Reviewer Report

Title: SeQuiLa-cov: A fast and scalable library for depth of coverage calculations

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Reviewer name: Brent Pedersen

Reviewer Comments to Author:

The authors present SeQuiLa-cov to enable fast coverage calculation within the SeQuiLa framework. The algorithm is described clearly and the software appears to have great scalability, especially in comparison to existing
solutions. I do have several points to address:
1. In the intro the authors motivate the need for fast coverage. One example is that it is used by CNV callers.
However, it's not clear to me that existing CNV callers could utilize the coverage information in SeQuiLa-cov as it's
in their table format. Would it require export? Can tools other than SeQuiLa use the full coverage information available?
How are the timings affected if export to a standard (BED) text format is required?
2. Since scalability and speed are a key focus of the paper, the authors should show how this scales on CRAM data.
Most centers and even small labs are moving to CRAM. In mosdepth, we show that we can get better speed with CRAM
especially in --fast-mode.
3. From the benchmarking scripts here:
http://biodatageeks.org/sequila/benchmarking/benchmarking.html it's not clear
to me how the window mode was run with mosdepth. Much of the time in mosdepth in spent writing the
per-base coverage which can be avoided if only the window information is needed by passing the `-n` flag.
4. This is related to 1. But, given the relative youth of SeQuiLa, it would be good to have a clear statement about how/if
SeQuiLa-cov results can be used outside of the SeQuiLa environment. If this is not feasible, that should be clear in the
text. If use of these fast coverage results does not require buy-in to the full SeQuiLa ecosystem, that would be a boon
for the software.
signed,
-Brent Pedersen

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