

# Microbiome Premature

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# Contents

<b>1</b>	<b>Introduction</b>	<b>3</b>
1.1	Microbiome . . . . .	3
1.2	rRNA . . . . .	3
1.3	Premature . . . . .	3
<b>2</b>	<b>Materials</b>	<b>3</b>
2.1	16S rRNA Sequencing . . . . .	3
2.1.1	Helixco Data . . . . .	3
2.1.2	EBI Data . . . . .	3
2.1.3	HMP Data . . . . .	3
<b>3</b>	<b>Methods</b>	<b>3</b>
3.1	QIIME 2 . . . . .	3
3.2	Denoising Algorithms . . . . .	3
3.2.1	DADA2 . . . . .	3
3.2.2	Deblur . . . . .	5
3.3	Taxonomy Classification Algorithms . . . . .	5
3.3.1	Greengenes . . . . .	5
3.3.2	SILVA . . . . .	5
3.4	Mothur . . . . .	5
3.5	t-SNE . . . . .	5
3.6	Python Packages . . . . .	5
3.6.1	Pandas . . . . .	5
3.6.2	Scikit-Learn . . . . .	5
3.6.3	Matplotlib . . . . .	5
3.6.4	Seaborn . . . . .	5
<b>4</b>	<b>Results</b>	<b>5</b>
4.1	t-SNE for Brief Information . . . . .	5
<b>5</b>	<b>Discussion</b>	<b>5</b>
<b>6</b>	<b>References</b>	<b>5</b>

## List of Tables

1	Metadata of Data . . . . .	4
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## List of Figures

1	Concept of a core human microbiome. (Turnbaugh et al., 2007) . . . . .	4
2	Definition of Premature (Tucker & McGuire, 2004) . . . . .	4
3	Workflow of QIIME2 . . . . .	4
4	Denoising Algorithms . . . . .	6
5	Taxonomy Classification Algorithms . . . . .	6
6	t-SNE Visualizations of handwritten digits from MNIST data (Maaten & Hinton, 2008) . . . . .	6
7	Workflow of t-SNE for Brief Information . . . . .	6
8	Count of Intersected Taxa Information . . . . .	7
9	t-SNE for Brief Information . . . . .	7

# 1 Introduction

## 1.1 Microbiome

After the Human Genome Project was finished, the microorganisms which live along humans, as known as the microbiota, are considered overwhelmed human cells (Turnbaugh et al., 2007). Moreover, the microbiome, the collective genome from these microbiota (Gill et al., 2006), serve as the trait of individual have not to evolve on their own (Turnbaugh et al., 2007). Furthermore, human microbiome is effected by host's life style as figure 1.

## 1.2 Ribosomal RNA

Ribosomal RNA (rRNA) plays the main roles in a cell. This main roles include mRNA selection, tRNA binding, proof-reading, factor binding, and *et cetera* (Noller, 1991). Because of its momentous roles, rRNA could be preserved amongst whole bacteria throughout the evolution.

## 1.3 Premature

Premature (PTB; stands for Preterm Birth) is the birth of a baby earlier than 37 gestational weeks, as Figure 2 (Tucker & McGuire, 2004). Premature infants have more risk such as hearing problems and sight problems.

# 2 Materials

## 2.1 16S rRNA Sequencing

rRNA has been kept among bacteria; thus, 16S rRNA exists in almost bacteria, and its functions has not changed over time. Also, 16S rRNA is large enough for bioinformatics (Janda & Abbott, 2007). Hence, 16S rRNA sequencing is the reference method for bacterial taxonomy classification and identification (Mignard & Flandrois, 2006).

There are three databases which for machine learning: Helixco data, EBI data, and HMP data. Metadata of these databases is as table 1.

### 2.1.1 Helixco Data

### 2.1.2 European Bioinformatics Institute Data

EBI data was collected by European Bioinformatics Institute (EBI) (Dominguez-Bello et al., 2016). EBI data aimed to compare Cesarean section birth and vaginal birth; thus, every participants in EBI data is on term, not PTB.

### 2.1.3 Human Microbiome Project Data

HMP data was collected by Human Microbiome Project (HMP) (Fettweis et al., 2019). HMP data aimed to compare PTB and on-term birth; thus, every participants in HTMP data is PTB.

# 3 Methods

## 3.1 QIIME 2

QIIME 2 is a next-generation microbiome bioinformatics platform which is extensible, free, open-source, and community developed (Bolyen et al., 2019; Mandal et al., 2015; McDonald et al., 2012).

## 3.2 Denoising Algorithms

There are two denoising algorithms which are provided by QIIME as figure 4: DADA2 (Callahan et al., 2016) and Deblur (Amir et al., 2017).

### 3.2.1 DADA2

DADA2 is an open-source software package for modeling and correcting Illumina-sequenced amplicon errors (Callahan et al., 2016).

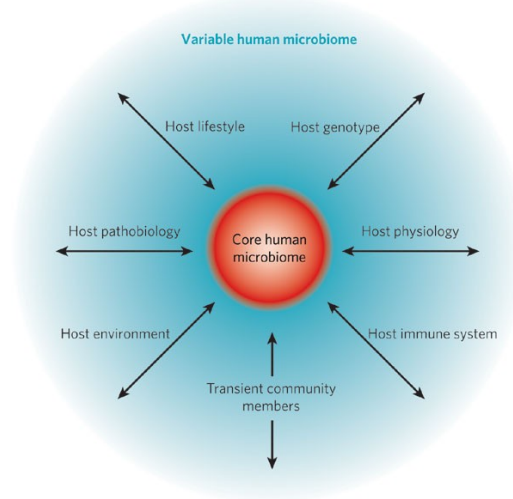


Figure 1: Concept of a core human microbiome. (Turnbaugh et al., 2007)

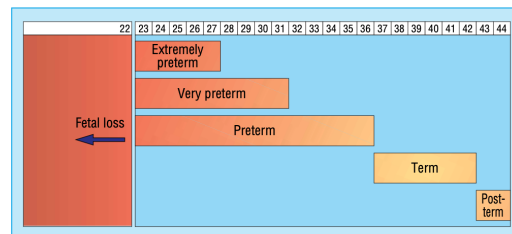


Figure 2: Definition of Premature (Tucker & McGuire, 2004)

Table 1: Metadata of Data			
Data	Participants	Samples	Remarks
Helixco	24	107	-
EBI	18	1016	Only Normal
HMP	1572	9205	Only Premature

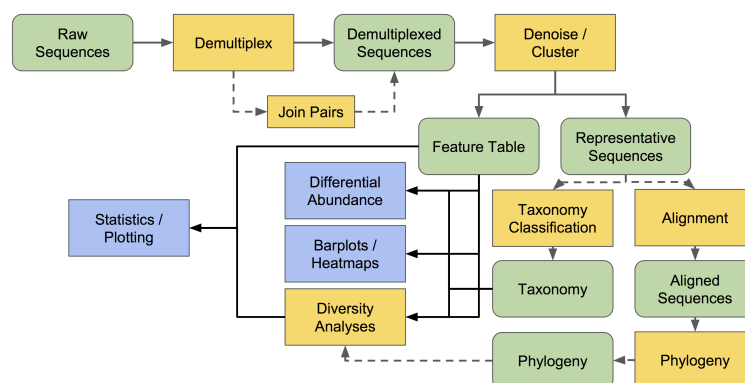


Figure 3: Workflow of QIIME2

### 3.2.2 Deblur

Deblur is a software packages which uses error profiles to obtain putative error-free sequences from Illumina MiSeq and HiSeq sequencing platforms (Amir et al., 2017).

## 3.3 Taxonomy Classification Algorithms

There are two taxonomy classification algorithms which are provided by QIIME as figures 5: Greengenes (DeSantis et al., 2006) and SILVA (Pruesse et al., 2007; Quast et al., 2012).

### 3.3.1 Greengenes

Greengenes (GG) is a chimera-checked 16S rRNA gene database (DeSantis et al., 2006).

### 3.3.2 SILVA

SILVA is a comprehensive web resource for up-to-date, quality-controlled databases of aligned rRNA gene sequences from the Bacteria domains (Pruesse et al., 2007; Quast et al., 2012).

## 3.4 Mothur

Mothur is an open-source software package for bioinformatics data processing, especially for the analysis of DNA from microbes (Schloss et al., 2009).

## 3.5 t-distributed Stochastic Neighbor Embedding

T-distributed stochastic neighbor embedding (t-SNE) visualizes high-dimensional data by giving each data-point a location in a two-dimensional map (Maaten & Hinton, 2008).

## 3.6 Python Packages

### 3.6.1 Pandas

Pandas is a Python library of rich data structure and tools for working with structured data sets (McKinney et al., 2011).

### 3.6.2 Scikit-Learn

Scikit-learn is a Python module which integrating a wide range of state-of-the-art machine learning algorithms for medium-scale supervised and unsupervised problems (Pedregosa et al., 2011).

### 3.6.3 Matplotlib

Matplotlib is a two-dimensional graphics package used for Python for image generation (Hunter, 2007).

### 3.6.4 Seaborn

Seaborn is a Python data visualization library based on Matplotlib (Waskom et al., 2020).

## 4 Results

### 4.1 t-SNE for Brief Information

To compare three databases, workflow, which as figure 7, was executed.

## 5 Discussion

## 6 References

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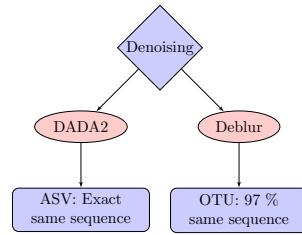


Figure 4: Denoising Algorithms

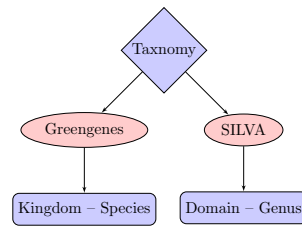


Figure 5: Taxonomy Classification Algorithms

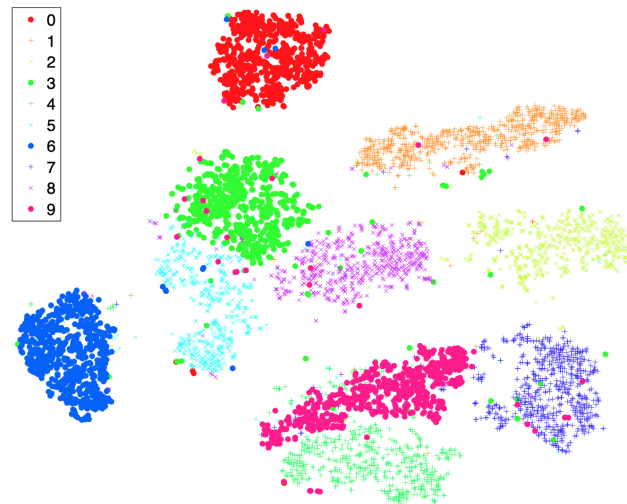


Figure 6: t-SNE Visualizations of handwritten digits from MNIST data (Maaten & Hinton, 2008)

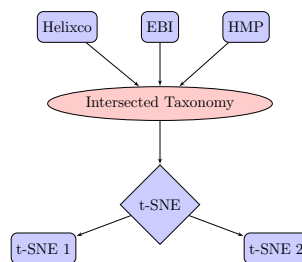
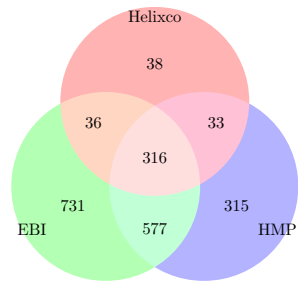
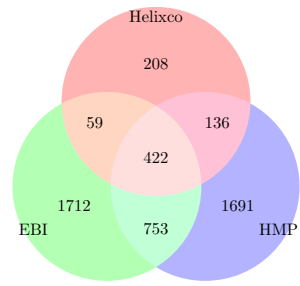


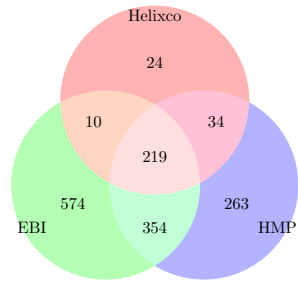
Figure 7: Workflow of t-SNE for Brief Information



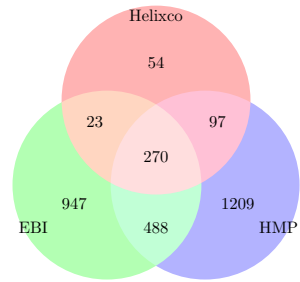
(a) DADA2 + GG



(b) DADA2 + SILVA

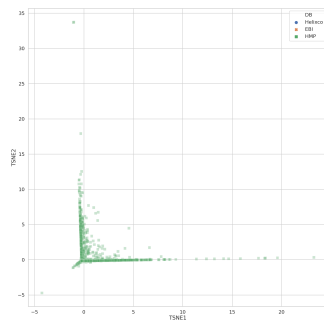


(c) Deblur + GG

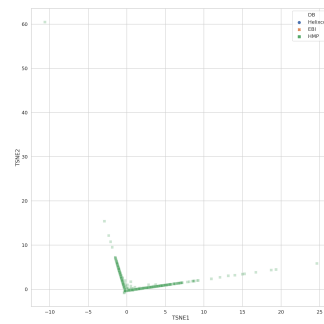


(d) Deblur + SILVA

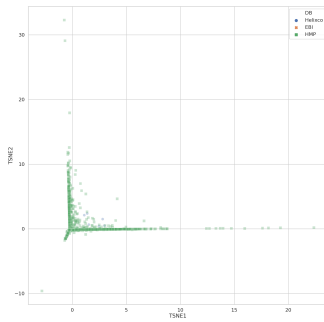
Figure 8: Count of Intersected Taxa Information



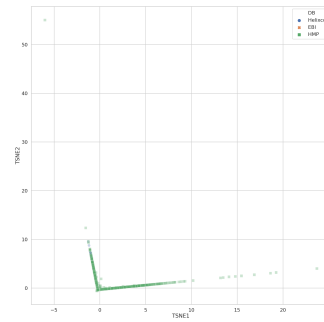
(a) DADA2 + GG



(b) DADA2 + SILVA



(c) Deblur + GG



(d) Deblur + SILVA

Figure 9: t-SNE for Brief Information

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