AI-powered Human-on-Chip: Redefining Biomedical Frontiers

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AI-powered Human-on-Chip: Redefining Biomedical Frontiers

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Abstract: Human-on-chip technology heralds a transformative paradigm in biomedical frontiers, furnishing diminutive replicas of human organs and tissues on microscale substrates. These platforms offer an unprecedented avenue for scrutinizing human physiology, diseases, and pharmacological responses with heightened precision, efficiency, and ethical consideration vis-à-vis conventional methodologies, contributing to the achievement of the Sustainable Development Goal (SDG) related to good health and well-being (SDG-03). This perspective explores the integration of human-on-chip technology with artificial intelligence (AI) to enhance the efficacy of these systems. AI algorithms assume a pivotal function in deciphering intricate datasets emanating from human-on-chip experiments, prognosticating outcomes, fine-tuning experimental parameters, and even orchestrating chip operations. This investigation illuminates the contemporary state-of-the-art human-on-chip technology, the critical role of AI in propelling this domain forward, and the prospective synergy between these innovations in the biomedical frontiers, thereby contributing to the advancement of health-related sustainable development goals.

Keywords: Human-on-Chip; Artificial intelligence; Biomedical frontiers; Sustainable development goals

1 Introduction

The field of biomedical research has witnessed remarkable advancements in recent years, fueled by innovations at the intersection of engineering, biology, and computer science. One such groundbreaking technology is human-on-chip, which offers a transformative approach to studying human physiology, diseases, and drug responses in vitro [1]. Human-on-chip platforms, also known as organ-on-chip systems, utilize microscale models of human organs and tissues to replicate their structure and function in a controlled laboratory environment. These miniature systems provide researchers with a powerful tool to investigate complex biological processes with unprecedented precision and relevance [2]. Conventional methods for studying human biology and disease often rely on animal models, cell cultures, and clinical trials. While these approaches have contributed significantly to our understanding of human physiology and pathology, they also present inherent limitations, including interspecies differences, ethical concerns, and high costs [3]. These limitations indicate that the traditional method is a high-energy, low-precision research approach, which is certainly contrary to the urgent pursuit of sustainable development goals globally. Human-on-chip technology addresses these challenges by providing a more physiologically relevant and scalable alternative that advances the health-related SDGs.

The U.S. Food and Drug Administration (FDA), National Institute of Health (NIH), and Defense Advanced Research Project Agency (DARPA) have responded to the demand for human-on-chip by providing funding and regulatory guidance [4, 5]. In Europe, the DMT consortium has teamed up with several companies, institutions, and foundations to develop a versatile "SMART Organ-on-Chip" with the help of a grant. The Asia-Pacific region, particularly China, is experiencing rapid growth in this field due to government funding and an increase in cell-based clinical trials. Startups, particularly in academic settings, are actively contributing to the advancement of human-on-chip technology. Such as, Emulate, based at Harvard's Wyss Institute, collaborates with major pharmaceutical companies to improve drug testing accuracy. Other startups like InSphero, AxoSim, TaraBiosystems, Nortis Bio, and TissUse are focused on various aspects of human-on-chip development. TissUse, for example, has recently developed a chip integrating four organs and aims to expand to ten. Successful implementation of human-on-chip relies on collaborative efforts among stakeholders to integrate this technology into existing methodologies effectively. However, most of the current biochips (including multi-organ human chips and single-organ chips) are still difficult to deploy for clinical applications. A key problem is that the human chip provides the hardware basis for conducting large-scale multivariable experiments with ultra-high throughput, but the software methods for designing experimental conditions, data processing, and result analysis for such complex multivariable experiments are not yet complete. Researchers are in urgent need of consistently efficient auxiliary means to truly unlock the working potential of the human chip.

The integration of AI with human-on-chip technology represents a paradigm shift in biomedical frontiers. AI algorithms, including machine learning and deep learning techniques, have the potential to revolutionize the way we analyze data, predict outcomes, and optimize experimental conditions in human-on-chip systems [6]. By harnessing the power of AI, researchers can extract meaningful insights from complex biological datasets, accelerate the pace of discovery, and ultimately improve human health aligning with SDG-03. There is no doubt that AI will effectively promote the efficiency of the current body chip, so that it is truly from a laboratory technology to medical field.

This perspective aims to explore the synergistic integration of human-on-chip technology and AI in biomedical frontiers, aligning with the goal of promoting good health and well-being as charted in the Sustainable Development Goals (SDG-03). We will discuss the principles and applications of human-on-chip system, the role of AI in advancing this field, and the future prospects for these transformative technologies. Through a comprehensive review of the current state-of-the-art and emerging trends, we seek to provide insights into the potential impact of AI-powered human-on-chip platforms on biomedical research. In the following sections, we will investigate into the principles of human-on-chip technology, the applications of AI in biomedical frontiers, the integration of AI with human-on-chip system, and the future directions and challenges of this exciting field. By examining the convergence of these two cutting-edge technologies, we expect to create a low-power, high precision sustainable research model of human physiology, disease, and drug responses, and inspire further innovation and collaboration in the pursuit of improving human health and well-being, thereby contributing to the advancement of SDG-03.

2 Human-on-chip technology

Human-on-chip technology signifies a revolutionary rise in biomedical frontiers, offering a transformative approach to modeling human physiology and diseases in vitro. These innovative platforms comprise microscale devices meticulously designed to replicate the intricate structure and dynamic functionality of human organs and tissues [7]. By harnessing the capabilities of human-on-chip systems, researchers can investigate into biological processes with unparalleled precision and relevance, opening new avenues for understanding disease mechanisms and drug responses [8]. The evolution of human-on-chip systems has been pushed by significant advancements in microfabrication techniques, biomaterials, and tissue engineering methodologies. These advancements have facilitated the development of sophisticated, multicellular models capable of faithfully recapitulating crucial aspects of organ function and intercellular interactions. By providing physiologically relevant platforms for studying human biology, human-on-chip devices offer a more ethical and efficient alternative to traditional animal models and two-dimensional cell cultures [9]. These systems enable researchers to simulate complex disease states, test the efficacy of potential therapeutics, and explore personalized treatment strategies tailored to individual patients' unique physiological profiles. In this context, human-on-chip technology represents a powerful tool for accelerating the pace of scientific discovery, improving healthcare outcomes, and advancing the field of medicine.

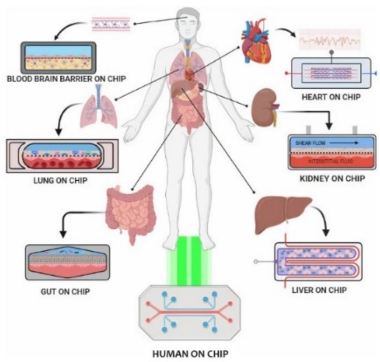

Figure 1 Schematic of Human-on-Chip Technology

2.1 Principles of human-on-chip platforms

Human-on-chip technology represents a groundbreaking approach to modeling human physiology and diseases in vitro. At the core of these innovative platforms are microfluidic channels that intricately regulate the flow of nutrients, drugs, and signaling molecules. These channels enable researchers to recreate dynamic physiological conditions within the microscale environment of the chip, mimicking essential aspects of in vivo biology such as blood flow patterns, shear stress, and nutrient gradients [10, 11]. By precisely controlling these parameters, human-on-chip devices provide a more accurate representation of the cellular microenvironment compared to traditional static cell culture methods, thus ensuring the viability and functionality of cells over extended periods.

Human-on-chip devices are meticulously designed to replicate the architecture and microenvironment of human organs and tissues, a concept known as biomimetic design. This approach involves engineering scaffolds, extracellular matrices, and cellular interfaces to closely resemble the native tissue structure [1, 12]. By emulating the intricate organization and composition of human tissues, biomimetic human-on-chip platforms create a conducive environment for cells to organize, differentiate, and function as they would in vivo. This not only enhances the physiological relevance of in vitro models but also allows researchers to study complex biological processes and disease mechanisms with greater fidelity [13].

One of the key features of human-on-chip systems is the integration of multiple cell types relevant to the modeled organ or tissue. These cell types may include parenchymal cells responsible for the primary function of the organ, as well as supporting cell types such as stromal cells, immune cells, and endothelial cells [5]. By incorporating diverse cell populations, human-on-chip platforms enable the recreation of multicellular interactions that are characteristic of the in vivo microenvironment. This integration is essential for capturing the complexity of biological systems and accurately modeling physiological responses to stimuli such as drugs, pathogens, or environmental cues.

The combination of microfluidics, biomimetic design, and integration of multiple cell types distinguishes human-on-chip technology as a powerful tool for biomedical research. By faithfully recapitulating the complexity of human biology in vitro, these platforms hold great promise for advancing our understanding of disease mechanisms, accelerating drug discovery and development, and ultimately improving patient outcomes in healthcare [4].

2.2 Examples of organ-on-chip models

Liver-on-chip models represent sophisticated platforms designed to mimic the complex structure and functions of the human liver within a controlled laboratory setting [14, 15]. These models accurately replicate key hepatic processes such as drug metabolism, detoxification, and bile production, providing researchers with a powerful tool to study liver physiology and pathophysiology. Liver-on-chip systems have been instrumental in advancing our understanding of liver diseases, including hepatitis, fibrosis, and drug-induced liver injury [16]. By recapitulating disease-relevant features and cellular interactions, these models enable the investigation of disease mechanisms and the identification of potential therapeutic targets. Liver-on-chip platforms play a crucial role in drug development by providing a predictive preclinical model for assessing the efficacy and toxicity of pharmaceutical compounds, ultimately contributing to the development of safer and more effective therapeutics [17].

Lung-on-chip devices offer a physiologically relevant platform for studying respiratory diseases and drug responses in vitro. These models recreate the alveolar-capillary interface of the human lung, allowing researchers to investigate lung inflammation, fibrosis, drug response, and respiratory or infectious diseases such as pneumonia [18, 19]. Lung-on-chip platforms have been particularly valuable for studying chronic respiratory conditions like asthma and chronic obstructive pulmonary disease (COPD), as well as lung cancer. These systems enable the assessment of drug efficacy and toxicity in a lung-specific context, providing insights into the effectiveness of inhalation therapies and potential adverse effects.

Heart-on-chip models simulate the contractile function and electrical signaling of human cardiac tissue, offering unique insights into cardiovascular diseases and drug cardiotoxicity. These platforms allow researchers to study arrhythmias, myocardial infarction, and heart failure in a controlled environment, facilitating the development of novel therapeutic strategies [20, 21]. By incorporating patient-specific cells and disease-relevant parameters, heart-on-chip models provide personalized insights into cardiac physiology and pathology, paving the way for precision medicine approaches in cardiology. These systems serve as valuable tools for evaluating the efficacy of cardiac therapies and modeling congenital heart defects, ultimately contributing to improved patient care and outcomes in cardiovascular medicine.

2.3 Applications of human-on-chip technology

Human-on-chip platforms represent a transformative paradigm in disease modeling, offering researchers unprecedented opportunities to mimic and study human diseases in vitro. By recapitulating key aspects of human physiology and organ function within microscale environments, these platforms provide a more accurate representation of disease mechanisms compared to traditional cell culture methods or animal models. Researchers can leverage human-on-chip technology to explore the underlying molecular and cellular processes driving diseases such as cancer, neurodegenerative disorders, and cardiovascular diseases [1, 20]. This deeper understanding of disease pathogenesis can lead to the identification of novel therapeutic targets and the development of more effective treatment strategies.

Human-on-chip systems have emerged as powerful tools for drug screening and toxicity testing, addressing critical challenges faced by the pharmaceutical industry. Traditional drug development pipelines often rely on animal models or simplified cell culture systems to predict drug responses in humans, leading to high failure rates and significant costs. Human-on-chip platforms offer a more predictive and cost-effective alternative by recreating the complex interactions between drugs and human tissues [22]. Researchers can use these platforms to evaluate drug efficacy, assess pharmacokinetics, and predict potential adverse effects with greater accuracy, ultimately accelerating the drug development process and reducing reliance on animal testing.

Human-on-chip technology has the potential to revolutionize personalized medicine by enabling researchers to tailor treatments to individual patients. By incorporating patient-specific cells derived from induced pluripotent stem cells (iPSCs) or primary tissues, human-on-chip platforms can model the genetic and phenotypic diversity observed in human populations [1, 23]. Researchers can use these patient-specific models to predict individual responses to drugs, identify optimal treatment regimens, and develop personalized therapeutic strategies. This approach holds promise for improving patient outcomes, reducing adverse drug reactions, and optimizing healthcare delivery.

2.4 Advantages and limitations

Human-on-chip technology represents a transformative advancement in biomedical frontiers, offering a multitude of advantages over traditional methods. One of the key advantages is the increased physiological relevance provided by these platforms. By closely mimicking the microenvironment and cellular interactions found in human organs, human-on-chip systems offer a more accurate representation of in vivo physiology compared to traditional cell culture techniques [1, 13, 24]. This enhanced physiological relevance enables researchers to study complex biological processes, such as cell-cell interactions, tissue morphogenesis, and disease progression, in a controlled laboratory setting.

Human-on-chip platforms offer higher throughput capabilities, allowing researchers to conduct multiple experiments simultaneously and rapidly screen large numbers of compounds or conditions. This increased throughput accelerates the pace of biomedical frontiers, enabling researchers to explore a broader range of hypotheses and identify promising leads more efficiently. The reduced costs associated with human-on-chip technology make it a cost-effective alternative to traditional animal models and clinical trials, ultimately leading to more economical drug development.

Another significant advantage of human-on-chip technology is the decreased reliance on animal models. Animal studies are often costly, time-consuming, and ethically challenging, and may not always accurately predict human responses to drugs and diseases [25, 26]. Human-on-chip platforms offer a more ethical and human-relevant approach to preclinical research, reducing the need for animal testing while providing more predictive and translatable results.

Despite these advantages, human-on-chip technology also faces several limitations that need to be addressed for its widespread adoption and application. Scalability remains a challenge, as current human-on-chip systems are often limited in their capacity to model complex multicellular interactions or entire organ systems. Standardization and validation of models are also critical for ensuring reproducibility and reliability [1, 27]. Recreating the full complexity of human organ function in vitro presents significant technical challenges, requiring further advancements in tissue engineering, cell culture techniques, and biomaterials.

Firstly, there is a lack of standardized evaluation criteria for human chip performance. The variability in experimental outcomes across different human chip models makes it challenging for researchers to ascertain which results most accurately represent human physiological conditions. Establishing a standardized human chip model remains a critical issue in this field. Secondly, current human chips often overlook aspects of biomimicry and system robustness. To enhance biomimicry, these chips must replicate the microenvironment of various organs, necessitating advanced micro-nano processing, multicellular co-culture, and tissue engineering technologies. This also requires precise control over factors such as temperature, oxygen levels, and nutrient composition, which complicates the system and undermines its robustness, posing challenges for large-scale application. The need for accurate replication of the human body's microenvironment is crucial for the chips to provide meaningful and reliable data. However, achieving this replication involves significant technological challenges and resources, which can hinder widespread adoption and practical utility.

Lastly, while human chips offer high-throughput experimental capabilities, they lack comprehensive data processing solutions. Although these chips have the potential to achieve results comparable to those obtained from thousands of animal experiments or traditional two-dimensional culture methods using minimal resources, data collection and processing still depend heavily on manual efforts. This reliance significantly limits experimental throughput, preventing the full utilization of the high-throughput advantage of human chips. The manual nature of data handling introduces a bottleneck, reducing the efficiency and speed of research processes. Consequently, the anticipated benefits of human-on-a-chip technology, such as rapid and large-scale screening of drug candidates or toxicity testing, are not fully realized.

3 AI in biomedical research

In recent years, AI has risen to prominence as a formidable asset in biomedical research, presenting novel approaches to analyzing complex biological data, forecasting outcomes, and refining experimental conditions. AI, in its broad spectrum, encompasses diverse techniques such as machine learning, deep learning, and natural language processing, each lending its expertise to various domains of biomedical investigation [28, 29]. From scrutinizing medical images and deciphering genomic sequences to uncovering potential drug candidates and guiding clinical decisions, AI offers unparalleled opportunities for advancement across the biomedical landscape. With its ability to discern patterns, extrapolate insights, and streamline processes, AI stands poised to revolutionize the field of biomedical research, accelerating the pace of discovery and opening doors to innovative avenues of exploration.

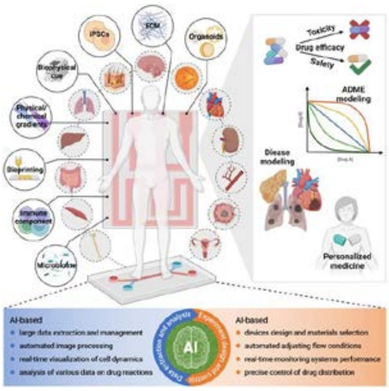

Figure 2 Schematic of Organ-on-a-Chip Meets AI in Drug Evaluation [30].

3.1 Overview of AI techniques

Machine learning algorithms, including supervised learning, unsupervised learning, and reinforcement learning, play a crucial role in enhancing the capabilities of human-on-chip technology [6, 31]. These algorithms enable computers to analyze complex datasets generated from human-on-chip experiments, identify patterns, and make predictions about drug responses, disease mechanisms, and physiological processes. Supervised learning algorithms, for example, can be trained on labeled datasets to recognize patterns indicative of specific disease states or drug effects. Unsupervised learning algorithms can uncover hidden patterns or structures in unlabeled data, providing insights into complex biological interactions. Reinforcement learning algorithms can optimize experimental designs and conditions through trial and error, maximizing the efficiency and effectiveness of human-on-chip experiments.

Deep learning, a subset of machine learning, further enhances the capabilities of human-on-chip technology by leveraging neural networks with multiple layers to learn representations of complex biological data [1, 31, 32]. Deep learning algorithms, such as convolutional neural networks (CNNs), recurrent neural networks (RNNs), and generative adversarial networks (GANs), have demonstrated remarkable success in various biomedical applications relevant to human-on-chip technology [33]. CNNs are commonly used for analyzing medical images generated from human-on-chip experiments, facilitating the detection of subtle changes indicative of disease states or drug effects. RNNs are employed for sequential data analysis, enabling researchers to model dynamic physiological processes and temporal dependencies. GANs can generate synthetic data to augment existing datasets, enhancing the diversity and representativeness of training data for machine learning models.

Natural language processing techniques enable computers to extract and analyze information from text-based sources relevant to human-on-chip technology, such as scientific literature and electronic health records. NLP algorithms can facilitate literature mining, information retrieval, and clinical decision support, enabling researchers and clinicians to access relevant information and insights from vast amounts of textual data [33, 34]. By leveraging NLP, researchers can stay abreast of the latest developments in human-on-chip technology, identify relevant research articles, and extract key findings to inform their own experiments and analyses. NLP can aid in the integration of textual data with experimental data generated from human-on-chip experiments, facilitating interdisciplinary research and knowledge discovery.

3.2 Applications of AI in healthcare

AI algorithms, particularly deep learning models, are increasingly utilized to analyze medical images in diagnostic settings, such as X-rays, MRIs, and CT scans [35, 36]. These AI-powered image analysis techniques enhance the capabilities of human-on-chip technology by providing advanced tools for visualizing and interpreting experimental results. For example, convolutional neural networks (CNNs) trained on large datasets can detect abnormalities and classify diseases with high accuracy, assisting researchers in identifying phenotypic changes and assessing drug effects in human-on-chip experiments. By leveraging AI-powered medical imaging analysis, researchers can improve diagnostic accuracy, reduce interpretation time, and enhance the overall utility of human-on-chip platforms in disease modeling and drug discovery.

AI techniques are increasingly applied to genomic data analysis, offering valuable insights into the genetic basis of diseases and personalized treatment strategies [37, 38]. These AI-powered approaches complement human-on-chip technology by providing a deeper understanding of the molecular mechanisms underlying disease pathogenesis and drug responses. Machine learning algorithms can analyze large-scale genomic datasets to identify genetic variants associated with diseases, predict disease risk, and stratify patient populations based on their genetic profiles. By integrating genomic data with experimental data from human-on-chip platforms, researchers can enhance the predictive power of disease models, identify biomarkers for patient stratification, and optimize personalized treatment.

AI-powered drug discovery platforms are revolutionizing the drug development process by accelerating the identification of novel drug candidates, predicting drug-target interactions, and optimizing drug design [39, 40]. These AI-powered approaches complement human-on-chip technology by providing computational tools for predicting drug responses and toxicity in silico. Machine learning models trained on chemical and biological data can expedite virtual screening, lead optimization, and toxicity prediction, enabling researchers to prioritize promising drug candidates for further validation on human-on-chip platforms. By integrating AI-powered drug discovery approaches with experimental data from human-on-chip experiments, researchers can streamline the drug development pipeline, reduce development costs, and address unmet medical needs more effectively.

4 Integration of AI with human-on-chip

Artificial intelligence (AI) can significantly enhance the capabilities of human-on-chip technology by addressing some of the challenges and limitations associated with these platforms. One way AI can contribute is by optimizing experimental design and data analysis processes. AI algorithms can analyze large datasets generated from human-on-chip experiments to identify patterns, correlations, and trends that may not be apparent to human researchers. By mining complex biological data, AI can enable researchers to uncover novel insights into disease mechanisms, drug responses, and physiological processes, ultimately enhancing the predictive power of human-on-chip models.

AI algorithms can aid in the standardization and validation of human-on-chip models by analyzing data from multiple experiments and platforms to identify common features and benchmarks [41]. This can help establish standardized protocols and quality control measures, ensuring reproducibility and reliability across different research groups and platforms. AI-powered predictive modeling can assist in overcoming scalability challenges by predicting how changes in experimental parameters or conditions may impact the outcomes of human-on-chip experiments, enabling researchers to optimize experimental designs for efficiency and effectiveness.

AI can contribute to the development of more sophisticated human-on-chip models by integrating data from diverse sources, such as omics data, clinical data, and environmental data. AI-powered integration of multidimensional data can provide a more comprehensive understanding of human physiology and disease processes, enabling researchers to design more physiologically relevant human-on-chip models that better mimic the complexity of human organs and tissues.

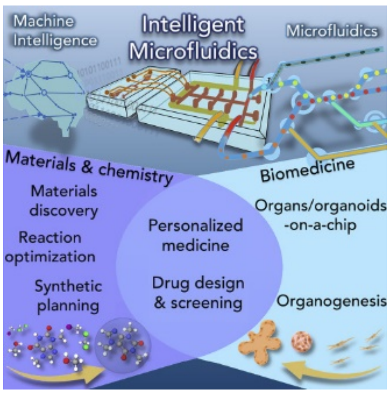

Figure 3 Applications of Intelligent Microfluidics in Materials Science and Biomedicine [42].

Human-on-chip systems, comprising microscale devices that mimic the structure and function of human organs and tissues, have already revolutionized the study of biological processes. However, the fusion of AI algorithms with human-on-chip platforms may further enhance their capabilities by harnessing the power of data analysis, prediction, optimization, and real-time control [43, 44]. AI algorithms serve as the backbone of this integration, playing a pivotal role in extracting valuable insights from the complex data generated by human-on-chip experiments. These algorithms leverage machine learning, deep learning, and other AI techniques to discern patterns, correlations, and trends within large datasets, providing researchers with a deeper understanding of biological processes and disease mechanisms. By analyzing multi-dimensional data streams in real-time, AI enables researchers to make more informed decisions and derive actionable insights from human-on-chip experiments.

The integration of AI with human-on-chip technology represents a paradigm shift in biomedical frontiers, offering researchers unprecedented insights into human biology and disease mechanisms. By leveraging AI algorithms to analyze complex data, predict outcomes, optimize experimental conditions, and control microscale devices in real-time, researchers can accelerate the pace of discovery, develop more effective therapeutics, and ultimately improve human health. This synergistic approach holds immense promise for advancing personalized medicine, drug development, and precision therapeutics, ushering in a new era of innovation and progress in biomedical frontiers and healthcare.

4.1 Role of AI in data analysis and interpretation

AI algorithms play a pivotal role in analyzing large datasets generated from human-on-chip experiments, complementing the capabilities of these platforms in disease modeling and drug discovery. By leveraging advanced data mining and pattern recognition techniques, AI enables researchers to uncover hidden patterns, correlations, and trends within complex biological data. This enhances our understanding of disease mechanisms, drug responses, and physiological processes, facilitating the identification of novel insights and therapeutic targets relevant to human health.

Human-on-chip experiments often yield high-dimensional datasets containing diverse biological measurements, such as gene expression profiles, metabolite concentrations, and cellular responses [32, 45]. AI techniques, such as principal component analysis (PCA) and t-distributed stochastic neighbor embedding (t-SNE), are instrumental in extracting relevant features and reducing the dimensionality of data [46, 47]. This enables researchers to visualize and analyze complex datasets more effectively, uncovering underlying patterns and relationships that may inform subsequent analyses and experimental design.

AI algorithms, including machine learning and deep learning models, empower researchers to build predictive models using human-on-chip data, facilitating drug discovery and personalized medicine initiatives. By training AI models on experimental data, researchers can predict outcomes such as drug efficacy, toxicity, or disease progression, aiding in the identification of biomarkers and predictive signatures [48, 49]. This enables researchers to stratify patient populations, personalize treatment regimens, and develop targeted therapies tailored to individual patients' needs, ultimately advancing precision medicine and improving patient outcomes.

4.2 Optimization of experimental conditions

AI algorithms play a crucial role in assisting researchers with the design of human-on-chip experiments, optimizing experimental parameters to enhance the efficiency and effectiveness of biomedical research. By leveraging optimization algorithms, AI helps researchers navigate the complex experimental space of human-on-chip technology, considering factors such as cell culture conditions, media compositions, and drug concentrations [1, 50]. This enables researchers to systematically explore different experimental conditions, identify key variables influencing outcomes, and design experiments that maximize the generation of meaningful data.

AI-powered human-on-chip systems can incorporate adaptive control mechanisms and feedback loops to dynamically adjust experimental conditions based on real-time data and observations. By continuously monitoring cellular responses, physiological parameters, and environmental cues, AI algorithms can regulate fluid flow rates, nutrient delivery, and drug administration within human-on-chip devices to maintain homeostasis and mimic physiological conditions more accurately [9]. This adaptive control capability enables researchers to create more dynamic and responsive experimental platforms, improving the fidelity and reliability of human-on-chip experiments for disease modeling, drug screening, and personalized medicine applications.

4.3 Control and automation of human-on-chip

AI algorithms are instrumental in implementing closed-loop control systems within human-on-chip devices, enhancing their functionality and utility in biomedical research. By integrating sensors and detectors to provide real-time feedback, AI algorithms can adjust system parameters, such as flow rates, pressures, and temperature, to maintain optimal experimental conditions [51, 52]. This closed-loop control enables precise manipulation of experimental variables, ensuring the viability and functionality of cells within human-on-chip platforms. By maintaining physiological conditions and responding dynamically to changes, closed-loop control systems improve the accuracy and reproducibility of experimental results, enhancing the reliability of human-on-chip technology for disease modeling and drug screening applications.

AI-powered human-on-chip platforms have the potential to revolutionize biomedical research by enabling autonomous experimentation, where AI algorithms oversee the entire experimental process from start to finish. Building on closed-loop control capabilities, autonomous systems can autonomously design experiments, execute protocols, monitor responses, and analyze data, without the need for direct human intervention. This autonomous experimentation paradigm holds promise for accelerating the pace of discovery, reducing experimental variability, and enabling continuous experimentation, ultimately advancing our understanding of human physiology, diseases, and drug responses [1, 53]. By leveraging AI-powered autonomy, human-on-chip platforms can unlock new opportunities for innovation and discovery in biomedical research, paving the way for transformative advancements in healthcare.

5 Future directions and challenges

The integration of AI with human-on-chip promises to revolutionize biomedical frontiers. AI, including deep learning networks and automated machine learning, has propelled the development of generative AI, which can cater to the specific needs of human-on-chip and accelerate their progress. For example, AI addresses challenges in human-on-chip hardware development, such as the issue of drug absorption in polydimethylsiloxane (PDMS) materials commonly used in microfluidic devices. AI suggests alternatives like inorganic or elastomeric materials and coatings to mitigate this issue, while also streamlining fabrication processes through technologies like 3D bioprinting [54, 55]. AI augments the physiological relevance of human-on-chip by facilitating the integration of multiple cell types, metabolites, and gradients, as well as by optimizing culture conditions and media compositions. AI enhances the throughput of human-on-chip platforms, enabling their application at various stages of drug discovery, and aids in data processing, making analysis and interpretation more efficient. Despite these advancements, challenges like interpretability, repeatability, and industrial adoption remain, necessitating continued collaboration and innovation to realize the full potential of AI-powered human-on-chip in biomedical frontiers.

5.1 Opportunities for further integration

Future advancements in human-on-chip technology may involve the development of multi-organ systems interconnected through microfluidic channels, replicating the complexities of human physiology and enabling the study of organ-organ interactions [23]. AI algorithms can play a crucial role in facilitating the integration of data from diverse organ models within these platforms, enabling comprehensive analysis and prediction of complex physiological responses [56]. By leveraging AI-powered data integration and analysis techniques, researchers can gain insights into the systemic effects of drugs and diseases, advancing our understanding of human biology and improving the predictiveness of preclinical models.

AI-powered human-on-chip systems have the potential to revolutionize personalized medicine by incorporating patient-specific data, such as genetic information, cellular phenotypes, and clinical profiles [57]. By modeling individual variability and disease heterogeneity, researchers can tailor treatment strategies to specific patient populations, optimizing therapeutic outcomes and minimizing adverse effects. AI algorithms can enable the integration of diverse data sources and the development of predictive models that account for patient-specific factors, paving the way for more precise and effective healthcare interventions.

AI-powered human-on-chip platforms have the capacity to streamline drug discovery pipelines by enabling high-throughput screening of compound libraries and rapid evaluation of drug candidates. By automating experimental protocols and data analysis workflows, AI-powered platforms accelerate the pace of discovery and identify novel therapeutic targets more efficiently [58, 59]. AI algorithms can enhance the scalability and efficiency of high-throughput screening assays, enabling researchers to screen large numbers of compounds and prioritize candidates for further validation, ultimately expediting the drug development process and bringing new therapies to market more quickly.

AI algorithms enable real-time monitoring and adaptive control of human-on-chip systems, enhancing experimental reproducibility and the relevance of in vitro models. By integrating sensors and detectors to provide real-time feedback, AI-powered control systems can dynamically adjust experimental conditions, such as fluid flow rates and nutrient concentrations, to maintain physiological homeostasis and mimic in vivo conditions more accurately [60, 61]. This closed-loop control mechanism improves experimental reliability, enhances the reproducibility of results, and enhances the utility of human-on-chip technology for disease modeling, drug screening, and personalized medicine applications.

5.2 Challenges and future considerations

Maintaining high data quality and ensuring standardization of experimental protocols are critical aspects of AI-powered human-on-chip research. Standardized protocols, data formats, and quality control measures facilitate data sharing, comparison, and validation across different research groups and platforms. By establishing standardized practices, researchers can enhance the reproducibility and reliability of experimental results, enabling more robust scientific discoveries and accelerating progress in biomedical frontiers.

The integration of AI with human-on-chip technology necessitates the development of robust ethical and regulatory frameworks to address privacy concerns, informed consent, and responsible use of AI algorithms [31]. Collaboration between healthcare organizations, regulatory agencies, and policymakers is essential for establishing guidelines that ensure transparency, accountability, and ethical conduct in AI-powered biomedical frontiers. By upholding ethical principles and respecting patient rights, stakeholders can promote trust and confidence in AI-enabled technologies and foster responsible innovation in healthcare [62].

Promoting accessibility and equity in AI-powered human-on-chip technologies is essential for fostering scientific innovation and improving healthcare outcomes worldwide. Efforts to democratize access to AI and IoT tools, resources, and expertise, particularly in resource-limited settings, can empower researchers to collaborate and share knowledge, accelerating progress towards common sustainable development goals [63, 64]. By promoting inclusivity and diversity in research initiatives, stakeholders can harness the full potential of AI-powered technologies to address global health challenges and reduce disparities in healthcare delivery.

6 Conclusion

The integration of AI with human-on-chip technology signifies a remarkable achievement in biomedical frontiers, heralding a new era of exploration into human physiology, diseases, and drug responses. At its core, human-on-chip technology aims to replicate the complex interactions and dynamics of human physiology within miniature, controlled environments. These microscale devices offer a unique opportunity to study biological phenomena with unprecedented precision and relevance. By integrating various cell types, extracellular matrices, and physiological cues, human-on-chip platforms strive to recreate the structural and functional complexity of human organs and tissues, providing researchers with a powerful tool for unraveling the mysteries of human biology. By incorporating AI algorithms into these platforms, researchers can harness the power of data analysis, experimental optimization, and system control to enhance the accuracy, efficiency, and ethical integrity of in vitro investigations into biological processes. The convergence can ensure the accuracy of the experiment and greatly reduce the unnecessary loss in the process of scientific research, which is undoubtedly helpful to promote the realization of the sustainable development of experimental mode in the biomedical frontiers and contributing to the achievement of health-related sustainable development.

Declaration of Competing Interest: *The authors declare no competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.*

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