Reviewer Report

Title: TGS-GapCloser: A fast and accurate gap closer for large genomes with low coverage of error-prone long reads

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Reviewer Comments to Author:

The authors present a new method for gap closing with low coverage raw long reads. Experiments on draft genomes with contigs assembled from short reads and scaffolds from long range reads show the tool works well, and more efficiently compared to other tools. The manuscript overall is written and organized well. But I have the following concerns:
1. With more long reads sequenced, more genomes are directly assembled from long reads and then scaffolded or phased together with HiC and/or linked reads. Even though the cost is higher than short reads, different from applications like SV calling, genome assembly is done once and most of the cases the cost could be tolerated. The target application of the proposed method is using low coverage long reads to fill the gaps on draft genome assembled from short reads. The authors need to clearly define how "low" coverage they could perform better than with direct assembly from long reads. The authors show the performance of their tool on different coverage of long reads, but only on the draft genome assembled from short reads. How about the genome directly assembled from long reads? Say at 20X? If it is already good enough, then no need for gap closing at this coverage. This is pretty important as it defines the potential roles the proposed method could play.
2. The major advantages in speed and memory cost over other tools come from using other third party tools that perform good, like minimap2, while the compared tools use slow tools like "blast". It's not from method innovation or better algorithm design, although selecting proper tools is also important.
3. HG001 has HiFi long reads released by GIAB from last year (2019). The authors may consider switching to it.

Level of Interest

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