

Review of: "A Novel Variable Neighborhood Search Approach for Cell Clustering for Spatial Transcriptomics"

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Potential competing interests: No potential competing interests to declare.

- 1. As stated in the abstract, initially, the challenge was "confronted" or addressed as an Integer Linear Programming minimization problem. Did the considered problem type change later? The confronted word feels a little harsh.
- 2. A number of clustering and embedding methods are discussed in great detail in the Background section. The reason why some are and some are not useful in the current research would have been sufficient.
- 3. A literature survey of similar problems was expected.
- 4. A schema or block diagram could better convey the underlying idea in this article to a reader. This article really lacks diagrams that would have explained the techniques and their usefulness better.
- 5. In the "VNS for the cell clustering problem" section
 - 1. The definition of F at the end of the first paragraph could be written as a separate equation.
 - 2. How the LocalSearch() function keeps or updates Y' based on a random integer "ind" could also be written using an equation.
- 6. This research aims to improve the understanding of cell interactions within tissues by clustering cell types depending on cell properties represented as vectors. It gives k clusters of the given n cells by an unsupervised approach. However, Maynard et al. annotated a 10x Visium dataset. Is it possible to give a glimpse of the annotated data (five samples)?
- 7. How are the embedding dimensions (to which the number of genes is reduced using different dimensionality reduction techniques) decided?

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