Reviewer’s report

Title: Modified Entropy-Based Procedure Detects Gene-Gene-Interactions in Unconventional Genetic Models

Version: 0 Date: 07 Oct 2019

Reviewer: Ruzong Fan

Reviewer's report:

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I have read the paper by Malten and Konig which develops IGENT estimator for second order genetic interactions to test 2nd order gene-gene interactions, which exploits the advantages of the entropy methods.

The area is full of many methods already and I would like to see power comparison with existing method to see if the method is good or not. Specifically, the authors can compare with TIG in Fan et al. (2001). The software can be found at

https://sites.google.com/a/georgetown.edu/ruzong-fan/about

In addition, the type I errors are based on 1000 simulated datasets. This is far from enough and one can't tell if the methods can be used in GWAS (at most the method can be used in candidate gene analysis, and then why one would need this method?). The authors need to perform at 100,000 simulated datasets to check if the type I error rates are well controlled.

Some minor comments:

IGENT needs to be defined when first used.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
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Yes
Are the conclusions drawn adequately supported by the data shown?  
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I am able to assess the statistics

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