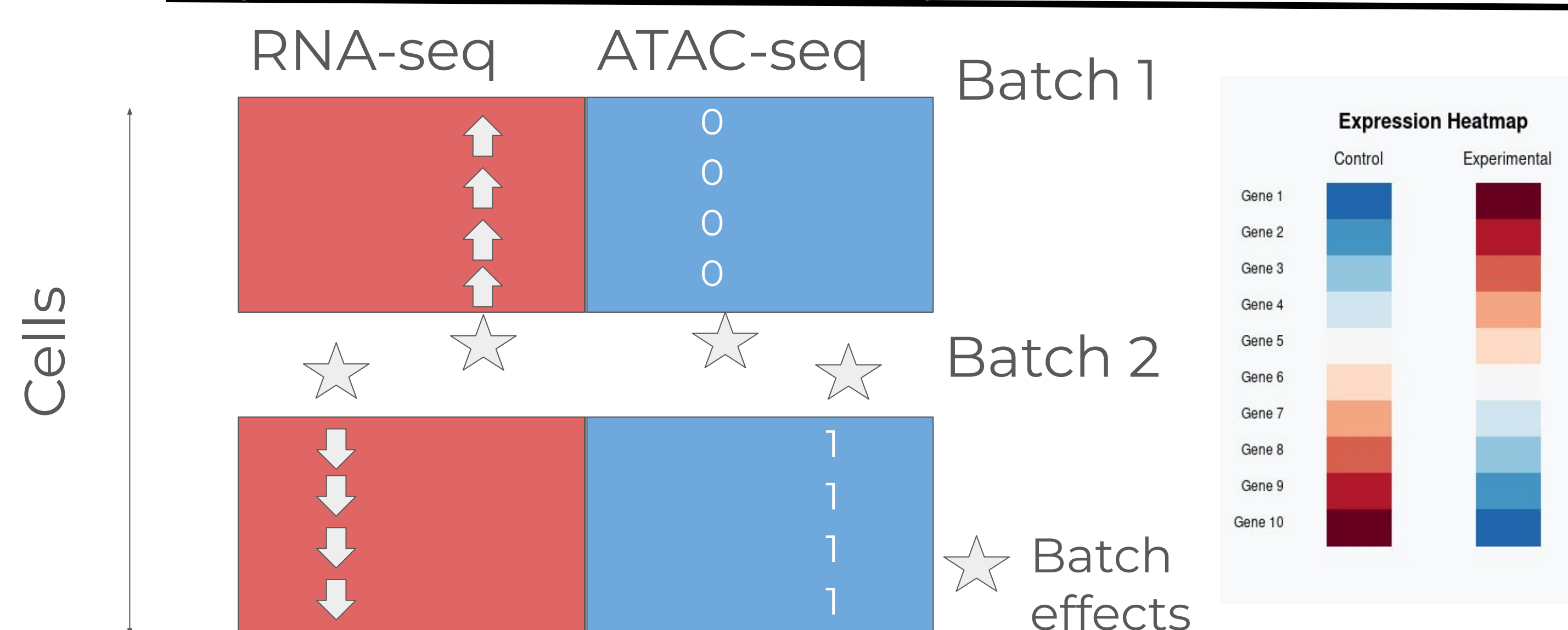


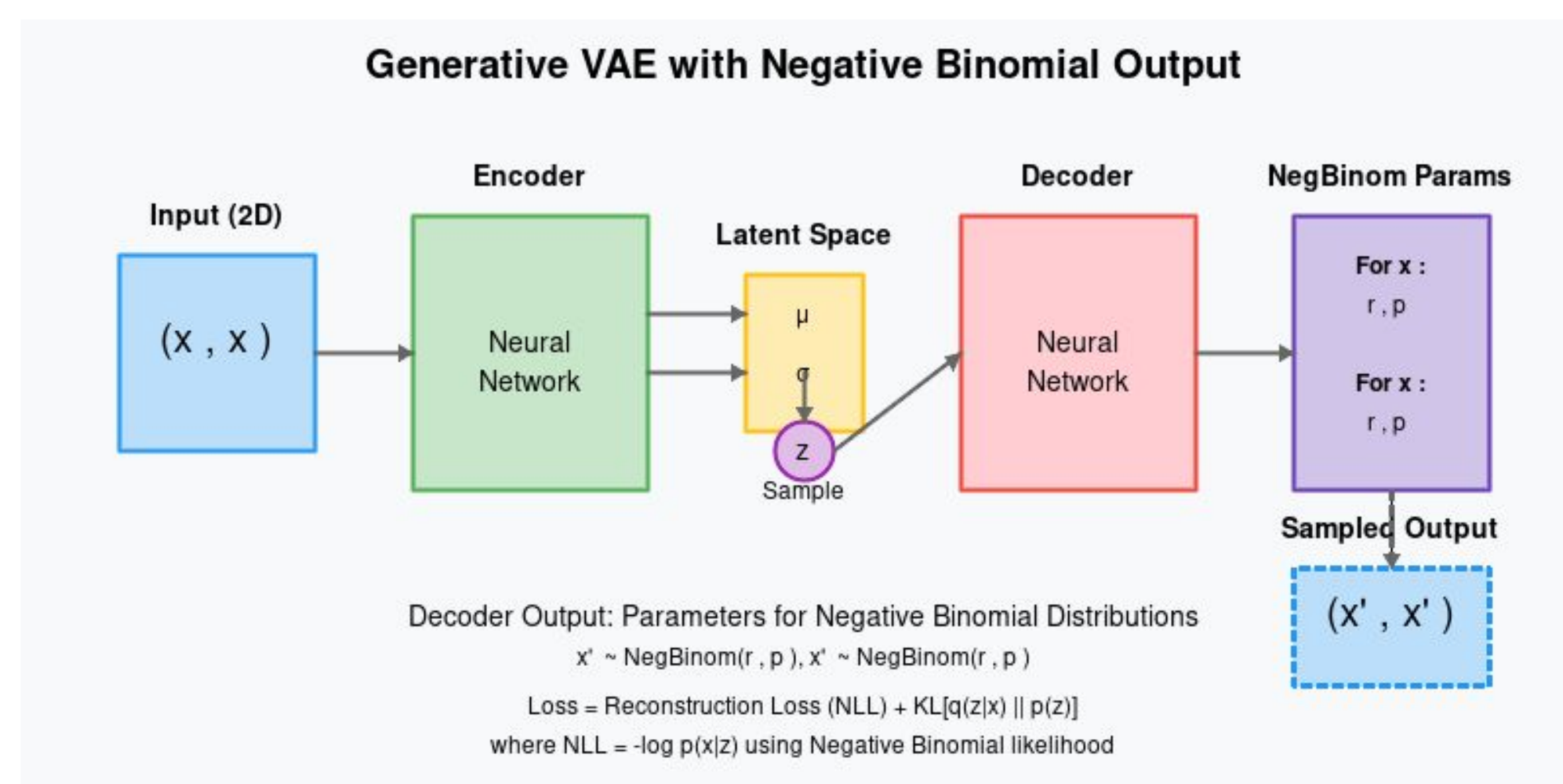
Deep generative single-cell representation learning

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Background & motivation



- **Analogy:** each **cell** is a **factory**. **RNA** counts the **products**. **ATAC** records which **patents** are available for production.
- **Motivation**
 - Compare healthy/diseased cells
- **Challenges**
 - **Compression:** >100k (sparse) features make analysis computationally challenging
 - **Normalization:** Batch effects create spurious cell signals



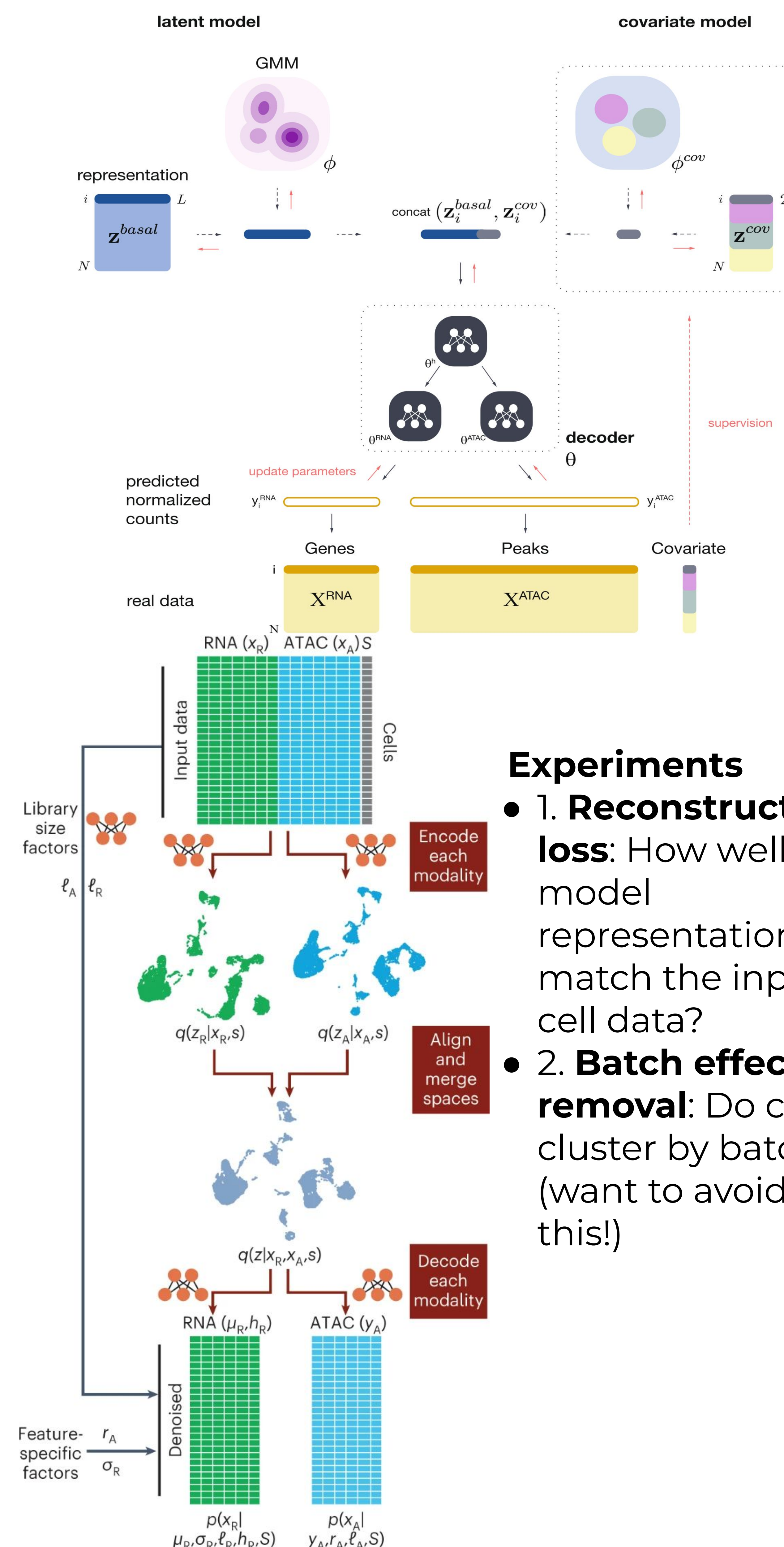
Generative representation learning models

- **Example:** Variational autoencoder
- **Goal:** Produce “latent representations” that compress and normalize input data
- **Architecture**
 - Encoder: outputs a latent representation
 - Decoder: outputs a reconstruction of input data, given the latent representation

Methods

Review and compare state-of-the-art models

- 1. MultiDGD (top-middle): a Gaussian Mixture Model (GMM) and generative decoder
- 2. MultiVI (bottom-left): a generative variational autoencoder

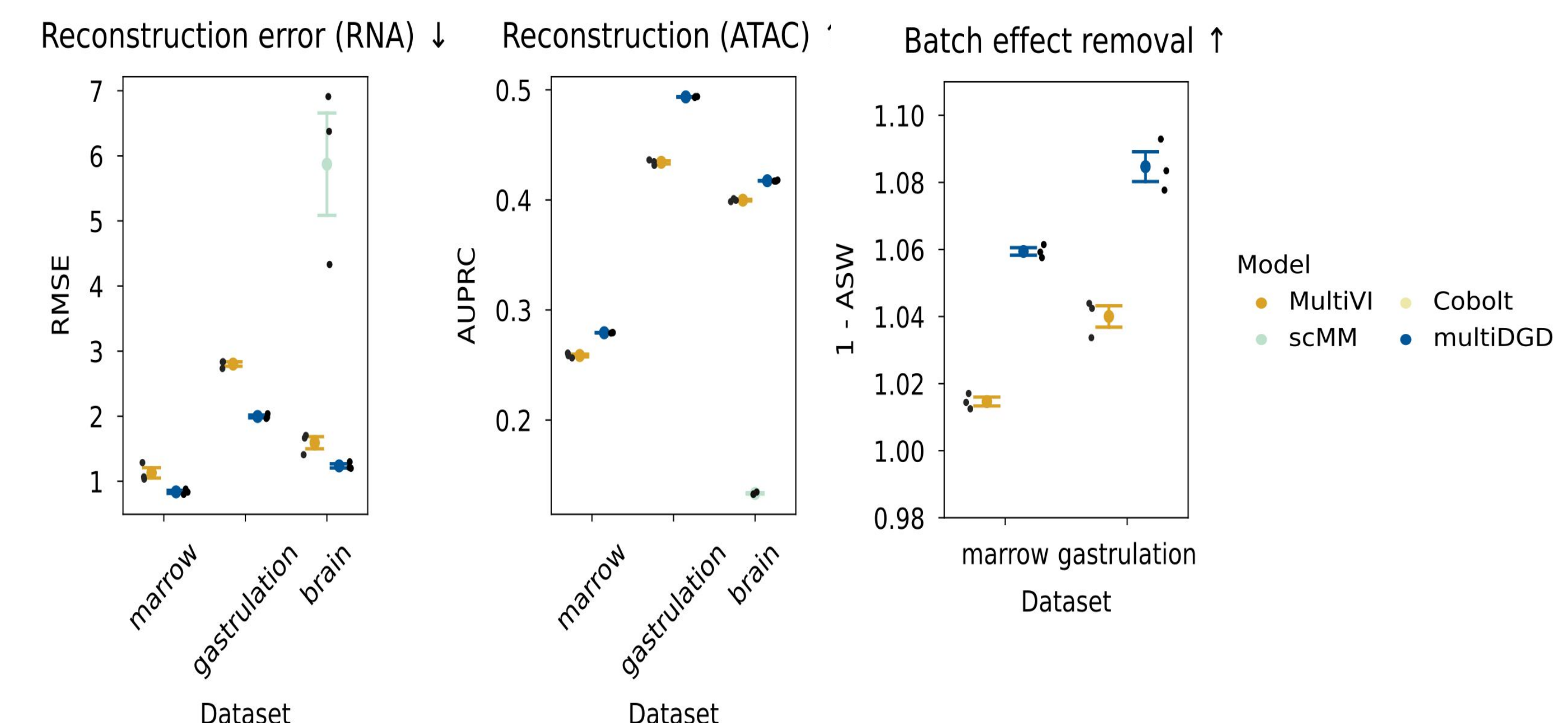


Experiments

- 1. **Reconstruction loss:** How well do model representations match the input cell data?
- 2. **Batch effect removal:** Do cells cluster by batch (want to avoid this!)

Results

Reported results



- Reconstruction is easier for RNA than ATAC
- Both models' representations do not cluster by batch

Reproduced results

Model	Dataset	RMSE (RNA)	Bal. Acc (ATAC)	1-ASW
MultiDGD	Human bonemarrow	0.925	0.764	1.061
MultiDGD	Mouse gastrulation	2.293	0.7318	1.078

Discussion

1. multiDGD's RNA reconstruction and batch effect removal was **successfully reproduced** (Bal. Acc used instead of AUPRC due to code constraints)
2. **Slow inference:** Both MultiVI and MultiDGD do “latent representation optimization” at test time

References

1. Schuster, V., Dann, E., Krogh, A., et al.: multidgd: A versatile deep generative model for multi-omics data. Nature Communications 15(1) (2024) 10031
2. Ashuach, T., Gabitto, M.I., Koodli, R.V., et al.: Multivi: deep generative model for the integration of multimodal data. Nature Methods 20 (2023) 1222–1231