### **Reviewer Report**

# Title: parSMURF, a High Performance Computing tool for the genome-wide detection of pathogenic variants

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**Reviewer name: Maria Chikina** 

**Reviewer Comments to Author:** 

This paper describes a parallelized extension of an existing method for classifying pathogenic non-coding mutations (hyperSMURF). The specific implementation choices are reasonable and indeed achieve the desired decrease in running time.

One issue needs a bit more motivation. The entire premise of this effort is based on the assumption that it is necessary to perform the training many times, thus necessitating that it is efficient. Where does the need to continuously retrain the models arise from? The input features hardly change, they are standard genomic annotations. Is it the addition of labels? If so it would be interesting to see some examples where the predictions have actually changed over time or over different training inputs. 139: "Nevertheless these imbalance-aware methods suffer from low scalability" It is unclear why sampling suffers from low scalability. Please expand on this point.

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