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AI-Driven Quality Monitoring and Control in Stem Cell Cultures: A Comprehensive Review

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ABSTRACT

Recent advancements in stem cell research forge them into one of the most promising sources for cell therapy applications. Quality monitoring in stem cell culture is essential for ensuring consistency, viability, and therapeutic efficacy. Traditional methods involve periodic sampling for conducting endpoint assays such as cell viability, proliferation, and differentiation using microscopy and flow cytometry, which are labor-intensive and often lack the real-time monitoring of the processes for scale-up applications. This paper explores artificial intelligence (AI)-driven approaches for real-time quality control, integrating machine vision, predictive modeling, and sensor-based monitoring. AI models analyze high-resolution imaging and multi-sensor data to dynamically track critical quality attributes (CQAs), including cell morphology, proliferation rate, differentiation potential, environmental stability (pH, oxygen, and nutrient levels), genetic integrity, and contamination risks. These models enable automated anomaly detection, differentiation tracking, and adaptive culture optimization. By leveraging real-time feedback systems and multi-omics integration, AI-driven techniques enhance scalability, reproducibility, and process automation in stem cell biomanufacturing. This review outlines current advancements, challenges, and future directions in AI-assisted quality monitoring and highlights its potential to improve fully automated, scalable production of stem cell lines for clinical translation and regulatory compliance in regenerative medicine.

1 | Introduction: The Role of AI in Stem Cell Quality Monitoring

Stem cell culture and manufacturing represent the cornerstone of regenerative medicine, tissue engineering, and personalized therapies, offering immense opportunities to address a wide range of medical conditions [1–3]. The ability to cultivate, expand, and differentiate stem cells into functional cell types has propelled this field into the spotlight of biomedical research.

However, the inherent complexity of stem cell cultures—including their sensitivity to environmental conditions, variability in behavior, and dependence on precise handling—underscores the urgent need for rigorous and scalable quality control measures [4, 5]. Maintaining consistent safety and culture quality is critical for both reproducibility and therapeutic success [6, 7].

Despite advances in imaging, sensor technologies, and omics profiling [8–10], traditional quality control practices remain labor-intensive, destructive, and poorly scalable [11, 12]. Widely used methods such as semi-automated microscopy, flow cytometry, and immunostaining offer limited temporal resolution and often fail to provide real-time, actionable

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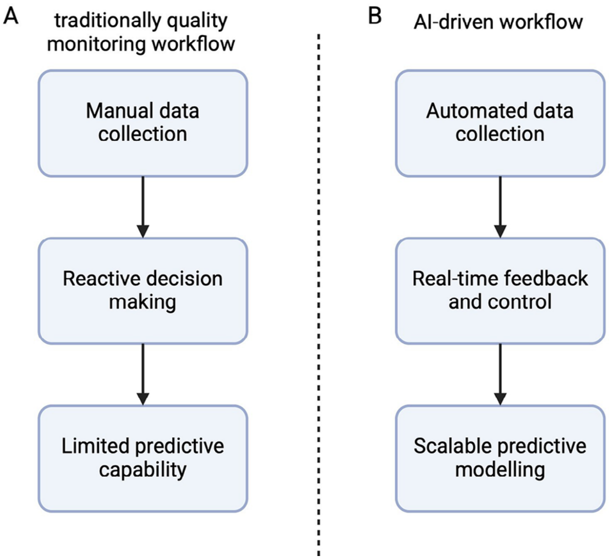

FIGURE 1 | A visual comparison of conventional quality control approaches—based on manual endpoint assays—and AI-enabled monitoring systems that integrate real-time imaging, predictive modeling, and feedback control (created using biorender.com).

insights during critical stages of culture growth and differentiation [13, 14].

As shown in Figure 1, conventional methods largely rely on fixed time-point sampling and destructive assays, limiting their utility for large-scale or dynamic applications. This gap is especially evident in clinical-grade production, where robust, scalable, and minimally invasive monitoring systems are required [15, 16]. Artificial intelligence (AI) has emerged as a transformative enabler in this space, offering capabilities for real-time data analysis, predictive modeling, anomaly detection, and automated feedback control [17–19]. By integrating heterogeneous data streams—including high-resolution imaging, environmental sensor data, and multi-omics profiles—AI systems can dynamically track critical quality attributes (CQAs), forecast culture trajectories, and proactively guide process interventions [20, 21].

However, integration of AI into stem cell workflows remains fragmented. Key challenges—such as data heterogeneity, lack of interpretability, and the absence of validated frameworks for regulatory compliance—have limited its widespread adoption and translation beyond proof-of-concept studies [22–24].

Recent developments in large-scale mesenchymal stem cell (MSC) production for therapeutic applications have further underscored the need for robust quality control and scalable automation strategies to ensure consistency and clinical efficacy [25]. In parallel, scaling cell therapy bioreactors to industrial levels presents significant challenges, necessitating innovative control approaches to manage turbulence, maintain homogeneity, and ensure reproducible cell yields [26].

To address these gaps, this review introduces a structured analytical framework for AI-driven quality monitoring in stem cell cultures. We systematically explore: (i) CQAs relevant to stem cell applications, (ii) AI technologies enabling real-time monitoring and predictive control, (iii) practical applications with comparative insights, (iv) integration challenges, and (v) innovative future directions. By synthesizing current technologies and proposing a unified perspective, we aim to provide a roadmap toward scalable, reproducible, and clinically compliant stem cell biomanufacturing (Figure 2) [27, 28].

The remainder of this paper is structured as follows: Section 2 details CQAs in stem cell cultures, Section 3 describes AI technologies enabling quality control, Section 4 discusses practical applications and comparative case studies, Section 5 analyzes

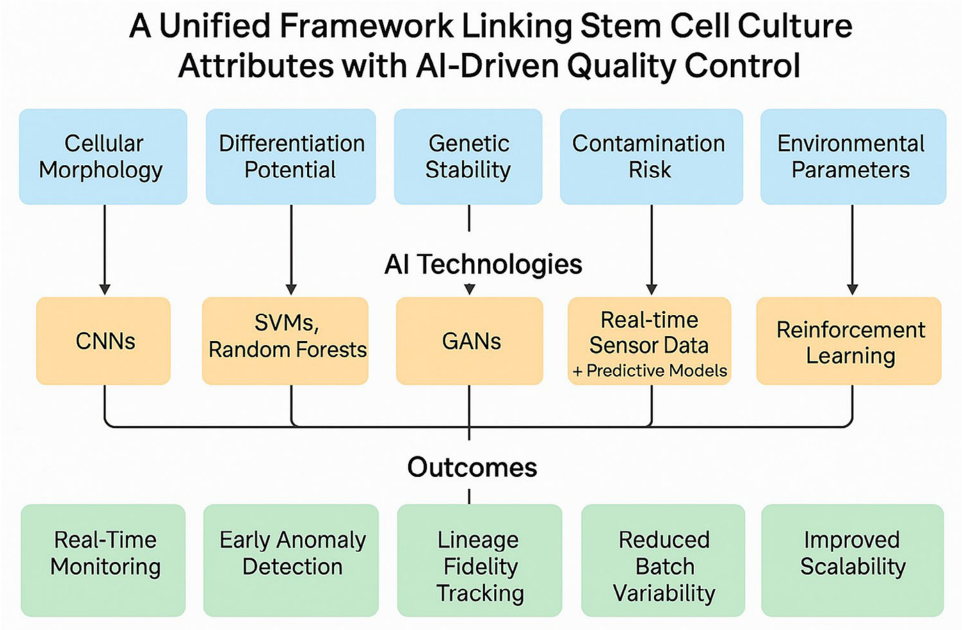

FIGURE 2 | Conceptual framework for AI-driven quality monitoring in stem cell cultures, linking critical quality attributes (CQAs) with corresponding AI technologies and control strategies. This framework structures the discussion in the subsequent sections (created using biorender.com).

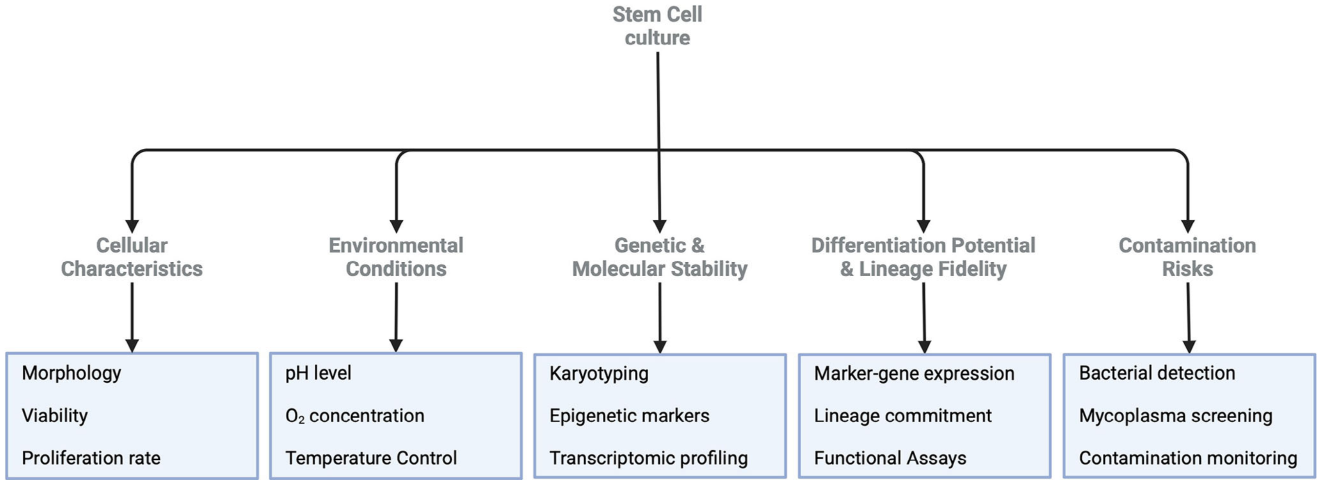

FIGURE 3 | Key CQAs and their monitoring approaches. AI tools enable earlier, noninvasive, and dynamic tracking compared to traditional static assays (created using biorender.com).

integration challenges, Section 6 proposes future directions, and Section 7 concludes the review.

2 | CQAs in Stem Cell Cultures

CQAs refer to the physical, chemical, biological, or microbiological properties that must be maintained within specific limits to ensure the safety, efficacy, and quality of stem cell-derived products [6]. Unlike critical process parameters (CPPs), which are operational variables such as pH or oxygen levels, CQAs directly influence cell fate and function [4, 7].

Figure 3 summarizes the major CQAs relevant to stem cell-derived product manufacturing and highlights corresponding AI-enabled monitoring strategies. By leveraging diverse AI models—ranging from CNNs for morphological assessment [29], to predictive algorithms for environmental condition control [30], and deep learning tools for tracking genetic integrity [31]—this framework enables earlier, more accurate, and noninvasive quality assessment compared to traditional endpoint assays. These AI-assisted approaches serve as the foundation for dynamic, real-time quality monitoring pipelines essential for scalable and robust stem cell biomanufacturing [32].

Table 1 outlines the mapping between major CQAs and AI tools used to monitor or control them.

TABLE 1 | Mapping critical quality attributes to AI monitoring strategies.

Critical quality attribute (CQA)	AI-based monitoring strategies
Cell morphology and viability	CNN-based image analysis [29, 33], GAN-generated synthetic data [34], automated time-lapse tracking [35]
Differentiation potential	SVMs for lineage classification [36], regression models for stage prediction and multitask learning [37]
Genetic stability	Multi-omics data fusion using deep learning [9]; attention-based models [38]
Contamination risk	Anomaly detection via sensor data and random forest classifiers [32], CNNs on microscopy images [39]
Environmental conditions	Predictive modeling from IoT sensor data [30], Reinforcement Learning for feedback control [40, 41]

AI offers a more scalable, interpretable, and proactive approach compared to traditional endpoint assays, which are often destructive, labor-intensive, and fail to capture dynamic trends [11, 12].

2.1 | Cellular Characteristics

Cell morphology, viability, and proliferation rate are primary indicators of stem cell quality. Traditional assessment methods—such as manual microscopy and flow cytometry—offer only static snapshots and are highly dependent on human expertise [42, 13]. These techniques are time-consuming and lack the resolution to detect subtle phenotypic changes [43].

AI-driven approaches, particularly convolutional neural networks (CNNs), enable continuous, noninvasive tracking of morphological changes. For instance, Fan et al. [29] demonstrated over 90% accuracy in predicting iPSC colony formation without labeling or destructive sampling.

In addition to morphology, proliferation trends can be inferred in real time via AI-assisted live-cell imaging. Padovani et al. [44] applied automated image segmentation to track cell cycle phases, which could be enhanced by AI for real-time application. While EdU and BrdU incorporation offer precision, AI models analyzing label-free data—for example, confluency progression—are now being evaluated as viable surrogates [45].

2.2 | Environmental Conditions

Stem cells are acutely sensitive to their microenvironment, including nutrient availability, gas exchange, pH, and shear forces [46, 47]. Deviation from optimal conditions can significantly impact viability, differentiation, and lineage fidelity [48, 49].

Traditional environmental monitoring relies on offline sampling or threshold-based control. In contrast, AI-powered real-time monitoring systems use predictive models trained on historical sensor data to detect subtle anomalies. For example, Xie et al. [30] implemented a model to predict future oxygen saturation dips hours in advance based on high-frequency input from dissolved oxygen and lactate sensors.

Reinforcement learning has also been used to dynamically adjust environmental parameters. Komarova et al. [40] showed that gas composition adjustments guided by an RL algorithm improved expansion efficiency of stem cell cultures by 15%.

2.3 | Genetic and Molecular Stability

Maintaining genetic and epigenetic integrity is crucial for the safety and reproducibility of stem cell-based therapies [50, 51]. Extended passaging often leads to genetic drift, chromosomal abnormalities, and epigenetic reprogramming [52, 53], threatening clinical viability.

Traditional assessments rely on low-throughput techniques like karyotyping or microarrays. AI enables multi-omics integration—fusing genomics, transcriptomics, and epigenomic data—to model patterns of instability. For example, Smith et al. [31] used deep learning to detect latent instability trajectories by combining RNA-seq and SNP profiles. Similarly, Shahir et al. [38] proposed graph-based models for identifying subpopulations with early aberrant gene expression.

2.4 | Differentiation Potential and Lineage Fidelity

The ability of stem cells to commit to target lineages while avoiding off-target differentiation is central to their therapeutic utility [54, 55]. Monitoring this transition in real time has remained a challenge, as traditional methods rely on endpoint marker expression or immunostaining.

Recent AI approaches have shifted toward trajectory-based modeling. For instance, Buggenhagen et al. [56] developed a classifier trained on time-series imaging and gene expression to forecast differentiation outcomes with 88% accuracy. In pancreatic beta cell protocols, SVM classifiers trained on brightfield images have achieved over 90% sensitivity in distinguishing endocrine lineage commitment stages [36]. Seeding strategies critically influence the metabolic profiles and differentiation potential of human induced pluripotent stem cells (iPSCs) into pancreatic progenitors, underlining the importance of precise process controls to maintain desired CQAs [57].

2.5 | Contamination Risks

Contamination remains one of the most costly risks in stem cell manufacturing. Detection is traditionally done through visual inspection, microbial assays, or mycoplasma tests [58, 59]. These methods are time-delayed and reactive.

AI-based contamination detection uses pattern recognition on both sensor streams (e.g., sudden pH or O_2 shifts) and microscopy data. For example, Burnett et al. [32] trained a Random Forest model on 48-h pH, oxygen, and glucose trends to predict contamination with 93% accuracy—12 to 24 h earlier than manual identification. CNNs applied to time-lapse imagery can detect subtle visual markers—such as granular debris or disrupted monolayers—indicative of microbial growth [39].

3 | AI Technologies Enabling Quality Control

AI has introduced powerful new capabilities to automate, accelerate, and enhance the quality control of stem cell cultures [20]. Rather than simply replacing manual observation, AI technologies enable real-time, dynamic, and predictive monitoring of critical culture attributes.

Figure 4 outlines how different AI methods are mapped to specific quality monitoring challenges. Rather than an exhaustive listing, this figure aims to contextualize the selection of AI tools based on the type of CQA being assessed.

3.1 | Machine Vision for Image Analysis

Traditional microscopy relies heavily on manual interpretation, which is prone to subjectivity and limited scalability [60]. AI-driven machine vision, particularly CNNs, enables high-throughput, objective analysis of stem cell images. CNN-based classifiers, as illustrated in Figure 5, have achieved over 90% accuracy in identifying morphological indicators of pluripotency, outperforming manual assessments by a margin of 15%–20% in precision and reproducibility [29, 61]. These models detect subtle shifts in morphology—such as changes in colony shape or granularity—that human observers often miss. CNN-based models, illustrated in Figure 6, enable high-resolution tracking of morphological shifts during proliferation and differentiation with improved precision and scalability.

However, CNNs are highly dependent on training dataset quality. Variations in imaging conditions, microscope settings, or staining methods can significantly impact model performance [39]. Data augmentation and domain adaptation techniques are increasingly employed to mitigate these challenges.

3.1.1 | Dynamic Tracking Through Time-Lapse Imaging

Dynamic behaviors such as proliferation, motility, and colony expansion provide critical insights into culture health. Traditional tracking is labor-intensive and prone to error. Highly sensitive real-time quantitative PCR (qPCR) assays have been developed to

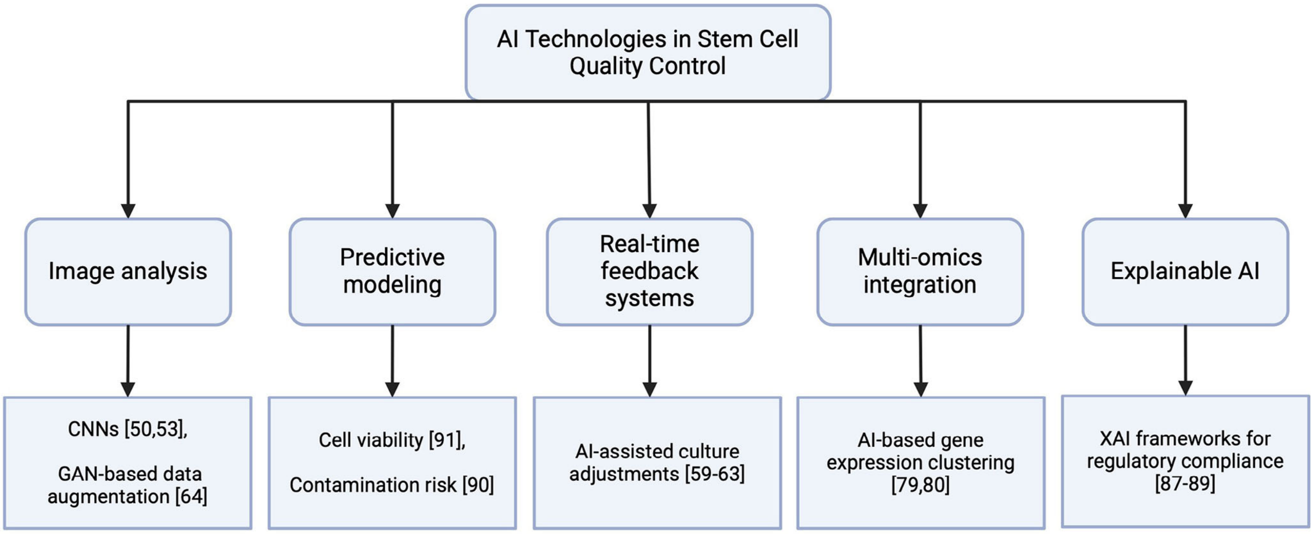
AI Technologies in Stem Cell Quality Control

Image analysis

Predictive modeling

Real-time feedback systems

Multi-omics integration

Explainable AI

CNNs [50,53], GAN-based data augmentation [64]

Cell viability [91], Contamination risk [90]

AI-assisted culture adjustments [59-63]

AI-based gene expression clustering [79,80]

XAI frameworks for regulatory compliance [87-89]

FIGURE 4 | Mapping of AI tools to critical quality monitoring tasks in stem cell manufacturing. Each technique addresses specific limitations of traditional QC workflows, enhancing scalability, reproducibility, and predictive capacity (created using biorender.com).

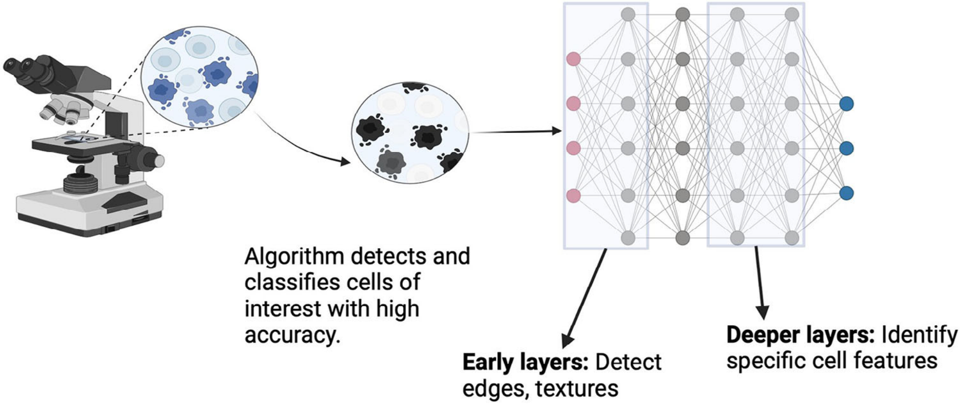

FIGURE 5 | Illustration of AI-driven machine vision techniques applied to microscopic images of stem cell cultures, enabling automated identification of morphological changes, proliferation rates, and differentiation status (created using biorender.com).

precisely quantify MSCs in vivo, supporting noninvasive monitoring methods necessary for clinical-grade stem cell manufacturing [62]. AI models applied to time-lapse microscopy—such as those developed by Schwarz et al. [35]—automate tracking with higher temporal resolution. They reduce manual annotation time by up to 70% and detect early deviations from expected proliferation rates. Despite these advantages, dynamic tracking systems must address drift and identity loss in long-term imaging. Integrating imaging data with environmental metadata may improve robustness in future implementations.

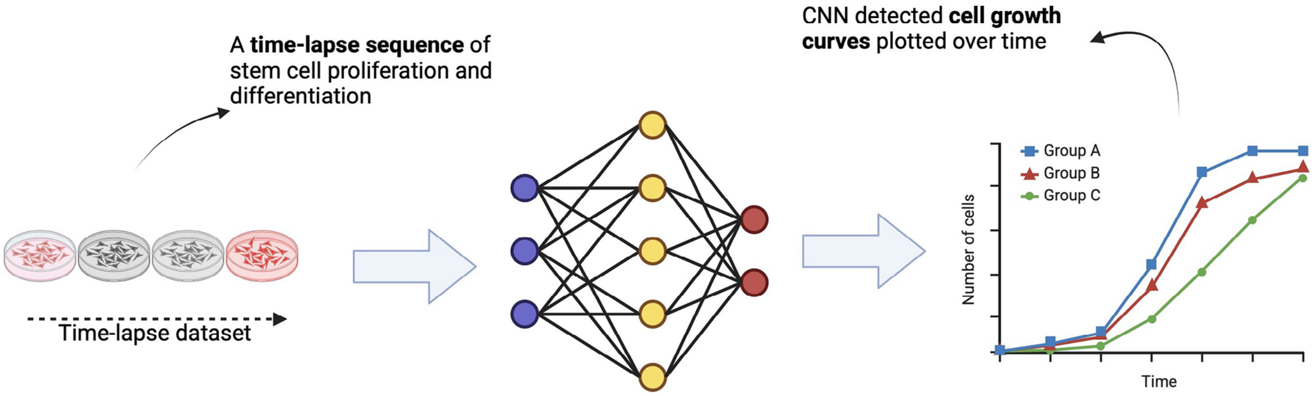

FIGURE 6 | Illustration of CNNs enabling automated cell morphology assessment and real-time tracking of proliferation and differentiation (created using biorender.com).

3.1.2 | Synthetic Data Generation Using GANs

Limited annotated datasets hinder the training of robust image-based AI models. Generative adversarial networks (GANs) offer a solution by creating realistic synthetic images to augment datasets. For example, Khanal et al. [34] demonstrated that GAN-augmented datasets improved CNN classification accuracy by 12% when identifying differentiated versus undifferentiated colonies. GANs help balance rare classes, enhancing the ability to detect rare events such as early apoptosis or off-target differentiation. Nevertheless, GAN-generated data risks introducing artifacts if not properly validated. Techniques such as visual Turing tests and biological plausibility metrics are recommended for quality control of synthetic datasets.

3.2 | Predictive Modeling for Quality Control

Predictive modeling forms the backbone of proactive quality management in stem cell manufacturing. Rather than detecting failures after they occur, AI models forecast CQAs based on historical and real-time data [63]. Regression models, such as support vector regression (SVR) and random forest regressors, have been widely used to predict continuous variables like confluency, metabolic activity, or differentiation stage. For instance, Xie et al. [64] demonstrated that predictive modeling based on phase-contrast imaging could anticipate optimal subculture timing with 92% accuracy, reducing unnecessary manipulations and improving batch viability. Classification models, such as SVMs and decision trees, are applied to categorical outcomes. Singh et al. [36] used SVM classifiers on phase contrast microscopic images to predict differentiation status, achieving sensitivities above 90% across multiple lineage markers.

Despite promising results, model overfitting remains a concern—particularly when training data do not capture batch-to-batch variability or protocol deviations. Active learning and uncertainty quantification strategies are being explored to mitigate these limitations.

3.2.1 | Multistage and Longitudinal Prediction

AI models incorporating sequential datasets—spanning multiple days of culture—enable dynamic predictions of culture trajectories. Multistage modeling approaches, as shown by Zhang et al. [65], track changes over time rather than static snapshots, improving the early detection of differentiation failures by 20%–30%. Multitask learning further enhances model utility by simultaneously predicting multiple CQAs (e.g., viability and differentiation stage), reducing computational cost, and improving interpretability [66]. However, managing temporal data increases complexity. Temporal models must address missing data, variable sampling rates, and nonlinear progression trends, which require careful model architecture design.

3.3 | Real-Time Feedback Systems

Real-time feedback systems leverage AI to create closed-loop biomanufacturing processes. By continuously monitoring environmental and cellular parameters, they autonomously adjust culture conditions to maintain optimal growth environments.

Early work by Csaszar et al. [41] demonstrated real-time cytokine feedback to optimize hematopoietic stem cell expansion. More recently, reinforcement learning (RL) models have been used to dynamically optimize gas composition, feeding schedules, and temperature controls, improving yield consistency by up to 18% in test environments [40].

Nevertheless, challenges such as sensor drift, biofouling, and communication lags between sensors and control algorithms must be addressed. Digital twin technologies—virtual models of bioreactor systems updated in real time—are emerging as promising strategies to enhance feedback accuracy and robustness.

A schematic overview of how AI-driven predictive models integrate real-time data to forecast CQAs and dynamically guide process interventions is presented in Figure 7.

3.4 | Multi-Omics Integration

Multi-omics analysis—combining genomics, transcriptomics, proteomics, and metabolomics—provides a comprehensive view of stem cell culture health [9]. However, the high dimensionality and complexity of multi-omics data necessitate advanced AI tools for integration and interpretation.

Deep learning models such as autoencoders, graph neural networks, and multi-view clustering have been successfully applied to fuse omics layers. For instance, Wang et al. [67] integrated transcriptomic and proteomic profiles to predict pluripotency maintenance markers with a 15% improvement in predictive accuracy over single-omics models.

Despite these successes, challenges include data normalization across modalities, missing value imputation, and biological interpretability of latent features. Graph-based models such as Cello-Graph [38] have shown promise by explicitly modeling cell-cell communication networks.

Scalability remains a bottleneck, particularly as culture systems move toward industrial-scale manufacturing requiring real-time multi-omics surveillance.

Figure 8 illustrates how AI techniques fuse multiple omics modalities to provide a holistic view of stem cell quality and differentiation trajectories.

3.5 | Explainable AI in Stem Cell Research

Interpretability is critical for the clinical translation and regulatory approval of AI-driven stem cell quality monitoring systems, as it enables researchers to validate and trust the outcomes of these models. Explainable AI (XAI) methods enhance the robustness and reliability of real-time monitoring by making AI decision-making transparent, a benefit demonstrated in recent chromatographic protein purification processes, where deep learning interpretability significantly improved process control

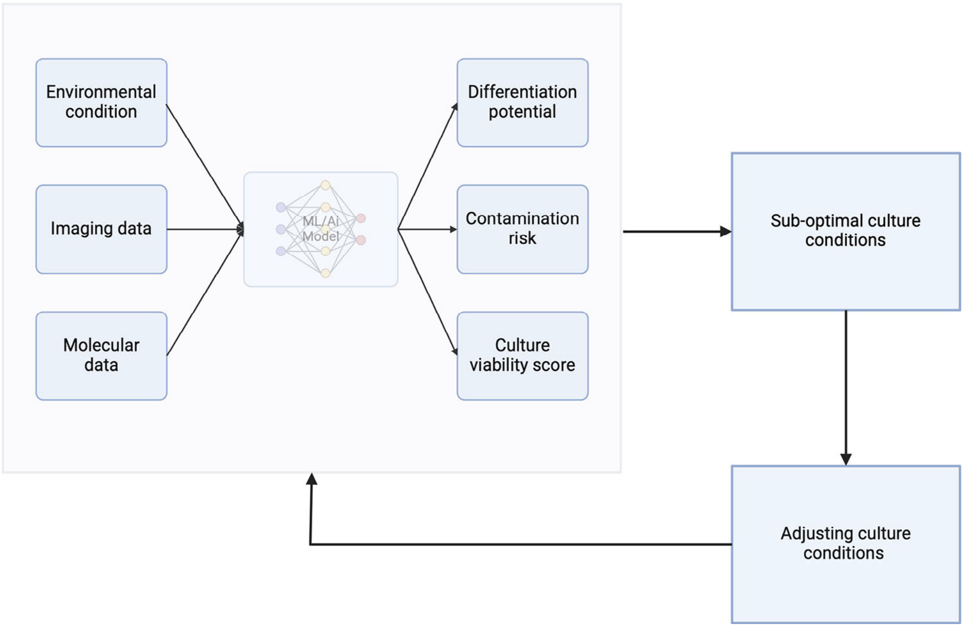

FIGURE 7 | A step-by-step flowchart demonstrating how AI models process historical and real-time data to forecast CQAs, detect deviations, and optimize stem cell culture conditions dynamically (created using biorender.com).

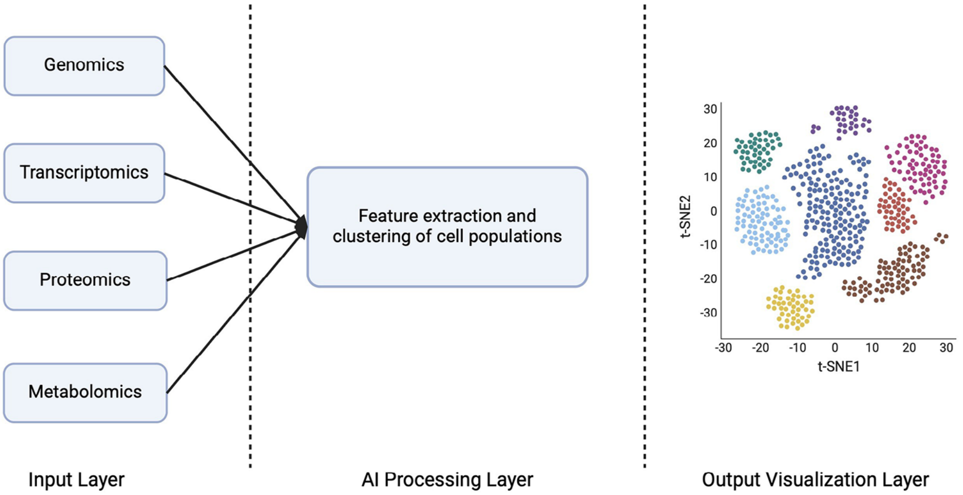

FIGURE 8 | A schematic representation of how AI integrates genomics, transcriptomics, proteomics, and metabolomics data to provide a holistic assessment of stem cell quality and differentiation potential (created using biorender.com).

and operational trust [68]. In stem cell contexts, attention-based models such as SCEMILA have been employed to identify diagnostically relevant cells in hematological datasets, offering insights into the most influential features driving classification decisions [69]. For image-based analysis, techniques like Grad-CAM (Gradient-weighted Class Activation Mapping) help visualize which regions of stem cell colony images contribute most to AI predictions [70], while in multi-omics applications, feature attribution approaches such as SHAP (SHapley Additive exPlanations) rank genetic, proteomic, or metabolic markers based on their importance in outcome predictions. Despite their advantages, these interpretability tools can sometimes come at the cost of reduced model complexity or predictive performance, making it essential to strike a balance between transparency and accuracy, particularly when working with deep learning models applied to high-dimensional biological data. Figure 9 illustrates XAI enabling transparency.

Table 2 summarizes the key strengths, limitations, and applications of the various AI technologies discussed in this section.

4 | Challenges in AI Integration

Despite its potential, the integration of AI into stem cell culture workflows faces critical barriers that must be addressed

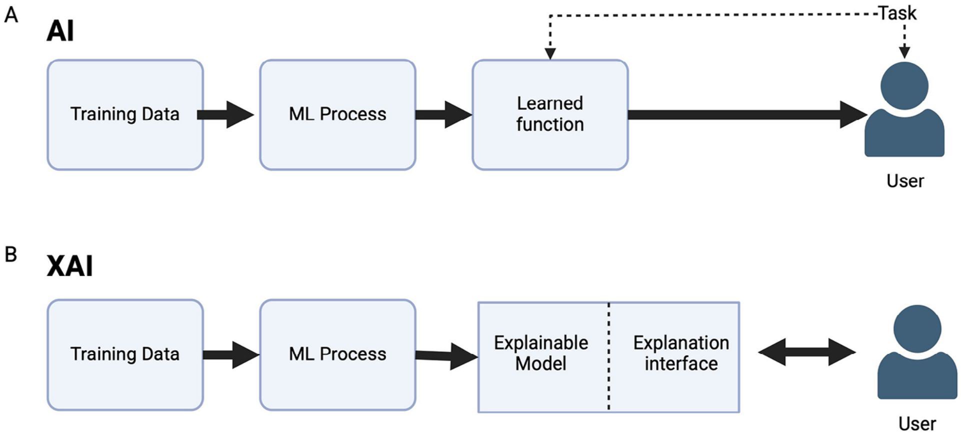

FIGURE 9 | Illustration of explainable AI (XAI) techniques enabling transparency in quality control models by identifying critical features influencing predictions (created using biorender.com).

TABLE 2 | Comparative summary of AI technologies for quality control in stem cell cultures.

AI technology	Key strengths	Limitations	Example applications	Refs.
Machine vision (CNNs)	High-throughput automated analysis, superior accuracy	Dependence on dataset quality, sensitive to imaging conditions	Morphology tracking, proliferation assessment	[29, 35, 61]
Dynamic tracking (time-lapse)	Continuous, precise temporal monitoring	Issues with drift and identity loss over time	Real-time proliferation and motility analysis	[35]
Synthetic data generation (GANs)	Data scarcity solutions, enhance rare-event detection	Potential artifact introduction, validation required	Dataset robustness, apoptosis detection, differentiation status	[34]
Predictive modeling	Proactive, reduces interventions	Overfitting, variability in batch-to- batch data	Confluency prediction, differentiation stage prediction	[64, 36]
Real-time feedback (RL)	Dynamic environment optimization, yields consistency	Computational complexity, sensor drift	Automated environmental condition adjustments	[41, 40]
Multi-omics integration	Comprehensive analysis, improved predictive accuracy	Data complexity, scalability bottlenecks	Genetic stability, pluripotency prediction	[38, 67]
Explainable AI (XAI)	Enhances transparency, supports regulatory compliance	May reduce model complexity or predictive power	Diagnostic feature identification, regulatory approval	[69, 70]

for widespread clinical and industrial adoption [18]. These challenges span technical, ethical, regulatory, and operational domains.

Key technical, ethical, and operational barriers to AI implementation in stem cell manufacturing are summarized in Table 3, highlighting the need for data standardization, scalable infrastructure, and improved clinical integration strategies.

4.1 | Data Heterogeneity and Standardization

Stem cell culture generates heterogeneous datasets—ranging from high-resolution microscopy images to real-time bioreactor sensor outputs to multi-omics profiles. These datasets differ widely in dimensionality, noise levels, and sampling frequencies [71].

Without standardized data preprocessing and integration protocols, AI models risk overfitting to specific datasets, thereby reducing generalizability across laboratories or production sites. This severely limits regulatory acceptance, where models must demonstrate reproducibility under good manufacturing practice (GMP) conditions.

Collaborative initiatives, such as open annotated datasets and harmonized data pipelines, are crucial to overcome this barrier [72].

TABLE 3 | Summary of key challenges in AI integration for stem cell quality monitoring.

Challenge category	Key challenges and implications
Data heterogeneity	Multimodal data (images, omics, sensors) vary in scale, quality, and format, complicating AI training. Poor data harmonization risks model failure and impedes regulatory validation.
Scalability for large systems	Real-time AI processing demands high computational resources. Data overload in bioreactor-scale systems can overwhelm models, leading to missed anomalies or control failures.
Ethical and privacy concerns	Use of patient-derived data introduces GDPR/HIPAA compliance issues. Biases in datasets can propagate into model decisions, raising fairness and liability concerns in clinical applications.
Limited clinical adoption	High costs of implementation, lack of interoperability with legacy systems, and absence of standardized validation frameworks slow down real-world integration.

4.2 | Scalability for Large-Scale Culture Systems

Scaling AI models from benchtop systems to industrial bioreactors presents major operational challenges. The volume and velocity of data—terabytes per day in large facilities—strain both computational infrastructure and model inference speeds.

Real-time feedback systems, if overwhelmed, can miss critical anomalies or fail to adjust environmental parameters in time, leading to batch losses. Edge computing, federated learning, and hierarchical control systems are emerging as solutions, but adoption remains limited [22].

Furthermore, maintaining model robustness during scale-up (e.g., in the face of gradient heterogeneity in large bioreactors) requires extensive retraining and validation [15].

4.3 | Ethical and Privacy Concerns

AI models trained on patient-derived stem cells or disease-specific iPSC lines involve sensitive personal data. Compliance with data protection laws such as GDPR and HIPAA is non-negotiable but technically challenging, especially in cross-border collaborations [73, 74].

Beyond privacy, bias in training datasets—such as overrepresentation of certain demographic groups—can propagate into quality predictions or lineage differentiation assessments, raising concerns about fairness and liability [24].

Moreover, informed consent frameworks often do not yet cover the secondary AI uses of biomedical data. Addressing these gaps will be crucial to build public and regulatory trust [75].

4.4 | Operational and Regulatory Barriers

Despite technological readiness, AI adoption remains limited in clinical and industrial settings. High upfront costs for infrastructure upgrades, lack of trained personnel, and resistance to changing established protocols are major operational hurdles [23]. Regulatory bodies require clear documentation, validation, and explainability for AI-driven decision systems under GMP. Currently, there are no universally accepted validation frameworks for AI in stem cell manufacturing. Lack of standards for model robustness, retraining frequency, and performance under adverse conditions further complicates approval pathways [76]. Bridging this gap requires joint efforts from AI researchers, biomanufacturers, and regulatory agencies to establish clear, pragmatic validation pathways [77].

5 | Future Directions

The integration of AI into stem cell quality monitoring has made remarkable progress but remains at a transitional stage. Addressing current challenges through targeted innovations could unlock the full potential of scalable, reproducible, and personalized regenerative therapies.

This section outlines specific, feasible strategies to drive the next generation of AI-enhanced stem cell manufacturing.

5.1 | Toward Autonomous Biomanufacturing Systems

Building fully autonomous stem cell biomanufacturing systems will require the integration of real-time AI monitoring, adaptive control algorithms, and digital twin technologies. Current AI models rely heavily on labeled datasets, which limits their scalability and adaptability across diverse cultural systems. Self-supervised learning approaches, capable of extracting meaningful representations from unlabeled data, offer a promising solution to reduce annotation bottlenecks and improve model generalizability for monitoring heterogeneous stem cell environments [78]. In parallel, embed- ding reinforcement learning agents into bioreactors could enable continuous optimization of critical parameters such as feeding, oxygenation, and shear stress based on real-time sensor feedback, reducing the need for manual intervention. Digital twins—real-time virtual simulations of stem cell cultures updated continuously with sensor and image data—can be used to predict differentiation trajectories, identify early signs of anomalies, and suggest targeted interventions to maintain optimal culture conditions [81]. Several early prototypes of autonomous systems in hematopoietic stem cell culture have already demonstrated feasibility [41]; however, scaling these frameworks to support pluripotent stem cells and lineage-specific differentiation remains a critical next step.

5.2 | Federated Learning for Multisite Model Training

Data privacy and variability across institutions remain major barriers to AI model generalization. Federated learning frameworks offer a promising solution by enabling decentralized model training across multiple laboratories without the need to share raw data, thereby preserving privacy while still leveraging diverse datasets [79]. To ensure the effectiveness of these frameworks, it is essential to harmonize data collection and preprocessing protocols across participating institutions, which will help improve model convergence and robustness. Pilot federated learning networks for biomedical imaging have already demonstrated the technical feasibility of this approach [82], and extending these frameworks to stem cell culture data represents a natural and necessary progression.

5.3 | Explainable AI for Regulatory Approval and Trust

For clinical and GMP-grade stem cell manufacturing, AI models must offer transparent and interpretable decision-making processes. Techniques such as attention mechanisms and feature attribution enable models to highlight which morphological or molecular features influence quality assessments, facilitating human validation and easing the path toward regulatory review [69]. In addition, the development of standardized validation pipelines—including consistency checks across production batches, robustness testing against adversarial inputs, and correlation with clinical outcomes—will be crucial for gaining regulatory acceptance. Explainable AI will not only enhance trust among biologists and clinicians but also streamline compliance with regulatory standards.

5.4 | Ethical AI Governance Frameworks

As AI-driven stem cell manufacturing moves closer to clinical application, ethical oversight must evolve in parallel. One key area is the evolution of informed consent processes, which should explicitly account for the secondary use of data in AI model development and quality monitoring, thereby anticipating future regulatory requirements [75]. Furthermore, regular audits for demographic and procedural biases in training datasets must become a routine part of AI model quality control to ensure fairness and reliability. Global initiatives, such as the WHO's guidance on ethics and governance of AI in health, offer a foundational framework upon which more specific, domain-tailored governance models can be built [83].

5.5 | Expansion to Organoid and Tissue Engineering Systems

AI-driven quality monitoring tools initially developed for stem cell cultures are also highly applicable to complex three-dimensional systems, including organoids and engineered tissues. Temporal AI models capable of predicting morphogenesis trajectories could allow for earlier detection of off-target developments, improving the reliability of organoid production. Moreover, integrating multimodal data sources—such as imaging, transcriptomics, and metabolomics—can produce dynamic, high-resolution fingerprints of organoid quality [80]. Scaling and refining these approaches will significantly accelerate advancements in disease modeling, high-throughput drug screening, and personalized tissue therapies.

6 | Conclusion

The application of AI in stem cell quality monitoring is transforming the landscape of regenerative medicine—from static, labor-intensive assessments to dynamic, predictive, and scalable systems. However, meaningful progress requires more than technological capability: it demands critical integration, validation, and a clear roadmap for implementation.

This review provides a structured analytical framework that links CQAs in stem cell cultures to AI-driven monitoring and control strategies. We critically evaluated key technologies—such as CNNs, generative models, predictive analytics, and explainable AI—and presented comparative benchmarks to demonstrate their practical impact. Through case studies and quantitative insights, we highlighted how AI enables early anomaly detection, improves lineage fidelity, and reduces batch variability.

At the same time, we identified core barriers—including data heterogeneity, ethical constraints, and regulatory uncertainty—that currently limit widespread adoption. We proposed actionable future directions including federated learning, digital twins, self-supervised models, and standardized validation protocols that can bridge the gap between innovation and clinical translation.

By advancing from descriptive summaries to a comparative, implementation-oriented perspective, this review aims to guide researchers, engineers, and regulators toward building autonomous, ethical, and robust stem cell manufacturing pipelines. Addressing the outlined challenges will not only improve process quality but also accelerate the broader adoption of AI-enhanced regenerative therapies worldwide.

Author Contributions

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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