

scMultiNODE: Temporal Single-Cell Data Integration across Unaligned Modalities



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Codes & Paper

github.com/rsinghlab/scMultiNODE

Introduction

Problem

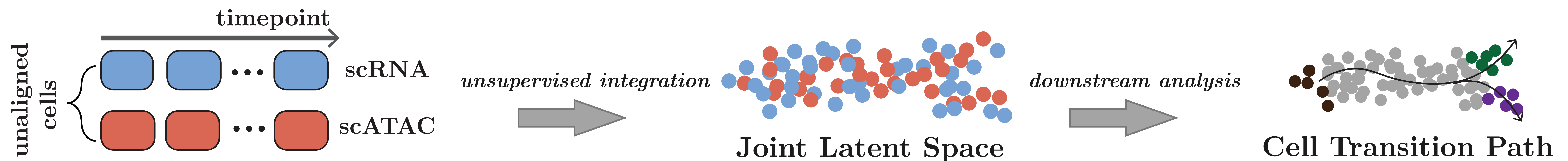
- Temporal scRNA-seq data are only profiled at discrete and sparsely spaced timepoints due to laborious and expensive lab experiments
- Obtaining different sequencing assays on the same cells across developmental stages is technically challenging

Goal

- Integrate unaligned cell profiles from two modalities: gene expression and chromatin accessibility
- Retain both **cell type variations** & **cellular dynamics** during integration

Solution

- Auto-Encoders (AEs) learn complex latent representation and preserve cell type variations
- Gromov-Wasserstein (GW) Optimal Transport aligns cells across timepoints and modalities
- Neural Ordinary Differential Equation (ODE) captures cellular dynamics



Method: single-cell Multi-Modal Neural Ordinary Differential Equation (scMultiNODE)

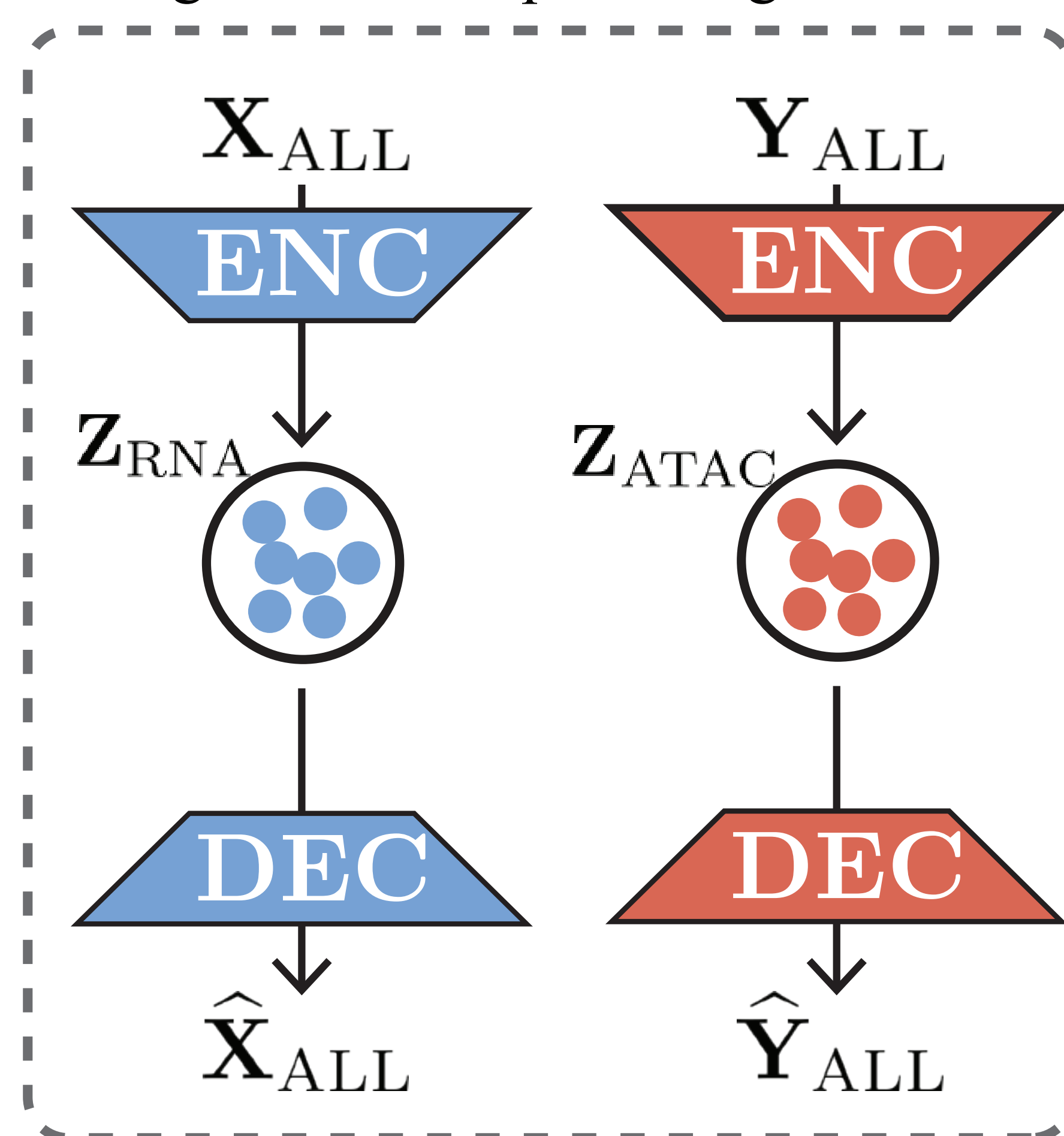
Input (e.g., scRNA-seq + scATAC-seq)

- Gene expression $\mathbf{X}^{(t)}$ at measured timepoints $t \in \mathcal{T}_{\text{RNA}} \subset \{0, 1, \dots\}$
- Chromatin accessibility $\mathbf{Y}^{(t)}$ at measured timepoints $t \in \mathcal{T}_{\text{ATAC}} \subset \{0, 1, \dots\}$

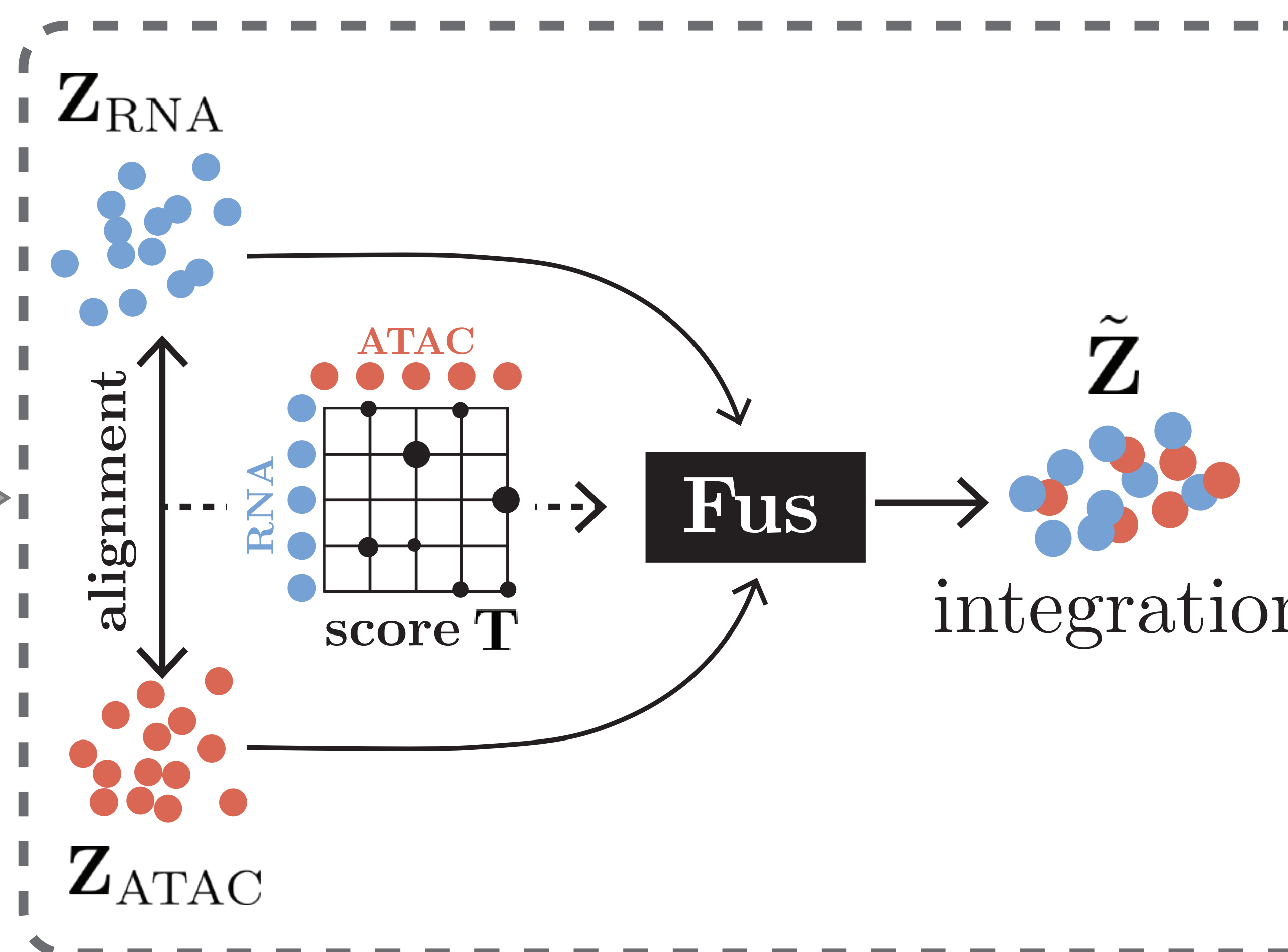
Advantage

- Quantization GW enables efficient alignment across large-scale multi-modal data
- Integrations capture both cell type variations and developmental dynamics

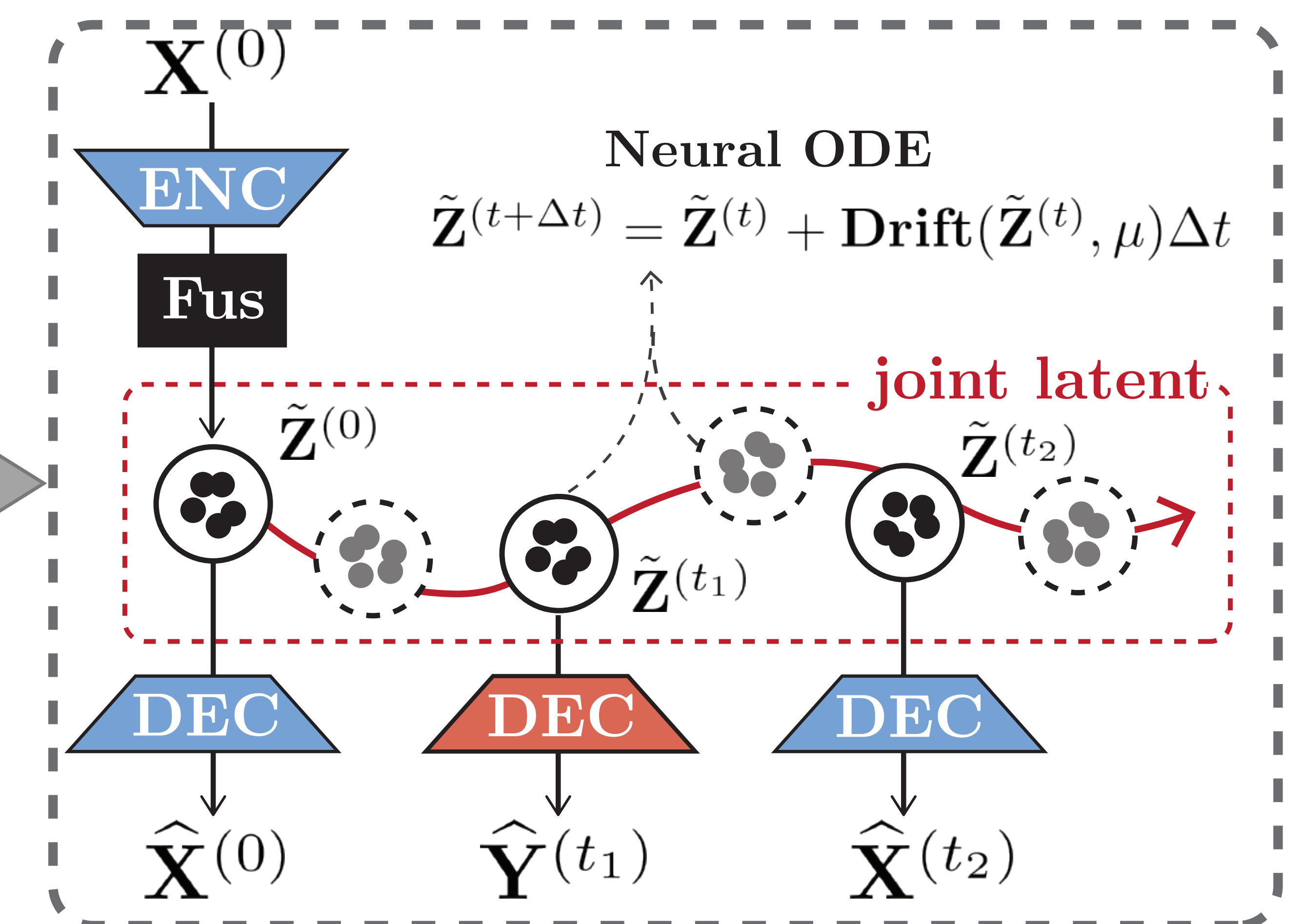
Stage I: Pre-train separate AEs to compress high-dim. and sparse single-cell data



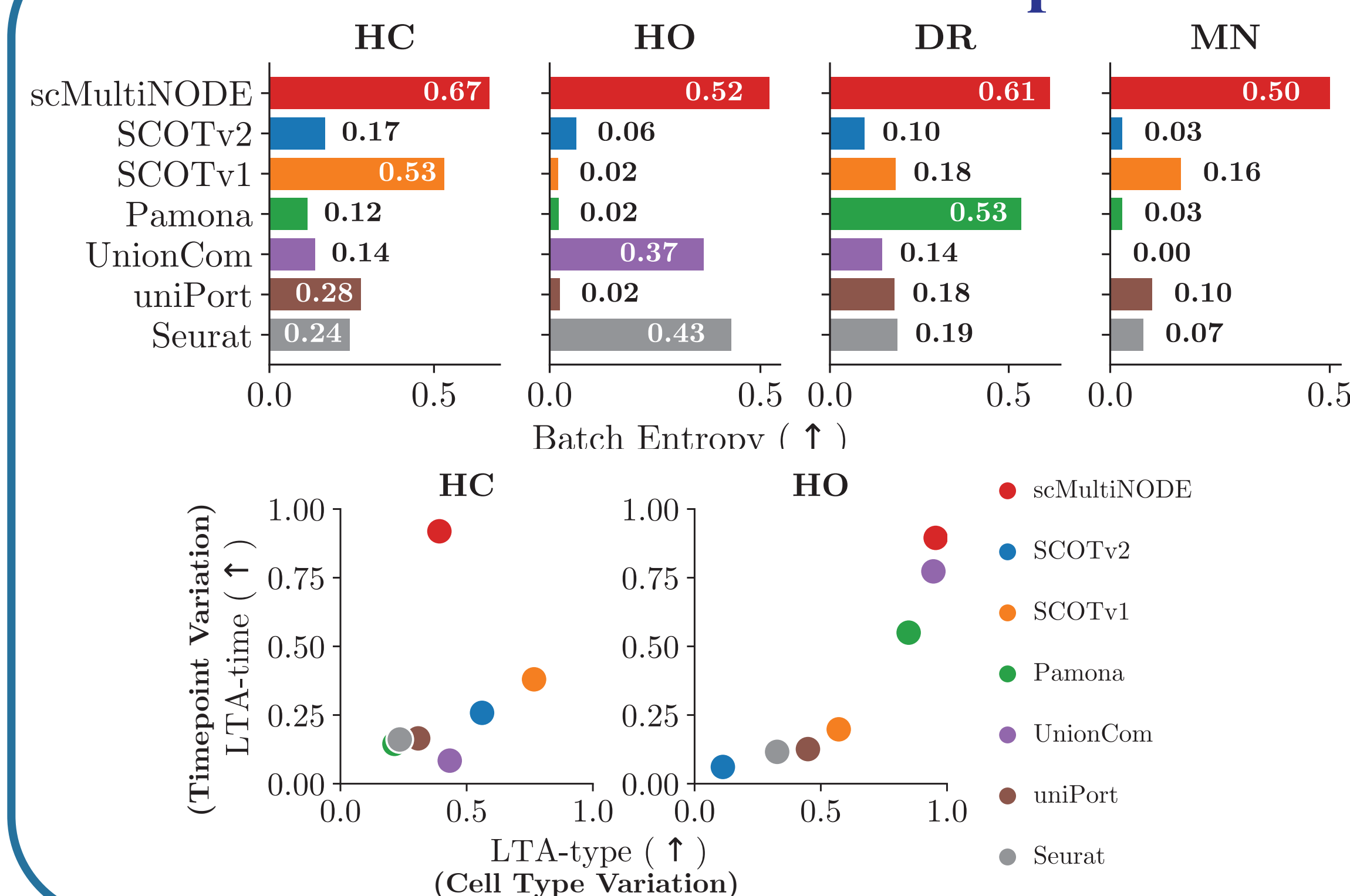
Stage II: Align modalities with GW Optimal Transport



Stage III: Incorporate cellular dynamics with Neural ODE



scMultiNODE Captures Cell Type Variations & Cellular Dynamics in Integration



Understanding Cell State Transition

