Reviewer Report

Title: A workflow reproducibility scale for automatic validation of biological interpretation results

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Reviewer name: Stephen R Piccolo, Ph.D.

Reviewer Comments to Author:

This manuscript describes a methodology for automating evaluation of the reproducibility of data-science workflows for genomics analyses. The authors explain that reproducibility should be evaluated on a scale rather than on a binary basis. They explain concepts related to these issues and apply their methodology to real-world data.

The manuscript was well written and addresses an important issue. I believe this manuscript provides new insights. I have a few minor concerns that I would appreciate being addressed:

- The manuscript indicates that it's not feasible to compare images automatically. However, this is actually pretty easy. For example, using the Pillow package in Python, you can calculate a percentage similarity between two image files. I'm not suggesting that the authors should do this in their study. But the text should not preclude this as a possibility.
- The authors describe scenarios where the outputs might be different but these differences would be immaterial to the overall conclusions. They also describe a few scenarios where the outputs differ for biological features but that the differences are relatively small and could be considered to be acceptable. Examples include when BAM files are sorted differently. I think it would be helpful to add a bit more discussion of scenarios where differences in biological features could occur and what would cause those differences.
- Although a person checking the outputs can change the numeric threshold, it would be difficult to know what that threshold should be. Perhaps the authors could describe additional situation(s) where having relatively large differences would be acceptable and other situation(s) where they would not. For example, you could have a single difference in the biological feature outputs and perhaps that would make a huge difference in the interpretation in some cases. Additional discussion would be helpful.
- This paper focuses on automating the verification process. I think the big picture could be explained more. Who might perform this verification process in a scientific context? In what context would they do it?
- Please add brief discussion about generalizing this methodology beyond Tonkaz.

Methods

Are the methods appropriate to the aims of the study, are they well described, and are necessary controls included? Choose an item.

Conclusions

Are the conclusions adequately supported by the data shown? Choose an item.

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