Trends in Information Management (TRIM)
ISSN: 0973-4163
13(1), pp. 80-91

Towards Intelligent Cancer Subtyping: Integrating Multi-Omics Data Using Diverse Machine Learning Strategies

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Abstract
Precision oncology heavily relies on dividing cancer into different subtypes. Single-omics data do not accurately reflect the complex ways in which molecules interact and collaborate in tumor growth and development. Advances in high-throughput methods have enabled the generation of genomic, transcriptomic, epigenomic, and proteomic data, providing new opportunities to examine cancer. However since various types of data must be used together, there are large computational obstacles involved. In this paper, we look into ways that combine different machine learning (ML) methods for integrating various kinds of data to find cancer subtypes. We describe the main data forms, methods for data integration, model design strategies, testing techniques, and new difficulties. In addition, we address the impact of biological significance, easy understanding, and medical application on the future of intelligent cancer subtyping.
***Keywords**: Multi-Omics Integration, Cancer Subtyping, Precision Oncology, Machine Learning, Translational Bioinformatics*

Introduction

Cancer is a leading cause of death around the world and better recognition of its subtypes greatly helps with the diagnosis, prognosis, and treatment (Zhang et al., 2023). To date, using traditional methods just to look at tissues and symptoms is often not enough to detect all the detailed molecular changes that occur in many tumors (Ma et al., 2024). Many genomic changes such as mutations, gene expression, patterns of DNA methylation, and modifications in proteins, can now be analyzed in large populations with the help of modern sequencing technology (Satam et al., 2023). The variety of biological data now makes it possible to study cancer at the level of its molecules (Wang et al., 2023). They could pave the way for more targeted and helpful ways to subtype different cancer types for patients. Even so, making different and complicated types of data compatible in a single analytical framework is challenging methodologically and computationally. Here, intelligent machine learning techniques, mainly those built for handling complex multi-modal datasets, have proven very useful (Ahmed et al., 2023). This work focuses on how blending omics (Chakraborty et al., 2024) techniques with advanced machine learning approaches (Mokoatle et al., 2023) may find cancer subtypes linked to successful clinical results, strengthening the design of therapies (Kumar et al., 2024).

Background and Significance

Cancer Subtyping: A Clinical Imperative

Cancer is not a singular disease but a complex collection of diverse conditions, even within what appears to be a single type (Brown et al., 2023). How the disease develops and how effective treatment is depends on the underlying variety of cancer types (Swanton et al., 2024). We find that breast cancer which is widely treated, can be diagnosed in several different forms. Instead, the disease is separated into subtypes according to specific types of molecules, for example, luminal A, luminal B, HER2-enriched, or basal-like (Mayrovitz, 2022). Every subtype is identified by its own set of genes expressed, proteins present, and the behaviors of its cells. Clinical decisions often depend on molecular classifications of cancer. In the case of luminal breast cancer, hormone therapy tends to help patients, who usually have a better chance of recovering (Grimm & Mazurowski, 2020;Testa et al., 2020). In contrast, persons with HER2-enriched or basal-like (most likely triple-negative) cancer subtypes may be treated more aggressively with targeted medications and chemotherapy (Zagami & Carey, 2022). That’s why making sure these subtypes are precisely labeled is crucial for successful care (Fusco & Viale, 2024). Tailoring cancer treatment becomes much easier for oncologists when they can classify types of cancer and how they grow inside a patient. Cancer treatment is more accurate, more likely to be successful, and less likely to result in unnecessary problems (Riedl et al., 2024). Besides, using pathology helps doctors predict the severity of the disease, its likelihood of returning, and the chances of successful treatment. How we categorize cancer based on its genes affects the treatment results and the quality of life patients will experience. Supplying and studying biomarkers is vital for clinical reasons and helps close the gap between labs and the care patients receive, making it more likely they will survive cancer (Das et al., 2024; Prasanth et al., 2023).

The Multi-Omics Revolution

Multi-omics technologies have allowed biomedical researchers to see cellular processes from a new, multidirectional perspective. By not depending on one method, the multi-omics approach shows how diverse parts of a cell interact. Genomics is important for finding genetic differences in DNA, among them mutations and copy number changes that could be the main causes of cancer. Meanwhile, transcriptomics studies the various patterns of gene activity that determine how RNA is formed from the initiation of gene transcription. Thanks to epigenomics, we can now see how methylation and similar chemical changes can change gene activity without touching the core genetic code. In the end, proteomics examines proteins that make up the majority of a cell’s ability to function and are the result of transcription and translation. Every omics provides different, important information and these fields are linked. Because of their integration, researchers can build a clear and united understanding of cancer biology, spotting molecular signatures that cannot be found when studied separately. The use of this whole-body strategy is important for recognizing cancer's seriousness and may benefit progress in precision oncology (Chen et al., 2023; Gutierrez Reyes et al., 2024;Hayes et al., 2024).

Machine Learning for Multi-Omics Integration

ML strategies for multi-omics integration can be broadly categorized based on their learning paradigms (supervised, unsupervised, and semi-supervised) and data integration frameworks (early, intermediate, and late integration).

Early Integration (Concatenation-based)

Concatenation-based integration means merging all of the different omics information into a single feature matrix before training. Since all the data is seen as one input, this process is easy to understand and use. However, since omics datasets can be very different in size and shape, it is often hard to avoid overfitting and work with such a large amount of information. Many people in this field use PCA, t-SNE, and autoencoders to reduce the number of dimensions in datasets. These methods make the data take up less space, remove background noise, and pick out key features which improves how easy it is for the model to learn and be used in other situations.

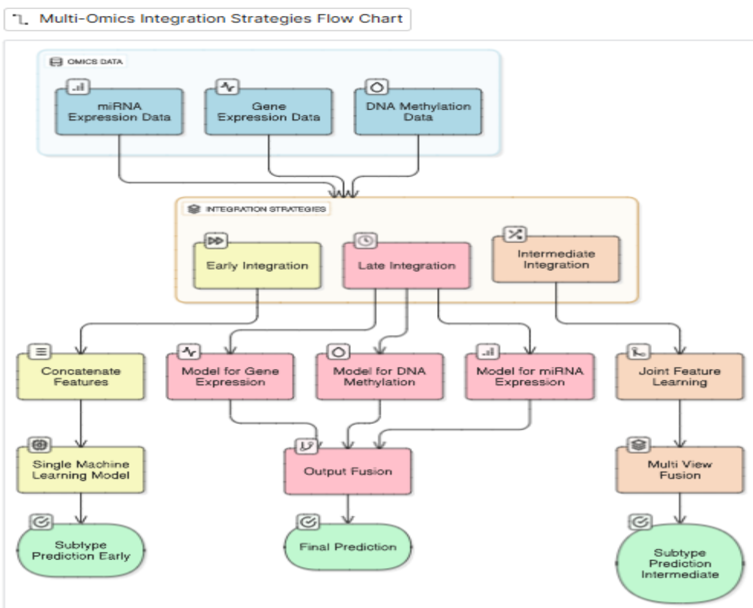
Intermediate Integration (Latent Representation Learning)

Intermediate Integration is known as latent representation learning and handles the fusion of multi-omics data more precisely. Rather than combining the raw data from every omics type, the method first does independent processing on each dataset to generate useful lower-dimensional representations. By using these compact representations, we clear some of the noise and unnecessary redundancy found in the original data. Afterward, the different latent features from all omics layers are put together to create a single fused feature space for further work. Applying this method fixes data problems and makes it easier to link and compare several omics datasets. In this level of integration, researchers use Multi-Omics Factor Analysis to observe both common and unique parts in the data, CCA to search for relationships, and a range of deep learning solutions to extract complex features. Thanks to latent features, intermediate integration can better mix and use the complementary information between omics than simple concatenation alone.

Late Integration (Model-level Fusion)

In Late Integration, each dataset is managed independently during the early stages, rather than by using any kind of mixed model. With this strategy, several models are trained on different omics data independently, so every model can learn what is special about its dataset. All the outputs from the individual models are merged when making the most critical decision. Unifying results can be done by ensemble learning which combines many predictions from different neural networks to get better accuracy or by using multi-view learning, mixing details from several data sources to come to a single conclusion. Using late integration means that data scientists can gain from using varied models which helps them process complex data with diverse characteristics (Ballard et al., 2024;Picard et al., 2021).

Fig. 1: ML Integration Strategies: Early, Intermediate, Late



Diverse Machine Learning Strategies

Unsupervised Learning

In cancer subtyping, unsupervised learning is very important and k-means, hierarchical clustering, and spectral clustering are commonly used to this end. They organize patients using similar molecular tests to see if any groups perform similarly and show a pattern of the disease. Lately, modern clustering solutions have appeared to help overcome the difficulties of handling data from multiple types of "omics." SNF, iClusterBayes (Mo et al., 2018), and NEMO (Rappoport and Shamir, 2019) techniques are available to bring together different data from omics research. They achieve this by combining and blending the similarity information found in data types such as microarray, methylation, and copy numbers. Comprehensive sample networks permit the identification of resilient and meaningful groups that symbolize various cancer subtypes, increasing our knowledge of tumor heterogeneity and options for treatment (Trezza et al., 2024).

Deep Learning Approaches

Deep learning is becoming an important way to integrate multi-omics data because it can find complex connections between different biological data sources. Because of this, deep learning models are highly effective at working with the high-dimensional and potentially noisy data found in omics. For instance, autoencoders are frequently used to separate important biological signals from the raw information in the data they receive. VAEs (Ranjbari and Arslanturk, 2023) and GANs (Ahmed et al., 2022) make use of probabilistic methods and the production of synthetic data to improve how well we understand the data and increase the models' ability to adapt to unseen situations. Besides, state-of-the-art frameworks MOGONET (Lan et al., 2025) and SUPREME (Kesimoglu and Bozdag, 2023) combine information from several omics layers at the same time. Because these architectures process data from multiple omics groups and recognize device differences, they present a fuller and more detailed image of the mechanisms involved in different cancer subtypes (Ballard et al., 2024).

Graph-based and Manifold Learning Methods

Graphs and manifold learning are useful ways to emphasize the details in relationships in big multi-omics datasets. In these methods, samples and features are part of a graph which lets them capture activities that nearby and separate units interact with. GCNs make it possible to pass information across elaborate biological networks and gain knowledge from the relationships among the data. Hypergraph (Wang et al., 2024) learning takes this now by including relationships where a single hyperedge is connected to more than two nodes. Also, using spectral clustering on P-Laplacian graphs (Valous et al., 2024) allows one to uncover the organization of the data and cluster cancer samples, revealing different cancer subtypes. This combination of graph approaches offers a clear and mathematically sound way to work with and understand multi-omics datasets (Patton-López, 2022; Valous et al., 2024;Wandy & Daly, 2021).

Evaluation Metrics and Validation

The reliability, usefulness for healthcare, and scientific meaning of cancer subtyping techniques should be evaluated. To confirm that clustering is effective, the Silhouette Score, Adjusted Rand Index (ARI), and Normalized Mutual Information (NMI) are used. These methods tell us how accurate and consistent the groupings are in contrast to the rest of the data. To test how the subtypes are relevant for patients, survival analysis workers often use a log-rank test to see if they result in different survival times. Enrichments in selected pathways and biomarkers are examined to determine if the clusters are associated with particular functions or associated with various diseases. Strong validation methods are critical to guarantee good performance and general application which includes verification in different sections of the same data, cohort evaluation, and comparison with the major divisions defined in the TCGA. These multilayer evaluation strategies help us fully assess a method, guiding us in making better and clinically important divisions of subtypes (Rainio et al., 2024).

Case Studies and Applications

Several large-scale studies have highlighted the promising impact of machine learning-driven multi-omics integration in advancing cancer subtyping and personalized medicine. For the integration of genomic data, the Cancer Genome Atlas (TCGA) The National Cancer Institute(n.d.) has helped as a reference, by supplying large, comprehensive datasets used to measure and check new methodologies. With that resource on hand, advanced models have shown good results. By using MOGONET, researchers were able to find meaningful subtypes of glioblastoma and lung cancers (Huang, 2021). In chronic lymphocytic leukemia, MOFA+ showed it was useful by revealing interpretable latent factors that affect the differences seen between patients, giving helpful insight into how the leukemia develops. Using these examples, it becomes clear that smart methods in subtyping which rely on machine learning, can take complex data from omics to improve both diagnostics and treatment choices in oncology.

Challenges and Future Directions

Despite significant advancements in multi-omics integration, several key challenges continue to hinder progress and present opportunities for future research. One major challenge is **data heterogeneity and missingness**. Handling the difference in data formats and missing values is a major difficulty for big data analysis. A lack of certain omics data for a patient is usual in clinical and research fields because it is often limited by things such as costs or space. A lack of full data during integration makes it necessary to build reliable procedures for filling in the gaps using information from similar data sources. Another critical issue is **model interpretability** is yet another important matter to address. Many leading integration methods that rely on deep learning give results without clearly explaining how they came to that decision. To help these models be used in clinical practice, their workings must be explained in a way that helps understand the biological reasons for the results. **Computational scalability**, many issues related to processing large amounts of data still need to be resolved. Small algorithms will not work well, as multi-omics data is usually spread out over a large number of dimensions and comes from different sources. As data becomes bigger and more complicated, there is a greater need for efficient tools and fast computers, showing that new ideas in algorithms and computer design are still necessary. Finally, **ethical and privacy concerns** loom large as integration methods become more powerful and widely used. Ensuring all patient data is safe and genetics data is managed according to ethical guidelines is most important. Keeping data secure and acting ethically is necessary for researchers, doctors, and others involved to maintain the public's trust and respond to new methods of sharing and receiving consent in the field of genomics research. Addressing these challenges through interdisciplinary collaboration and innovative methodologies will be essential to fully harness the potential of multi-omics integration for precision medicine in the years to come.

Future Directions

The future brings many innovative and significant developments to multi-omics integration. Federated learning shows much promise because it lets different institutions study data together while still protecting patient privacy. Federated learning keeps sensitive data on users' local devices and doesn't move it between servers, protecting privacy and providing access to different kinds of data. Because of this breakthrough, multi-center studies may happen faster and make us confident that results can be applied elsewhere. At the same time, there is more attention being given to XAI which aims to help explain the ways complex machine learning models arrive at their decisions. When insights are easily understood, XAI allows clinicians to trust the models, choose the best actions, and use these advanced health technologies more widely. With the help of detailed medical information and imaging data, multidimensional maps of disease can be made from multi-omics data. It helps detect not just changes at the molecular level but also changes in appearance and body structure, giving a better snapshot of a patient's health and making diagnoses, predictions, and treatment choices more accurate. Now, researchers are investigating multi-omics analyses of cells or tissues as time goes by, helping to describe the development of cancer. Tracking changes over time in these analyses provides information about disease development, how well treatments work and patient outcomes, helping to develop better and more flexible treatments. Overall, these new directions suggest a promising route ahead, ensuring multi-omics integration is safer, easier to explain, covers more areas, and results in better progress for personalized medicine.

Conclusion

The integration of multi-omics data through a variety of sophisticated machine-learning strategies marks a profound transformation in the field of cancer subtyping. Classifying cancer by simple clustering was traditionally difficult because it did not capture the many biological differences inside tumors. Recently, using powerful new tools, we have discovered patterns in tumors that show much greater levels of detail than before. Such smart frameworks take advantage of all the omics fields like genomics, transcriptomics, proteomics, and epigenomics and also handle the unusually complex way biological data works, making us notice incredibly fine subtypes that were difficult to notice before. When computational tools can explain what they are thinking interpretably and deal efficiently with an increasing amount of data—scalable they are more and more useful in everyday healthcare. Because of this transition, cancer treatments can now be shaped perfectly to fit the individual changes in each patient's tumor. When multi-omics data are combined with advanced machine learning methods, precision oncology sees real progress, giving us valuable new evidence and uses in medical practice. It (sys/enabling services) improves diagnostics, leads to better forecasts, and helps create therapies that are customized for different patients, boosting the achievements of biomedical research and changing our approach to cancer.

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