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Leveraging Transformer Architectures to Learn Biologically Meaningful Cellular Representations

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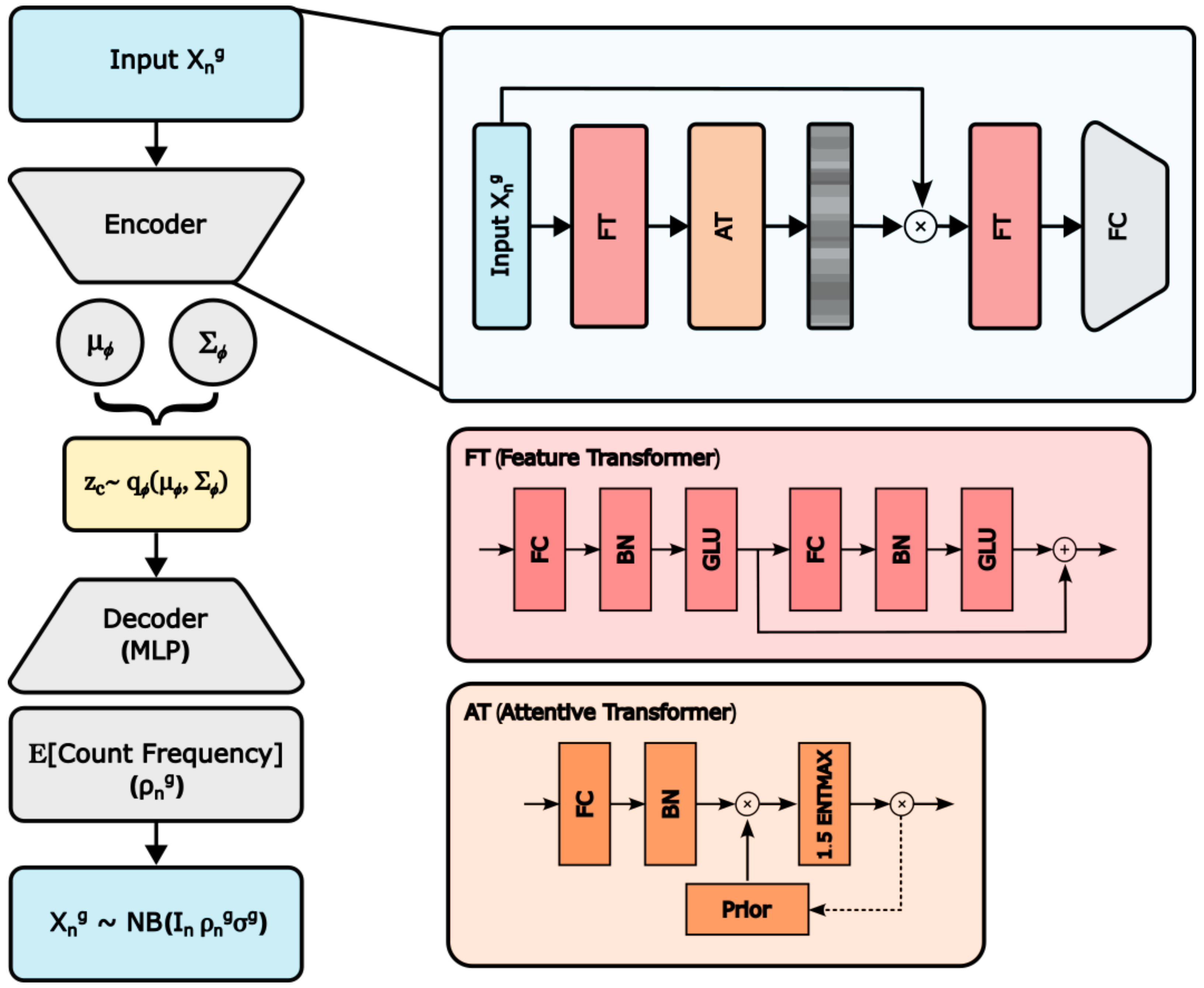
Introduction

- **We propose TabVI**: A probabilistic transformer model for **single-cell genomics**.
- Adapts transformer architectures to gene functionality, which is hierarchical and modular, unlike the sequential structure of natural language.
- Improves latent embedding learning. Validated on cell type annotation and integration benchmarks.
- Robust to dataset scaling using interpretable, sample-specific feature attention.
- Excels where large-scale foundation models are less effective in single-cell analysis.



Architecture combines the latent space interpretability of VAEs with a sample efficient tabular feature transformer.

References

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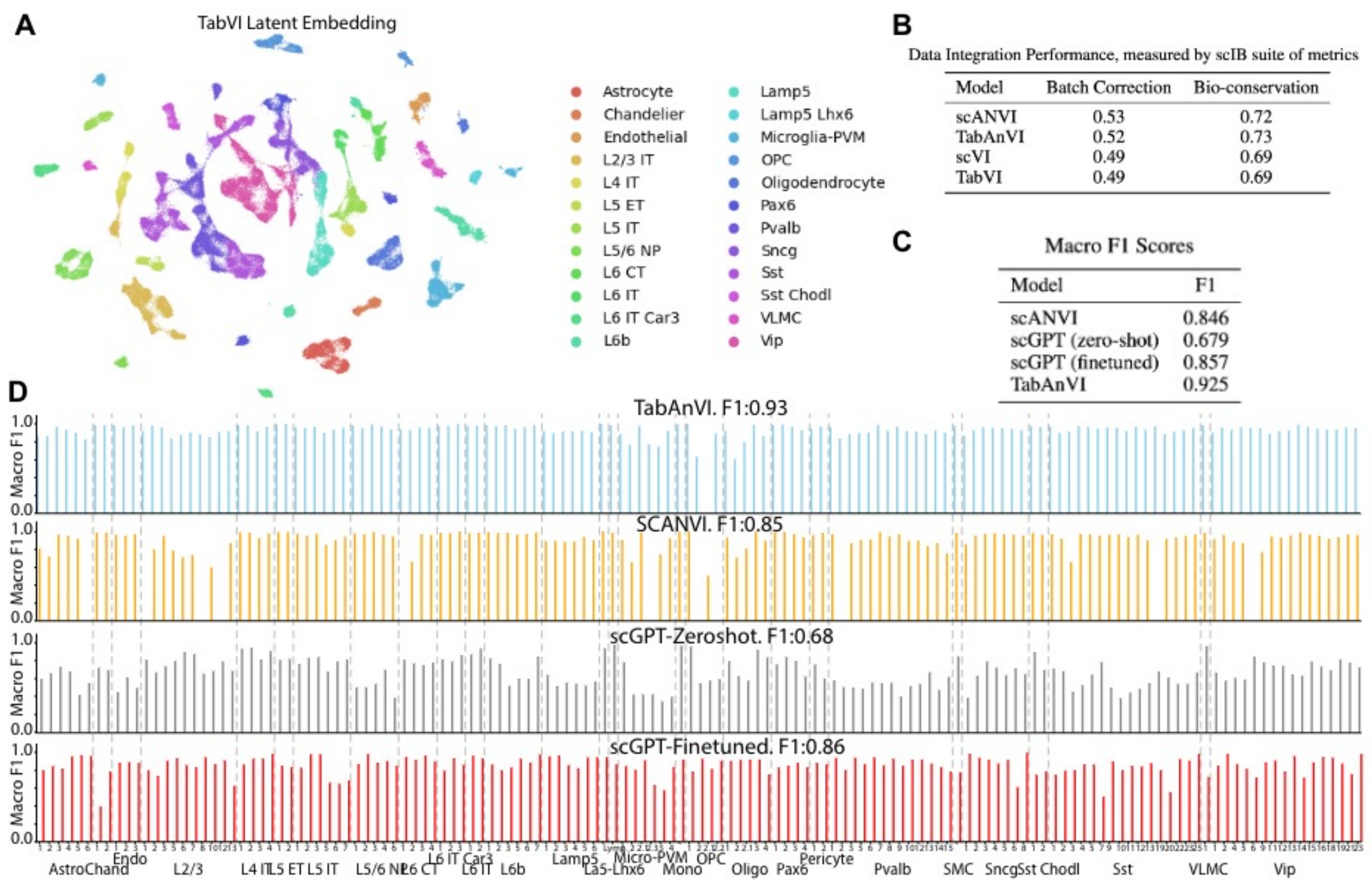
Results

Benchmarking across integration and annotation tasks.



B

Data Integration Performance, measured by scIB suite of metrics

Model	Batch Correction	Bio-conservation
scANVI	0.53	0.72
TabAnVI	0.52	0.73
scVI	0.49	0.69
TabVI	0.49	0.69

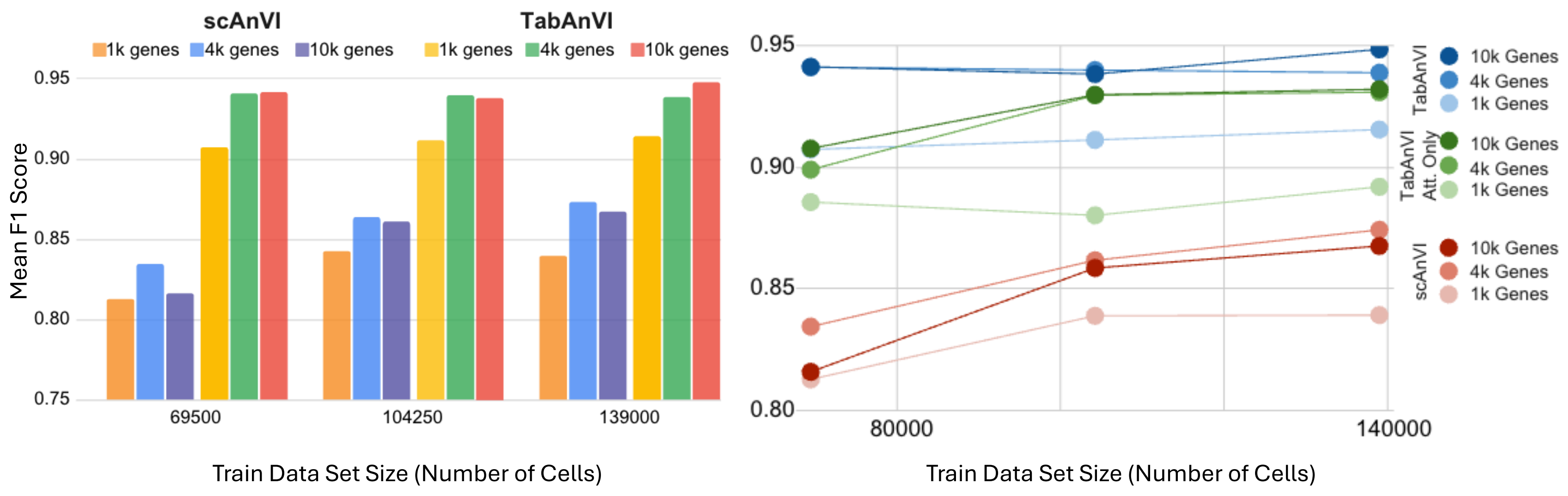
C

Macro F1 Scores

Model	F1
scANVI	0.846
scGPT (zero-shot)	0.679
scGPT (finetuned)	0.857
TabAnVI	0.925

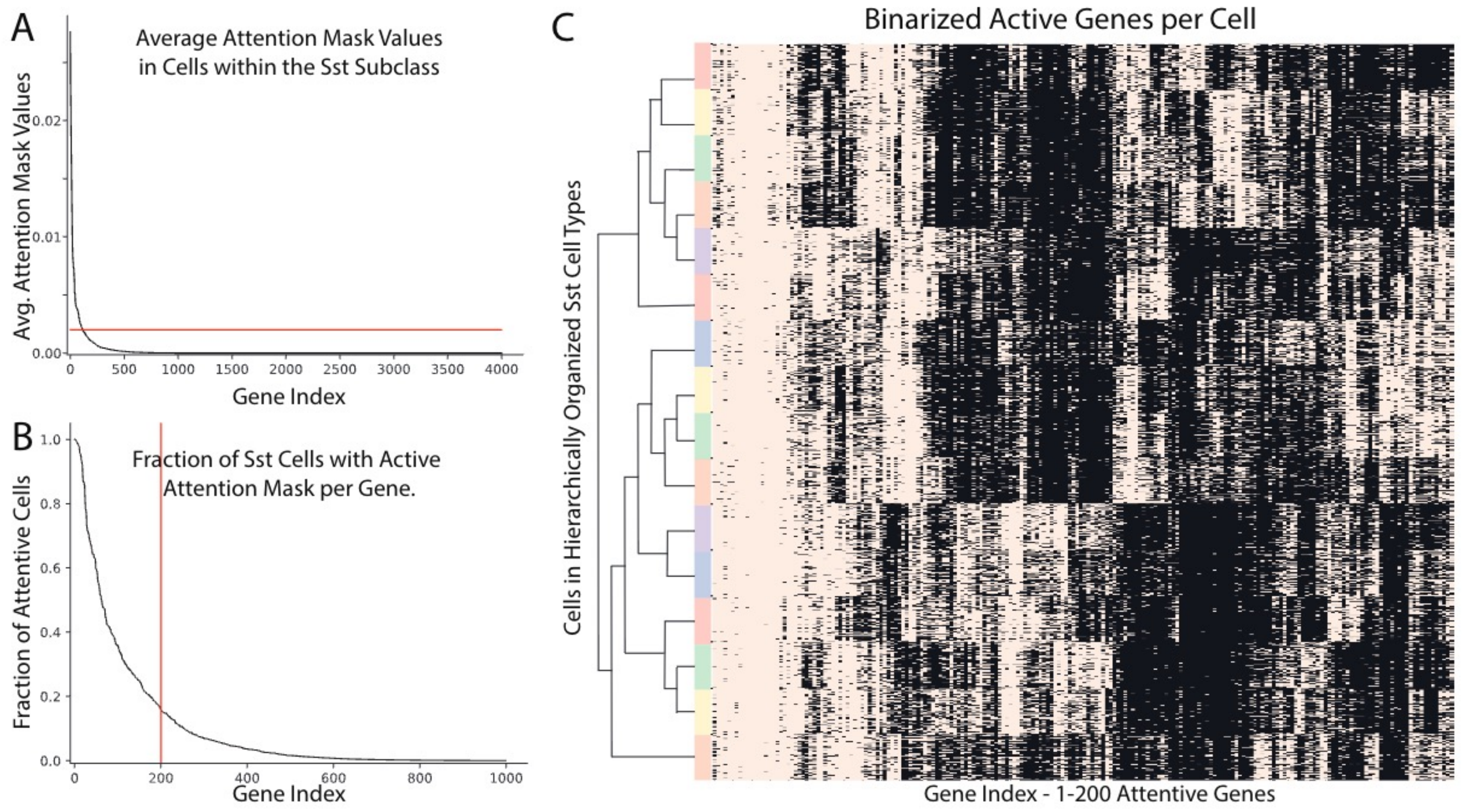
- TabVI's latent representations of human middle temporal gyrus cells originating from SEA-AD donors spanning the entire spectrum of AD (A).
- TabVI achieves higher overall classification performance compared to scAnVI [5] or scGPT [1] representations (B), while maintaining scVI's [3] representation capabilities (C).
- TabVI achieves high classification performance across cell types (D).

Scalability performance evaluated on subsets of features and observations.

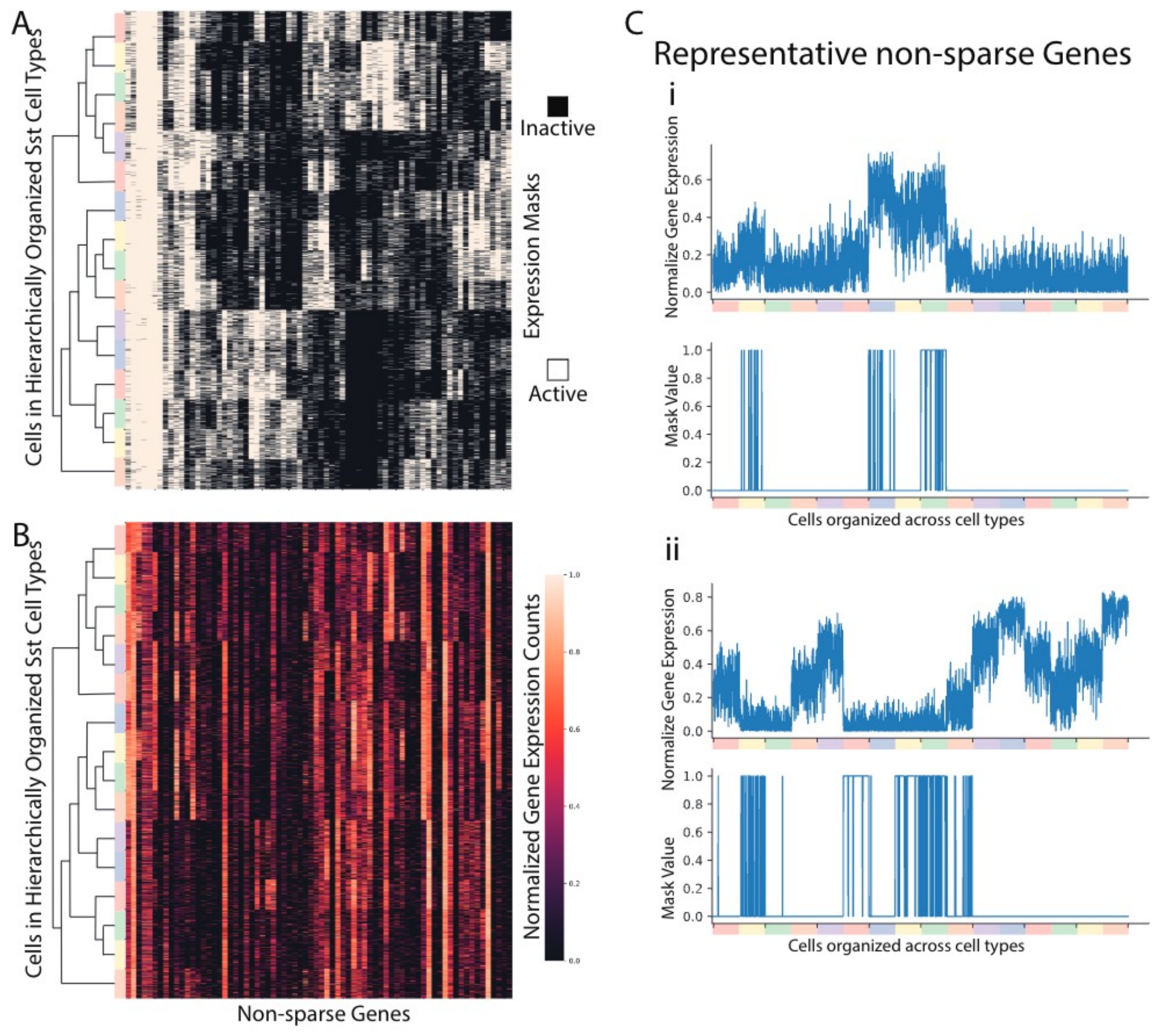


- We compare macro F1 annotation metrics from TabVI against scAnVI [5] when training data consists of fewer genes, fewer cells, or both.
- TabVI performance consistently improves when more features are introduced in the input data. *(left)*
- Each component of TabVI is necessary to produce peak performance (we show scAnVI [5], a model with attentive masking only, and TabVI, the model with both attentive masking and a tabular transformer)

Cell Type-specific Feature Selection



A. Threshold for "attended to" genes.
B. Fraction of Sst cells in which each gene is attended to (y-axis).
C. Heatmap of binarized attention mask values, arranged hierarchically by genes and stratified by cell types. Color denotes cell types within the Sst subclass.



A. Attention mask of non-sparsely expressed genes.
B. Normalized expression values corresponding to non-sparsely expressed genes. Cells and genes organized as in **(A)**.
C. Expression and mask values for representative, non-sparse genes.

- **The attention mechanism captures cell type-specific and combinatorial attention patterns.**
- These patterns are amplified when we select against sparsity.

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