

## Reviewer Report

**Title:** Loop detection using Hi-C data with HiCEXplorer

**Version:** Revision 2      **Date:** 11/23/2021

**Reviewer name:** Aleksandra PÄ™kowska

### Reviewer Comments to Author:

Thank you for the feedback and for including more analyses. Figure S 5 is hard to read (it is unclear where the loops are), in Figure S 6, HiCEXplorer looks in fact worse than HiCCUPS. Both tools have issues at noisy loci but seem to be calling the most relevant interactions. The authors decided not to address the issue of pixel merging and its impact on the analysis which might have perhaps helped to understand the discrepancies between tools. Given that almost half of the loops detected by HiCEXplorer are not detected by HiCCUPS, it would be interesting to check what these loops connect - convergent CTCF sites, cis regulatory elements to each other? This point could be addressed either in this or in another study.

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