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Sensitive detection of copy number alterations in low-quality liquid biopsy sequencing data

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Liquid biopsies, coupled with analysis of copy number alterations (CNAs), have emerged as a promising tool for non-invasive monitoring of cancer progression and tumor composition. CNAs, which involve large genomic gains or losses, are prevalent in cancer and can be detected using low-pass liquid biopsy sequencing. This approach offers a cost-effective and minimally invasive alternative to traditional tissue biopsies. However, methods utilizing CNA data from liquid biopsies are limited by the low signal in the samples, caused by a low percentage of cancer DNA in the blood, and the inherent noise introduced during sequencing, which limits the strength of the detectable signal. To address this challenge, we employ a Bayesian changepoint detection algorithm [1, 2] to improve signal detection from low-pass liquid biopsy sequencing. We identify positions in the genome with high posterior changepoint probability to identify the locations of CNAs. We show the effectiveness of the method on synthetically generated datasets, and compare the method to state-of-the-art bioinformatics tools under noisy conditions. Our results show that this novel approach increases sensitivity in detecting CNAs, particularly in low-quality cases.

References

[1] D. Barry, J. A. Hartigan, Product Partition Models for Change Point Problems, *The Annals of Statistics*, 20:260–279, 1992.

[2] D. Barry, J. A. Hartigan, A Bayesian Analysis for Change Point Problems, *Journal of the American Statistical Association*, 88:309–319, 1993.