MEM 2016

Identity sheets of the 9 funded projects

Project acronym:	ENIGME
Project title:	Engineering interactions in methanogenic communities at the ecosystem level

Axes:

	Axis 1		
	1.1 Bioinformatics	1.2 Statistics	1.3 Modeling
Axis 2			
2.1 Relations between diversity and functioning of microbial ecosystems		x	x
2.2 Role of biotic and abiotic factors on spatial and temporal structures of microbial communities		x	
2.3 Relations between functioning and interaction networks		x	x
2.4 Ecological engineering		x	

Abstract:

In ENIGME, mathematical and ecological modelers and microbial ecologists join forces to disentangle putative microbial interactions in a biorefinery process: anaerobic digestion, i.e. the conversion of waste organic matter to the renewable energy source methane. We are experimentally trying to force different functionally redundant communities to engage in interactions by mixing them. Our novel combinatorial model assigns interaction properties to elements in these mixtures, in our case, the various initial source communities or OTUs within the mixtures. Our key hypothesis is that more strongly interacting communities degrade a complex substrate more efficiently. In our experiments, we test three levers to modify interactions: (1) degree of mixing (the more source communities are mixed, the more interactions develop); (2) degree of maturation (younger communities develop interactions more easily with a large metacommunity), (3) degree of substrate complexity (higher complexity of substrates favors more interactions). The basic knowledge generated in ENGIME will be translated into a pragmatic answer to the engineering question: How can we best compose and maintain microbial communities with optimized and stable performance of an ecosystem function? In ENGIME, we apply concepts from theoretical ecology to control a biotechnological process. However, our experimental and modeling approach are generic and can be applied to various ecosystems of interest to INRA.

Key words:

Interactions; microbial communities; ecological engineering;

Partners and expertise:

Partner N°	PI family name	PI first name	Institute	Unit type and N°	Acronym of the Unit	Name of the Division	Expertise / skills brought in the project by the team*
Coordinator	MILFERSTEDT	Kim	INRA	UR0050	LBE	MICA	Environmental engineering and Microbial ecology
Co-coordinator	HAMELIN	Jérôme	INRA	UR0050	LBE	MICA	Microbial ecology
Partner 1	JAILLARD	Benoît	INRA	UMR1222	Eco&Sols	EA	Ecological modeling

Project acronym:	HANTAGULUMIC
Project title:	Spatio-temporal interactions between hantavirus, gut and lung microbiota

Axes:

	Axis 1		
	1.1 Bioinformatics	1.2 Statistics	1.3 Modeling
Axis 2			
2.1 Relations between diversity and functioning of microbial ecosystems			
2.2 Role of biotic and abiotic factors on spatial and temporal structures of microbial communities	x	x	x
2.3 Relations between functioning and interaction networks			
2.4 Ecological engineering			

Abstract:

Much of our current understanding of the interactions between microbiota, immune system and diseases has been acquired from gut microbiota and human or germ-free animal studies. High throughput sequencing technologies now offer the possibility to study microbiota complexity, well beyond the intestinal lumina and the bacterial community, in any wild animals. Our objectives are to describe and analyze how bacterial and fungal microbiota may interact to modulate rodent susceptibility to infectious diseases. In this pilot study, we will focus on hantavirus infections in bank voles and investigate the potential impacts of gut and lung microbiota on these infections. We will first develop metagenomic lab and bioinformatics tools required to describe microbiota (especially fungal one) from different organs and excreta of wild rodents. Next, we will use rodent samples from previous large-scale cross-sectional and longitudinal surveys to analyze spatio-temporal associations between hantavirus and microbiota. This project will provide innovative results in biological (fungal microbiota; pathobiome/microbiota interactions) and mathematical (coinfection analyses) front sciences that may be further valorized in human/animal health. Three European partners participate in this project. Microbiota studies will bring an important added-value to their research on biological invasions or zoonosis emergence. These collaborations will strengthen our leadership position in wild rodent metagenomics.

Key words:

Gut and lung microbiota; mycobiome; rodent-borne zoonoses; biotic interactions; statistical associations

Partners and expertise:

Partner N°	PI family name	PI first name	Institute	Unit type and N°	Acronym of the Unit	Name of the Division	Expertise / skills brought in the project by the team*
Coordinator	CHARBONNEL	Nathalie	INRA	UMR 1062	CBGP	EFPA	Evolutionary ecology of zoonoses, metagenomics
Co-coordinator	CRESPIN	Laurent	INRA	UR 346	EPIA	SA	Ecology, biostatistics, population dynamics
Partner 1	PASCAL	Géraldine	INRA	UMR 1388	GenPhyse	GA PHASE	Bioinformatics
Partner 2	BERNARD	Maria	INRA	UMR 1313	GABI	GA	Bioinformatics
Partner 3	ROCHE	Benjamin	IRD	UMR IRD 224	MIVEGEC		Mathematics, modeling, epidemiology, theoretical ecology
Partner 4	VAPALAHTI	Olli	Univ Helsinki, Finland	Dept Virology			Rodent Ecology, virology
Partner 5	LEIRS	Herwig	Antweerp University, Belgium				Population ecology of rodents, modeling
Partner 6	HOLAND	Celia	Trinity College, Ireland				Biological invasion, parasitology

Project acronym:	LEARN-BIOCONTROL
Project title:	Learning microbial networks from metabarcoding data: application to biological control

Axes

	Axis 1		
	1.1 Bioinformatics	1.2 Statistics	1.3 Modeling
Axis 2			
2.1 Relations between diversity and functioning of microbial ecosystems			
2.2 Role of biotic and abiotic factors on spatial and temporal structures of microbial communities			
2.3 Relations between functioning and interaction networks	x	x	
2.4 Ecological engineering			

Abstract:

Ecological interactions underpin ecosystem services, including those of disease regulation. The microbial interactions that regulate disease are usually identified by using co-culture experiments. This is a tedious and time-consuming process that cannot, therefore, be extended to the whole microbial community with which a pathogen interacts. The challenge is to reconstruct microbial interaction networks directly from environmental DNA. The purpose of the project will be (1) to develop generic methods for learning microbial interaction networks from metabarcoding data and (2) to prove that these new methods can be used for improving biological control of pathogens because they reveal antagonistic interactions between pathogen species and other microorganisms. This proof-of-concept study will be performed by using foliar pathogens of grapevine as a model system. We will specifically develop and test two methods: a Bayesian framework for network inference and a novel machine-learning approach (meta-interpretive learning). The aim will be to integrate environmental covariates, for the first time, and to apply the methods to high-dimensional datasets. We will evaluate the methods based on their ability to identify potential antagonists of grapevine powdery mildew. We will disseminate the methods to co-workers in MEM and INRA, and internationally, by organizing a workshop on network inference and ecological performance in agriculture.

Key words:

pathobiome; ecological networks; statistical models; machine-learning algorithms; grapevine

Partners and expertise:

Partner N°	PI family name	PI first name	Institute	Unit type and N°	Acronym of the Unit	Name of the Division	Expertise / skills brought in the project by the team*
Coordinator	VACHER	Corinne	INRA	UMR1202	BIOGECO	EFPA	Network ecology, metagenomics of the phyllosphere
Co-coordinator	VALLANCE	Jessica	INRA	UMR1065	SAVE	SPE	Microbiology, plant pathology, biological control, metagenomics of the phyllosphere
Partner 1	BOHAN	David	INRA	UMR1347	Agroécologie	SPE	Network ecology, agro-ecology
Partner 2	ROBIN	Stéphane	INRA	UMR518	MIA	MIA	Statistics, networks
Partner 3	TAMADDONI-NEZHAD	Alireza	Imperial College, London				Machine-learning, networks

Project acronym:	METAFOLDSCAN
Project title:	Metafoldscan a user-friendly interface -experimentally validated- dedicated to wide-genome scanning to identify fold hits associated to a 3d characterized target protein.

Axes

	Axis 1		
	1.1 Bioinformatics	1.2 Statistics	1.3 Modeling
Axis 2			
2.1 Relations between diversity and functioning of microbial ecosystems			
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2.3 Relations between functioning and interaction networks			
2.4 Ecological engineering			x

Abstract:

Human gut microbiota clusters more than 1,000 different species of bacteria. Balanced biodiversity of microbiote associates with healthy patients whilst imbalance correlates with dysbiosis and defective host-microbial interactions. Among adequate interactions, Faecalibacterium prausnitzii secrete bioactive peptides derived from Microbial Anti-inflammatory Molecule (MAM) whose expression blocks the inflammation pathway. Conversely, bacteria sustain Mutation Frequency Decline (Mfd) to repair DNA in response to host chemical secretion. Freshly, Mfd reports essentiality in bacterial virulence. Despite these promising properties, microbiome is underexploited and microbiota-based high value products remain scarce. One bottleneck is the lack of molecules that specifically drive probiotic responses. Because protein fold is endurable and strongly indicates its function, accurate prediction of proteins folded identically to a relevant target, despite distant sequence, is highly valuable. Thus we compute a predictive solution dedicated to wide-genomes screening and identification of hits, structurally homologous to protein targets. Such wide-genomes scanning to detect fold is nonexistent. MetaFoldScan project associates 1.1 and 2.4 MEM sub-axis to integrate in Galaxy a suite of tools able to fish, among ecological systems, structural homologs of target protein. Promising competitors Mfd and MAM are chosen for set up. Their in silico structural hits will be experimentally tested.

Key words:

functional genomics; wide-genome screening; structural homologous hits; HMM profile; MAM & Mfd

Partners and expertise:

Partner N°	PI family name	PI first name	Institute	Unit type and N°	Acronym of the Unit	Name of the Division	Expertise / skills brought in the project by the team*
Coordinator	LEROUX	Gwenaëlle	Inra	UR1014	MAIAGE	MICA/MIA	Structural bioinformatics, molecular modeling, coordination
Partner 1	RAMA RAO	Nalini	Inra	UMR1319	MICALIS	MICA	Pathogenesis, Host pathogen Interaction, host immune response
Partner 2	CHATEL	Jean-Marc	Inra	ProbiHote	MICALIS	MICA	Bacteria (commensal and probiotics)-host interactions, Immune response
Partner 3	LOUX	Valentin	Inra	UR1014	MaIAGE-Migale	MICA/MIA	Bioinformatics, Galaxy developer

Project acronym:	MICROFIT
Project title:	Unraveling the genetic determinants of fitness of a food microorganism in its natural ecosystem by a Tn-seq approach (massive sequencing of transposon insertion libraries)

Axes:

	Axis 1		
	1.1 Bioinformatics	1.2 Statistics	1.3 Modeling
Axis 2			
2.1 Relations between diversity and functioning of microbial ecosystems	x	x	
2.2 Role of biotic and abiotic factors on spatial and temporal structures of microbial communities			
2.3 Relations between functioning and interaction networks	x	x	
2.4 Ecological engineering			

Abstract:

Understanding how microorganisms function and interact in their natural habitats requires “omics” approaches for dealing with the biological and physico-chemical complexity of such ecosystems. This is in particular the case of food ecosystems which, through their role in nutrition and health, have huge economical importance. In addition, they also constitute very relevant models for academical studies of the adaptation of microorganisms to their natural habitat. We previously validated a model cheese ecosystem of nine species (three yeasts and six bacteria) that allows us to study interactions within a cheese microbial community in a model curd. We propose here to study the adaptation of a yeast, Yarrowia lipolytica, to its dairy environment. Besides transcriptomics and metabolomics studies, we aim to demonstrate here the feasibility of an alternative Tn-seq approach for studying food microbiota. Tn-seq consists in massive sequencing of transposon/chromosome junctions from transposon insertion mutant libraries grown in various conditions. This method determines a fitness value for each gene in the considered growth condition. We will focus on adaptation to its ecological niche of the yeast Yarrowia lipolytica, cultivated alone or with other microorganisms from dairy ecosystem. This innovative approach should allow identifying the genetic determinants involved in the adaptation of this yeast to its habitat and in its interactions with other microorganisms in the ecosystem.

Key words:

Functional ecology; Tn-seq; adaptation; yeast; cheese ecosystem

Partners and expertise:

Partner N°	PI family name	PI first name	Institute	Unit type and N°	Acronym of the Unit	Name of the Division	Expertise / skills brought in the project by the team*
Coordinator	MADZAK	Catherine	INRA, AgroParisTech	UMR0782	GMPA	MICA CEPIA	Microbial ecology (yeast, bacteria), Biotechnology of cheese, Genomics, Molecular biology, Genetic engineering (Yarrowia lipolytica)
Partner 1	LOUX	Valentin	INRA	UR1404	MaIAGE MIGALE	MIA MICA	Bioinformatics, Data integration, Statistics

Project acronym:	MODCHOCYCLE
Project title:	Modeling the cholesterol cycle with the interplay between the host and gut microbiota

Axes:

	Axis 1		
	1.1 Bioinformatics	1.2 Statistics	1.3 Modeling
Axis 2			
2.1 Relations between diversity and functioning of microbial ecosystems			x
2.2 Role of biotic and abiotic factors on spatial and temporal structures of microbial communities			
2.3 Relations between functioning and interaction networks			
2.4 Ecological engineering			

Abstract:

Cholesterol plays a vital role in the human body for cell membranes, bile acids, steroid hormones and vitamin D synthesis but cholesterol level in blood (especially LDL-cholesterol) is also the main marker for cardiovascular diseases, a pathology with worldwide increasing occurrence. Therefore modeling the complex cholesterol cycle in the body taking into account all the players including the microbiota is a key step toward the identification of efficient levers to manage this component and to better understand the respective roles and cross-talk between host and its digestive ecosystem.
Few mathematical models of the cholesterol cycle in the human body exist however none integrates the role of the intestinal microbiota despite numerous reports on microbiota activities impacting this cycle (bile acids deconjugation, cholesterol conversion in coprostanol and other derivatives, and trapping by microbial envelops).
As MEM-recruited young researchers working in the fields of mathematical modeling and functional metagenomics, we propose to join our knowledge in this multidisciplinary project. Our project ModChoCycle aims at building a complete model of the human cholesterol metabolism using all available knowledge including those regarding the gastro-intestinal microbiota and biological data obtained in the project on the metabolism of deuterated-cholesterol in a rodent model. The outcome of the project is a better understanding of the cholesterol cycle in rodents and humans and, a model allowing to evaluate the importance of the microbiota versus human physiological processes and to identify levers or combination of levers to better manage cholesterol.

Key words:

Modeling; Gut microbiota; Germfree animal model; microbiota transplantation; metabolism

Partners and expertise:

Partner N°	PI family name	PI first name	Institute	Unit type and N°	Acronym of the Unit	Name of the Division	Expertise / skills brought in the project by the team*
Coordinator	RHIMI	Moez	INRA	UMR1319	MICALIS	MICA	Functional metagenomics, Biochemistry, animal experimentation, microbiology
Co-coordinator	LABARTHE	Simon	INRA	UR1404	MaIAGE	MIA	Applied Maths, dynamical systems modelling and simulation.
Partner 1	MAGUIN	Emmanuelle	INRA	UMR1319	MICALIS	MICA	Functional metagenomics, microbiology, molecular biology.
Partner 2	ABRAHAM	Anne-Laure	INRA	UMR1319	MICALIS	MICA	Bioinformatics, 16S analysis
Partner 3	LAROCHE	Béatrice	INRA	UR1404	MaIAGE	MIA	Applied Maths, dynamical systems modelling, Bayesian inference.
Partner 4	GERARD	Philippe	INRA	UMR1319	MICALIS	MICA	Gnotobiotic experiments, human microbiota transplantation in animal.

Project acronym:	POPART
Project title:	Regulation of the poplar microbiome by its host: is the immune system involved?

Axes:

	Axis 1		
	1.1 Bioinformatics	1.2 Statistics	1.3 Modeling
Axis 2			
2.1 Relations between diversity and functioning of microbial ecosystems		x	
2.2 Role of biotic and abiotic factors on spatial and temporal structures of microbial communities		x	
2.3 Relations between functioning and interaction networks		x	
2.4 Ecological engineering			

Abstract:

Tree roots are colonized by complex microbial communities that participate to the growth of their tree host and its resistance to abiotic and biotic stresses. The main factors that drive the composition and the structure of these microbial communities have been identified but their precise mechanisms and their relative importance as drivers of the community structure are unknown. The goal of this project is to test whether the phytohormones salicylic and jasmonic acids have a role in shaping the fungal and bacterial communities of the roots of Poplar and to the study the ways by which they could shape these microbial communities. To do so, we will compare the composition and structure of the fungal and bacterial communities of Poplar roots that have been treated with jasmonic acid, salicylic acid or with a mock treatment by Illumina sequencing of fungal and bacterial gene markers. In parallel we will study the direct impact of the two phytohormones on soil microbial communities and we will test whether the phytohormones induce a change in the active microbial community of the roots through an indirect effect on the root exudates. Illumina sequencing data will be analysed using standard procedure in terms of composition and structure. Potential interactions between microorganisms will also be assessed and the best methods to do so will be tested. The project will be built on a collaborative effort between biologists, statisticians and computer scientists.

Key words:

tree root microbiome; phytohormones; microbial interaction network inference; graph analysis

Partners and expertise:

Partner N°	PI family name	PI first name	Institute	Unit type and N°	Acronym of the Unit	Name of the Division	Expertise / skills brought in the project by the team*
Coordinator	DEVEAU	Aurélie	INRA-UL	UMR1136	IAM	EFPA	Microbial Ecology, metagenomics
Co-coordinator	AIGLE	Bertrand	INRA-UL	UMR1128	DYNAMIC	MICA	Ecology of streptomyces and forest soil
Partner 1	PLAIN	Caroline	INRA-UL	UMR1137	EEF	EFPA	isotopic labelling
Partner 2	GUEUDIN	Aurélie	CNRS-UL	UMR7502	IECL		Statistics, estimation, graph inference
Partner 3	GUEGOUT-PETIT	Anne	CNRS-UL	UMR7502	IECL		Statistics, estimation, graph inference
Partner 4	RAISSI	Chedy	INRIA		Orpailleur		
Partner 5	TSCHAPLINSKY	Tim	ORNL				Metabolome analysis of poplar
Partner 6	MIEZSKIN	Sophie	INRA-UL	UMR1336	IAM	EFPA	Fungal-bacterial interactions

Project acronym:	SYSTOMICS
Project title:	Systems approaches to study microbial consortia: integrating meta-omics data to elucidate the functioning of lignocellulolytic microbial consortia.

Axes:

	Axis 1		
	1.1 Bioinformatics	1.2 Statistics	1.3 Modeling
Axis 2			
2.1 Relations between diversity and functioning of microbial ecosystems	x	x	
2.2 Role of biotic and abiotic factors on spatial and temporal structures of microbial communities	x	x	
2.3 Relations between functioning and interaction networks	x	x	
2.4 Ecological engineering			

Abstract:

Lignocellulosic biomass (LC) is the main renewable carbon and energy source in the world that maybe transformed to produce energy and target chemicals (synthons) useful for the industry. In nature, the recycling of lignocellulose is performed by LC-utilizing microbial communities which are equipped of the enzymatic machinery that is fully adapted for LC deconstruction. Thus, the processes naturally occurring in lignocellulolytic microbial ecosystems could be taken as a model to design efficient bioconversion processes. The complex composition of microbial communities found in microbial ecosystems is supposed to reflect a highly interlinked metabolic system with multiple dependencies between the various species. In order to design more efficient LC bioconversion processes using microbial consortia, it is thus evident that we need a precise knowledge of such dependencies and interactions and they response to different biotic and abiotic factors. Such knowledge could be acquired thanks to the recent advances in high-throughput 'omics' technologies and applying systems biology approaches to study microbial ecosystems. The aim of SystOmics is to combine meta-OMICS data sets in order to obtain a comprehensive and delicate view of interactions of the lignocellulolytic microbial community. Such data will be correlated to those obtained from bioconversion performance observations during LC transformation by microbial consortia under different substrate constraints.

Key words:

Lignocellulose bioconversion, inocula effect, process constraints, microbial community functioning, meta-omics, systems approach.

Partners and expertise:

Partner N°	PI family name	PI first name	Institute	Unit type and N°	Acronym of the Unit	Name of the Division	Expertise / skills brought in the project by the team*
Coordinator	HERNANDEZ RAQUET	Guillermina	INRA	UMR 792	LISBP	CEPIA	Microbial ecology, Biotechnology, LC degradation
Partner 1	LEBERRE ET DUMON	Véronique et Claire	INRA CNRS	UMR 792	LISBP	CEPIA	BioChip analysis, molecular biology, enzymology, biochemistry
Partner 2	PLANCADE ET MARIADASSOU	Sandra et Mahendra	INRA	UR 1404	MaIAGE	MIA	Statistics
Partner 3	DEJEAN	Sébastien	GeT Biostatistics Platform	UPS	BSP	UPS	Statistics, Bioinformatics
Partner 4	JEHMLICH	Nico	UFZ		UFZ	Proteomics	Metaproteomics, biochemistry

Project acronym:	VIROME ACCESS
Project title:	Accessing to virus genomes out of metagenomics data: improving statistical and bio-informatics analytic tools to better assess the contribution of phages on microbial ecosystems

Axes:

	Axis 1		
	1.1 Bioinformatics	1.2 Statistics	1.3 Modeling
Axis 2			
2.1 Relations between diversity and functioning of microbial ecosystems			
2.2 Role of biotic and abiotic factors on spatial and temporal structures of microbial communities	x	x	
2.3 Relations between functioning and interaction networks			
2.4 Ecological engineering			

Abstract:

Phages are present in all ecosystems where bacteria are present but it is still hard to assess their contribution to ecosystem functioning because they are difficult to count, to identify and their genome are difficult to assemble from metagenomic data. The aim of VIROME ACCESS project is to provide researchers in metagenomics with a set of sampling strategies and protocols to include phages in their ecosystems analysis. The project encompasses a large panel of microbial ecosystems studied at INRA, because we want to use the specific and increasing complexity of each of these environments as a strategy to check the efficiency of the methods which will be developed for the scientific users: meat/seafood products, mature cheese rind, human feces and waste anaerobic digestor. The first two tasks of the project is to use a new imaging technology based on optical interference to accurately count and describe phage morphologies in the various ecosystems studied and to evaluate, before sequencing, whether phages are important players in these bacterial communities. The third task is to tailor tools to improve phage genome assemblies out of metagenomics samples based on recent breakthrough in co-variance analysis and by sequencing both viral and bacterial fractions of the ecosystems. The fourth task is to predict which bacterial hosts are targeted by the dominant phages by a comparative tetramer-based strategy.

Key words:

phage metagenomic; co-variance analysis; optical interference; phage annotation; host prediction

Partners and expertise:

Partner N°	PI family name	PI first name	Institute	Unit type and N°	Acronym of the Unit	Name of the Division	Expertise / skills brought in the project by the team*
Coordinator	CHAILLOU	Stéphane	INRA	UMR 1319	MICALIS	MICA	SC is a microbial genomist, food microbial ecologist and a bio-informatician involved in metagenomics data analysis. SC studies meat and seafood spoilage ecosystems.
Co-coordinator	PETIT	Marie-Agnès	INRA	UMR 1319	MICALIS	MICA	MAP is a Phage genomists studying the role of phages in human gut microbiota. MAP is also a bioinformatician involved in phage metadata analysis in collaboration with F. Enault (UBP Clermont-Ferrand).
Partner 1	SCHBATH	Sophie	INRA	UR 1404	MaIAGE	MIA	SS and MM are statisticians and bio-informaticians, involved in metagenomics data analysis
Partner 2	DE PAEPE	Marianne	INRA	UMR 1319	MICALIS	MICA	As MAP, MDP is a Phage genomists studying the role of phages in human gut microbiota.

Partner 3	DUGAT-BONY	Eric	INRA	UMR 0782	GMPA	MICA	EDB is a microbial ecologist and genomist. He is also a bio-informatician involved in meta-omics data analysis. EDB studies the role of complex communities in French cheese rind
Partner 4	MARIADASSOU	Mahendra	INRA	UR 1404	MaIAGE	MIA	SS and MM are statisticians and bio-informaticians, involved in metagenomics data analysis
Partner 5	HAMELIN	Jérome	INRA	UR 0050	LBE	MICA	JH and KM are microbial ecologists focusing on biodiversity-functioning relationship, with anaerobic digestion as model ecosystem
Partner 6	MILFERSTEDT	KIM	INRA	UR 0050	LBE	MICA	JH and KM are microbial ecologists focusing on biodiversity-functioning relationship, with anaerobic digestion as model ecosystem