University of California, Irvine
Statistics Seminar

Analysis of Single-cell Data with Time-variant Clustering

Sheng Zhong
Professor, Bioengineering
UC San Diego

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(Bldg. #314 on campus map)

It remains an open question when and how the first cell fate decision is made in mammals. Using single-cell RNA sequencing of embryonic cells (a.k.a. blastomeres), we report highly reproducible inter-blastomere differences among ten 2-cell and five 4-cell mouse embryos. Inter-blastomere gene expression differences dominated between-embryo differences and noise, and were sufficient to cluster blastomeres into distinct groups. Dozens of protein-coding genes exhibited reproducible bimodal expression in sister blastomeres, which cannot be explained by random fluctuations. These data suggest that reproducible cellular differences may have occurred at earlier developmental time than what's previously thought (Genome Res, 24:1787-1796). Inspired by this biological question, we initiated theoretical work to tackle the clustering problems for time course data in which the cluster number and clustering structure change with respect to time, dubbed time-variant clustering. We developed a hierarchical model that simultaneously clusters the objects at every time point and describes the relationships of the clusters between time points (PNAS, 111:E4797–E4806). Our method inferred three genes to be associated with the earliest cell fate decision, which was corroborated by experimental validations.

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