LABORATOIRE LRGP REACTIONS ET GENIE DES PROCEDES

REACTIONS AND CHEMICAL ENGINEERING LABORATORY

BIOREFINERY ENGINEERING

Skills of the Reactions and Chemical Engineering Laboratory in:

- **Processes of extraction, fractionation, separation and purification.**
- **Processes of biotechnological, chemical and thermal transformation.**
- **Multi-scale modelling: molecular, meso-scale, PSE, LCA.**

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1. Biorefinery: numerous products from renewable resources

The concept of biorefinery is defined as *the sustainable processing of biomass into a spectrum of marketable products and energy.* This concept is thus analogous to today's petroleum refinery, which produces multiple fuels and products from petroleum. Because it uses renewable raw materials in place of fossil resources, it is a cornerstone of green and sustainable production future strategies (Figure 1).

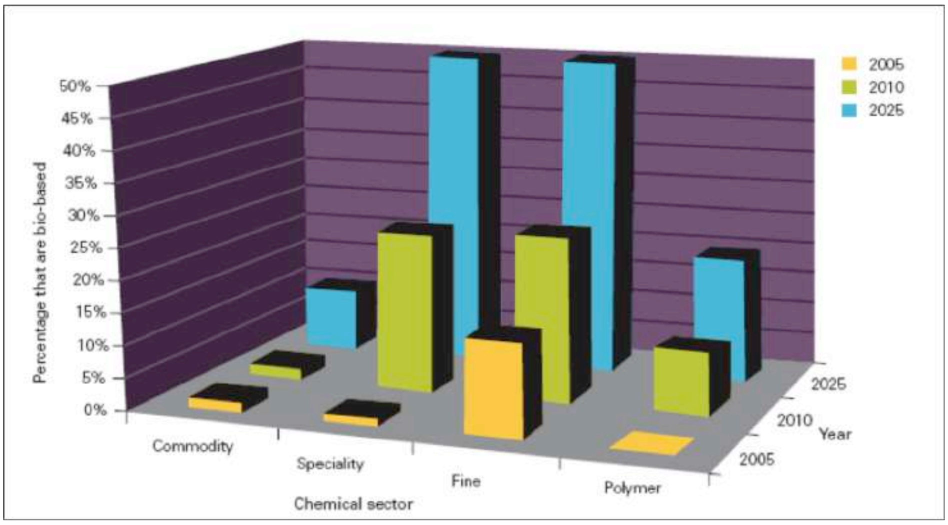


Figure 1. Predicted market penetration of bio-based chemicals in world chemical production, excluding pharmaceuticals (Advisory group for bio-based products, European Commission Enterprise and Industry, Nov. 2009).

By producing multiple products, the biorefinery takes advantage of the various components in biomass (starch, hemicellulose, cellulose, lignin, oil, protein) and their intermediates, therefore maximizing the value derived from the biomass feedstock. The biorefinery can produce, for example, one or several, low-volume but high-value, chemical or biochemical products such as cosmetics or neutracetics, and, low-value but high-volume, liquid transportation fuels such as biodiesel or bioethanol. A very large variety of products can be thus obtained opening a wide field of applications (Figure 2).

Although some facilities exist that can be called biorefinery plants, scientific and technological knowledges are yet required to improve and to optimize them. Consequently a large spectrum of research and development activities has to be undertaken in order to make the concept of biorefinery an industrial reality. Henceforth, multidisciplinary skills, including biology, chemistry and chemical engineering, are required to reach such ambitious goals. Several initiatives are under progress throughout the world based on collaborative programs.

In this general context, the objectives of this White Paper are to highlight the various processes involved in a biorefinery plant and to point out the scientific challenges that need to be adressed at each stage of the biomass refining process, through a Biorefinery Engineering point of view. Then, it describes the skills available at LRGP-Nancy (Laboratoire Réactions et Génie des Procédés), which could be advantageously used for the better knowledge and the development of processes dedicated to biorefinery plants. At the end of the document, some examples of LRGP research projects in this area are given.

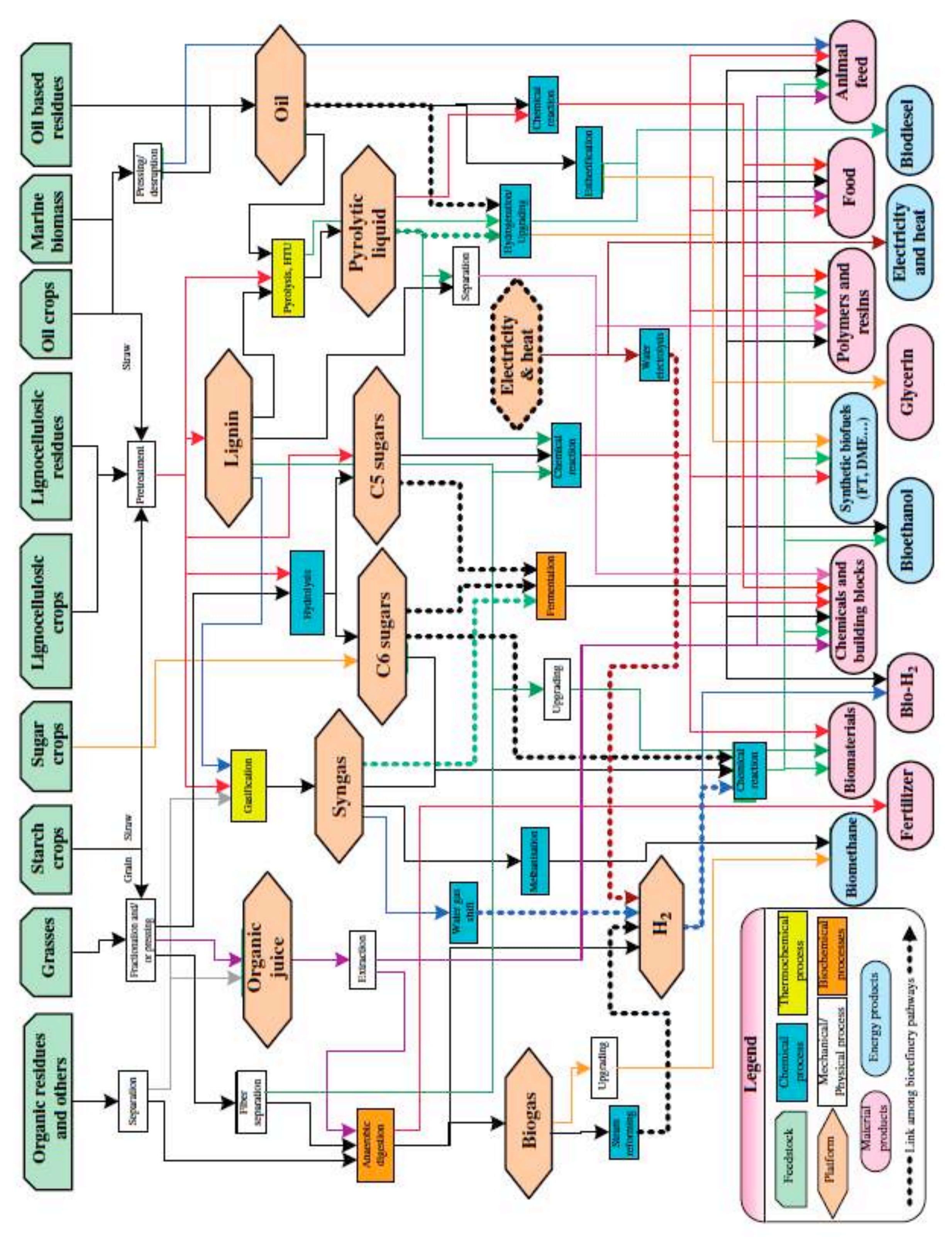


Figure 2. Complex network from biomass feedstocks to products.

(Cherubini et al., Biofuels, Bioprod. Bioref., 2009).

2. Biorefinery: many processes to implement

The concept of biorefinery is largely multifaceted and requires implementing various types of processes. Figure 3 presents the different connections between processes from raw materials to application areas.

2.1. Extraction and fractionation processes

From renewable raw materials, which are mainly vegetables, wood or algae, and on the basis of a thorough characterization of these complex resources, fractionation and/or extraction processes allow to reach major biochemical species such as starch, lipids, proteins, cellulose or lignin. These processes are mainly based on mechanical operations or on solid/liquid extraction, heat treatment, supercitical CO_2, and membrane separation.

2.2. Thermal and biotechnological transformation processes

The obtained biochemical molecules can be then, either purified and directly used, or transformed through various thermal or biotechnological processes. Thermal processes mainly include pyrolysis and gasification. Biological processes can use enzymatic biocatalysts for the hydrolysis of the polymeric molecules or for the transesterification and functionalization of the intermediates. Viable biocatalysts, mainly bacteria or yeasts, are also available to transform small molecules in products of interest by microbial processes. Additionally, it should be noted that hybrid transformation schemes, making use of an interplay between biochemical and thermochemical processes are also possible and can be of interest with regard to energy integration aspects.

2.3. Purification processes

Then, depending on the type of application of the final products, such as green chemistry, energy, food and feed, health, some purification processes have to be implemented. They are mainly based on membrane processes (micro, ultra and nanofiltration) or chromatographic processes (size exlusion, ion exchange, adsorption, centrifugal partition chromatography).

2.4 Global biorefinery system

From a global overwiew of the biorefinery factory, process system engineering must also be used in order to organize the process unit operations, to optimize the mass flows and to limit energy requirement. Indeed, a large number of possibilities exists concerning the architecture of the global system and the combination of the process steps. Finally, the life cycle analysis of the overall biorefinery system can be proposed to ensure sustainability and protection of the environment. Beside, multi-scale modeling can be required at molecular, meso, reactor and factory scale.

It should be noted that there is, to the best of our knowledge, no research team covering the complete spectrum of biorefinery, starting from raw biomass materials down to a final ready to sale end product.

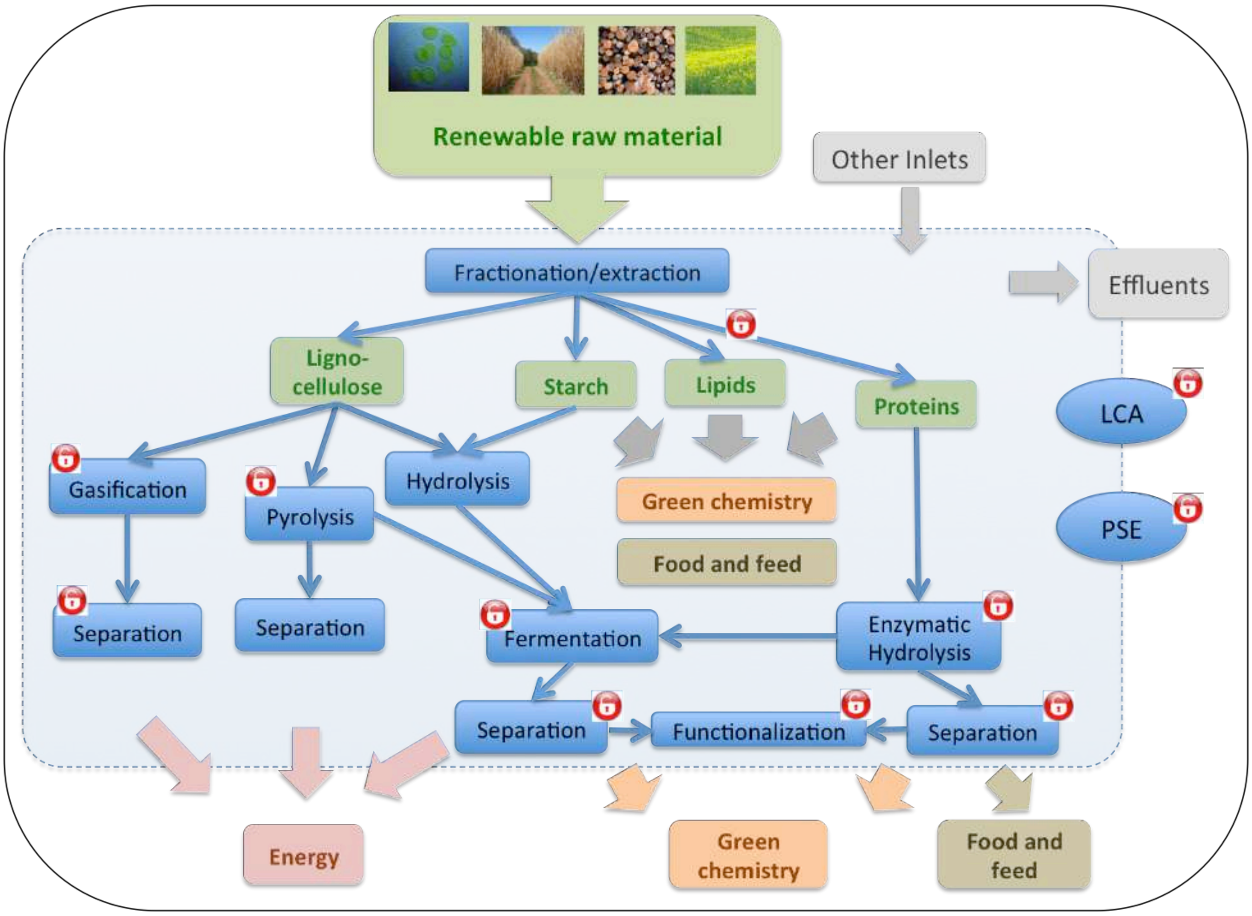


Figure 3. Various processes (in blue) required for renewable raw material refining. Red padlocks correspond to main research challenges addressed at LRGP *(PSE: Process System Engineering, LCA: Life Cycle Analysis).*

3. Research challenges in biorefinery engineering and strategic targets at LRGP

This section is dedicated to the presentation of the main research challenges in biorefinery engineering. For easy reading, they have been intentionally limited to challenges, which are currently being addressed at LRGP.

3.1. Specificities of biorefinery

To better identify the research challenges in biorefinery engineering, it is first necessary to identify the specificities of this domain, which will significantly impact the performances of the involved processes. In contrast to refinery of fossil resources (oil, gas, coal), these specificities can be summarized as follows.

- **Chemical composition**. The chemical composition of renewable raw materials is much more complex, because they contain a wide variety of chemical molecules, which are often mixed and/or associated in various proportions. Most of the time, these molecules are polymers of very different sizes. Starch, mainly issued from crops, as well as cellulose and hemicellulose, from wood or straw, are polymers of different carbohydrates, which are more or less soluble and fermentable. Proteins, which can be extracted from various vegetables seeds, are polymers of amino acids. Lipids, such as oil from oleaginous plants, are composed of fatty acids. Lignins from wood are polymers of monolignols such as coumaryl, coniferyl or sinapyl alcohols. Moreover, the ratio of oxygen per carbon is often much higher than in fossil materials. Finally, feedstock is highly dependent on the plant variety or on the harvest period, and can possibly be tuned in order to achieve the most appropriate molecular composition and morphology.

- **Molecular and ultra structures**. These polymeric substances often exhibit multifunctional molecular structures. Moreover, the bioresources are not based on a simple mixture of chemical components. Most often time, there are solid material structures with a complex anisotropic ultrastructure.

- **Transformation reactions**. The kinetic reaction pathways of biomass transformation are usually extremely complex due to the molecular specificities of the resources. Highly selective chemical or enzymatic catalysts are needed for reactions of dehydration, hydrolysis, cyclization, ring opening, hydrogen transfer, functionalization, etc. Furthermore, microorganisms have to be screened or genetically modified to be able to consume molecules issued from biomass and to synthesize desired products.

- **Final product composition and structure**. The thermal or biological transformation processes lead to complex mixtures, containing several by-products, and wherein the product of interest is often diluted. As the end product functionality is mostly linked to its structure, it is required to develop expensive and multiple steps downstream processes coupled to innovative analytical methods.

- **Energetic aspects**. Ideally in a biorefinery, steam and electricity integration has to be taken into account together with the polygeneration of materials and products.

3.2. Challenges and targets for extraction and fractionation processes

Taking into account the competitions in land use between food and non-food applications, the selection of the available biomass resource first requires an accurate quantification of its availability within a reasonable transportation distance. Furthermore, precautions are needed to reduce the export of soil nutrients by over-intensive biomass harvesting. Biomass with lower cost or faster growing is to be favored and the process should match with its various compositions in minerals or pollutants.

- **Ligno-cellulose.** For ligno-cellulosic raw materials, the fractionation of the starting feedstock into different families of molecules is of major interest. This enables the different molecules to be used according to dedicated transformation processes (thermal, chemical or biological). The extraction and purification of cellulose can be done by using ionic liquids, while lignin and hemicellulose can be solubilized with organic solvents (organosol process). The main issues are to reduce solvent consumption, to research green solvent (such as ethanol) and to recycle them. Heat recovery is also an important challenge.

- **Proteins**. Protein extraction processes are rather simple and depend on the nature of the raw material. It may consist in mechanical operations (for leaves) and/or solid/liquid extraction in aqueous solvents (for solid residues like seeds or meals). However, protein functionalities as foaming, emulsifying, gelifying, adhesive properties, nutritional properties etc…are very sensitive to extraction operating conditions. Furthermore, undesirable compounds like polyphenols or antinutritional molecules released from vegetal sources react with proteins in the extract and limit their performances. The bottleneck in term of chemical engineering at this level lies on the complex optimization of the step since many operating conditions (pH, S/L ratio, T, solid size repartition, agitation, etc…) and antagonist performance criteria (yield, purity, concentration, phenol complexation, properties, aggregation etc…) are involved.

→ ***Strategic targets proposed by LRGP***:

- Combining advanced modeling of the forest (or agricultural crops) growth and wood availability with detailed models of biorefinery chains (including biomass pretreatment, transportation and biorefinery process). Hence the biomass needed to supply the process matches with the available resource, with a limited transportation distance.
- Ligno-cellulosic biomass fractionation by liquid ionic and organosolv methods with detailed process modeling to reduce solvent consumption, improve solvent recycling and heat integration.
- Multi-criteria optimization of rapeseed meal proteins extraction including protein qualities criterion, such as structure, phenol complexation and protein functionalities.
- Enzymatic treatments for improving protein extraction from industrial rapeseed meal.
- Integration of protein extraction and lignocellulosic residue valorization.

3.3. Challenges and targets for thermal transformation processes

The thermochemical conversion of biomass produces gas, liquid (bio-oils) and solid (char). The selectivity in these products depends on the operating conditions (temperature, oxidation, residence time, pressure, etc.). The different processing routes, which can be used for biomass thermal treatment, are combustion, pyrolysis, gasification or liquefaction. A considerable know how has been accumulated for decades at LRGP for gasification and pyrolysis process, especially for syngas and bio-oil production. In biorefinery, the biomass thermal treatment uses two major processes:

- gasification producing essentially syngas, followed by a Fischer Tropsch reaction for alcane synthesis, a methanation reaction for CH_4 production, or hydrogen production through water gas shift.

- flash pyrolysis or liquefaction, followed by a catalytic treatment to produce alcanes or aromatics from the bio-oils.

The catalytic conversion step is the major bottleneck due to undesirable coking effects leading to catalyst deactivation. To that respect, numerous catalysts (namely Ni/Co/MoS, zeolites (H-ZSM5), or Fe/Ni were investigated. One of the main roles of catalyst is to achieve the selective desoxygenation of the feedstock molecules.

Very little is known on the chemical reactions and mechanisms leading to biomass liquefaction (high pressure solvolysis) or pyrolysis. Hundreds of compounds are involved and numerous by products (including undesired ones like tars) are generated. The expertise gained in gas reaction could possibly be attempted to these challenging systems.

Reactor design for thermal processes can be considered as reasonably mature, nevertheless, challenges remain for the rational design of trickle bed or ebullated bed such as for viscous and reactive (oxygenated) feed treatment.

Reactor optimization could be investigated through modern CFD approaches, but requires relevant reaction schemes and kinetics knowledge to be available for biomass thermal treatment.

→ Strategic targets proposed by LRGP:

- Detailed kinetics modeling of gaseous or liquid/solid reactions for thermochemical processes
- Advanced spectroscopic techniques for pyrolysis mechanisms identification or bio-oils characterization
- Dedicated thermodynamic models for ligno-cellulosic biomass and oxygenated products
- Tailor made catalysts for cracking or desoxygenation reactions
- Reactor design and development of intensified processes: liquefaction, hydrotreatment (ebullated or trickle bed)
- Detailed modeling under Aspen Plus of the thermal processes for further improving selectivity, heat efficiency and reducing environmental impacts.

3.4. Challenges and targets for biotechnological transformation processes

The biological transformation of feed stocks deriving from natural resources can be carried out through two main ways, involving bio-catalysts alive or not. Such bioprocesses usually generate products in solution, are specific and can reach production yields equivalent compared to their chemical counterparts.

- enzymatic processes, often performed under mild operating conditions, such as ambient temperature, non-extreme pH or atmospheric pressure, even if other conditions (water, sCO_2, ionic liquid) are still under study.

- microbial processes use cellular catalysts (bacteria, yeasts, ...) to transform small intermediate or complex molecules in molecules for energy (hydrogen, alcohol,...), food (glutamate), cosmetics (hyaluronic acid) or chemicals (succinic acid, 1,3-propanediol…).

Regardless of the catalysts used, lack of knowledge about structure, physiology or biochemical mechanism could be the main bottleneck of bioprocess development. It includes the identification of rate limiting steps of reactions at various scales (micro, meso and marcroscopic), the understanding of metabolic routes through partitioning of carbon and electron fluxes, and the stability of biocatalysts such as cell viability and genetic, or enzyme structure.

Besides, bioreactor design for biological reactions is relatively classical, including scale-up aspects. Nevertheless, integrated approaches combining reaction kinetics and operating conditions should be more systematically investigated. CFD methods are also likely to improve the understanding of gas-liquid or liquid-solid transfers, as well as shear stresses, opening innovative developments for bioreactor design.

→ *Strategic targets proposed by LRGP:*

- Enzymatic processes to hydrolyze plant proteins in bioactive peptides.
- Regio- and chemo-specificity of lipase B for peptide acylation: optimal conditions to get improved peptide derivatives, prediction of enzyme specificity by molecular modeling using docking simulation.
- Reverse engineering focused on new enzymes: seeking new activities from natural diversity and enzymatic engineering by direct mutagenesis based on structural molecular modeling.
- Microbial transformation of biomass or derivatives (starch, cellulose, glycerol…) into higher value metabolites such as acids (succinate, butyrate), alcohols (ethanol, butanol) or gas (H2, CH4).
- Better understanding of metabolic pathways for development and control of the production process.
- Kinetic studies of aerobic/anaerobic transitions in bi-phasic fermentation processes.
- Modeling of metabolism kinetics at various microbial process scales (microscopic and macroscopic).

3.5. Challenges and targets for separation and purification processes

A general bottleneck of biorefinery development comes from the fact that product concentrations are typically low and several by-products are produced. Consequently, the different separation processes used for isolation, concentration and purification, usually referred as downstream processing, have an important impact on the economics of the system, causing up to 80 % of the production costs. There is thus a crucial need for efficient, novel, sustainable, intensified and low cost separation processes to unlock biorefinery applications. Major challenges concern separation and purification technologies, mostly based on nano and microfiltration membrane processes, electrochemical processes, classical chromatographies (affinity, adsorption, size exclusion) or promising ones (centrifugal partition chromatography), and their reliable scale-up methodologies.

Separation processes for solutes in liquid phase

Mixtures from biochemical conversion or extraction from bioressources are most often time very complex (classically hundreds of different solutes) and the solutes (or group of solutes of interest) in these mixtures are often in low concentrations. In many cases, the purification, enrichment or concentration of targeted solutes has to be implemented. Membrane and chromatographic processes are used for such applications in most of the cases. To date, the choice of operating conditions and the chaining of operations for reaching the satisfying purity, yield or environmental print is often made empirically.

There are three main issues related to bioseparations for biorefineries, both of them due to the complexity of the mixtures: i)- improving separation selectivities and productivities, ii)- rational chaining of operations (for multi-steps separation processes), iii)- limiting environmental print (reduction of effluent and/or energy consumption). To tackle these issues, a deep knowledge of: solute mass transport limitations in separation media, modeling separation systems, and multicriteria optimization methodologies, are required independently or in association with analytical chemistry (for dealing with complex mixture characterization), chemistry and/or material sciences (for designing advanced separation media).

LRGP has pioneered mass transport phenomenon in porous media like chromatographic stationary phases and has developed advanced methodology for dynamic optimization as well as has undertaken researches on various field of bioseparations for biorefinery, especially concerning peptides (from enzymatic proteolysis) and carbohydrate polymers for years.

Separation processes in gas phase

The LRGP also develops some research works on processes for biogas mixture separation. Even if these methods and tools could have an interest in biorefinery, they will not be described in this white paper, because they rather belong to the field of energy.

→ Strategic targets proposed by LRGP:

- Modeling and design of separation processes (membranes, chromatography, electrochemical technologies)
- Fast cartography of peptide properties (molar weight, charge, hydrophily, hydrophobicity and composition) in complex peptide mixtures (hydrolysates) by liquid chromatography- and capillary electrophoresis-mass spectrometry
- Methodology development for predicting separation performances (yield, enrichment and productivity) of complex protein hydrolysates in a peptide of interest by membrane or chromatographic separation
- Development of hybrid techniques combining ion exchange and bipolar membrane electrodialysis (zero effluent/continuous ion exchange processes)

3.6. Challenges and targets for global biorefinery study

The design and optimization of sustainable biorefineries include various challenges that can be first classified with respect to the underlying phenomena they are based on:

- the design of routes synthesis: due to the large number of potential chemical pathways from the raw products to the final products, the choice of the synthesis route can be a challenge. Whereas this step could be seen as a chemical choice, the impact on the final process flow sheet is huge and the pathway selection cannot be totally decoupled from the flow sheet design and rating.

- the design of separation steps: various PSE methods and tools have been developed for design of separation of common mixtures. Unfortunately, the variability of mixtures involved in biorefinery flow sheets strongly widens the complexity of the problem, and a lack of mixture properties enlarges the uncertainties related to the relevance of technical potential solutions. This variability must be taken into account not only during the design and rating of the flow sheet and devices but also during the operation, planning and scheduling of the plant.

- the flowsheet synthesis: based on the above-mentioned difficulties, the flow sheet synthesis must be based on dynamic and rapid tools and methods so that various scenarios can be tested and compared. Criteria for this comparison should include various levels of accuracy depending on the current development of a project. The flow sheet synthesis should also be able to tackle with a specific feature of biorefineries: should the production be performed in a single large-size plant or distributed into various delocalized small-size plants?

In addition to these challenges that mainly concern the development of new biorefineries, PSE methods to be developed should also include the fact that biorefineries may also be developed by coupling them to or by retrofitting existing conventional refineries. New sets of constraints should then be included in the flow sheet synthesis, but such combinations could help accelerate their development and test new industrial-scale technical solutions.

To optimize the complete biorefinery factory, additional studies have to be developed in:

- Process System Engineering (PSE), including matter flows and energy integration issues: fast and flexible first-screening methods for process flow sheet generation and comparison, appropriate methods for process design and scheduling under uncertainty, PSE tools for one-site and multi-site scenarios design and comparison, advanced retrofitting methods and tools for optimal flow sheet reshaping.

- Life Cycle Analysis (LCA) of the overall biorefinery system to ensure the sustainability and the environment protection: the development of eco-efficient processes is a very important issue especially for bio-refining processes, which require interesting environmental performances compared to fossil fuels without competition with the food chain. LCA is a standardized method that takes into account each constituent process of the life cycle of the system considered. It is obviously necessary to quantify emissions of greenhouse gases, consumption of resources (renewable or not), occupation or change of land use, or human health impacts. However, it is often used only in the final stages of designing a process or for comparison of different sectors. But the integration of this method in the initial stages of design of the process is essential. Indeed, consider the environmental constraints from the preliminary steps offers opportunities and additional degrees of freedom. Thus, the coupling of LCA and PSE methods is an ideal tool for developing an eco-efficient bio-refining process.

→ Strategic targets proposed by LRGP:

- Optimization methods for process and energy integration.
- Molecular mesoscale modeling.
- Tailor made PSE tools for simulation and process synthesis: advanced process models including resource growth, its mobilization, pretreatment as well as bio- and thermo-chemical processes to the final purified products.
- Evaluation of the environmental impact (LCA, carbon and water footprint) of biorefineries.
- Development of an effective methodology for coupling LCA and PSE to reflect environmental impacts from the preliminary stages of developing biorefining processes.

4. Biorefinery research activities at LRGP

The research activities performed at LRGP in the area of biorefinery on a broad sense have been gathered and presented through summary sheets (see annex). A total number of about 20 permanent researchers from the five departments of LRGP are involved:

1. Processes for the environment, safety and recovery of resources
2. Architecture and process intensification
3. Bioprocesses - Biomolecules
4. Kinetics and Thermodynamics for Energy and Products
5. Processes, Products, Materials

This inventory highlights the following points:

- **Multiscale approach**. In terms of research objectives, different levels are investigated, leading to a multiscale approach, from molecules, local mechanisms, unit processes to overall plant.

- **Large number of equipments**. From a technical point of view, a large number of different types of reactors and separation devices can be used from lab to pilot scale. Moreover, different characterization methods and analytical tools, such as various spectroscopies including mass spectrometry, gas and liquid chromatographies, biochemical analyzors, particule analysis, ... are available in the laboratory. They have been already applied to the complex initial raw materials as well as to the mixtures of molecules that are generated through biomass transformation in solid, liquid or gaseous state.

- **Methodological tools**. Several methodological tools and methods are developed in the laboratory such as molecular modeling, modeling and simulation of unit operations (reactors, separators), complete process chain simulation through Process System Engineering softwares, generic approaches and softwares for security and Life Cycle Analysis (LCA) concepts.

- **Integrated approach**. LRGP offers a broad spectrum of know-how covering the different processes of the whole flowsheet of biorefinery: raw biomass treatment, biotechnological or thermochemical transformations, separation and purification processes (liquid-liquid extraction, electrochemical processes, membranes, chromatography), final product production from intermediate (i.e. acrylic polymer from glycerol).

- **Complementary skills**. A specificity of LRGP, in particular at the national level, is to gather in the same unit researchers having expertise in both thermochemical and biotechnological transformation processes.

Annexes: Summary sheets of research activities at LRGP

(The e-mail adress of the contact always finish by: @univ-lorraine.fr)

Extraction and fractionation processes

1. Dissolution and extraction of carbohydrates using ionic liquids (Fabrice.Mutelet@...)
2. Extraction, enzymatic hydolysis and transformation of proteins from oleoproteaginous plants (Romain.Kapel@...)

Biotechnological and chemical transformation processes

3. Transesterification processes (Jean-Francois.Portha@...)
4. Microbial processes for production of molecular building blocks (Emmanuel.Guedon@..., Stephane.Delaunay@...)
5. Coupling between bioreactor hydrodynamics and cell biological responses (Eric.Olmos@...)
6. Ways of raw glycerol valorization (Isabelle.Chevalot@...)
7. Catalytic processes for biorefinery (Eric.Schaer@...)
8. Bio-based monomers/polymers, and polymer recycling (Sandrine.Hoppe@...)

Thermal transformation processes

9. Lignin valorisation (Anthony.Dufour@...)
10. Biomass pyrolysis and gasification (Guillain.Mauviel@...)
11. Modelling of thermal transformation processes (Anthony.Dufour@...)
12. Gas/Dust hybrid mixtures explosion (Olivier.Dufaud@...)

Separation and purification processes

13. Membrane and chromatographic processes for fractionation, concentration and purification of biomass products (Romain.Kapel@...)

Global biorefinery study

14. Molecular and meso modelling for bioraffinery (Catherine.Humeau@..., Latifa.Chebil@...)

Extraction

and fractionation

processes

1. Dissolution and extraction of carbohydrates using ionic liquids

Projects

- Extraction of cellulose and carbohydrates from biomass using ionic liquids ((ICEEL, Coord. F. Mutelet, 2012).
- Mutiscales modeling of the behavior of carbohydrates in methylphosphonate based ionic liquids.
- Phase equilibria of biomass carbohydrates in ionic liquids and deep eutectic solvents.
- Pretreatment of miscanthus using 1,3-dimethyl-imidazolium methyl phosphonate (DMIMMPh) ionic liquid for glucose recovery and ethanol production

LRGP Skills

- Study of the dissolution of carbohydrates, cellulose and lignin in various ionic liquids (dissolution rates, influence of the presence of impurities and of thermodynamic properties).
- Extraction process using the antisolvent method.

Results

- Ionic liquids have been suggested to replace volatile organic compounds in industrial separation processes (HASSAN, 2013). Antisolvent method was found a good technique for the extraction of sugars from Ils: the decrease of sugar solubility in binary mixtures proves ethanol ability to be an excellent antisolvent for separating sugars from various types of ionic liquids.
- A successful extraction process requires high ethanol/ IL ratio, low temperature and low water content.
- Influence of the structure of both IL and sugar on the extraction performance.
- A new process for cellulose bio-conversion into fuels and chemicals has been patented and sold to 10 companies in the world.

Figure 1. Dissolution rate of sucrose in a mixture of (BMIMCl + EtOH)

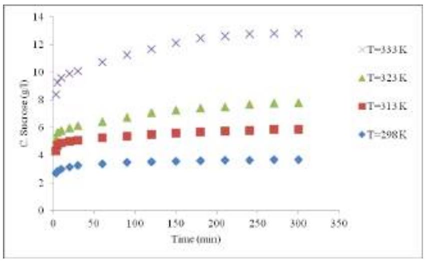
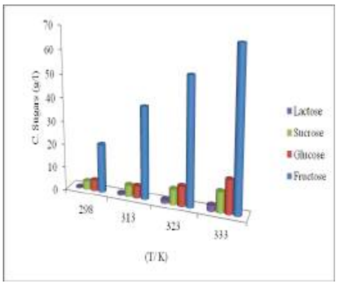


Figure 2. The solubility of carbohydrates in a binary mixture of (BMIMCl+EtOH)



Reference

. HASSAN E.S. et al., Environ. Sci. and Techn., 47, 2809-2816, 2013.

Contact: fabrice.mutelet@univ-lorraine.fr

2. Extraction, enzymatic hydrolysis and transformation of proteins from oleoproteagineous plants

Projects

- Rational production of bioactive hydrolysates from rapeseed proteins. Coord. R.Kapel. Regional funding (2011-2013), CNRS funding (2009).
- Large-scale production of casein hydrolysates. Coord. R.Kapel (2013), Industrial funding (YOPLAIT).
- Peptides engineering: enzymatic reactions for the production of peptides and peptides derivatives (CPER Fabelor, Coord. I. Chevalot, 2007-2013)
- Peptides acylation in sCO_2 (ICEEL, Coord. I. Chevalot, 2013).

LRGP Skills

- Structural characterization of proteins (Fluorescence, m-DSC, circular dichroism).
- Enzymatic proteolysis reactors (kinetics and modeling).
- Peptide characterizations and sequencing (HPLC and CE-MS).
- Bioactivity assessment and screening (anti-microbial, animal cells growth, anti-oxydant…).
- Production of peptide derivatives by fatty acids grafting catalyzed by hydrolytic enzymes.
- Bioacatalysis for O and N-acylation in organic solvents, ionic liquids and sCO_2.
- Aminoacylases production from *Streptomyces ambofaciens* for the biocatalysis of acylation reactions in aqueous media.

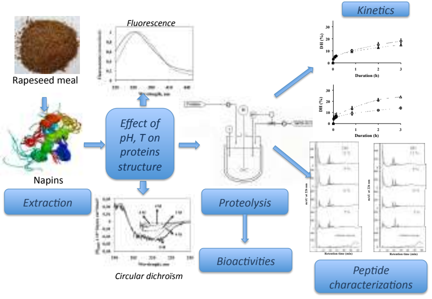
Results

- Characterization of antifungal activity of rapeseed albumins.
- Kinetics of proteolysis improvement by protein structure modifications.
- Modulation of peptide production by pH, T and proteins pre-incubation.
- Study of regio- and chemo-selectivities of lipases for N- and O-acylation of peptides depending on reaction media.
- Synthesis of dipeptides derivatives such as carnosine acylation catalyzed by the lipase B of *C. antarctica*.

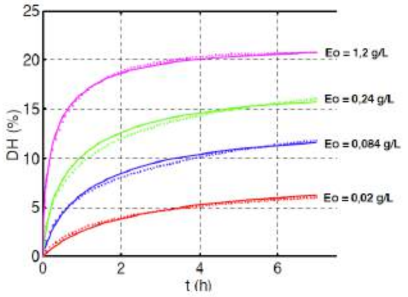
Contact: romain.kapel@univ-lorraine.fr

Extraction
and fractionation
processes

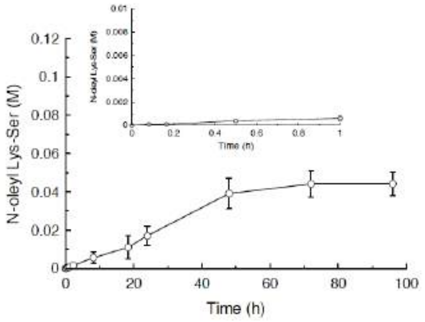
Proteolysis study: general scheme



Kinetics modeling of DH



Kinetics of Lys-Ser acylation by $C_{18:1}$



References

. Farges et al., Process Biochemistry, 2006, 41, 2297-2304
Chabanon G., Bioressource Technology, 2008, 99 (15), 7143-7151.
. Husson E. et al., Process Biochemistry, 2009, 44, 428-434.
. Husson E. et al., Process Biochemistry, 2011, 46, 945-952.
. Nioi C. et al., Food Chemistry, 2012, 134 (4), 2149-2155.

3. Transesterification processes

Projects

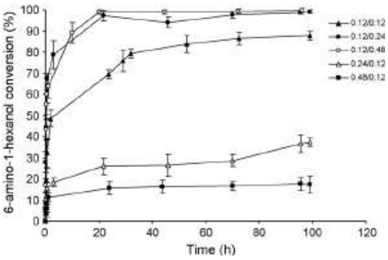
- Methodology for the intensification of a multi-staged catalytic process: experimental and theoretical study. Application to the transesterification of vegetable oils (Partner: IFP Energies Nouvelles)
- Enzymatic transesterification and transamidification of bifunctional molecules: applications for amino acids based biosurfactants production (Partner: SEPPIC-Air Liquide)

LRGP Skills

- Development and building of a modular pilot unit for kinetic measurements, working under severe conditions (T=200°C, P=50bar). Modelling of the reactors by the finite volume method.
- Enzymatic process in different reaction media (organic solvents, ionic liquids, sCO2) for amino acids and peptides acylation by fatty acid esters. Modelling of the reaction kinetics.

Results

- Understanding of the behaviour of the coupled phenomena (thermodynamic equilibrium, external and internal mass transfer, kinetics). Determination of the kinetic parameters by optimization. Study of the staging impact on equilibrium shifting and ester yield.
- Study of the behaviour of biocatalysts such as lipases for the amidification and/or esterification of bifunctional molecules: regio- and chemo-specificities of the enzymes depending on reaction media. Kinetics studies in stirred reactors and in packed-bed microreactors.



References

. Portha J.F. et al., Chem. Eng. Sc., 207-208, 285-298, 2012.
. Husson E. et al., Journal of Molecular Catalysis B: Enzymatic, 55, 110-117, 2008.
. Husson E. et al., Enzyme and Microbial Technology, 46, 338–346, 2010.

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Biotechnological and chemical transformation processes

4. Microbial processes for production of molecular building blocks

Projects

- Bio-based production of chemical building blocks: *Corynebacterium glutamicum* as a platform for new and efficient bioprocesses. Industrial Biotechnology Era Net project-ADEME (coll. Ulm Univ, Bielefd Univ, Forsch. Jülich, INBIOTEC Spain, ITQB Portugal, Delft Univ.
- Effect of oxygen availability on the production of diacide compounds (succinate, malate, fumarate, oxaloacetate…) by *C. glutamicum* during fermentation processes. ICEEL project.
- Antibiotic production by *Streptomyces pristinaespiralis* during a fermentation process using raw date juice (coll. King Faisal Univ).
- Coupling between cellulose thermic treatment and fermentation processes using *Clostridium* species for the production of chemical building blocks.

LRGP Skills

- Culture of industrial microorganisms in bioreactors fully instrumented.
- Metabolic analysis at micro and macro scales using analytical tools (HPLC, ICP-MS, GC-MS, LC-MS, UV-VIS spectroscopy).
- Genetic engineering and metabolic engineering of industrial microbial strains.
- Characterisation of gas transfer, mixing and hydrodynamics in bioreactors dedicated to bioconversions

Results

- Effect of bioreactor hydrodynamics on the physiology of Streptomyces during process.
- Oxygen supply controls the onset of pristinamycins production by *Streptomyces pristinaespiralis* in shaking flasks.
- Elucidation of mecanisms involving OdhI dephosphorylation in *C. glutamicum* during glutamate production processes.
- Metabolic engineerring of *C. glutamicum* for the production of itaconic acid, lactic acid or di-acid compounds such as succinate, oxaloacetate, malate or fumarate.

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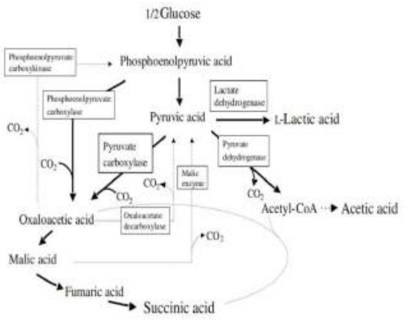
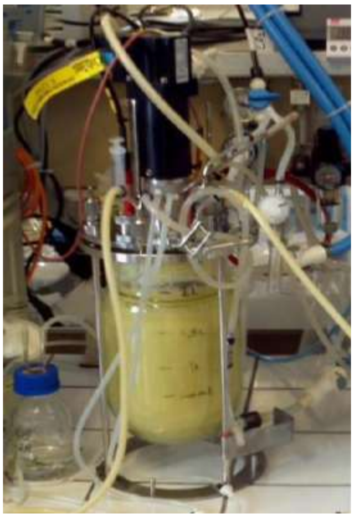


Anaerobic metabolism of *C. glutamicum*



Batch fermentation process of micro-organisms carried out in a fully instrumented bioreactor

References

. Bokas D et al., Appl Microbiol Biotechnol. 2007.76:773-81.

. Olmos E, et al., Bioprocess Biosyst Eng. 2012 In press.

. Mehmood N. et al., Biotechnol Bioeng. 2011. 108 :2151-61.

. Khuat HBT et al., Réc Prog en Génie des Procédés, 101-2011.Ed. SFGP, Paris

. Boulahya KA. et al., Appl Microbiol Biotechnol. 2010. 87 :1867-74.

5. Coupling between bioreactor hydrodynamics and cell biological responses

Projects

- Date juice as substrate for antibiotic production by filamentous bacteria. (coll. Univ Saudi Arabia).
- Micro-measurements of dissolved oxygen concentrations in *Streptomyces pristinaespiralis* cultures. 2012-2014**.** (Coll. Univ Reims).
- Scale-down of succinate production bioprocess**.** ICEEL project, 2011-2014.
- Intensification of production of fermentable organic acids in methanizer; biochemical valorization of CO_2. ADEME-ArcelorMittal 2013-2016.
- Anaerobic processes for wastewater treatment and biogas production. ANR PROMET, 2011-2014.
- Processes for sludge valorisation. SLUDGEPRO project, 2013-2016 (Coll. Veolia Innovation).

LRGP Skills

- Study of transport phenomena in bioreactors at macro-, meso- and micro-scales (flow, turbulence, multiphase flow, mass transfer).
- Filamentous and planktonic bacteria in shake flasks, mini-bioreactors and bench-top bioreactors (stirred and sparged vessels, airlifts).
- Methanisation of urban and agricultural waste at the pilot scale.
- Particle Image Velocimetry (PIV), μ-PIV, Laser Induced Fluorescence (LIF), Laser Doppler Anemometry (LDA).
- Micro-measurements of dissolved oxygen concentrations.
- Bioengineering tools for the characterization of cellular response.
- Numerical simulation of liquid-solid (Euler-Lagrange) and gas-liquid flows (Euler-Euler / PBM) in bioreactor.
- Kinetics modelling coupled to bioreactor hydrodynamics.
- Lattice-Boltzmann simulations

Results

- CFD of gas-liquid-solid bioreacting flows in airlift bioreactor.
- New insights of bioreactor impacts on antibiotic production.
- Multi-scale modelling in anaerobic bioreactor.

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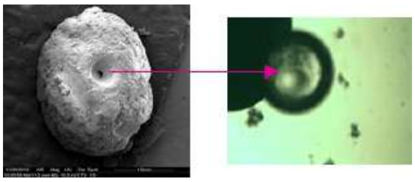
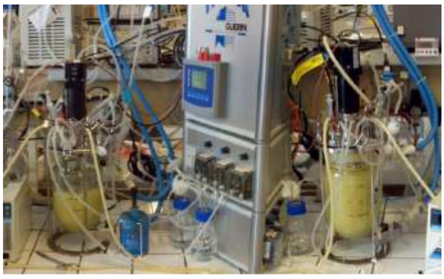
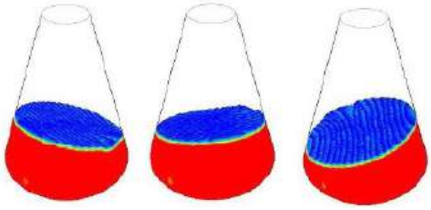
Biotechnological and chemical transformation processes


Growth of a microbubble of methane on a sludge in wastewater


Scale-down set-up for industrial bioprocess study at the lab-scale.


CFD Simulations in bioreactors (here, shaking flasks)

References
. Olmos et al. (2013),Bioprocess Biosyst Eng.36
. Mehmood et al. (2012) Biochem. Eng J. 68
. Zhang et al. (2012), Env. Sci. Tech., 46
. Wu et al. (2012), Water Res., 46
. Wu et al. (2012), Process Biochem., 47
. Mehmood et al. (2011), Biotechnol Bioeng, 108
. Mehmood et al. (2010), Process Biochem, 45
. Zhang et al. (2011), Chem. Eng. Sci., 66

6. Ways of raw glycerol valorization

Projects

- Biotechnological valorisation of raw glycerol discharged after bio-diesel (fatty acid methyl-esters) manufacturing process: production of 1,3-propanediol, citric acid, carotenoids and single cell oil.
- Synthesize of acrylic acid from glycerol through gas phase acrolein formation on solid catalyst.

LRGP Skills

- Kinetic studies and modelling of different microorganisms growing on glycerol in bioreactors fully instrumented.
- Metabolic analysis at micro and macro scales using analytical tools (HPLC, ICP-MS, GC-MS, LC-MS, UV-VIS spectroscopy).
- Determination of kinetic mechanisms and deactivation processes.
- Simultaneous online and continuous condensable and permanent gas analysis by chromatography.

Results

- Production of polyunsaturated fatty acids by *zygomycetes* fungi growing on glycerol.
- Bioconversion of raw glycerol into 1,3-propanediol by *Clostridium butyricum* under anaerobic conditions.
- Lipid production by *Yarrowia lipolytica* yeasts growing on industrial glycerol.
- Influence of glycerol and lipids-glycerol mixtures on cell growth and carotenoid production by *Sporobolomyces ruberrimus* yeasts.
- High level selectivity of acrolein during dehydration of glycerol.
- Determination of primary and secondary product pathways during dehydration of glycerol.

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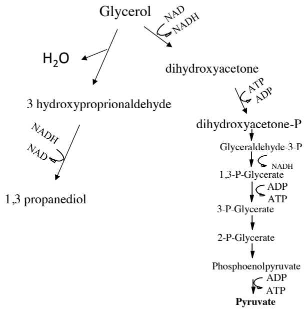
Biotechnological and chemical transformation processes

Sporobolomyces ruberrimus growth kinetics and carotenoid production on 3 L bioreactor



Metabolic pathway of glycerol bioconversion by microbial strains

Experimental set-up for kinetics determination in an isothermal fixed bed reactor using online and continuous gas-chromatography analysis

References
. Papanikolaou S., et al., Biomass and Bioenergy, 32, 60-71, 2008
. Papanikolaou S, et al., Current Microbiology. 52, 134-42, 2006
. Papanikolaou S., et al., Journal of Applied Microbiology, 92, 737-744, 2002

7. Catalytic processes for biorefinery

Projects

- Low oxidation kinetics reactor. FUI project (coll. Air Liquide).
- Oxydation catalytique en film liquide activée par plasma, ANR Oxyfilm.
- Valorisation industrielle et energétique du CO_2 par utilisation efficace d'électricité décarbonée, stabilisation du système électrique et stockage d'électricité. ANR Vitesse2 (coll. Rhodia).
- Bioenergy ANR Project GAMECO (coll. EDF).
- Acryliques issus du vegetal (coll. AME-Arkema)
- External transport intensification for catalytic reactions in monolith reactors,
- Methane and ethanol autothermal reforming process for hydrogen production,
- Intensification of triolein transesterification for biodiesel production,
- Intensification and optimisation of fatty acid esterification on a sulfonated resin,
- Analysis of coupled reaction, transport and material structural evolution in chemical looping combustion,
- Catalytic pyrolysis of lignin to produce green aromatics
- Catalytic high pressure liquefaction of lignin
- Dehydration of glycerol in gas phase over a solid acid catalyst
- Conception and design of a microstructured reactor for steam methane reforming
- Technology comparison and design for flexible and modular process units for methanol synthesis from CO_2 and H_2

LRGP Skills

- Pilot scale units and micro-pilot scale units for experimental studies of catalytic reactions and kinetics identification.
- Fixed and fluidised bed (20g or 1kg of catalyst).
- Modeling and analysis of transient coupled kinetic, mass and energy transport phenomena, using Comsol or home-developed codes
- Analysis of catalysts by temperature programmed oxidation (for coke analysis), desorption, advanced spectroscopy (coll. IJL-Nancy)
- Online and continuous gas chromatography analysis.

Results

- Analysis and identification of coupled kinetic and transport phenomena in catalytic and multiphasic systems.
- Identification of catalytic mechanisms and kinetics.
- Catalytic processes design, optimisation and intensification.
- Green and cheap iron-based catalysts developed for the hydrotreatment of bio-oils.

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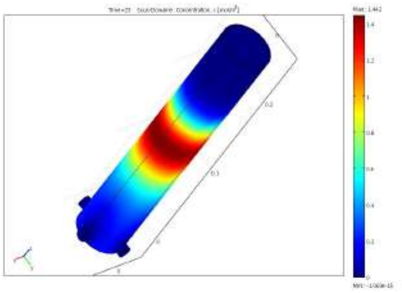
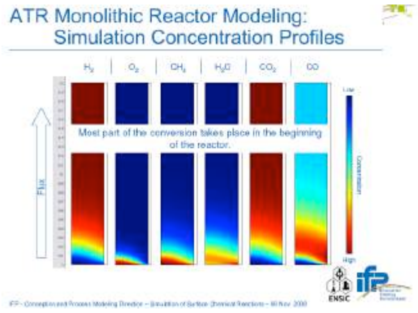
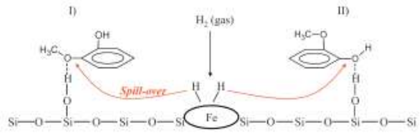
Biotechnological and chemical transformation processes





ATR Monolithic Reactor Modeling:
Simulation Concentration Profiles

Most part of the conversion takes place in the beginning of the reactor.



Mechanism of bio-oil catalytic hydrotreatment over iron/silica catalyst

References
. Vincent G. et al. Process Safety Enviro. Protection, **89**, pp 35-40, 2011.
. Queffeulou A. et al., Chem. Eng. Sc., **65**, pp 5067-5074, 2010.
. Portha J.F. et al., Chem. Eng. Sc., **207-208**, pp 285-298, 2012.
. Mbodji M.et al., Chem. Eng. J., **207-208**, pp. 871-884, 2012.
. Olcese et al., Appl Catal B 115-116, pp. 63-73, 2012.
. Olcese et al., Appl Catal B 129, pp. 528-538, 2013.
. Olcese et al., Energy Fuels 27 (2), pp. 975-984, 2013.
. Olcese et al., ChemSusChem, in press
. Dufour et al., Appl. Catal. A, 346, pp. 164–173, 2008.

8. Bio-based monomers/polymers, and polymer recycling

Projects

- Natural fibers/Bio-polymer composites: A sustainable alternative to traditional plastics. AME project (coll. FIBRASTRAL, A Composite, Les Chanvriers de l'Est, Poirot Injection Plastique, Trolitan).
- Cassava starch-Kaolinite composite: A new bio-material for packaging (coll. LEM).
- Biodegradable blends based on thermoplastic starch and poly(lactic acid): compatibilization, extrusion and uses. ICEEL project (coll. LCPM)
- Nanoparticles for improving the impact strength of poly(lactic acid) : synthesis of Poly(buty acrylate)-Laponite nanocomposites. ICEEL project.
- Design and multicriteria optimization of manufacturing processes, by extrusion of nanocomposites with recycled polymers strengthened by nanocelluloses. PCP project (coll. IPICYT-Mexico).
- New developments in multiobjective optimization of the development of materials based on biopolymers for the inclusion of industrial and commercial constraints. PICS project (coll. Univ Ottawa, Univ Quebec)
- Recycling of ground tire rubber as impact modifiers for brittle polymers (coll. Sao Paulo Univ)
- Purification of bio-sourced acrylic acid by crystallization in melt. F3 Factory (coll. Arkema, Erhfeld).

LRGP Skills

- Functionalization of biopolymers in batch/continuous reactors
- Extrusion processes for: blending of bio-based polymers; elaboration of bio-sourced composites, chemical/physical modification, functionalization, plasticization, depolymerization, COV extraction/ purification of biopolymers.
- Recycling of ground tire rubbers.
- Kinetic's modeling of batch and continuous reactors.
- Multicriteria optimization of processes and material's properties.
- Analysis of bio-macromolecules (NMR, SEC, IRTF,...), thermo-mechanical and rheological characterization of bio-composites.

Results

- New bio-based polymers and composites processes.
- Polymer recycling processes.
- Patent on the purification and crystallization of bio-based acrylic acid.

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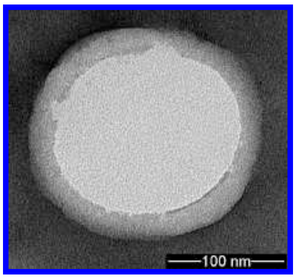
Figure 1. : Natural hemp fiber/Bio-polymer composites

Figure 2. Core-shell nanoparticle as impact strength agent for poly(lactic acid): *Core : Polybutyl acrylate* ; *shell : Polymethyl methacrylate + Laponite clay*



References

. Fang Y., Hoppe S., Hu G.H., Durand A., Journal of Applied Polymer Science, 2013

. M'Bey J.A., Hoppe S., Thomas F., Carbohydrates Polymers, 88, 213-222, 2012

. Mostefa, MLP; Muhr, H; Plasari, E; Fauconet, M., J. of Chemical and Engineering, vol.57 (4), p. 1209-1212, 2013

. Rebouillat S., Pla F., J. Biomaterials and Nanobiotechnology, vol.4, p.165-188, 2013

. Renaud J., Thibault J., Lanouette R., Kiss L.N., Zaras K., Fonteix C., European Journal of Operation Research, vol.177 (3), p.1418-1432, 2007

9. Lignin valorisation

Projects

- Pyrolysis of lignins with in-situ analysis and detailed modelling. ANR PYRAIM.
- Catalytic hydrodeoxygenation of lignin pyrolysis bio-oils over iron-based catalysts to produce green aromatics.
- Catalytic high-pressure liquefaction of lignin to produce fuels and chemicals.

LRGP Skills

- Production and characterization of lignins by NMR, rheology, thermogravimetry-calorimetry, etc (coll. LERMAB).
- Pyrolysis of lignin in batch reactor. Lignin/Char oxidation.
- Catalytic hydrotreatment of lignin pyrolysis vapours in fixed bed reactor.
- Analysis of coke deposit over catalysts.
- High pressure liquefaction and hydrotreatment of bio-oils.
- Analysis of lignin liquefaction or pyrolysis products by advanced GC*GC/MS and high resolution mass spectrometry.

Results

- Iron-based catalyst supported over silica or activated carbon developed, with high selectivity for aromatics production from lignin pyrolysis.
- In-situ analysis by rheology, 1H NMR and ex-situ 2D NMR revealed new mechanism of lignin pyrolysis.
- Synchrotron light photo-ionisation mass spectrometry was used for the first time to on-line analyse the evolution of lignin pyrolysis markers.
- High resolution mass spectrometry showed new findings on the catalytic treatment of heavy lignin oligomers.
- Mass and energy balance of the integrated lignin to aromatics process.

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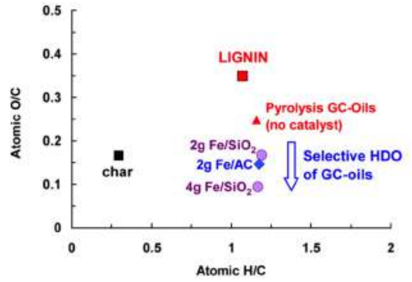
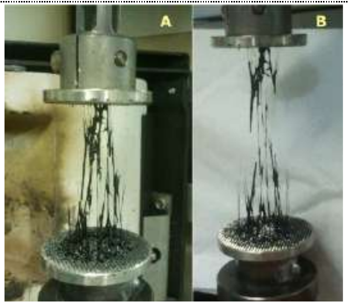
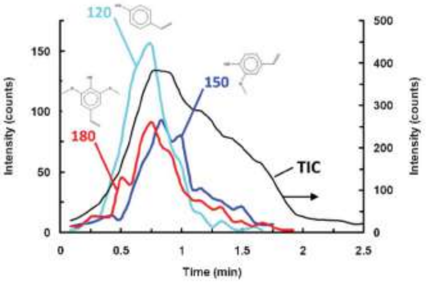
Thermal transformation processes



Good selectivity for the hydrodeoxygenation (HDO) of lignin oils over iron-based catalysts



In-situ rheology reveals softening behaviour of lignin during pyrolysis



Analysis of lignin markers by synchrotron photo-ionisation-mass spectrometry

References

. Olcese et al., Appl Catal B 115-116, pp. 63-73, 2012.
. Olcese et al., Appl Catal B 129, pp. 528-538, 2013.
. Olcese et al., Energy Fuels 27 (2), pp. 975-984, 2013.
. Olcese et al., Energy Fuels 27 (4), pp. 2135-2145, 2013.
. Olcese et al., ChemSusChem, in press
. Dufour et al., RSC Advances 3 (14), pp. 4786-4792, 2013.
. Dufour et al., Energy Fuels 26 (10) , pp. 6432-6441, 2012.
. Dufour et al., ChemSusChem 5 (7), pp. 1258-1265, 2012.

10. Biomass pyrolysis and gasification

Thermal transformation processes

Projects

- Methodological study of biomass pyrolysis with in-situ analysis. ANR PYRAIM**.**
- Improved gasification for CHP applications. ANR GAMECO (coll. EDF).
- Production of substitute natural gas from biomass gasification**.** ADEME project GAYA (coll. GDF Suez).
- Life Cycle Analysis of combined heat and power processes. Federation J.V.
- Environmental and economic assessment of biomass valorization. CNRS project FORêVER

LRGP Skills

- Experimental study and kinetic modelling of solid fuels primary pyrolysis and tar catalytic or gas-phase conversion.
- Experimental study and modelling of pyrolysis / gasification reactors: fluidized beds, cyclone, fixed beds.
- Analysis of bio-oils and tar by advanced mass spectrometry.
- Modelling of thermo-chemical processes under Aspen Plus.

Results

- The image furnace: a unique setup for primary pyrolysis study [2]
- An original model of biomass pyrolysis [3]
- The origin of molecular mobility during biomass pyrolysis revealed by in situ 1H NMR spectroscopy [4]
- A complete fluidized bed pilot plant (3 kg/h) for pyrolysis or gasification of biomass (cf. Figure)
- An integrated DFB gasifier model implemented in Aspen Plus [1]
- A complete gasification process simulated under Aspen Plus [5]

Fluidized Bed pilot plant
(3kg/h of biomass)

References

. Abdelouahed L. et al., Energy & Fuels 26 (9), 3840-3855, 2012

. Christodoulou M. et al., JAAP, 10.1016/j.jaap.2012.11.006

. Dufour A. et al., Chem. Eng. Res. Des. 89 (10), 2136-2146, 2011

. Dufour A. et al., ChemSusChem, 5 (7) , 1258-1265, 2012

. Francois J. et al., Biomass Bioenergy, 51, 68–82, 2013

. N. Jendoubi et al., JAAP, 92 (1), 59-67, 2011

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11. Modelling of thermal transformation

Projects

- Life Cycle Analysis of combined heat and power processes. Federation J.V.
- Lignin to green aromatics: catalysts design and modelling of the integrated process.
- Environmental and economic assessment of biomass valorization routes: from forests to final use. CNRS project FORêVER.

LRGP Skills

- Advanced models of reactors, which combine heat and mass transfer, hydrodynamic and kinetics.
- Detailed reactor and separator models included under Aspen Plus®, by specific Fortran programs.
- Biomass production and pre-treatment chain included in Aspen Plus, eg. forest management, biomass harvesting, transport, crushing, drying, torrefaction or fast pyrolysis (etc.).

Results

- An advanced model of biomass gasification in dual fluidized bed developed under Aspen Plus.
- Detailed mass, energy and exergy balances of combined heat and power units, including pollutants (NOx, SOx, PAH, tar, etc.) and ash issues.
- Mass and energy balances of an integrated lignin to aromatic process including lignin pyrolysis, bio-oil hydrotreatment and aromatics refining (by absorption) and heat revocery.
- Improvement/recommendations for biorefinery design to improve mass (selectivity), energy, exergy balances and to reduce environmental impacts (pollutants issues).
- A model for biomass growth, mobilisation and pretreatment included for the first time into Aspen Plus model. First model to handle the whole carbon and nutrient balances from the ecosystem (soil/forest) to the biomass final use.

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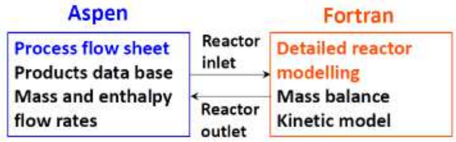
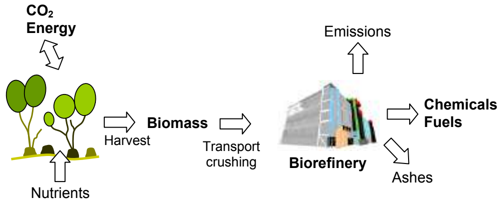
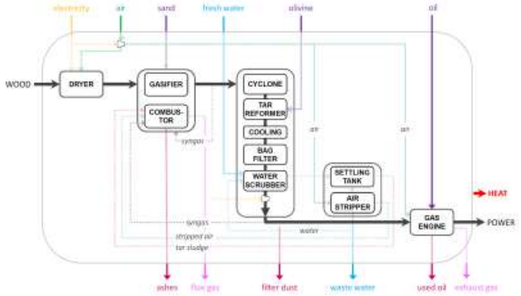
Thermal transformation processes



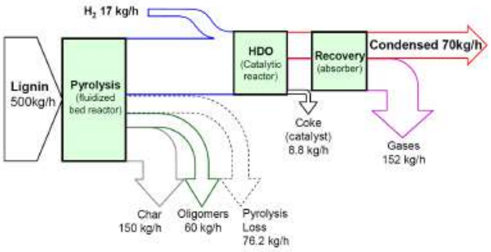
Aspen Plus® models associated with Fortran models give detailed mass/energy balances



Biomass production in the ecosystem is handled under Aspen Plus



Gasification unit modelled under Aspen Plus



Mass balance of the integrated lignin to aromatics process

References
. Abdelouahed L. et al., Energy Fuels 26 (9), pp. 3840-3855, 2012.
. Francois J. et al., Biomass Bioenergy, 51, pp.68–82, 2013.
. Olcese et al., Energy Fuels 27 (4), pp. 2135-2145, 2013.

12. Gas/Dust hybrid mixtures explosion

Projects

- Specificities of gas/dust explosions: application to biofuels and feed industries, Tecaliman.
- Turbulence/combustion interactions in hybrid mixtures explosions (coll. IRC Naples).

LRGP Skills

- Determination of ignition and explosion characteristics of dust and hybrid mixtures.
- Application of inherent safety principles to explosions in the process industries.
- Characterization of flame propagation and turbulence/combustion interactions.
- Determination of the rate limiting step of the combustion.

Results

- Tests done on various oilseeds and hexane with applications to industry of oleaginous plants and biofuels (trituration, desolvation of the oil cakes, storage...).
- Hybrid mixtures can be explosive when both dust and gas concentrations are below their minimum explosive concentration (MEC) and lower explosive limit (LEL) (figure 1).
- Classical laws (Le Chatelier...) are not always conservative from a safety standpoint (figure 1).
- Ignition sensitivity of hybrid mixtures is increased even for low gas concentration down to 0.5 % v. (figure 2) and is linked to the critical ignition diameters.
- Maximum rates of explosion of pure compounds greatly affected by presence of few amounts of gas or dust; synergistic effects observed; gas addition changes rate-limiting step of the combustion reaction; combined impacts on thermal transfer, hydrodynamics and combustion kinetics (turbulence/combustion interactions) ?
- Results can be used in the scope of ATEX directives application and to develop new prevention and protection barriers such as flame arresters (figure 3).

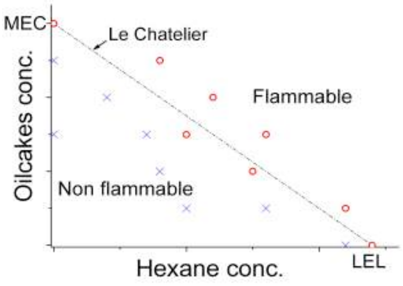


Figure 1.

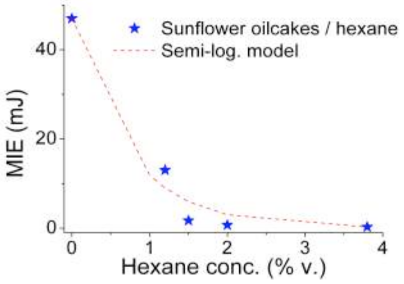


Figure 2.

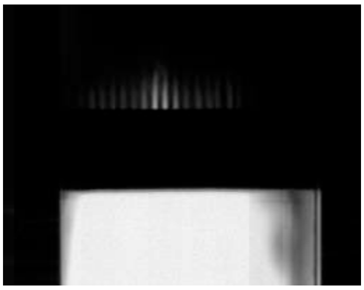


Figure 3.

References

. Khalili I. et al., Powder Technol., 217, 199–206, 2012.

. Dufaud O. et al., Ind. & Eng. Chemistry Research, 304-310, 90 (4), 2012.

. Khalili I. et al., 13th Int. Symp. Loss Prev.in Proc. Ind., Bruges, 2010.

. Dufaud O. et al., Powder Technol., 190, 269-273, 2009.

. Dufaud O. et al., J Loss Prev Process Indust., 21 (4), 481-484, 2008.

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13. Membrane and chromatographic processes for fractionation, concentration and purification of biomass products

Projects

- Design of new membrane chromatographies using macroporous PVC/silica material (Coll. AMERSIL, Lux), 2011-2013,
- Oside separation and purification (Coll. Industry), 2011-2014,
- Yeast extract fractionation for animal cells growth activity improvement (Coll. BioSpringer), 2009-2012,
- Purification and characterization of antioxydant Ni^{2+}-binding peptide by IMAC, ICEEL project, 2013,
- Recovery and concentration of organic acids from fermentation broths using a hybrid technic combining IEX and EDMB (Coll. ENIG) 2012-2015,
- Extraction and purification of therapeutic molecules from wood, FUI project, LBS Le Bois Santé, 2012-2015.

LRGP Skills

- Tangential ultrafiltration for peptide, protein and polyoside separations (flux and performances modeling),
- Low pressure preparative chromatography for peptide purification / enrichments (SEC, CEI, IMAC…),
- Chromatography elution modeling/simulation/optimization
- Membrane chromatography,
- High performance liquid chromatography and capillary electrophoresis coupled to mass spectrometry,
- Electrical Swing Ion Exchange,
- Multi-Column Chromatographic Process.

Results

- New modeling strategy for UF performance,
- Peptide mapping of complex hydrolysates by RP, NP-HPLC-MS,
- Peptide enrichment by CPC from complex hydrolysates (Collab. Univ Reims),
- Peptide enrichment by ED-UF (Collab. INAF, Canada),
- Effluentless ion exchange: application to organic salt conversion, biomolecules separation,
- Strategy / gradient elution / multi-column chromatographic processes.

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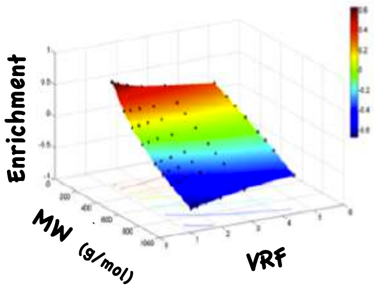
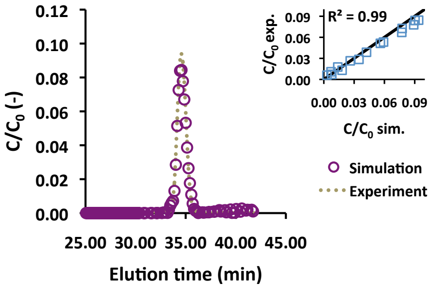
Separation
and purification
processes

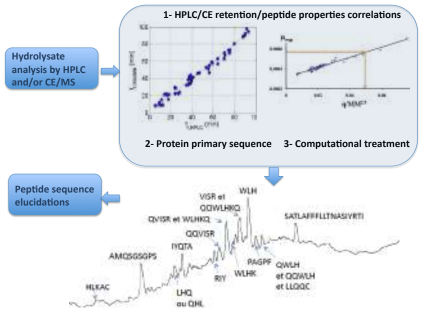
Prediction of peptide enrichment in UF



Chromatography elution simulation



Analytical separation of hydrolysates



References

. Schab *et al.*, 2010, Separation Science and Technology, 8, 1015-1024.
. Lu *et al.*, 2010, Desalination and Water Treatment, 14, 1-6
. Kapel R. *et al.*, 2011, Journal of Membrane Science, 383, 26-34
. Lu et al. 2011, Separation Science and Technology, 46 (12) 1861-1867
. Boudesoque L. *et al.*, 2012, Journal of Chromatography B, 905, 23-30
. Mosser L. *et al.*, 2012, Process Biochemistry, 47, 1178-1185
. Harscoat C. *et al.,* 2012, Analytical Bioanalytical Chemistry, 403, 1939-1949.
. Rehouma *et al.,* 2013, Desalination and Water Treatment, 51/1-3, 511-517

14. Molecular and mesoscale modelling for the design of meso-structures and enzymes

Projects

- Modelling of protein/ligand interactions in enzymatic bioprocesses. CPER MISN, Coord. C. Humeau, 2007-2013.
- Modelling of biomolecule structuration in complex matrices. CPER MISN, Coord. L. Chebil, 2007-2013, Regional fundings (2012).
- Modelling of enzyme/ligand binding modes. Regional fundings, Coord. C. Humeau (2009).
- Enzyme engineering guided by molecular models. Regional fundings, C. Mathé (2013).

LRGP Skills

- Modelling of enzyme/ligand binding modes (docking, molecular dynamics, energy calculation).
- Chemical reactivity of enzyme/ligand complexes.
- Determination of the molecular rules for enzymatic selectivity and substrate specificity.
- Enzyme redesign.
- Structure/function relationships.
- Prediction of thermodynamics and physico-chemical parameters (free energy calculations, solubility).

Results

- The molecular rules for selectivity and substrate specificity have been elucidated for lipase-catalyzed transesterification bioprocesses.
- Molecular modelling methodologies have been developed to explain and predict the regio- and the chemo-selectivity of lipase-catalyzed bioconversion of peptides and phenols.
- New enzymes with improved selectivity properties are under development.
- Molecular modelling methodologies have been developed to explain and predict the solubility of biomolecules in organic solvents.
- Mesoscale modelling simulations have been carried out to explain the aggregation mechanism of biomolecules in organic solvents.

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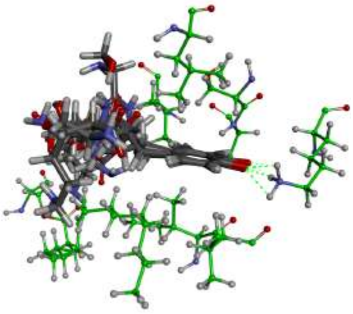
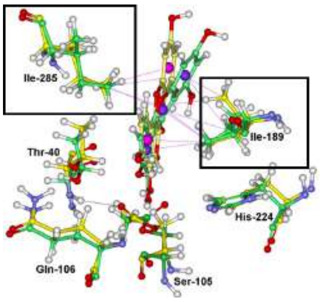
Global biorefinery study

Molecular modelling of enzyme/substrate binding modes.

Elucidation of molecular rules for enzymatic selectivity.

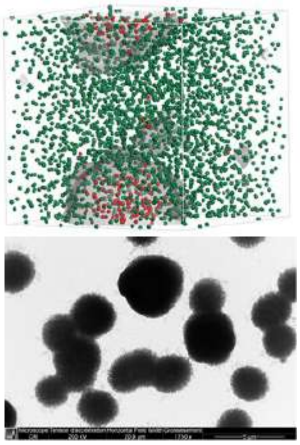


Determination of molecular guidelines for enzyme redesign.



Mesoscale modelling of biomolecule structuration in organic media

Elucidation of aggregation mechanism



References

. L. Chebil et al., Journal of Physical Chemistry B. 114, 38, 12308-12313, 2010
. L. Chebil et al., Industrial & Engineering Chemistry Research. 31, 1464–1470, 2012
. C. Bidouil et al., Journal of Biotechnology, 156, 203-210, 2011
. F. Ferrari et al., Journal of Molecular Catalysis B: Enzymatic. 101, 122–132, 2014.

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JULY 2015