

# 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.

## **Strong aspects: Comments to the author: what are the strong aspects of the paper**

The authors propose a novel cell clustering for spatial transcriptomics by tuning the Variable Neighborhood Search. To achieve that, the authors evaluated the distance between cells as a linear combination of the Cosine Similarity and the Euclidean distance between cells. The optimization problem has been reduced to the minimization of the distance between cells.

The authors considered two real datasets to validate their proposal. Their comparison with existing clustering and embedding methods shows significant improvement. The results are well presented, and the figures are clear.

The paper is well-written, easily readable, and has very few typos. The contribution and the research field of the paper are very exciting, and we would like to congratulate the authors.

## **Weak aspects: Comments to the author: what are the weak aspects of the paper?**

The choice of the meta-heuristic VNS is not justified; the authors should mention why VNS is more suitable than other powerful metaheuristics such as PSO, ABC, ACO, etc.

Furthermore, assuming that the authors' main contribution is the novel metaheuristic based on VNS, comparing their proposal with other metaheuristics should be more meaningful.

## **Recommended changes: Please indicate any changes that should be made to the paper if accepted.**

- In Eq. (3), the parameter "qj" is not defined;
- The expression of D is not very clear; if it is a well-known representation of the distance between cells, please add some refs. Otherwise, the authors should provide additional comments to justify this expression.
- Before the presentation of the contribution, we suggest the authors add a subsection to remind clearly the problem statement.
- Adding an algorithm (or a flowchart) that summarizes the proposed VNS could be nice; thus, the differences with the basic VNS would be highlighted.
- Provide the expression of the parameter "ARI" ;
- For a better understanding, the authors should provide parameters such as the number of iterations, the time of

convergence, etc., of their proposal in order to improve the results part.