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Scalable and Accurate Detection of Pathogens from Whole-Genome Shotgun Sequencing

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Abstract : Next-generation sequencing, especially whole genome shotgun sequencing, is becoming a common approach to gain insight into the microbiomes in a culture-independent way, even in clinical practice. It does not only give us information about the species composition of an environmental sample but opens the possibility to detect antimicrobial resistance and novel, or currently unknown, pathogens. Accurately and reliably detecting the microbial strains is a challenging task. Here we present a sensitive approach for detecting pathogens in metagenomics samples with special regard to detecting novel variants of known pathogens. We have developed a pipeline that uses fast, short read aligner programs (i.e., Bowtie2/BWA) and comprehensive nucleotide databases. Taxonomic binning is based on the lowest common ancestor (LCA) principle; each read is assigned to a taxon, covering the most significantly hit taxa. This approach helps in balancing between sensitivity and running time. The program was tested both on experimental and synthetic data. The results implicate that our method performs as good as the state-of-the-art BLAST-based ones, furthermore, in some cases, it even proves to be better, while running two orders magnitude faster. It is sensitive and capable of identifying taxa being present only in small abundance. Moreover, it needs two orders of magnitude less reads to complete the identification than MetaPhLan2 does. We analyzed an experimental anthrax dataset (B. anthracis strain BA104). The majority of the reads (96.50%) was classified as Bacillus anthracis, a small portion, 1.2%, was classified as other species from the Bacillus genus. We demonstrate that the evaluation of high-throughput sequencing data is feasible in a reasonable time with good classification accuracy.

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