

Benchmarking single cell RNA sequencing integration

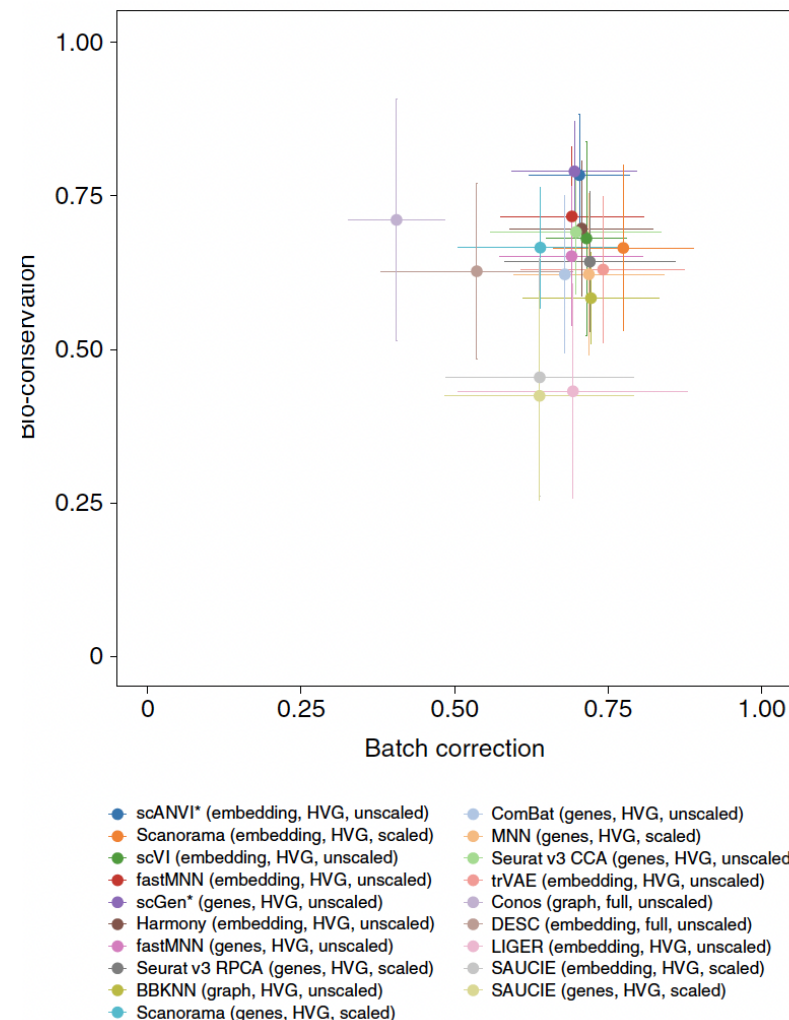
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05/02/2022

Background

- **Dataset:** Single-cell RNA sequencing (scRNA-seq) datasets.
 - each dataset consists of a **cell** by **gene** expression matrix, where cells are annotated with batches and labels.
- **Goal:** Combining high-throughput sequencing datasets to produce a self-consistent version of the data for downstream analysis.
- **Reason:** Integrating scRNA-seq helps biological findings.
- **Challenges:**
 - Dealing with noise, sparsity, batch effects and rare cell types.
 - Evaluating integration methods.

Background

- (Luecken, Büttner, Chaichoompu, Danese, Interlandi, Müller, Strobl, Zappia, Dugas, Colomé-Tatché, and others, 2022) benchmarked 19 methods in 13 integration tasks.
- They used 14 metrics to evaluate integration methods on their ability to
 - **remove batch effects**, and
 - **conserve biological variations**.
- They provided guidelines to choose an integration method given a task.
- For all methods, they used default parameters.



Methods

- Integrating scRNA-seq datasets usually include two parts:
 - jointly **embedding** high-dimensional input onto a shared latent space, and
 - (soft) **clustering** cells that incorporates annotated information (e.g. cell type).
- In this presentation, we aim to study the dependence of integration methods on the dimension of latent space.
- We focus on three methods that build deep generative models:
 - **scVI** (Lopez, Regier, Cole, Jordan, and Yosef, 2018),
 - **scGen** (Lotfollahi, Wolf, and Theis, 2019), and
 - **scANVI** (Xu, Lopez, Mehlman, Regier, Jordan, and Yosef, 2021).

Evaluation

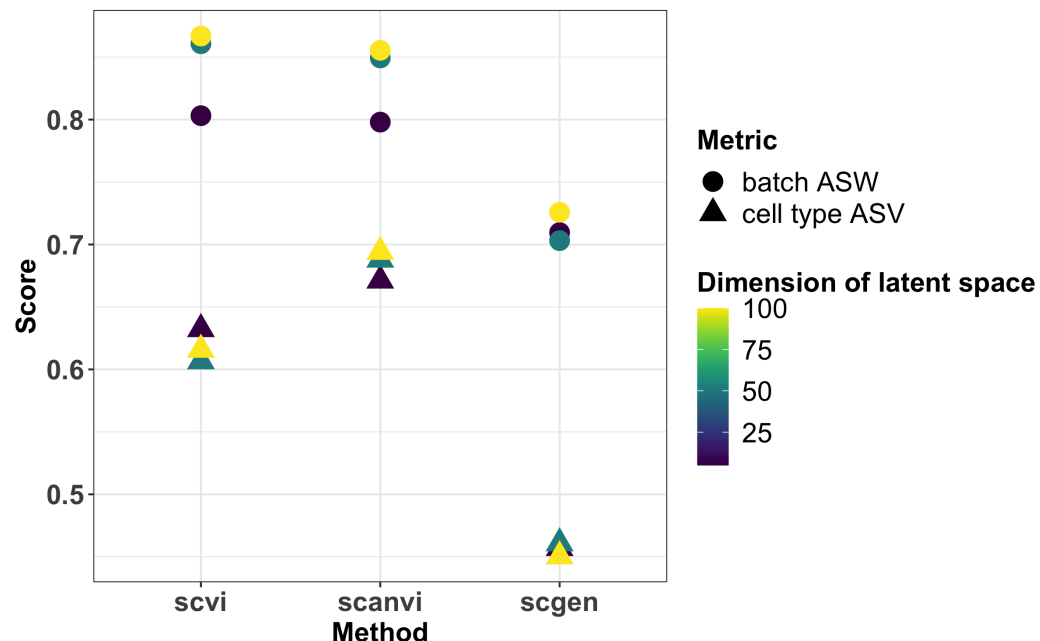
- Average silhouette width (ASW) measures the separation of clusters.
- We use modified **batch ASW** and **cell type ASW** to evaluate the ability of batch removal and biological conservation, respectively.
- For both, the larger ASW we have, the better.

Real-data analysis: human immune cell integration

- Task: integrating 5 datasets of 10 batches (donors) with cells from peripheral blood and bone marrow, annotated by cell types
- According to (Luecken, Büttner, Chaichoompu, et al., 2022), [scANVI](#) is one of the best methods, evaluated by a weighted mean of 14 metrics.

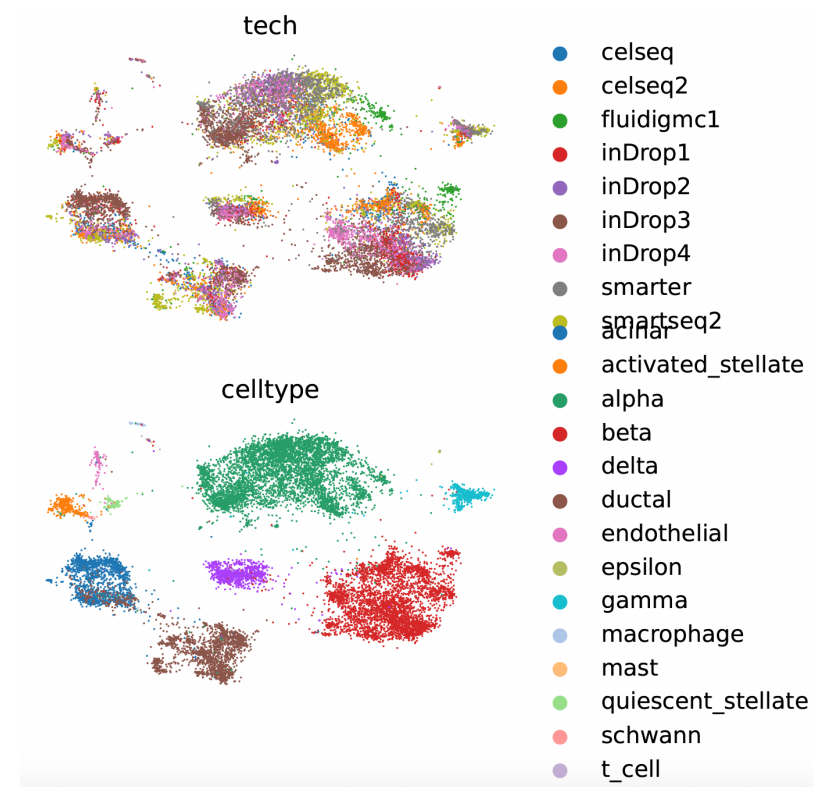
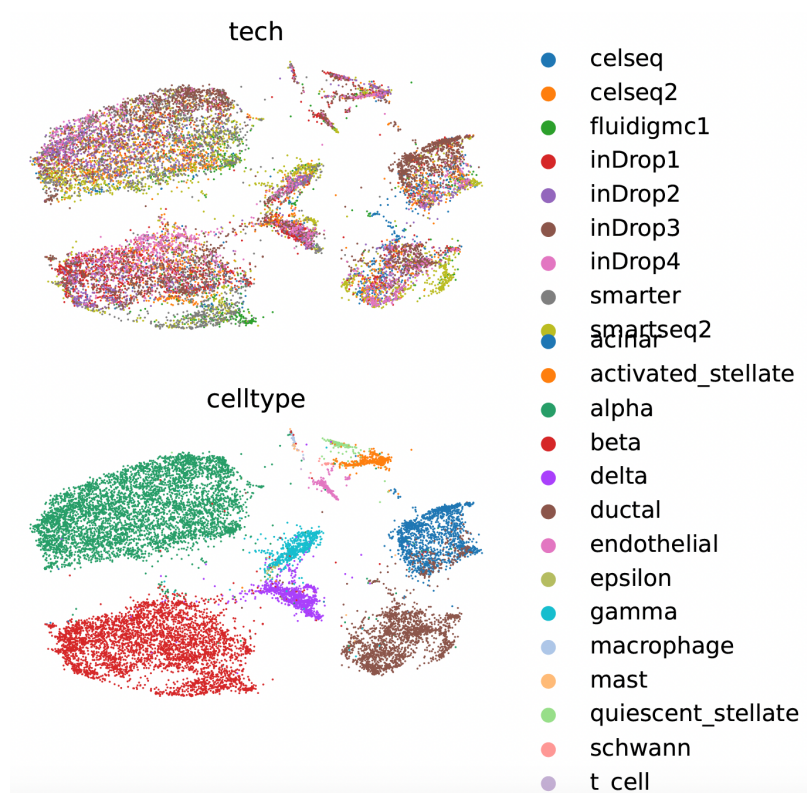
Results

- We vary the dimension of latent space, and evaluate **scvi**, **scanvi** and **scgen** using batch ASW and cell type ASV.
- Overall, **scgen** works worst.
- For **scvi** and **scanvi**, there is a trade-off between removing batch effects and conserving biological variations.
 - High-dimensional latent space leads to better batch removal and worse biological conservation.
 - The choice of latent space dimension doesn't affect the rank across methods.



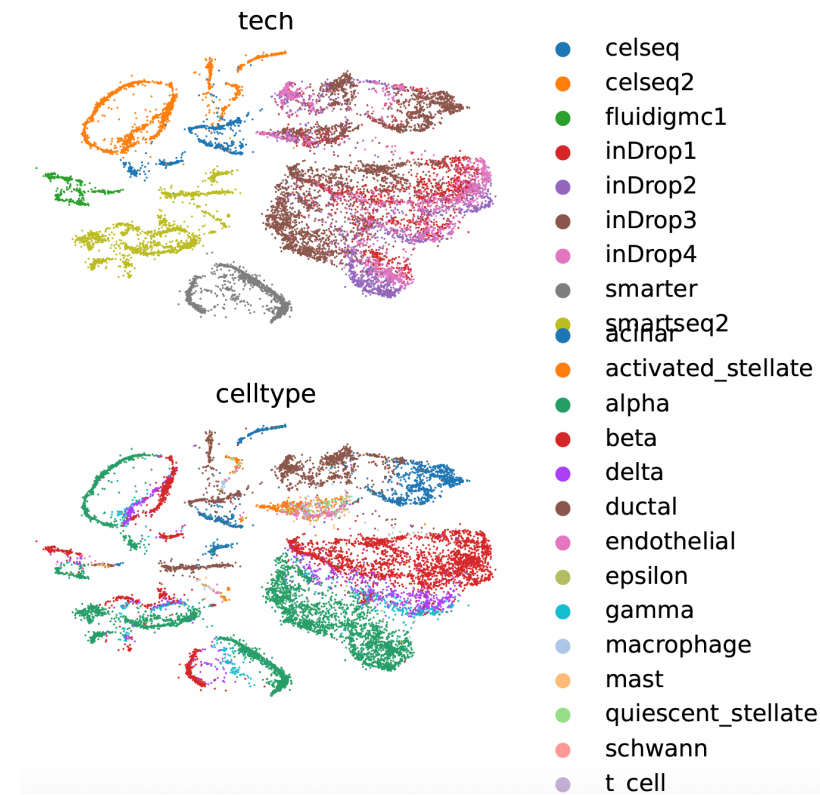
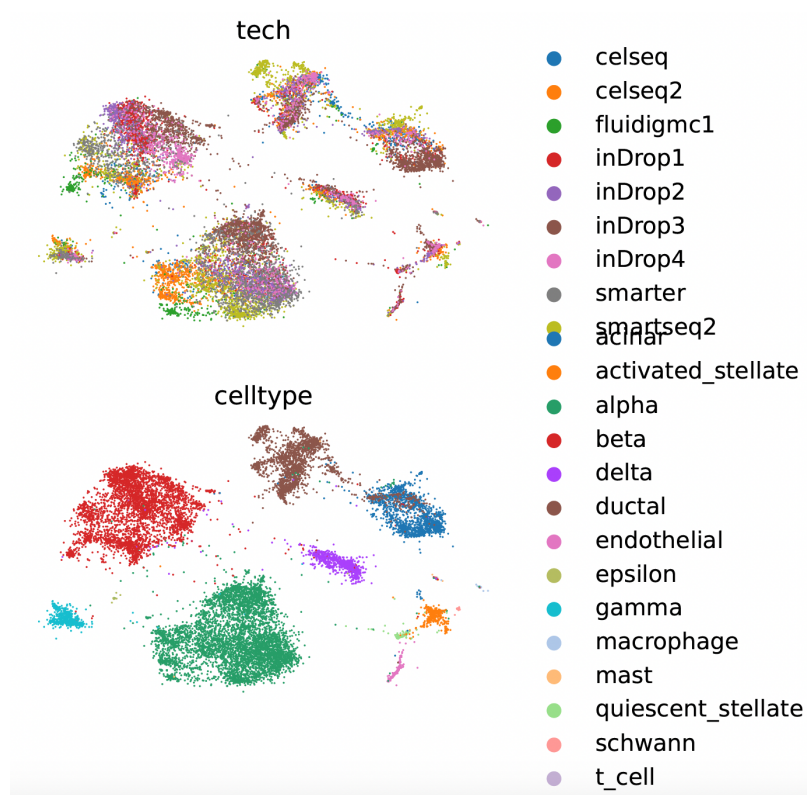
Results

Latent space fitted by **scvi** projected onto 2d space, with dimension of latent space (left) 5 and (right) 100, colored by (top) batches and (bottom) cell types.



Results

Latent space fitted by (left) **scanvi** and **scgen** projected onto 2d space, , colored by (top) batches and (bottom) cell types.



Takeaways

- For each method, the performance of integration methods is dependent on the dimension of latent space.
 - High-dimensional latent space leads to better batch removal and worse biological conservation.
 - That being said, it's hard to tell the difference in visualizations on 2d space.
- The choice of latent space dimension doesn't affect the rank across methods.

Reproducibility

- Results can be reproduced via https://github.com/XinranMiao/scRNA_int (not yet finished).



Thank You!
Questions?

References

Luecken, M. D., M. Büttner, K. Chaichoompu, et al. (2022). "Benchmarking atlas-level data integration in single-cell genomics". In: *Nature methods* 19.1, pp. 41–50.