

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.

Grammar and Wording:

- The grammar and wording in the abstract are clear and effectively convey the purpose of the study.
- The language used throughout the introduction and background sections is appropriate for an academic paper.

Logic and Science:

- The abstract provides a clear overview of the research problem, approach, and results. It effectively highlights the novelty and potential impact of the proposed method.
- The paper addresses an important problem in the field of spatial transcriptomics, and the proposed approach of using Variable Neighborhood Search (VNS) for cell clustering is innovative and promising.
- The authors provide a clear statement of need, explaining the importance of cell clustering and spatial transcriptomics in understanding cellular dynamics and disease etiology.
- The authors provide a solid rationale for the study, emphasizing the importance of cell clustering for understanding cellular dynamics within tissues.
- The integration of spatial transcriptomics into the analysis expands the scope of traditional genomics and allows for a more comprehensive understanding of gene expression patterns across complex tissue structures.
- The authors effectively highlight the limitations of existing clustering methods and argue for the need for a novel approach based on the Variable Neighborhood Search technique.
- The background section provides a good overview of popular clustering methods from the literature, but it would benefit from a more detailed explanation of how Variable Neighborhood Search differs from these methods.

Innovation:

- The authors' use of the Variable Neighborhood Search metaheuristic for cell clustering in spatial transcriptomics is a novel approach that has the potential to advance current clustering methodologies.
- The adaptability of the method to both cell-type clustering and spatial domain clustering is a significant innovation that



can have broad applications in various fields.

- But the proposed approach should be compared to other new metaheuristics and AI techniques (machine learning, deep learning, ...).
- The used references must be updated, some of them are very old.

General Evaluation:

Overall, the article presents a novel approach to cell clustering in spatial transcriptomics using the Variable Neighborhood Search metaheuristic. The paper is well-written, with clear and concise language. The rationale for the study is well-supported, and the innovation of the approach is highlighted. The background section provides a good overview of existing clustering methods, but further clarification on the differences between Variable Neighborhood Search and these methods would be beneficial. Overall, the article is suitable for publication in the journal, but some minor revisions are recommended to improve clarity and address the mentioned shortcomings.

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