

Integrative Approaches of Artificial Intelligence and Multi-Omics in Cancer

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Abstract: AI-based multi-omics research has brought lots of outcomes and improvements in biological science, especially in cancer research and clinics. However, these cutting-edge techniques are inevitably facing lots of challenges. To clearly illustrate the advances and challenges in this interdisciplinary field, an updated overview of AI and multi-omics applications in cancer studies and an exploration of current paradigms of AI & omics in cancer research are lacking. Here we explore this question in three different aspects: application field, algorithms, and application paradigms of AI and multi-omics for cancer. This research brings out a high-resolution, well-structured landscape of AI and omics for cancer by summarizing reviews and recent related papers, and finally indicates the future direction of AI-powered multi-omics cancer study and research gaps that need to be explored.

Keywords: Artificial intelligence, multi-omics, cancer research, machine oncology, machine learning

1. Introduction

Artificial intelligence (AI) and multi-omics techniques are two fields with great potential that are in rapid development. AI is being increasingly integrated into scientific discovery, helping researchers gain scientific insights [1]. Multi-omics, as part of bioinformatics, on the other hand, is poised to revolutionize the future of healthcare [2]. AI combined with multi-omics creates tremendous research value and application value, especially in cancer, an important aspect of health care. Various breakthroughs were accomplished using AI and omics techniques. For example, in cancer drug discovery, unlike traditional drug discovery methods, AI and multi-omics techniques can efficiently create new, cost-effective cancer therapies by harnessing computing power [3]; AI-based omics data empowered the biomarker discovery of cancer; for example, precision immunoncology, such as immune checkpoint inhibitors (ICIs) selection from high-dimension data (including genomics, radionics, pathology, and real-world and multimodality data), exhibits a tendency of meta-biomarker discovery using AI-based multimodal and multi-omics data [4]; by combining images (including mammography (DM), digital breast tomosynthesis (DBT), magnetic resonance imaging (MRI), ultrasound (US), and nuclear medicine techniques) and omics data, AI algorithms can increase breast cancer diagnosis accuracy, classification accuracy, and prognosis

prediction, such as metastasis, treatment response, and survival [5]. Although analysis of cancer and tumor heterogeneity suffers from genetic and epigenetic complexity, multi-omics, spatial omics, and AI show advantages in advanced precision medicine [6]. Reviews on AI-based systems biology methods analyze omics data and emphasize the advances of these approaches in cancer classification, prognosis, and precision medicine. Novel information dimensions, including clinical data, radiation, and patient environment information, were discussed and analyzed to facilitate the realization of precision patient healthcare [7, 8]. Till now, integrative multi-omics approaches have been proven to precede single data types when dealing with complex patterns and accessing meaningful information from large-scale omics big data; AI exhibits exceptional capacity, indicating a future trade of AI and multi-dimensional omics cancer studies. But at the current stage, multi-omics analysis and AI are still facing lots of challenges, and new perspectives for oncology research are desired [9, 10]. Although all kinds of reviews and research have been done, an overview of the AI method and the paradigm of AI & omics research is lacking. To illustrate these views, this review focuses on the application field, algorithms, and application paradigms of AI and multi-omics for cancer. A high-resolution, well-structured landscape of AI and omics for cancer lays out the inadequacy of this field, points out the future direction of such work, and fills in the gaps that need to be explored.

2. AI algorithms and methods for multi-omics cancer analysis

Artificial intelligence (AI) has rapidly transformed research across many fields. It can be broadly categorized into four core components. First, perception—technologies like computer vision, speech recognition, and language processing enable machines to collect and interpret external data. Second, reasoning, planning, and acting encompass both deterministic and probabilistic approaches to decision-making, such as propositional logic, probabilistic models (e.g., Markov chains, Bayesian networks), and reinforcement learning. Third, knowledge representation focuses on structuring information in ways that support inference and action, using tools like logic, knowledge graphs, and ontologies. Fourth, integrated systems—such as robotics, expert systems, and multi-agent frameworks—combine these capabilities to perform complex tasks. Deep learning, in particular, enhances many of these components. These interconnected subfields allow AI to replicate or surpass aspects of human intelligence. Based on this framework, we categorize multi-omics cancer research by its application of key AI technologies [11, 12].

2.1. Signaling and language processing

Pathology slides, cancer staging information, and genomic mutation profiles, along with the associated pathology reports, can be processed by Prov-GigaPath, a whole-slide pathology foundation model, and generate accurate pathomics task results, such as cancer subtyping tasks. Prov-Gigapath was pretrained using GigaPath, a novel vision transformer for pathology slides, and then they paired each slide with an associated report using PubMedBERT, an advanced biomedical language model, which makes Prov-Gigapath a state-of-the-art pathology vision-language model. This model successfully combined a computer vision (image, in this case) model and a language model using two transformer architectures [13].

2.2. Reasoning in omics-cancer research

Causal relationship is important in cancer research. By using a causal reasoning model such as COSMOS (Causal Oriented Search of Multi-Omics Space), researchers can access mechanistic hypotheses for experimental observations across multi-omics datasets. COSMOS integrates phosphoproteomics, transcriptomics, and metabolomics datasets and combines prior knowledge of signaling, metabolic, and gene regulatory networks with computational methods to estimate transcription factor activities, kinase activities, and network-level causal reasoning. The core algorithm of COSMOS is CARNIVAL, which uses an integer linear programming (ILP) optimization strategy to find the smallest coherent subnetwork causally connecting as many deregulated TFs, kinases/phosphatases, and metabolites as possible [14].

2.3. Machine learning in omics-cancer research

Machine learning constitutes a big part of AI. Here we list out a table of ML sub-aspects and their application in omics cancer research as follows. We also describe several sub-aspects in detail [15].

Table 1. ML algorithms in cancer omics

Category	Representative Algorithms	Key Applications in Cancer Omics
Supervised Learning	Regression (Linear, SVR, RF), Classification (SVM, RF, XGBoost)	Biomarker discovery, drug response modeling, cancer classification and staging [16-31]
Supervised Learning	Ensemble Methods (AdaBoost, Gradient Boosting, deep forest)	Cancer diagnosis, prognosis, and stage prediction [16, 32-35]
Unsupervised Learning	Clustering (k-Means, HAC, DBSCAN), PCA, Autoencoders	Tumor subtype identification, omics data dimensionality reduction and latent feature extraction [17, 36-41]
Unsupervised Learning	Visualization and Dimension Reduction (t-SNE, UMAP, MDS)	Visualization of tumor clusters and subtypes [42-47]
Semi-Supervised Learning	Label Propagation	Drug repositioning and discovery via semi-supervised node labeling [48]
Deep Learning	CNN (ResNet, iSEGnet), RNN (LSTM, BiLSTM)	Gene expression prediction, transcription factor discovery, cancer stage classification [34,49]
Deep Learning	Autoencoders (VAE, DAE, SAE)	Omics data compression, chemotherapy response prediction [50-53]
Deep Learning	Generative Adversarial Networks (GAN, WGAN)	Synthetic data generation, patient risk stratification [54, 55]
Reinforcement Learning	Value/Policy-based Methods (Q-Learning, SARSA, PPO)	Optimizing therapeutic strategies and hybrid detection models [56]
Graphical Models	Graph Neural Networks (Node2Vec, GraphSAGE), Knowledge Graphs (SPOKE, Hetionet)	Integration and analysis of multi-omics data, cancer gene prediction [57-59]
Natural Language Processing (NLP)	Transformers (BERT, ChatGPT), Topic Modeling (LDA)	Literature review automation, clustering, DIA proteomics analysis [60-62]
Recommender Systems	Collaborative and Content-based filtering (SVD, Cosine Similarity)	Prioritizing candidate cancer drugs based on functional similarity [63]

2.3.1. Supervised ML and unsupervised ML

The core AI techniques for the whole chain of cancer care contain machine learning (ML), deep learning (DL), and natural language processing (NLP). Supervised ML is normally implemented in classification and regression, such as cancer subtype classification and prognostic prediction. Popular supervised learning tools for oncology include Naive Bayes, logistic regression, k-nearest neighbors (KNN), decision tree (DT), support vector machines (SVM), random forest (RF) [64], and generalized linear model (GLM) [65]. Unsupervised ML is a statistical tool that is typically used for clustering data based on its features and is commonly implemented in prognosis analysis, key marker extraction, dimension reduction, and gene functional clustering. Popular algorithms in unsupervised ML for oncology include principal component analysis (PCA), singular value decomposition (SVD), k-means, mean-shift, hierarchical clustering, DBSCAN, optics clustering, et al.

2.3.2. Deep learning

Deep learning algorithms are skilled at handling large datasets and extracting potentially advanced, yet uninterpretable, semantic features through multilayer nonlinear transformations, and have been proven to be accurate on target tasks. It is widely applicable in the clinical situation. The basic modes include convolutional neural networks (CNN), recurrent neural networks (RNN), long short-term memory (LSTM), fully convolutional networks (FCN), generative adversarial networks (GAN) [64], multilayer perceptrons (MLP) [65], et al. More recent and innovative network structures include graph convolutional networks (GCN), attention, multi-head attention, transformers, vision transformers (ViT), autoencoders (AE), variational autoencoders (VAE), deep clustering, et al. For non-annotation data such as digital pathology, single-cell omics, and spatial transcriptomics, a contrastive learning algorithm is an effective tool for learning latent information automatically in a self-supervised manner.

2.3.3. Natural language processing

Natural language processing (NLP) receives language or text data and transforms it using hand-crafted or self-learned symbolic rules or using statistical approaches such as ML to learn language phenomena and finally generate valuable information. NLP based on DL is dominant, as there are many successful models under this track, such as ULMFiT, bidirectional encoder representations from transformer (BERT), Transformer-XL, Google PaLM, GPT-3, et al. In cancer research, medical records can be generated automatically, and key information can easily be extracted from non-structured text data, including pathology and radiology reports and oncological clinical notes.

2.4. Knowledge representing and representing individuals' knowledge and relations

Knowledge and relation representation are crucial in the interpretability of AI and omics-related cancer research. To improve biocentric interpretability, knowledge and relation of knowledge are represented as domain knowledge and relational knowledge, and integrated with DL models. This new trend of converging external domain knowledge and the design of architectures that reflect the structure of known biological mechanisms with DL models can bring expert-level model explainability, more plausibility of these models, improved explanation quality, and fundamentally of pos-hoc methods and repositioning of DL models from pure black box to explainable models which provides new biological insight [66].

2.5. Multi agent system, expert system, and robotics

2.5.1. Robotic process automation

In addition, robotic process automation (RPA), as an integrated intelligence of sensors, automation, and AI, is widely used in research and clinical settings such as surgery, radiation oncology, oncology nursing, and rehabilitation [64]. Omics data are somewhat inherently interconnected in the biological processes, and although single omics data could contribute to a specific problem in cancer research or clinical practice, it is inadequate to consider the interactions between all omics data. To consider as much omics data as possible, one should integrate high-dimensional and heterogeneous multi-omics features. Data cleaning and normalization methods such as Z-score normalization and Min-Max scaling are required. Concatenating data from multi-omics and circumventing the “curse of dimensionality” commonly requires conducting dimensionality reduction, which is achieved using feature selection or feature extraction.

3. Application of AI for multi-omics

There are lots of applications when it comes to the combination of AI and multi-omics for cancer. According to reviews, omics often includes genomics, transcriptomics, proteomics, metabolomics, epigenetics [2, 67], radiomics [68], clinlabomics [69], pathology [70], and fragmentomics [71].

There are two aspects of applications in AI and multi-omics for cancer. One is based on the healthcare process of cancer patients; the other is based on the biological mechanism of cancer. The aspect of the healthcare process of cancer patients includes three subclassifications: diagnosis, treatment, and prognosis. There are also studies in this aspect that cover all three subclassifications, such as precision oncology and translational application. The aspects of the biological mechanism of cancer include the molecular mechanism of cancer, signaling pathways of cancer, and cancer-related biological mechanisms such as tumorigenesis, immune responses of cancer, tumor microenvironment, and homeostasis, etc.

3.1. Application field paradigm

Application fields based on the medical or clinical care of cancer often include diagnosis, treatment, and prognosis [72]. For diagnosis, pathological biopsy, radiomics imaging, and liquid biopsy are frequently used. Pathology combined with DL exhibits better efficiency and accuracy compared with traditional pathological diagnosis [73]. Radiomics, such as MRI, PET, and CT enhanced by AI, show promising results too [74-76]. Liquid biopsy as an innovative noninvasive method for early detection represents a great potential when integrated with AI technology [77]. Multi-omics liquid biopsy was recently invented and can identify clinically valuable biomarkers [78]. As part of the diagnosis, AI and omics are widely used in cancer classification too [72, 79, 80]. For treatment, omics and AI are utilized in drug discovery, therapy decision-making using biomarkers, and therapy decision-making or studies such as radiation, chemotherapy [65], vaccines, surgery, and immunotherapy [81-85]. For prognosis, AI-based omics are often used in prognosis biomarker [81], therapy efficiency prediction [86], and survival prediction [87].

Application fields based on the mechanism of cancer often include cancer-related molecular and pathway studies, which might offer valuable information, such as potential diagnosis-to-prognosis biomarkers and treatment targets [88]. AI-driven interpretable biomarker profiling has the potential to identify targets based on biological mechanisms [89]. Cancer-related biological mechanisms such

as inflammation [90], immune processes [91], homeostasis [92], tumor microenvironment (TME), and therapy resistance mechanisms [88].

3.2. Framework paradigm

AI-driven multi-omics for cancer typically follows a structured framework that integrates biological data generation, computational processing, and interpretability-driven modeling.

3.2.1. Data acquisition and engineering

To maximize the potential of multi-omics, large-scale, tissue-specific datasets are essential [2]. Advances in bioengineering enable the capture of diverse molecular features using top-down and bottom-up approaches. Top-down methods maintain the physiological context of tissues, whereas bottom-up techniques use microfluidic interfaces to reconstruct dynamic tissue-like environments, producing highly reproducible data [82].

Domain knowledge, including biological pathways and protein–protein interaction (PPI) networks, is increasingly integrated into model architecture. Incorporating such knowledge improves post-hoc interpretability, suggesting that domain-informed designs are crucial for revealing mechanistic insights [66].

Before integration, omics data require rigorous pre-processing, including normalization and cleaning [8]. Integration strategies include early integration, which concatenates raw or engineered features before modeling but struggles with heterogeneity and dimensional imbalance; late integration, where individual models are trained on separate omics and combined at the decision stage—a preferred strategy for heterogeneous data types like radiomics and genomics; and intermediate integration, which learns joint representations from each modality and combines them for downstream prediction [65].

3.2.2. Computational framework and feature strategies

Modern computing platforms such as DOE Leadership Computing Facilities (LCF) and HPC systems enable parallelized training of large-scale models through high-speed interconnects [93]. These resources are vital for deep learning-based multi-omics applications that require intensive simulation and training.

Dimensionality reduction is essential to mitigate overfitting in high-dimensional omics datasets. This can be achieved through feature selection or feature extraction. These methods can be either supervised or unsupervised, depending on label availability. Unsupervised feature selection methods include correlation analysis and variance-based approaches. Data with labels processed with supervised feature selection methods identify the most correlated features via univariate or multivariate tests, random forest (RF), least absolute shrinkage and selection operator (LASSO), etc. Unsupervised feature extraction methods include clustering, autoencoders, and matrix factorization techniques such as principal component analysis (PCA) and singular value decomposition (SVD). Supervised feature extraction methods include linear discriminant analysis (LDA), deep neural pursuit (DNP), etc. Model choice should reflect dataset characteristics: linear models are well-suited for small sample sizes, while random forests or deep neural networks may be feasible if combined with domain-appropriate data augmentation. Validation through cross-validation is necessary, and trade-offs among accuracy, interpretability, and computational cost must be considered. Different dimensionality reduction methods are already used to further reduce feature dimensions in treatment

response prediction. In addition, it may not be necessary to reduce feature dimensions before integrating multi-omic features when using DL methods because DL models can learn a representation from raw features [65, 89, 94].

3.2.3. Model design, interpretability, and validation

Initiatives such as JDACS4C, a collaboration between the NCI and DOE, demonstrate how AI systems can support cancer research through modular, interpretable model designs. Model features are categorized as experiment-related (design tools), data-related (synthetic data generation, modality conversion), and model-related (hyperparameter tuning, inference, uncertainty quantification). Interpretability plays a central role in bio-informed model evaluation. Architecture-centric approaches use schema-level representations to enhance transparency, while output-centric designs align domain knowledge with predictions. Post-hoc methods trace information flow within the model, highlighting the contribution of specific neurons or layers [66]. Finally, validation frameworks employing uncertainty quantification (UQ) assess robustness to noise, overfitting, and extrapolation. UQ is essential for detecting unreliable predictions and guiding experimental refinement, especially under multi-modal uncertainties [65].

4. Ethical and privacy issues

The development of intelligent oncology involves ethical, philosophical, moral, and economic issues as well as a variety of uncontrollable problems and unknown risks. Most of the ethical concerns related to healthcare applications of AI are summarized into the “fairness, accountability, and transparency (FAT) paradigm of AI ethics.” Explainability and interpretability of AI methods are still an issue. Sensitive information also raises concerns about data protection and privacy. Many countries have introduced relevant laws and policies to promote the reasonable applications of AI in healthcare systems. In 2021, the US Food and Drug Administration (FDA) identified a workflow for AI- and ML-based software as a medical device (SaMD) [64, 76].

To estimate the risk of bias and usefulness of the AI model, guidelines have been made to ensure the reproducibility and transparency of AI in medical conditions. For example, recommendations for the reporting of developing, validating, or updating a diagnostic or prognostic prediction model [65].

Supervision of medical AI has been adapted from approaches that ensure the safety and efficacy of drugs and conventional medical devices. The FDA considers clinical AI as a software-based medical device, and it involves the approval of a “static” model and additional approval when any change in data, algorithm, or intended use is made. More recently, the FDA took out a regulatory framework with new post-authorization considerations that are important for clinical AI, such as predetermined change control plans that specify parameters and methodology they intend to modify in the future [95].

5. State-of-the-art techniques

Advancements in nanophotonics have made Raman spectroscopy a non-invasive, label-free method capable of analyzing the tumor microenvironment, predicting biomarkers, and monitoring drug responses at subcellular resolution. When combined with AI and omics data, it offers deeper insights into tumor heterogeneity [96]. AI-driven optical nanosensors also enhance biomarker discovery and personalized treatment by enabling comprehensive multi-omics analysis [97].

Digital omics standardizes clinical and omics data into secure, interpretable digital formats, improving healthcare delivery through transparency and efficiency [98]. Digital twin (DT) technology, originating from aerospace, creates real-time virtual models of tumors using patient data, simulating disease progression and optimizing treatment plans. As DT systems evolve, they may become essential tools for precision oncology, bridging real-world data with predictive modeling [99].

6. Conclusions

This review provides an updated overview of AI and omics techniques in cancer research and applications. Based on previous reviews, we list out common algorithms of AI and multi-omics for cancer and summarize the application field paradigm of AI and multi-omics for cancer. In addition, we exhibited the omics data integration paradigm and the general framework paradigm of AI and omics cancer study. Although the existence of a general framework and analysis paradigms, biases are common in any of the steps of analysis. Further improvement should be made to enhance the reliability of the data and analysis tools with more advanced algorithms, omics-tech, interdisciplinary cooperation, and ethical policies. This review arranged the current development situation of the AI and omics techniques and patterns in cancer studies and pointed out the deficiencies of this field, calling for better outcomes in AI and omics cancer studies.

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