Spatial Transcriptomics Deconvolution Methods

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Spatial Transcriptomics

▶ Single cell RNA sequencing technologies (scRNA-seq) have allowed for low level cell-specific profiling of expression.

▶ However, this technique does not give any out information on the localized expression within a tissue sample - the expression rates are aggregates of each cell without spatial location context

▶ Spatial transcriptomics results in gene expression rates at each "spot" (a set sized group of cells) in a tissue sample, giving a spatial location on the tissue to each expression value

▶ One of the current challenges with spatial transcriptomics is its lack of specificity - each spot contains multiple cells of differing types in some proportion - which can can only be found through "deconvolution" of cell type proportions

MuSiC

- ▶ Bulk tissue RNA-seq data is similar to scRNA-seq data taken over various tissue states (ie progressions in a disease over time) and identifying cell type proportions within each state allows for exploration of its relationship with tissue state transitions

- ▶ MuSiC improves upon upon methods like CIBERSORT in that it does not require a pre-selection method to knock out insignificant genes and is sensitive to correlations/relationships between gene expression within a single cell across status

MuSiC

▶ Under some assumptions, the relative proportion of a particular gene across the tissues in a subject is proportion to a multiplicative combination of the proportion of that gene for a particular cell type, the molecular size (number of) that cell type, and the proportion of cells of that type - what we want to find

▶ The assumptions are: 1) the samples are all from the same population with the same distribution of gene proportions 2) the relative proportion of cell molecular sizes is the same across all states 3) the average read count is the same across varying cell types in all states

▶ The proportionality can be constrained since all cell type proportions must be non negative and the sum of proportions per each state must sum to 1