

Editor
Genome Biology

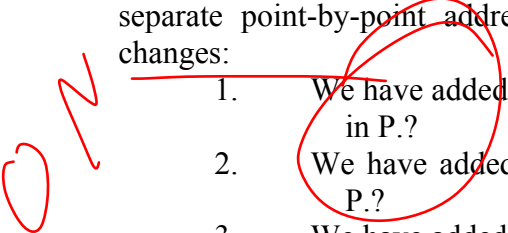
Feb 1, 2014

Re: OrthoClust: An orthology-based network framework for expression clustering across multiple species

Dear Editor,

We hereby resubmit our revised manuscript entitled “OrthoClust: An orthology-based network framework for clustering across multiple species” by Yan et al.

We want to acknowledge the two referees in providing us the valuable comments suggestions. We think the comments are really helpful in strengthening our manuscript. We therefore have performed extensive analysis in order to address their concerns. A separate point-by-point address is enclosed. In short, we have made the following changes:

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1. We have added a new section “Comparison with single-species clustering” in P.?
 2. We have added a new section “Comparison with network alignment” in P.?
 3. We have added a new section “Robustness analysis” in P.?
 4. We have added a new section “Weights associated with the orthology relationships” in P.? concerning with the exploration of the parameters space.
 5. We have added a new section “Benchmarking modules based on co-regulation patterns” in P.?
 6. We have adjusted the language to fit better Genome Biology’s broad audience.
 7. We have mentioned in the manuscript that we are willing to provide our MATLAB code upon request.

In addition, in the revised manuscript, we want to emphasis that OrthoClust is not limited to clustering expression profiles, but as a general network framework to cluster genomics data across species. The clustering of expression profiles was used as a demonstration. We therefore revised the introduction, the overall description of OrthoClust, and the discussion accordingly. Also, the title has been slightly adjusted.

Thank you for giving us the opportunities to revise our manuscript. We are looking forward to hearing from you.

Yours faithfully,

Mark Gerstein

Albert L. Williams Professor
of Biomedical Informatics

Thank you for submitting your manuscript entitled 'OrthoClust: An orthology-based network framework for expression clustering across multiple species' to Genome Biology and please accept my apologies for the delay in getting back to you about it. We have now received reports from two referees, and these are accessible as PDFs from the links below. Please let us know if you have any trouble with the files.

Referee 1: http://genomebiology.com/imedia/9489668651085495_comment.pdf

Referee 2: http://genomebiology.com/imedia/7445629611096570_comment.pdf

As you will see from the reports, although Referee 1 finds the manuscript potentially interesting, both referees raised some serious concerns about the lack of comparison with existing methods and an insufficient exploration of the parameter space. Referee 1 has also raised concerns about the technical language of the manuscript, and Referee 2 about the availability of the software. At this stage, therefore, we are not persuaded that an offer of publication in Genome Biology would be justified.

If you are able to address in full all of the issues raised by the referees, we would be happy to consider a revised version of the manuscript. You would have to submit this as a new manuscript, although we would consider it in the same way as we do all revised manuscripts. The exception is that we will take into account any work published in the intervening period.

In particular we ask that you perform a comparison with existing methods (both multi-species clustering and network alignment-based) as requested by both referees; that you perform a thorough exploration of the parameters space as suggested by both referees; that you demonstrate the robustness of the method as requested by Referee 2; that you improve the benchmarking and perform some form of biological validation as requested by Referee 1; that you ensure that the implementation of the method is made available as requested by Referee 2 and that you adjust the language to better fit Genome Biology's broad audience. The revised manuscript should address in full all the points raised by both referees; a separate list of the revisions made, specifying where in the manuscript the changes have been made, would also be helpful.

For the time being, however, we hope that you will find our referees' comments helpful in deciding how to proceed.

With best wishes,
Rafal

