

## **Readme\_file.pdf**

This directory contains all input data files and codes to identify metabolic influences between each pair of microbial entities. Microbes IDs and the Metabolites IDs have been provided in the ID\_Information.xlsx file. Input files have been provided in the “Inputs” folder and all output files will be generated in the “Outputs” folder upon successful execution of source code and executable file.

### **The output will be stored in following files:**

**Step\_1:** Calculation of the production and consumption attribute for each metabolite and microbial species. This step basically generate three different values for three different metabolic events i.e., macromolecular degradation, metabolic production, and metabolic consumption for each metabolite (i) and microbe (x) pair.

**Step\_2:** Here we calculate the different terms for  $W_{xy}$  based on the metabolic actions of microbial entities. For each microbial pair (x,y) we have calculated their metabolic influence on each other based on three different metabolic events i.e., metabolite 'i' directly produce by microbe 'x', 'i' produce by the macromolecule degradation of 'x' and 'i' directly consume by 'x'.

**$W_{xy}$  matrix:** Calculating the  $W_{xy}$  matrix by using the step 2 output values.  $W_{xy}$ , whose absolute value is smaller than the input 'thre' is filtered and set to zero.

The final output file is the specie-wide metabolic influence matrix ( $W_{xy}$ -matrix), which is a  $W - (a \times a)$  matrix, wherein a, is the total number of microbial entities. A value in the (x, y)th position of the matrix can be interpreted as metabolic influence of entity x (of row) towards other entity y (of column).

### **System requirement:**

In order to run the executable code, you need to have a Linux operating system with GCC compiler installed. One can use different compiler (other than GCC) that supports the execution of C++ code. Within the terminal, move to the “code” directory. Write the command: “make” to create the executable file, then run the command “. / getWxy\_matrix” to run the executable code. The output files will be generated in the ‘Outputs’ directory.

Description of the Input files:

#### **1. Information of microbial abundance**

File name: micr\_info.txt

Format interaction network. From the second row and onward, each row represents species ID and the average microbial abundance in the Bovine gut microbiota.

#### **2. Information of microbial groups**

File name: grp\_info.txt

Format: First row represents the total number of microbial groups. From the second row and onward, each row is in the group ID.

#### **3. List of small-molecule**

File name: sml\_info.txt

Format: First row represents the total number of small-molecule metabolites. From the second row and onward, each row represents the metabolite ID of each.

#### **4. List of macromolecules**

File name: mac.txt

Format: First row represents the total number of macromolecules. From the second row and onward, each row represents the macromolecule ID.

### **5 Species-wide metabolic interactions**

File name: net\_info.txt

Format: First row represents total number of links in the community-wide metabolic interaction network of Bovine gut microbiota. From the second row and onward, each row corresponds to each link. Each link represented as, metabolite ID, species ID, metabolite ID and type of metabolic activity.

#### **Types of metabolic activity are provided below:**

- 1: Consumptions of metabolite by the microbe
- 2: Production of metabolite by the microbe
- 3: Both consumption and production of a certain metabolic by the microbe
- 4: Macromolecule degradation events

**N.B:** The original algorithm for identifying metabolic influences have been described by Sung, J. *et al.* in the study of Global metabolic interaction network of the human gut microbiota for context-specific community-scale analysis. Nat. Commun. 8, 15393. doi: 10.1038/ncomms15393, 2017. We have utilized this published code with slight modification to analyze the metabolic influence inside bovine gut microbiota.