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SINGLE-CELL ANALYSIS USING HIERARCHICAL AUTOENCODER

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BACKGROUND

Defining cell types through unsupervised learning is considered one of the mainstay for single-cell RNA sequencing (scRNA-seq) analysis. However, the ever-increasing number of cells, technical noise, and high dropout rate [1] pose significant computational challenges in scRNA-seq analysis [2].

OBJECTIVES

Developing an accurate and scalable clustering method, single-cell Decomposition using Hierarchical Autoencoder (scDHA), for single-cell sequencing data.

METHODS

Normalization

Data is log transformed and rescaled to 0 and 1.

Gene Filtering

scDHA use a non-negative kernel autoencoder to filter out genes or components that have insignificant contribution to the data.

Dimension Reduction

scDHA uses Stacked Bayesian Self-learning Network that is built upon the Variational Autoencoder (VAE) to project the data onto a low dimensional space.

Clustering

scDHA uses k-nearest neighbor spectral clustering to separate the cells into different groups.

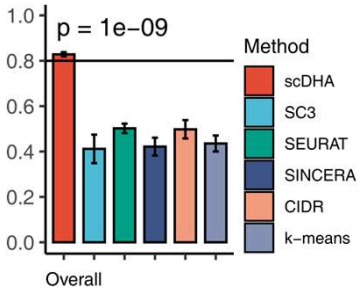
Visualization: Using the compressed data, scDHA project the data to 2-dimensional space for visualization.

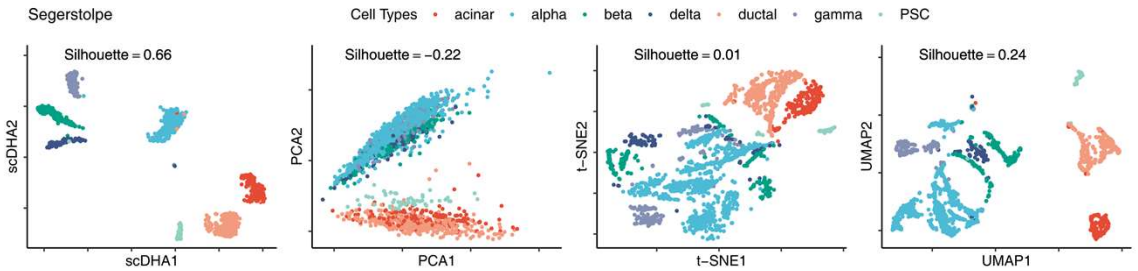
RESULTS

Data: The method is validated using 24 real single-cell datasets.

Clustering: scDHA outperforms current state-of-the-art (SC3 [3], Seurat [4], SINCERA [5], CIDR [6]) in clustering accuracy. Accuracy is measured by adjusted Rand Index (ARI).

Visualization: Using compressed data, scDHA is more efficient than both t-SNE and UMAP, as well as the classical principal component analysis (PCA) in visualizing single-cell data.





CONCLUSION

scDHA is an accurate method for scRNA-seq data clustering. Using two autoencoders in a hierarchical setting, scDHA can effectively transform high dimensional scRNA-seq data to a low dimensional space. This compressed data can be used in downstream applications.

FUTURE WORK

- Expanding scDHA to work with other data type such as Hi-C [7], network [8], or multi-omics data [9, 10].
- Applying hierarchical autoencoder concept to other areas such as predicting cellular spatial position [11], or pathway analysis [12].

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