

Reviewer Report

Title: SMIntegration: A Web Tool for Comprehensive Spatial Metabolomics and Transcriptomics Integrated Analysis and Visualization

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Reviewer name: Reviewer 3

Reviewer Comments to Author:

This manuscript presents a web application for the integrated analysis of spatial metabolomics and spatial transcriptomics data, which will be of great interest to many researchers. However, the tool currently lacks several important data preprocessing steps. Users must perform these steps using other software, which demands substantial programming skills and compromises user-friendliness. My specific comments are as follows: Major: 1. Data preprocessing for spatial metabolomics data was done using the Cardinal package, and for spatial transcriptomics data using Seurat in this manuscript. This significantly reduces user-friendliness and requires substantial programming skills to use SMIntegration, making this tool difficult for many users. Please consider integrating the data preprocessing steps directly into SMIntegration. 2. Please consider adding a registration function in SMIntegration using the SpatialData package, as this is one of the most critical steps for integrated spatial metabolomics and transcriptomics data analysis. 3. Line 143: LogNormalization does not work well for spatial metabolomics data due to its highly sparse nature. More common methods are TIC normalization and root mean squared normalization. Minor: 1. Line 90: Add the word "spatial" (e.g., "spatial metabolomics"). 2. Line 100: Your workflow does not include the complete processing steps. Please consider removing the word "preprocessing." 3. Line 159: Why is the default threshold for the fold-change value so small? 4. Line 189: The authors appear to confuse "mass features/peaks" with "metabolites." Please replace "metabolites" with "mass peaks" or "mass features" throughout the manuscript and in Figure 1.5. Line 188: SManalyst identifies metabolites only through monoisotopic ion matching, which is considered Level 3 metabolite identification. The authors should state this clearly in the manuscript and exercise caution when interpreting the data throughout the manuscript.

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