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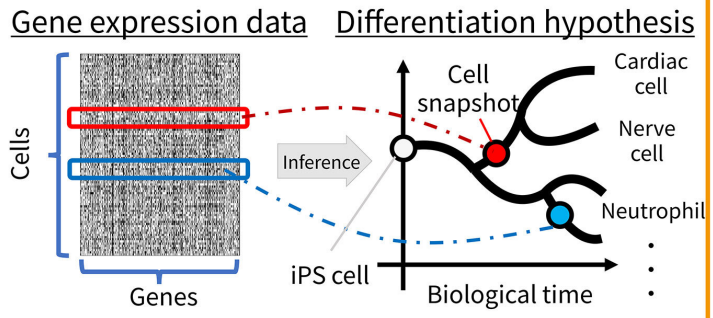
Interactive hypothesis testing on cell differentiation

Seeking to capture the growth trajectory of cells

Abstract

Biological cells develop into various organs and tissues through differentiation. How individual cells undergo this differentiation process is a critical and universal question in the life sciences. To elucidate these differentiation mechanisms, it is essential to both generate hypotheses and test them. Therefore, we are constructing a new mathematical framework for hypothesis generation and testing. Specifically, this technology assists life science researchers in interactively discovering hypotheses through AI, which aids in the visual design of differentiation structure hypotheses and in testing of their validity. Deeper insights into the mechanisms of biological cell differentiation may enable us to induce differentiation phenomena involving various genetic and environmental factors. By investigating the causes of congenital diseases and the efficacy of medications for designated intractable diseases, we aim to contribute to the advancement of regenerative medicine and artificial organ technology.

Cell differentiation inference



Purpose: Understanding of differentiation mechanism

Application: Regenerative medicine and gene therapy

Challenges of differentiation inference task

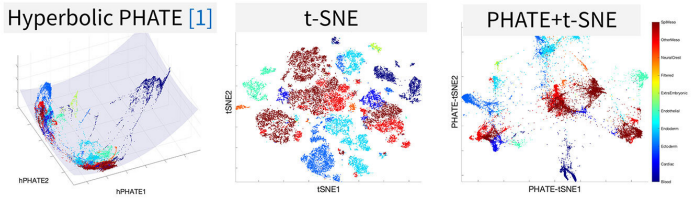
- **Current standard approach**：High-dimensional gene expression features are visualized in a lower dimension using dimension reduction techniques, and experts interpret them.

■ **#1: Unknown nature of genes responsible for local differentiation**

Each specific gene is thought to play a major role in the local differentiation of cells. However, in order to verify the genes-cause-differentiation hypothesis, the differentiation structure itself is required.

■ **#2: Lack of established metrics for assessing validity of visual rep**

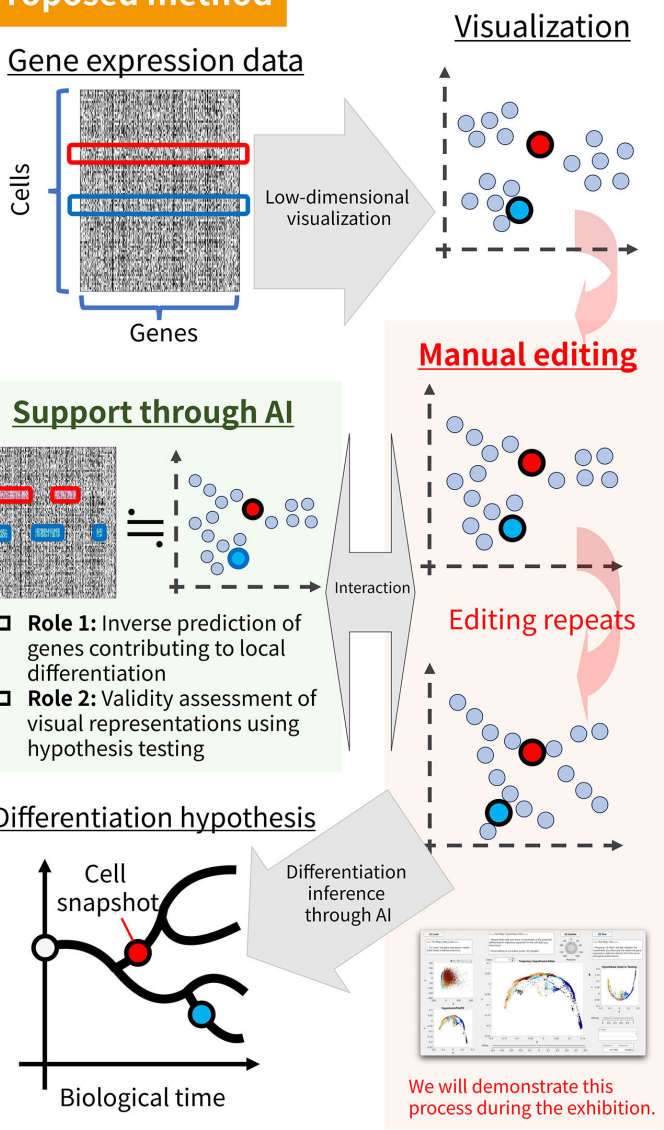
In general, visualization techniques carry the risk of removing important clues about the differentiation structure during compression, as well as the risk of introducing misunderstanding that were not present in the original data.



Examples of three types of visualizations for same gene expression data

Data：Han+, Single cell transcriptomics identifies a signaling network coordinating endoderm and mesoderm diversification during foregut organogenesis, Nature Communications 2020.

Proposed method



References

[1] M. Nakano, H. Sakuma, R. Nishikimi, K. Komiya, T. Iwata, K. Kashino, “HyperbolicPHATE: Visualizing Continuous Hierarchy of Latent Differentiation Structures,” *IEEE International Conference on Acoustics, Speech and Signal Processing (ICASSP)*, 2025.

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