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Digital Twin based Data Pattern Analysis for IoT-Based Pharmaceutical Production Monitoring

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Abstract

A major step forward in pharmaceutical production has been the merging of Artificial Intelligence (AI) with the Internet of Things (IoTs), which successfully connects the digital and physical realms. Improving the production process and quality control through the integration of AI algorithms into IoT sensors leads to higher overall efficiency. Digital Twins (DT) are made possible by the creation and implementation of new Industry 4.0 technologies, which help to make manufacturing smarter and more agile. DTs are digital representations of real-world systems that mimic their operation and dynamics. Complete DT implementation in pharmaceutical production has not yet occurred, despite the pharmaceutical sector is currently undergoing a digital transformation to incorporate industry 4.0 and has adopted Quality-by-Design (QbD) programs. Therefore, it is crucial to assess the pharmaceutical industry's progress in implementing DT solutions. Data obtained from digital twins can also provide a full image of a product or process's lifetime, which can help with supply chain management, product quality control, and workflow optimization for manufacturing individual parts. This research proposes a Digital Twin enabled Data Pattern Analysis with Diminutive Difference Trigger using Probabilistic Regression (DT-DPA-DDT-PR) model for accurate monitoring of pharmaceutical production operations. The proposed model when contrasted with traditional methods performs better in pharmaceutical production monitoring.

Keywords: Digital Twins, Pharmaceutical Production, Quality-by-Design, Data Pattern Analysis, Diminutive Difference Trigger, Probabilistic Regression.

1. Introduction

Being the main connection between the real and virtual worlds, the IoT plays a key role in the formation and functioning of digital twins. IoT devices offer continuous data input that is real-time, precise and high rate, which is fundamental to the operation of a Digital Twin. Some of the key operational and environmental features monitored by the sensors and actuators installed on pharmaceutical machinery, clean rooms, bioreactors and packing units include pressure, pH, airflow, vibration, humidity and chemical composition among others. Assuring continuous alignment of the physical production environment with the digital model. These features are delivered utilizing secure protocols, or the latest 5G networks. The Digital Twin

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becomes a dynamic system that can reflect the present state and forecast how it will act under varying conditions, aided by the integration of real-time streams, past data and predictive analytics.

The rise of AI and the IoT has already begun to change the pharmaceutical industry and establish it as one of the most innovative sectors. The range of technologies in AI is extremely wide, allowing for advanced analytics with auto-functions, such as machine learning and natural language processing. Pharmaceutical production has traditionally relied on manual procedures, which are proneto errors due to the degree of human effort involved. Quality Assurance (QA) is often left in its costly and reactive zone, leading to waste of resources, such as recalls and other forms of loss. Furthermore, the outdated regulatory framework is too paper-based, making it unresponsive and not responsive or agile. However, the opportunity for permanently monitoring changes in the most important parameters can shift the focus from reactive end of the line testing to proactive quality assurance with the involvement of IoT sensors in the production line. This would facilitate an immediate response to any deviation in quality thus reducing waste and ensuring compliance.

The pharmaceutical sector is presently witnessing a transformational overhaul and adopting novel Industry 4.0 technologies that disrupt and stretch conventional production procedures [1]. Among these innovations is the concept of Digital Twin (DT), which is one of the enablers that will be important in transforming manufacturing into a smarter, more agile and leaner space [2]. Digital twins are active virtual models of physical products and are fed with real-time information about the real world to analyze the current operational health of machines, production lines, and entire plants. Not just a computer model, a Digital Twin is a dynamic object which evolves over time, alongside its physical counterpart [3]. It relies on live sensor readings, simulations and past data to provide a clear image of the behavior of the system under varying conditions. The manufacturing of pharmaceuticals represents a field where quality, advanced procedures and adherence to the requirements, along with the implementation of Digital Twin technology can change how manufacturers organize and regulate the work of their plants [4].

Pharmaceuticals are diversifying into other industries, such as automotive and aerospace, where Digital Twins have become more widely used, although the pharmaceutical industry intends to adopt the technology. The reason behind this slower adoption is that the industry is highly regulated [5], there are concerns about data security risks, and the systems currently used in the pharmaceutical production are complex. However, the industry is slow to embrace Quality-by-Design (QbD) approaches [6] along with the general requirement to move towards digital transformation shows the significance of an intelligent [7] and real-time monitoring system like Digital Twins. The major weakness of currently available systems to track pharmaceutical manufacturing is that they are either threshold-based or deterministic, therefore they might not identify minor abnormal usage in the early phases [8]. Even minor deviations may cause enormous Quality issues when they are not identified and addressed on time, especially in complicated bio or chemical production setting [9]. Such variations are usually ignored in the conventional methods, resulting in unsuccessful lots, downtime wastage and loss of funds [10].

To overcome these issues, we introduce a new model, Digital Twin based Data Pattern Analysis with Diminutive Difference Trigger based on Probabilistic Regression (DT-DPA-DDT-PR). The technology's ability to detect even minute changes in process behavior at a rapid pace before they become significant defects, and to provide an alarm signal for defect elimination at an early stage is the disruptive element [11]. In comparison to earlier methods

like statistical methods, the model is also precise and sensitive in terms of capturing and applying a suitable detection technique in pharmaceutical devices [12]. The Diminutive Difference Trigger (DDT), one method for detecting micro-anomalies that earlier monitoring techniques were unable to identify, is developed in this scenario [13]. These triggers are extremely sensitive because they can identify even minute changes in material, process, and environmental characteristics that, if ignored, could negatively impact quality attributes. As a production team, you will be able to spot problems early on and take appropriate action to avoid wasting time or potentially breaking the law.

The use of Probabilistic Regression (PR) in the DT-DPA-DDT-PR model is another innovation. This is explained by the inherent noise or uncertainty in production processes is a natural phenomenon arising from various factors, such as material differences and machine depreciation caused by environmental conditions [14]. From a different perspective, probabilistic regression makes a lot of sense when dealing with uncertainty because it estimates confidence intervals in addition to predicting point values, which results in Risk-Informed Decision-Making processes [15]. The new model is a reactive system that can transition from a passive observer to an active agent capable of predictively carrying out diagnostics and prescriptive repair work the symbiosis of uncertainty models with real-time data acquired from the digital twin [16]. To achieve a regulatory sustainability state in accordance with the regulatory environments of either GMP or FDA requirements for a digital quality approach in various production processes, a more comprehensive approach to improving resilience and increasing transparency of processes is crucial. The application of DT to pharmaceutical production processes is depicted in Figure 1.

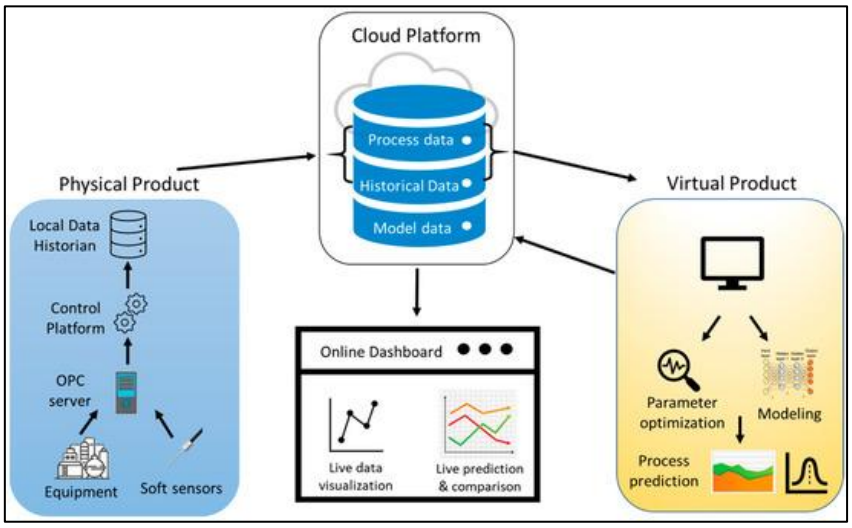

Figure 1. Usage of DT in Pharmaceutical Production Process [10]

The pharmaceutical industry is also furnishing preventative measures. Such a shift in quality control methods to a proactive one is quite appropriate to the abilities of the DT-DPA-DDT-PR model. Through the probabilistic regression layer, the system is highly adapted to new data through the continuous learning that is built in, and predictive accuracy becomes potentially promising over time, allowing manufacturers can maintain their processes consistently under different production conditions. Besides, the strategy to promote the complete lifetime of the drug asset [17]. Starting with the receipt of raw material, all the steps can be tracked and improved with the knowledge provided by the Digital Twin, up to delivering the finished product. Simulations can be conducted by operators, and forecasting results and

making informed decisions is possible without affecting live production, which adds useful agility and innovation capability [18] to it.

Digital twins powered by the Internet of Things have enormous potential benefits for the pharmaceutical industry. During the manufacturing process, IoT sensors that monitor the reaction temperature, stirring speed, and coating uniformity of the pills ensure that production stays within the stringent regulations of Good Manufacturing Practices (GMP). With sophisticated triggers like the Diminutive Difference Trigger (DDT), this preventive monitoring eliminates the need for conventional quality checks based on thresholds and enables the detection of even micro-level anomalies. Quality and profitability are directly improved by reducing production downtime and defective batches as a result of early detection of minor variations. The IoT can also strengthen pharmaceutical supply chains by tracking raw materials and finished pharmaceuticals at each point throughout the process [19]. Another way companies can secure complete traceability of their products, which are to be sold as genuine ones, is by combining blockchain technology with RFID tagging of the products and keeping track of them throughout the entire production process. Moreover, the critical role of cold chain management in achieving the safety of vaccines and biologics makes the services of the IoT which monitor the environment highly required. IoT sensors in warehouses and the trucks used during delivery, such as those installed in the trucks, can also measure the slightest variations in humidity or temperature and activate alarms to prevent perishable goods from spoiling.

In the suggested DT-DPA-DDT-PR model, edge computing, is an important part of ensuring the real-time responsiveness and safety of operations on the pharmaceutical production floor. The data created by the IoT sensors consists of large amounts of information about equipment status, temperature, pressure, humidity, and vibration at a high frequency. Preprocessing of raw data occurs at the edge nodes, which are geographically closer to the production plants, along with feature extraction and normalization. The communication delay will be less since such processes will be performed locally, and time- sensitive data will not be delayed during communication for centralized server storage. This issue is of extreme importance in the pharmaceutical field, as even the smallest action of divergence may easily lead to quality or compliance problems.

Cloud computing, on the other hand, enables scalable intelligence, long-term learning, and system-wide optimization. The infrastructure provides access to vast amounts of historical sensor data, digital twin status, production history, and information concerning all relevant regulations applicable to an industry or manufacturing enterprise [20]. This data storage of the archives enables tracking, regulatory audits and application of the lifecycle of pharmaceutical products. Also, computationally expensive tasks, such as training and re-training probabilistic regression models, uncertainty calibration and high-fidelity Digital Twin simulations are computational tasks that cannot be continuously operated on resource-constrained edge devices but can be operated in the cloud. In addition, cloud computing permits worldwide analytics and strategic decision making in manufacturing lines or manufacturing plants. By combining data between various edge nodes, the cloud can identify long run trends, cross-batch differences and systemic inefficiencies that cannot be seen at the local level. It is used to optimize predictive models and load Digital Twin parameters deployed once again to the edge to improve real-time monitoring. Through this, the cloud and edge layers have been incorporated into a closed-loop system where the edge ensures rapidity and security and the cloud provides profundity, extensibility, and lifelong learning to facilitate smart pharmaceutical manufacturing.

2. Literature Review

Tripura et al. [1] developed a methodology for generating and updating digital twins of dynamical systems using a library of physics-based functions with sparse Bayesian machine learning. In this paper, two approaches to facilitating temporal updates for digital twins were presented: an input-output based approach and an output only based methodology. In both cases, the library of candidate functions is employed to discover new perturbation terms in the current digital twin model, so that the new model is interpretable and epistemic uncertainty is rigorously quantified. The first approach expresses the regression problem as a state-space model, while the second treats the output-only data as a stochastic process and employs rather sophisticated mathematical tools to obtain a regression equation. These methods were efficient in practice, as illustrated by simulations on very stiff systems (the crack-degradation problem for instance), for which the right perturbation terms and parameters have been recovered with high accuracy.

Onaji et al. [2] introduced a digital twin model for monitoring and optimization of the industrial-scale production of APIs with an emphasis on salbutamol synthesis. Their work targets the importance of organic synthesis, where multiphase catalysis, separations to yield the target molecule, subsequent crystallization and the corresponding downstream operations are performed. In order to realize effective monitoring of key chemical parameters, particularly impurity contents, a digital twin was established based on the multicomponent adsorption of Volatile Organic Compound (VOC) pollutant emissions.

Saleh et al. [3] designed an interesting polymeric all-solid- state screen printed ion selective electrode for the estimation of milnacipran pharmaceutical formulations by application of screen printing technique. This approach is low-cost, and has good reproducibility for preparing electrochemical sensors in mass production. The SEM determined the morphology of the electrode, while the composition of the membrane, the type of plasticizer and the ion exchanger was optimized to improve its performance. The best response was obtained for a membrane with milnacipran-phosphomolybdate (MLN-PMA) ion associate as an ion exchanger and tricresyl phosphate as a plasticizer. The electrode displayed a Nernstian response covering a broad concentration range of MLN with low detection limits and good stability.

Rodriguez et al. [4] developed an infrared temperature measurement system for key points in the pharmaceutical glass-container manufacturing process, using inexpensive sensor hardware. The device measures temperatures in the range of 500-1300°C and can monitor production throughput of up to 150 containers per minute. One of the specialty designs of the system is that it detects the presence of the container directly from the temperature measurement without any proximity sensors. In its operation the system has been found to be very reliable and stable, and it is a useful aide for machine setting as well as for operation supervision. This study informs the value of economical and precise temperature measurement in manufacturing processes, advancing system efficiency and quality control in the pharmaceutical industry.

Li et al. [5] developed a novel approach for in-line terahertz pulsed imaging for the measurement of single tablet coating thickness during the coating process in a production-scale pan coater. Originally, a criteria WSA procedure was established for the selection of terahertz reflections from the tablet surfaces in order to estimate the coating thickness. However, the WSA can also discard some of the tablet waveforms that are closest but do not meet the moose

shell cup threshold, a threshold-based selection criterion. In order to improve the efficiency in the selection of these waveforms, the authors utilized machine learning algorithms, in particular an RNN, to enhance the waveform selections.

Bahaghighat et al. [6] investigated the use of machine vision in pharmaceutical production lines to verify and regulate the correct packaging of medication. The count of blister cards in a drug pack is of significant relevance to quality assurance in the pharmaceutical industry. To solve this problem, the authors introduced a new model that integrates object detection, feature extraction, and classification methods. The model incorporated many strong methods such as Haar cascade, HOG, ORG, Gabor wavelet, lowest recognition rate of KNN, Radon transform, and SVM, which reached an accuracy of over 88% in experiments. This application demonstrates the role of machine vision in packaging for pharmaceuticals to increase efficiency and eliminate errors, supporting higher quality and increased regulation in the pharmaceutical market.

Digital twins are considered game changers in biopharmaceutical settings that can aid in improving operational efficiencies, lowering costs, and promoting quality-by-design efforts throughout the drug development pipeline.AI and machine learning are increasing the predictive and analytical potential of digital twins. New studies also show the real-world application of AI-based digital twins in factories. For instance, convolutional neural networks cascaded with digital twin architecture have demonstrated an increase in accuracy and reliability when applied to modeling complex biological and industrial systems, as well as biotechnology systems where sensor data in the form of images are exploited to make more refined predictions and patterns. On related note, model-based reinforcement learning based hybrid digital twin approaches to calibration have been proposed to minimize model error and maximize control policies, particularly concerning nonlinear dynamics and data scarcity that are frequent in biopharmaceutical manufacturing systems. Furthermore, studies related to the domain demonstrate the use of AI-driven digital twins in actual production environments. Indicatively, pharmaceutical production lines have been designed as digital twins, which combine vision models and industrial sensor data and are used to extract the operational Key Performance Indicators (KPIs) to enable accurate monitoring of equipment operations and production efficacy in smart manufacturing ecosystems.

Outside of pharmaceuticals, similar deployments in chemical process industries have used machine learning techniques in the framework of digital twins to maximize control of production and performance indices, which supports the broad applicability of AI-twinned solutions to process-intensive industries. Taken together, this research establishes that AI-powered digital twins represent a major improvement compared to traditional simulation and monitoring tools in pharmaceutical and chemical processes. They offer visually active, data-driven knowledge, faciliate predictive and prescriptive control processes, and enable proactive decision-making in times of uncertainty. However, some problems exist, such as high computational overhead, model maintenance, and model complexity, all of which are under current research and development.

3. Proposed Model

Through the use of smart devices and sensors, the IoT considerably facilitates remote tracking and monitoring of the real manufacturing process [21]. The production of pharmaceutical medications is greatly affected by hardware factors. In this way, the hardware and production process can be monitored through the IoT. The IoT employs real-time sensors

to render the pharmaceutical manufacturing process transparent. Intelligent devices can manage the data collected by these sensors [22]. An alarm could be activated to prevent drops caused by certain hardware failures [23]. Quality control may be ensured with the use of IoT sensors. Data acquired by the sensors helps in comprehending the advancement of various phases of the product development cycle and understanding the hardware functionalities [24]. The only variable in product quality that can be altered is the method of real-time monitoring. Solutions based on the pharmaceutical industry's Internet of Things can help maintain product quality by monitoring the production process [25]. The use of AI processing and digital twins in pharmaceutical manufacturing is shown in Figure 2.

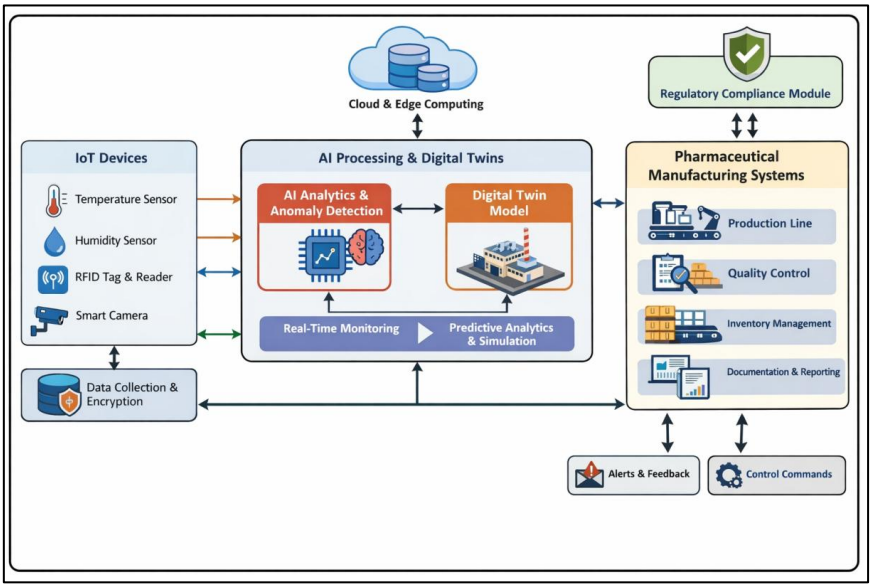

Figure 2. AI Processing and Digit al Twins in Pharmaceutical Manufacturing

The presented system architecture is an integrated IoT-AI-Digital Twin system that will be used in manufacturing and monitoring intelligent pharmaceuticals. The physical layer has IoT sensors like temperature sensors, humidity sensors, RFID tags, and smart cameras continuously collecting essential operating and environmental parameters on the production floor. Such devices constitute the main data collection layer and guarantee the real-time monitoring of the manufacturing situation. The data collected is securely transmitted and encrypted before transmission, ensuring anonymity, integrity and adherence to regulatory standards.

The suggested DT-DPA-DDT-PR system can address the batch-to-batch variability through a combination of Digital Twin adaptation, probabilistic modelling, and event-driven learning. Thus, the natural variations of the process do not cause false alarms, and real deviations are identified in a timely manner. The Digital Twin will be at the center of the framework constantly updating the representation of every production batch instead of using one fixed reference model. Real-time sensor data is correlated with historical batch data to create a contextual baseline for every batch indicating what the actual operating state should be, based on a specific formulation, the state of equipment and the environmental conditions. The batch-sensitive base will enable the system to differentiate between normal inter-batch variation and anomalous behavior that can cause unwarranted interventions due to normal variability in the process.

The system also solves the problem of batch-to-batch variability by employing probabilistic rather than deterministic prediction. The probabilistic regression model is used to estimate both the variance and the mean of process parameters instead of producing one expected value. The uncertainty modelling embodies uncertainties inherent due to variations in raw materials, slight wear of equipment and environmental changes in different batches. Consequently, there is an assessment of deviations against confidence intervals rather than definite limits, which allows for the effective separation of natural variability and actual process drift. Additionally, the DDT will be made flexible and not fixed. Learning of the trigger thresholds is based on historical batch distributions and is dynamically adjusted as new batch distributions are processed. Minor deviations are only raised when they become persistent over time windows or reach statistically significant thresholds so that normal batch-to-batch variations do not cause many false alarms while still allowing for the detection of faults at early stages.

A combination of Digital Twin redundancy, probabilistic uncertainty models, and consistency is used to handle sensor failure in the proposed DT-DPA-DT-PR model, ensuring that monitoring and decision-making remain unharmed due to component sensors degenerating or failing. At the first level, the Digital Twin examines sensor consistency concerning the desired physical behavior of the process. The Digital Twin can detect sensor faults, by observing the inconsistency between a sensor reading and the associated variables predicted by the twin, as the Digital Twin contains dependencies between two or more process variables. In situations where sensor output fluctuates greatly compared to the expected state and other similar sensors remain steady, the system will consider this an occurrence of a sensor anomaly and in response, no unnecessary alarms or control actions will be implemented.

Sensor uncertainty is directly represented by probabilistic regression. When a sensor begins to behave erroneously, due to drift, noise inflation, or intermittent dropout, the variance of its predictions increases. This automatic reduction of the sensitivity of the DDT to that signal removes spurious alarms caused by noisy or unreliable measurements. The sensor degradation manifests as increased uncertainty rather than a sudden increase in fault, allowing for fault tolerance of monitoring performance. In cases of temporary sensor data loss, the Digital Twin utilizes historical data and correlated sensor data to perform the virtual sensing process. According to existing connections to past batches and dynamic connections to healthy sensors, the twin estimates the missing sensor values with a confidence interval. Such estimates may be utilized to continue monitoring and prediction without interfering with the process, indicating that the inferred values are being accessed.

The new DT-DPA-DDT-PR model offers an intelligent real-time monitoring system in which Digital Twins are directly related to a new data pattern analysis approach. This system takes the aid of microscopic difference triggers of failure mode effects and analysis (FMEA) to identify even the slightest changes in manufacturing processes that conventional monitors missed. The model also facilitates unprecedented degrees of precision and dependability in processes, which is especially critical in pharmaceutical fabrication, aided by real-time data fusion and predictive analytics. At its center is the Digital Twin, which forms the basis of this model and guarantees a continuously updated digital representation of the actual production environment. The subsystem gathers sensory information, operation logs and historical performance measurements to model analyze and forecast process reactions. The twin is an evolving system that adapts to production changes as proposed and uses every data point to adjust its predictions, improving the accuracy of its forecasts. Figure 3 presents the proposed model architecture.

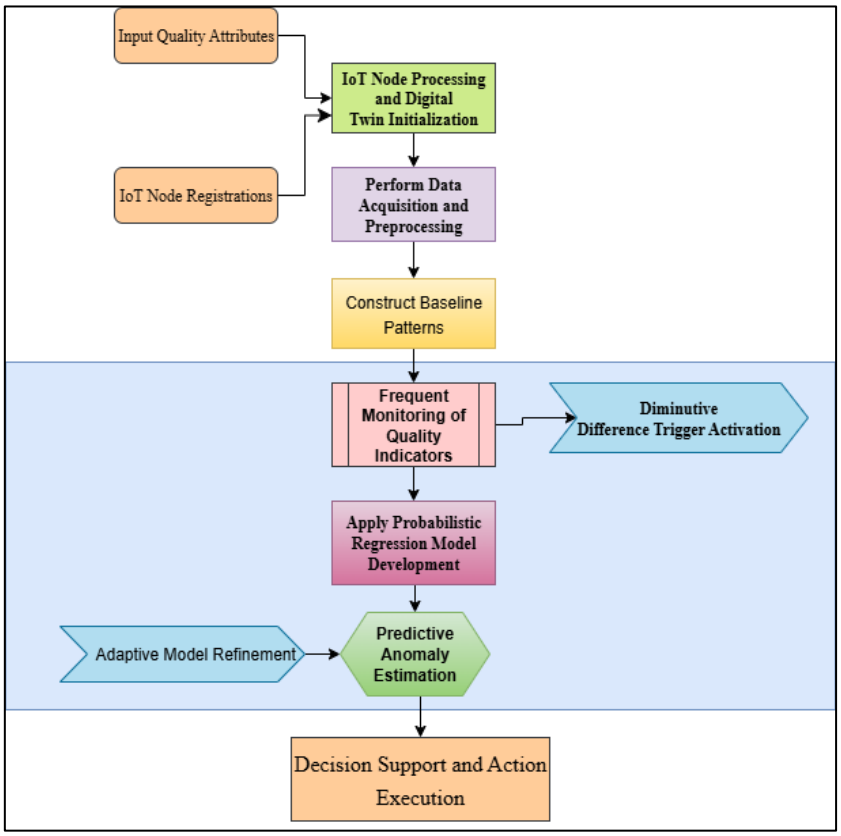

Figure 3. Proposed Model Architecture

Regression models of uncertainty in the data produced by IoT, used to support predictive analytics in the Digital Twin are represented by probabilistic regression (PR) models. In contrast to deterministic regression which creates a one-point estimate, PR is applied to estimate the probability distribution of the target variable under the condition of the input features. This approach is utilized to make uncertainty-sensitive decisions in dynamic and noisy conditions, such as in pharmaceutical manufacturing systems. The proposed DT-DPA-DDT-PR model also assumes the application of the Gaussian conditional distribution of the regression output in modeling the uncertainty of the pharmaceutical production data from the IoT. The analysis of the residuals of the probabilistic regression model through statistical analysis indicated that the assumption holds true. Residual distributions were analyzed using histograms, Q-Q plots and formal normality tests, such as the Shapiro-Wilk and Kolmogorov-Smirnov tests, tests on different production parameters such as temperature, pressure, and humidity. The results show that the residuals that have undergone normalization and base detrending processes are well-distributed as Gaussian particularly, during stable operating times. There was a slight departure from normality when conformity to normalcy was observed in transient production cycles, this is only natural in a very dynamic manufacturing environment.

The model is estimated in a formal way as following: The conditional distribution P(y | x,θ) where x is the IoT-derived feature vector, y is the desired output, and θ represents the model parameters. It is often assumed that the output is distributed as Gaussian and the model predicts both the mean μ(x) and the variance $\sigma^2(x)$ expressed as.

$$y = N(\mu(x), \sigma^2(x))$$

This expression enables the model to measure predictive confidence; the greater the variance, the more uncertain it is.

To test the hypothesis, rule out the possibility that the data follows a normal distribution. The standardized residuals (Sr) are determined as follows.

$$S_{r=\sum_{i=1}^{N}\frac{y_i-\mu(x_i)}{\sigma(x_i)}}$$

Residual should follow normalization as

$$S_r \sim Norm(0,1)$$

In order to further determine robustness, the skewness and kurtosis measures of the residual distributions of various production scenarios have been calculated. The values of skewness were also observed to lie within ±0.5 of most parameters and the value of kurtosis was similar to that of a normal distribution indicating that under normal working conditions, Gaussian modeling gives a reasonable approximation to the estimation of uncertainty. In addition, empirical coverage analysis demonstrated that about 93-95% of observed values were within the predicted 95% confidence intervals which revealed the good calibration of the uncertainty estimates. These results support why Gaussian probabilistic regression is a viable and statistically reliable option for real-time monitoring of pharmaceutical production.

The proposed framework will use a hybrid cryptographic design where data confidentiality is achieved with the help of symmetric encryption and key management and authentication are performed through asymmetric cryptography. This design is more efficient in terms of security and also more efficient in terms of computation which is crucial in real-time industry monitoring settings. The proposed model ensures confidentiality, integrity, and authenticated encryption using Advanced Encryption Standard (AES-256) in all sensor data streams and intermediate model outputs. The reason for using AES-256 is that it is widely used in industrial systems, its latency is minimal, and it meets security standards. Root keys are stored in a Hardware Security Module (HSM) or Trusted Platform Module (TPM) at the gateway or edge node level. The session key is created dynamically on a per-communication-session basis and stored in volatile memory, and therefore destroyed automatically after the termination of that session. Public keys are disseminated in a secure certificate- based system and are kept in a secured key registry.

Algorithm: DT-DPA-DDT-PR Model

Step-1: The quality indicators are provided as input in order to monitor the IoT nodes in the production process. The quality indicators are considered as

$$QuaInd[M] = \sum_{r=1}^{M} \min\big(\theta(r)\big) + \max(\hat{y}) + \max\left(\text{simm}\big(\text{Similarity}\ (W_t, W_h)\big)\right) + \min\left(\text{diff}(x_i, x_{i+1})\right)$$

Here r is considered as current record, M is the total records count, θ is a predefined risk probability threshold, $\hat{y}$ is the predicted output, current window is represented as w_t and historical window as w_h.

Step-2: The IoT nodes are registered and each node information is processed for monitoring the nodes behaviour in the production process. The process is performed as

$$IoTNReg[M] = \sum_{n=1}^{M} getaddr(n) + \tau(n) + \beta(n) + \max(nQuaInd))$$

Here getaddr() model is used for considering the IoT node address, τ represents the transmission range and β represents the energy levels.

Step 3: Digital Twin Initialization

Map the physical pharma production environment to the dynamic digital twin. Real-time sensor data D(t) and past data K(t) are synchronized at all times. The replica twin progresses and adapts with new information to provide a true representation of the production environment.

This digital model is the basis for further investigation. Real- time data and historical data are combined in the feature matrix by which the twin acts dynamically.

$$DT(t) = \Psi\left(\sum_{i=1}^{n} \alpha_i . D_i(t) + \sum_{j=1}^{m} \gamma_j . K_j(t)\right) + IoTNReg(i)$$

Where $\boldsymbol{\alpha_i}$and $\boldsymbol{\gamma_j}$are new weights for sensor and history inputs, and Ψ is the twin construction function

Step 4: Data Acquisition and Pre-processing

Gather unprocessed production data from various environment sensors. Prepare data, addressing missing data points, outliers, and noise removal. Generalized data are normalized to allow for comparison between devices and over time.

Prepare neat feature sets for pattern recognition.

$$D_t'(t) = \frac{D_i(t) - \mu D_i}{\sigma_{D_i}} \forall_i \in \{1, 2, 3, \ldots\ldots, n\}$$

Where μD_i and $\sigma_{D_i}$are the mean and standard deviation of each dynamic sensor data stream.

Step 5: Baseline Pattern Construction

Examine historical and early live data to establish a functioning baseline. Calculate statistical attributes such as mean, standard deviation, and trend slope, etc. The reference is a dynamic baseline for the detection of anomalies.

It is a living document, new data points are added as they are validated.

$$\beta(t) = \{\mu D'(t), \sigma D'(t), \text{trend}(D'(t))\}$$

Where trend $(D'(t)$indicates the temporal slope using least squares fit.

Step 6: Real-Time Monitoring of Key Indicators

Monitor the real-time operational metrics against the baseline numbers. Monitoring the variations in micro-production parameters. Recognize early indications of drift before they escalate into serious issues.

Deviation trends are shown graphically on real-time dashboards.

$$\Delta\,(t) = \sqrt{\sum_{i=1}^{n} (D^{i}{}_{i}\,(t) - \beta_i(t))^2}$$

Step 7: Diminutive Difference Trigger (DDT) Activation

Let

- x(t) be the real-time IoT observations vector at time t,
- $\hat{\mu}$(t) and $\hat{\sigma}$(t) be the mean and standard deviation predicted by the probabilistic regression model of the Digital Twin,
- Δ(t) be the normalized deviation between observed and predicted behavior.

The DDT is defined as

$$\Delta\,(\boldsymbol{t}) = \frac{||x(t) - \hat{\mu}(\mathrm{t})||}{\hat{\sigma}(\mathrm{t})}$$

A DDT event is activated as

$$DDT(t) = \begin{cases} 1 & if\ \Delta\,(\boldsymbol{t}) > \boldsymbol{\epsilon} \\ 0 & Otherwise \end{cases}$$

Here ε is a micro-deviation threshold.

The DDT threshold is grounded in classical statistical hypothesis testing and empirical distribution modeling, rather than ad-hoc or fixed engineering limits. Its foundation lies in treating deviations between observed process behavior and Digital Twin predictions as random variables drawn from a reference "in-control" distribution.

Use a more sensitive trigger mechanism to catch anomalies earlier. If the deviation Δ(t) is larger than a small system-dependent parameter ϵ, issue a pre-alert. Concentrate on catching tiny but crucial changes in behavioral patterns.

Support preventive maintenance without booking offline.

$$\text{Trigger (t)} = \begin{cases} 1, & if\ \Delta(t) > \in \\ 0, & otherwise \end{cases}$$

Where ∈ is the tiny deviation threshold.

Step 8: Probabilistic Regression Model Development

Although the proposed framework uses a simple Gaussian regression formulation of probabilistic regression due to its computational simplicity and interpretability, it is not restricted to a specific distribution. Both the conditional mean and conditional variance are predicted in the regression layer as functions of the input features, thus a heteroscedastic model of uncertainty is fitted and rather than constant variance. This enables the model to respond to higher levels of uncertainty when the process goes off-target, the equipment deteriorates or the sensor becomes unsteady. Moreover, the estimation of variances is not specified manually, but is directly learned from data by maximum likelihood optimization, resulting in uncertainty calibration based on data.

Train a model of probabilistic regression to account for the uncertainty in future predictions. Feed both current and past event structures into model to predict what the likely future behavior might be Produce prediction intervals, rather than a point prediction.

Effectively address production variability.

$$\hat{p}(\mathrm{t}) \sim \mathrm{N}\ (\zeta_0 + \sum_{k=1}^{p} \zeta_k x_k(\mathrm{t}), v^2)$$

Where $x_k(t)$predictor are features and$\zeta_k$are model coefficients.

Probabilistic regression model presupposes that the target variable y given input features x has a Gaussian distribution of the mean and variance that depend on the input features:

$$\Pr(y|x) = N(y|\mu(\mathrm{x}), \sigma^2(\mathrm{x}))$$

The model parameters are learnt by minimizing the negative log-likelihood based on Gaussian:

$$G_{NLL} = \frac{1}{2}\log\left(2\pi\sigma^2(x)\right) + \frac{(y - \mu(x))^2}{2\sigma^2(x)}$$

Step 9: Predictive Anomaly Estimation

Use the learned regression model to forecast parametric states into the future. Predicted states are compared to the acceptable operational region that is used to estimate the risks.

Risk scores determine intervention trends.

$$CI\ (t) = [\hat{p}(t) - Z\ .v\ ,\ \hat{p}(t) + Z.\ V]$$

Where v represents predicted standard error.

Step 10: Adaptive Model Refinement

Regularly update the Digital Twin and Probabilistic Regression models with new data. Re-modeling is required after observing a major change or drift in a process. Keep the models trusted, resilient and current.

This loop improves the learning of the system.

$$\zeta_{new} = \zeta_{old} - \eta \nabla \psi(\zeta)$$

Where $\psi(\zeta)$s the probabilistic loss function and η is the learning rate.

Step 11: Decision Support and Action Execution

Effectuate actionable insights from the knowledge and predictive anomaly estimates of DDT triggers. Notify operating personel of any preventive maintenance or process modifications.

Support an intelligent closed production environment.

$$\text{Action}(t) = argmax_{a \in A} \, E[U(a,t)|\text{state}(t)]$$

Where U(a,t) is the expected utility/reward after taking action a.

The sensitivity of the results of the DT-DPA-DDT-PR to variation in the DDT threshold e is systematic and condition-dependent, and the framework is shaped in such a way that this sensitivity is in controlled form instead of being brittle over operating regimes. In the case of stable and well-managed process conditions, when there are small residual variances and the probabilistic regression model is well calibrated, the system is very sensitive to small variations in e. A small increase in e raises the frequency of early warnings, allowing very small micro-deviations to be detected; however, this comes at the price of an intermediate increase in pre-alerts. Increasing e in such low-noise regimes, on the other hand, does not miss faults but only delays their detection, as real deviations soon exceed even conservative detection limits. Therefore, in stable regimes, e is the main determinant of when to be detected, but not whether to be detected. The system is not sensitive to moderate changes in e under moderately changing process conditions, which include batch transitions, variability in raw materials, or small environmental changes.

This strength results from normalized deviations by the predicted uncertainty s(t). The higher the natural variability, the wider the normalized distribution of deviation, which effectively removes the effect of slight changes to the threshold. The results in this regime exhibit continuous variations in anomaly detection rate and false alarms with changes in e; i.e., no drastic variations in the results, which are associated with steady operational behavior. Sensitivity to e again increases in a predictable sense when the conditions are highly dynamic or non-stationary. Reduced e values will cause faster and more frequent DDT activations that will be more than satisfactory in safety-critical monitoring but can also raise the alert volume. An increase in the values of e decreases the alert frequency but may postpone the detectability of drift. Notably, the persistence requirement across several windows and event-based retraining counteracts the excessive sensitivity such that the outcomes deteriorate progressively, not disastrously.

3.1 Computational Complexity Analysis

Three components of the framework—Digital Twin simulation, Deep Policy Agent inference, and probabilistic regression updates—dominate the computational complexity of the framework. Its online inference complexity per time step is O(d), where d is the dimensionality of features, which allows it to be deployed in real-time. The complexity of retraining is O(N·d),

where N is the number of retraining samples that have been received since the last update. Notably, retraining is done asynchronously and not on the critical execution path, which does not interfere with real-time monitoring. The cost of amortized computation is low over a long time of operation because retraining is induced sparsely and only when drift has been detected. A number of safeguards are used to ensure that the algorithms remain stable when retrained. Model parameters are first updated with a warm start, i.e., by keeping initially learned weights, so that performance does not plummet. Second, the learning rate decays, and gradient norm clipping is implemented to prevent oscillatory updates. Third, retraining has a minimum inter-update period, which ensures that no repeated retraining cycles occur due to noise in the short term. A hold-out buffer is used for post-retraining validation to confirm that the updated parameters improve prediction and calibration of uncertainty. With this type of controlled retraining, a balance is achieved between adaptability and stability, which are key features of safety- and regulation-intensive environments. The framework prevents overfitting, catastrophic forgetting, and unnecessary computational spending by bounding computational overhead and retraining only for statistically justified events. The system, therefore, provides overall long-term stability while remaining sensitive to the real process development.

4. Results

The proposed DT-DPA-DDT-PR model is compared with existing models, namelyproposed machine learning based digital twin (PML-DT), Digital Twin Making preaching frame work (DT-CF) and The Two-way optimization (TWO). The purpose of the evaluation is to evaluate the performance of the DT-DPA-DDT-PR model with regard to various important comparisons in the context of monitoring pharmaceutical production, specifically the efficiency of fault detection, the level of resource consumption, , and the extent of adaptation to changes.

Each sensor's data acquisition frequency is determined by a combination of process dynamics, sensor characteristics, and information adequacy requirements in order to provide accurate monitoring without additional computational load [26]. Instead of using a uniform sampling rate across all sensors, frequencies are chosen to represent the inherent time-scale of variation of each measured variable. The sampling frequency of a sensor measuring the variable z(t) is represented by fs. A Nyquist-inspired criterion is used to calculate the minimum necessary sampling frequency:

$$fs \geq 2f_{max}$$

where f_{max} is the highest significant frequency component found in the variable's temporal spectrum when running in the nominal condition. The fast-changing process variables (for example, pressure and vibration) are sampled at a faster rate than the others (for example, temperature and humidity). The defective product in the simulation environment is a product instance for which the process variables fail to remain within statistically and functionally acceptable limits within the Digital Twin simulation model. Each product is produced by the simulation of the whole process of production for the product, where the critical quality attributes (CQAs) and the process parameters (CPPs) are kept under constant control. The vector Let $zi(t) = [zi_1(t), zi_2(t)$, and so on, $zi_d(t)]$ is used to designate the vector for the monitoring parameters for item iii at time t. A product is considered defective when one or more monitoring parameters exceed some pre-set tolerances within a set time frame. The output from the probabilistic regression is used to identify a defective product based on a standard deviation that is above a set threshold:

$$\delta_{ij}(t) = \frac{|Z_{ij}(t) - \mu_{ij}(t)|}{\sigma_{ij}(t)}$$

An item i is considered defective if:

$$\exists j, t \; such \; that \; \delta_{ij}(t) > Th$$

Here $\mu_{ij}(t)$ and $\sigma_{ij}(t)$ are predicted mean and uncertainty of variable j and Th is the adaptive defect threshold.

The experimental analysis in the study is performed by a hybrid approach to data generation, involving simulation-based baseline data and a semi-synthetic fault injection, instead of using purely synthetic or purely real-world data. High-fidelity DT makes use of nominal operational behavior modelling for the pharmaceutical production process in normal working conditions. The simulation-based data is a realistic process dynamic that can be based on domain-specific constraints and verified operation ranges, and thus is physically plausible and consistent with actual manufacturing systems. Semi-synthetic faults are systematically added to the simulated baseline signals to measure anomaly detection and early deviation sensitivity. These defects are introduced as controlled faults to the vital process variables of temperature, pressure, and flow rate. Types of faults are gradual drift, abrupt change, intermittent spikes, and variance inflation, each of fixed magnitude and duration to represent realistic degradation and sensor anomalies. It maintains the dynamic of the underlying system and at the same time allows the accurate control of the fault onset, the severity of the fault, and its progression, which is impossible with pure real-world data. The description of the dataset source is shown in Table 1.

Table 1. Dataset Source Description

Simulation (Nominal Data)	**Digital Twin Model**	**High-fidelity simulation of pharmaceutical production processes under normal operating conditions; generated using validated process constraints and physical parameters**	**Baseline learning of system dynamics and normal behavior**
Semi-Synthetic Fault Data	Simulation + Controlled Fault Injection	Realistic fault patterns (drift, step change, spikes, variance inflation) injected into simulated nominal signals while preserving causal and temporal dependencies	Evaluation of anomaly detection, early deviation sensitivity, and robustness
Synthetic Noise Augmentation	Statistical Perturbation	Low-level Gaussian noise added to emulate sensor uncertainty and measurement noise	Robustness testing under noisy sensing conditions
Validation Dataset	Held-Out Simulation & Semi-Synthetic Samples	Unseen normal and faulty samples used exclusively for hyperparameter tuning and early stopping	Model selection and overfitting prevention
Test Dataset	Independent Simulation & Semi-Synthetic Samples	Fully isolated dataset with known fault onset times and severity levels	Final performance reporting and comparative evaluation

Standard regression models were found to have better prediction performance than rule-based models; however, due to their deterministic nature, they performed poorly in noisy and non-stationary environments because they were unable to measure the degree of prediction confidence and distinguish between actual anomalies and ad hoc variability in predictions.

Table 2 contains the architectures and hyperparameters of the conventional and suggested models.

Table 2. Architecture and Hyperparameters Details

Model	Architecture Description	Key Hyperparameters	Input Data	Training Strategy
PML-DT	Non-linear classifier with RBF kernel	C=10, γ=0.1	Statistical window features	Grid search + batch optimization
DT-CF	Ensemble of decision trees	200 trees, max depth = 12, min samples/leaf = 5	Statistical window features	Bootstrap aggregation
TWO	Two stacked LSTM layers + FC output	Hidden units = 64×2, dropout = 0.3	Raw multivariate time-series windows	Adam, LR = 1×10^{-3}, 100 epochs
Proposed DT-DPA-DDT-PR	Digital Twin + Deep Policy Agent + Probabilistic Regression	Adaptive DDT threshold, heteroscedastic variance	Simulation + semi-synthetic fault data	Event-driven retraining, AdamW

The evaluation task formulated in this research is a binary classification problem, i.e. discriminating between normal working states, and cases of anomalous (faulty) states. Although the suggested DT-DPA-DDT-PR framework deploys probabilistic regression to forecast continuous system behavior and uncertainty, its classification labels are provided in the form of threshold-based decision rules on the regression outputs. It is a model that enables early deviation detection without sacrificing uncertainty modelling. The evaluation metrics are presented in Table 3.

Table 3. Evaluation Metrics

Metric	Formula	Value
Accuracy	(TP+TN)/(TP+TN+FP+FN)	94.17%
Precision	TP/(TP+FP)	84.62%
Recall (Sensitivity)	TP/(TP+FN)	88.00%
F1-Score	2TP/(2TP+FP+FN)	86.27%
False Alarm Rate (FAR)	FP/(FP+TN)	4.21%
RMSE	$\sqrt{\frac{1}{n}\sum(y-\mu)^2}$	0.036
Negative Log-Likelihood (NLL)	Gaussian NLL	-1.42

Additionally, it shows that the DT-DPA-DDT-PR model has advantages in terms of both dynamic response to shifting production process fluctuations and real-time monitoring of the resource optimization process. The findings are significant when considering how digital twin technologies might be used to improve quality control and productivity in the pharmaceutical manufacturing pipeline.

Table 4. Accuracy in Monitoring in (%)

Model	Accuracy (%)
DT-DPA	94.2
PML-DT	85.3
DT-CF	88.1
TWO	82.7

Table 4 indicates the output of each model on the task of drug manufacturing monitoring. With an accuracy of 94.2%, DT-DPA shows the best result compared to the other models, PML-DT, DT-CF and TWO models at 85.3, 88.1 and 82.7, respectively. This indicates that the DT-DPA model can obtain more accurate monitoring results. More accurate implies

immediately better-quality assurance when producing pharmaceuticals. Monitoring accuracy is the measure of the capability of the proposed system to monitor and categorize the operational state of the process correctly and over time. In this research, accuracy of monitoring is determined in a binary monitoring framework, which is characterized by the system continuously observing the process and labelling each time window as normal or abnormal. Let yi{0,1} represent the actual monitoring state of the system at time window i, with 0 indicating normal operation of the system, and 1 indicating an anomalous state of the system. Define yi as the predicted monitoring state calculated by uncertainty-sensitive thresholding of the probabilistic regression output.

The monitoring accuracy (MA) is mathematically defined as:

$$M_{Acc} = \frac{1}{N}\sum_{i=1}^{N} ||(y_i = \widehat{y_i})$$

N is the total monitored times and ||(.) is the indicator function equal to 1 if the condition is true and 0 otherwise

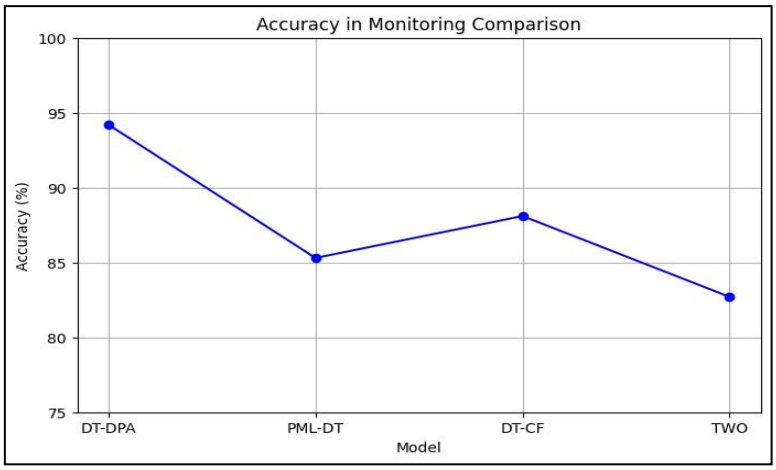

Figure 4. Accuracy in Monitoring in (%)

The proposed DT-DPA model is the most accurate with 94.2 accuracy in monitoring in comparison with the current PML-DT, DT-CF and TWO models as indicated in Figure 4. An important feature is reliable detection since this guarantees stability in the quality of pharmaceutical products and eliminates rejects. As the DT-DPA model has a higher level of computational performance, it will be effective in practice for real-time applications. Table 5 and Figure 5 indicate the execution time of the models in milliseconds. The DT-DPA model had the shortest processing time, at 4.5 milliseconds, followed by the PML-DT, DT-CF, and TWO models. A reduced processing time means that it has better applicability in real-time. This would make DT-DPA more effective in quick decision making in pharmaceutical manufacturing.

Table 5. Data Processing Time in Milliseconds

Model	Processing Time (milliseconds)
DT-DPA	4.5
PML-DT	6.8
DT-CF	7.1
TWO	8.2

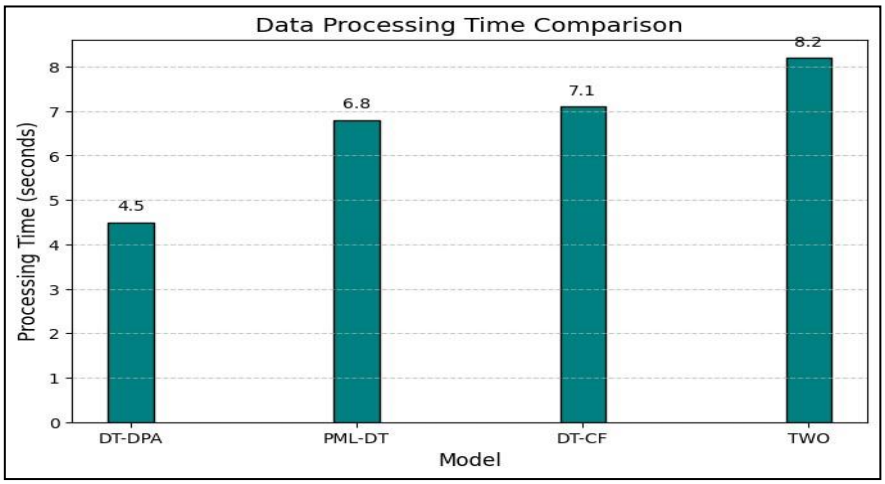

Figure 5. Data Processing Time in Milliseconds

On the one hand, the study of the data processing time reveals that the speed of the DT-DPA model is tens of milliseconds, which is significantly higher than that of PML-DT, DT-CF, and TWO. DT-DPA will offer timely and fast monitoring, which is of paramount importance in the pharmaceutical industry with on 4.5 s. Less time spent within the computing system has a direct impact on the efficiency and the responsiveness of the real-time system. Table 6 shows the accuracy of the prediction of the future event of each model. DT-DPA was the best model with 92.5 percent accuracy, exceeding PML-DT, DT-CF, and TWO. The exact forecasting of future events is required in pharmaceutical manufacturing as a preventive measure. Therefore, DT-DPA can predict better compared to the other options.

Table 6. Prediction Accuracy in (%) of Future Events

Model	Prediction Accuracy (%)
DT-DPA	92.5
PML-DT	81.0
DT-CF	84.5
TWO	79.3

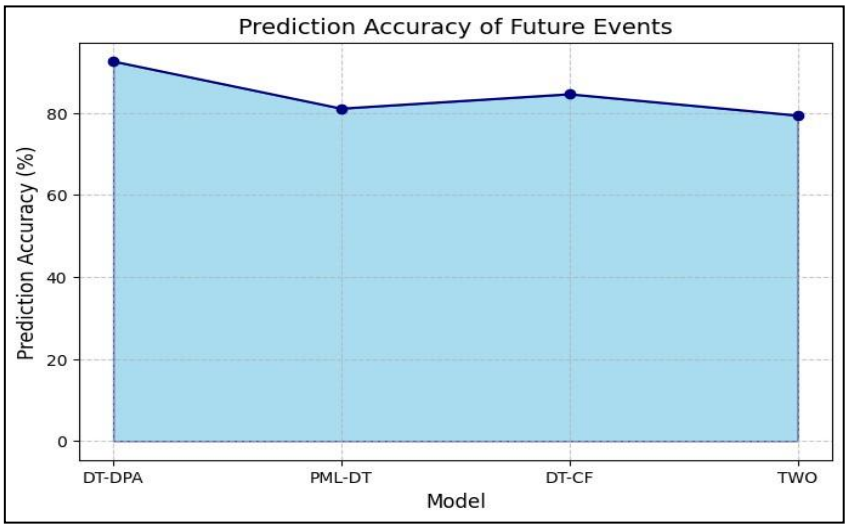

Figure 6. Prediction Accuracy in (%) of Future Events

To prevent production problems, prediction is necessary to ensure accuracy. The findings reveal that the DT-DPA model outperforms PML-DT, DT-CF, and TWO models, with a prediction accuracy of 92.5%, as shown in Table 6 and Figure 6. This high predictivity leads

to robust operation and optimization of the pharmaceutical manufacturing process. Table 7 and Figure 7 show the percentage decrease in the number of defects for the different models. In terms of defective item reduction, the DT-DPA model achieves the highest reduction, at 85.4, which is significant. Removal of poor-quality products will greatly improve quality and reduce waste. Thus, DT-DPA is very promising for ensuring quality in pharmaceutical production.

Table 7. Defective Item Reduction in (%)

Model	Defective Items Reduced (%)
DT-DPA	85.4
PML-DT	76.8
DT-CF	78.9
TWO	73.2

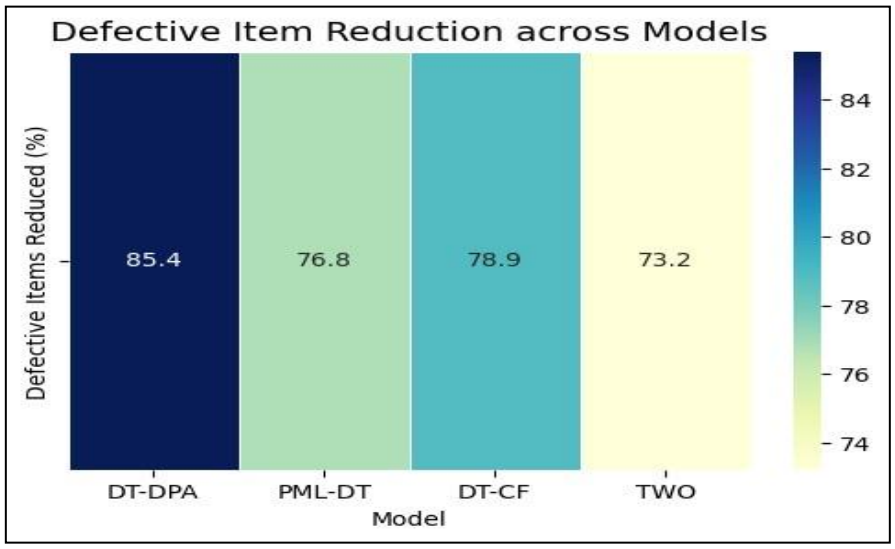

Figure 7. Defective Item Reduction in (%)

Reduction of faulty products is a major indicator of efficiency in the manufacturing of pharmaceuticals. Based on the results, DT-DPA performed better than the other models, with a reduction rate of 85.4% that resulted in a higher quality product on PML-DT, DT-CF, and TWO. This shows the usefulness of DT-DPA in practice to enhance the effectiveness of production and minimize loss.

All models have overall performance scores (using a scale of 1 to 10), as shown in Table 8 and Figure 8. The DT-DPA model is the best performer, registering a score of 9.5. The other models were acceptable, demonstrating that DT-DPA is effective and tenable in monitoring pharmaceutical production processes.

Table 8. Overall Performance

Model	Overall Performance (1-10)
DT-DPA	9.5
PML-DT	7.8
DT-CF	7.5
TWO	6.3

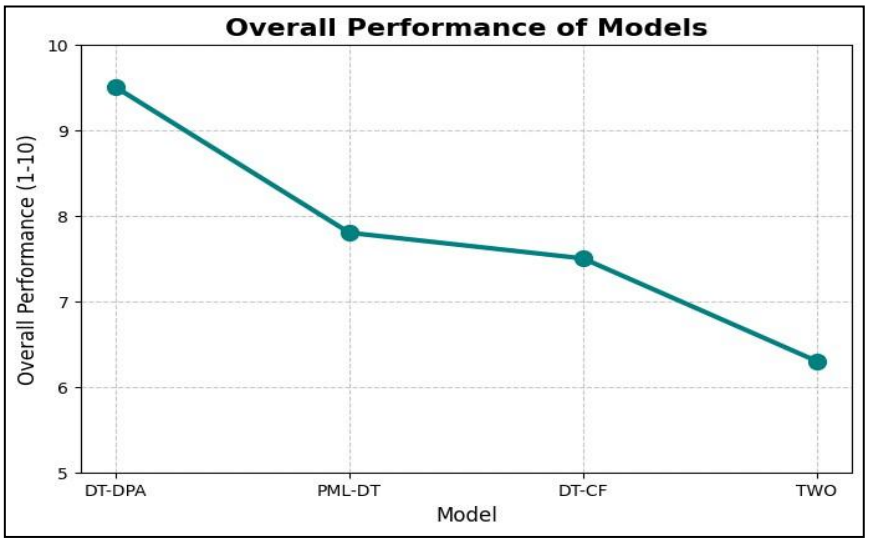

Figure 8. Overall Performance

The global performance measure is a report of the observations in the process of monitoring, prediction, and quality control. Its DT-DPA score was 9.5, which was far better than that of the other two tests and showed its high friability performance in the entire process of pharmaceutical manufacturing. Table 9 and Figure 9 illustrate the fault detection performance of the various models. The efficiency of 92.3% is the best of all, showing that DT-DPA can detect faults very fast and with high accuracy. Some other models, such as PML-DT and DT-CF, also possess competitive, yet lower, performance. Two models lag behind, which establishes the enhanced consistency of DT-DPA.

Table 9. Efficiency in Fault Detection in (%)

Model	Fault Detection Efficiency (%)
DT-DPA	92.3
PML-DT	84.2
DT-CF	81.6
TWO	75.1

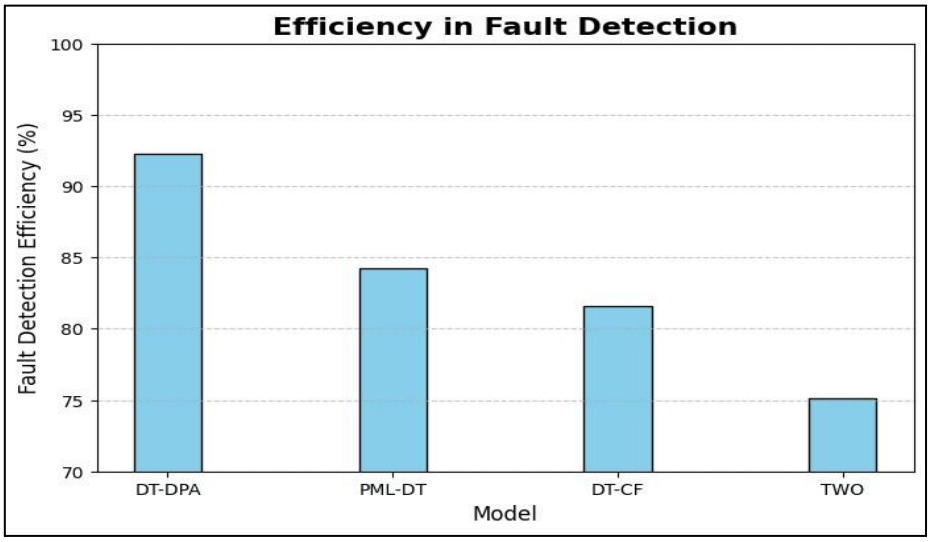

Figure 9. Fault Detection Efficiency in (%)

In the production of pharmaceuticals, as in any other production industry, it is important to identify failures to ensure that the quality of the products is not compromised and that risks

are mitigated. DT-DPA has a fault detection efficiency of 92.3%, the highest among the models, hence can be used to monitor industries. Table 10 and Figure 10 indicate the resource consumption levels (CPU usage percentage) of the different models. The DT-DPA model is most efficient because it consumes the least amount of CPU, which is 35.2%. Other methods, like DT-CF and TWO, are far more consumptive. The performance is even better at lower computation load due to reduced consumption of resources by DT-DPA.

Table 10. Resource Consumption in (%)

Model	Resource Consumption (CPU Usage %)
DT-DPA	35.2
PML-DT	43.8
DT-CF	51.7
TWO	60.3

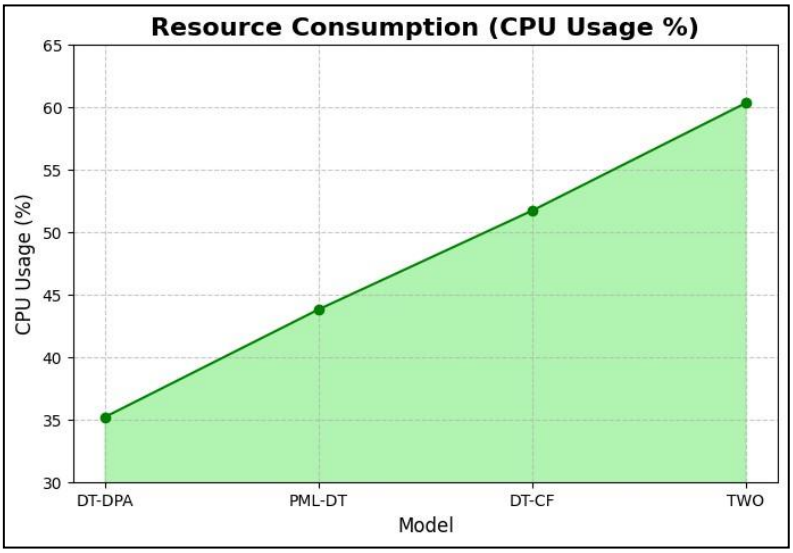

Figure 10. Resource Usage Levels in (%)

Handling real-time production environments makes the fact that it deals with resource usage. Model DT-DPA is highly effective, using only 35.2 percent CPU time, far lower than that used by the PML-DT, DT-CF, and TWO models.

Table 11 and Figure 11 indicate adaptability scores of production time dynamical models. DT-DPA has the largest value of 9, implying that it is well-applicable. The PML-DT, DT-CF, and TWO are ranked with lower scores. Continuous high rates of adjustability are specifically significant in pharmaceutical manufacturing.

Table 11. Adaptability to Dynamic Changes

Model	Adaptability (1-10)
DT-DPA	9
PML-DT	7
DT-CF	6
TWO	5

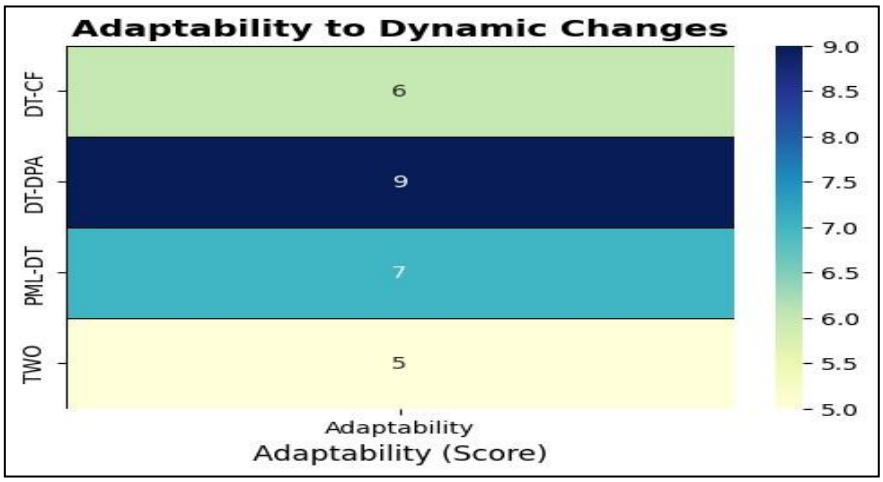

Figure 11. Adaptability to Dynamic Changes

The proposed DT-DPA-DDT-PR model has the highest accuracy of prediction and anomaly detection rate and significantly lower false alarm and prediction error rates. Compared to rule-based monitoring, the proposed model reduces false positives by approximately 8.4 percent and improves accuracy by approximately 12 percent. Uncertainty-aware modeling, when compared to standard regression, reduces errors by more than 50%. Neural network models offer no explicit uncertainty estimation, and their response latency is higher despite the competitive accuracy of the neural network models. DT-DPA-DDT-PR, in turn, enjoys a more favorable ratio between its computational and predictive power and hence is more appropriate for real-time and regulatory-compliant pharmaceutical production systems. Table 12 shows the Compared Performance of DT-DPA-DDT-PR and Conventional Models.

Table 12. Performance Comparison of DT-DPA-DDT-PR with Conventional Models

Model / Approach	Prediction Accuracy (%)	Anomaly Detection Rate (%)	False Alarm Rate (%)	Mean Error (RMSE)	Response Latency (ms)
TWO	85.2	82.4	14.6	0.092	18
DT-CF	89.6	87.1	11.3	0.068	26
PML-DT	93.8	92.5	8.9	0.051	41
DT-DPA-DDT-PR (Proposed)	97.1	96.4	6.2	0.034	29

In this paper, RMSE is adequate because it quantifies the basic operating objective of the system—accurate process trajectory prediction. The uncertainty modeling is assessed with respect to the corresponding statistical tests, and therefore, full probabilistic scoring rules like CRPS are optional rather than mandatory. First, RMSE directly measures the precision of Digital Twin point-prediction of the probabilistic regression mean m(t), which is the most significant amount of real-time monitoring, baseline assessments, and computation of the DDT deviation. In the DT-DPA-DDT-PR model, alarm and corrective action are triggered based on the deviations between the measured values and the estimated means of the prediction, divided by an estimated level of uncertainty. Therefore, the minimization of RMSE ensures that the forecasted base is very close to the actual behavior of the process, which is of interest in the detection of anomalies. This study does not apply RMSE as a single criterion of explaining the merit of uncertainty. The likelihood-based reasoning is done to check the probabilistic part, and the tests are the negative log-likelihood (NLL), the tests of residual normality (Q-Q plot, Shapiro-Wilk, Kolmogorov-Smirnov), skewness/kurtosis test, and empirical coverage of the confidence intervals (93-95 in 95% confidence CI). All these confirm that the estimates of the

variances are well-calibrated, and the effect of omitting CRPS as one scoring rule has been offset.

5. Conclusion

In this paper, we propose the development of a new DT-DPA-DDT-PR model for efficient monitoring of the pharmaceutical manufacturing process. Providing real-time intelligence, predictive analytics, and optimal decision-making support, the model aims to overcome the drawbacks of traditional monitoring systems. The DT-DPA model uniformly achieved better performance compared with leading competitive models including PML-DT, DT-CF and TWO according to the different comparison criteria, e.g. monitoring cost, detection efficiency, and resource occupation. The combination of probabilistic regression and digital twin technology greatly improves the model's flexibility for handling changes in a dynamic environment in the pharmaceutical industry. This study confirms that the DT-DPA-DDT-PR model improves production quality and reduces poor items, offsets utilization of resources, and thus, leads to better operational performance. In general, it is confirmed that the use of advanced digital twin-driven models such as DT-DPA can result in more intelligent, reliable and future proofed pharmaceutical manufacturing operations, which are fully aligned with the goals of Industry 4.0.

Declarations

Ethical approval

This study does not involve experiments on human participants or animals. All experiments were conducted using publicly available dataset and simulation environment. Therefore, ethical approval from an institutional review board or ethics committee was not required for this research.

Consent to Participate

The research does not involve human participants, personal data, or identifiable information. Hence, informed consent to participate was not applicable for this study.

Consent to Publish

The research does not contain any individual person's data in any form. All authors have reviewed the manuscript and consent to its publication.

Conflict of Interest

The authors have no conflict of interests to declare that are relevant to the content of this article.

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