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Machine Learning Analysis of Gut Microbiome Profiles in Infants from Different Feeding Practices

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Introduction. The importance of breast milk in infant health is well established, recent research suggests that early nutrition affects the infant’s gut microbiome, development of their immune system, and their health throughout life [1]. Feeding patterns significantly influence the gut microbiota in infants, and several studies have compared the effects of human milk versus formula milk on the infant microbiome [2, 3, 4].

Objectives. We will use Machine learning-based feature selection algorithms to identify taxonomic differences between breast milk and formula, and analyze its relationship with infant health.

Methods.

Data. Table 1 details the three datasets, downloaded from NCBI repository, used in this study.

Table 1: Characteristics of the selected datasets

Accession Number	Samples	Labels	Taxa (features)
PRJNA633365 [2]	65	22 - breastfeed 43 - formula-feed	1,202
DRA007599 [3]	60	24 - breastfeed 36 - formula-feed	2,521
PRJNA515307 [5]	40	20 - breastfeed 20 - formula-feed	1,779

Feature Selection. We applied a methodology that combines a DADA2-based script and the Recursive Feature Selection (REFS) algorithm designed for biomarker discovery [6], to identify taxa differences between breast milk and formula using three independent datasets: one as a discovery dataset (PRJNA633365) and the remaining two for testing (DRA007599 and PRJNA515307).

Results. After applying the methodology to the three datasets, nine bacteria were identified in the discovery dataset PRJNA633365. At the genus level, these bacteria are: Cutibacterium, two Lactobacillus, Bacteroides, two Bifidobacterium, Bilophila, and Romboutsia. At the order level, Enterobacterales were identified. After searching the resulting bacteria in the testing datasets DRA007599 and PRJNA515307 we found five out of nine and tree out of nine respectively. For the tree datasets, the algorithm with the best performance after the testing phase was KNeighbors with AUCs of 0.77 for PRJNA633365, 0.63 for DRA007599 and 0.75 for PRJNA515307. In Fig. 1 is illustrated the effectiveness of the nine bacteria in making the difference between the breastfeed and formula-feed groups.

Certain microbes provide protection to gut health, while others are more prevalent in infants with allergic diseases. For example:

- Cutibacterium and Bacteroides play a protective role in atopic dermatitis (AD) [7, 8].
- Bilophila increases in infants with AD [9].
- Bifidobacterium serves as a biomarker for investigating allergic infants [10], including those with asthma [11] and cow’s milk allergy [12].

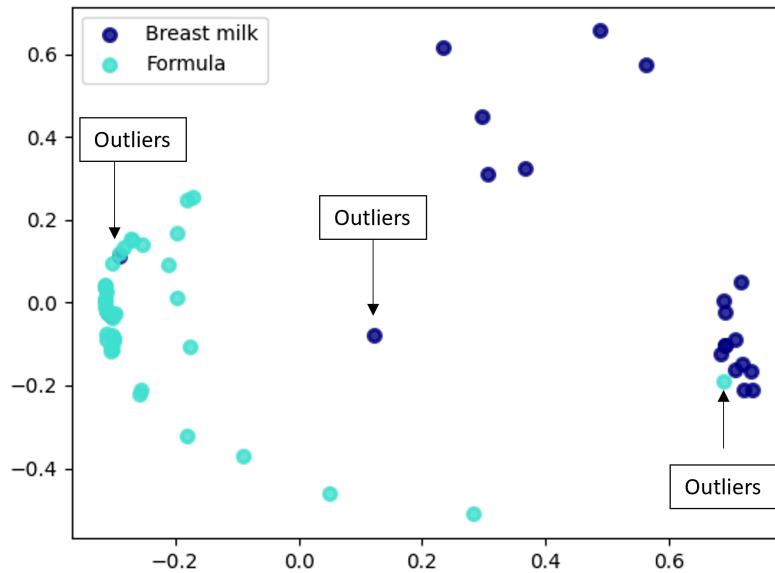


Figure 1: PCA plot using rbf kernel.

- Lactobacillus is used as a probiotic in the treatment of allergic rhinitis [13]. Both Lactobacillus and Bifidobacterium seem to be protective against the development of food allergies (FA) [8].
- Romboutsia is found more frequently in patients with neurodevelopmental disorders (NDD) [14]. Specifically, Romboutsia timonensis has been associated with autism diagnosis [4].
- Phylum Proteobacteria class and Gammaproteobacteria (Enterobacterales order) may be associated with the development of allergic respiratory diseases [9].

Conclusion. We identified taxonomic differences between breast milk and formula by applying a methodology to analyze microbiome datasets. The literature analysis of the resulting taxa show that breast-fed infants have a higher abundance of beneficial microbes, such as Bifidobacterium and Lactobacillus, which protect against allergic diseases and infections. The next steps of this work will be to expand the analysis to more datasets and study the relationship between infant health and the microbiome present in breast milk and formula.

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