### **Reviewer Report**

Title: Hybrid-denovo: A de novo OTU-picking pipeline integrating single-end and paired-end 16S

sequence tags

**Version:** Original Submission **Date:** 11/13/2017

Reviewer name: Jeffrey Werner

#### **Reviewer Comments to Author:**

This work has been through several rounds of review, so I won't repeat my comments from previous rounds, which have been addressed by new comparisons with more consistent methods and more clearly documented methods. I still feel that this work presents conclusions that are valid and well-supported, although they are limited to a very specific question regarding the limitations of a low quality non-overlapping paired end HTP bacterial 16S rRNA gene sequencing survey. My only critical comment is that the authors' conclusion statement in the Abstract, "Hybrid-denovo is more powerful than de novo OTU picking approaches based on paired-end or single-end 16S sequence tags," sounds more grandiose and all-encompassing than the modest scope of the article. It seems that the authors have made additional improvements to the work in response to comments from another reviewer, and that reviewer may not be available to check those responses in this round. I've reviewed the reviewer's comments as well as the authors' responses, and changes to the manuscript. All the concerns seem to have been addressed by the authors, and I'm recommending publication.

#### **Level of Interest**

Please indicate how interesting you found the manuscript: An article whose findings are important to those with closely related research interests

# **Quality of Written English**

Please indicate the quality of language in the manuscript: Acceptable

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