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Differential variability and consensus clustering of genes in spatial transcriptomics

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Spatial transcriptomics enables genome-wide profiling of gene expression while preserving tissue architecture, providing new opportunities to study cellular heterogeneity and the tumor microenvironment. Current differential expression methods in this field primarily target mean differences across tissue domains, whereas differential variability of expression has been less explored. We propose a two-part framework for variance differential expression in spatial transcriptomics. The first part extends Levene's test to identify genes showing differential variability across pre-defined tissue domians. The second part applies multi-metric consensus clustering to these genes, grouping them into stable clusters that capture shared spatial patterns of variability across tissue regions. These clusters may highlight gene modules that reflect heterogeneity among tumor, stromal, and immune-infiltrated regions. We applied the framework to a 10x Genomics melanoma brain metastasis dataset and an invasive ductal carcinoma breast tissue dataset, where it revealed spatially variable genes and gene clusters linked to tumor microenvironment.