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

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The authors presented a novel clustering approach, VNS-based, to deal with clustering of cells in spatial transcriptomic analyses. They have compared their approach with several known clustering algorithms such as Kmeans under several embedding methods. This work is very interesting but needs to be clearer in certain places of the paper. The paper is well-written and easy to read.

In what follows, some remarks and questions that, I hope, could help the authors to improve the paper:

Line 84: Could you please give a reference to the assessment?

In mathematical statements, there are some ambiguities:

- x and y are coordinates of c, are they the same as those defined in lines 201 and 204?

Line 204: Replace « centrod » by « centroid »

Line 209: What « qj » represents?

Line 211: The variables are already defined as binary in 203 and 204? Aren't they?

Line 206: In equation (1), the purpose is to minimize this objective function. The objective function would be according to a distance between the cells and the k chosen centroids, why in the second sum, j varies from 1 to n and not from 1 to K?

- In the method description, it would be better to add some illustrations or figures for better comprehension.

Line 226 : What do the authors mean in « vectors $'$ that **have a difference of the th order** from the solution   » ? Could you please precise for the readers ?

Line 249: Sometimes « ci » is called centroid and in others it's « yi », furthermore, « yi » is a binary variable ? Could you precise this ambiguity ?

The VNS cell clustering is difficult to follow; please add an explicit algorithm to the description.

Line 332 : Could you be more precise, which results ?? In « to **evaluate the results** and compare them with.. ». Are the used datasets supervised ones ?

Line 345 : How many features do the datasets have ? We don't have an idea of the rate of reduction !

From line 351 to 365, there is a redundancy; in my opinion, it's enough to consider the explanation from 350 to 365.

Line 390 : Why are the authors focused on results given using PCA and STAGATE embedding only, while CCST has given the best results with the lowest f(VNS) and t(VNS) with more features (128)? In PCA, the authors don't specify how the cumulated variances are when taking 50 features.

From line 407 : In Table 2, VNS gave the highest score of ARI in all cases, but these scores are still closer to « 0 » than to « 1 », how could we in this case assess that the clustering is better ??

Line 427 : This phrase « dataset. Other slices imply. Thus,.. » seems wrong !

In general, the results have to be more discussed regarding the embedding methods and the clustering methods. The impact of feature reduction, the impact of « alpha »,…..