A Modular Hybrid Simulation Framework for Complex Manufacturing System Design

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Abstract

For complex manufacturing systems, the current hybrid Agent-Based Modelling and Discrete Event Simulation (ABM–DES) frameworks are limited to component and system levels of representation and present a degree of static complexity to study optimal resource planning. To address these limitations, a modular hybrid simulation framework for complex manufacturing system design is presented. A manufacturing system with highly regulated and manual handling processes, composed of multiple repeating modules, is considered. In this framework, the concept of modular hybrid ABM–DES technique is introduced to demonstrate a novel simulation method using a dynamic system of parallel multi-agent discrete events. In this context, to create a modular model, the stochastic finite dynamical system is extended to allow the description of discrete event states inside the agent for manufacturing repeating modules (meso level). Moreover, dynamic complexity regarding uncertain processing time and resources is considered. This framework guides the user step-by-step through the system design and modular hybrid model. A real case study in the cell and gene therapy industry is conducted to test the validity of the framework. The simulation results are compared against the data from the studied case; excellent agreement with 1.038% error margin is found in terms of the company performance. The optimal resource planning and the uncertainty of the processing time for manufacturing phases (exo level), in the presence of dynamic complexity is calculated.

Keywords: *Complex manufacturing, Modular hybrid simulation, Multi-agent system, Resource planning, Agent-based modeling*

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1. Introduction

Manufacturing system simulation focuses on operation and system design [1]. System operation studies maintenance planning & scheduling, real-time control and performing policies & regulations [2, 3]. Whereas, system design studies facility and plant layout, material handling and flexible manufacturing [4, 5, 6, 7]. Facility design considers the allocation of different machinery in a system and, therefore, impacts manufacturing performance. Moreover, material-handling design has been the centre of attention for numerous research studies due to its significant effect on total production efficiency. Flexibility can be described in terms of labour, products, raw materials, machines, inventory, routing or as a combination; known as mix flexibility. In manufacturing processes, flexibility is vital to accommodate the production capacity and customers' demand. One of the key elements for developing a flexible manufacturing process is to measure the capacity of the process, known as manufacturability, where the system must be developed and refined to have a robust and error proof-process [8, 9]. Complex manufacturing systems consist of multiple sub-systems that operate simultaneously - referred to as the manufacturing phase in this study. Manufacturing processes in different phases can interact with each other; for instance, the interaction can emerge from labourers who are responsible for performing several tasks in different phases, or can arise from equipment and information, which are shared between different processes. In this study, such interactions are referred to as parallel interactions. These considerations are essential to achieve mix flexibility. Moreover, complex systems are highly time-dependent, multifunctional and possess diverse characteristics. In this context, a manufacturing module is described as a sequence of events that are repeated frequently; such as quality control and feedback procedures. The existence of repeating modules in multiple sub-systems is a characteristic of complex manufacturing. Complexity in manufacturing systems can potentially arise from complications in the physical structure of systems and sub-systems, as well as multifunctionality of system components, known as static complexity. The unpredictability in system behaviour presents dynamic complexity over time [10]. The later complexity is more likely to arise in highly regulated manufacturing systems, including manual handling processes and with interactive behaviour. The complexity study necessitates the use of advanced simulation techniques to certify high quality, economically viable processes and final products. [11]. Evaluating and optimising the behaviour of such systems requires an integrated framework that considers all aspects and characteristics of manufacturing processes.

1.1. Research gaps

In the current hybrid ABM–DES simulation frameworks, the agent-based technique is mostly employed to model the global manufacturing system and components as macro and micro-level agents respectively [12, 13]. However, global manufacturing systems can also be split into multiple sub-systems (exo-level agents) which can interact with each other in a parallel manner. Each sub-system has an individual dynamical discrete event structure composed of multiple repeating modules. In this study, these modules are considered as the *meso-level* of agent-based modelling. The multi-layer ABM structure for complex manufacturing systems is illustrated in Figure 1.

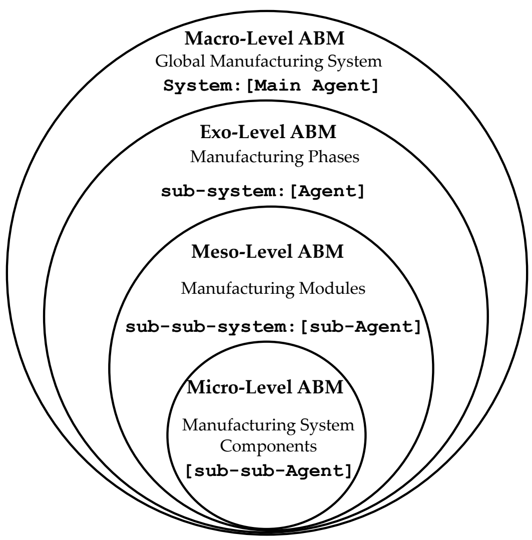


Figure 1: Modular hybrid ABM–DES method (MHSM): Multi-layer ABM structure for complex manufacturing systems

Regarding the context of complex manufacturing system design [10], the following research gaps are identified: (i) In the existing ABM–DES hybrid simulation methods, the dynamical structure at meso level is not fully covered for manufacturing systems with highly regulated and manual handling processes; (ii) system design and simulation are not integerated and typically carried out by individual procedures including logical design, floor planning and physical design [14]; (iii) A degree of static complexity has been considered to study optimal resource planning [15, 16, 17]. In [16], static complexity arises from the variability in production line since each product batch may take different route though the preparation process with different queue capacity. Hao & Shen [17] proposed a hybrid simulation approach to model material handling processes in an assembly line. Complexity in their work is due to the variability of operations on different products which is also known as static complexity. Literature addressing dynamic complexity is scarce. Studies regarding dynamic complexity in manufacturing processes with several random events and uncertainties require stochastic data analysis and performance measures, which are addressed in this paper; (iv) Developing a simulation framework for system design, in particular by using the ABM technique, was mainly covered in social sciences and supply chain studies [18], rather than complex manufacturing processes in plants.

In this work, a Modular Hybrid Simulation Framework (MHSF) for complex manufacturing system design is presented. In this framework, the concept of modular hybrid ABM–DES technique is introduced to demonstrate a novel simulation method called Modular Hybrid Simulation Method (MHSM) using a dynamic system of parallel multi-agent discrete events. In this context, the stochastic finite dynamical system is extended to allow the description of discrete event states inside the agent at the meso level. This extension creates a modular structure for the hybrid ABM–DES technique called *modular hybrid*. Dynamic complexity regarding uncertain processing time and resource allocation is investigated to quantify uncertainty in the processing time.

The remainder for the rest of this paper is organised as follows: the modular hybrid framework is developed in Section 2. A case study in the cell and gene therapy industry is conducted in Section 3 to test the validity of the framework, following the research methodology illustrated in Figure 2. Moreover, the simulation results are verified and validated with the actual data from the studied case. This is followed by further simulation and optimisation results. Summary of critical discussion on the framework and the simulation outcomes are presented in Section 4. Finally, Section 5 highlights the conclusions and the potential future research work.

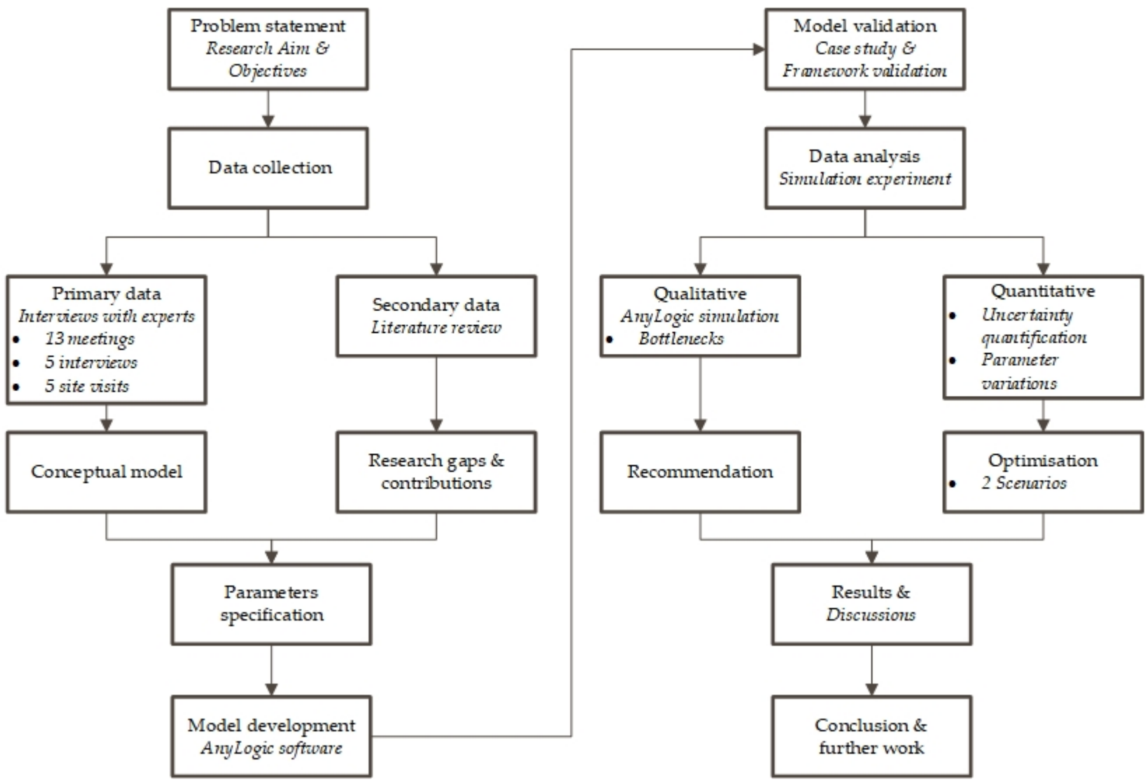


Figure 2: Research Methodology

2. Proposed Modular Hybrid Simulation Framework (MHSF) for complex manufacturing system design

Analytical modelling provides mathematical formulations to describe and predict the performance of manufacturing systems. However, for complex manufacturing processes, mathematical complexity grows rapidly. Even when the manufacturing performance is formulated, it is challenging to find the analytical solution due to inherent stochastic emergence phenomenon. Moreover, designing the physical structure including a dynamic network of interactive behaviours add more complexity to the analytical model. Therefore, advanced simulation techniques can be deployed to study complex systems. Within this context, modular hybrid ABM–DES simulation method is presented in Section 2.1. This is followed by the modular hybrid framework development in Section 2.2.

2.1. Modular hybrid ABM–DES simulation method

A dynamic system of multi-agent discrete events is deployed to model complex manufacturing processes. MHSM is introduced as an extension to the Stochastic Finite Dynamical System

(SFDS) approach which allows the description of discrete event-based states within an agent using Discrete Event System Specification (DEVS) modular formalism. The method consists of three main parts as illustrated in Figure 3:

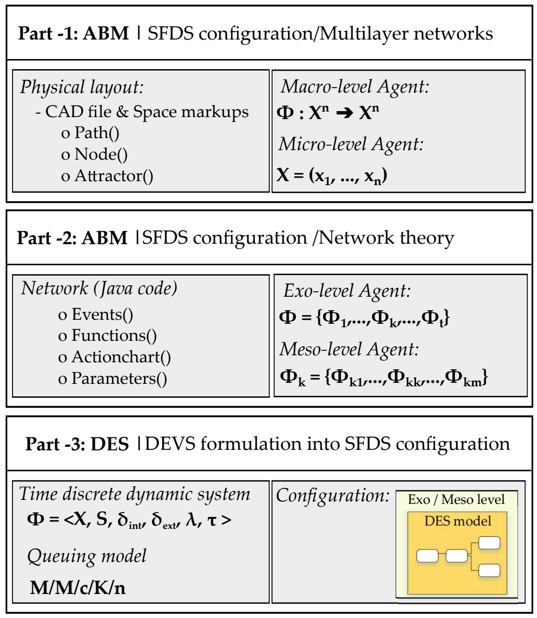


Figure 3: Modular hybrid ABM–DES method (MHSM): SFDS and DEVS configuration using network theory

Part-1: Objected-oriented approach for macro and micro level agents: in this study ABM approach has been selected to create the global system of complex manufacturing, multiple local sub-systems, repeating manufacturing modules and components. The global system is a top-level or macro-level agent called `Main()` class. Moreover, `Main()` agent may contain several manufacturing components such as staff members, products, machines, information, *etc.*, which are modelled at a micro-level agent so-called `<sub-sub-Agents>` class. These agents are created as *population* agent type where a number of entities of the same type living in the same environment. Micro-level agents have specific characteristics which can be described by several *parameters* (e.g. rate, capacity, constraints) and *schedule* elements (e.g. working shifts) and can be divided into different *resource* units. The type of resource units can be categorised as *static*, *moving* or *portable*. The behaviour algorithm of each micro-level agent can be defined by an *Action chart*. The interaction rules between multiple agents can be defined using *Functions* and *Events* for algebraic and non-algebraic rules respectively. Some of the labourer related rules can be task delays & timeouts; and machine related rules can be breakdowns, time of failure, and time to maintenance for equipment.

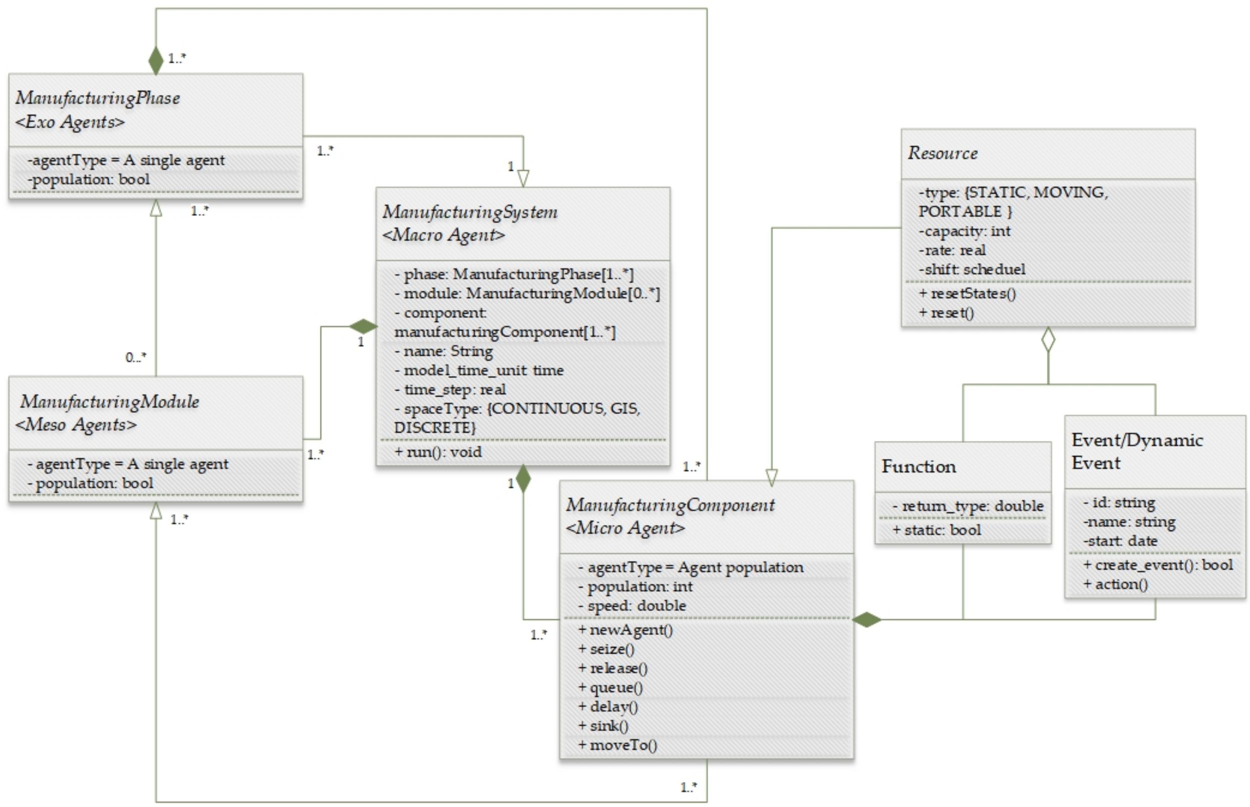


Figure 4: UML Class diagram of MHSM

The UML class diagram is shown in Figure 4

Part-2: Objected-oriented approach for exo and meso level agents: the ABM approach has been also selected to simulate the interactive structure of manufacturing sub-systems and repeating modules, which are modelled at exo and meso level agents so-called `Agents()` and `sub-Agents()` class respectively. Such agents are created as a *single* agent type that will always exist within the Main. Meso-level agents are modular and can be deployed in multiple sub-systems.

Part-3: Process-oriented approach for exo and meso level agents: The finite dynamical system of manufacturing processes at each manufacturing phase and modules are modelled inside the exo and meso level-agent classes using DES modelling approach. Utilising the modular technique will simplify the complicated structure of DES model and will ease the simulation error tracking through the modelling procedure. Moreover, the structure of the modular hybrid model becomes more neat and understandable for non-experts. In this study, dynamic complexity is introduced in the hybrid model by considering uncertainties in the form of probabilistic distribution in design parameters, schedule and shifts and sequence of events within each sub-system.

2.2. Modular hybrid ABM–DES framework development

The research gaps highlighted previously, led to the development of the modular hybrid simulation framework for complex manufacturing system design as illustrated in Figure 5. The framework is composed of six steps.

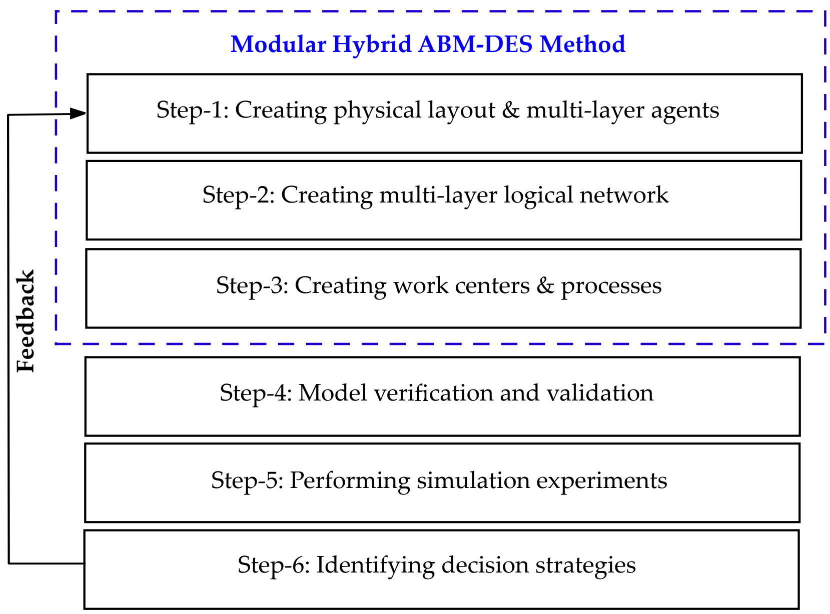


Figure 5: Modular hybrid simulation framework (MHSF) for complex manufacturing system design.

Step-1: Creating physical layout & multi-layer agents

The structure of complex manufacturing systems has multiple layers of connectivity. Layout of manufacturing systems and configuration of each layer in the global `Main` agent (Macro-level) can be introduced in the simulation environment using space markups. The physical network representation between different layer can be developed in terms of *Path* (e.g. movement), *Node* (e.g. reside, intersection) and *Attractor*; Attractors control the entities (Micro-level) inside a node. In this context, SFDS formulation can be used as a configuration to perform ABM and to simulate the communication networks between the agents, where the model space and network are considered as continuous. State of locations and dynamics of complex interactions between the agents can be modelled using *Network theory*. Moreover, states of each node updates using a permutation $\pi \in T$ together with a given probability distribution, where, T is the subset of permutations and for any random permutation π, Φ_π is the phase space function for a parallel dynamical system. Let $x_1, \ldots, x_n$ collection of entities in a finite set X and the elements in X represent the state of the entities at micro-level agent. SFDS configuration is a set of parallel dynamical systems Φ_π together with a probability distribution, therefore the phase space of Φ at exo-level agent can be described as a directed graph on the vertex set X^n written as $\Phi : X^n \to X^n$ and all micro-level agents in Φ_k have the probabilities $p_1, p_2, \ldots, p_t$ and the finite collection of agents, Ω, are $\Phi_1, \ldots, \Phi_k, \ldots \Phi_t$. The stochastic phase space of Φ_Ω is Γ_Ω and calculated as thus:

$$\Gamma_\Omega = p_1\Gamma_1 + p_2\Gamma_2 + \cdots + p_t\Gamma_t$$

The stochastic phase space Γ_Ω can be introduced as a Markov chain over the state space X^n and therefore the adjacency matrix can be described as the Markov transition matrix [19]. Similarly, considering the finite collection of meso-level agents, Ω_m, as $\Phi_{k1}, \ldots, \Phi_{kk}, \ldots \Phi_{km}$. The stochastic phase space of Φ_{Ω_k} is Γ_{Ω_m} and calculated as thus:

$$\Gamma_{\Omega_k} = p_{k1}\Gamma_{k1} + p_{k2}\Gamma_{k2} + \cdots + p_{km}\Gamma_{km}$$

Step-2: Creating multi-layer logical network

The logical network in a complex manufacturing system necessitates consideration of the interactions between micro-level agents among the upper layers. Base on the mathematical formulation of multilayer networks [20], suppose two set of nodes x_i and x_j represent different micro-level agents who interact with each other, where $i, j = 1, 2, \ldots, n$. The associated state with each node set can be represented by a canonical vector $\mathbf{e}_i$ and $\mathbf{e}_j$ in the vector space $\mathbb{R}^N$. In this regard, the second-order canonical tensor describes the relationship between the sub-agents and can be defined by $\mathbf{E}_{ij} = \mathbf{e}_i \otimes \mathbf{e}_j^\top$, where $\top$ is the transposition operator. Concerning multilayer networks, let $e^\alpha(i)$ as the αth component of the ith contravariant canonical vector $\mathbf{e}_i$, and $e_\beta(j)$ as the βth component of the jth covariant canonical vector $\mathbf{e}_j$ in the space $\mathbb{R}^N$. Following a similar approach, for the agents layers $l_{\tilde{i}}$ and $l_{\tilde{j}}$, where $\tilde{i}, \tilde{j} = 1, 2, \ldots, L$. Thus, $e^{\tilde{\alpha}}(\tilde{i})$ and $e_{\tilde{\beta}}(\tilde{j})$ are the canonical vectors in space $\mathbb{R}^L$. The multilayer adjacency tensor can be written as thus:

$$\Phi^{\alpha\tilde{\alpha}}_{\beta\tilde{\beta}} = \sum_{\tilde{i},\tilde{j}=1}^{L} C^{\alpha}_{\beta}(\tilde{i}\tilde{j}) E^{\tilde{\alpha}}_{\tilde{\beta}}(\tilde{i}\tilde{j}), \tag{1}$$

where the second order tensors $E^{\tilde{\alpha}}_{\tilde{\beta}}(\tilde{i}\tilde{j}) = e^{\tilde{\alpha}}(\tilde{i}) e_{\tilde{\beta}}(\tilde{j})$ represent the canonical basis of the space $\mathbb{R}^{L\times L}$ and the second-order interlayer adjacency tensor $C^{\alpha}_{\beta}(\tilde{i}\tilde{j})$ is thus:

$$C^{\alpha}_{\beta}(\tilde{i}\tilde{j}) = \sum_{i,j=1}^{N} w_{ij}(\tilde{i}\tilde{j}) E^{\alpha}_{\beta}(ij), \tag{2}$$

where $w_{ij}(\tilde{i}\tilde{j})$ is the intensity of the relationship between nodes n_i in layer $\tilde{i}$ and nodes n_j in layer $\tilde{j}$. Therefore Equation 1 can be expressed as:

$$\begin{aligned} \Phi^{\alpha\tilde{\alpha}}_{\beta\tilde{\beta}} &= \sum_{\tilde{i},\tilde{j}=1}^{L} \left[\sum_{i,j=1}^{N} w_{ij}(\tilde{i}\tilde{j}) E^{\alpha}_{\beta}(ij) \right] E^{\tilde{\alpha}}_{\tilde{\beta}}(\tilde{i}\tilde{j}), \\ &= \sum_{\tilde{i},\tilde{j}=1}^{L} \sum_{i,j=1}^{N} w_{ij}(\tilde{i}\tilde{j}) \mathcal{E}^{\alpha\tilde{\alpha}}_{\beta\tilde{\beta}}(ij\tilde{i}\tilde{j}), \end{aligned} \tag{3}$$

where $\mathcal{E}^{\alpha\tilde{\alpha}}_{\beta\tilde{\beta}}(ij\tilde{i}\tilde{j}) = e^{\alpha}(i) e_{\beta}(j) e^{\tilde{\alpha}}(\tilde{i}) e_{\tilde{\beta}}(\tilde{j})$ is the forth-order canonical basis in space $\mathbb{R}^{N\times N\times L\times L}$. Equation 3 is a general form of the multilayer adjacency tensor to represent the interactions between the agents in a complex manufacturing system.

Step-3: Creating work centres & processes

In this section an extension to the SFDS approach is proposed to include the description of process-oriented states in the canonical vector specification of an agent at both exo and meso-level agent. According to MHSF, different work centres, assembly and disassembly procedures, and quality check procedures can be simulated using DES technique within an agent and modelled mathematically using Discrete Event System Specification (DEVS). Accordingly, DEVS provides a mathematical description of the time discrete dynamical systems for agent Φ with a modular formalism and structure as [21]:

$$\Phi = \quad < \chi, S, \delta_{int}, \delta_{ext}, \lambda, \tau >, \tag{4}$$

where, χ is input set for external events, S is a set of sequential states, δ_{int} and δ_{ext} are internal and external transition functions respectively, λ is the output function and τ is the time advance function. Equation 4 has the following constraint that τ is mapping from states

S to a non-negative real with infinity $\tau: \; S \rightarrow R^{+}_{0,\infty}$, where $\tau(s)$ represents the time the system is allowed to stay in state s, if no external event occurs. Considering e_τ as the elapsed time for state s, the total state-set of the sub-system Φ is thus:

$$Q = \{(s, e_\tau) | \; s \in S, 0 \leq e_\tau \leq \tau(s)\}. \tag{5}$$

Moreover, considering $x \in \chi$ as an input function at the state s for an elapsed time e_τ, $\delta_{int}(s)$ and $\delta_{ext}(s, e_\tau, x)$ transition mappings are thus:

$$\delta_{int} : S \rightarrow S, \qquad \delta_{ext} : Q \times S \rightarrow S. \tag{6}$$

Considering the DES simulation approach, the queuing model typically follows the $M/M/1$ rule which indicates a single-server system with unlimited queue capacity and infinite calling population. However, in multi-agent DES models with parallel servers, the queuing model can be expressed as $M/M/c/K/n$ where, the number of parallel services $c > 1$; K, the system queue capacity varies based on the system policies and regulations and n is the number of entities. Hence, the modified steady state probability P_n of having n arrivals in the systems is thus:

$$P_n = \begin{cases} \frac{\bar{\lambda}^n}{n!\mu^n} P_0 & 1 \leq n < c \\ \frac{\bar{\lambda}^n}{c! c^{n-c} \mu^n} P_0 & c \leq n < K \end{cases}, \text{where} \quad P_0 = \begin{cases} \left(\sum_{n=0}^{c-1} \frac{r^n}{n!} + \frac{r^c}{c!} \frac{1-\rho^{K-c+1}}{1-\rho} \right)^{-1} & \rho \neq 1 \\ \left(\sum_{n=0}^{c-1} \frac{r^n}{n!} + \frac{r^c}{c!} (K - c + 1) \right)^{-1} & \rho = 1 \end{cases}, \tag{7}$$

where $\rho = \bar{\lambda}/c\mu$ and $\bar{\lambda}$ is the mean arrival rate which is equal to inverse of expected value of inter-arrival time; μ denotes the service rate which is equal to inverse of expected value of service-time. In a complex manufacturing system, entity n represent a quantity of different sub-agents at different parts of the manufacturing system. It can be a number of customers, orders, deliveries and raw materials.

Step-4: Model verification & validation

Comparing the simulation outcome with real system requires application of real system initial states. For instance, the state of all agents at the start-time, Work-In-Progress (WIP) data, non-zero stock size for the raw materials and storing goods and pre-scheduled orders for dispatching. Initial conditions can be introduced using *statechart* or *actionchart* functions. It is not the goal of this article to introduce the different validation approaches for complex manufacturing systems; within this study however, the validation procedure for the case study is discussed in Section 3.1.

Step-5: Performing simulation experiments

To measure the system performance under uncertainty, a wide range of stochastic analysis techniques is required. The system performance can be evaluated by identifying the current-state bottlenecks, and performing multiple time-in-system analysis, flexible optimisation, and resource and space utilisation analysis. For instance, by introducing the objective function of random variable $\mathcal{X}$ as $f(\mathcal{X}) = E[\mathcal{X}] + \theta$, where $E[.]$ is the expected value operator and θ is the associated uncertainty, *optimisation* experiments under uncertainty provides the optimum value of a parameter set corresponding to the best value of $f(\mathcal{X})$ with respect to the system's constraints. *Parameter Variation* experiment is run multiple times to evaluate the value of $f(\mathcal{X})$ by varying one or several parameters.

Step-6: Identifying decision strategies

Performing numerical and mathematical experiments provides the information required for decision makers to evaluate and describe the behaviour of a complex manufacturing system. Within the final step of the proposed framework, the final sestem design outcomes could support decision and policy makers to enhance and modify strategies. These strategies can be in terms of product commercialisation, sourcing and procurement, value and supply chain, bidding strategy and planning, risk mitigation and management, environment and sustainability strategies, *etc*. The optimal decision strategy can be formulated in a general form as [22]: $\mathcal{X}^* = argmin(\text{or } \ argmax) f(\mathcal{X})$ for $\mathcal{X} > 0$. The outcomes with respect to the associated constraints improve the knowledge of decision and policy makers and subsequently their wisdom to modify policies and regulations within the complex manufacturing system. These knowledge and wisdom are ultimately fed back into the system.

3. Framework validation: Case study

In this study, manufacturing system at a Cell and Gene Therapy (CGT) cryogenic storage company is selected as the case study to test the validity of the proposed framework. The manufacturing system includes highly regulated and manual handling processes with multiple repeating modules. A typical CGT supply chain is illustrated in Appendix A, Figure A.1. For such complex manufacturing processes, generating the performance model are constrained by various boundaries and regulatory conditions. The interrelationship between different CGT manufacturing procedures in multiple phases develops complexity in such systems. Such complexity arises from multiple response time requirements and consideration of numerous policies and regulations. MHSF has been followed to model the case study intending to identify the manufacturing bottlenecks and to optimise the system performance.

3.1. Step–1: Physical layout & multi-layer agents

To define the physical layout and to map the manufacturing processes, a series of industrial site visits (5 site visits; 4 hours each), meetings (13 meetings and teleconferences; 2 hours each) and interviews (5 interviews; 3 hours each) with the global director, head of operations and the project team manager were carried out. Three main manufacturing phases have been investigated, which are: Phase I–receipt & inventory, Phase II–storage & monitoring, and Phase III–distribution of cryo-products. These phases are modelled as single type agents, $\Phi = \{\Phi_1, \Phi_2, \Phi_3\}$ at exo-level in the global Main CGT system. The parallel interactive procedures of the three phases are initiated when the products are transmitted from the CGT manufacturer or other healthcare institution to the CGT cryogenic storage companies. A detailed schematic for these phases are presented in Appendix A, Figures A.2–A.4. Staff members with different expertise and equipment were modelled as `sub-sub-agents`, X with individual attributes. These characteristics include sub-agents population, working hours and shifts, movement speed (meter/second) and shape (2D/3D animation sketch). The collection of micro-level agents in a finite set $X = \{x_1, x_2..., x_8\}$ as technicians, recycle & refill, load & unload, QA, QC, QP, Cryocart and trolley respectively. Moreover, three manufacturing modules are created as meso-level agents $\Phi_k = \{\Phi_{21}, \Phi_{31}, \Phi_{22}, \Phi_{32}, \Phi_{23}, \Phi_{33}\}$; the 'Quality checking' module to perform quality checks required to release the products in Phase II, Φ_{21} and III Φ_{31}, the 'Picking products' module form quarantine storage in Phase II Φ_{22} , and from storage in Phase II, Φ_{32} and the 'Packaging' module in Phase II, Φ_{23} and III, Φ_{33} to model the sequence of activities to pick the products from the storage area for quality check at quarantine stage and dispatch respectively.

3.2. Step–2: Multi-layer logical network

The logical network of the global manufacturing system at the studied CGT cryogenic storage is as follows: after shippers with/without products are delivered to the storage site, Phase–I starts by verifying and documenting deliveries. The products are initially stored in quarantine storages and may be released, recycled or disposed - considering the type of the supply - after multiple quality checks. The stored products are then quality checked and documented based on the policies and regulations in Phase–II. In this phase, the approved products will be moved to the long-term cryogenic storages. In parallel to the activities in Phase I and II, the company receives orders to dispatch the products to the healthcare institutions such as hospitals, medical clinics, *etc.* at Phase–III. This phase starts with planning and scheduling the shipments (daily, weekly, *etc.*) and continue by products' secondary packaging (it is not required for all shipments), verification, multiple checking procedures and finally dispatching containers. The three phases include highly interactive machine and material handling processes as shown in Figure 6.

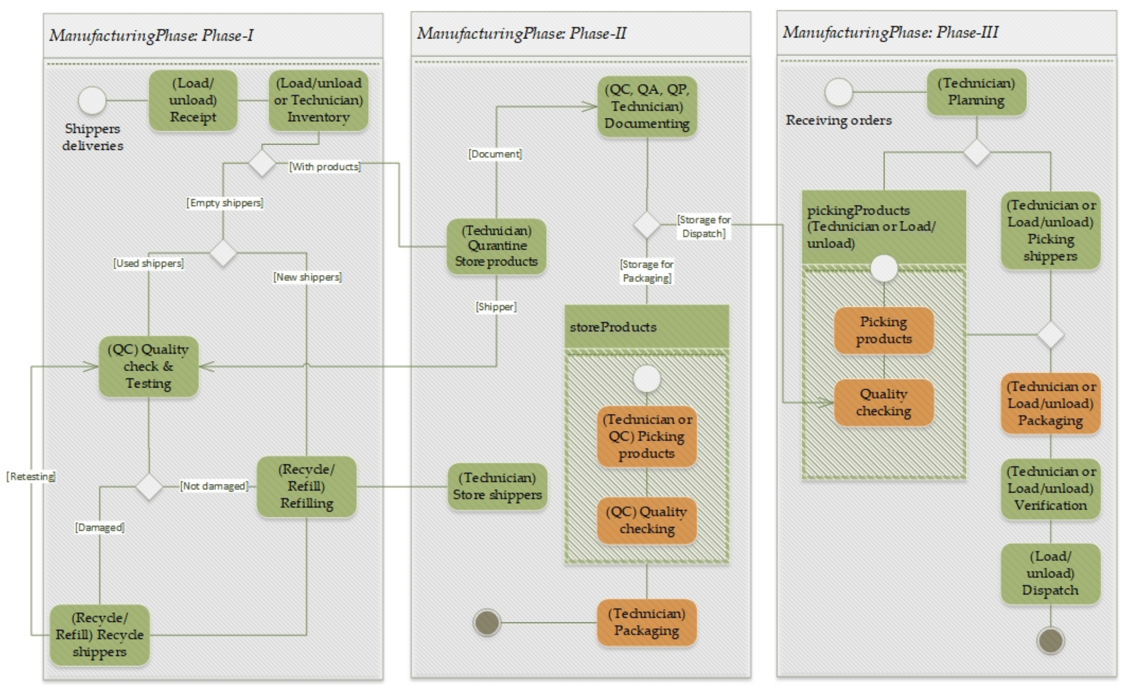


Figure 6: Case study: UML composite structure diagram for the logical network between classes with role-based annotations; manufacturing phase processes (in green) and repeating modules (in brown) are simulated using DES (see Appendix B, Figures B.6–B.8).

3.3. Step–3: Manufacturing processes

The course of the processes in details are presented in Appendix B, Figures B.5–B.8. The Figures present the discrete event modelling interface of each sub-system based on the sequence of events illustrated earlier in Figures A.2–A.4 respectively.

3.4. Step–4: Model validation

In this paper, the CGT cryogenic storage processes of the Fisher BioServices UK (FBS) Company have been studied to develop the simulation model. The micro-level agents and the corresponding attributes are summarised in Table 1.

Table 1: Simulation micro-level agents, X for the case study system design.

Agents (X)	Technician (x_1)	Recycle/Refill (x_2)	Load/Unload (x_3)	QA (x_4)	QC (x_5)	QP (x_6)	Cryocart (x_7)	Trolley (x_8)
No.	16–20	2–6	2	4	6	2	3–4	4

The uncertainty of the collected data regarding the manufacturing processes were analysed. The continuous probability distributions are used as the input data in the simulation model as summarised in Table 2. The simulation modelling tool, AnyLogic version 8 has been selected. Validation of the model is accomplished using the data from the case study. The simulation time unit is set as 'minute'. Initially, the model generates the results for one working day. Then, the time is set as 'day' to generate the simulation results for one working month. The total number of daily orders and dispatches over time are illustrated in Figure 7.

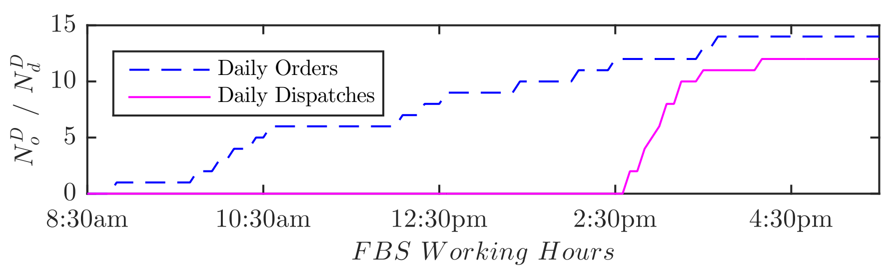


Figure 7: Simulation results for the total number of daily orders N_o^D and dispatches N_d^D on average.

The graph shows that the company received orders during the daily working hours between $8:30am$ and $4:30pm$. However, orders are dispatched between $2:30pm$ and $4:30pm$ when the delivery trucks are available at the company. Furthermore, the results for total number of monthly orders and dispatches are summarised in Table 3.

Table 2: Input data for the case study simulation model; Note that [1] new shippers' validation takes about 1 month and includes 20-day temperature monitoring process; [2] after cleaning process, shippers should be left for 12 hours so the shipments adapt to the room temperature.

	Task	Expertise	Distribution (minute)
Agent: Phase–I Receipt & inventory	Unloading	Loading person	Triangular(2, 6, 10)
	Arrival checking	Technician	Uniform(2, 3)
	Documenting	Technician	Triangular(5, 7, 10)[1]
	Recycling	Recycling person	Triangular(15, 32, 50)[2]
	Refilling	Refilling person	Triangular(10, 15, 20)
Agent: Phase–II Storage & monitoring	Storing/Picking shippers	Technician	Uniform(3, 5)
	Storing/Picking products	Technician	Uniform(5, 10)
	QA quality check	QA person	Triangular(25, 30, 35)
	QC quality check	QC person	Triangular(15, 20, 25)
	QP quality check	QP person	off-site, > 1 day
Agent: Phase–III Distribution	Documenting	Technician	Uniform(30, 45)
	Verification	Technician	Uniform(5, 10)
	Packaging/Second checking	QC person	Triangular(10, 15, 20)
	Loading shippers	Loading person	Uniform(5, 8)

Table 3: Simulation results for the total number of monthly orders N_o^M and dispatches N_d^M on average.

Time	Week-1	Week-2	Week-3	Week-4
N_o^M	48	87	132	199
N_d^M	47	87	131	199

The number of the total daily dispatches N_d^D, and the total monthly dispatches N_d^M fall into the FBS dispatch ranges which are $8 - 11$ and $150 - 250$ respectively. FBS company sets an schedule for the daily and monthly dispatches and therefore the difference between the orders and dispatches represents the WIP in the system. Actual data of the number of dispatches for an eight-month period between Jan–Aug 2016 has been provided by FBS for validation. The simulation time has been set accordingly. The real data has been compared to the results derived from the simulation model in a longitudinal study as illustrated in Figure 8.

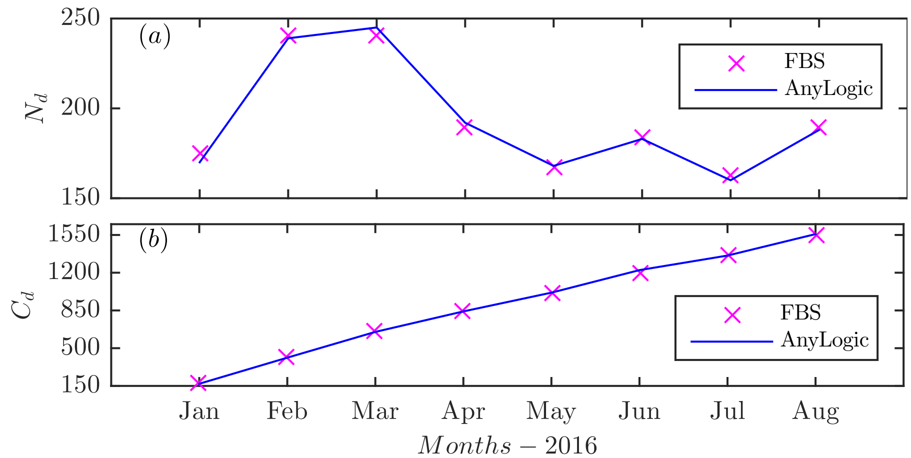


Figure 8: Simulation results against the FBS case study for the total number of dispatches (a) in each month N_d and (b) the cumulative monthly sum of the number of dispatches C_d between January and August 2016.

Initially, the simulation model generates the output for each month, and therefore it has been compared with the company monthly dispatches as presented in Figure 8(a). Moreover, the cumulative monthly sum of the company dispatches has been compared with the simulation results as shown in Figure 8(b). In order to generate the cumulative simulation output, the model time has been set to the target period (*i.e.* the last month) in every cycle. The graphs illustrate a highly representative comparison between the simulation model and the case study data with an average error of 1.038% for the monthly dispatches and 1.05% for the cumulative monthly sum of the number of dispatches.

3.5. Step–5: Simulation experiments

The simulation model has been verified and validated against the case study previously. The model represents the actual behaviour of the interactive system. To quantify the uncertainty in processing time, a range of simulation experiments has been performed and presented in this section. In this regard, the simulation time is set as ‘minute’, and the model generates the outputs from January to August. The uncertainty is quantified using stochastic data analysis. The histogram graphs have been developed to calculate the Probability Density Function (pdf) for the time period which has been spent in each sub-system. The pdf graphs for the processing time in Phase I–III have been illustrated in Figures 9(a–c) respectively. Considering the results, during the receipt & inventory process, 86.73% of deliveries are being received and documented in less than 50 minutes, see Figure 9(a).

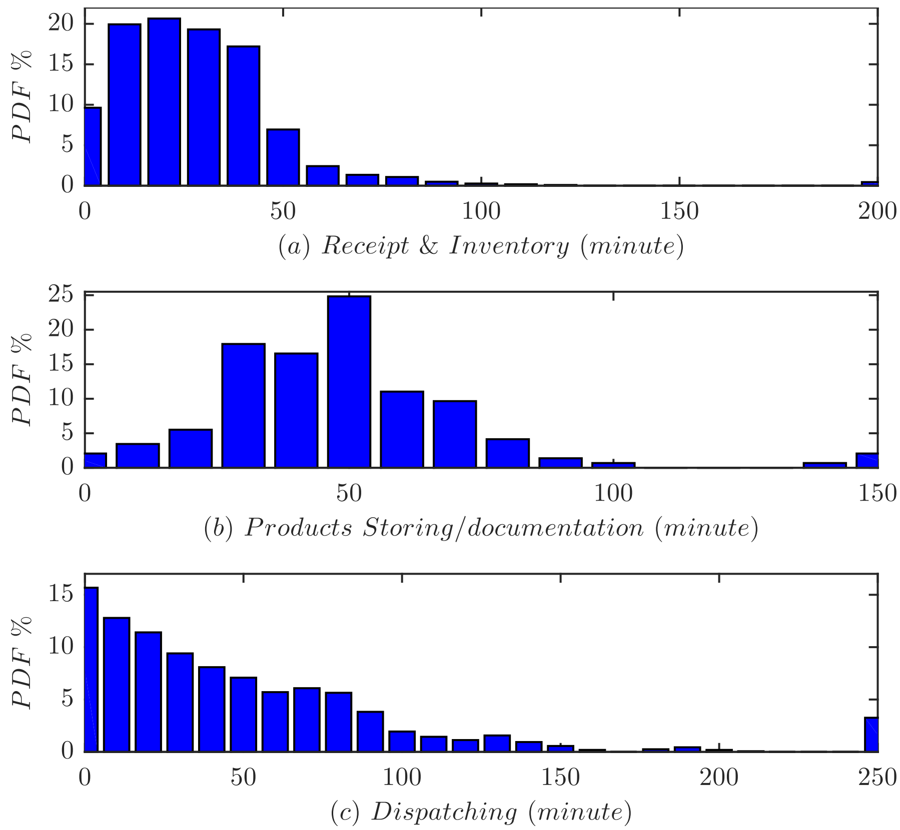


Figure 9: Histogram pdf for the processing time in each sub-system (a) receipt & inventory; (b) product storing/documentation and (c) dispatching, between January and August 2016.

Moreover, the corresponding pdf has a Poisson distribution with $\lambda_p = 52.76$ minutes. Besides, the pdf for the processing time in the products' 'storing and documentation' phase has a Poisson distribution with $\lambda_p = 71.15$ minutes. Moreover, the graph shows that 45.52% of the products are being stored in about 50 minutes. However, just above 50% of the products are being stored in between 50–100 minutes, and for just below 4%, the process takes more than 100 minutes, see Figure 9(b). Furthermore, pdf for the processing time in the dispatching phase has an exponential distribution with $\lambda_e = 0.1567$, see Figure 9(c).

Parameters variation experiment

As mentioned earlier, studying current practices is the initial step in manufacturability. Such a study attempt to identify the current-state bottlenecks and therefore to highlight the enhancement requirements and criteria in a complex manufacturing system. Hitherto, the simulation results outline the existing company's throughput and quantify the uncertainty in processing time of each sub-system. These results are based on the current practice, the storage capacity and the layout of the company. Following the simulation experiment results, the following manageable bottlenecks during the daily practices are identified:

1. refilling and recycling zone, between 9:00am–4:30pm, due to the shortage of staff working in this section,
2. receipt zone, between 10:30am–11:30am,
3. dispatching zone, between 2:30pm–4:30pm, due to the interactive processes between receipt and dispatching zones.

Moreover, by increasing the number of daily orders by 5 times, apart from the current practice bottlenecks, the following new bottlenecks have been identified:

4. picking products and shippers for dispatching, around 10:00 am–3:00 pm,
5. quality checking zone, around 10:30 am–3:30 pm,
6. shortage in the number of validated shippers.

It is also found that by the 20% increase in the number of orders, only about 80% of the orders could be successfully dispatched, and this is mainly due to the shortage in the number of validated shippers. Afterwards, Parameters Variation experiment is developed to evaluate the impact of the number of staff working on the shop floor on the company's performance (throughput). The experiment is created by focusing on the total number of monthly dispatches N_d^M and the total number of available validated shippers in a monthly practice N_v^s versus the number of staff members in the company. The aim is to find the optimum number of staff members intending to maximise the number of dispatches where the difference between N_d^M and N_v^s is minimum (*i.e.* $N_d^M \simeq N_v^s$). It is assumed that the bottlenecks $[1-5]$ have been removed in the system. To perform the Parameters Variation experiment, the model has been run multiple times with varying the number of staff members between 1 to 40 as presented in Figure 10.

The optimum number of staff members N_{opt}^* and the corresponding values for the N_d^M and N_v^s have been highlighted. Furthermore, it is found that the N_d^M and N_v^s values are insensitive to the number of staff members working in the quality check section N^Q. Therefore, this parameter is not considered as a variable for the optimisation study.

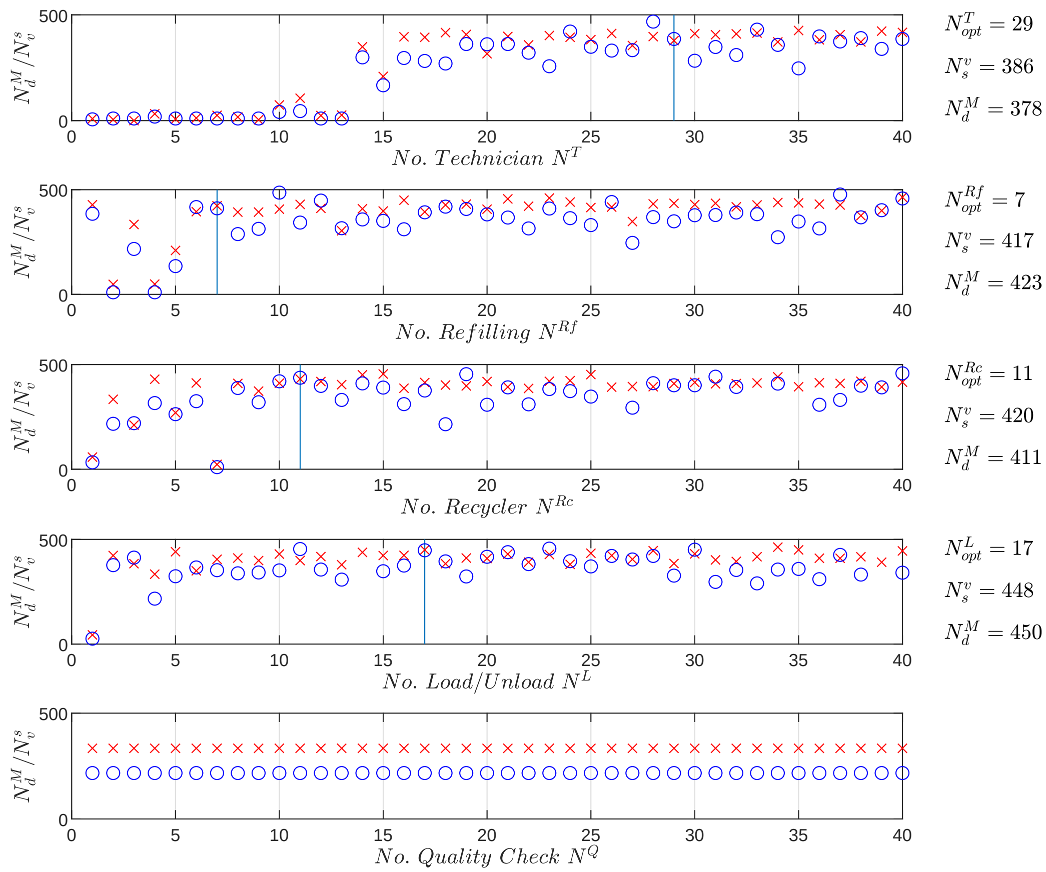


Figure 10: Parameters Variation experiment: number of staff members versus the monthly number of dispatches N_d^M with ($\times$) symbol, and validated shippers N_v^s with (o) symbol.

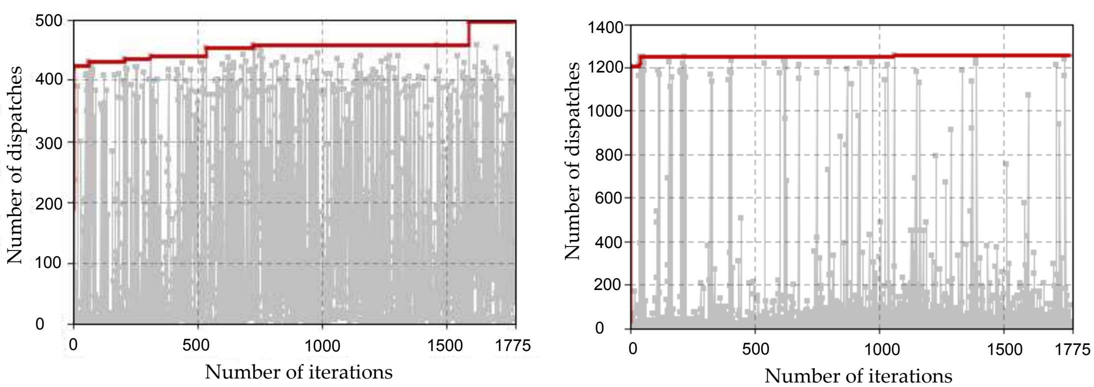
3.6. Step–6: Decision strategies

Flexible optimisation experiment has been conducted in order to find the best decision strategy regarding the optimum throughput of the case study. The optimum solution for the studied manufacturing processes has been evaluated with a view to maximise the total number of dispatches. In an initial scenario, it is assumed that (i) the company has no intention to recruit more shop-floor staff members; (ii) the bottlenecks [1–5] have been removed from the system; (iii) the required initial inventory capacity (see Figure B.5) for the validated shippers is minimum in the company and therefore $N_d^M \simeq N_v^s$, as thus:

$$f_{1,opt} = \max\ f_1(\mathcal{X}) = \max\ N_d^M$$

$$f_{2,opt} = \min\ f_2(\mathcal{X}) = \min\ N_d^M - N_v^s$$

According to the interviews with the Head of Operations and the Project Team Manager, staff working as technicians also cooperate with the other activities when the workload in other sections are high. Hence, this collaboration has been considered in the simulation. In order to find the optimum staff combination, optimisation experiment has been conducted with a view to maximise the number of monthly dispatches in the Company. The optimisation experiment is developed in AnyLogic using the built-in Opt-Quest optimisation technique [23]. optimisation is initiated by defining the objective function, model constraints, and parameters that can be varied. The objective function is set as the "number of monthly dispatches"; the variables are the staff numbers. By running the experiment, the AnyLogic automatically generates the User Interface (UI) for the experiments, which is embedded within the software. The UI includes the current and best solutions and the dynamic chart of the optimisation progress with respect to the simulation time. The optimisation results have been presented diagrammatically in Figure 11(a).



(a) (b)

Figure 11: AnyLogic results of the optimisation experiments for (a) Scenario-2 and (b) Scenario-3, intending to maximise the number of monthly dispatches in the Company. The graph presents the results for all possible iterations presented in dotted line.

Note that, the total number of staff should be constant and equal to 24 and the number of staff can obtain any value between 1 and 21. Therefore, the total number of iterations to perform optimisation experiment has been calculated as 1771. The optimisation result illustrates that, the total number of monthly dispatches can be increased up to 497 and the optimum staff combination would be $N^T = 11$, $N^{Rf} = 2$, $N^{Rc} = 2$ and $N^L = 9$. In another scenario, it is assumed that there are no bottlenecks in the system and therefore there is no limit for the initial inventory capacity of the validated shippers in the company. In this case, the total number of dispatches can be increased up to 1259 and the optimum staff combination would be $N^T = 18$, $N^{Rf} = 1$, $N^{Rc} = 3$ and $N^L = 2$ in the company. The optimisation results have been presented diagrammatically in Figure 11(b).

4. Discussion

The current hybrid ABM-DES simulation frameworks are limited to micro and macro levels of agent based modelling [12, 3, 13] and a degree of static complexity to study optimal resource planning [16, 17]. In [13], the behaviour of multiple agents at micro level are specified through state-charts. In a recent study by Mathieu, *et al.* [12], four possible interaction patterns between a micro and a macro level of agents are proposed. The example models, advantages and limitation of each pattern have been discussed. They focused on models which are composed of two relative micro and macro levels. This paper extends the current literature to investigate how a complex system of manufacturing processes can be simulated using MHSF, in the presence of dynamic complexities at different levels of the agent-based model (see Figure 1). The modular model was formed by creating a discrete event-based state to the SFDS approach for each agent using the DEVS modular formalism at the meso-level of the agent-based model. Integrating MHSM with stochastic data analysis and flexible optimisation led to the development of MHSF for simulation and optimisation of complex manufacturing systems. The developed method is applicable for manufacturing systems with highly regulated and manual handling processes, including multiple repeating manufacturing modules. The modular model reduces the simulation complication by introducing the meso-level agents and reducing the simulation elements. This assists the user with more insight in identifying and tracking the bottlenecks and the root-causes. Utilising the framework, such systems can be analysed regarding uncertainty quantification on processing time and performance. Such detailed analysis can ultimately facilitate strategic decision making for the system.

Based on the case study, this paper investigates four main outcomes: First, the impact of bottlenecks on the system performance was evaluated by completing several simulation experiments. The results show a 1.56 and 5.49-fold increase in the throughput with and without the limit on inventory size respectively. Second, the uncertainty on processing time at exo-level was quantified in the form of pdf graphs using stochastic data analysis. Third, this paper investigated how the flexibility in manufacturing design regarding labour and inventory affects production performance. In this regard, Utilising parameter variation and optimisation experiments, optimal resource planning and inventory size were calculated, as discussed in detail in Section 3.5. Finally, the weaknesses and strengths of the system have been identified. This led to the identification of three high priority strategies for the Company; (i) implementing the optimal resource planning and inventory size at the shop-floor and elimination of bottlenecks; (ii) using the Radio-Frequency Identification RFID technology to track and trace products and shippers; (iii) applying lean principles to reduce waste at the shop floor.

5. Conclusions and further work

This paper has presented the modular hybrid simulation framework for manufacturing systems with highly regulated and manual handling processes, composed of multiple repeating modules using the modular hybrid ABM–DES method. The theoretical aspects and the mathematical formulation of the modular method have been introduced as an extension to the dynamical system approach. The framework considers dynamic complexity in terms of uncertain processing time and resources and present a systematic user guide through the system design. To test the validity of the framework, a case study in the cell and gene therapy industry was conducted. Following the framework, the case study system was designed and simulation results compared against data from the company; excellent agreement was found in terms of current performance of the company. Furthermore, the optimal resource planning and the uncertainty of the processing time at each sub-system was calculated. The outcomes from the simulation model provide clear, scalable and detailed information to support users. The framework can be used by decision-makers as a tool to improve or modify policies and regulations in manufacturing sectors with a highly regulated and complex nature. In summary, the main contributions of this paper are thus: 1) A modular hybrid framework is developed for complex manufacturing system design, 2) An extension to the finite dynamical system for manufacturing modules is presented, 3) Uncertainty in processing time is quantified in the presence of dynamic complexity, 4) The optimal resource planning to maximise the manufacturing performance is analysed.

Further to this study, adding manufacturing cost information as an input data can deliver a cost analysis model to support users. The developed computational model can be used as a virtual platform to assess further real-world scenarios such as disruptions, breakdowns, fire alarm and emergency events to enhance decision-making strategies. The simulation model can be integrated with several sensitivity analysis techniques to perform failure modes and effects analysis in a complex manufacturing system.

Acknowledgements and Funding

This research study is funded by the Innovate UK [IUK project No. 102396] and the EPSRC [grant reference No. EP/N508937/1] for Innovative Manufacturing at Cranfield University's Through-Life Engineering Services (TES). The main partners of the project are Fisher BioServices (FBS), the leader in critical biological material management, Cryogatt, specialists with significant cutting edge RFID-based systems and Cell and Gene Therapy Catapult (CGT). The authors would like to express their especial thanks to all management and shop-floor personnel of the FBS Company who were working closely with the Cranfield University.

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Appendix A. Case study supply chain & Manufacturing processes Phase I–III

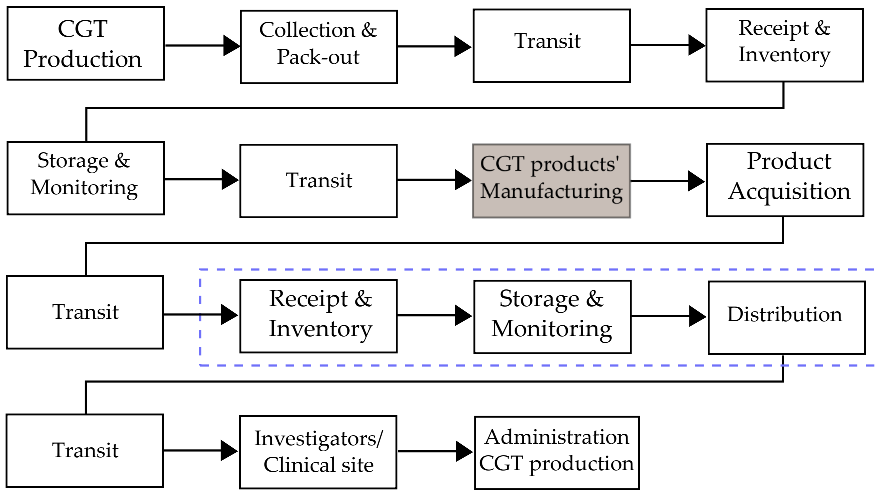

Figure A.1: A typical CGT supply chain network and logistics; the dashed line shows the considered CGT manufacturing phases in this study, [24].

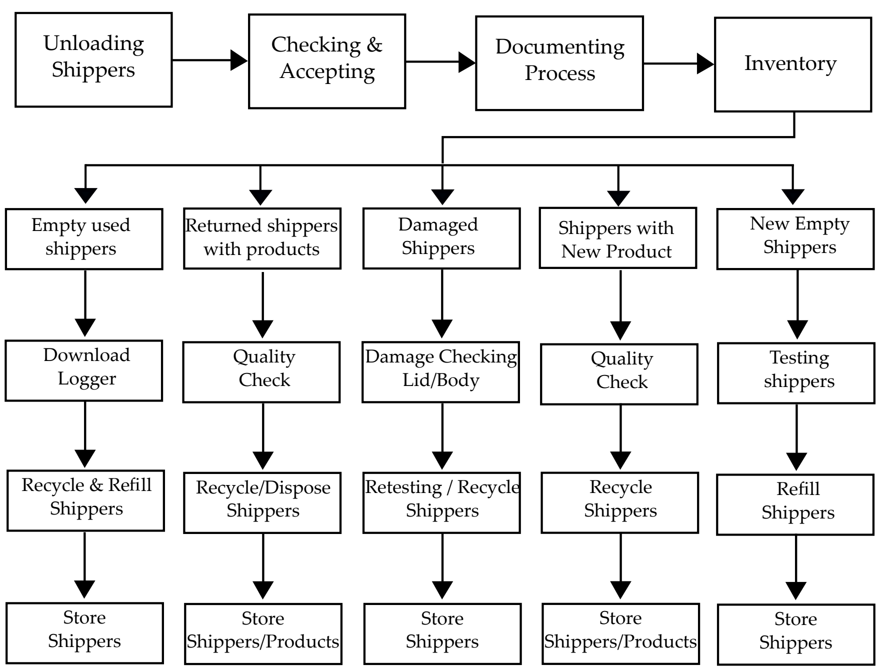

Figure A.2: Conceptual model for Phase–I: Current practice layout of the receipt & inventory phase.

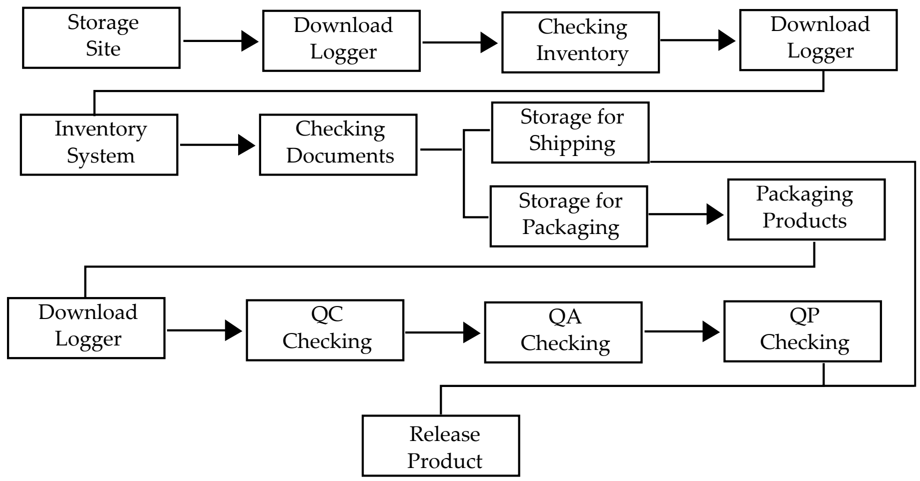

Figure A.3: Conceptual model for Phase–II: Current practice layout of the storage & monitoring phase.

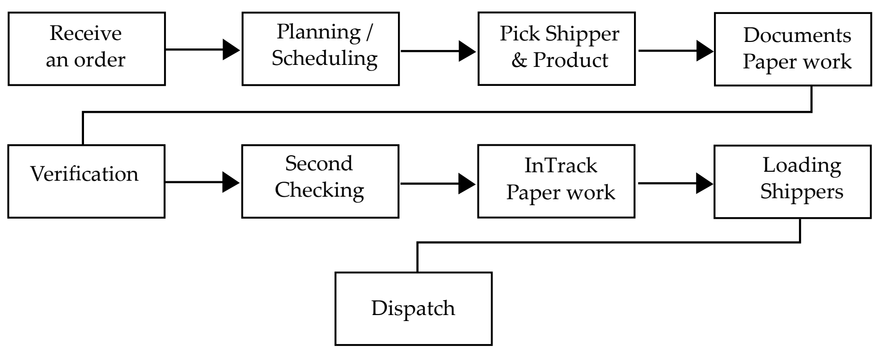

Figure A.4: Conceptual model for Phase–III: Current practice layout of the distribution phase.

Appendix B. The computational simulation model and demonstration

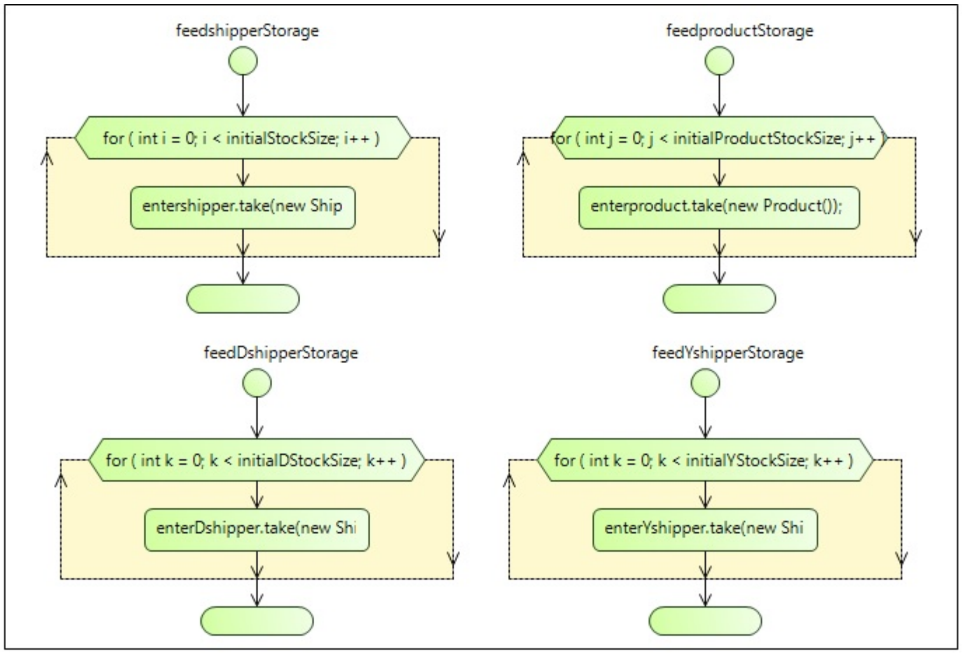

Figure B.5: AnyLogic interface of the ABM model of initial storage capacity for the sub-agent store shippers & store products

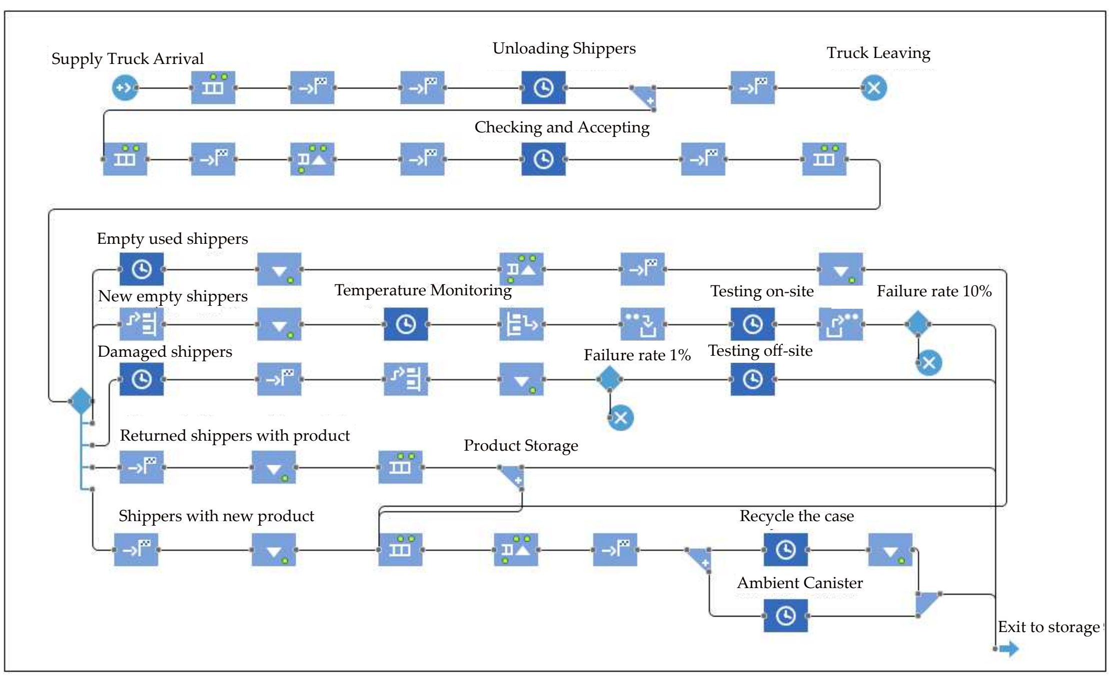

Figure B.6: Phase–I: AnyLogic interface of the DES model for the sub-system receipt & inventory.

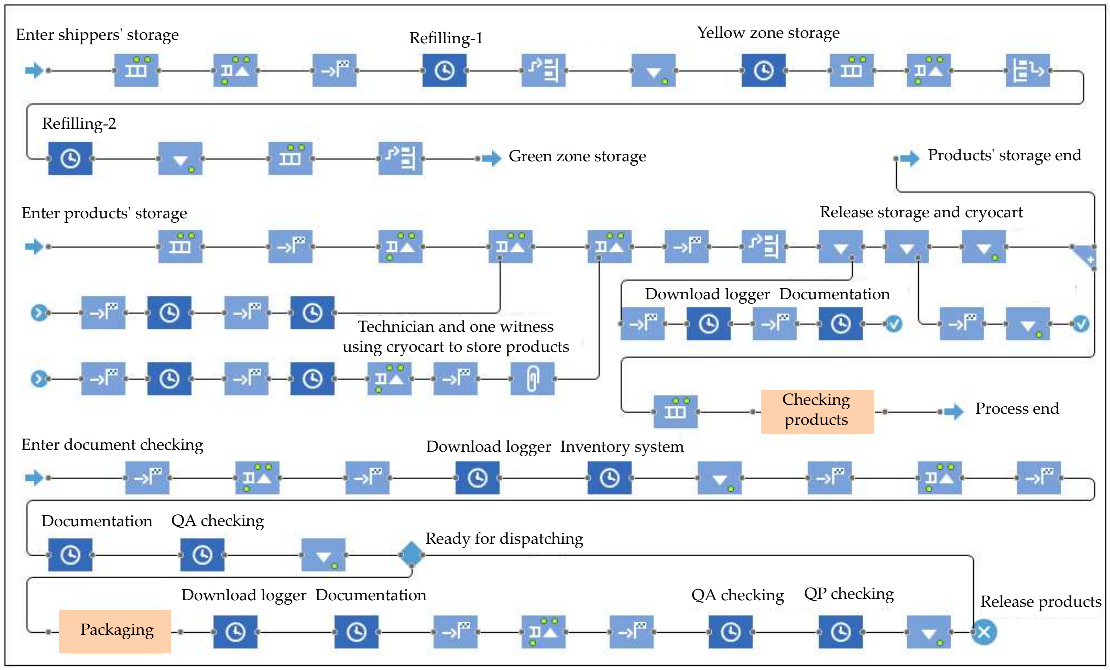

Figure B.7: Phase–II: AnyLogic interface of the DES model for the sub-system shippers & products' storage processes. The 'Checking products' and 'Packaging' modules are modelled as sub-sub-systems (sub-agent).

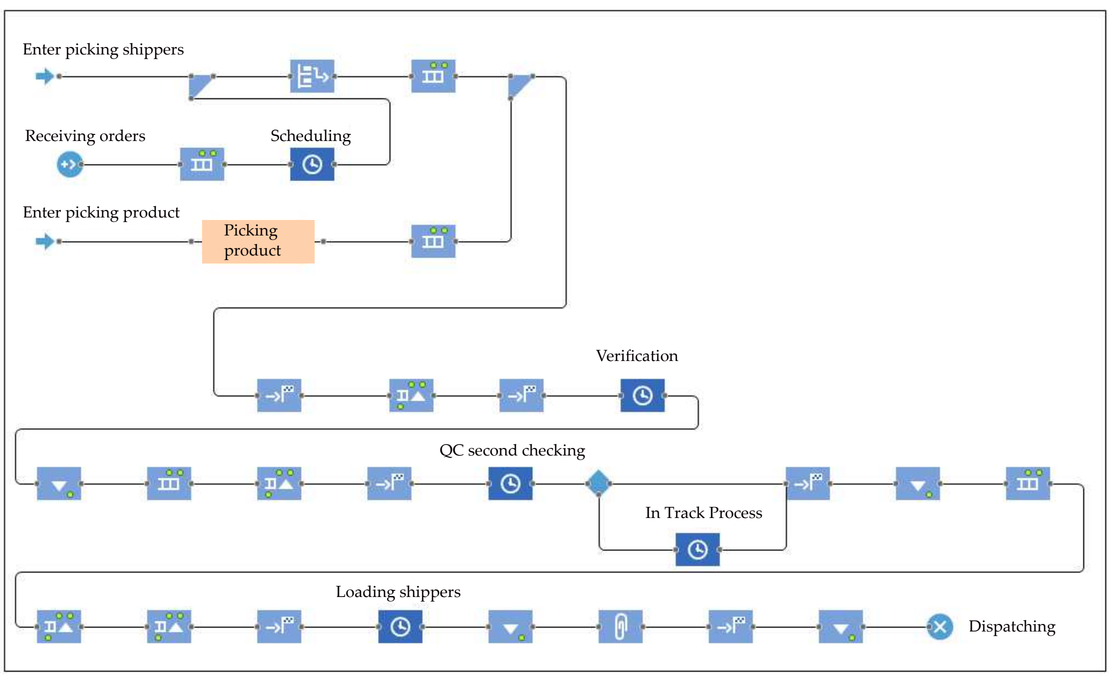

Figure B.8: Phase–III: AnyLogic interface of the DES model for the sub-system receiving orders and dispatching. The 'Picking product' module is modelled as sub-sub-system (sub-agent).