

## Reviewer Report

### Title: **Clustering trees: a visualisation for evaluating clusterings at multiple resolutions**

Version: **Original Submission** Date: 3/16/2018

Reviewer name: **Vladimir Kiselev**

#### Reviewer Comments to Author:

The authors in the manuscript try to answer an important and biologically relevant question. The manuscript is written well and the message is clearly explained. However, we have some concerns and comments on the manuscript.

1. The presented method is conceptually equivalent to visualisation of hierarchical clustering, only applicable to other clustering methods. This should be made more clear in the text.
2. We think more datasets should be considered in the study.
3. Clustertree considers cluster stability measured across  $k$ s. Cluster stability is not a novel concept and the authors should include an brief overview of the existing literature on cluster stability in the introduction (e.g. Ben-Hur et al. 2002, Luxburg 2010) and explain how their method is different from the existing approaches.
4. In application to scRNAseq the elements of the clustering tree are methodologically very similar to the cluster stability index introduced in the SC3 package (<https://www.nature.com/articles/nmeth.4236>). It would be good to have a comparison of the two methods.
5. (major) It is not obvious (at least for us) to understand from the clustering tree which  $k$  is the best. Even for a simple iris dataset it was hard for me to guess that  $k=3$  is the right  $k$ . Maybe there are too many colours in the tree picture. Could the authors provide an algorithmic approach to suggest the appropriate  $k(s)$  based on the tree perhaps in conjunction with some kind of metadata laid over the tree?

Reviewed by Tallulah Andrews and Vladimir Kiselev

## Methods

Are the methods appropriate to the aims of the study, are they well described, and are necessary controls included? Yes

### **Conclusions**

Are the conclusions adequately supported by the data shown? Yes

### **Reporting Standards**

Does the manuscript adhere to the journal's guidelines on [minimum standards of reporting?](#) Yes

Choose an item.

### **Statistics**

Are you able to assess all statistics in the manuscript, including the appropriateness of statistical tests used? Yes, and I have assessed the statistics in my report.

### **Quality of Written English**

Please indicate the quality of language in the manuscript: Acceptable

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