PhD offer: Tools and methods for modelling the dynamics of complex microbial ecosystems from temporal experimental observations: application to the dynamics of the intestinal microbiota.

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Biological context and motivation

Microbiotas are communities of microorganisms formed by bacteria, phages, viruses, archaea, fungi associated with a living (plant, animal or human) host. Microbiotas and their host establish a continuous dialogue that plays a crucial role in the physiology and health of the host. For example, in mammals and humans in particular, the functions of the digestive tract, such as digestion or protection against pathogens, are carried out by a tight association between the epithelial and immune cells and the intestinal microbiota. It has been shown that the mutual benefit (mutualism) existing between the host and its intestinal microbiota is influenced by the environment, diet and more generally for humans by lifestyle, and that the alteration of this balance, called dysbiosis, is associated with certain pathologies such as inflammatory bowel diseases. Understanding the determinants and detecting the warning signs of these imbalances, related to the composition, diversity, metabolic activity of the microbiota and host physiology, is therefore an important issue in human and animal health. The thesis subject is grounded by this applicative issue, the objective is to develop mathematical models, methods and tools that contribute to the understanding of the dynamics of a complex microbial ecosystem and to the prediction of its composition and activity.

Thematic key words

Biomathematical models in microbial ecology, modelling, dynamic systems, data analysis, estimation.

Domain

Biomathematics

Objectives

The objective of the thesis work will be

1) the formulation of generic models of ecosystem dynamics, in the form of ordinary differential equations (ODE) or possible PDE if structured populations are needed, stochastic differential equations (EDS) or jump processes, and their study. In particular, the Lotka-Volterra model or other EDO models or processes proposed for example in [1,2], which correspond to phenomena of interest in ecosystem studies such as critical transitions or interactions, should be used. The links between the different model types (jump process->EDS->EDO) will be established using the scaling techniques proposed in [3,4], in conjunction with other modelling work currently being conducted in the team.

2) the development of generic methods for data reduction, in particular functional data (time series). These time series could either be measured on the same individual, in which case the methods could be related to curve clustering or shape descriptor extraction, or they could be obtained through the monitoring at the population level in different individuals, which raises more challenging issues.

3) the development of methods for estimating parameters for the models developed in 1) and 2). This work will be based on work in progress in the team in collaboration with the LAMME laboratory at the University of Evry, which is based on semi-parametric methods [5,6].

4) the analysis of experimental data sets, in rodents and humans, and the interpretation of the results obtained with the teams of partner biologists.

Scientific context and collaborations

The project will take place in the MaIAGE unit (Mathematics and Applied Informatics, from Genome to Environment) of the INRA centre in Jouy-en-Josas and will be part of the future MUSCA project team of the INRIA Saclay-Île-de-France centre, currently being created. It is part of the research collective involved in the ERC Homo.symbiosus project of Professor Joël Doré, a member of the FInE team (Intestinal Ecosystem Functionality) at the MICALIS INRA-AgroParisTech Institute (see http://www.jouy.inra.fr/Toutes-les-actualites/ERC-Joel-Dore). This collective includes teams of microbiologists, bioinformaticians and statisticians, nutritionists and physicians at the forefront of global research on the human intestinal microbiota.

Several models integrating various aspects of microbiota activity have been developed within MaIAGE. In particular, we have modelled the dietary fiber hydrolysis by the microbiota in humans [7,8], we have developed in collaboration with the Denis Poisson Institute a spatialized model coupling fluid mechanics and the presence of the microbiota [9] and microbiota/host /pathogen interaction models in animal epidemiology [10]. The thesis work will benefit from this expertise, and more broadly from the expertise in statistics and modelling present within MaIAGE and MUSCA and from collaborations and interactions (Denis Poisson Institute, CMAP, COSY IPL, GDR MABIOME).

Expected outputs

From a biomathematics perspective, the expected outputs are original models of complex ecosystem dynamics and methods for estimating and processing data to compare them with experimental data. From the applicative perspective in microbial ecology and physiology, the expected outputs are a quantitative analysis of experimental results, and the proposal of quantities of interest or markers to follow to predict the installation of dysbioses. Both aspects will lead to scientific publications.

References

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Material & financial conditions

The thesis will take place at the University of Paris-Saclay, in the MaIAGE unit and the future INRIA MUSCA project team (MUltiSCAle population dynamics for physiological systems). The hosting doctoral school will be the Hadamard School of Mathematics (EDMH) and the main workplace will be the INRA research center in Jouy-en-Josas. The doctoral student will have full access to the resources of both structures (libraries, computing clusters, file servers, computer licenses), and will benefit from funding for short stays and conferences abroad.

Candidate background and skills

Candidates with a Master's degree in Applied Mathematics or equivalent, with skills in modelling: expertise in deterministic (EDO/EDP) and stochastic (SDE, processes) dynamical systems, solid background in statistics and data analysis, proficiency in scientific programming (R, Matlab or Python). Interest for biology.