introduced in this research. The agent detects anomalies and identify bottlenecks through communicating with other agents in different levels automatically. The DT-CPS provides feedback automatically to the physical space to remove and mitigate the identified bottlenecks. The proposed DT based multi-agent CPS has been tested successfully on a real case study in a cryogenic warehouse shop-floor from the cell and gene therapy industry. The performance of the studied cryogenic warehouse is continuously measured using real-time sensor data. The analyses of the results show that the proposed DT-CPS improves the utilisation rates of human resources, on average, by 30% supporting decision making and control in complex manufacturing systems.

1. Introduction

The integration of digital twins (DT), cyber physical systems (CPS) and the cutting-edge information technologies, including Internet of Things (IoT), cloud computing, big data processing and Artificial Intelligence (AI), have formed one of the main pillars of the fourth industrial revolution, Industry 4.0 (I4.0) [30]. With the rapid development of digital and information technologies in the Industry 4.0 era, DT in manufacturing sectors and supply chains has grown rapidly, enabling automation, digitalisation and intelligence [59]. Over the last two decades, digital manufacturing has brought great benefits to the entire industry by improving processing quality and reducing production cost in an efficient and dynamic way [34,36]. In digital manufacturing, computational models and simulation techniques play key role in capturing the dynamic behaviour of an asset or process through virtual representations of facilities, information, test equipment, spares and people, including the skills, roles, and priorities of personnel [3,34,36,53].

Although DT was introduced by Grieves in 2003 as a concept for product lifecycle management [11] a fast growth of this model has been mostly observed in the last five years [34,36]. DT, thus, progressively moves from its infancy to a stage of quick transformation where real industry applications and technologies are investigated. Haag and Anderl [13] defined DT as "a comprehensive digital representation of an

* Corresponding author.
E-mail address: christina.latsou@cranfield.ac.uk (C. Latsou).

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individual product that plays an integral role in a fully digitalised product life cycle". Similarly, CPSs represent an emerging research area due to the increasing importance of the interactions between interconnected computing systems and the physical world [47]. CPSs can be described as a computer-based control system with an integrated network of hardware devices and software platforms [57]. Physical devices communicate within the cyber network through a transportation layer of an IoT infrastructure. CPSs enable the connectivity between physical and computational domains over the Internet and provide access to information and application services for the user [24]. CPSs and DTs can provide manufacturing systems with greater efficiency, resilience and intelligence [47]. In the context of CPSs, DTs can be defined as a cyber-representation of a real system in real time. Tao et al. [47] have discussed the importance of integration of CPSs and DTs, highlighting the differences and correlation between them. According to ISO 23247-1 [21], in the context of manufacturing sector, among other purposes, DTs are intended to improve the manner in which a process or system is designed, manufactured and operated. Similarly, CPSs are intended to support system integration and DT implementation by monitoring and controlling physical manufacturing systems and cyber-supporting systems with the help of a computing and communication core. In this research work, DT is employed to improve the operation of complex manufacturing systems, while CPS to support DT implementation by monitoring and controlling complex manufacturing systems via the integration of sensing (i.e. RFID) and computing devices.

Despite the plethora of academic and industrial research, DT has not yet been properly understood and adopted by many industries, as several challenges are identified in the literature in the development of accurate DTs. Considering the existing literature, mechanisms to enable automated anomaly detection, bottleneck identification and response in DTs in manufacturing are limited and relatively new [50,54]. Neglecting the detection of anomalies (i.e. deviations from expected behaviour) or identification of bottlenecks (i.e. work stages that cannot meet the desired outcome and hence stop or slow the system's operation) limits the purpose of DTs to act as enablers for enhanced asset or process performance [15]. Current research on anomalies detection and bottlenecks analysis is typically conducted using top-down approaches, lacking a formal comprehensive method for capturing emergent behaviours in complex manufacturing systems [32,40]. Moreover, in the context of DT-CPS for complex manufacturing systems, the literature on the development of models and architectures for integrating DTs in CPSs is sparse and relatively new [26,47]. The architecture of integrated DT-CPS can be composed of multiple digital representations for different cyber-elements. The agent-based modelling technique can be applied effectively to develop a multi-agent CPS [26,8]. The challenge in DT-CPS is to develop an integrated DT architecture that aggregates multiple cyber elements and allows data communication and integrity within a multi-agent CPS. However, the development of advanced computational models and simulation techniques to design modular and comprehensive DTs for complex manufacturing systems is also scarce [26,39,7]. Additionally, the literature emphasises on the importance of a bidirectional flow of information between physical and cyber spaces in which the change in one space in one entity is directly reflected in another entity and vice versa. However, only a limited number of studies facilitates this communication providing feedback automatically from the cyberspace to the physical space for on-demand predictive services [23,34,36,4].

Considering the existing literature on the automated anomaly detection in DTs, the research question considered is: "How can an agent-based technique be applied to develop a DT-CPS to automatically detect anomalies, identify bottlenecks and provide control to remove the bottlenecks in complex manufacturing systems[1]?". This research question is addressed by developing a novel Agent-Based Modelling (ABM) approach for a DT-CPS that can automatically detect anomalous values in sensor data, identify and diagnose bottlenecks that emerge during the system operation and provide feedback to physical space to self-optimise the system's performance by removing the diagnosed bottlenecks. The agent-based technique can be employed to effectively capture the probabilistic variability and aggregate parallelism and dynamism of such interactions, providing a mechanism for automated anomalies detection and dynamic performance evaluation that can improve decision making and control in multi-agent manufacturing systems.

In this work, a multi-agent system is formed by a network of agents[2] that interact and communicate with each other and the environment. Moreover, an agent-based model of a complex manufacturing system consists of macro, exo, meso and micro level agents. A macro-level agent is introduced for modelling the operation of complex manufacturing systems using an ABM approach. Hierarchically, this is the top-level agent of the global manufacturing system design in which exo, meso and micro agents belong, operate and interact to each other. Manufacturing phases are modelled at the exo-level agent as single agents that will always exist within the macro-level agent and communicate with the meso and micro level agents. Manufacturing modules, described as a sequence of activities that are repeated frequently such as picking products or quality control procedures, are modelled at the meso-level agent. These modules are modular and can be deployed in multiple manufacturing phases. ABM approach is employed to simulate the interactive structure of phases and modules. Discrete Event Simulation (DES) modelling approach is additionally employed to model the finite dynamical system of manufacturing processes within each manufacturing phase and module. A bottom-level agent, called micro, is developed using ABM approach for modelling manufacturing components, which are included in the meso, exo and macro level agents. At this level, population of agents are created for manufacturing components such as human, equipment and material resources. At a multi-level ABM structure, in the context of complex manufacturing systems, the detection of anomalies in data, captured from sensors, is carried out by the 'monitoring agent' introduced at the exo-level. Additionally, bottlenecks and their root causes are identified at the micro, meso, exo and macro level agents.

This research work contributes to the literature by proposing a DT-CPS approach, employing the ABM technique, for detecting anomalies in sensor data, and identifying and resolving bottlenecks in multi-agent manufacturing systems in an automated way. By adopting a bottom-up ABM approach for the DT-driven approach and a hybrid ABM-DES technique for real-time simulations, the proposed solution can support decision making and control of complex manufacturing systems, contributing to the automated monitoring of such systems in a flexible, interactive and efficient way. Therefore, the main contributions of this work can be summarised as follows:

[1] It is noted that complex manufacturing systems may consist of several manufacturing phases, modules and components. The complexity of these systems, including labour-intensive processes and random events, may arise from the multiple manufacturing phases in which various activities can be performed simultaneously, resulting in parallel dynamic interactions within the system [7].

[2] An agent may represent people, products, equipment, facilities, or intangible aspects such as task ordering (e.g. a series of activities that compose a manufacturing phase) or a mechanism responsible for monitoring the behaviour of other agents and acting accordingly based on defined rules and conditions. An agent can be, thus, used to accomplish an activity based on resource and time constraints or exercise control by assigning activities, monitoring activities execution, and collecting and combining results.

- A novel DT-CPS model for automated anomalies detection, and bottlenecks identification and removal is developed using a bottom-up ABM technique, by conceptualising the data architecture as a multi-agent system using a UML Class diagram. Moreover, a new simulation model is developed employing the ABM technique (bottom-up approach) by conceptualising the automated anomaly detection and bottlenecks identification in complex manufacturing systems using a UML State Machine diagram.
- This research work expands the research by Farsi et al. [7] by introducing a single agent at the exo-level of the multi-level ABM structure to monitor the performance of the complex manufacturing system. This new 'monitoring agent' can automatically detect anomalies and identify bottlenecks through communicating with other agents in different levels automatically.
- Anomalous values found in sensor data of the system are automatically detected by the proposed 'monitoring agent' at the exo-level. The experienced anomalies may include variations in daily orders and delivery rates, cycle times or faulty product type, batch size, etc. In the case of anomalies being detected, the system's performance is monitored in terms of throughput rates and lead times to uncover bottlenecks emerged from the anomalies and understand the root causes. The emergence of unplanned bottlenecks, identified dynamically at the macro, exo, meso and micro level agents by the 'monitoring agent', is quantified in terms of throughput, lead times, inventory levels, and human and equipment resources utilisations. Moreover, the proposed DT-CPS approach automatically provides feedback to the physical space through the process of self-optimisation. In self-optimisation, the system's parameters at the micro-level agent are autonomously and continuously updated in such a way to manage the identified bottlenecks and improve system's productivity and performance.

The remainder of the paper is structured as: Section 2 discusses the literature review on DT development and simulation approaches for the anomaly detection and diagnosis in manufacturing. The proposed DT based multi-agent CPS structure, data architecture and method including the automated anomaly detection and bottlenecks identification are discussed in Section 3. Section 4 validates the proposed architecture through a case study in a manufacturing system at a Cell and Gene Therapy cryogenic warehouse. The simulation results are verified and validated against actual data obtained from the case study. Section 5 presents a summary of critical discussion on the DT-CPS approach and the simulation outcomes. Finally, the conclusions and future research work are highlighted in Section 6.

2. Literature review

2.1. Anomaly detection in digital twins in manufacturing

The literature behind DTs in manufacturing systems highlights that this emerging technology can effectively contribute to both capture the state of systems in real-time and predict potential anomalies and failures [14,29,64]. According to the survey on anomaly detection techniques, conducted by Rubio et al. [41], DTs create new opportunities to the areas of condition monitoring for anomaly detection,[3] fault detection and diagnosis,[4] and fault prognosis.[5] In this regard, Liu et al. [35], highlighted that DT can: (i) monitor the deviations between collected data and expected values; and (ii) identify anomalies and unwanted variations in performance metrics by reproducing the state of physical entity in virtual space and comparing DT simulated data against collected data. However, only a few research works have been proposed to use DTs for detecting anomalies and performing fault diagnosis in manufacturing [18], while there is still a lack of systematic research on fully employing DT for performing accurate fault diagnosis with standardised data processing flows in complex systems [19].

In the area of fault detection and diagnosis, Jain et al. [22] proposed a DT-based mathematical model and simulation study to detect and identify faults in distributed photovoltaic systems in real-time. MATLAB/Simulink was used for developing the simulation model, employing the piecewise linear electrical circuit simulation toolbox. Additionally, an intelligent digital twin (i-DT) for health monitoring and prognosis of electric vehicle motor, using artificial neural network and fuzzy logic, was presented by Venkatesan et al. [52]. The i-DT model can predict the health and remaining useful life of electric vehicle motors but cannot be updated according to the current status of the motor, i.e., digital shadow. Similarly, Wang et al. [56] proposed a DT reference model for rotating machinery health management, focusing on the dynamic behaviour of rotor system. A model-updating scheme based on parameter sensitivity analysis was employed to enable fault diagnosis and enhance model adaptability. In the same year, Xu et al. [59] developed a DT for fault diagnosis in the development and maintenance phases in a smart manufacturing environment employing deep transfer learning. In this work, a virtual model, simulating the physical system, is developed and data produced from this model is used as the training set for the deep neural network. The training data is then used to build a diagnosis model. The model is developed based on the virtual space simulation rather than the physical system and it is validated by its application to a case study in a car-manufacturing environment. Akin to the two previously discussed works, the actual model developed by Xu et al. [59] is a digital shadow as only unidirectional communication between the physical and virtual entities is enabled [10]. Recently, Q. Xu et al. [60] proposed an Anomaly deTection with DT (ATTAIN) approach to detect anomalies in CPSs. The proposed approach enables the continuous and automated construction of the DT using real-time data acquired from a CPS. ATTAIN considers time constraints by building the DT model as a timed automaton, while captures the spatial and temporal characteristics of input data by implementing Graph Convolutional Networks. Although the model developed is a DT, it remains a challenge to handle complex tasks such as the detection of simultaneous attacks in CPS.

As mentioned earlier, the literature on the development of DTs for smart manufacturing highlights the importance to implement autonomous learning agents [46,54]. This learning capability can help effectively detect anomalies [42] and greatly advance the dependability of the current approaches to develop DTs where the value of knowledge for supporting autonomous operations is mostly ignored [54]. The capability of autonomy in DTs that can be realised if performance is always delivered under any circumstances can, thus, lead to high dependability. Additionally, dependability can be enhanced by predicting future behaviour through self-monitoring, self-diagnosis and self-repair [50].

In the area of autonomous monitoring and control in DTs, Tomiyama and Moyen [49] in their work proposed an architecture for cyber physical production systems (CPPS) to autonomously detect faults and respond to them by maintaining the system's performance at an acceptable level. However, the proposed architecture lacks the capability of handling complexities including parallel interactions and heterogeneity. Moreover, Stark et al. [46] proposed an approach that enables simulating the positions of objects in a smart factory DT, as well self-monitoring and self-diagnosing the status of processes and objects. However, the case study for the mill and the pick-and-place robot assumes that the positions of moving objects used in the DT simulation are updated accurately and continuously in real-time. More recently, Vrabič et al. [54] in their work developed an approach where the learning capability is realised by introducing a learning agent. This agent can detect and diagnose faults to the DT, as well determine a response and

[3] Anomaly detection refers to any observed behaviour of the system that deviates from the expected behaviour as captured by the historical data.

[4] Fault detection and diagnosis is the process of discovering the presence of a fault and tracing its symptoms.

[5] Fault prognosis refers to the capability to use available observations to predict the fault before it occurs.

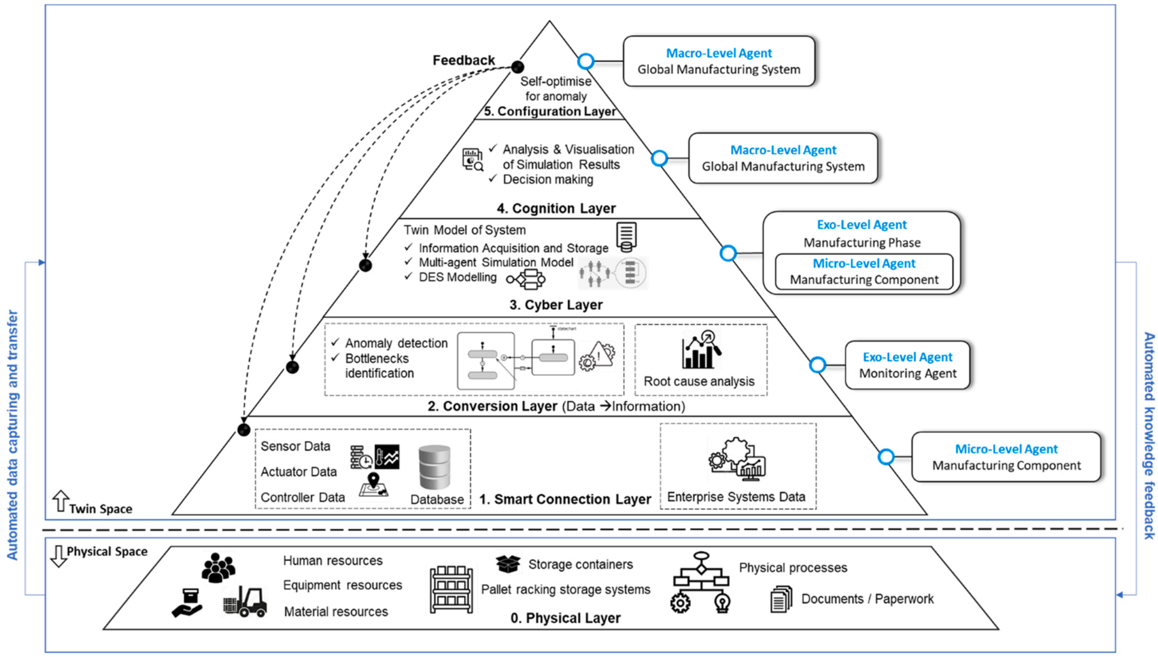


Fig. 1. Digital twin-based multi-agent cyber physical system architecture in manufacturing.

self-adapt the DT. This approach lacks the ability to provide feedback from the virtual to physical system in the form of changes to improve the resilience of the physical system in the presence of faults. The integration of bidirectional flow of data between physical entity and its digital counterpart closes the loop between DT and physical twin and realises digital-physical convergence [1,33]. This bidirectional communication needs to be controllable, i.e., changes on one entity should control the other entity. However, most of the existing works develop digital models or digital shadows as they focus on unidirectional data flow from physical to digital [4]. Therefore, the dynamic and fully integrated bidirectional mapping of data flow from digital to physical after executing DT simulation requires deeper research [33].

2.2. Agent-based approach in the development of digital twins

The adoption of the agent-based approach can play key role in the development of DTs and CPSs [32,38]. ABM offers advanced capabilities including complexity management, decentralisation, intelligence, modularity, flexibility, robustness, adaptation and responsiveness [31,48,9]. In this regard, flexibility and adaptation to changes in DTs are crucial considering the probabilistic variability, and dynamic and highly interactive nature of complex manufacturing systems [7]. In the area of agent-based approaches in DTs and CPSs, Laryukhin et al. [25] proposed a multi-agent approach for the conceptual development of an integrated CPS-DT for managing farms. In this research, a knowledge base with domain ontology, DT agent and data mining methods for supporting decision making of farmers were considered. Moreover, Tran et al. [51] presented an approach for developing a smart cyber physical manufacturing system (CPMS). In their research, cognitive agent technology was integrated enabling the CMPS to have autonomous characteristics such as perception, communication and self-control. More recently, in the context of complex manufacturing systems, Latsou et al. [26] developed a DT architecture integrated in a multi-agent CPMS where the DT represents the data flow for radio frequency identification (RFID) tagged products processed on a shop floor. Furthermore, Zheng et al. [63] proposed a conceptual DT modelling method based on a multi-agent architecture to examine the factors influence the product quality during the manufacturing phase. A multi-agent system component and a semantic engineering component are integrated for the development of the DT approach. Moreover, in the area of dynamic scheduling for smart manufacturing, conceptual models [44] and top-down approaches [12,62] for the development of DTs using agents have been proposed. Similarly, in the context of production systems, Dittrich & Fohlmeister [6] proposed a cooperative multi-agent system using reinforcement learning to handle the complexity of order scheduling and overcome the local optimisation problem. Another research work on multi-agent systems was proposed by Seitz et al. [43] for the development of a CPPS that enables the dynamic organisation of production resources required to execute a production order. The configuration of production resources for enabling the adaptability of an individual facility through (physical) modification is also discussed. With the increasing availability of data, the current literature on agent-based CPSs and DTs gives emphasis to data-driven approaches using artificial intelligence [59,20,45].

Such approaches where the model is composed of multiple digital representations for different cyber elements can facilitate the development of a flexible and adaptable digital architecture. The agent-based approach can, thus, empower the development of such architectures with advanced capabilities and be successfully applied to establish a multi-agent DT [25,26,31]. The challenge, though, is to develop a DT that aggregates multiple cyber elements allowing data communication and integrity within a multi-agent CPS. In this regard, the existing literature shows that the majority of the current approaches discusses the development of multi-agent CPS at a conceptual level.

Moreover, the existing literature suggests that the currently known approaches for developing DT simulations, including mathematical algorithms, ontology-based approaches and discrete-event simulation methods, lack suitability for advanced computational modelling [55,8]. Compared to the other dynamic modelling techniques, i.e., system dynamics and discrete-event, ABM supports a higher degree of autonomy and offers opportunities for a more flexible, interactive and effective approach [31]. Additionally, hybrid system design and engineering approaches are proposed as a suitable technique for the specification and analysis of DTs due to the limitation of individual methods [25,8]. The bottom-up approach and the multi-agent structure of ABM can, thus, provide innovative opportunities in the development of DT simulation models through computational experiments, what-if scenarios, and prediction for decision making support, offering prospects for reduced complexity, high modularity and flexibility [37,45].

3. Digital twin-multi agent cyber physical system development in manufacturing

Deployment of mechanisms to dynamically analyse the operational conditions of complex manufacturing systems is an ongoing research topic. To address the complex, dynamic and highly interactive nature of manufacturing systems, this work presents a DT-CPS architecture, model and method that enhance the interactivity between physical and cyber spaces and allow data communication within a multi-agent CPSs. The proposed architecture of the integrated DT in a multi-agent CPS is discussed in detail in Section 3.1. This is followed by the data architecture of the DT-CPS in Section 3.2. The method employed to formulate mathematically the DT-CPS to derive formal results is discussed in Section 3.3.

3.1. Digital twin-based multi-agent cyber physical system architecture

A well-known CPS structure that has been adopted by Jay Lee et al. [28] is proposed to build the DT-CPS architecture of complex manufacturing systems. The architecture considers a sequential workflow from data capturing and storage to development of simulation model as exact replica of the system in the physical space and analysis of the simulation results to gain insights for informed decision making. The DT is governed by the same control inputs as the system in the physical space, while automated knowledge feedback from the cyber to the physical spaces is provided for performance improvement. A dynamic system of multi-agents is deployed to model DTs for complex manufacturing systems. Additionally, the ABM approach, adopted by Farsi et al. [7] and extended by introducing the 'monitoring agent', has been selected to create the global manufacturing system, multiple manufacturing phases, 'monitoring agent' and manufacturing components. The architecture of the integrated DT-CPS, as illustrated in Fig. 1, is outlined as:

3.1.1. Physical layer

Physical layer can be referred to any physical component including resource, system or process that is relevant to a given manufacturing system or installed at the shop floor and exists at the two spaces: the physical space and the twin space. Physical layer may include human, equipment and material resources, plants or facilities, storage containers and pallet racking storage systems, physical processes (e.g. picking, storing or assembling products, etc.), documents or paperwork (e.g. checklists and forms to perform inventory or quality assurance audit, etc.).

3.1.2. Smart connection layer

Smart connection layer is used to capture data measured directly by sensors, actuators or controllers, or obtained from enterprise manufacturing systems (e.g. product lifecycle management (PLM), enterprise resource planning (ERP), manufacturing execution systems (MES), etc.). Reliable integrated data management solutions should be developed to enable effective collection and efficient transmission of data acquired from various fixed or mobile sources such as ERP, MES or sensors. The diversity of data sources and data latency, the different data types, heterogeneous structures and various dimensions, as well as the representation of structured, semi-structured and un-structured data, are, among others, key aspects in data acquisition that should be considered. In terms of the ABM approach, data acquired in the smart connection layer is referred to as manufacturing components, modelled at the micro-level agent. A *database* at this level is employed for storing the remotely collected sensor data (e.g. quantity of material resources, cycle times, etc.) for tracking and tracing physical components at a manufacturing system. Additional data available from enterprise systems refers to the status of human, equipment and material resources, inventory size, storage capacity, etc.

3.1.3. Conversion layer

Conversion layer can be referred to as all the physical processes to convert data into information. Once the data is acquired in the smart connection layer, data processing, including filtering process, artificial intelligence-based processing and data analytics, is required to transform the data into information. This information, revealing key failures, brings self-awareness to physical components (e.g. product, machine, equipment, facility, etc.) and can later help users take actions to increase system's performance. In this work, a novel 'monitoring agent' has been introduced at the exo-level agent to dynamically detect anomalies in the sensor data of the *database*, identify bottlenecks related to resources availability, inventory levels and storage space availability and analyse their root causes. Bottlenecks may occur due to obstacles or delays at different locations and times within the manufacturing system that slow processing physical components. Such root causes can be identified by measuring performance metrics, including work in progress, waiting time, lead times, utilisation levels of resources, throughput or available inventory, and comparing these to historical data of the daily operations of the manufacturing system. Monitoring agent is, thus, able to provide self-awareness and self-prediction to physical manufacturing system in terms of anomalies detection, bottlenecks identification and root cause analysis of the latter.

3.1.4. Cyber layer

Cyber layer operates as a central hub of information that is acquired from the connection layer, stored and processed to develop the cyber twin model of system in the twin space (see Fig. 1). Information from every physical component for sharing and exchanging data is being stored in an *information base* at the micro-level agent. This helps create the network of all connected physical components. *Information base* may store the conditions under which an anomaly has been detected (e.g. date, time and location within the manufacturing system), equipment failure types, downtime and repair status, processing times of materials/products, etc. Utilising this information, cyber avatars for physical components can be created. Advanced data analytics can be then employed to extract knowledge from these avatars, providing insights beyond the status of individual components. Knowledge will be aggregated to the components information to monitor their status and generate the cyber twin of each component. The performance of these cyber-twin components can then be compared to relevant historical information to predict their future behaviour. For managing and analysing information effectively, a hierarchical structure to develop the cyber twin model of manufacturing systems is proposed. The hierarchy of ABM approach in the cyber layer consists of exo and micro level agents for modelling the manufacturing phases and manufacturing components (i.e. *information base*), respectively. Meso-level agent, if repeated manufacturing modules exist, may be also considered. Cyber layer provides the necessary data analytics to the cognition layer.

3.1.5. Cognition layer

Cognition layer is employed to transfer knowledge to the users to make appropriate decisions for improving system's performance and productivity. Cognition of the monitored manufacturing system is achieved by thoroughly analysing and effectively visualising the results obtained from modelling and simulating the twin model as discussed in the cyber layer. Results in terms of anomalies detection, bottlenecks identification with root cause analysis and a comparison of these results against corresponding historical data to show deviations can be presented. Key performance indicators of manufacturing system, phases and components that can be also visualised in this layer may include system's throughput, lead time, work in progress, utilisation of human and equipment resources, available storage space and stock size of material resources. These indicators are obtained at macro, exo, meso and micro level agents. Thus, throughput of the manufacturing system is

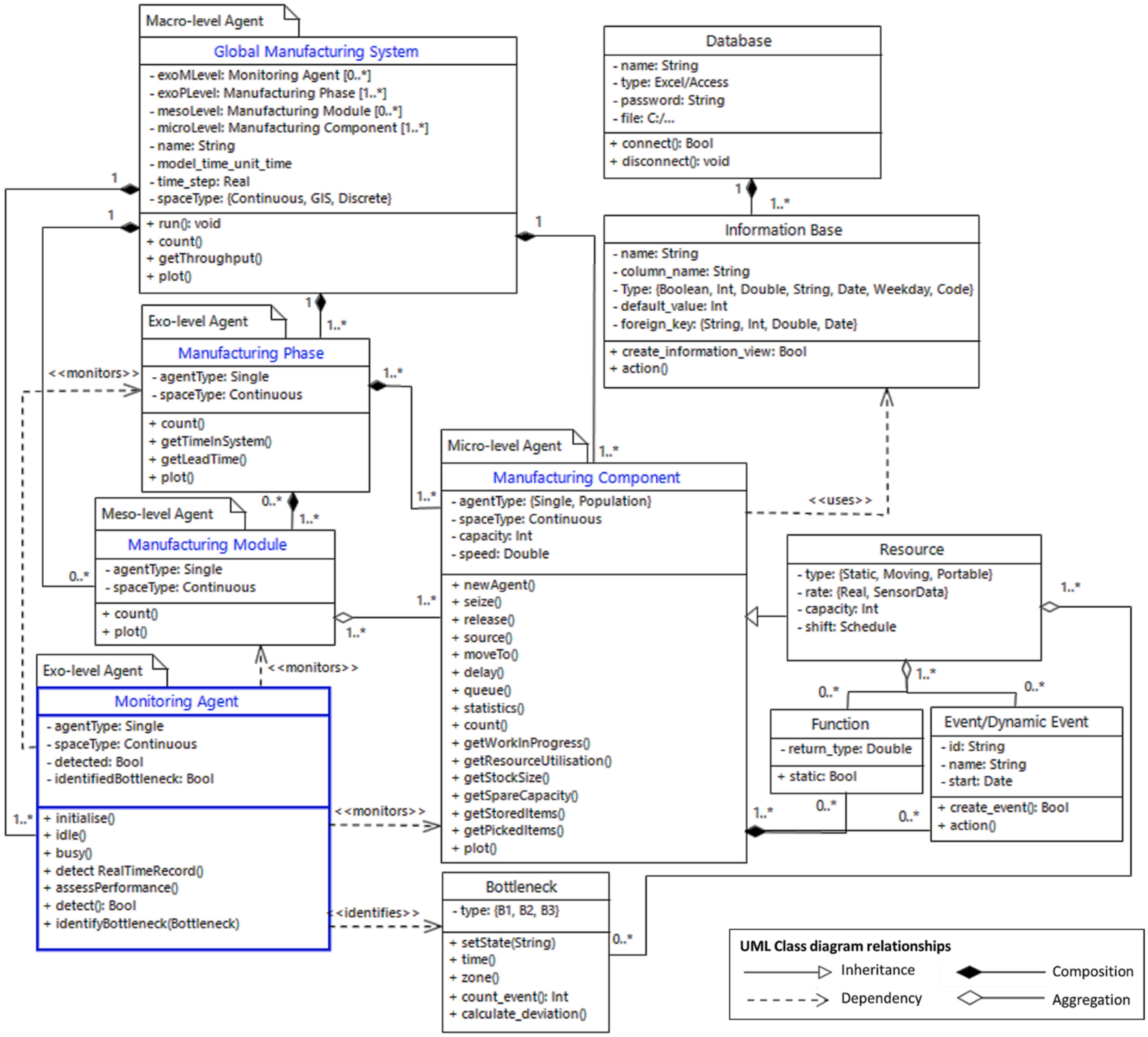


Fig. 2. UML class diagram of digital twin based multi-agent cyber physical system model in manufacturing.

obtained at the macro-level agent. Lead times and time in system are obtained at the exo and meso level agents, while anomalies detection, resources utilisation, work in progress, available storage spaces and stock sizes at the micro-level agent.

3.1.6. *Configuration layer*

Configuration layer acts as an intelligent control for self-configuration of resilience, self-adjustment of variation or self-optimisation of anomalies [28], by providing feedback to the smart connection, conversion and cognition layers, as seen in Fig. 1. The feedback, obtained at the macro-level agent of the manufacturing system, should be implemented at the other agent levels automatically to create a synchronised DT. Feedback in manufacturing systems can be applied to achieve optimal throughput, resource planning, initial inventory capacity and inventory control, dispatch planning and space layout planning or job order control. This work focuses on finding a decision strategy that proposes the optimal solution, e.g., for the real-location of human or equipment resources, optimal initial inventory level or storage space, to eliminate the bottlenecks caused by anomalous values in input sensor data as identified in the conversion layer. Feedback to the smart connection layer is applied to the micro-level agents which are updated based on the optimal solution; to the conversion layer is employed to check if the bottleneck remains in the system; and to the cyber layer to simulate the cyber-twin model with the updated parameters at the micro level and obtain updated results visualised in the cognition layer. This process stops only if the bottleneck is eliminated, otherwise, a new self-optimisation for handling anomalies and their emergent bottlenecks is performed.

Communication between physical and twin spaces for automated data capturing and transfer (left arrow in Fig. 1) and knowledge feedback (right arrow in Fig. 1) can be realised through wired or wireless network connections. The network coverage for accessing these networks and transmitting data can be enabled using personal area networks (PAN), local area networks (LAN), or wide-area networks (WAN) based on the characteristics of physical system, digital twin purpose and environmental conditions. In this work, a server computer in the physical system holds the sensor data repository system (e.g. relational or non-relational databases, data lakes, etc.). If several manufacturing sites exist, such as in a supply chain, one server computer should exist at each site. The sensor data repository system should provide improved performance, security and excellent data restoration and recovery mechanism. For allowing any device, from desktop computers to smartphones, connected to the same network to view and process the stored sensor data, each server computer can run a web service. Moreover, the sensor data repository system can be hosted on a cloud computing service, enabling cross-site communication and providing interconnection between different devices and sites. Seamless exchange of data between the sensor data repository system and *database* can be enabled through Application Programming Interfaces (API). Similarly, the knowledge feedback obtained from the cyber space is automatically available to the operators at the physical space i.e., shop floor (right arrow in Fig. 1). The implementation of this feedback in manufacturing systems for realising improvement in the operation of the system requires human intervention at the shop floor. A mechanism for enabling real-time data exchange can enhance the responsiveness in process monitoring and operation optimisation. Real-time DTs are linked to the frequency so called twinning rate at which control process or decision making is required or realised by the DT. In this study, control refers to the process at which a state or data changes frequently (i.e. seconds to hours) and handling is needed to control the process. For instance, quality control in manufacturing often requires immediate action to eliminate defects in production.

3.2. Data architecture of digital twin-based multi-agent cyber physical system

The data architecture of the multi-level agent-based structure, illustrated in Fig. 1, is discussed in this section. The DT-CPS model, employing a bottom-up ABM approach, is conceptualised using the UML Class diagram in Fig. 2. The proposed simulation method defines a hierarchical agent-based structure of the DT-CPS model where any agent is living within another agent and can host populations of other agents. In this work, the model consists of four levels of agents: macro, exo, meso and micro, as viewed in Fig. 1 and blue blocks in Fig. 2. The global manufacturing system is composed of one or more manufacturing phases, monitoring agents, manufacturing components, and zero or more manufacturing modules (composition relationships). Similarly, each manufacturing phase is composed of one or more manufacturing components, while owning zero or more manufacturing modules. Each manufacturing module can have one or more manufacturing components (aggregation relationship).

The 'monitoring agent', hosted by the macro-level agent for modelling the manufacturing system, is introduced within the exo-level agent using ABM approach. The role of this agent is to provide a mechanism to constantly monitor the behaviour of manufacturing components of the *database* (i.e. the sensor data) at the micro-level agent (dependency relationship) and detect anomalies in this data by comparing it with corresponding values obtained from the steady state performance of the system. Anomaly is, thus, any deviation between the behaviours of the sensor data and expected behaviour (i.e. historical data). The experienced anomalies can consider variations in daily orders and delivery rates, cycle times, product type, batch size, etc. Exo-level agent can also identify unplanned *bottlenecks*, as indicated by the dependency relationship that emerge from the detected anomalies, by comparing a set of performance metrics (e.g. lead times, work in progress, resources utilisation rates, etc.) with a set of properties of the expected behaviour of the physical system (i.e. historical data). *Bottlenecks*, are measured in terms of throughput at the macro-level agent, time in system and lead times at the exo and meso levels, and inventory levels or resource utilisation rates at the micro-level agent. A state machine diagram, using the Nondeterministic Finite Automata formalism, is developed to automatically detect anomalies and identify bottlenecks in complex manufacturing systems. *Bottlenecks* can be modelled as variables at the 'monitoring agent' to store information obtained from the bottlenecks identified during the system's operation including when (date and time), where (location at the manufacturing shop floor) and what type of bottlenecks has been identified. The types of bottlenecks can be associated to shortage of human resources (type B1), equipment resources (type B2) or material resources/storage space (type B3).

Moreover, the ABM approach is also employed to model the inherent complexity of manufacturing phases and modules, by developing an individual or single agent for each manufacture phase and module, respectively. Exo-level agents are created considering how the manufacturing phases operate over time. The 'monitoring agent' and manufacturing phases, created at this stage, can communicate and interact in parallel to each other during simulation. Similarly, meso-level agents are introduced as a single agent to simulate the interactive structure of repeated manufacturing modules. The 'monitoring agent' monitors the behaviour of manufacturing phases and modules, as indicated by the dependency relationships. Performance measures captured by the operation of manufacturing phases and modules in terms of lead times and time in system are automatically realised by the 'monitoring agent' to analyse emergent *bottlenecks* within the system. Additionally, at this stage, DES approach is used within each agent created for each manufacturing phase and module. DES modelling approach is employed to model the operation of each manufacturing phase and module, at the exo and meso level agents, respectively, as a sequence of activities that occur over time and capture the changes observed in the system state.

Similarly, to enable the 'monitoring agent' to measure *bottlenecks* at the micro-level agent, population of agents are created for manufacturing components such as human, equipment and material *resources*, inventory-related information, etc. The characteristics of each micro-level agent can be represented by parameters for specifying the type, unit, capacity and rate of the agent; and shift schedules for defining how some value changes in time according to the defined pattern. Other elements including *functions* that return the value of an expression every time it is called from the model, *events* used to schedule some action in the model or modelling delays and timeouts, and collections to define data that group multiple elements into a single unit are also included at micro-level, determining the interactions between agents. Thus, each manufacturing component owns zero or more functions and events (composition relationship). Each *resource* is a manufacturing component (inheritance relationship), while having zero or more *functions*, *events* and bottlenecks (aggregation relationships). Key element in the presented architecture is a built-in integrated database that captures multidimensional (e.g. asset, time, activity) and heterogeneous data from multiple time periods from physical components. This is accomplished with the help of sensors, actuators or controllers located at the manufacturing shop floor. *Database* element included at micro-level agent reads data from the sensor data repository system, as discussed in the smart connection layer in Section 3.1. This data may include date, time and location of data created, contact details of suppliers and recipients, order number, delivery location, sample types, batch number, container type, etc. The file holding this data is automatically updated at a regular basis retrieving new data from the sensor data repository system via APIs. An *information base* that retrieves data from the *database*, stores in a structured form and processes it is then generated dynamically. Each *database* is composed of one or more *information bases* (composition relationship). For the data to create meaningful information, such as date and time stamps, processing times of products or equipment failure types and repair status, retrieved data is further processed to create the *information base*. The latter is the result set of a query on the data stored in the *database*. The *information base* is at the micro-level agent and its contents are used by the manufacturing components (dependency relationship) and, by extension, by the manufacturing phases and modules at exo and meso level agents to mimic the behaviour of physical components.

Moreover, variables or collections are used to store the simulation results of the manufacturing system, manufacturing phases, modules and components. Such variables are used to measure system's throughput at macro-level agent, time in system and lead times at exo and meso level agents, and resource utilisation levels for people and equipment, work in progress, number of stored and picked items, stock

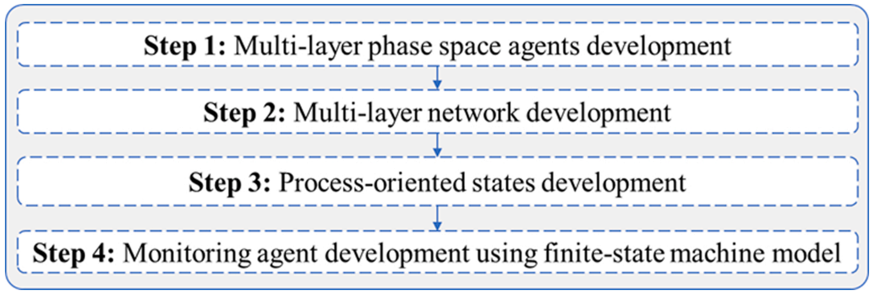


Fig. 3. DT-CPS: multi-agent simulation method.

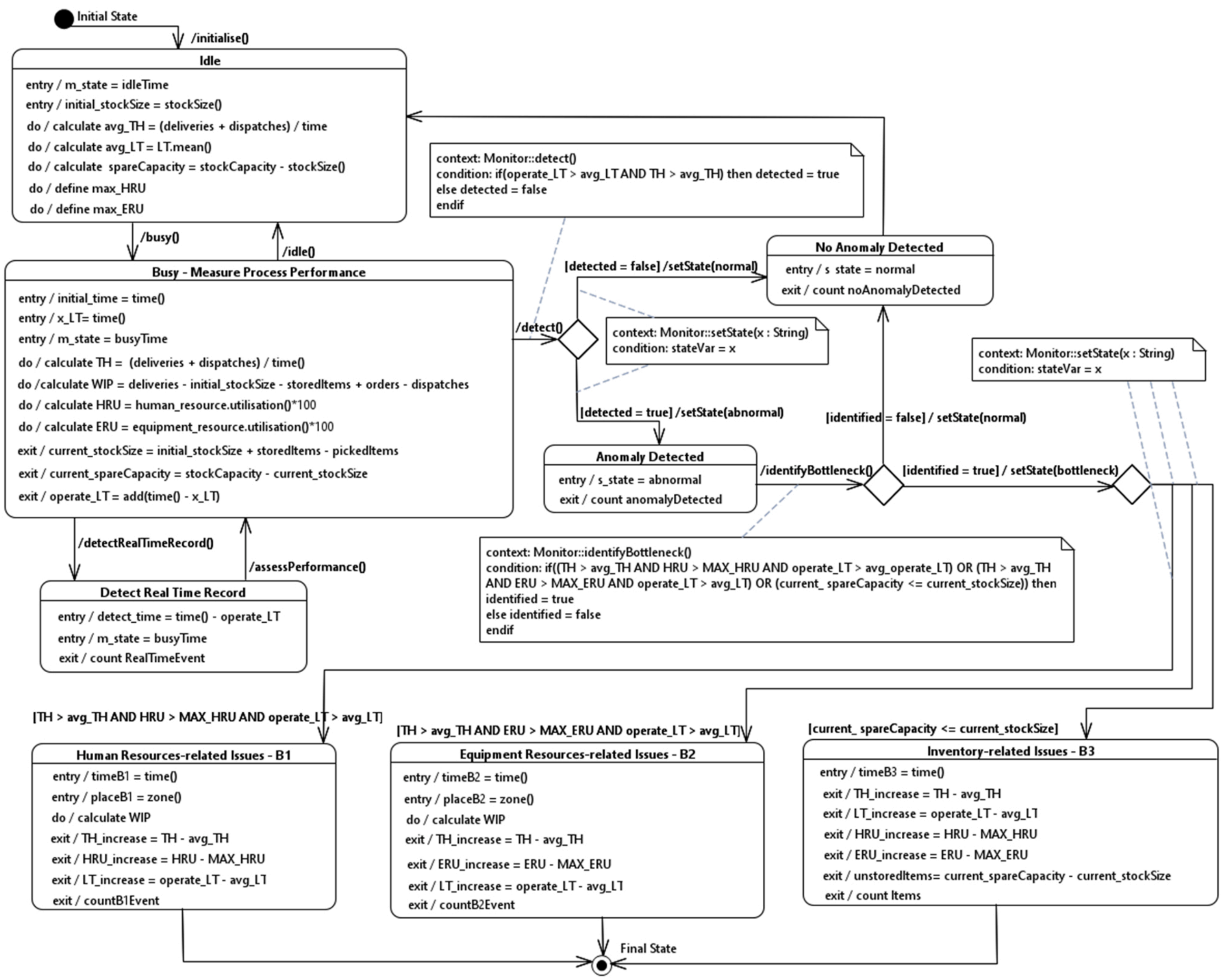


Fig. 4. UML state machine diagram of the monitoring agent for automated anomaly detection and bottlenecks identification in manufacturing.

size and space storage capacity at micro-level agents. Plots can be also employed at all levels of the multi-agent model to graphically display how variables change over time capturing the dynamic behaviour of complex manufacturing systems. Visualising the simulation results and performing self-optimisation of the global manufacturing system in the cognition and configuration layers, respectively, (see Fig. 1) generates knowledge to inform decision makers about the current or future state of the physical system. The added value of knowledge can be provided through real-time monitoring and data analysis, performance evaluation, bottlenecks identification and self-optimisation. Employing the multi-agent ABM approach, knowledge provides actions to physical space in the form of feedback, for making corrective and preventive decisions for performance improvement. According to the knowledge, generated from the cyber space, human intervention is required in the manufacturing shop floor for developing actions to synchronise the communication between physical and cyber spaces and realise improvement in the rectification, optimisation, and resilience of the physical space.

In this work, the anomalies are identified in the remotely collected sensor data that measures the physical position or state of physical components in a manufacturing system. Any identified anomaly that can lead to the emergence of unplanned bottlenecks requires action to meet the demand of the physical system. The proposed DT-CPS is able to continuously update the cyber space, generate knowledge and actuate this as productive feedback to its physical space. Therefore, if an anomaly is detected, the integrated DT-CPS is updated accordingly. As previously discussed, anomaly detection is enabled by the 'monitoring agent' at the exo level (conversion layer in Fig. 1) that determines how the sensor data, obtained from the *database* at micro-level agent (smart connection layer), deviate from expected behaviour. If a bottleneck is then identified by the 'monitoring agent', the simulation model (cyber layer) provides results for the impact on the performance of the physical system which are visualised and realised at macro-level agent as knowledge (cognition layer). In this study, knowledge such as the identification of bottlenecks needs further action to be removed and optimise the system's performance. The model is able to perform self-optimisation of the global manufacturing system at macro-level agent (configuration layer) and find the optimal reallocation of resources, initial inventory level or storage space that would reduce the eliminate the identified bottleneck. The optimisation results (i.e. number of resources, stock size and storage space), obtained at the macro level, automatically update the associated parameters at micro-level agent (smart connection layer). The 'monitoring agent' and simulation model in the conversion and cyber layers, respectively, are also updated based on the optimised parameters and new results are obtained. The simulation and optimisation methods are carried out until the associated bottleneck has been removed. In this work, for the decision and realisation of knowledge in the physical space (i.e. manufacturing system), managers and operators are responsible to take actions considering further economic, environmental and social impacts. What-if scenarios can also be explored off-line with the help of flexible and customisable dashboards. Such dashboards can be used to perform different scenarios and evaluate the system's performance by modifying the input parameter values of the simulation model. Overall, knowledge may allow for better performance simulation, monitoring and visualisation, diagnosis and prognosis, scenarios analysis, optimisation and decision making for resource planning, time-in-system and dispatch planning. Cloud-based applications can also allow multiple users with remote access to the digital twin to explore various scenarios.

Deploying a multi-level ABM method, decision makers gain a better understanding of system structure, operation and abilities, as the multiple agents of a system are specified at various scales providing system granularity. Additionally, ABM and DES approaches are able to capture the dynamic behaviour and interdependencies in complex manufacturing systems. The mathematical formalism of the DT-CPS method is discussed in Section 3.3. In this section, a generic conceptual model of the 'monitoring agent' for detecting anomalies and identifying bottlenecks in complex manufacturing systems is also presented.

3.3. Digital twin-based multi-agent cyber physical system method

A hybrid agent-oriented and process-oriented approach has been employed in the proposed DT-CPS architecture to model and then simulate the complex nature of manufacturing systems. The process followed to develop the hybrid multi-agent ABM-DES simulation method for detecting anomalies and recognising any associated bottlenecks in a dynamic and automated way is composed of four steps, as outlined in Fig. 3. As mentioned earlier, this work extends the hybrid simulation method proposed by Farsi et al. [7] that employs an ABM-DES technique to simulate a dynamic system of parallel multi-agent discrete events. In the current work, the hybrid ABM-DES simulation method is extended by introducing the 'monitoring agent' at the exo-level of the multi-layer ABM structure. In this section, the steps of the proposed multi-agent simulation method will be discussed. A more detailed explanation for steps 1–3 can be found in Appendix, Section 1 and the work proposed by Farsi et al. [7].

This section emphasises on step 4 of the proposed multi-agent simulation method, i.e., on the development of the 'monitoring agent' using finite-state machine model. Thus, an agent-based simulation model is proposed to create the 'monitoring agent' at the exo-level that continuously observes the behaviour of the micro, meso, exo and macro level agents, while real-time sensor data is captured by the database at the micro-level agent. The UML State Machine diagram, as shown in Fig. 4, is used to model the dynamic nature of the proposed agent-based model for automated detection of anomalies in the input data and for identification of any unplanned associated bottlenecks in complex manufacturing systems. The anomalies in input data are detected through a set of system's parameters considering variations in deliveries or orders, or delivery of the wrong quantity of products, or increased cycle times, i.e., time required for human resources to complete an activity (e.g. receive, store or dispatch products). The system throughput rates and lead times of the manufacturing phases are then measured to investigate if the anomalies create bottlenecks to the manufacturing system. In this study, the bottom-up ABM technique is selected to simulate the exo-level agent so called Agent () class. The Agent class consists of *states* that represent a location of control with a particular set of reactions to conditions and/or events, and *transitions* that denote a switch from one state to another. Three subclasses of Transition () class are considered, which based on their trigger type can be categorised into Condition (<TransitionCondition>), Message (<TransitionMessage>) and Rate (<TransitionRate>) subclasses. Moreover, *actions* can be associated with transitions, and with entering and exiting states. Thus, within each state, three types of actions can be defined, including (<EntryAction>) and (<ExitAction>) that are executed when the statechart enters and exits the state respectively, and (<DoAction>) to calculate performance indicators. All these state actions use data from the micro, meso and macro level agents, as well as from the exo-level agents of the manufacturing phases where a sequence of activities are carried out.

Considering a complex manufacturing system, the UML State Machine diagram, in Fig. 4, starts with an 'Initial State' entry point. Once *initialise()* transition is triggered, 'Idle' state is activated and average values for throughput (TH) and lead times (LTs) measured in various parts in the manufacturing system are obtained. This data can be obtained from: (i) databases where recorded historical data, including resources utilisation, operating conditions and lead times, has been stored; (ii) business process management software systems (e.g. PLM, ERP, MES, or other DTs); or from (iii) user data that is collected from human input while monitoring the operating levels of the physical asset.

Employing the modified format of Little's Law proposed by Hopp and Spearman [17], the system's throughput (macro-level agent) can be formulated:

$$TH = \frac{WIP}{LT} \tag{1}$$

where WIP is the work in progress i.e., the average number of items processed in a specified part of system per unit time; and LT is the lead time i.e., the average time an item spends as WIP. The system's WIP (micro-level agent) can be calculated as:

$$WIP = \sum_{i=1}^{n} del_i - \sum_{i=1}^{n} stc_{ini} - \sum_{i=1}^{n} sr_i + \sum_{j=1}^{m} ord_j - \sum_{j=1}^{m} dis_j \tag{2}$$

where del_i is the number of delivered items for $i = 1, \ldots, n$, stc_{ini} is the initial stock size of stored items, sr_i is the number of items stored after delivered items are received, ord_i is the number of received orders and dis_i the number of dispatches for $j = 1, \ldots, m$. Moreover, the stock size ($Stock_{size}$) at the micro-level agent can be calculated as:

$$Stock_{size} = \sum_{i=1}^{n} stc_i - \sum_{i=1}^{n} sr_i - \sum_{i=1}^{n} pck_i \tag{3}$$

where stc_i is number of stored items and pck_i is the number of items picked from storage for further processing, packaging or dispatch. The stock size (i.e. item readily available) and stock capacity (i.e. total volume of items that can be stored), retrieved from the micro-level agent, are used to calculate the storage spare capacity in the system, expressed as:

$$Spare_{capacity} = Stock_{Capacity} - Stock_{size} \quad (4)$$

The lead time (exo-level agent) of i-th item to complete a process can be thus:

$$LT_{operate} = \frac{1}{N}\sum_{i=1}^{N} W_i \quad (5)$$

where W_i is the difference between the start time and end time for the i-th item for $i = 1, 2, \ldots, N$, and N is the number of items in a batch. In addition, maximum allowable levels for the utilisations of human resources (HRU) and equipment resources (ERU) at the micro-level agent are defined. The rate of resource utilisation can be expressed as:

$$RU = \sum_{i=1} \frac{bill^{i}_{hrs}}{av^{i}_{hrs}} * 100 \quad (6)$$

where $bill^{i}_{hrs}$ is the total billable hours of i-th resource; and av^{i}_{hrs} is the number of total available hours of ith resource (e.g. based on the shift schedule).

When inputs, i.e., deliveries and/or orders are captured by the micro-level agent, *busy()* transition fires and 'busy' state where the system performance is measured is activated. The 'busy – measure process performance' state can dynamically calculate several metrics including stored items, items picked from storage, TH, WIP, HRU, ERU, stock size, spare capacity and operating LTs. Once real-time data is detected at the micro-level agent, *detect Real Time Record()* transition fires and 'detect Real Time record' state is activated and parameters associated to the real-time data, including tag ID, date and time stamps, location and user ID are detected. The model via *assess Performance()* transition moves back to 'busy' state. At this point, the *detect()* transition is enabled and the performance of the manufacturing system is assessed by comparing the real-time sensor data and performance metrics (i.e. TH and operating LT at macro and exo level agents, respectively) against average nominal values that either are provided as inputs to the model or derived from historical data (e.g. ERP system). If the performance metrics are greater than the nominal values, an anomaly is detected (i.e. *set State (abnormal)* transition is enabled) and the system state is set as disrupted, otherwise as normal (i.e. *set State(normal)* transition is enabled). Based on the state, 'Anomaly Detected' state or 'No Anomaly Detected' state is activated, respectively. The latter state leads to the 'idle' state, whereas if an anomaly is detected, the *identify bottleneck()* transition is triggered and the simulation model explores if the anomaly may cause potential unplanned bottlenecks related to human resources, equipment resources or inventory. A bottleneck, thus, is identified if:

- TH (macro-level agent) is greater than the average TH, operating LTs (exo-level agent) greater than the average LTs and the rate of HRU (micro-level agent) greater than the maximum allowable HRU rate; or
- TH is greater than the average TH, operating LTs greater than the average LTs and the rate of ERU (micro-level agent) greater than the maximum allowable ERU rate; or
- spare capacity (micro-level agent) equal to the stock size or stock size is less than the number of orders.

If a bottleneck is identified, the *set State (bottleneck)* transition fires and the type of the bottleneck is recognised, otherwise *set State (normal)* transition is enabled leading to the 'no disruptive event diagnosed' and 'idle' states. Three types of associated bottlenecks are categorised, based on their root causes, into human resources-related issues (type B1), equipment resources-related issues (type B2) and inventory-related issues (type B3), as seen in Fig. 4. Once a bottleneck is identified, various key performance indicators are measured, becoming available to the user. For instance, the time and the activity performed (i.e. zone) when the bottleneck is detected, the WIP, increase in TH, LT and HRU/ERU as well as the number of items cannot be stored due to lack of storage space are obtained from the simulation model, as viewed in Fig. 4.

From a mathematical perspective, a Nondeterministic Finite Automata (NFA), as defined in Hopcroft et al. [16], can be employed to formulate the 'monitoring agent' at the exo-level and derive formal results as:

$$A = (Q, \Sigma, \delta, q_0, F) \quad (7)$$

where Q is a finite set of states, Σ is a finite set of input symbols, δ is the transition function that takes a state in Q and an input symbol in Σ as arguments and return a subset of Q, q_0, a member of Q, is the start state, and F, a subset of Q, is the set of final states.

4. Case study: digital twin-cyber physical system development of a cryogenic warehouse

In this study, a complex manufacturing system of a cryogenic warehouse company in the Cell and Gene Therapy (CGT) sector has been selected as the case study to test the validity of the proposed architecture. The impact of the DT-based multi-agent CPS model on the automated anomaly detection, and bottlenecks identification and removal in complex manufacturing systems is evaluated. The complexity of CGT manufacturing systems, originated from multiple response time requirements and numerous policies and regulations, can result in parallel dynamic interactions within the system. Common example of such parallel interactions is when operators are required to perform manufacturing activities at different locations within the facility at the same time. In this study, radio-frequency identification (RFID) technology has been installed at the cryostorage company for recording, monitoring and auditing of cryomaterials. Devices including sensors, RFID readers and tablets have been used to capture the real-time data from the shop floor.

The approach proposed in this research work is followed to formulate the selected case study. The proposed DT-CPS architecture that represents the data flow of RFID tagged cryomaterials being processed on the shop floor of the studied warehouse is developed in Section 4.1. The dynamic behaviour of the cryogenic warehouse is captured by considering real-time data for performing simulation experiments. AnyLogic software (version 8) has been used to develop the hybrid multi-agent ABM-DES simulation method. The simulation time unit has been set as 'minute'. In Section 4.2, the DT-CPS is validated against actual data obtained from the studied warehouse.

After validation, in Section 4.3, a scenario to assess the impact of the 'monitoring agent', its applicability in relation to the other agents and how it improves the cognition and configuration layers is simulated and analysed. This scenario emphasises on the capability of the 'monitoring agent' to automatically detect anomalous values to sensor data and identify bottlenecks that arise in the system and affect its performance and productivity. Moreover, the automated knowledge feedback provided to the physical space to remove and mitigate the identified bottlenecks is demonstrated. The selected scenario considers increased number of orders, dispatches and time for picking material from cryostorage and assigning it to shippers for dispatch. This scenario has been selected as it captures common challenges faced during the daily practices in the studied cryogenic warehouse. A stochastic data analysis to quantify the uncertainty in lead times is also carried out.

4.1. Digital twin based multi-agent cyber physical system architecture

In this section, the DT-CPS architecture that represents the data flow for RFID tagged products processed on the shop floor of the studied cryogenic warehouse is developed. The studied warehouse is responsible for receiving cryogenic material from manufacturers, storing and

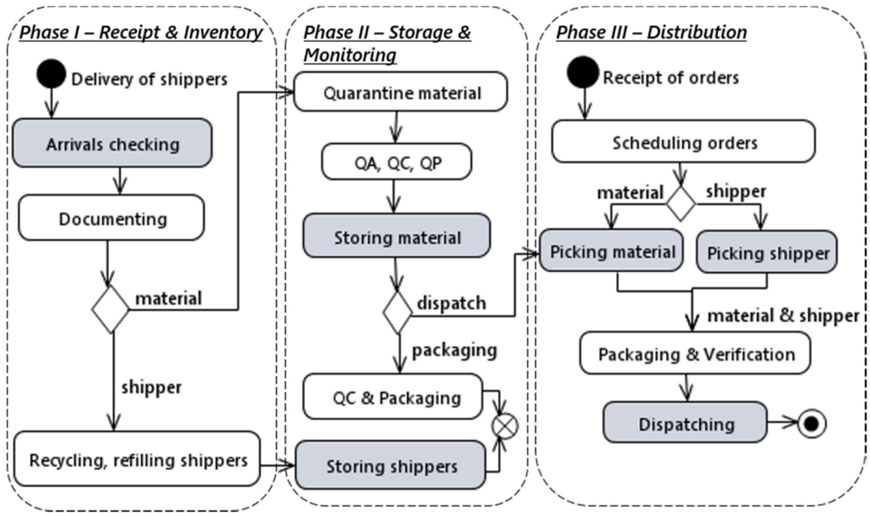


Fig. 5. Case study: UML activity diagram for the CGT cryogenic warehouse; RFID implementation (in blue).

monitoring the material, and dispatching it when requested from manufacturers and healthcare institutions. According to these processes, three manufacturing phases are considered: Phase I – Receipt & Inventory; Phase II – Storage & Monitoring; and Phase III – Distribution. The manufacturing phases act in parallel with the 'monitoring agent' at the exo-level. The 'monitoring agent' interact with the phases to identify bottlenecks, by comparing performance measures (e.g. lead times and time in system) obtained from each phase to the corresponding average numbers observed during the normal daily operations of the cryogenic warehouse. The flow of cryomaterial and information in the warehouse is demonstrated in the UML Activity diagram in Fig. 5. Moreover, RFID devices have been implemented in the areas of goods in, cryogenic storage and goods out of the warehouse, as highlighted in blue in Fig. 5. The DT-CPS architecture as discussed in Section 3.1 is followed.

4.1.1. Physical layer

Physical layer refers to the operators working at the cryostorage company (i.e. human resources), cryocarts and trolleys for the transportation of the cryomaterials on the shop floor (i.e. equipment resources) and cryomaterials and liquid nitrogen (LN2) for the preservation of cryomaterials (i.e. material resources). Moreover, cryovials and cryo/freezer bags for the storage of cryomaterials and packaging items, including boxes for the storage of vials, racks for the storage of bags and boxes, and shippers for the transportation of the biological material within the cryogenic supply chain are considered. Pallet racks for the storage of shippers are also considered. RFID tags are embedded to the containers and packaging items. In this study, three types of RFID readers have been implemented to the shop floor of the warehouse, including: (i) 'shipping readers' for reading dry shipper tags attached to cryostorage containers; (ii) 'proximity readers' for close up reads of bags and racks; and (iii) 'cold 10 × 10 readers' for reading cryoboxes containing up to 99 vials. Each vial slot in the cold readers has a unique antenna, enabling individual readings. All reader types can automatically update the location of stored items without requiring human intervention (i.e. manual data entry). Moreover, the physical processes (e.g. arrivals checking, documenting, picking and storing materials, etc.) carried out on the shop floor are captured, as demonstrated in Fig. 5.

4.1.2. Smart connection layer

Smart connection layer acquires sensor and other input data associated with the operations occur at the shop floor of the cryogenic warehouse. The innovative cryogenic RFID system, integrated at the warehouse, has the ability to read, interpret and process RFID signals. The RFID system, used for the automated data capture, is deployed on MS Azure, a cloud computing service. The system driver is a component that reads RFID signals from a tag and produces an open standard file format and data interchange, JSON, which is then consumed by the RFID software. In this work, the Internet, the world's largest WAN, has been selected to transmit data between physical system and digital twin due to its wide availability and applicability. In terms of the software, the data captured by the RFID system is stored to MS SQL Server 2019 (i.e. the sensor data repository system) that is hosted on Azure Virtual Machines and transmitted using the Internet. This allows using full versions of MS SQL Server in the cloud without having to manage any on-premises hardware, enabling cross-site communication and interconnection between different devices and geographical regions.

To facilitate data communication among different software systems, a web server based on FLASK micro web framework, written in Python, was created. FLASK has an extension called Flask-RESTful that provides support to quickly building REST APIs for Create, Read, Update, and Delete (CRUD) endpoints. Hence, to retrieve the data to AnyLogic, MS SQL Server is connected to Google Sheets to read the RFID data from the database, by whitelisting the IP, creating 'Apps Script' project, creating a connection to MS SQL Server database, reading data from MS SQL Server database and writing data to Google Sheets. Google Drive API is also used to allow leverage Google Drive storage. AnyLogic software has Cloud APIs in Python that enable compatibility with other programs and processing JSON files. However, this feature is only available for commercial license and hence, XLSX file format used for data exchange between Google Drive and AnyLogic by building a REST API. The data in XLSX is updated dynamically every twenty minutes, as configured via the Azure and Google Drive APIs. For the *database* deployment, XLSX data is imported in the built-in *database* in AnyLogic via the Database.getConnection method call and retrieved in the model by querying the *database* table to mimic the behaviour of the physical components, using SQL queries. The *database* table is set to be updated automatically on each model start up, as provided by the software. For the RFID readings at the shop floor, the types of collected sensor data from the RFID system to the *database* table include RFID sensor tags unique identifier (UID), activity identification and user UID. After each tag is scanned by an RFID reader, recordings of date and time stamps of the commencement and completion of manufacturing activities, and location are also captured. Moreover, data related to the number of orders, deliveries, dispatches' location, carrier information, type and quantity of biological material, batch number, type and quantity of container are recorded.

Other input data obtained from the enterprise system employed in the studied system is considered. The company's working hours is between 8:30 am and 16:30. The number of operators, working at the cryogenic facility, based on their expertise is shown in Table A1. Each operator is trained to carry out multiple activities and the number of operators needed for the daily activities at the warehouse can also be found in Table A1. Moreover, the cycle time distributions for the manufacturing activities are listed in Table A2. An asterisk (*) denotes the activities affected by the RFID implementation. Additional input data collected from the daily operations of the selected cryogenic warehouse is summarised in Tables A1, A2 and A3.

All data acquired in the smart connection layer is modelled at the micro-level agent. For the implementation of micro-level agents, a population of agents of the same type living in the same environment is created in AnyLogic software. These micro-agents have dynamic properties including movement speed (metre/second), location (X, Y, Z, rotation Z coordinates of Java type double), shape (2D/3D animation sketch) and recurrence update time. A function that returns the colour type value, using getFillColor () function, has been considered to get the fill colour of the (human, equipment and material) resources when simulation is animated in 2D. This enables to visually track the movement of resources on the shop floor when running the model. The space type of micro-level agents is defined as continuous, allowing the user to set and retrieve the current agent location, and move the agent with the specified speed from one location to another.

4.1.3. Conversion layer

Conversion layer transforms sensor data stored in the *database* to meaningful information for the health status of RFID tagged products. Anomalies identified in the *database* can be related to an increased number of deliveries and/or orders than it is expected on a daily basis, or delivery of wrong quantity of products, or increased time (i.e. cycle time) required for receiving, processing or dispatching cryomaterials compared to the nominal time required to complete these tasks. Anomalies are detected by the 'monitoring agent' at the exo-level agent that can then predict dynamically unplanned emergent bottlenecks related to human and equipment resources availability and inventory levels and storage space availability. Moreover, the root cause of the bottleneck is identified in terms of unstored products, queues of products waiting to be processed and any increase identified in the TH, LTs, WIP, HRU or ERU compared to average numbers observed during the normal daily operations of the cryogenic warehouse.

Thus, following the finite-state machine model, discussed in Section 3.3, the 'monitoring agent' is deployed in AnyLogic, considering the different states of the monitoring agent-based model for automated anomaly detection and bottlenecks identification (see Fig. 4). The required parameters and variables that define the average nominal values used for the case study are summarised in Table A3. This data, being input to the micro-level agent, has been collected with the RFID system from the shop floor of the case study company for a five-week period. The maximum allowable utilisation rates for the human and equipment resources have been set at 50% of the company's working hours, as seen in Table A3. This is explained as only part of the operations carrying out at the cryogenic warehouse has been considered in this case study. Anomaly detection, bottleneck identification and diagnosis are further discussed in Sections 4.2 and 4.3.

4.1.4. Cyber layer

In this layer, *information base*, modelled at the micro-level agent, is deployed as a built-in fully integrated database for reading input data from the *database* table and writing simulation output. As discussed in the smart connection layer, the raw data collected from the RFID system is uploaded to AnyLogic software. In the cyber layer, this data is then processed using SQL queries to create timestamps and calculate the time required for performing various activities within the cryogenic warehouse. In AnyLogic, *information base* tables and views are created. *Information base* table is a collection of related data held in a structured format consisting of fields (i.e. columns) and rows. Each table has a column storing unique IDs of the table rows. Additional fields are the activities in which the RFID system has been implemented (e.g. arrivals checking, storing material, etc.), date and time stamps recorded after each tag is scanned, cycle time required for each activity to be carried out and users' UID. *Information base* views, are relational tables representing a subset of data contained in the *information base* table. A view is computed dynamically from data in the table when access to that view is requested. In this work, one view has been created for each RFID activity. SQL queries for creating the views are developed in the 'View definition' field using the SELECT statement. One *information base* table and six views, one for each RFID activity as highlighted in blue in Fig. 5, have been created. Moreover, '*Source*' block from the Process Modelling Library, modelled at the exo and meso level agents, is used to generate one agent per one *information base* view record. To make 'Source' blocks generate agents according to the view records, arrivals are defined by '*Arrival table in Database*' property. The *information base* view containing the data on agent arrivals is then selected in the '*Database table*' parameter. Moreover, the column (datetime) of the view that contains the agent arrival timestamps is selected in the '*Arrival date*' parameter. Therefore, '*Source*' blocks can generate agents according to the records in the view. Each record defines one agent arrival. Agent attributes such as ID, activity, date, time, and process time are read and stored in the corresponding parameters at the micro-level agent.

The multi-agent simulation method discussed in Section 3.3 is employed to develop the cyber-twin model of the cryogenic warehouse. The multi-agent architecture of macro, exo, meso and micro level agents is developed according to Appendix Section 1.1. The 'monitoring agent' is modelled as a single agent type at the exo-level agent in the global manufacturing system, macro-level agent, of the cryogenic warehouse. The three manufacturing phases, including Phase I – Receipt & Inventory, Phase II – Storage & Monitoring, and Phase III – Distribution, are implemented as single type agents $\Phi_W = \{\Phi_1, \Phi_2, \Phi_3\}$ at the exo-level agent. According to Eq. (A1) in Appendix, Section 1.1, the stochastic phase space of $\Phi_W$is Γ_W, the probabilities are $p_1 = p_2 = p_3 = 1/3$ and can be obtained as:

$$\Gamma_W = p_1\Gamma_1 + p_2\Gamma_2 + p_3\Gamma_3 \tag{8}$$

It is noted that in this case study there are no repeated manufacturing modules, and hence the meso-level agent is not considered. Human and equipment resources are implemented as sub-sub-agents, X, at the micro-level agent with dynamic properties including population, working hours, breaks and shifts, movement speed, home location and 2D/3D animation shape and capacity. The collection of micro-level agents is described in a finite set X = {x1, x2, …, x9} modelling operators for receiving deliveries, general activities, shippers filling, QA, QC, QP, trolleys, cryocarts and cryotanks. Each sub-sub-agent contains parameters to capture the dynamic parametric operation of the corresponding agent and entire system.

With regard to the development of the multi-layer network, in Appendix, Section 1.2, the logical network (i.e. transition(s) from one activity to another) of the manufacturing system at the cryogenic warehouse is demonstrated in the UML Activity diagram in Fig. 5. The parallel interactive activities in the three manufacturing phases that include highly interactive and manual handling processes are initiated once a delivery arrives at the company in Phase I and/or an order to dispatch cryoproducts to healthcare institutions is received in Phase III. After the shippers are delivered at the cryogenic warehouse, in Phase I, they are verified and documented (arrivals checking). The shippers are recycled and refilled, before they are stored in pallet racks in Phase II. The cryomaterials are initially stored in quarantine storages, checked in terms of policies and regulations and once approved, they are stored in the cryotanks. Phase III initiates once an order is received followed by the shipment planning and scheduling. After picking the right material and shipper from storage, and assign the material into the shipper, secondary packaging (if necessary), verification and dispatch are carried out. For the network of agents, let two sets of nodes $x2_1$ and $x2_2$ that represent micro-level agents, e.g., operators for general tasks,

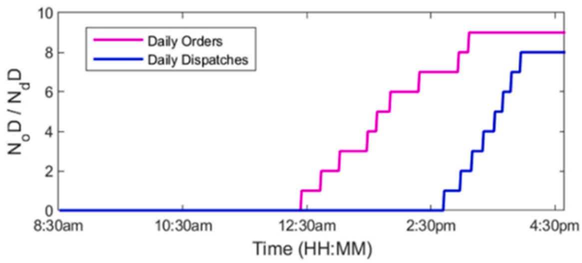


Fig. 6. Case study: simulation results for the total number of daily orders (N_o^D) and dispatches (N_d^D) for the 'without DT-CPS' scenario.

interacting with each other. The state for each node set is represented by a canonical vector $\varepsilon 2_1$ and $\varepsilon 2_2$ in the space $\mathbb{R}^{20}$, as there are 20 operators for performing general tasks. According to Eq. (A3) in Appendix, Section 1.2, the interactions between the agents can be expressed as:

$$\Phi 2^{\widetilde{\alpha\alpha}}_{\widetilde{\beta\beta}} = \sum_{\widetilde{i,j=1}}^{20} \sum_{i,j=1}^{20} w2_{12}\left(\widetilde{12}\right) \varepsilon 2^{\widetilde{\alpha\alpha}}_{\widetilde{\beta\beta}}\left(12\widetilde{12}\right) \tag{9}$$

where $w2_{12}(\widetilde{12})$ is the intensity of the relationship between nodes $x2_1$ and $x2_2$; $\varepsilon 2^{\alpha}(1)$ and $\varepsilon 2^{\beta}(2)$ are the αth and βth components of the 1st and 2nd contravariant canonical vectors $\varepsilon 2_1$ and $\varepsilon 2_2$ in $\mathbb{R}^{20}$, respectively; and $\varepsilon 2^{\widetilde{\alpha\alpha}}_{\widetilde{\beta\beta}}\left(12\widetilde{12}\right)$ is the fourth-order canonical basis in space $\mathbb{R}^{20\times 20\times 20\times 20}$.

Additionally, discrete event simulation, discussed in Appendix Section 1.3, is used to develop the process-oriented states, by capturing the manufacturing activities carried out at the warehouse in a step-by-step process, as illustrated in Fig. 5. For instance, according to Eq. (A4), 'Arrivals checking' activity has: X the input control flow of the shippers delivered at the start node, named 'Delivery of shippers'; Y the output control flow after the completion of 'Arrivals checking'; and s_0 the initial state of 'Arrivals checking' activity before its execution. The AnyLogic Process Modelling Library was selected to model these activities as a sequence of activities using queue, delay, resource pool, seize and release blocks.

4.1.5. Cognition layer

Cognition layer is employed to transfer knowledge to the users to make appropriate decisions for maintaining or improving the performance and productivity of the cryogenic warehouse. Such knowledge obtained from the computational results includes the system TH, modelled at macro-level agent, time required for performing the several activities within the three manufacturing phases modelled at the exo-level agent, and WIP, HRU, ERU and space utilisation rates, levels of inventory size and availability of storage space modelled at the micro-level agent. Additionally, the daily numbers of shippers delivered and dispatched and cryomaterials stored in the cryotanks, the space availability of cryotanks, and stock size of cryomaterials and consumables are considered. For utilisation rates of human and equipment resources, the billable hours over the eight working hours of the company are obtained from the simulation model. The performance and productivity of the cryogenic warehouse is continuously monitored and measured, while knowledge is obtained by running the simulation experiment with animation displayed. In the case of a disruptive event is diagnosed, at the exo-level agent, the user is warned about the abnormality in the system's performance through an alert that appears in the screen with the associated bottleneck to be highlighted.

To collect data analytics from the multi-agent system, as discussed in Section 3.3, different methods have been deployed in AnyLogic using Java. Thus, utilisation.mean() method is used to measure the daily average (collected over time) number of hours that the human/equipment resources are busy/used over the daily working hours of the cryogenic warehouse. Additionally, count() and out.count() methods are used to measure how many agents (i.e. deliveries, orders, shippers and cryomaterials) entered the input and left the output ports of different blocks (i.e. manufacturing activities) over time. count() method is also used to measure the stock size of cryomaterials and shippers available for dispatch. TH is calculated by finding the difference between the agents left and entered blocks or a set of blocks (i.e. manufacturing phase). LTs are measured using Time Measure Start blocks from the Process Modelling Library in AnyLogic and distribution() method is used to calculate the time distribution the agents spent between given points within the manufacturing phases. Time plots, bar charts, pie charts and histograms can be used to visualise the results in an interactive and self-explanatory way, as can be seen in Sections 4.2 and 4.3.

4.1.6. Configuration layer

The configuration layer is employed to automatically optimise the performance of the cryogenic warehouse by providing feedback to the smart connection, conversion and cognition layers. Self-optimisation is implemented at the macro-level agent of the cryogenic warehouse system. In the studied system, decision strategies including sourcing and procurement, risk mitigation and management, environment and sustainability strategies, are considered according to managers' knowledge and experience, but also with the help of computational models where various simulation and optimisation scenarios can be executed. By realising the automated knowledge feedback from the cognition layer, actionable insights can be derived for improvement in the control and decision making. Thus, relevant data analytics can be performed to make informed decisions considering dispatch planning, queue management to reduce WIP limits and queue sizes, resource planning, space layout planning and inventory control. In this study, the selected decision strategy proposes reallocation of operators within existing groups in order to handle bottlenecks identified in the conversion layer and increase system's flexibility, while maximising the number of deliveries completed, while minimising the WIP and excessive use of human resources. The self-optimisation is deployed in AnyLogic employing OptQuest® search engine that uses the metaheuristic algorithms of Scatter Search, Tabu Search and Neural Networks, combining them into a single search heuristic.

The results obtained from the optimisation experiment are used to modify the properties of the asset, (e.g. resource planning) and its environment (e.g. shop floor planning and control). In this study, the optimisation results, i.e. optimal values of operators required within each group, are automatically updated to the human resources parameters at the micro-level in the smart connection layer. Monitoring agent in the conversion layer is then updated based on the new reallocation of human resources and checks if the bottlenecks previously identified have been removed. Based on the updated parameters, the cyber-twin model in the cyber layer is then simulated and provides updated results visualised in the cognition layer. In the case of the bottlenecks remain or new are identified, a new self-optimisation for handling bottlenecks should be carried out. Additional decision strategies can be explored finding the optimal number of equipment resources to improve the performance and productivity of the digital twin and, by extension, physical system. It can be also explored the optimal TH, initial stock size and storage space to improve the warehouse capacity and shipping speed, minimise the LTs of manufacturing phases and avoid the occurrence of queues, and emergence of bottlenecks. Self-optimisation is further discussed in Section 4.3.

4.2. Digital twin – cyber physical system model validation

Validation of the simulation model and DT-CPS architecture is accomplished using real data obtained from the studied cryogenic warehouse. The validation of the model has been carried out at three stages. At Stage 1, the simulation model developed for the shop floor warehouse is validated against real data for the state without the DT-CPS

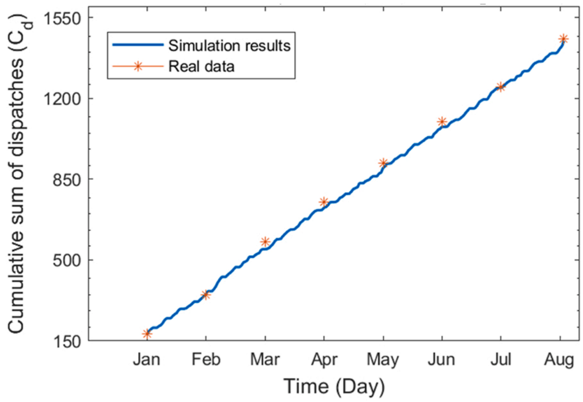


Fig. 7. Case study: simulation results against real data for the cumulative total of dispatches (C_d) for an eight-month period for the 'without DT-CPS' scenario.

Table 1
Case study: real-time RFID input data – cycle times for the 'DT-CPS without anomaly' scenario.

Activity with RFID	Test Procedures							
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Arrivals checking (seconds)	9	9	9	15	15	15	15	15
Storing material (minutes)	2	2	2	4	4	4	4	4
Picking material (minutes)	1	1	3	3	3	1	3	1
Dispatching (seconds)	9	9	15	15	15	9	15	9

and RFID system implementation ('without DT-CPS' scenario). This is important for later testing the validity of Stage 2 that builds on and extends the model of Stage 1. At Stage 2, the DT-CPS architecture is validated using real-time data collected from the RFID system for the normal operation of the warehouse ('DT-CPS without anomaly' scenario). This is also necessary for validating Stage 3 that builds on and extends the model of Stage 2. At Stage 3, anomalous values are captured in the RFID data due to disruptions that occur on the shop floor of the warehouse. The 'monitoring agent' is validated in terms of its capability to automatically detect these anomalies and capture their impact on the system's performance ('DT-CPS with anomaly' scenario).

At Stage 1 ('without DT-CPS' scenario), the total number of daily orders (N_o^D) and dispatches (N_d^D) over time are obtained from the simulation model as illustrated in Fig. 6. The graph shows that the warehouse receives orders during the daily working hours between 8:30 am and 16:30. However, orders are dispatched between 14:30 and 16:30 when the trucks are available at the company. Moreover, real data for the cumulative total of monthly dispatches, provided by the studied company for the validation, is compared to the results obtained from the simulation model for an eight-month period, between January and August, as viewed in Fig. 7. The simulation time has been set accordingly. The number of monthly dispatches obtained from the simulation results fall into the monthly ranges provided by the company, which are 150 – 185. The graph for the cumulative monthly dispatches shows the accuracy of measurements with a highly representative comparison between the simulation model and the real data, having an average percentage error of 0.81% in terms of the company performance.

At Stage 2 ('DT-CPS without anomaly' scenario), after validating successfully the simulation model for the 'without DT-CPS' state, the proposed DT-CPS architecture is validated using RFID data collected under the normal operation of the cryogenic warehouse. Real data on the RFID cycle times for a six-week period has been collected from the shop floor of the company. The average cycle times taken for each test procedure carried out within a trial are summarised in Table 1. According to this data, obtained from the *database*, the histogram graphs have been developed to calculate the Probability Density Function (pdf)

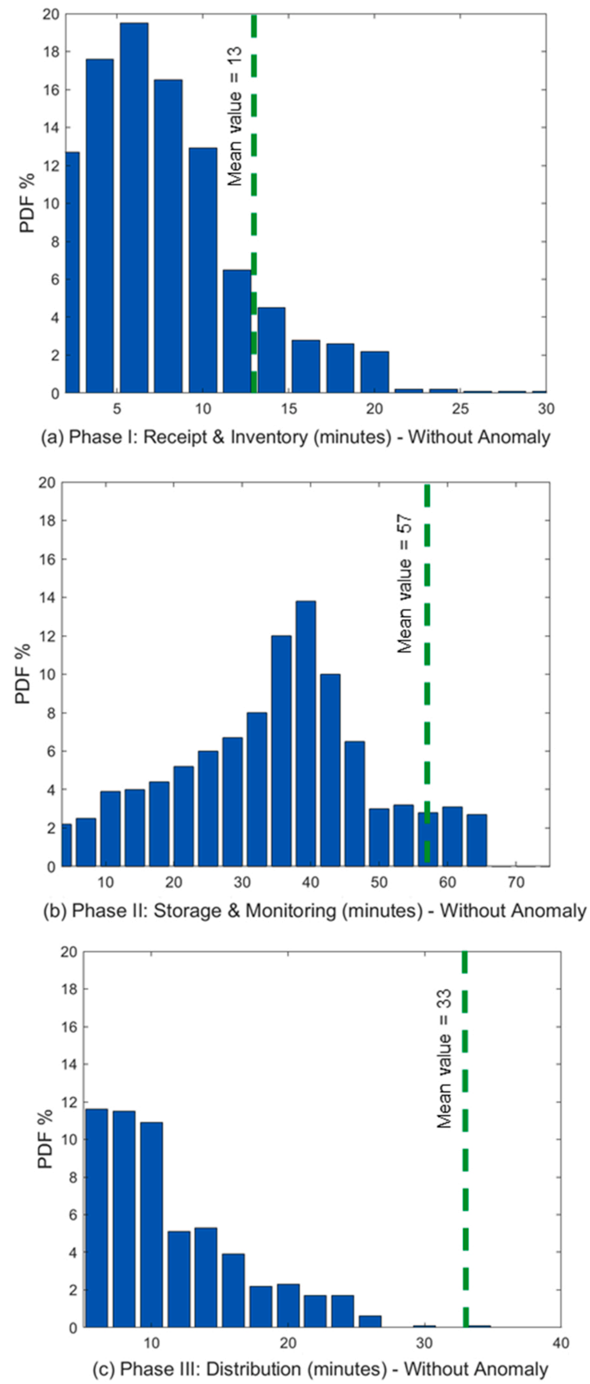


Fig. 8. Case study: Pdf graphs for the lead times for the 'DT-CPS without anomaly' scenario: Phases I – III (a-c).

for the arrivals checking, storing material, picking material and dispatching cycle times. The mean values of the corresponding pdf graphs are $\lambda_{Arrivals\ checking} = 12.81sec$, $\lambda_{Storing\ material} = 3.3\text{min}$, $\lambda_{Picking\ material} = 2.05\text{min}$ and $\lambda_{Dispatching} = 12.3sec$. Comparing the cycle times in Table A2 and these obtained from the pdf graphs for the four manufacturing activities, excellent agreement is found, with an average error of 1.503%. This validates the operation of the DT-CPS architecture under normal operation.

Moreover, the histogram graphs, developed in the cognition layer, calculate the pdf for the time spent in each manufacturing phase. The pdf graphs for the lead times in Phases I–III for the 'DT-CPS without anomaly' scenario and mean values can be viewed in Fig. 8. According

Table 2
Case study: RFID input data of disruption scenario – cycle times for the 'DT-CPS with anomaly' scenario.

Activity with RFID	Test Procedures									
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Picking Material (minutes)	8	10	10	12	25	27	15	17	20	22

Table 3
Case study: average lead times for the 'DT-CPS without anomaly' and 'DT-CPS with anomaly' scenarios.

Lead time for Phases I–III	'Without anomaly' (minutes)	'With anomaly' (minutes)	Increase (%)
Receipt & Inventory	13	14	7.7
Storage & Monitoring	57	65	14
Distribution	33	47	42.4

Table 4
Case study: average human resource utilisation rates for the 'DT-CPS without anomaly' and DT-CPS with anomaly' scenarios.

Human resource utilisation for Phases I–III	'Without anomaly' (minutes)	'With anomaly' (minutes)	Increase (%)
Receipt & Inventory	40.2	40.8	1.5
Storage & Monitoring	50.7	53.6	5.7
Distribution	45.6	77.4	69.7

to the pdf graphs, it is observed that 95.5% of deliveries are being received and documented in less than 20 min, see Fig. 8(a). The corresponding pdf graph has a Poisson distribution with $\lambda_{Phase\ I-Without\ Anomaly} = 13\text{min}$. Additionally, the pdf for the storage and monitoring lead time in the 'DT-CPS without anomaly' state shows that 89% of the products are being stored in about 50 min, and only 11% of the products in between 50 and 70 min, see Fig. 8(b). The corresponding pdf graph has a Poisson distribution with $\lambda_{Phase\ II-Without\ Anomaly} = 57\text{min}$. Finally, in Phase III, the pdf graph for the distribution lead time has an exponential distribution, as illustrated in Fig. 8(c). The average time needed to complete a product dispatch is much less as 97% of the orders are being dispatched in less than 30 min. The corresponding pdf graph has an exponential distribution with $\lambda_{Phase\ III-Without\ Anomaly} = 0.1158\text{min}$. The pdf graphs and analysis are included as they will be used for the validation of the next stage for the 'DT-CPS with anomaly' scenario.

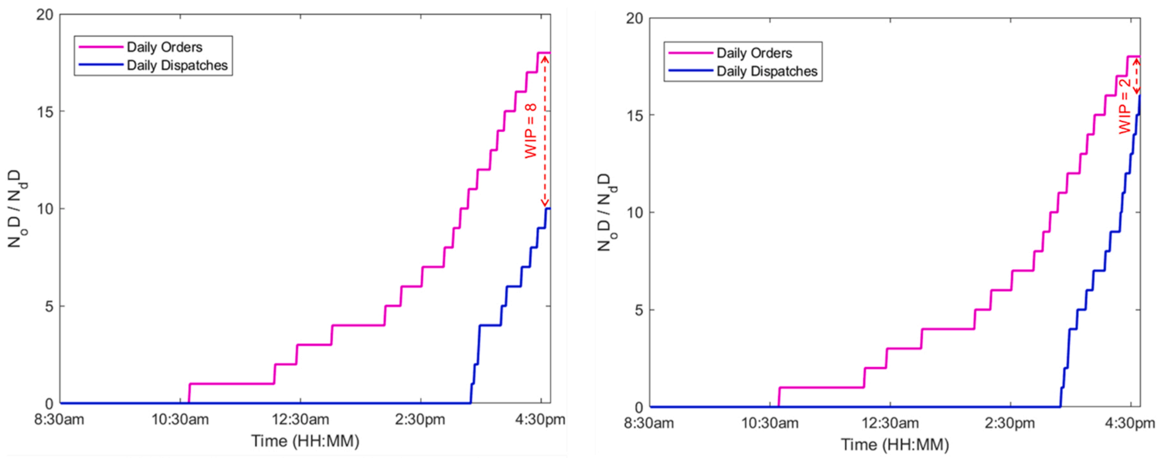
At Stage 3 ('DT-CPS with anomaly' scenario), an anomaly detection scenario with ten test procedures has been considered to validate that the proposed 'monitoring agent' can detect anomalous values in input RFID data and realise their impacts to the system performance. In these trials, the cycle times for picking materials from storage and assigning them to shippers for dispatch have been deliberately increased compared to the normal operations of the system. The average cycle times taken for each test procedure carried out within a trial are summarised in Table 2. The cycle time for 'Picking material' under normal operating conditions is between 1 and 3 min, as seen in Table A3. The cryogenic warehouse carried out these scenarios and collected the data using the RFID system. The cycle time distributions are implemented to the simulation model at micro-level agent and the mean value of the corresponding pdf graph is$\lambda_{Picking\ material} = 16.8\text{min}$. Comparing the cycle times in Table 2 and these obtained from the pdf graph for 'Picking material, excellent agreement is found, with an average error of 1.21%. The 'Anomaly Detected' state in AnyLogic statechart is activated, validating the ability of the 'monitoring agent' to detect anomalous values in input sensor data. Additionally, average lead times for the three manufacturing phases, for the DT-CPS with anomaly' scenario are obtained. The results are compared with the corresponding computational data obtained for the 'DT-CPS without anomaly' scenario (Stage 2) and the average lead times are summarised in Table 3. Similarly, the average human resource utilisation rates for the three manufacturing phases for the 'without anomaly' and 'with anomaly' scenarios are obtained, as seen in Table 4. From the computational results in Tables 3 and 4, obtained in the cognition layer, it is seen that the model can capture the impacts of these anomalies to the operation of the manufacturing phase (i.e. Phase III - Distribution) and to entire system in terms of lead times and human resource utilisation rates. According to the results, the lead time of Phase III – Distribution has increased by 42.4% (Table 3), while the utilisation rates of human resources by 69.7% (Table 4) compared to the normal operations of the cryostorage warehouse. Although the anomaly occurs in Phase III, an increase in the lead times and resource utilisation in the other two phase (Phases I and II) has been observed due to parallel dynamic interactions within the three manufacturing phases.

4.3. 'Monitoring agent' validation

The proposed 'monitoring agent' within the DT based multi-agent CPS architecture has been validated against actual data obtained from the studied cryostorage company as discussed previously in Section 4.2. The architecture enables real-time communication between the RFID system and DT-CPS, and the computational model represents the actual behaviour of the interactive system. In this section, a 'Disruption' scenario is studied to demonstrate that after the 'monitoring agent' at the exo-level captures anomalous values in input real-time data, collected by the RFID system, can analyse the impact of anomalies (i.e. bottlenecks identification) to the system at the macro, exo and micro level agents. Self-optimisation is then employed to automatically update the micro-level agents and remove the identified bottlenecks. To demonstrate the impact of the 'monitoring agent' and self-optimisation, key performance indicators (KPIs) are tested and compared for the 'Disruption' scenario for two cases: 'without feedback' (i.e. without self-optimisation) and 'with feedback', obtained from the configuration layer.

The simulation experiments for the 'Disruption' scenario have been performed for a three-day period. For this experiment, the daily number of orders and deliveries have been increased by 100% and the time required for 'Picking material' (Phase III) by about 500% times on average compared to the normal operation of the facility. The average cycle times taken for each test procedure carried out within a trial are summarised in Table A4. After obtaining the RFID data to the database in the smart connection layer (i.e. micro-level agent), the 'monitoring agent' at exo-level agent in the connection layer informs the user that an anomaly has been detected in the input data in terms of large numbers of deliveries and orders, and increased time for materials picking. The simulation model of the cryogenic warehouse is then executed in the cyber layer and the results are visualised in the cognition layer. For the 'Disruption – without feedback' scenario, the anomaly is diagnosed identifying that it causes high rates of human resource utilisation at the micro-level agent (bottleneck), greater than the maximum allowable level of 50% (see Table A3). Moreover, during the third day of operation, the simulation model stops due to lack of validated shippers (bottleneck), modelled at micro-level agent, to assign cryomaterials for dispatch. The AnyLogic interface of the monitoring agent-based model for automated anomaly detection and bottlenecks identification for the 'Disruption – without feedback' scenario is presented in Fig. A1. Analysing the simulation results, the bottlenecks, identified during the daily practices for this scenario in the cognition layer, are:

- Shortage of human resources in the refilling and recycling zones at the warehouse between 9:00 am – 14:30. Queues of cryomaterials waiting to be stored are identified, with average waiting time 21 min. The utilisation levels of the operators trained in the shipper



(a) Disruption – without feedback scenario

(b) Disruption – with feedback scenario

Fig. 9. Case study: Simulation results for the total number of the daily orders (N_o^D) and dispatches (N_d^D) for the: (a) 'Disruption – without feedback' and (b) 'Disruption – with feedback' scenarios.

filling and verification tasks are 81% and 74%, respectively. Considering that only LN2 cryogenic products have been studied in this work, these utilisation levels are greater than the maximum allowable limit (50%) set by the company. This ultimately may result in shortage of operators to perform the tasks on the shop floor.

- Shortage of human resources in the storage zone between 11:30 am - 16:30, due to interactive actions between the three manufacturing phases.
- Shortage of human resources in the dispatching zone between 14:30–16:30, due to queues in the quality check completion, due to interactive actions between the receipt (Phase I) and distribution (Phase III) zones.
- Shortage of validated shippers (≤ 5). This bottleneck, identified by the 'monitoring agent', makes the simulation model to stop, as there is no available shipper to assign the cryomaterials for dispatch. This bottleneck informs users that based on the demand and supply there is insufficient initial inventory and the company may miss out on sales opportunities.

The root causes of the bottlenecks are further explored. Thus, the computational model captures that the cryogenic warehouse accepts 18 orders daily from which only the 10 are completed and dispatched. The total number of daily orders (N_o^D) and dispatches (N_d^D) over time are obtained from the simulation model as illustrated in Fig. 9(a). The graph shows that the average WIP per day (at micro-level agent) is 8 orders, while only 56% of the orders accepted daily can be dispatched.

The bottleneck root causes are further investigated through a stochastic data analysis, quantifying the uncertainty in lead times as visualised in the cognition layer. The results are compared against these from the 'DT-CPS without anomaly' scenario to show the capability of the 'monitoring agent' to capture the impact of the anomalies on KPIs. The histogram graphs have been developed to calculate the pdf for the time spent in each manufacturing phase at the exo-level agent. The pdf graphs for the lead (i.e. processing) times in Phases I–III for the 'Disruption – without feedback' scenario can be viewed in Fig. 10 (a–c). The pdf graphs have a Poisson distribution with $\lambda_{Phase\ I} = 22.1$min, $\lambda_{Phase\ II} = 68.4$min and $\lambda_{Phase\ III} = 47.4$min respectively. It is observed that 23% of deliveries are being received and documented within 16 – 18 min and for about 61% the process takes more than 20 min see Fig. 10 (a). On the contrary, in the 'Without anomaly' scenario, 95.5% of deliveries are being received and documented in less than 20 min, see Fig. 8(a). Additionally, the pdf for the storage and monitoring processing time in the 'Disruption' scenario shows that 35% of the products are being stored in about 68 min, 62% of the products in between 68 and 73 min, and for about 3% the process takes more than 73 min, see Fig. 10 (b). Moreover, the pdf for the storage and monitoring processing time in the 'Without anomaly' scenario, shows that 95.5% of the products are being stored in about 60 min, and only 4.5% of the products in between 60 and 70 min see Fig. 8(b). Finally, in Phase III, the pdf graphs for the distribution processing time for the 'Disruption' scenario, 87.5% of orders are being dispatched in less than 48 min see Fig. 10 (c). In terms of the 'Without anomaly' scenario, the average time needed to complete a product dispatch is much less as 97% of the orders are being dispatched in less than 30 min, see Fig. 8(c).

Additionally, the average daily utilisation rates of human resources for the 'Without anomaly' and 'Disruption – without feedback' scenarios are 47% and 57%, respectively. The daily utilisation rates of the human resources for the two scenarios are illustrated in Fig. 11 (a). According to the results, the 'monitoring agent' can capture the impact of the studied anomalies on the utilisation rates of the operators at the warehouse. In the 'Disruption – without feedback' scenario, an increase in the utilisation rate is observed from 9:00 am, exceeding the corresponding rate of the 'Without anomaly' scenario during the daily operations (Fig. 11 (a)). This rise is explained due to the unexpected increase in TH and LTs for picking materials for dispatch at the macro and exo level agents, respectively.

After identifying the bottlenecks and their root causes, relevant data analytics at the configuration layer of the proposed DT-CPS architecture can be carried out to find the best decision strategy to eliminate the bottlenecks. In this study, a decision strategy on eliminating the bottlenecks related to the shortage of human resources will be investigated. An optimisation experiment to find the best allocation of human resources required within each role, as discussed in Section 4.1.6, in order to maximise the number of completed orders, while reducing the HRU rates and WIP in Phase III – Distribution is employed. For the formulation of the optimisation, the objective function, namely maximising the number of deliveries completed daily on the shop floor, in initially defined. The decision variables considered for the human resources within each role vary between 1 and 19, while ensuring that the total number of human resources remains equal to 40 which is the current number (Table A1), as the cryogenic company will not recruit more operators. In terms of the model constraints, the operators should be able to accept all the daily deliveries, WIP in Phase III – Distribution be less than or equal to 3 orders, while keeping the HRU rates lower or equal to 50% to prevent excessive use of resources. For this experiment, it has been assumed that the number of orders received daily equals the number of validated shippers on the shop floor. The optimisation has been carried out in AnyLogic OptQuest® that automatically builds the

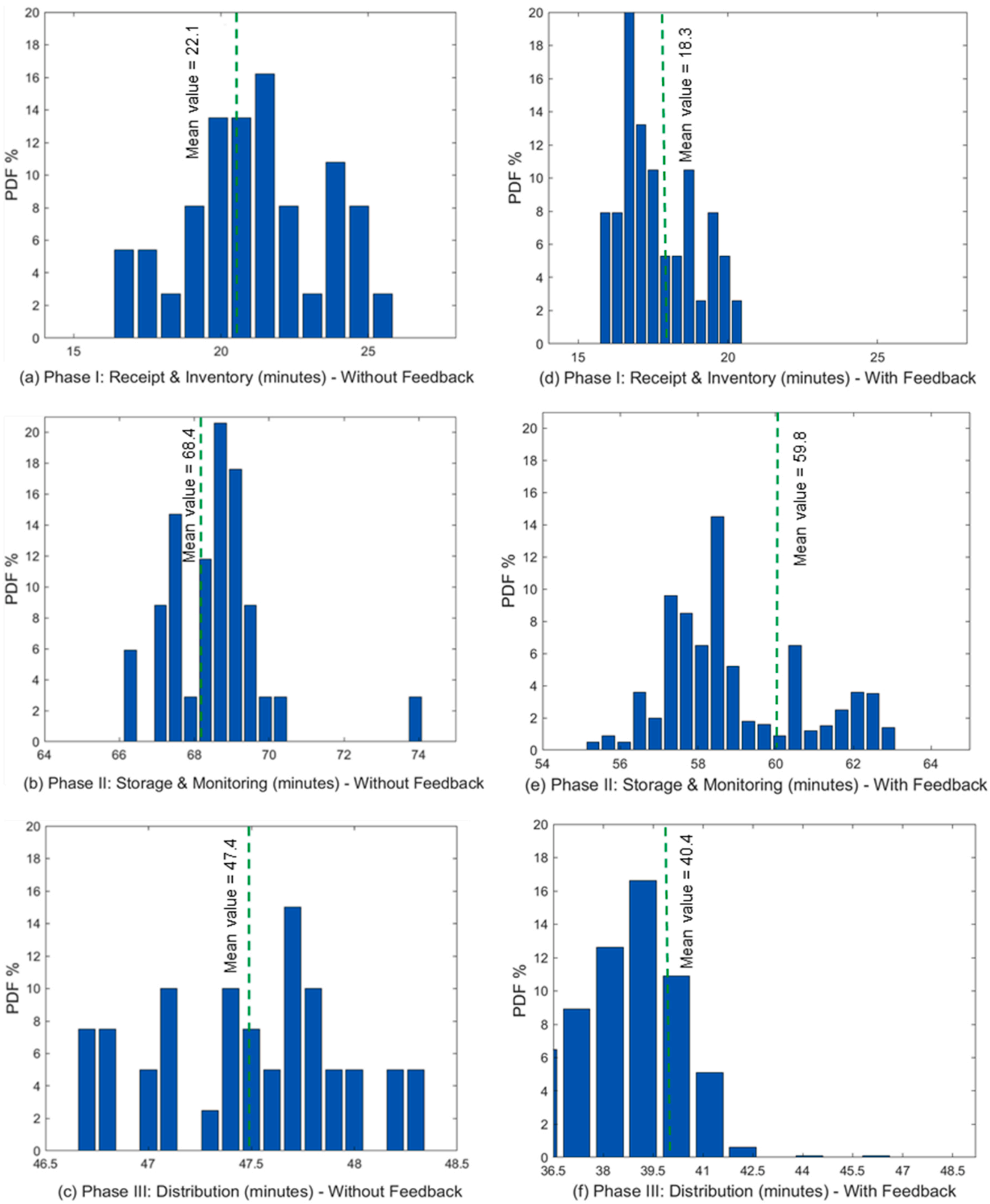


Fig. 10. Case study: Pdf graphs for the lead times for the: 'Disruption – without feedback' scenario: Phases I – III (a-c) and Disruption – with feedback' scenario: Phases I – III (d-f).

User Interface, displaying the current and best feasible solutions and the dynamic optimisation progress with respect to the number of iterations performed. The optimisation results for the maximisation of the daily dispatches (N_d^D) are presented in Fig. 12 for 1750 iterations. No change in the results has been observed beyond this number of iterations. Additionally, the proposed allocation of human resources within each role is: receipt of deliveries (1), receipt of material (5), shipper filling (14), inventory (7), verification (10), and dispatch (3). The number of human resources required for each activity is denoted in the parentheses. The optimisation results show that if the proposed allocation of human resources is adopted by the cryogenic company, the number of daily dispatches can increase up to 16, i.e., 60% more orders can complete compared to the current figures (see Fig. 9(a)).

Once the optimisation experiment is conducted, the proposed allocation of human resources is automatically embedded as feedback into the corresponding human resources parameters, modelled at the micro-level agent, in the smart connection layer using the getBestParamValue () method for the best iteration. After the human resources-related parameters are updated, the 'monitoring agent' detects the anomalous values in RFID data, but no bottlenecks related to the human resources utilisation rates are identified. The simulation model runs and new results are visualised in the cognition layer as illustrated in Figs. 9(b) and

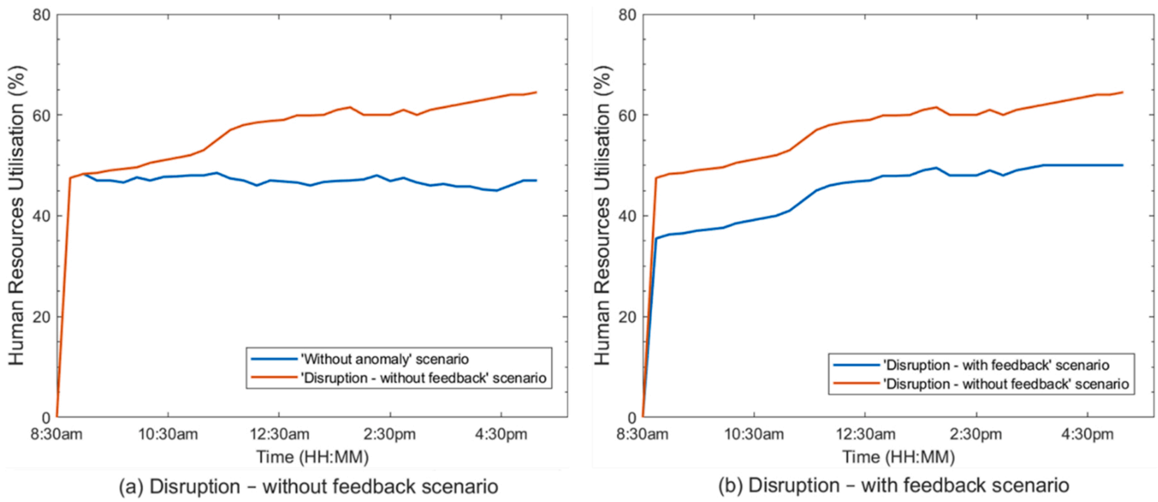


Fig. 11. Case study: Daily human resources utilisation rates for the: (a) 'Disruption – without feedback' and (b) 'Disruption – with feedback' scenarios.

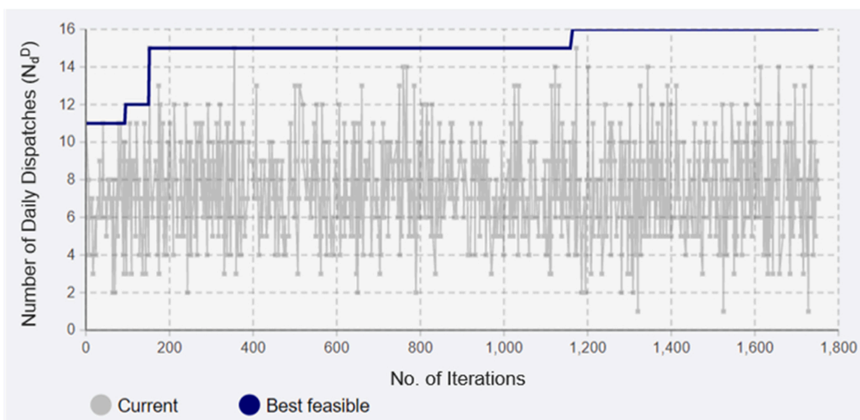


Fig. 12. Case study: optimisation results for the total number of the daily dispatches (N_d^D) for the 'Disruption' scenario.

Table 5
Case study: average lead times for the 'the Disruption – without feedback' and 'Disruption – with feedback' scenarios.

Lead time for Phases I–III	'Without feedback' (minutes)	'With feedback' (minutes)	Reduction (%)
Receipt & Inventory	22	18	18.2%
Storage & Monitoring	68	60	11.8%
Distribution	47	40	14.9%

11 (b). Thus, the total number of daily orders (N_o^D) and dispatches (N_d^D) for the 'Disruption – with feedback' scenario are obtained from the simulation model as presented in Fig. 9(b). The computational results show that the cryogenic warehouse accepts 18 orders daily from which the 16 can be completed and dispatched. The graph shows that the average WIP per day in Phase III - Distribution is 2 orders, while 89% of the orders accepted daily can be dispatched. After the feedback implementation, the new simulation results suggest that 33% more orders can be completed compared to the 'Disruption – without feedback' scenario, seen in Fig. 9(b). Moreover, the average daily utilisation rates of the human resources for 'Disruption – without feedback' and 'Disruption – with feedback' scenarios are illustrated in Fig. 11 (b). It is observed that if the system is under disruptions and no action is taken (i.e. 'without feedback' scenario), the HRU rate increases and remains at high levels, making the system unable to efficiently handle the disruptions (orange line in Fig. 11 (b)). On the contrary, once the reallocation, obtained from the optimisation, is applied, a significant drop is observed (blue line in Fig. 11 (b)) and, hence, the HRU-related bottlenecks are eliminated. With the feedback implementation, the daily HRU rate slightly increases after 10:30 am at around 45%, satisfying the relevant constraint defined during the optimisation.

It is also found that with the new allocation of the operators, the average queue waiting time in the refilling and recycling zones at the warehouse between 9:00 am – 14:30 has been reduced from 21 to 15 min. The utilisation levels of the operators trained in the shipper filling and verification tasks have been reduced from 81% and 74%, to 50% and 47%, respectively. Minor decrease of 4 min is also observed in the queue waiting time for quality check in the dispatching zone between 14:30 am - 16:30. The pdf graphs for the lead times in Phases I–III for the 'Disruption – with feedback' scenario can be viewed in Fig. 10 (d – f). The pdf graphs have a Poisson distribution with $\lambda_{Phase\ I} = 18.3$min, $\lambda_{Phase\ II} = 59.8$min and $\lambda_{Phase\ III} = 40.4$min respectively. The average lead times for the three manufacturing phases, for the 'without feedback' and 'with feedback' scenarios are summarised in Table 5. According to the results, the reallocation of human resources as proposed by the optimisation experiment can reduce the lead time of Phase III – Distribution by 15% compared to the 'without feedback' scenario. From the simulation results, it can be seen that the proposed reallocation of human resources can maximise the daily dispatches, complete all the deliveries, eliminate the WIP and prevent excessive use of human resources, while

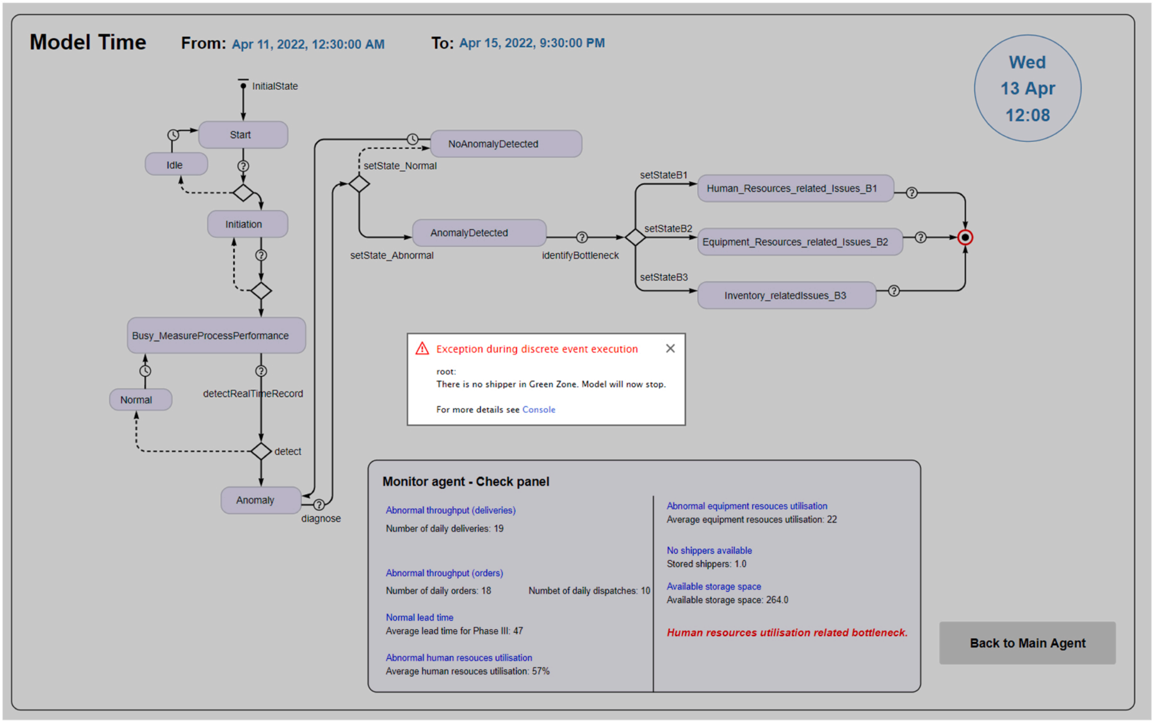


Fig. A1. AnyLogic interface of the monitoring agent-based model for automated anomaly detection and bottlenecks analysis for the 'Disruption – without feedback' scenario.

Table A1
Case study: input data – human, equipment & material resources.

Parameter/variable	Value
Weekly number of deliveries	12
Weekly number of orders	10
Initial stock size of shippers	35
Storage capacity of shippers	280
Initial stock size of cryomaterial	3000
Storage capacity of cryomaterial	30,000
Number of trolleys	2
Number of cryocarts	6
Number of tanks for cryomaterial storage	12
Shippers' storage capacity of pallet racks	420
Number of operators for: receiving deliveries	2
general activities	20
shippers filling	4
Quality Assurance (QA)	4
Quality Control (QC)	6
certified Qualified Person (QP)	2
Number of operators required for daily activities: receipt of deliveries	2
receipt of material	9
shipper filling	4
inventory	13
verification	18
dispatch	12

Table A2
Case study: input data – cycle time distributions.

Manufacturing Phase	Manufacturing Activity	Distribution (minutes)
Phase I – Receipt & Inventory	Arrivals checking*	Uniform(2, 3)
	Documenting	Triangular(7 ± 3)
Phase II – Storage & Monitoring	Recycling & Refilling	Triangular(47 ± 23)
	Storing/Picking material*	Triangular(18 ± 10)
	Storing/Picking shipper*	Uniform(5, 10)
	QA quality check	Triangular(30 ± 5)
	QC quality check	Triangular(20 ± 5)
	QP quality check	Off-site, > 1 day
	Documenting & Verification	Uniform(35, 55)
Phase III – Distribution	Packaging	Triangular(15 ± 5)
	Dispatching*	Uniform(0.08, 0.17)

satisfying the constraints defined during the optimisation experiment in terms of WIP and HRU rates. Therefore, it has been demonstrated that the optimal values for the reallocation of human resources can be effectively applied for eliminating the bottlenecks emerged in the cryogenic warehouse from the occurrence of anomalies in the sensor data.

5. Discussion

Most of the existing literature on agent-based CPSs and DTs in manufacturing is limited to conceptual models [25,44,63], top-down approaches [46,51,54,62], static complexity for optimal routing strategies without considering uncertainty in lead times or resources (i.e. dynamic complexity) [2] and data-driven approaches [59,20]. Similarly, top-down approaches are greatly used by the current DT and CPS approaches on detecting and diagnosing anomalies in manufacturing [12,19,32,49,51]. The existing top-down approaches are modelling systems at the macro and micro levels, while lacking a formal comprehensive method for capturing emergent behaviour [32,40]. Such approaches where systems are developed at an abstract level are more appropriate if the detail of level of the available input data is aggregated at a high level. On the contrary, if data about the system is available, bottom-up approaches are more beneficial to represent the system by modelling external interactions with the environment and internal interactions between sub-systems (i.e. exo-level agents) and components (i.e. micro-level agents) [48].

In manufacturing, systems are built by increasingly dynamic complexity at different levels of an agent-based model [7,9,20]. These

Table A3
Case study: average nominal RFID input data.

Parameter/variable	Value/Distribution	Unit
Average number of: deliveries	Uniform (9, 10)	/day
orders	Uniform (8, 10)	/day
(*continued*)		
Parameter/variable	**Value**	
dispatches	Uniform (6, 8)	/day
Maximum allowable rate: human resource utilisation	50%	
equipment resource utilisation	50%	
Average lead times with RFID: Arrivals checking	Uniform (9, 15)	seconds
Storing material	Uniform (2, 4)	minutes
Picking material	Uniform (1, 3)	minutes
Dispatching	Uniform (9, 15)	seconds
Phase I – Receipt & Inventory	Uniform (12, 14)	minutes
Phase II – Storage & Monitoring	Uniform (55, 58)	minutes
Phase III – Distribution	Uniform (30, 35)	minutes

systems, typically, consist of multiple manufacturing phases where various manufacturing activities operate simultaneously. Dynamic complexity, arising from manual activities with interactive behaviour, can create parallel dynamic interactions (i.e. collaborative interdependencies) in the system, affecting its productivity and performance. Advanced computational modelling such as bottom-up ABM approaches help represent such interdependencies and obtain a formal and flexible description of the system [20]. Using the agent-based technique, the probabilistic variability and aggregate parallelism and dynamism of parallel dynamic interactions in complex manufacturing systems can be captured [7,9].

This work contributes to the literature of complex manufacturing systems by proposing a generic, yet novel approach using the ABM technique for developing a DT-based multi-agent CPS model. The scope of the DT is to improve the operation of complex manufacturing systems, while the purpose of the CPS is to support the implementation of DT by automatically enabling anomaly detection and emergent bottlenecks identification (exo-level) through communicating with other agents in macro, exo, meso and micro levels dynamically. The DT-CPS provides knowledge feedback automatically to the physical space to remove the identified bottlenecks through self-optimisation. The agent-based technique is more flexible, interactive and effective compared to the other dynamic modelling techniques, defining the agents' behaviour and how this changes in real-time while interactions with other agents at the same or other levels occur [39,9]. Moreover, to derive formal results, the SFDS modelling framework is employed to formulate the DT-based multi-agent CPS method (Section 3.3). In addition, the SFDS framework and NFA theory are used to mathematically formulate the hybrid multi-agent ABM-DES simulation method and monitoring agent-based model at the exo-level (Section 3.3), respectively.

This study goes beyond the existing conceptual research, providing a formal comprehensive DT-CPS approach for complex manufacturing systems able to continuously monitor operation, detect anomalies, and identify and remove bottlenecks. This work enhances the current understanding, by employing the agent-based technique to create a flexible and functional DT-based multi-agent CPS that captures the elements of a system that move around and interact with other parts of the twin. Agent-based models single acting entities of the system and the sophisticated interactions between agents and heterogeneous state space during simulation in order to determine the macro behaviour of the system. The DT-CPS model offers prompt anomaly detection and bottlenecks identification by introducing the exo-level agent. This offers users more insights in identifying the anomalies in input data and tracking bottlenecks and root causes. Utilising the approach, complex manufacturing systems can be analysed considering uncertainty quantification on lead times and resources utilisation. Such in-depth analysis can facilitate enhanced decision making for the complex manufacturing systems.

According to the case study, this research work examines: (i) the DT-based multi-agent CPS architecture for a complex manufacturing system; (ii) the ability of the 'monitoring agent' to automatically detect anomalous values to sensor data and identify emergent bottlenecks that affect the system's performance and productivity in terms of throughput, lead times, resources utilisation and inventory levels; and (iii) the capability of the DT-CPS to provide automated knowledge feedback from macro to micro, meso and exo level agents to remove and mitigate the identified bottlenecks though reallocation of human resources. The results show that the proposed DT-CPS for complex manufacturing systems can effectively detect anomalies in input data, generated by the RFID system, and evaluate the impact of the bottlenecks these anomalies cause on the system performance. In terms of this latter point, the results show that the 'monitoring agent' of the DT-based multi-agent CPS has effectively detected an increase in the system's throughput by about 100% and, in turn, identify an increase in the utilisation rate of human resources by about 21.4%, in lead times by about 25.6%, and a shortage of human and material resources at certain times during the daily operations of the cryogenic company. Self-optimisation for removing the identified bottlenecks and reduce lead times and utilisation rates of human resources to normal operating levels is successfully employed by reallocating the human resources of the cryogenic warehouse. The reallocation of human resources has been provided automatically from the configuration layer to the smart connection layer reducing the utilisation rates of operators by 30%, throughput by 33% and lead time by 15% on average.

6. Concluding remarks

This paper has presented a DT-CPS approach, composed of multiple agents, for automated anomaly detection, and bottlenecks identification and removal for complex manufacturing systems with dynamic parallel interactions, using the bottom-up ABM technique. Anomalous values in model input data, captured from RFID sensors, are detected at the micro-level agent and bottlenecks that deteriorate the system's performance are identified at the micro, meso, exo and macro level agents. The theoretical aspects and the mathematical formulation of the DT-based multi-agent CPS method have been introduced as an extension to the hybrid simulation method, introduced by Farsi et al. [7], that uses an ABM-DES technique to simulate a dynamic system of parallel multi-agent discrete events. The hybrid ABM-DES simulation method has been extended by introducing the 'monitoring agent' at the exo-level that interactively communicate with the micro, meso, exo and macro level agents to detect anomalies, and identify and handle bottlenecks in an automated and dynamic way. The UML Class diagram of the DT-based multi-agent CPS model and the UML State Machine diagram of

Table A4
Case study: RFID input data - cycle times for the 'DT-CPS – Disruption' scenario.

Activity with RFID	Test Procedures																						
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**
Picking Material (minutes)	10	9	10	8	8	15	12	10	11	9	12	15	8	8	8	10	12	10	11	10	10	10	10
(continued)																							
	24	**24**	**25**	**26**	**27**	**28**	**29**	**30**	**31**	**32**	**33**												
Picking Material (minutes)	9	9	10	10	12	11	12	11	10	9	9												

the monitoring agent-based model for automated anomaly detection and bottlenecks identification have been presented. Moreover, the impact of the 'monitoring agent' on the performance of complex manufacturing systems in terms of throughput, lead times, inventory levels and resource utilisations has been measured. To test the validity of the proposed approach, a case study in the CGT industry was employed. Following the DT-based multi-agent CPS architecture, the case study for the selected cryogenic warehouse was developed and the results obtained from the simulation for different scenarios were compared against data from the company; excellent agreement was found in terms of anomalies detection and bottlenecks identification. The outcomes from the DT-based multi-agent CPS model provide support and detailed information in terms of prompt and accurate detection of anomalies, and identification and removal of bottlenecks in complex systems.

The DT-based multi-agent CPS architecture, model, mathematical method, and simulation model can be used as an automated monitoring tool of anomalies detection, and bottlenecks identification and removal for more informed decision making and control in manufacturing sectors with a highly regulated and complex nature. The proposed architecture and method differ from the existing models as anomalies in input data are detected and unplanned bottlenecks are identified and eliminated automatically over time using real-time data. The bottom-up approach of the model using the multi agent-based technique for DTs can enhance the flexibility, interactivity and modularity of DT-CPS design. The bidirectional communication between the physical and twin spaces is also considered. Additionally, the method and simulation model follow a stochastic bottom-up approach for DT-CPS, to detect anomalies and identify bottlenecks in complex manufacturing systems using the ABM, DES and pdf techniques.

Further to this work, the applicability of the DT-CPS approach can also be explored in other manufacturing or production systems and supply chains. Further research can also be conducted to quantify the impact of the 'monitoring agent' in terms of sustainability and evaluate the cost of goods and energy consumption. In this regard, cost information could be added to the simulation model to calculate the cost and profit for different scenarios considering unexpected and emergency events and their financial and environmental impacts. Additionally, the quality of simulation results could be improved with the integration of parameters variation and sensitivity analysis techniques to gain deeper understanding in terms of the operation of complex manufacturing systems. Another future direction could be to identify different uncertainties within the multi-agent DT architecture checking the accuracy of communication between physical system and its digital counterpart. The proposed DT could also be enhanced with cognitive capabilities through semantic technologies such as knowledge graphs. In this regard, actionable cognitive twins could be investigated to bring intelligence through cognitive capabilities to support execution of autonomous activities and provide insights and informed decision-making.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. DT-CPS: multi-agent simulation method: steps 1–3

See Fig. A1 and Tables A1–A4.

Step 1: Multi-layer phase space agents development

Complex manufacturing systems are structured from multiple layers that interactively communicate to each other. As proposed in the work by Farsi et al. [7], in the context of complex manufacturing systems with multiple layers of connectivity, Network theory can be used to model the state of locations and dynamics between agents, and stochastic finite dynamical systems (SFDS) formulation can be used to simulate the communication networks between agents in a continuous model space and network. The modelling framework of SFDS, as discussed in Laubenbacher et al. [27] has been employed to mathematically formulate the DT-CPS and derive formal results. A SFDS is defined as a set of parallel dynamical systems $\{\Phi_\pi : \pi \in T\}$, where T is the subset of permutations, with a given probability distribution. The states of the system are updated using a permutation $\pi \in$ T and a system Φ_π is selected randomly for the next iteration. The stochastic phase space of a SFDS, Γ_W, can be modelled as a Markov chain over the state space X^n and the adjacency matrix of Γ_W that shows the probabilities of moving from one state to another can be formulated as a Markov transition matrix. Thus, let W be a finite collection of systems $\Phi_1,\ldots,\Phi_t$, where $\Phi_i : X^n \rightarrow X^n$ for all i, and $p_1,\ldots,p_t$be the probabilities which sum to 1. The stochastic phase space of $\Phi_W$is Γ_W and can be obtained as:

$$\Gamma_W = p_1\Gamma_1 + p_2\Gamma_2 + \ldots + p_t\Gamma_t \tag{A1}$$

where Γ_i is the phase space of Φ_i. Thus, macro-level agent, enclosing the 'monitoring agent', phases, modules and components, can be expressed as a set of parallel dynamical systems $\{\Phi_\pi : \pi \in T\}$ with a given probability distribution, where *:* $X^n \rightarrow X^n$. Manufacturing phase at exo-level agent is defined as proposed in Eq. (1). Similarly, the finite collection of meso-level agents Ω_p are $\Phi_{m1,}\Phi_{m2},\ldots\Phi_{mp}$. The stochastic phase space of $\Phi_{W_m}$is Γ_{W_p} and can be calculated as:

$$\Gamma_{W_m} = p_{m1}\Gamma_{m1} + p_{m2}\Gamma_{m2} + \ldots + p_{mp}\Gamma_{mp} \tag{A2}$$

Finally, the collection of micro-level agents in a finite set X can be described as: $X = \{x_1, x_2, \ldots, x_n\}$.

Step 2: Multi-layer network development

In this section, a network of agents is represented by nodes and the topology, i.e., relationships and methods of interactions, of the agent-based model is developed. Let two sets of nodes x_i and x_j that represent micro-level agents interacting with each other, where $i,j = 1, 2, \ldots n$. The state for each node set is represented by a canonical vector ε_i and ε_j in the space $\mathbb{R}^N$. The interactions between the agents in a complex manufacturing system can be expressed with the mathematical formulation of multilayer networks, as proposed by Domenico et al. [5] and Farsi et al. [7], as:

$$\Phi^{\alpha\widetilde{\alpha}}_{\beta\widetilde{\beta}} = \sum_{\widetilde{i,j}=1}^{L} \sum_{i,j=1}^{N} w_{ij}\left(\widetilde{ij}\right) \varepsilon^{\alpha\widetilde{\alpha}}_{\beta\widetilde{\beta}}\left(ij\widetilde{ij}\right) \tag{A3}$$

where $w_{ij}\left(\widetilde{ij}\right)$ is the intensity of the relationship between nodes n_i in layer i and nodes n_j in layer j; $\varepsilon^{\alpha}(i)$ and $\varepsilon^{\beta}(j)$ are the αth and βth components of the ith and jth contravariant canonical vectors ε_i and ε_j in $\mathbb{R}^N$, respectively; and $\varepsilon^{\alpha\widetilde{\alpha}}_{\beta\widetilde{\beta}}\left(ij\widetilde{ij}\right)$ is the fourth-order canonical basis in space $\mathbb{R}^{N\times N\times L\times L}$.

Step 3: Process-oriented states development

In this section, the process-oriented states, i.e., the manufacturing processes that can be described as a sequence of separate discrete events such as picking and storing items, performing quality checks and verifications, are simulated at exo-level agents using the DES technique. Based on the Discrete Event System Specification (DEVS) formalism, developed by Zeigler et al. [61], discrete event simulation models can be expressed mathematically as:

$$M = < X, S, Y, s_0, \delta_{\text{int}}, \delta_{ext}, \lambda, t_\alpha > \tag{A4}$$

where X is a set of input events that occur outside the system; Y is a set of output events; S is a set of sequential states, $s_0 \in S$ is the initial state; $t_\alpha : S \rightarrow \mathbb{T}^\infty$ is the time advance function used to determine the lifespan of a state s; δ_{int} is the function that defines the change of a state s according to time progress when no external events occur; δ_{ext} is the function that defines how an input event changes state s of the system; and λ is the output of the system in the state s.

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