# Unlocking the Potential of Single-Cell Multi-Omics Data with Large-Scale Pre-Trained Transformer Models

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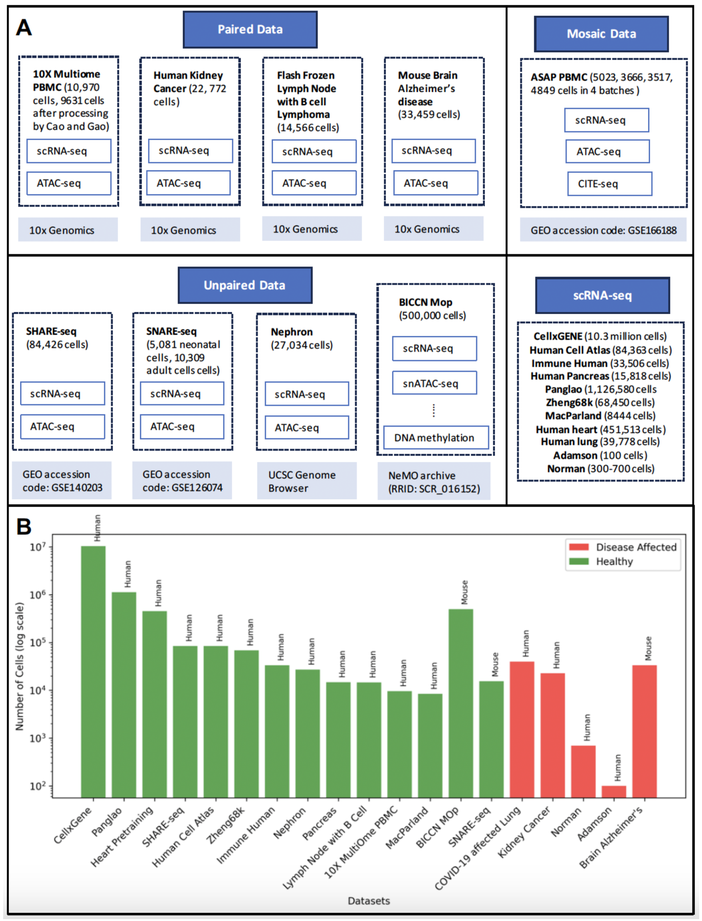
## Task 1: Training a Shared Encoder

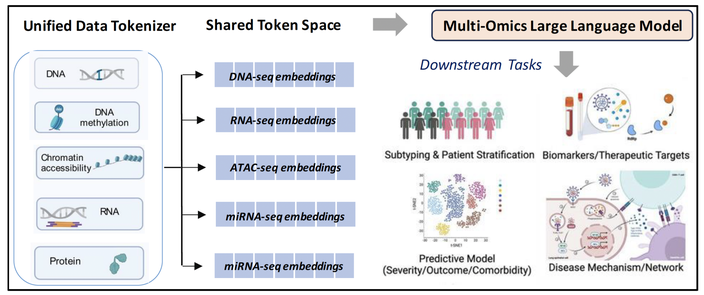
- We've amassed a large collection of single-cell multi-omics datasets with unique characteristics, including paired datasets from 10x Genomics and unpaired datasets such as SHARE-seq, SNARE-seq, and Nephron. These include massive single-omic and multi-omic resources, like the 10.3 million sample CELLxGENE and extensive ATAC-seq and gene expression datasets. Additionally, we have disease-specific datasets like COVID-19-affected human lung samples and Human Kidney Cancer, which are vital for understanding cellular differences in health and disease, and for developing multi-omics analysis models.




- Our multi-omics data processing approach utilizes a shared backbone inspired by multimodal learning, which doesn't rely on paired data. The cell-gene matrix for different omics types is processed using a unified tokenizer that maps data to a common token space, facilitating analysis with a shared token encoder.

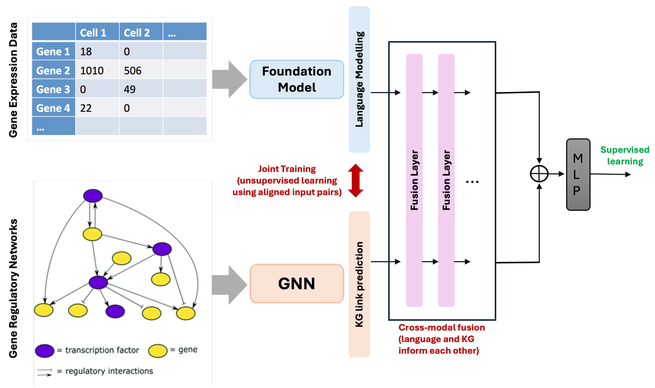
## Task 1: Training a Shared Encoder (continued)

- This shared encoder, part of a large language model, is trained across modalities to extract semantic features for each cell, enabling multi-omic understanding without paired training data. During pre-training, self-training objectives generate labels, and task-specific heads are applied post-training for various biomedical applications.



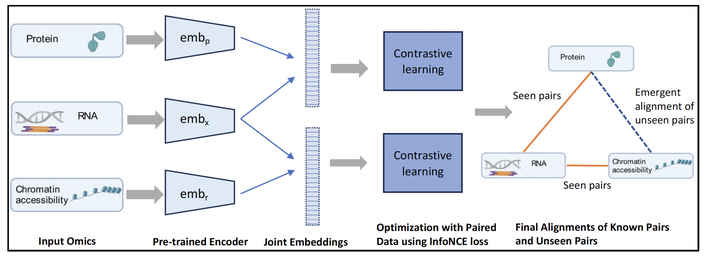

## Task 2: Integrate Gene Regulatory Networks

- Gene regulatory networks offer valuable insights into context-specific gene regulation. We propose a novel approach that integrates these networks into the pre-training of transformer models for single-cell multi-omics analysis.
- Our method involves a joint self-supervised training strategy, aiming to enhance the model's understanding of gene characteristics and interactions. Our co-training framework combines single-cell multi-omics data with gene regulatory networks using a multi-omics large language model and Graph Neural Networks (GNNs).
- This approach unifies masked language modeling and link prediction in the networks, providing a comprehensive understanding of gene interactions beyond simple co-expression relationships. By integrating biological network knowledge into the pre-training process, our approach enhances the identification of functionally related genes based on shared regulatory mechanisms.




## Task 3: Enhance Single-cell Multi-omics Data Integration

- This task enhances single-cell multi-omics data integration by using cross-modal translation and contrastive learning, techniques designed to utilize unpaired data. The goal is to boost the model's capacity to interpret and relate information across various omics modalities for a deeper biological insight.
- Our approach is focused on aligning unpaired multi-omics data using cross-modal translation, building on previous successful methods like BABEL and scCross that translate between RNA-seq and ATAC-seq data. Our approach expands on this by including a wider variety of omics data and employing a bidirectional transformer for pairwise alignment, aiming to minimize the distance between original and translated data across different omics types, thus enhancing alignment accuracy.




- By encoding each omics modality with a specific self-attention transformer encoder and optimizing embeddings through contrastive learning with the InfoNCE loss, the goal is to minimize the distance between paired omics, while maximizing it for unpaired ones.
- This approach aims to improve the model's accuracy in classifying and aligning multi-omics datasets, leveraging both the diversity and the specificities of the data.

## Acknowledgement

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