Tracking Complex Mixtures of Strains in the Vaginal Microbiome

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Single Nucleotide Variants (SNVs) Enable Accurate Strain Detection Where Phylogenetic Trees Fall Short

The vaginal microbiome plays a crucial role in maintaining women's health, with Lactobacillus species being key contributors to a stable and protective environment. Vaginal microbiota transplants (VMTs) from healthy donors aim to restore a Lactobacillus-dominated microbiome in women with vaginal dysbiosis. Because VMTs contain complex mixtures of microbial strains and species, advanced bioinformatic approaches are essential for assessing strain engraftment and treatment effectiveness.

Even when only a single species—or a few strains of the same species—is administered, precise strain-level tracking is needed to differentiate between strains originating from the product, the host, or the environment.

Phylogenetic trees (Figure 1) are often used to assess engraftment, but these methods typically detect only the dominant strain in a sample and are limited to identifying one strain per species. As a result, they often fail in scenarios involving complex microbial mixtures such as VMTs.

To overcome these limitations, we developed a machine learning-based method that leverages single nucleotide variants (SNVs, Figure 2) and benchmarked it using in silico-generated strain mixtures.
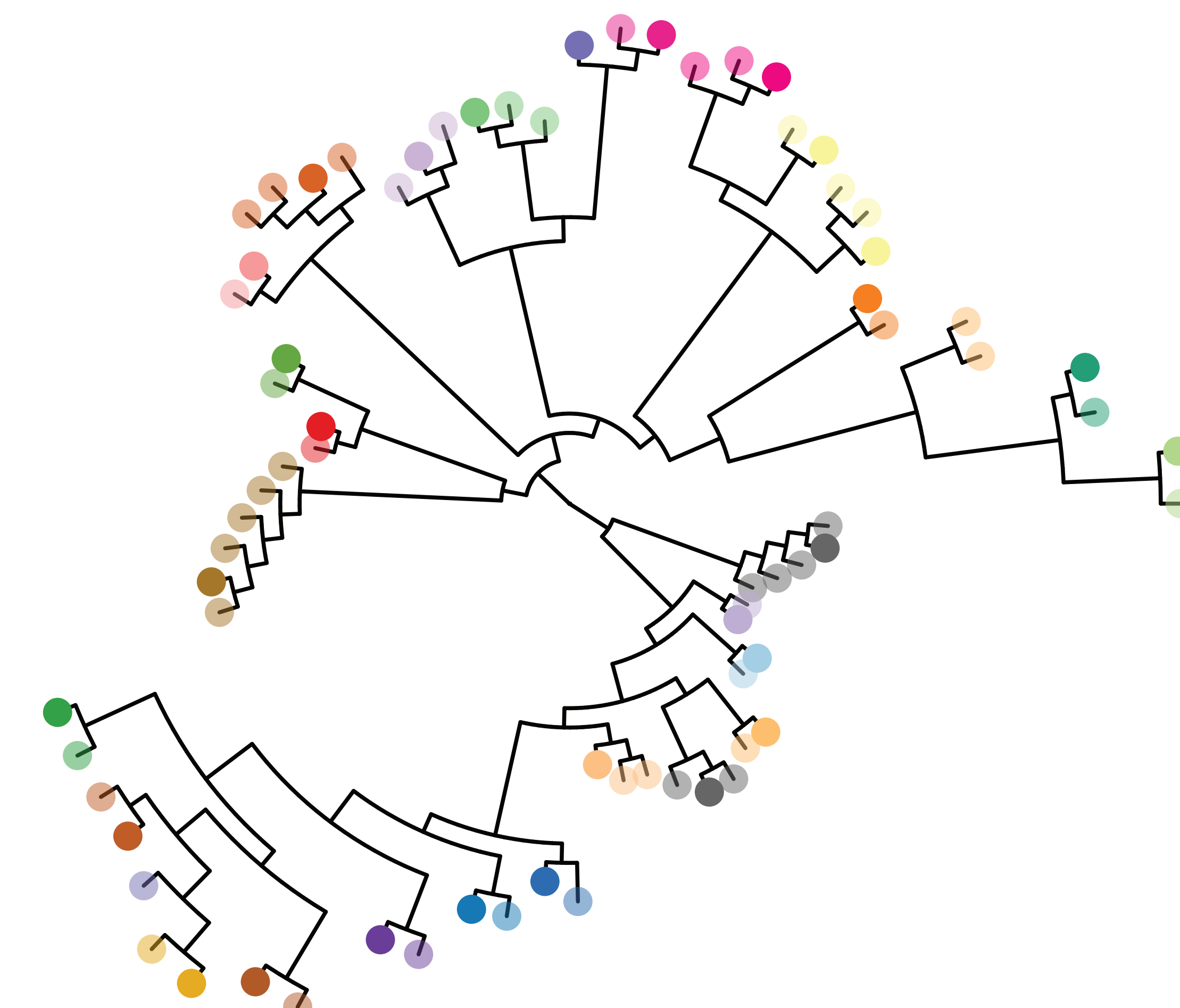

Figure 1: Phylogenetic tree of L. gasseri in 28 subjects who carry one dominant strain in 2 or more samples. Each subject is represented by a different color with the first sample having a more intense color than later samples.

CHAMP™ STRAINQ accurately detect mixtures of up to 7 probiotic (P) *Lactobacillus crispatus* strains in the presence of up to 7 endogenous (E) strains

Mix of Probiotic and Endogenous strains
Based on 20M simulated, host-filtered read pairs
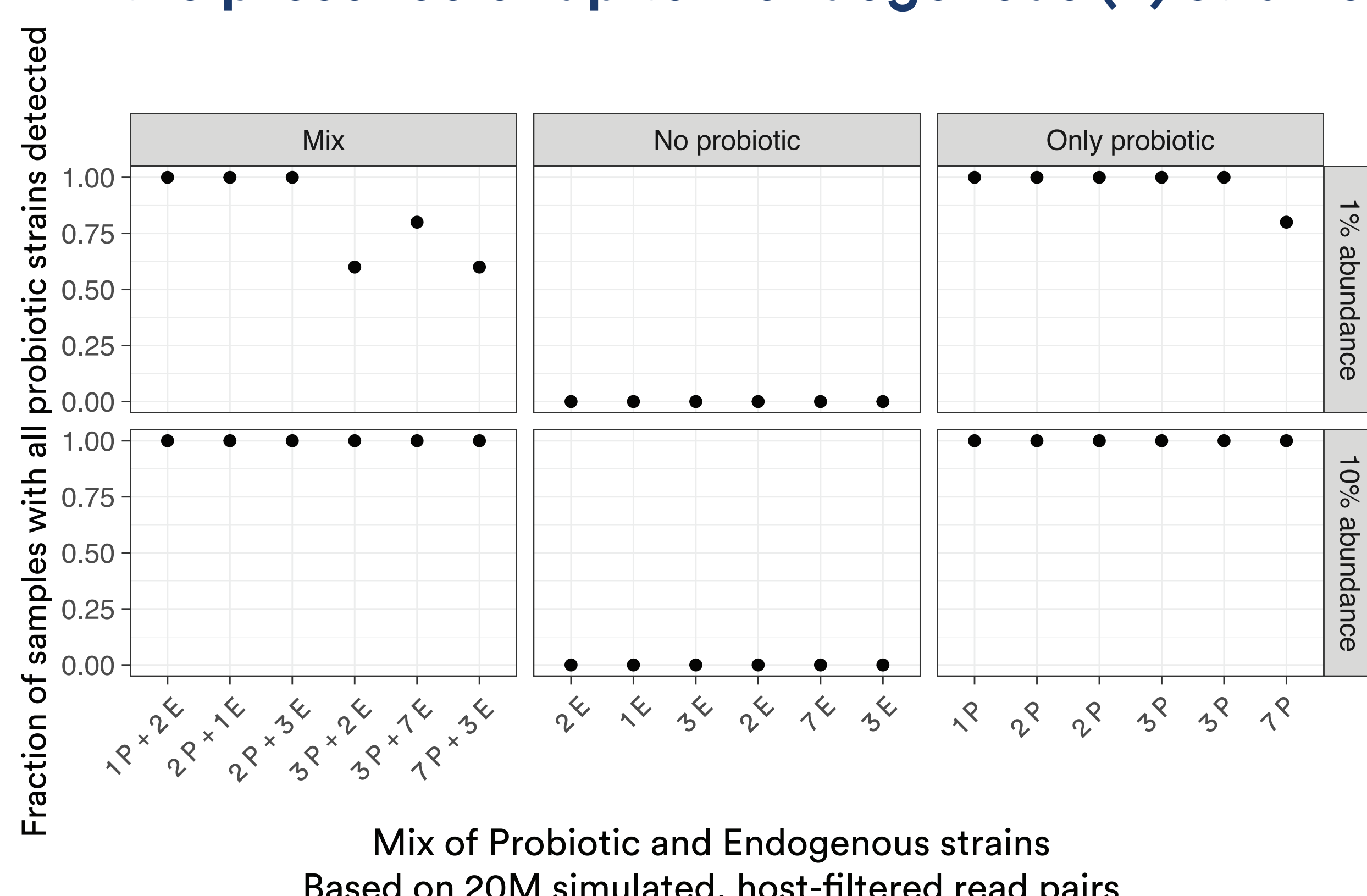
CHAMP™ STRAINQ boosts sensitivty by 131% across all abundance levels

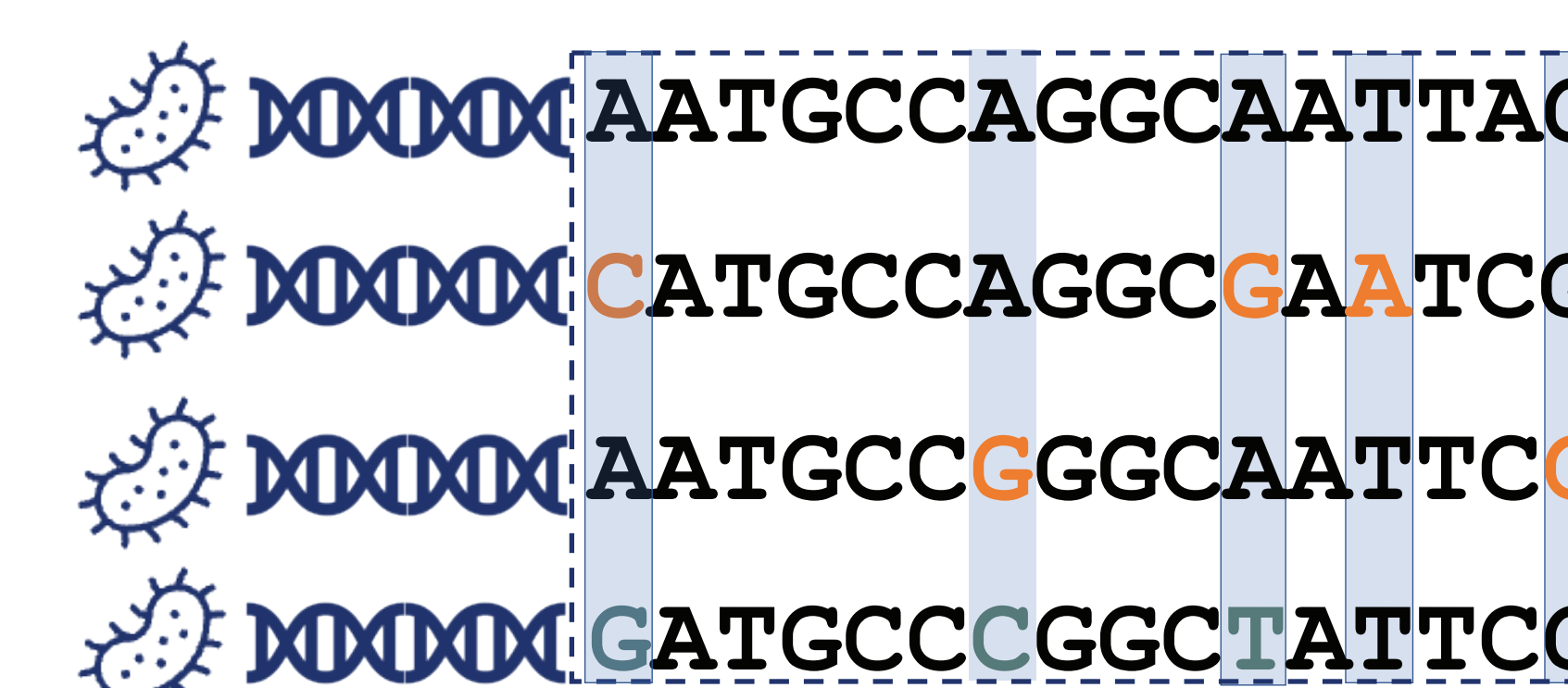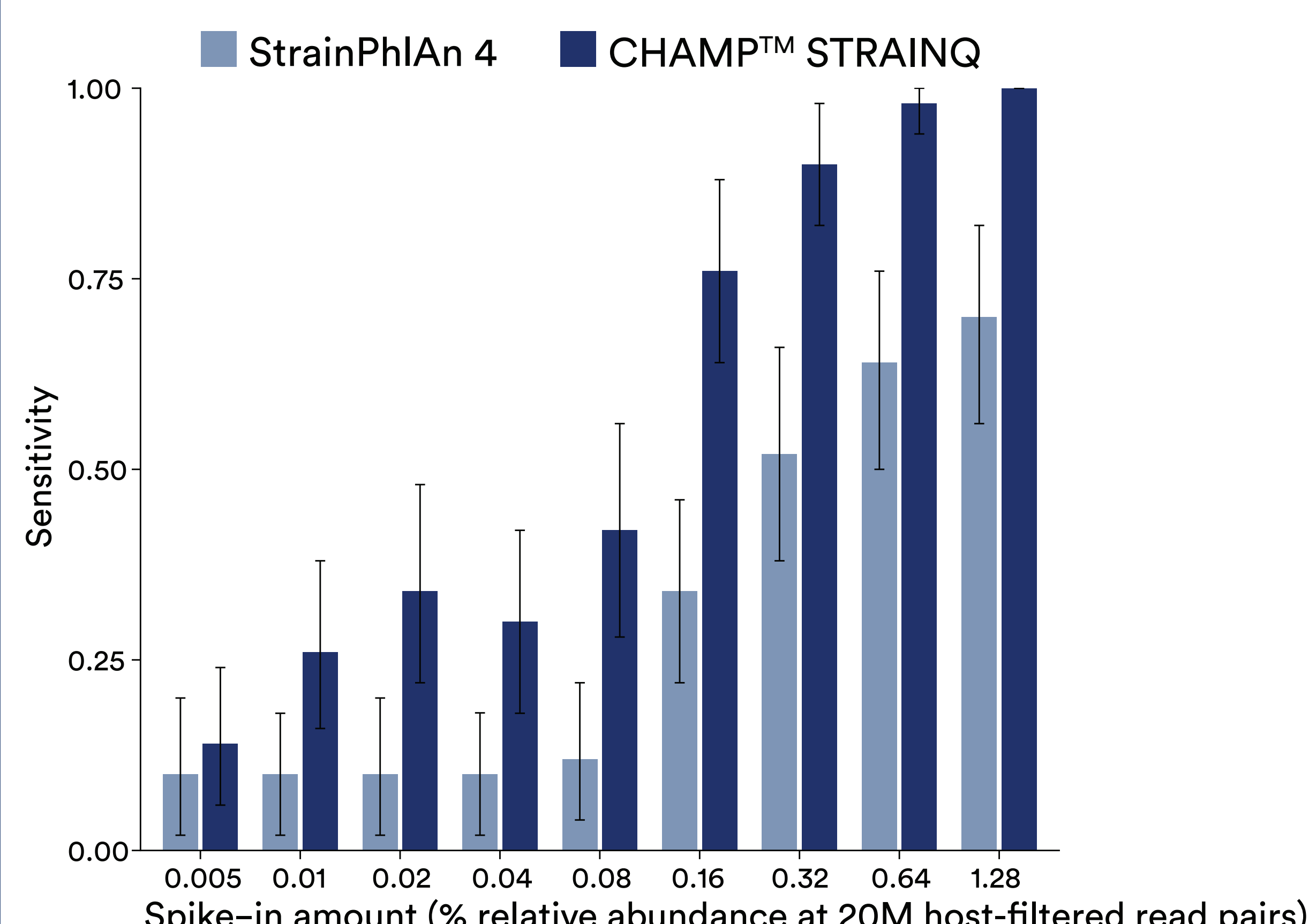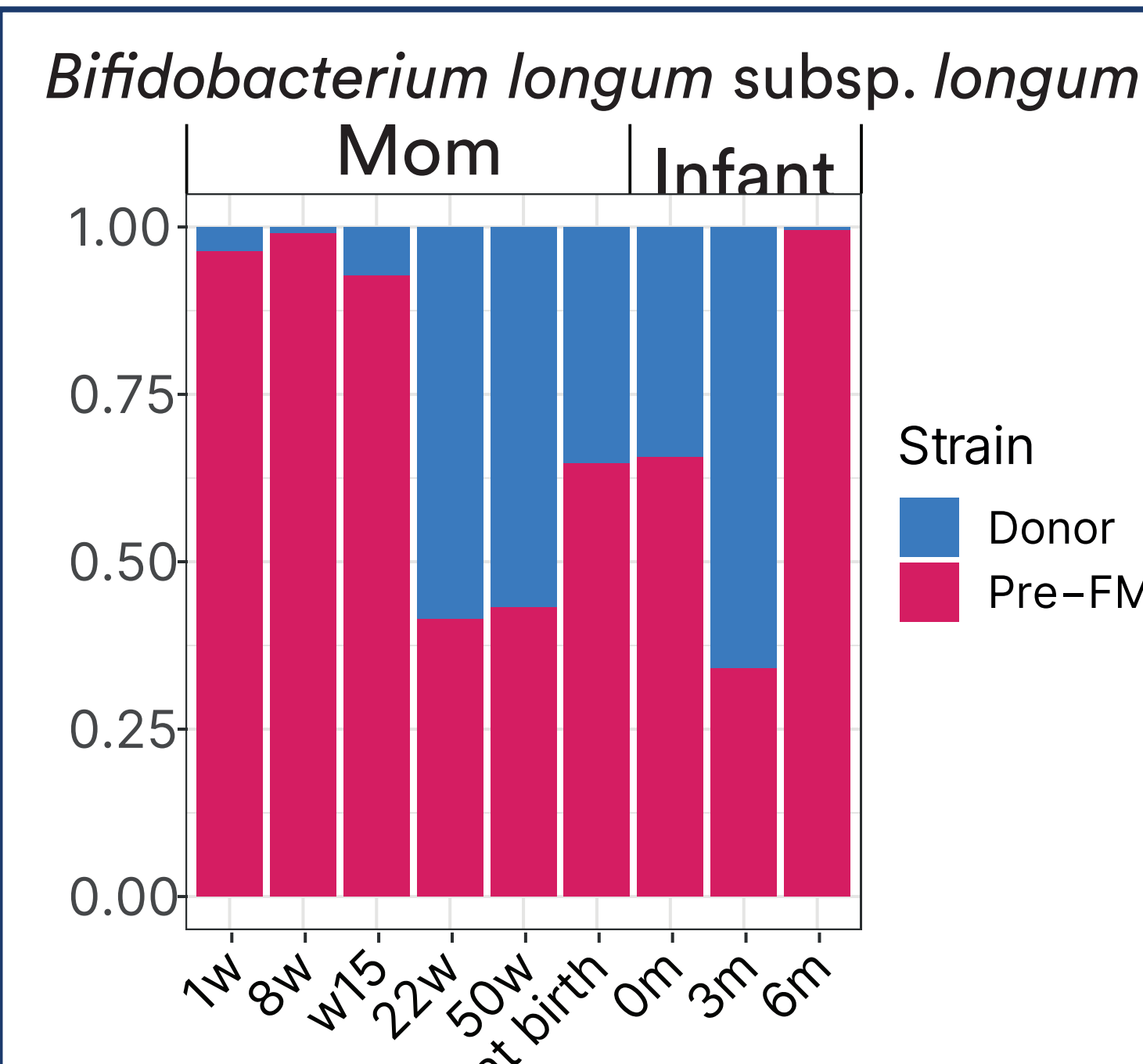Spike–in amount (% relative abundance at 20M host-filtered read pairs)

Figure 2: SNV profiles are used to discriminate between closely related strains. Machine-learning is used to determine number of strains in mixture made on allele frequency distributions.

Published Applications of CHAMP™ STRAINQ for Strain Tracking

Bifidobacterium longum subsp. *longum*

Establishment of vertical transmission of 120 bacterial strains from a fecal microbiota transplant (FMT) donor to a pregnant patient treated for Clostridioides difficile infection (CDI), culminating in the passage to the infant during vaginal delivery (1). Here is shown co-existence of two strains in mom and infant after the FMT.

(1) Wei et al. Cross-generational bacterial strain transfer to an infant after fecal microbiota transplantation to a pregnant patient: a case report. Microbiome, 2022.
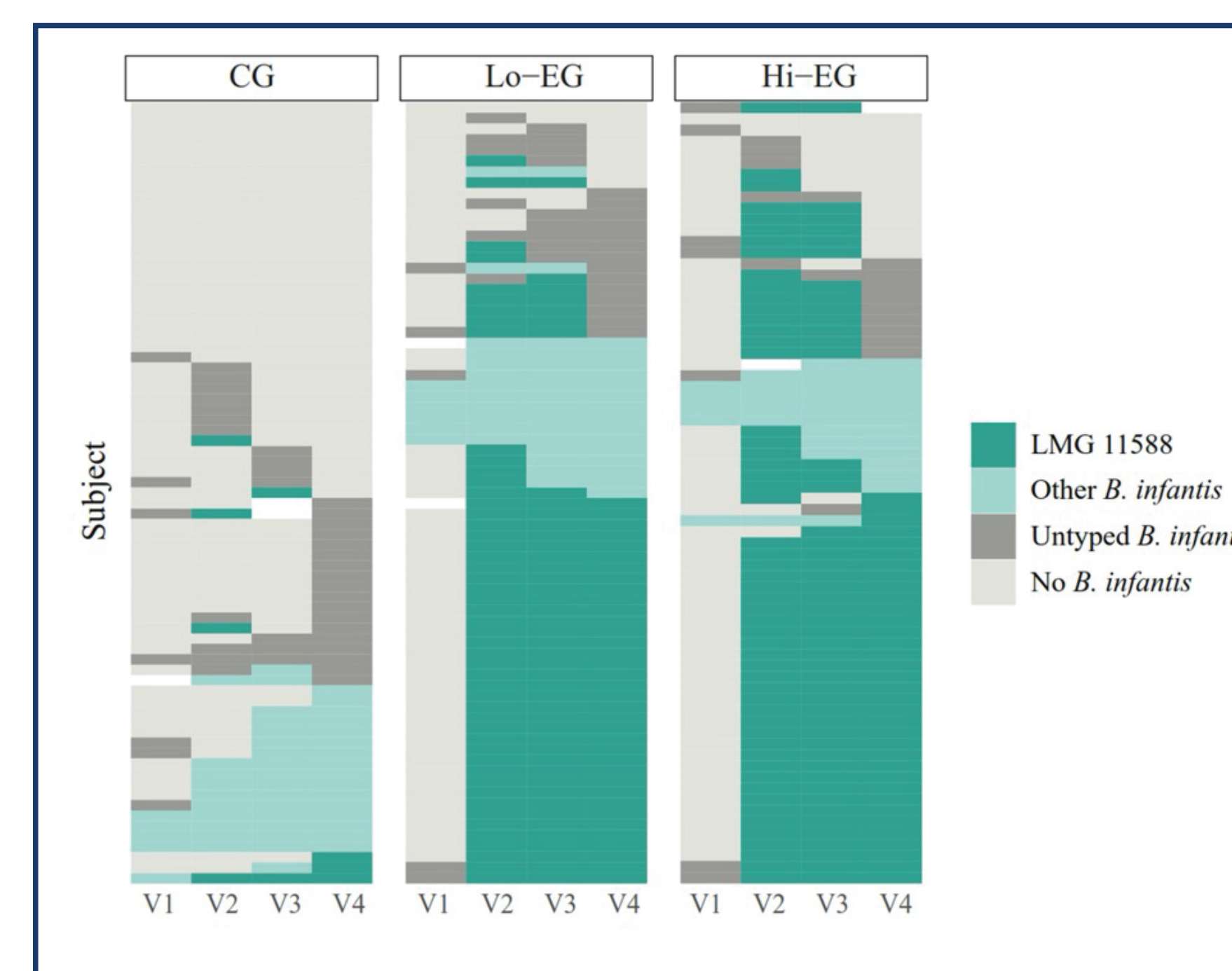
Low- and high-dose interventions with Bifidobacterium infantis LMG 11588 led to engraftment in most infants - except in those already colonized by an endogenous strain of the same species.

(2) Capeding et al. Safety, efficacy, and impact on gut microbial ecology of a Bifidobacterium longum subspecies infantis LMG11588 supplementation in healthy term infants: a randomized, double-blind, controlled trial in the Philippines. Frontiers in Nutrition, 2023.

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