

[A] Study Questions for “The art of using t-SNE for single-cell transcriptomics” by Kobak & Berens

1. What statistic do the authors use to quantify how well embeddings capture local structure in high-dimensional single-cell gene expression profiles? What about global structure? Think about what local and global mean in this context.
2. Why do the initial values for the t-SNE algorithm change the result? Do you think it makes sense to initialize with PCA?
3. The authors argue that tuning how you use an embedding algorithm is potentially more important than which algorithm you use (e.g., t-SNE vs. UMAP). Does this “art” aspect comfort you or make you nervous?

[B] Study Questions for “The specious art of single-cell genomics” (preprint) by Chari, Banerjee & Pachter

1. (*open ended discussion*) What do you think is the most surprising/unexpected result that the authors present in their analysis? How does this change your perspective on dimensionality reduction methods?
2. What statistic do the authors use to quantify how well embeddings capture local/global structure in high-dimensional single-cell gene expression profiles? Do you think their results are contradicting what has been reported in Kobak et al.?
3. What are equidistant cells? Can you find an example where this definition can be meaningful biologically?
4. What is (semi-) supervised dimensionality reduction and why do the authors think it can help in the analysis of single cell data? Are supervised methods always better than unsupervised methods?
5. How do the authors evaluate the performance of their proposed semi-supervised MCML method? Which benchmark/figure provides the most compelling evidence in favor of their approach?
6. (*open ended discussion, cont'd*) The paper is still in preprint form and is likely submitted for peer review. From a reviewer’s perspective, what would you consider as the major strengths/weaknesses of the paper?