

# Laboratoire d'Ingénierie des Systèmes Biologiques et des Procédés

*Nic Lindley*

UMR CNRS/INSA N°5504

*Engineering and Systems Sciences (INSIS)  
Biological Sciences (INSB)*

UMR INRA/INSA N° 792

*Microbiology and the Food Chain (MICA)  
Science and Process Engineering of Agricultural Products (CEPIA)*

*Laboratory evaluated A+ en 2005 et en 2009*

[www.lisbp.fr](http://www.lisbp.fr)



LABORATOIRE D'INGÉNIERIE  
DES SYSTÈMES BILOGIQUES  
ET DES PROCÉDÉS



# OUTLINES

Tuesday 23rd June



FILLAudeau Luc  
Overview of HTMS aims and context  
Description of LISBP

~15'  
~ 15'

**LINDLEY Nicholas (LISBP head)**  
**Presentation and visit of LISBP**

~ 30'

Lunch time (CEMES)

~ 90'

GOMA Gérard (LISBP)  
Biomass and bio-economy: the international context

PHAM Tuan Anh & CAO Bach Xuan (SBFT)

~ 60'

Pretreatment of lignocellulosic biomass: Steam explosion (rubber wood) and Organosolv (bagasse)

LABORATOIRE D'INGÉNIERIE  
DES SYSTÈMES BILOGIQUES  
ET DES PROCÉDÉS





**Laboratory evaluated A+ in 2005 & 2009. Considered unique and outstanding in 2014**

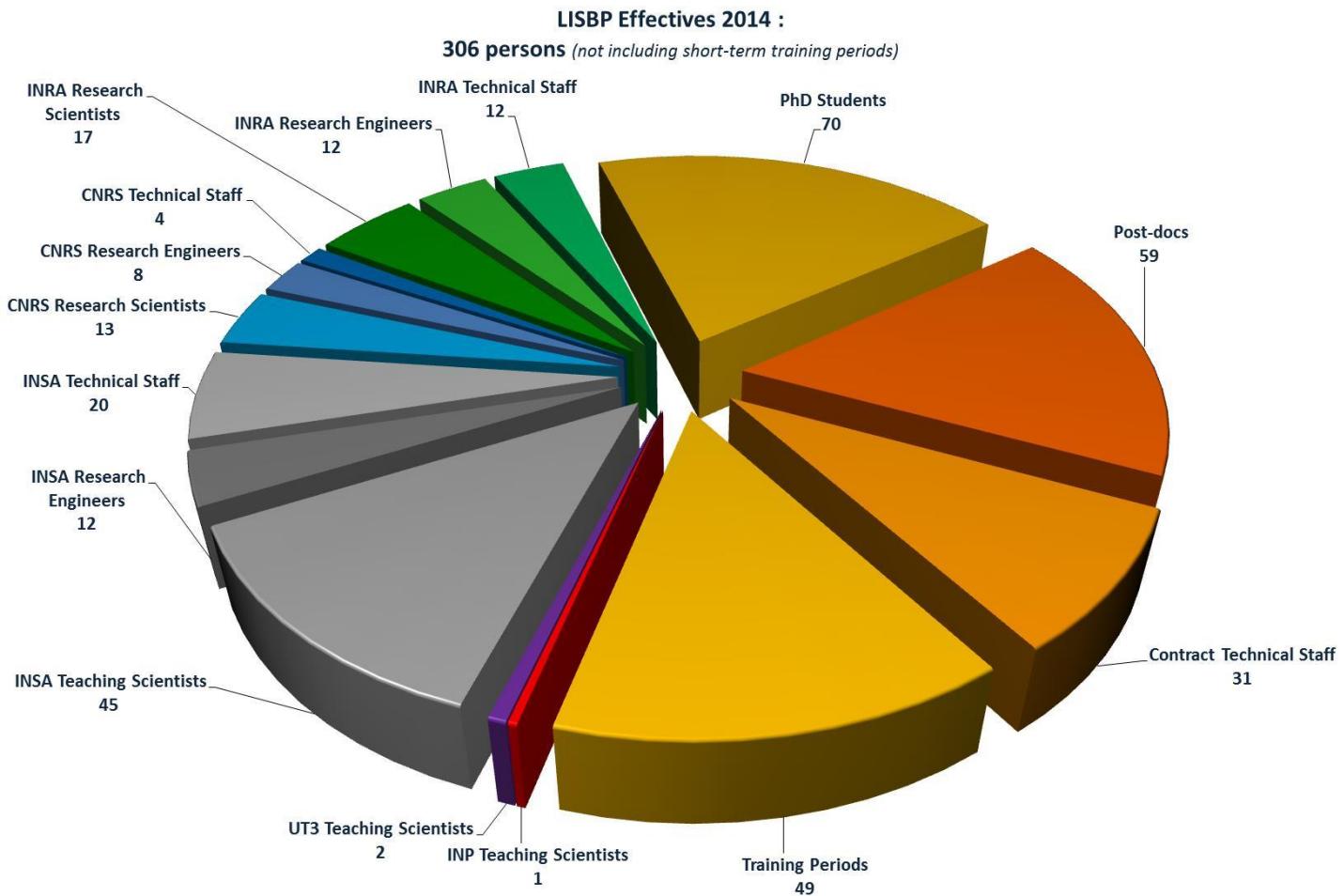
## Scientific Objectives in 3 Keywords



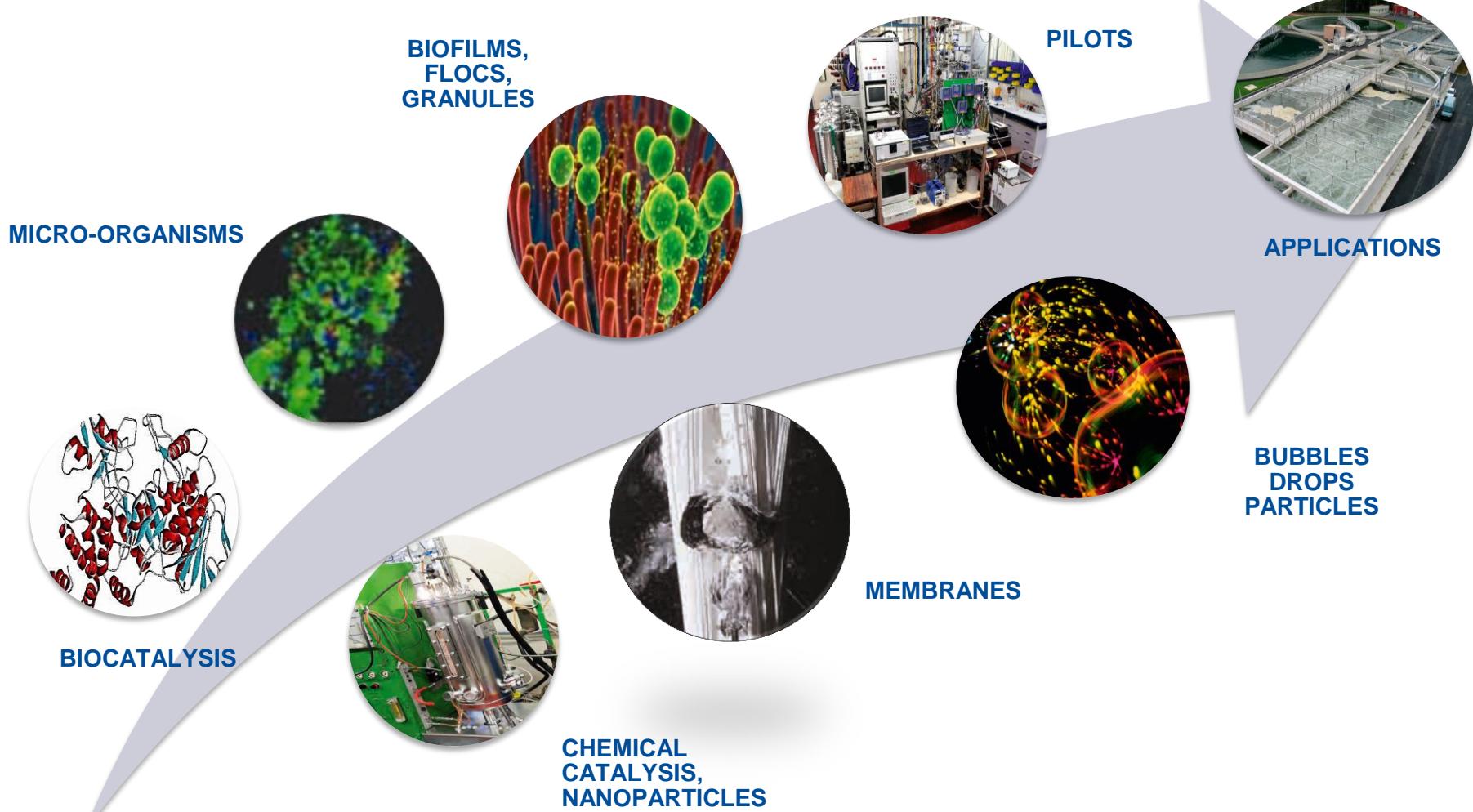
- **Engineering:** rational knowledge-driven improvement of a system's performance based upon in depth understanding of the underlying scientific mechanisms.
- **Systems Biology:** biological systems respond in a complex and dynamic manner to their ambient environment. Understanding these interactions and the basic regulatory networks involved is a key objective for modern industrial biotechnology.
- **(Bio)Chemical Engineering:** most of our research will find its application in industrial processes. Understanding and exploiting the fundamental characteristics of such processes is critical to realistic process development.

**Basic research input for an integrated approach to modern industrial biotechnology with wide applications in energy (biofuels), synthons, biomaterials, pharmaceuticals, food and feed, water resources, etc**

# Research Personnel at LISBP



# Cascade of competence



# LISBP Research Teams

3 major domains: biocatalysis, microbiology and (bio)chemical engineering

## Catalysis and Molecular Enzymatic Engineering

*M. Remaud Pr. INSA*

## Molecular and Metabolic Engineering

*G Truan DR CNRS*

### Biochips and Bionanotechnology

*V. Leberre CR CNRS*

### Engineering and Metabolic Pathway Evolution in Prokaryotes

*I.Meynil-Salles Ass.Pr. INSA*

### Metabolism of Prokaryotes

*M Cocaign-Bousquet DR INRA*

### Physiology and Functional Genomics of Eukaryotes

*JM. François Pr. INSA*

### Integrated Metabolism and Dynamics of Metabolic Systems

*JC. Portais Pr. UT3*

### Microalgal Genome Engineering

*F Daboussi DR INRA*

### Fermentation Advances & Microbial Engineering

*S Guillouet Pr.INSA*

### Microbial Ecosystems and Purification and Recovery Bioprocess

*M.Spérandio Pr.INSA*

### Transfer, Interface, Mixing

*A Cockx Ass Pr.INSA*

### Separation, Oxidation and Hybrid Processes for Environmental issues

*C.Guigui Pr. INSA*

## Technology Platforms



### Transcriptome-Biochips - <http://get.genotoul.fr>

Expertise and technology for the analysis of gene expression. Development of innovative technology for future generation of chip-based analysis.



### Engineering and Screening for Original Enzymes (ICEO) - <http://iceo.genotoul.fr>

Combinatorial engineering to modify or improve existing enzyme properties in order to adapt the catalysts to specific conditions of use. Generation of large libraries of mutant genes. Metagenomic screening.



### Metabolomics-fluxomics (MetaToul) - [www.metatoul.fr](http://www.metatoul.fr)

Expertise and state-of-the-art fluxomics NMR and MS methodologies for the functional analysis of metabolic networks. Major focus on approaches for the quantification of intracellular metabolite concentrations.



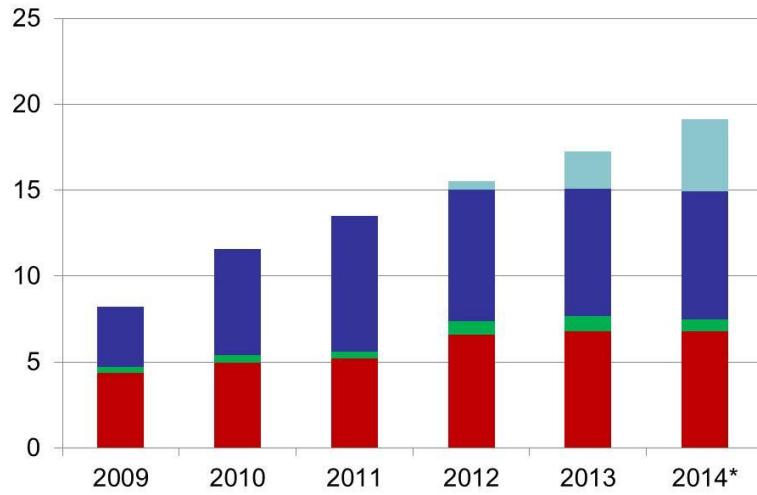
### iFERM fermentation platform

Multi-laboratory fermentation platform covering high throughput mini-fermenters to highly instrumented set-ups and 300L pilot scale plant.

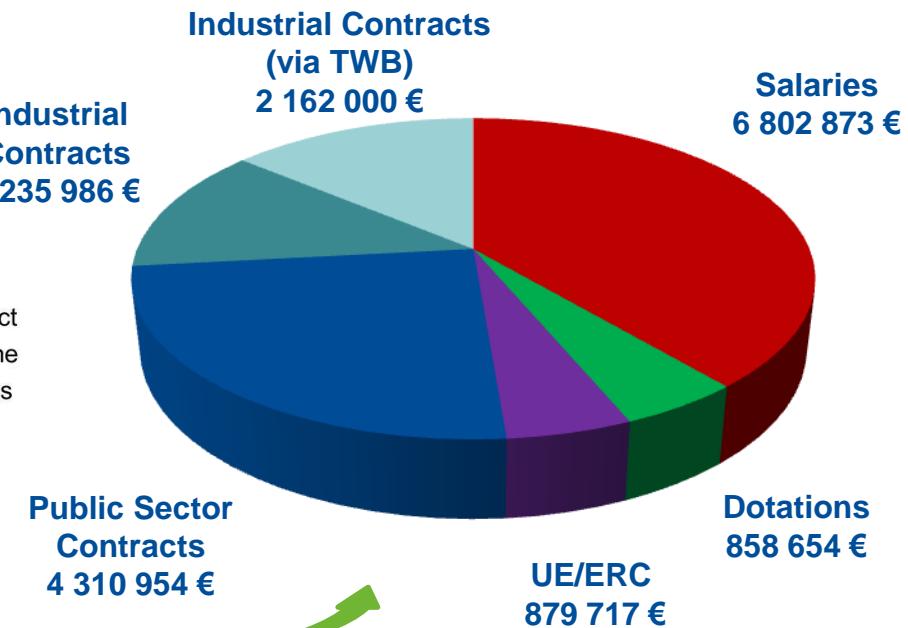
# Budget

## Consolidated Budget (salaries included)

- ❖ 8,5 M€ in 2009 to 15 M€ since 2012
- ❖ additional resources via TWB since 2012 (expected 4 M€ in 2014)
- ❖ 17 European Union/ERC contracts (2009-2014)
- ❖ 4 *Science for the Future* contracts
- ❖ high success rate at national calls (>35% en 2014)

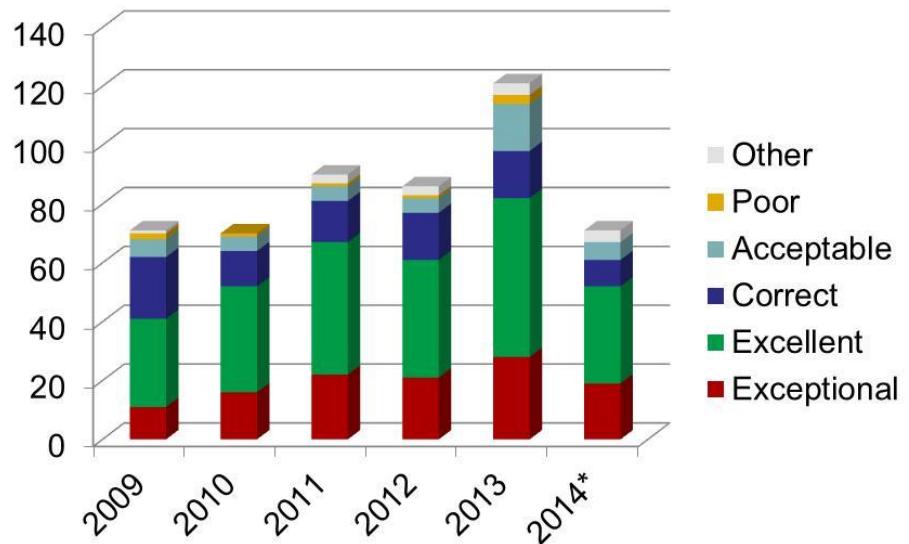


\* Provisional budget for 2014 at 1st July

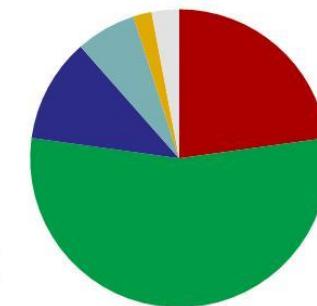


## Scientific Production (2009-2014)

- ❖ >500 publications in WoS journals
- ❖ >75% in 1st quarter journals (>20% in exceptional journals)
- ❖ Co-signatures (50% national / 30% international)

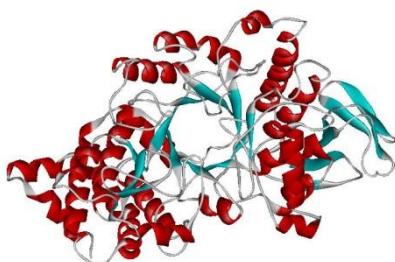
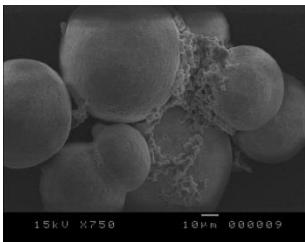


\* Values for 2014 represent only the first half of the year



**INPI Innovation Trophy in 2007**  
**>50 patents since 2007 (13 currently exploited)**

*Head of the group: Pr. Pierre MONSAN*

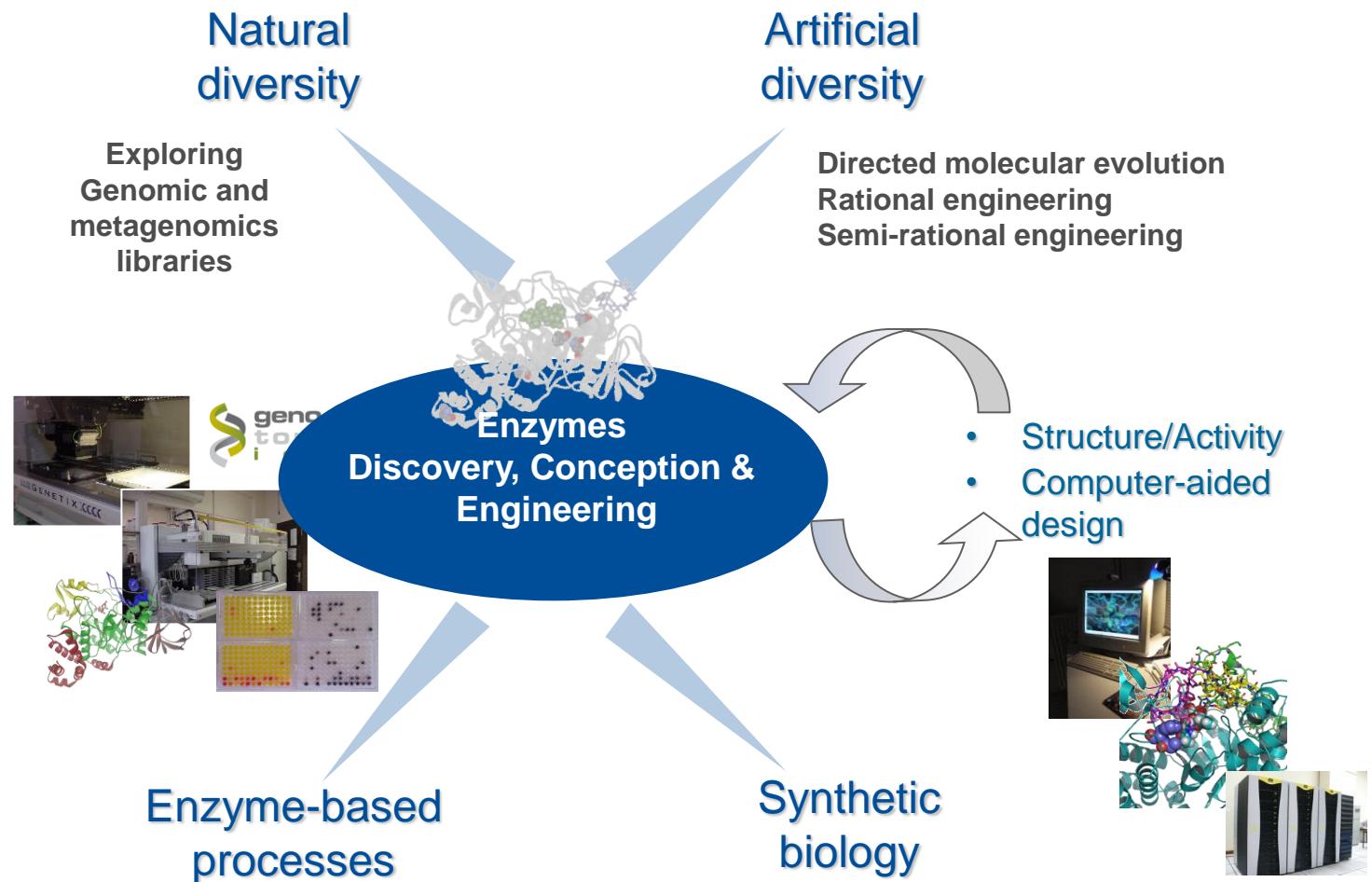


- ~ Discovery, improvement and rational exploitation of high performance enzymatic biocatalysts based upon structure-function analysis.
- ~ Efficient synthesis of novel products :
  - integrated use of microbiology, metagenomics and data mining coupled to molecular biology and 3D modelling
  - technological expertise in production, enzyme stability and immobilisation in both batch and continuous reactors

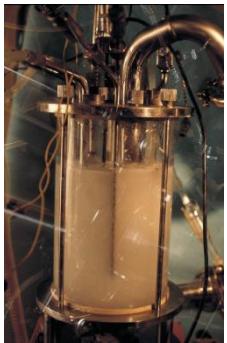
Catalysis & Molecular Enzyme Engineering – Pr. Magali REMAUD (INSA)

Molecular & Metabolic Engineering – Dr. Denis POMPON (CNRS)

# Biocatalysis



# Physiology and Microbial Metabolism



*Head of the group: Dr Nic LINDLEY*

- ~ Systems biology approach to understand and metabolically engineer the microbial system for biotechnological purposes:
  - production of high added value chemical synthons,
  - production of safer food and novel pharmaceutical products.
- ~ 6 teams with complimentary approaches:  
functional genomics, functional genetics, metabolic regulation of complex metabolic networks, metabolic flux analysis and mechanistic modelling based upon enzymes activities and quantitative transcriptomic, proteomic and metabolite analyses.



*Engineering & Metabolic Pathway Evolution in Prokaryotes – Ass.Pr. Isabelle MEYNAL-SALLES (INSA)*

*Metabolism of Prokaryotes – Dr. Muriel Cocaign-Bousquet (INRA)*

*Physiology & Functional Genomics of Eukaryotes – Pr. Jean-Marie FRANÇOIS (INSA)*

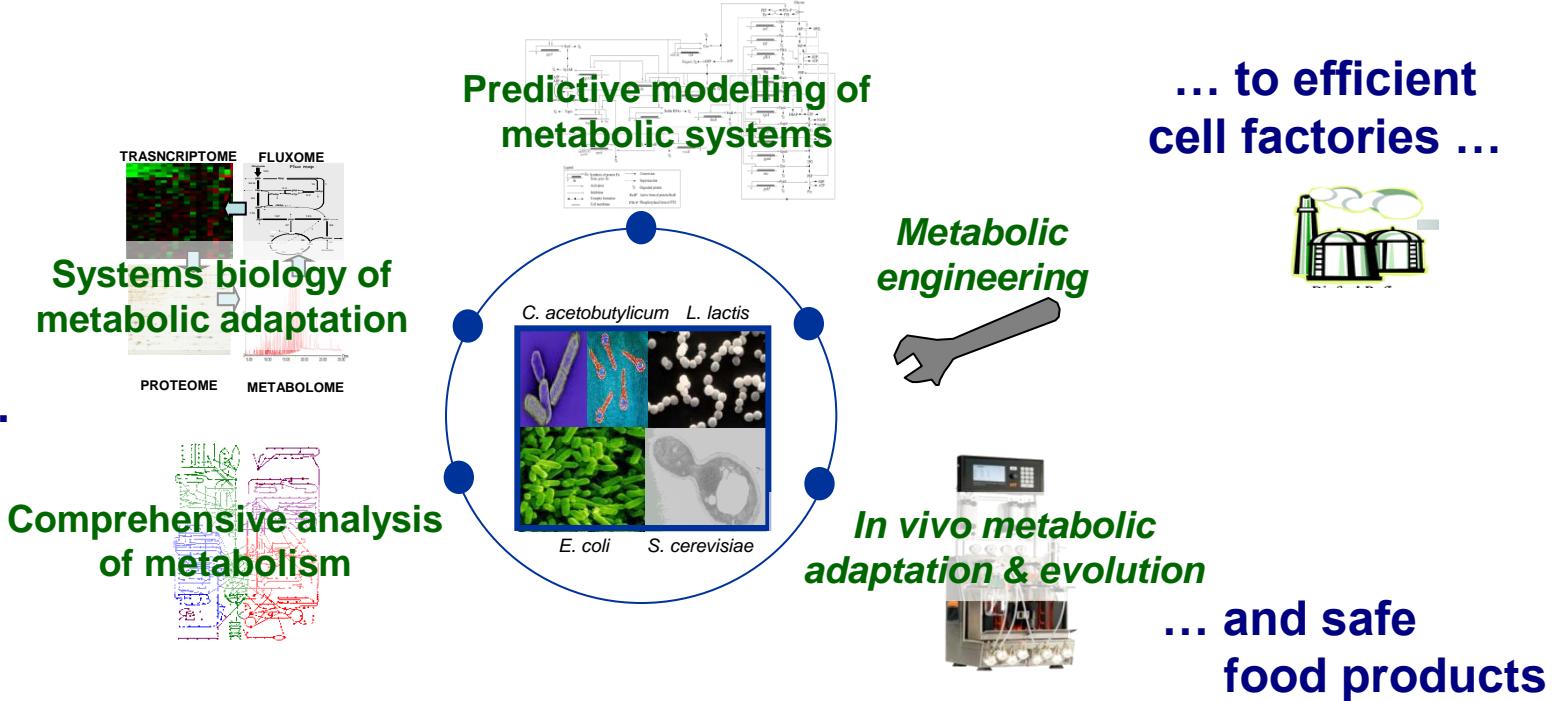
*Biochip & Bionanotechnology – Dr. Véronique LEBERRE (CNRS)*

*Integrated Metabolism & Dynamics of Metabolic Systems –Pr. Jean-Charles PORTAIS (UT3)*

*Microalgal Genome Engineering – Dr Fayza DABOSSI (INRA)*

# Microbial Physiology and Metabolism

**From basic knowledge ...**



**Applications:** biofuels, chemical synthons, nutrition, pharmaceuticals, etc

# Systems Biology Approach

**Phenotype**

Metabolite/  
flux

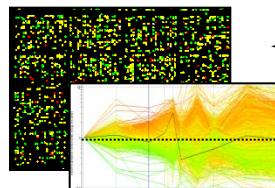
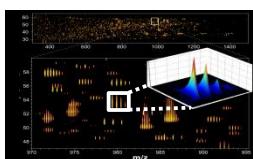
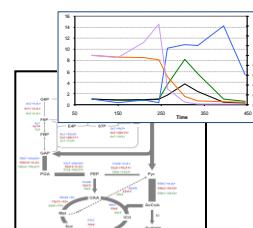
Protein

mRNA

Gene

**Adaptation**

**Systemic  
Biology**



**Mathematics**

$$\begin{aligned} \psi_i \cos(\omega t) &= \Phi \cos(\beta_i t) \\ \Phi^2 &= \sum_i \psi_i^2 + 2 \sum_{i,j} \psi_i \psi_j \cos(\beta_{ij} t) \\ \int \chi(t) dt &= \frac{\chi(t)}{dt} = k(\omega) \\ \alpha - \frac{1}{\sqrt{2}} \frac{\partial^2 u}{\partial t^2} + \frac{\partial^2 u}{\partial x^2} + \frac{\partial}{\partial x} &= 0 \\ V = \sqrt{\left(\frac{g \lambda}{2 \pi} + \frac{2 \pi \rho}{e \lambda}\right) \tan \theta} & \\ \psi = \int_{-\infty}^{\infty} (\alpha(k)) e^{i(kx - \omega t)} dk & \\ E = mc^2 & \end{aligned}$$

Understanding : system description

**Modeling**

Bacterial phenotypes

Predict

Understand

Determinant Identification

Nutritional Eng.  
Metabolic Eng  
Synthetic Biol.

Bacteria  
exploitation

Application

# Microbial Systems and Bioprocesses



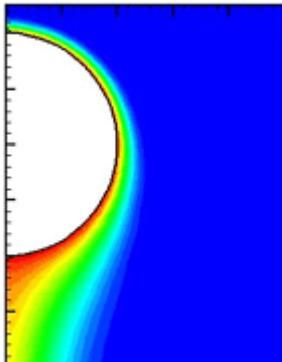
*Head of the group: Pr. Jean-Louis URIBELARRÉA*

- ~ Analysis and understanding of the dynamic behaviour of microbial populations within bioreactors with a controlled environment, based upon the integrated use of fermentation technology, microbial physiology and process engineering.
- ~ Study and exploitation of complex microbial consortia
- ~ Systemic analysis of microbial behaviour in reproducible and fully characterised fermentation conditions taking into account industrial constraints to develop innovative microbial bioprocesses.

*Microbiological Engineering Systemic Analysis & Process Innovation – Pr. Stephane GUILLOUET (INSA)*

*Microbial Ecosystems, Purification & Recovery Bioprocessing – Pr. Mathieu SPÉRANDIO (INSA)*

## Transfer-Interfaces-Mixing



*Head of the group: Pr. Philippe SCHMITZ*

- ~ Experimental analysis and mathematical modelling of hydrodynamic, mechanical and physico-chemical phenomena involved in multiphase and reactive process environments.
- ~ Fluid mechanics and chemical engineering principles to determine the diffusional transfer characteristics in fluids containing dispersed inclusions.
- ~ Detailed studies of specific phenomena identified in pilot studies are performed in model systems and then extrapolated to achieve knowledge of the functional behaviour of complex reactions at the bioreactor level.



*Transfer-Interfaces-Mixing – Dr. Arnaud Cockx (INSA)*

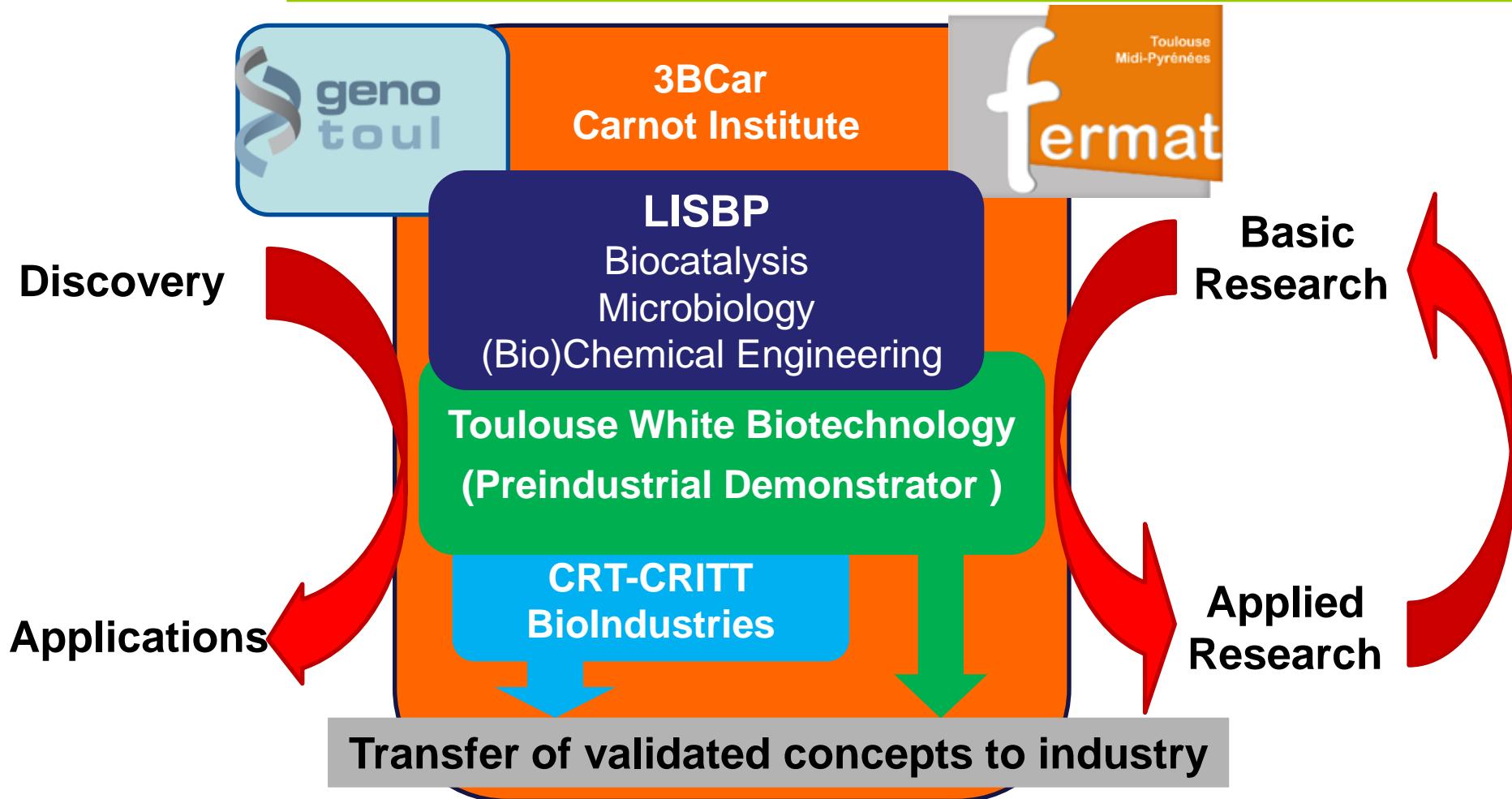
## Separation, Oxidation and Hybrid Processes for Environmental Issues



*Head of the group: Pr. Corinne CABASSUD*

- ~ New approaches in environmental engineering, water treatment and eco-designed processes.
  - separation (*membranes, adsorption, chromatography*)
  - reaction (*crystallization, oxidation*) and their limiting phenomena.
- ~ Analysis and optimization of these processes for complex liquids (*water, effluents, biological fluids, green juices, urine*) for their treatment or valorisation.
- ~ Sustainable and integrated processes involving hybrid processes based on separation and (bio) reactions (ex: *membrane bioreactors*)
- ~ Modelling tools for process eco-design and life cycle analysis.

## Toulouse Center for Industrial Biotechnology



*LISBP : a large panel of expertise and integrated approaches*

*...for understanding molecular phenomena underpinning biological systems*

*... the physico-mechanical characteristics of complex environments*

*...and to thereby rationally develop innovative processes for industrial biotechnology*

*see website [www.lisbp.fr](http://www.lisbp.fr) for further details*