PseudotimeDE: inference of differential gene expression along cell pseudotime from single-cell RNA sequencing data

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Abstract

To investigate molecular mechanisms underlying cell state changes, a crucial analysis is to identify differentially expressed (DE) genes along the pseudotime inferred from single-cell RNA-sequencing data. Therefore, we propose PseudotimeDE, a DE method that adapts to various pseudotime inference methods, accounts for pseudotime inference uncertainty, and outputs well-calibrated $p$-values.

Methods

We compare PseudotimeDE to existing DE methods on simulated datasets. PseudotimeDE generates well-calibrated $p$-values (a,b,g) and strongly correlates with true cell-cycle signals (b). PseudotimeDE also yields highest power (f).

Results: Comparison to Existing DE Methods on LPS-Dendritic Cell Dataset

Histograms show all genes' $p$-values by the three DE methods (a & e). Compared to other DE methods, many more GO terms are enriched in the PseudotimeDE-specific DE genes (c & g). Many of these GO terms are related to LPS, immune process, and defense to bacterium (d & f).

Results: Comparison to Existing DE Methods by Simulation

We compare PseudotimeDE to existing DE methods on simulated datasets. PseudotimeDE generates well-calibrated $p$-values (a,b,g), better FDR control (c & h) and higher power (e & j).