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Building the Gene Regulatory Network using Deep Learning

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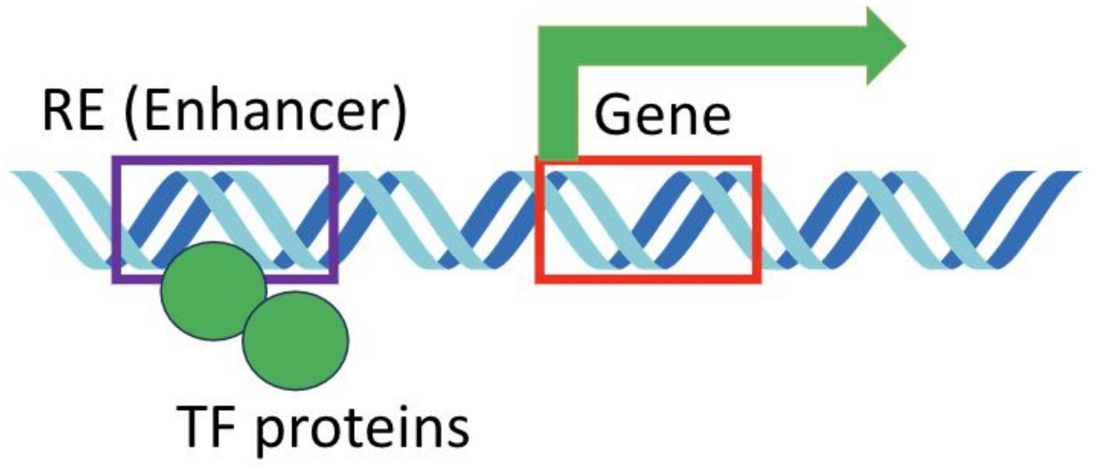
Introduction

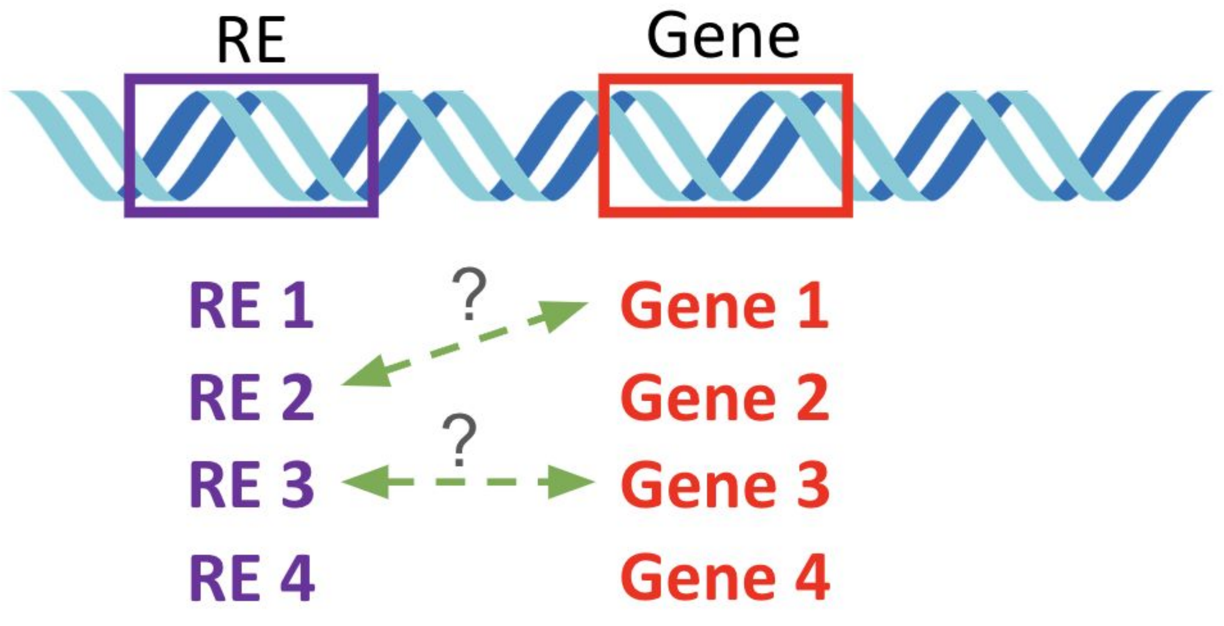
Gene regulatory networks (GRNs) consist of genes, regulatory elements (REs), and transcription factor (TF) proteins



Understanding GRNs is important for investigating disease origins and treatment

- Most disease-related mutations occur in non-coding regions (eg. REs such as enhancers) and cause target genes to be expressed in an incorrect amount
- Can use drugs/gene-editing techniques to correct enhancer behavior

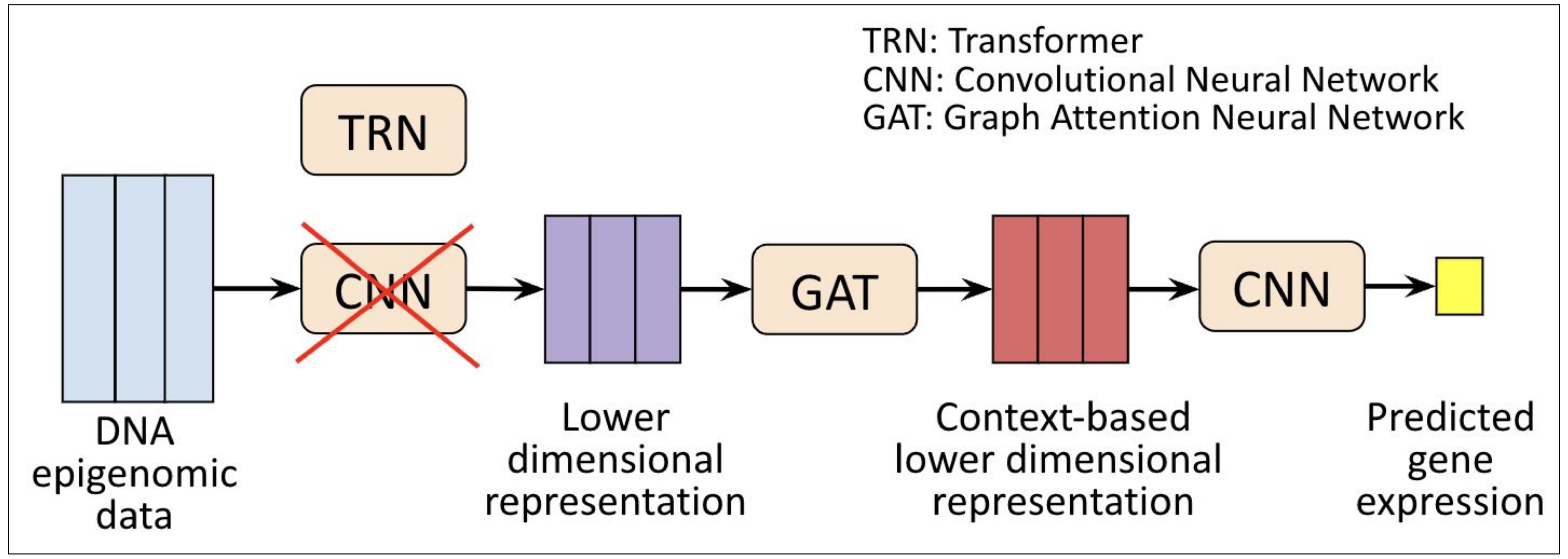
Problem: Many interactions between REs and genes still remain unknown



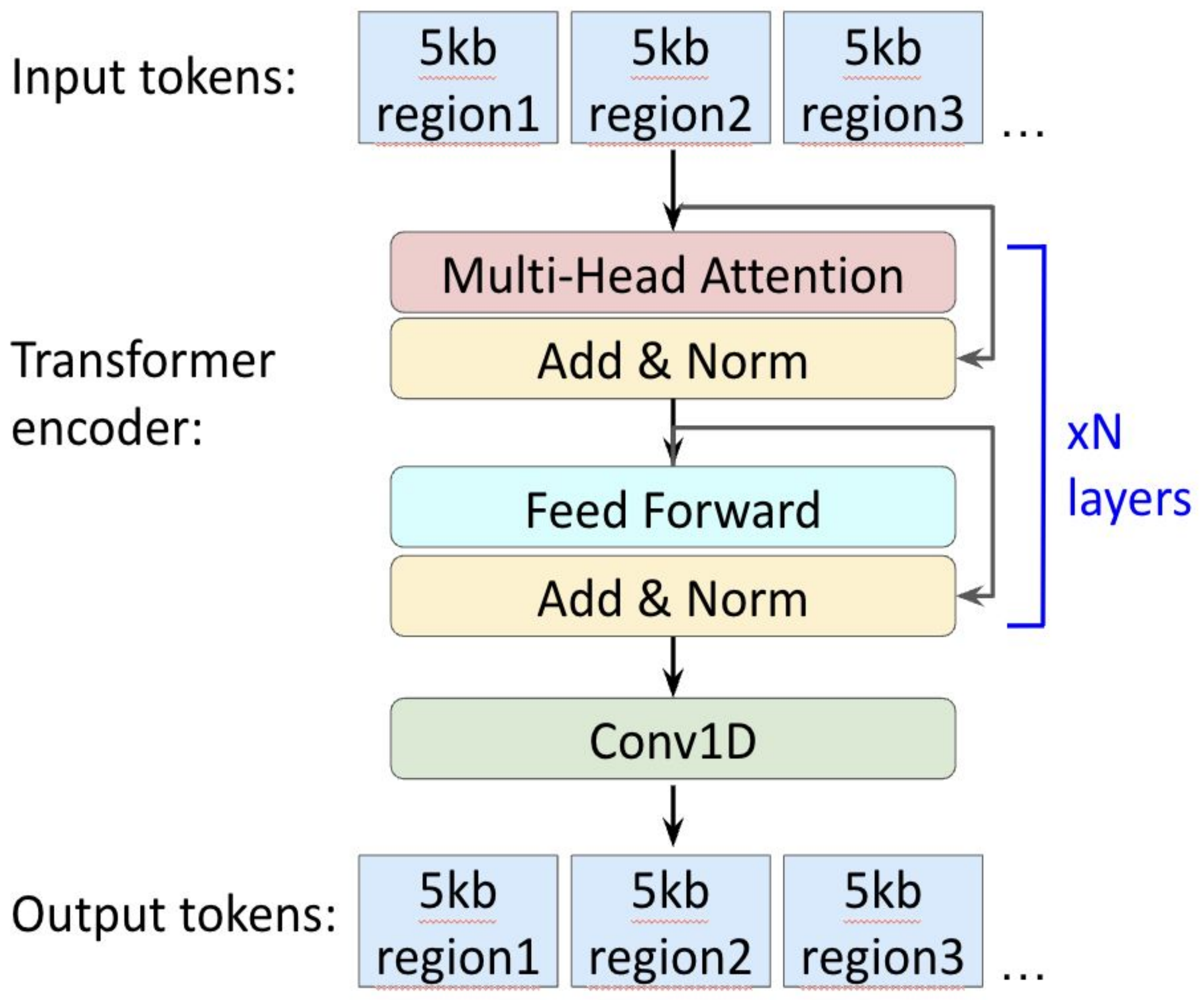
Goal: Discover interactions using deep-learning

Methods

Approach: Improve prediction accuracy of RE-Gene interactions by employing Transformer in existing GraphReg method (Alireza, et. al)



Transformer Architecture

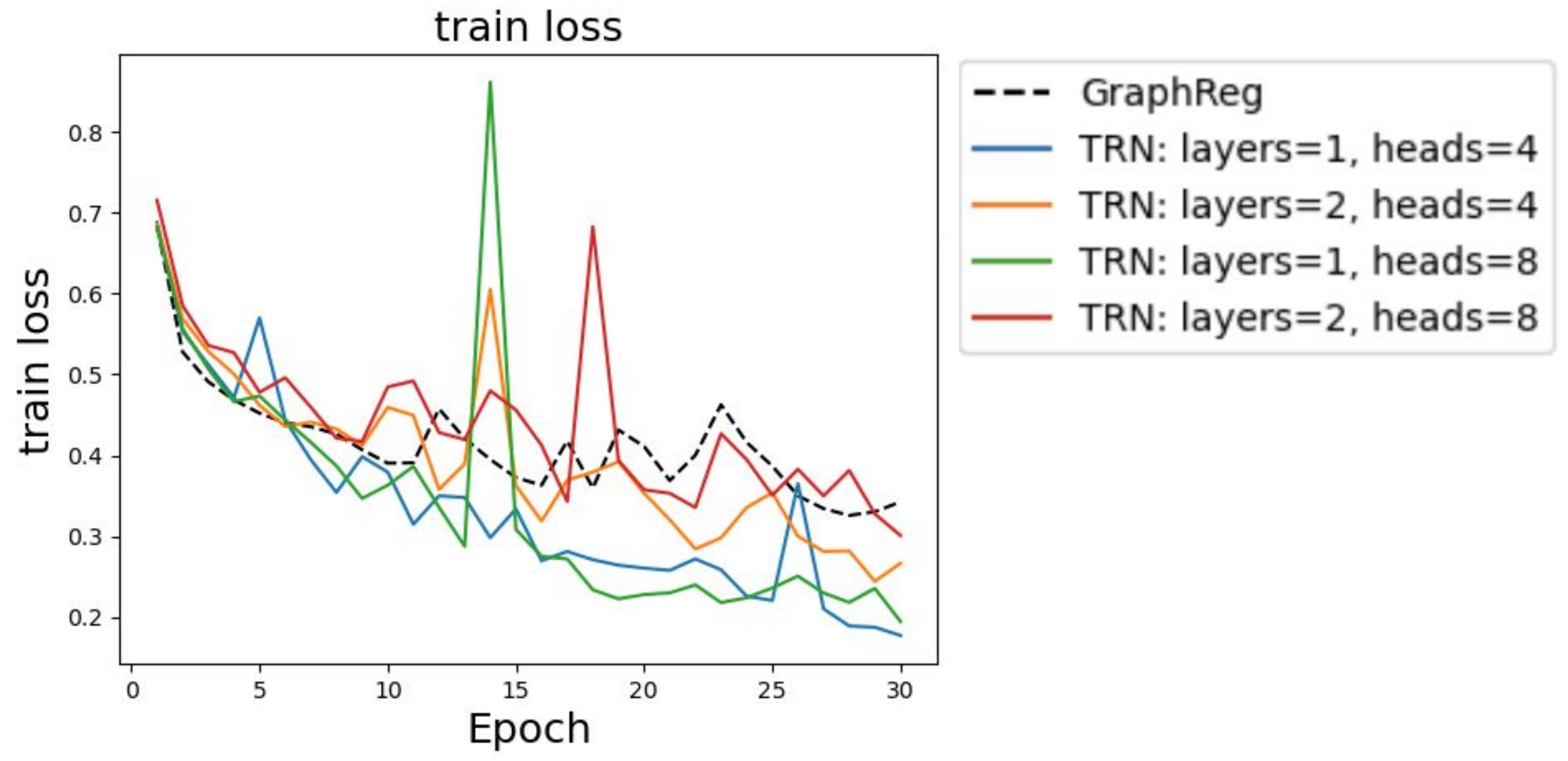


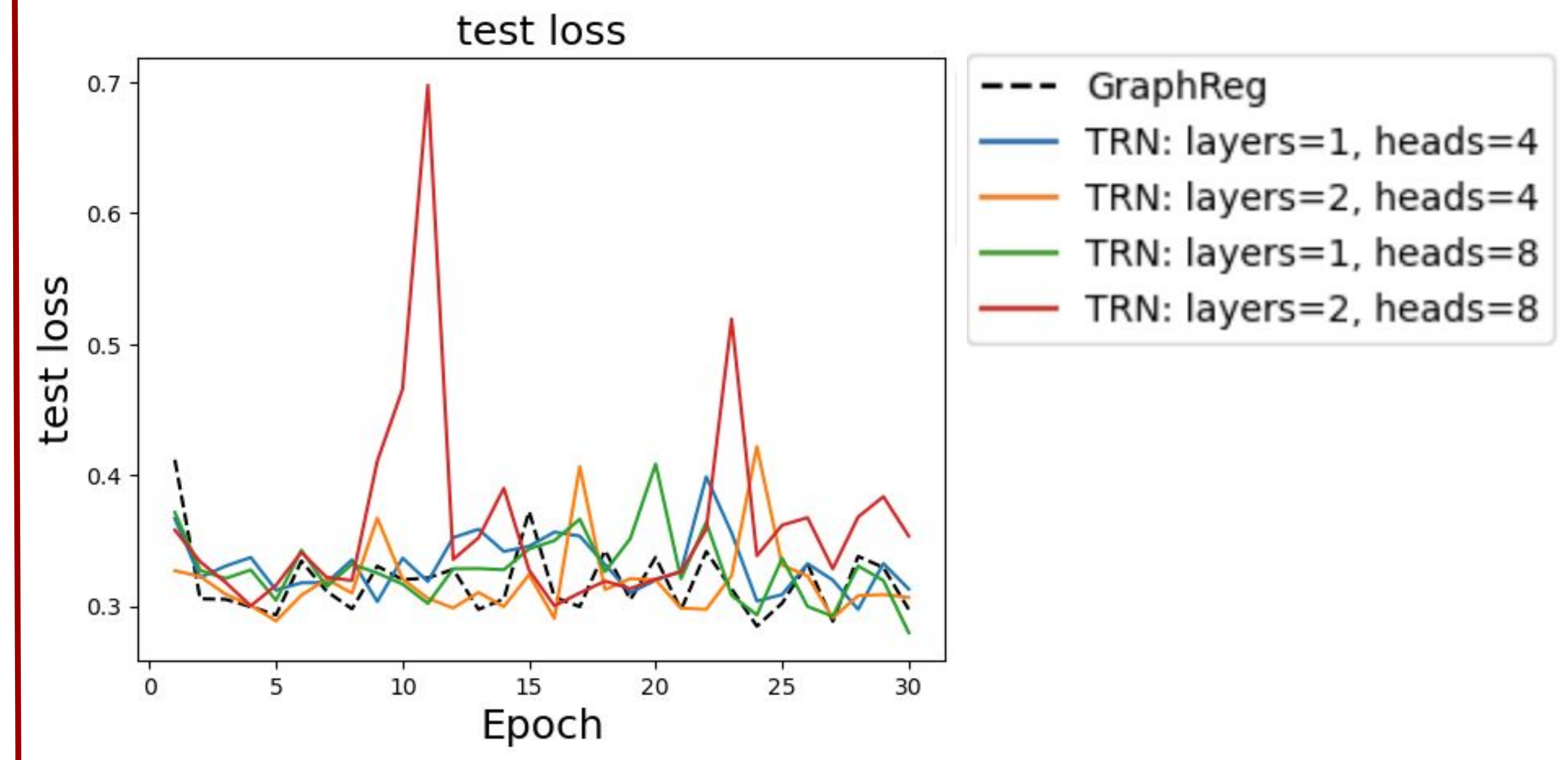
Self-Attention Matrix (example)

Unlike CNNs which learn relationships between a genomic region and its direct neighbors, Transformers learn relationships between a region and many other regions upstream and downstream by computing scores in the self-attention matrix below.

	5kb region1	5kb region2	5kb region3	…
5kb region1	0.71	0.04	0.07	
5kb region2	0.1	0.65	0.01	
5kb region3	0.2	0.01	0.6	
⋮				

Results





- For training, Transformer performs better compared to GraphReg, while testing losses are comparable
- Interestingly, Transformer's training performance decreases as # of attention layers/heads increases

Next Steps

1. Add positional encoding to the Transformer
2. Use scores in self-attention matrix to link REs with genes and compare results to GraphReg
3. Augment input data characterizing a genomic region (eg. ATAC-Seq data)