PhD DISSERTATION PROJECT

Human diet and digestion: a stoichiometry approach and gut microbial system dynamics

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The objective of this PhD project is to develop a new approach to describe the diet and the digestive process by a process-based model. A stoichiometric description and 13 C NMR spectroscopy will be employed to characterize the diet. Additionally, a mathematical model will be developed describing the interactions between the diet and the intestinal microbial community dynamics.

Dieta e digestione: approccio stechiometrico e dinamica della comunità microbica intestinale

L’obiettivo di questo progetto di dottorato è sviluppare un nuovo approccio di studio per la descrizione della dieta e del processo digestivo mediante un modello process-based. Una descrizione stechiometrica e la spettroscopia NMR a stato solido verranno utilizzate per caratterizzare la dieta. Parallelamente si svilupperà un modello matematico che descriva le interazioni tra la dieta e le dinamiche della comunità microbica intestinale.

# **State-of-the-Art**

* 1. *Stoichiometry and 13 C NMR approaches to describe human diet*

Dietary intake is widely identified as one of the most important lifestyle factors influencing human health at planetary scale. So far, human diet studies have been focused on macronutrients and calories composition (Dai et al, 2022; Diaz-Ruiz et al, 2021), with a specific emphasis on health (Katsouyanni et al, 1994; Studnicki et al, 2019). Likewise, (Schmidhuber et al, 2018) realized a comprehensive database of the macro and micronutrient distributions at country level, giving an overview of the global trends over time. Chemical stoichiometry and NMR spectroscopy have received considerable attention in ecology, environmental sciences, forestry, evolutionary biology and plant soil sciences, however those approaches have been less explored in describing human diet composition.

* 1. *Modelling gut diversity and functioning*

As all ecological consumers are limited by the quality of available resources, ample evidence shows that the human microbiome composition reflects human diet quality. As complex adaptive systems, microbial communities show higher-order properties that are not present in individual microbes, arising from their interactions (Song et al, 2014). In this context, predictive mathematical models are helpful to understand the underlying principles of the dynamics and emergent properties of microbial systems. In table 1, the main modelling approaches applied to gut microbial ecosystems are reported.

A main group of models is constituted by generalized Lotka Volterra models (gLV), describing the growth of the individuals, expressed as taxa or operational taxonomic unit (OUT), in the gut community and their interactions (Stein et al, 2013); (Chung et al, 2017). Those kind of models have been widely applied, with differences in the measure units utilized (Joseph et al, 2020), with the addition of terms representing an immigration effect (Li et al, 2021), and also considering the interference of diet and antibiotics (Joseph et al., 2020). Otherwise, some researches and tools (Moorthy & Eberl, 2017) have been developed about gut microbial community dynamics focusing on their dependences on resources availability in terms of macronutrients (Kettle et al, 2015; Moorthy & Eberl, 2017). Along with these methods, individual based models (IBMs), widely used in ecology for modelling both higher level organisms and, more recently, microbes (Kang et al, 2014), were also applied to the gut ecosystem (Shashkova et al, 2016).

A new definition of the diet pattern allows a different insight in the prediction and description of the interactions within the gut microbiota. In this context, this PhD project aims to propose a new mathematical model of the gut microbial dynamics and its relationship with the input resources described by the novel application of stoichiometry and 13 C NMR spectroscopy.

**Table 1** Main mathematical models applied to the gut microbial communities dynamics

|  |  |  |  |
| --- | --- | --- | --- |
| **Modelling**  **approach** | **Interaction**  **units** | **State**  **variables** | **Measure**  **units** |
| ODE | Individuals | Taxa | Relative concentration |
| ODE | Individuals | OTU | Absolute concentration |
| ODE | Individuals and resources | Bacterial functional groups and Polysaccharides | Absolute concentration |
| IBM | Individuals and resources | Species and Polysaccharides | Absolute concentration |

# **2. PhD Thesis Objectives and Milestones**

Within the overall objective mentioned above this PhD thesis project can be subdivided into the following activities according to the Gantt diagram given in Table 2:

1. **New approaches to describe human diet pattern** using the stoichiometric and 13 C NMR spectroscopy methods. Stoichiometry of Carbon and Nitrogen is applied to create a new global database of the human diet (A1.1) and then used to define different types of diets (A1.2). Then, to improve the carbon quality characterization of the human dietary pattern 13 C NMR spectroscopy can be used (A1.3).
2. **Identification of microbial community in the gut** using a process-based modelling approach. The model will be defined as the interaction between the microbiome species and the food intake expressed as macronutrients. The process of modelling will include the step of data analysis (A2.1), model design and calibration (A2.2), and model calibration and validation (A2.3).
3. **Identification of microbial community and food dynamics in the gut** using a process-based modelling approach**.** In this phase the model will be defined as the interaction of the microbiome community and the food intake dynamics including its digestion in the gut. The process of modelling will include the step of data analysis (A3.1), model design and calibration (A3.2), and model calibration and validation (A3.3).
4. **Writing and Editing** of the PhD thesis, scientific papers and oral and/or poster communications.

**Table 2** Gantt diagram for this PhD thesis project.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Activity Months | | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **13** | **14** | | **15** | **16** | **17** | **18** | **19** | **20** | **21** | **22** | **23** | **24** |
| A1) | ***New approaches to describe human diet pattern*** |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  |  |  |  |  |  |
|  | 1) Create a global database of C/N ratio in human diet |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  |  |  |  |  |  |
|  | 2) Calculate the C/N ratio associated to different diet |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  |  |  |  |  |  |
|  | 3) NMR spectroscopy of human diet |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  |  |  |  |  |  |
| A2) | ***Microbial community dynamics in the gut*** |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  |  |  |  |  |  |
|  | 1) Data analysis |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  |  |  |  |  |  |
|  | 2) Model design and implementation |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  |  |  |  |  |  |
|  | 3) Model calibration and validation |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  |  |  |  |  |  |
| A3) | ***Microbial community and food dynamics in the gut*** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  |  |  |  |  |
|  | 1) Data analysis |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  |  |  |  |  |  |
|  | 2) Model design and implementation |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  |  |  |  |  |  |
|  | 3)Model calibration and validation |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  |  |  |  |  |  |
| A4) | ***Thesis*** ***and Paper preparation*** |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  |  |  |  |  |  |

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