Reduced Metagenome Sequencing for strain-resolution taxonomic profiles

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Video Byte

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Abstract

Scientists seeking to understand the difference between a healthy and unhealthy gut microbiome often turn to sequencing microbial DNA. Two main approaches are currently used: metabarcoding, also known as targeted amplicon sequencing, and shotgun sequencing of random fragments. While metabarcoding has limited resolution, full shotgun sequencing has improved resolution but comes with a higher cost, restricting the number of samples sequenced. As an alternative, researchers evaluated the use of Reduced Metagenome Sequencing (RMS) to estimate microbial community composition. RMS involves double-digested restriction-associated DNA sequencing, meaning that only a small fraction of genomes are sequenced. RMS read sets are different from both amplicon and shotgun data, making it difficult to use analysis pipelines for either method. A new analysis pipeline is proposed that uses fragment clustering and constrained ordinary least square deconvolution, allowing for estimates of relative abundance. Tests with mock-community and real data sets showed the potential of RMS to clearly separate strains with very high resolution, making the technique useful for communities with very closely related genomes. RMS may therefore be a good alternative to metabarcoding and shotgun sequencing for resolving microbial communities at the strain level. A data analysis pipeline for RMS is available as an R package at <https://github.com/larssnip/microRMS>.