

## Reviewer Report

**Title: Deciphering spatial domains from spatially resolved transcriptomics with Siamese Graph Autoencoder**

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**Reviewer name: Ruoyan Li**

### Reviewer Comments to Author:

In the manuscript entitled 'Deciphering spatial domains from spatially resolved transcriptomics with Siamese Graph Autoencoder', Cao et al developed a new computational framework for spatial domain identification in spatial transcriptomics data. The new framework (SGAE) incorporates the power of Siamese Graph Autoencoder, which mitigates the information correlation at both sample and feature levels. Through a series of benchmarking based on ST datasets generated from different platforms, the authors show that SGAE outperforms other ST clustering methods. Particularly, SGAE has shown its potential for extension and application in multi-slice 3D reconstruction and tissue structure investigation. Overall, the manuscript describes a useful computational framework for ST data clustering and spatial domain identification. The method is sound and the manuscript is well-written. A few points need to be addressed before publication. 1. The authors used datasets from different ST platforms and various tissues to examine the performance of SGAE and benchmark against other ST clustering methods. The ST data used in the current manuscript are all from tissues with clear structures such as the mouse cortex and human dorsolateral prefrontal cortex. However, to show the versatility of SGAE, can the authors test its performance when handling more complex and heterogenous tissues like tumors. It would be useful to show the results. 2. The authors benchmarked SGAE based on several metrics including ARI, NMI, and FMI. However, the current description of these benchmarking metrics and how exactly benchmarking has been conducted (in the method section) is rudimentary in the manuscript. More detailed information in both the main text and the method section is essential for a better understanding of the method and manuscript. 3. More tutorials regarding how to use SGAE need to be included on the Github page. 4. The current resolution of all figures in the manuscript is poor, which largely influences the reading. Can authors improve the figure resolution in revision?

### Level of Interest

Please indicate how interesting you found the manuscript: Choose an item.

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