

From Environmental Omics to Eco-systems Metabolic Modeling of Microbial Communities

Microbial communities play crucial ecological roles on our planet, impacting all ecosystems at various levels. Notably, they sustain Earth's biogeochemical cycles in the oceans, but also impact and influence host nutrition, immunity and development in humans.

Next Generation Sequencing and functional genomics technologies (so called omics approaches) are revolutionizing the field of environmental microbiology and are reshaping our view on microbial ecosystems.

These approaches enable the study of ecological systems at the molecular scale and are revealing the under-explored diversity and complexity of microbial ecosystems.

Yet our ability to understand and predict the structures and functions of these complex and dynamic microbial communities is very limited.

Today, a great challenge is the global integration and mining of various environmental omics datasets (often very large) at various system levels of organization, from genes to ecosystems, in order to understand how microbial cells function within a community.

This is one of the main goals in Microbial Systems Biology, which tackles traditional but complex biological and ecological questions by coupling genomic and observational data (e.g. quantitative measurements about biological phenotypes or environmental features) with new computational techniques.

However, so far only a few studies have gone beyond the qualitative description of microbial communities.

ECOSYSMIC proposes to move toward the quantitative prediction and modeling of microbial community structure and function by combining omics data and measurements of quantitative traits through an integrative modeling platform.

Overcoming this challenge is a difficult task that still eludes us mainly because: (i) microbial communities are complex, (ii) most are described solely qualitatively, and (iii) quantitative understanding on how microbial communities interact with their surroundings remains incomplete.

Global large-scale ecosystem-wide or population-wide omics surveys are now opening the exciting possibility to characterize complex natural microbial communities, from genes to species to ecosystem functions, in an unbiased fashion.

ECOSYSMIC proposes to design integrative models and develop computational techniques to quantitatively model the structure and metabolism of natural microbial communities and predict their behavior in situ.

By (i) delineating genomes from metagenomes, it will be possible to (ii) reconstruct environmental metabolic networks in order to (iii) model the metabolism of microbial communities in situ.

As of today, the extensive large-scale sampling and sequencing of two relevant ecosystems, the human gut microbiome and the global ocean microbiome, for which enough metagenomic data are available, can be investigated using the ECOSYSMIC approach. This has never been done before and will give interesting insights into two globally important ecosystems: the medically relevant human gut microbiome and the ecologically relevant global ocean microbiome.

Through dedicated computational and modeling approaches, ECOSYSMIC will be particularly useful to investigate biological questions in various applied case studies, notably :

—ECOSYSMIC will improve our mechanistic understanding of the effect of diet on the gut microbiome metabolism and its influence on our own metabolism, and further our understanding of species interactions within our intestinal tract in health and diseases.

—ECOSYSMIC has the potential to help the design of synthetic microbiota cocktails to treat infections unresponsive to classical antibiotic treatments or as a strategy to treat the gut microbiota dysbiosis associated to various diseases.

—ECOSYSMIC will constitute a powerful platform for the functional investigation of the global Ocean microbiome and to acquire a true mechanistic understanding of key interacting players and associated metabolism driving primary production, flux of carbon and remineralization (by heterotrophic organisms), all three major components of the biological carbon pump. The platform will integrate environmental and molecular sequence information to better explain how microbial networks drive nutrient and energy cycling in marine ecosystems.

A global species-centered metabolic modeling approach using environmental sequence data is novel and should lead to significant new discoveries to help us better understand the dynamic and complex functioning of complex microbial communities inhabiting our gastrointestinal tract and the oceans.

The merging of genome-scale metabolic reconstruction into multi-species community-level models is a major goal of *Microbial Systems Biology*, and ECOSYSMIC will help to move toward the accurate modeling and prediction of microbial species in therapeutically and environmentally important contexts.

This research project on modeling natural microbial communities *in silico* will help to predict their behaviour *in situ* by merging omics technologies and microbial ecology to better understand, characterize and predict microbial ecosystems and their functions in our changing world.

In order to give access to the future ECOSYSMIC platform to a wide public, the developed computational tools will be deployed internally on the LS2N forge and externally on the BiRD bioinformatics platform.

Finally, the proximity of several Master degrees, in Bioinformatics (University of Nantes), in Computer Sciences for Biology and Health (École Centrale), and Genetics, Genomics and Systems Biology (University of Nantes and Nantes medical school) will facilitate the communication of ECOSYSMIC research.