

Reviewer's report

Title: Spatially Uniform ReliefF: Increasing the Power to Detect Epistasis in Genetic Association Studies

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Reviewer: David V Conti

Reviewer's report:

The authors present an extension to existing algorithms designed to detect interacting variants. Specifically, they introduce a Spatially Uniform ReliefF (SURF) algorithm that weights neighbors of a individual. Simply put, the original ReliefF algorithm uses a fixed number of neighbors, while SURF uses all neighbors within a fixed distance. The authors perform a simulation study to demonstrate increased power across a variety of heritabilities and sample sizes. In general, I found this manuscript very hard to follow. Most of the relevant information is included in the Appendix and only those that are already familiar with the approaches will follow the Methods section without constant reference to the Appendix. Since this is the case, the paper would benefit including more of the material within the Appendix in the main part of the paper to help guide the reader.

My biggest concern is the presentation of power. Power in this paper is defined as: "The percentage of time that a method scores both relevant SNPs above a given threshold..." This does not give us the complete story and thus the results do not allow for complete comparison of methods. Most investigations are also interested in:

Under the null when there are no simulated epistatic SNPs, how many SNPs do I score above a given threshold? This is typically called the Type I error and it is necessary for two methods to have the same Type I error in order to interpret power. It is unclear if these methods have the same Type I error. Related to this is the False Discovery Rate. Of those that I declare significant, how many are false? This would also be of interest. Does the use of spatially related weighting help reduce the False Discovery Rate, since I am utilizing information in a more efficient manner?

Currently, the results are very misleading. I view showing the complete context of these results as necessary for publication.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests