

Reviewer Report

Title: Parliament2: Accurate Structural Variant Calling At Scale

Version: Original Submission **Date:** 5/9/2020

Reviewer name: Ryan Layer

Reviewer Comments to Author:

The authors present a new method for executing and merging multiple SV callers into a single VCF. The problem is important, the paper is well written, and the performance of the method is impressive, but I have a 2 major issues.

There needs to be more details about what the ruleset is and how was generated, and the method needs to be tested against other genomes. The current manuscript just says it was based on GIAB deletions results, which means the samples was HG002. My concern is that you have essentially tuned Parliament2's performance on the same truth set that you test other methods against, which could possibly give us an overly optimistic view of this method's efficacy on unseen data. Even though you demonstrate this method's inter-platform concordance, this only partially assuages my concern here. The issue can be easily fixed by testing the methods from the paper against a few more samples with an existing truth set.

For example, Chaisson 2019 in Nat Com has SV call sets from three individuals that can serve as another gold standard to test against. A favorable comparison against these samples would make this result a lot stronger.

The authors totally missed FusorSV (Becker 2018, Genome Biology) which included a very similar set of SV tools, but used merge strategy that had was based on a similar observations (that different callers do better on different types and sizes), but FusorSV has an arguably more sophisticated method. I would also like to see this included in Figs 1 and 2 to know how Parliament2 stacks up to the ML machinery that FusorSV brings.

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