4.3.1 – Introduction

4.3.1.1 - The chemical industry in Italy.

The chemical industry in Italy has undergone a profound change over the past 10-15 years. The large Italian companies have disappeared and their plants have been sold to small companies or multinational groups. In Italy there are presently around 35 medium-size chemical industries (with over 100 Ml Euro in sales, corresponding to 23% of the overall production) and more than 1,500 small enterprises (accounting for 42% of the sales), almost all "Federchimica" members (see: www.federchimica.it). A great transformation has occurred also with respect to the location of the Italian enterprises, which are now more concentrated in northern Italy (69.2% of the production), in particular Lombardy (41.2%). The production is well balanced, being subdivided into commodities and fibres (31.5%), fine chemicals (29.4%), pharmaceutical products (25.6%), and products for public consumption (13.5%). In spite of their relatively small dimensions, Italian enterprises' R&D activity is high if compared to other manufacturing industries; it is, however, necessary to increase more and more the collaboration between these industris and public research institutions such as the CNR (National Council of Research), ENEA (an Italian alternative energy research institution), and university laboratories. Another problem for these companies – as well as for any other type of industry in Italy – is the strategic issue of the cost and availability of energy. Chemical research would therefore be strongly involved in solving this crucial problem for any kind of human activity.

4.3.1.2 – New guidelines for the research of a sustainable development in the field of Reaction and Process Design.

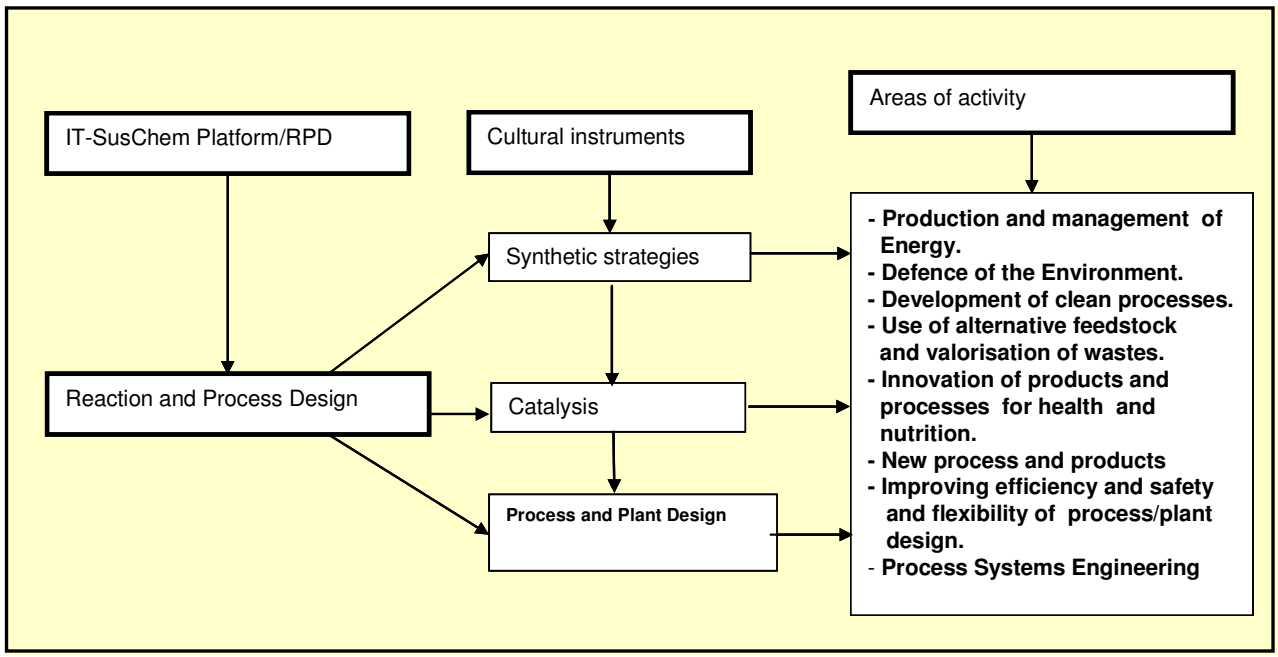
Nowadays, chemistry has a clear and important role in providing technological solutions to the many challenges which are facing developed countries in keeping their growth and competitiveness up with the pace of quickly developing economies, particularly from the Far East. The need for the development of technological processes matching the mainstays of the so-called *Sustainable Chemistry* will be a major factor in stimulating the growth of the European economy in the 21st century, by providing new opportunities that will benefit all citizens.

In spite of this general and widespread awareness, there are still too many important and large-scale processes which remain totally far from the concepts inspiring *Sustainable Chemistry*. Thus a massive flow of natural, non-renewable resources are steadily plundered from our planet every day and given back to the ecosphere in the form of economically exhausted matter. In this situation, the development of a *Sustainable Chemistry* is becoming imperative for addressing the multiform and serious problems affecting our modern technological society.

A resolute turn to the issues of Sustainable Chemistry may help to fulfil these requirements both by improving the current technologies for a more environmentally friendly use of energy, and by implementing alternative energy sources such as biomass-based resources, solar-thermal, and photovoltaic resources. The need for renewable resources for fuels and chemical feedstock is becoming a crucial topic due to: a) the decline of fossil resources (oil, natural gas, carbon) which is matched by the increased demand for oil by emerging economies, and b) political and environmental concerns over fossil fuels. In this respect, plant biomass is currently the only alternative sustainable source of organic carbon, fuels, and chemical feedstock. In particular, biofuels (fuels from biomasses) which are considered neutral as far as greenhouse effects are concerned, are expected to gradually replace fossil fuels (up to 40% by the end of 2040 in the EU). Transformation of biomasses into methanol or biodiesel fuels converts only a limited part of the total biomass (sugar, starch, or oil) into fuels. New and more efficient processes are necessary to convert a broader variety of biomasses (energy crops) into biofuels. Technologies available to transform biomasses include: pyrolysis, bio-oil refinement, gasification and Fischer Tropsch conversion. Most of these processes were developed around a century ago, in connection with the use of coal as primary resource. The need for modern, efficient and competitive processes requires an investigation of the complex chemistry involved in biomass transformation. Equally important issues to be pursued are both the study of more efficient and eco-benign technologies and the replacement of feedstocks for the chemical industry - mostly derived from fossil fuels - with renewable resources such as biomass and solar-thermal, for the short and medium/long term, respectively.

According to the European Technology Platform, the section related to "Reaction and Process Design" considers the development of products and related processes throughout their entire lifecycle. The complementary approaches of chemical synthesis, process design and engineering will be taken into account in any relevant step from the laboratory to the process plant, with the aim of introducing innovation, where possible, and of achieving a sustainable development.

As is well known, chemistry may have many interactions with human life and all the ecosystems of the environment. The social and economic impact of chemistry is impressive but not always positive. The main objective of "Sustainable Chemistry" is to save and improve the positive aspects, reducing or eliminating the negative ones. With this aim, the first important steps are to optimize the use of resources and minimize wastes and environmental impact. This requires the obtainment of new products, new synthetic pathways, new processes



and new technologies, which are more environmentally benign and address the human needs. Chemistry is also the basis for many innovations in other sectors, with beneficial effects for different manufacturing activities.

However, the main areas of activity for the Reaction and Process Design Section of the Italian Technology Platform for Sustainable Chemistry are the following:

- Products and technologies for energy management derived from alternative sources to oil, such as, for example, renewable sources.
- Products and technologies for a better safeguard of the environment.
- Improvement of active product delivery strategies for health.
- New products, new synthetic pathways, new processes and new technologies for the production of fine chemicals, pharmaceutical active principles, active ingredients for new materials and formulated products. Commodities must also be considered with the aim of studying more efficient and eco-benign technologies.
- Use of alternative feedstock, in particular renewable feedstock, and wastes used as sources for new products.
- Improvement of the efficiency of energy and water use in processes, as well as of the safety and flexibility of processes and plants.

To obtain satisfactory results in all the above-mentioned areas, it is necessary to achieve significant progress in three different cultural domains, which are: **synthetic strategies, catalysis, and process and plant design.**

A certain overlapping between synthetic strategies and catalysis cannot be avoided. The three above-mentioned cultural sectors are essential tools for all the activities of the Reaction and Process Design Sessions of the Italian Technology Platform for Sustainable Chemistry.In the development of a true *Sustainable Chemistry,* catalysis plays a pivotal role as more than 80% of all products of chemical industries are produced through catalytic processes. Catalysis is a discipline which has accomplished incredible results in the last century. However, topical problems concerning all of *Sustainable Chemistry*'s own issues have not yet been solved; thus, many conceptual advancement and technological improvements are needed to achieve better selectivity, efficiency and economy of the known processes as well as to design new catalytic cycles. A revolution in catalytic performances is expected, from the application of nanotechnologies to catalyst preparation. Also very important for the development of a *Sustainable Chemistry* is the search for new synthetic routes for reducing the number of reaction steps in the case of multistep reactions, converting stoichiometric processes into catalytic ones, and obtaining useful products from industrial waste materials.

Any new idea coming from catalysis and synthetic strategy needs to be developed at the industrial level by using chemical engineering, in order to improve the efficiency of existing processes, plant equipment and overall production systems, by promoting innovation through the development and use of more sophisticated techniques of simulation, optimization, automation and intensification.

4.3.2 - Novel Synthetic Strategies

4.3.2.1 - New reaction media.

Nowadays, reactions in unconventional media for sustainable organic synthesis focus on aqueous biphasic catalysis, supercritical media, fluorous biphasic catalysis, ionic liquids and biphasic combination. Several of these media, like fluorous and ionic liquids, allow intensified separation technologies by the selective recovery of the desired products, by-products, and catalysts in different phases, thus avoiding tedious and costly procedures which involve high volumes of organic solvents. Obviously, new systems like the previously mentioned ones need an accurate evaluation of all the requisites prescribed by Sustainable Chemistry before using them in an industrial process. The possible shift from the use of traditional organic solvents to water or supercritical systems in industrial processes is becoming more and more crucial, and several multi-national companies are already extensively investigating this field. The basic idea is to identify processes of general interest that could benefit from the use of non-traditional solvents and modify them accordingly. An in-depth patent literature investigation should guarantee the possibility to protect the new processes worth being industrially developed with patent applications. The advantages of supercritical carbon dioxide as a solvent have been indicated as its low toxicity, excellent gas-like transport properties, and very high solubilizing power with numerous kinds of small apolar molecules, including gases, whereas it is a poor solvent for most other molecules. Supercritical carbon dioxide extraction of natural products from solid plant matrices is currently an established application, with over a hundred industrial facilities of various sizes operating throughout the world. Also cleaning of specific materials, such as silicon wafers in the microprocessor industry, mechanical precision parts or dry-cleaning of clothes, have gone commercial. Owing to its high critical-point parameters, working with supercritical water requires high-pressure/high-temperature technology. Problems such as the considerable metal corrosion in sc-water and salt precipitation have been holding back the full industrial-scale implementation of potentially interesting applications of sc-water for some time. Even though high-T, high-P liquid water can be regarded as just another green expanded solvent, further studies are needed. Significantly, these two green solvents, water and CO_2, can be combined in relatively mild conditions in the form of microemulsions of water in CO_2, thus opening a wide and appealing range of applications if low cost-effective surfactants become available.

Ionic liquids (ILs) can be largely used in synthesis as alternative ‘solvents’ to classical organic reaction media and, in various cases, can be applied with advantages such as product yields, selectivity, and recycling of the IL. These processes can be considered clean when the products are sufficiently immiscible with the IL phase and can be separated by simple decantation. Multiphase catalysis, in particular liquid-liquid biphasic catalysis involving two immiscible phases and performed in ILs, can offer the possibility of circumventing classical problems occurring with classical homogeneous and heterogeneous catalysis in the chemical industry, such as product separation, catalyst recycling, and the use of organic solvents. The association of ILs with other green fluids such as supercritical carbon dioxide, will certainly boost clean extraction/ reaction protocols and will contribute to the generation of ‘sustainable’ catalytic processes.

Lastly, the coupling of two or more green technologies within a single process is a better approach to sustainability than reliance on a single technological opportunity. The goal can be achieved by developing new catalytic processes in innovative reaction media, in either mono- or polyphasic systems, capable of working selectively at room temperature. By a proper combination of the catalyst and solvent structure, in principle, it is possible to pursue selectivity (meaning a minimization of waste products) at temperatures close to room temperature: this means minimizing energy consumption and, indirectly, the contribution to the green house effect, etc.

4.3.2.2 - New substrates and/or reagents

Several reactions in traditional organic chemistry require reagents which lead to large quantities of waste materials in the reaction. In this perspective, a trivial but fitting example is the use of allyl bromide for amino group allylation. In this specific case, more than 60% of the starting material is discarded as waste material, and in addition an aggressive reagent is used. Now, using allylic alcohol could produce several evident advantages such as no waste, no hydrolysis, and no special tanks for storing this starting material. Unfortunately, alcohols are not as efficient as bromide in this type of reaction. A specific study in this direction could identify the suitable catalytic system that makes this reaction sustainable. The recent evolution in the Lewis acid area is a significant exemple of the great progress achieved in moving from conventional additives, such as aluminum trichloride, to lanthanide or scandium triflates: stoichiometric reactions with excess additives have now become catalytic reactions with high atom economy, in which substoichiometric amounts of water stable Lewis acid can be recycled indefinitely.

Another way to avoid the formation of waste and increase atom efficiency is by carbonylation and carboxylation procedures using CO and CO_2. Moreover, these processes appear well-suited for exploiting methanol, which is the most important basic product deriving from carbon monoxide. They are fully suitable not only in the field of bulk chemistry but also in the field of fine chemicals and pharmaceuticals such as ‘profens’ and in general arylacetic acids and esters. Also, the CO and H_2 (syn-gas) system - a well-assessed building block that can be produced from natural gas, petroleum, coal and biomasses - can be engaged into the direct synthesis of alcohols from olefins though more active and selective catalysts.

The use of carbon dioxide has not yet led to important industrial processes, but it will be the subject of further studies. Efficient methods for CO_2 use as building block for C1 chemistry have not yet been developed; however,

this achievement would be of paramount importance for both the reduction of the planetary global warming and the frequently invoked development of an *alcohol economy (either methanol or ethanol).* This is a very important issue, and efforts are being made to develop an efficient catalytic reduction of carbon dioxide.

To support development of new processes/products by intelligent and cost-effective testing methods/strategies, the evaluation of potentially toxic effects is necessary, with particular attention paid to priority issues as defined in REACH, e.g., *endocrine disruption.* Novel testing strategies for health effects should target *potentially vulnerable* groups, such as children (as indicated by the EU environment and Health Action Plan). Whereas the use of "conventional" toxicological testing (e.g., on rodents) cannot be fully replaced in the short/medium term, the development of such novel strategies has clear innovation requirements, which include the validation of *biotechnology-based tools*, such as "omics" approaches and sensors, as well as the development of *risk-to-benefit frameworks*.

4.3.2.3 - Introduction of alternative feedstock and novel building blocks.

The use of alternative fuels to the ones derived from oil makes available new raw materials and new building blocks derived, for example, from biomass. New syntheses can be developed starting from these new raw materials in order to obtain both new products and existing products at lower costs and with cleaner processes. Some of the most abundant chemicals on the planet that potentially have a place in fine chemical and commodities production are carbohydrates and polyphenols (lignin, residues from agroindustrial wastes and others), which represent a vast amount of biomass (in the range of hundreds of billions of tons), used by human activities only in small amounts. Despite the significant number of recent studies aimed at developing their industrial use (e.g., car mouldings, antioxidants, drugs, cosmetics, food), the systematic exploitation of this vast resource is still in its infancy. During the 1980s, a number of studies on the pyrolysis of lignocellulosic materials showed that a variety of interesting structures can be isolated from pyrolysis oils. These oils have been shown to contain heterocyclic derivatives such as 5-hydroxymethyl furfural, 2-furaldehyde (furfural), 2-methylfurfural, levoglucosenone, and levulinic acid. Consequently, there is a clear need for new and efficient technologies that effectively utilize low molecular weight compounds from lignocellulosic wastes by converting them into high-value added products in competition with classical oil chemistry. A similar strategy may be designed for organic components of other important wastes, e.g. olive oil mill, winemaking, rapeseed and sunflower wastes.

Moreover, also to be remembered is the more intensive use of coal as an energy source in power plants thanks to cleaner combustion processes based, for example, on the use of fluidized bed combustion technology. The usage of industrial and urban wastes as a raw material for new, more valuable products has both economic and environmental advantages. Examples are waste oils and fats that can be converted into biodiesel, and the possibility of re-using ash coming from coal-based combustion plants in traditional and non-traditional fields. Waste materials such as dead batteries that contain metal can be subjected to chemical treatment for the recovery of still-useful metals (commodities for national industry). Other examples are the recovery of chiral nonracemic by-products frequently discarded by the pharmaceutical industry and their transformation into valuable products.

4.3.2.4 - Reduction of the reaction steps and multicomponent reactions

The 'ideal synthesis' should lead to the desired product in as few steps as possible, in good overall yields and by using environmentally compatible reagents. In multistep synthesis, the temporal and preparation complexity increases in proportion to the number of steps in first approximation. It is reflected in many separation and purification operations, such as membrane processes, crystallization, extraction, distillation, or chromatography. Besides the multistep sequential synthesis of a target molecule, the desired product can also be obtained in one-pot reactions of a number of starting compounds. Multicomponent reactions (MCRs) are convergent reactions in which three or more starting materials react to form a product, where basically all or most of the atoms contribute to the newly formed molecule. In an MCR, a product is assembled according to a cascade of elementary chemical reactions. Thus there is a network of reaction equilibria, which all finally flow into an irreversible step yielding the product. The challenge is to conduct an MCR in such a way that the network of pre-equilibrated reactions channels into the main product and does not yield by-products. Especially thanks to their efficiency, ease of their control, and enormous number of possible products, MCRs have moved into the focus of contemporary endeavors to find new active substances in an environmentally sustainable manner and more quickly. The use of multivariate statistical instruments could be useful for novel synthetic strategies, because every single experimental result depends on many different factors which act simultaneously. In order to optimize experimental conditions, to get best results, all the occurring variables and their interactions are examined at the same time. This is possible by using the Design of Experiment (DoE) techniques. DoE techniques help the researcher plan experimental work by making different tests while changing all the factors at the same time, following a logical scheme, and obtaining the maximum information from the system being studied, with a small number of experiments. DoE techniques are useful in screening studies with many variables, in the optimization studies of different systems such as the synthetic reaction or step of an industrial process, and in finding the optimal compound or reagent composition (recipe) for the purpose studied (Mixture Design). The latter could be the keystone for facilitating the research on multicomponent reactions.

4.3.2.5 - More selective oxidation with hydrogen peroxide and/or oxygen

Stoichiometric oxidation processes, using toxic or dangerous oxidants, would be converted to catalytic processes using hydrogen peroxide and perspective oxygen, because both these oxidants are clean and non-polluting. The use of saturated hydrocarbons in place of unsaturated ones is paving the way towards the replacement, with direct oxidation processes, of the more complex processes achieved with unsaturated hydrocarbons. Butane oxidation to maleic anhydride has already been successful. Another objective is the direct enzyme-like oxidation of the terminal methyl group of saturated hydrocarbons; in the past decade, intensive research efforts in this field have led to many new oxidation systems, including biomimetic models. However, the progress towards environmentally friendly methods, which perform well in the presence of either H_2O_2 or O_2, (being highly catalytic and recyclable, selective, organic solvent-free, additive free), remains a current challenge. Catalysis is still significantly absent from industrial peroxide technologies, especially from the really large-scale processes that are found in pulp and paper manufacture, household laundering, industrial and institutional cleaning, and water disinfection, and much more is possible in environmental cleanup applications. In addition, better oxidation catalysts could contribute, among others, to the fields of commodity and specialty chemical syntheses, petroleum refining, and the decontamination of chemical and biological terrorism and warfare agents. Especially for wastewater detoxification, catalytic processes hosting multiple operating oxidation mechanisms are expected to promote an efficient degradation of the target pollutants. In this respect, photoactivated oxidations using inorganic photocatalysts and/or organic sensitizers or composite hybrids retain a major appeal.

In the fine chemical sector, an important breakthrough towards “green” oxidations has been the use of heterogeneous Ti(IV) silicalites (TS-1) as catalysts for H_2O_2 activation to effect a variety of highly interesting reactions including epoxidation of propene and other small alkenes, cyclohexanone ammoximation, the hydroxylation of aromatics and alkanes to alcohols and ketones. However, a general and efficient process for the selective production of terminal epoxides remains elusive together with the most desiderable co-reductant-free direct aerobic epoxidation. Despite the fact that water is the “ideal” solvent, catalytic systems operating in this environmentally friendly solvent are very rare and the high potential offered by the catalytic milieu of ionic liquids has yet to be explored, possibly in connection with alternative energy sources. In summary, catalyst innovation and the search for new eco-efficient processes demand a collective, multidisciplinary effort.

Finally, despite the different procedures reported in literature for the valorization of low molecular weight compounds that can be obtained from lignocellulosic wastes, little attention has been focused on their oxidative transformations, mainly in the case of low-cost, high-yield catalytic processes characterized by easy separation, purification, and efficient catalyst recovery schemes. In this case, also, the central requirement for achieving “green” transformations is the efficient activation of dioxygen and/or hydrogen peroxide with the use of novel catalysts.

Another field of interest includes selective catalytic oxidations of natural compounds such as terpenes and steroids, as well as organic molecules of interest to the pharmaceutical industry, with methyltrioxo-rhenium in association with hydrogen peroxide or with Jacobsen catalysts.

4.3.2.6 - Special Syntheses

In the past two decades, conjugated oligomers and polymers with semiconducting properties and phosphorescent metal complexes have been considered promising substitutes for conventional inorganic materials in electronic and optoelectronic devices. The most attractive feature of these organic materials is the possibility of tuning their electronic properties by acting on the backbone structure and/or on the nature of substituents on the main chain. In this context new molecular architectures of monomers, oligomers and metal complexes may be available for high-performance applications that exploit the high versatility of the transition metal-catalyzed coupling reactions of stable and easily prepared organometallic derivatives such as silicon, boron, and tin reagents. These are examples of special syntheses. The development of these methodologies for the preparation of organic compounds of interest in electronics and optoelectronics is becoming highly challenging for the synthetic organic chemist.

Within the field of special syntheses, of significant interest would be the development of novel synthetic protocols and processes that - while providing a convenient access to functional materials for advanced applications - are also modular, wide in scope, giving very high yields, and generating by-products that can be easily removed by non-chromatographic methods. Moreover, required characteristics should include simple reaction conditions, easily removable solvents and simple product isolation. Over the past few years, some innovative metal-catalyzed processes have appeared which are based on the use of a multistep/one-pot synthetic strategy for the preparation of polymeric conjugated systems. These processes are also characterized by a “modular approach” concept. In fact, they form materials that have a backbone made of regularly alternating (different) modules with the interplaying role of impressing mechanical and functional properties to the polymer. With this strategic approach, a wide variety of conjugated materials, which display a wide range of properties, have been conveniently accessed. Compared to conventional procedures, these synthetic protocols (named *Extended One Pot-EOP*), with their multiple and sequential one-pot metal-catalyzed processes, are characterized by a very low catalyst charge load, a sizable reduction in reaction time, easy operation, and low cost. During the multi-step one-pot process, reaction intermediates are formed *in situ* by complete re-conversion of the by-products generated in the same transformation. In addition, after the formation of the polymeric materials - which are recovered by simple filtration - final by-products are easily recovered and reused to form new reagents for a successive run.

Other synthetic methods based on carbon-carbon coupling reactions performed by commercially available catalytic systems are being developed for the preparation of novel conjugated polymers characterized by aryl-enyne alternating units.

4.3.2.7 - New means for energy input

Microwave irradiation (MWI) has become an established tool in organic synthesis, because of the rate enhancement, higher yield and often improved selectivity compared to conventional reaction conditions. There are several advantages when performing synthesis under microwave activation: short reaction time with energy savings; increased safety because the reaction is normally performed in milder conditions; economic and environmental advantages, because the reaction can be carried out in the absence of solvents. The use of MWI has become a common practice in the laboratory because organic synthesis performed with traditional methods requires a very long time and high temperatures. In other words, MWI is a useful tool for pursuing new synthetic strategies for laboratories. However, this very promising technique has some drawbacks, such as the high cost of the equipment and the difficulty in scaling-up. As a matter of fact, the volumes used in the laboratory for this technique are 1-5 cm^3 and no examples of industrial application are reported. The removal of the above-mentioned drawbacks would be a big step forward for the chemical industry.

Radiation processing makes use of ionizing radiation for chemical synthesis, and can be considered an alternative to other chemical processes. It can be considered an energy-saving and, in general, environmentally friendly process, thanks to the possibility of operating at low temperatures without solvents. Furthermore, generally speaking, no reaction initiators are needed, with positive consequences on the purity of the obtained products. This latter behaviour makes radiation processes strongly competitive when high--purity products are required, such as for pharmaceutical and biomedical applications. Also, it should be mentioned that this process can be controlled very easily through the control of the processing parameters, dose rate and total absorbed dose, which determine the kinetics and the completeness of the reactions, respectively.

The ability to build structures with nanometric precision is a very important characteristic of radiation processing. Nanofabrication involves nanolithography with nanopatterning, due to the small wavelength of the beam. Other studies concern the formation and synthesis of nanostructures, formed both by metallic or polymeric nanoparticles. Some examples are the radiation synthesis of nanoparticles of inorganic materials as copper, silver and other metals, as well as of polymers for the incorporation of active principles for drug delivery.

The use of plasma technology or light to trigger some reactions sometime produces exceptional results in the laboratory, but the difficult scale-up is still a problem. Similarly, in the activation of chemical bonds by means of photochemistry there are excellent premises for the promotion of organic reactions in the absence of any catalytic system, even though the serious problem concerning scaling-up remains unchanged.

4.3.2.8 - Conversion of batch processes to more intense continuous processes

Normally, fine chemicals and pharmaceutical active principles are produced in batch conditions as a consequence of the low production volume. It is well known that batch operations have lower performances than continuous devices. It can be useful, therefore, to consider the possibility of converting existing batch processes into small, more efficient continuous processes, also looking into the possible use of a unique plant, with a modular structure, for different productions (multipurpose continuous plant). Miniaturization and standardization of the unit operations, as modular systems, make it possible both to save energy and to operate more safely, simplifying the implementation of chemical plants. In the context of the development of continuous processes, the microreactor technique is offering a fast lane to optimizing processes either in the cases where unstable reactions or high exothermic/hazardous reactions (scale-up impossible for safety reasons) are involved or when products are formed which are unstable under applied reaction conditions. The already-achieved development and production of up to 5 kg of final product through microreactor tecnology envisages an environmentally safe revolution focused on improved yield and better safety for fine chemicals and pharmaceutical industries in the near future.

4.3.3 - New Catalysts for New Products and Processes

As already mentioned, catalysis is of paramount importance in order to reach the objectives of Sustainable Chemistry, because an appropriate catalyst makes it possible to selectively promote a specific reaction and obtain the desired product within a reasonable time. In catalyst preparation, the main focus must be the efficiency and specificity of the reaction in order to minimize as much by-products as possible and to maximize the yield. In this perspective, homogeneous catalysts would be more suitable than heterogeneous catalysts, as a consequence of the molecular dispersion. Unfortunately, it is difficult and expensive to recover and reuse homogeneous catalysts and the contamination of the final product with heavy metals is also a disadvantage. For these reasons, the use of heterogeneous catalysts is normally preferred in industry. Methods for heterogenizing homogeneous catalysts by grafting them onto the surface of a support which is characterized by high activity and selectivity have been developed, but this still remains a big challenge.

Sustainable Chemistry needs new and more efficient catalysts (homogeneous, heterogeneous and heterogenized) and biocatalysts for new reactions and new products. Lastly, it is interesting to observe that the characteristics of the used catalysts, together with the existence of a multiphase system, strongly affect the type of reactor to be used and the reaction procedure, either in the laboratory or in the industrial plant. The presence of different phases – that is, gas-liquid, liquid-liquid, gas-liquid-solid and gas-solid – makes it necessary to

maximize the interphase surface area, in order to achieve reasonable mass and heat transfer rates. The process design and development requires a chemical engineering approach at all scale levels, from laboratory to pilot and industrial plant.

4.3.3.1 - New highly efficient catalytic systems for the production of fine chemicals, pharmaceutical products and commodities with clean processes.

Two different R&D frontier problems deal with the need to design innovative catalysts for the production of fine chemicals, pharmaceuticals and bulk commodities. A common facet of these projects is that both are aimed at exploring new reaction pathways and conditions, by reducing the number of reaction steps, introducing intensified separation technologies and increasing energy savings. The improvement of a catalytic process in term of efficiency and selectivity (regio-, stereo- and enantio-) will be the most important deliverable of these research lines to be pursued through the use of either new specialized homogeneous catalysts or innovative heterogeneous systems specifically tailored to the nanoscale level. Issues actively pursued in these strategic areas also deal with the reduction of energy and resource requirements, the study of more efficient products, and the atom economization of the process with the aim of greatly reducing or eliminating waste formation (for example the use of benign and easy-to-handle oxidants). In the development of sustainable chemical transformations, the discovery of new efficient synthetic methods, especially for carbon-carbon bond formation, remains a great challenge.

4.3.3.2 - Metal mediated processes.

The study and development of new catalytic methods for the formation of complex molecules, based on the use of mono- or bi-metallic catalysts or mixtures, is very important, particularly for the pharmaceutical industry where complex molecules have to be handled. An important challenge in this field will be the design, synthesis and characterization of novel chelating N-donor ligands and of their corresponding Palladium (II) and Rhodium complexes as potential catalysts. Among many others, the application to an important process such as the oxidative carbonylation of phenols or bis-phenols to aryl carbonates or polycarbonates could be envisaged. Aromatic polycarbonates (PCs) are one of the most useful engineering plastics because of their good heat resistance, mechanical properties, and transparency. Market growth for aromatic polycarbonates has been almost 10% a year from the late 1990s. Recently developed effective catalytic systems for the direct synthesis of aromatic carbonates and polycarbonates consist of palladium(II) complexes with N,N'-carbene chelating ligands and with disubstituted-2,2'-bipyridyl ligands. It has recently been shown that even non-resonant bioxazolyl ligands are highly efficient and that increasing hindrance in positions adjacent to N-donor atoms of chelating ligands, such as bis-oxazolynes and N,N'-carbene ligands, affords higher TON of diphenyl carbonate (DPC). In this respect, there is a lack of knowledge about the influence of different anionic or neutral chelating donor ligands on the catalyzed manufacture of aromatic carbonates and polycarbonates. It could be interesting to investigate both the possibility of tuning the steric and electronic features of ligands and the catalytic properties of new palladium complexes containing new N-donor such as those indicated here.

A special attention should be devoted to the synthesis and structural characterization of Pd and Rh complexes, which are precursors of catalytic processes, mainly of C-C coupling of Heck, Suzuki, Sonogashira type, as well as to the detailed study of their catalytic and small-molecule activation properties. It is expected that N-coordinating ligands (for example imidazoles) will create proper coordination spheres of metals to achieve high activity compared to aryl halides, which are substrates of C-C coupling. This project could make it possible to elaborate new synthetic methods following green chemistry rules for the preparation of fine chemicals, pharmaceuticals and other materials such as conducting polymers. Lastly, possible synergic effects in the use of bimetallic catalysts or mixtures of catalysts and the replacement of the traditional metals with non-toxic and inexpensive metals like Cu and Fe in the coupling reactions deserve more general and deeper investigations.

4.3.3.3 - Asymmetric Catalysis.

There is an increasing demand for enantiopure chiral compounds to be used not only for pharmaceuticals but also for agrochemicals, flavours and fragrances, and specialty materials. This is due both to the knowledge that two enantiomers of a chiral substrate could show very different biological activities and to new regulations which will no longer allow the use of racemic mixtures. Among the different methods for producing enantiopure or enantioenriched compounds, enantioselective catalysis has proved to be quite useful. Exciting discoveries in the field of β- and γ-peptides have recently provided impetus for the development of new synthetic methodologies for the preparation of β- and γ-amino acids, the study of which has been very limited up to the past few years. The use of such amino acids for biomedical applications appears to be especially interesting as, for example, the incorporation of even isolated β-amino acid into α-peptides appears to protect against peptide degradation. Moreover, conformationally constrained amino acids such as cyclopropane-, cyclobutane-, cyclopentane-, and heterocycle-β- and γ-amino acids are especially appealing for the synthesis of foldamers, oligomers which adopt specific conformations. Such oligomers are useful both for the comprehension of the forces responsible for molecolar folding in natural systems, such as proteins, and for their potential application in medicinal chemistry as well as in synthetic organic chemistry as building blocks, ligands and catalysts in asymmetric synthesis. Therefore, investigations concerning catalytic methods for the preparation of this class of amino acids seem to be particularly stimulating.

4.3.3.4 - Organocatalysis.

This can be considered as based on an enzyme-like catalysis mediated by small organic molecules, which have become extremely significant over the last few years. Their benefits include not only atom economy and simplicity, but also the possibility of performing homogeneous asymmetric catalysis in the absence of any metal. Notably, preparation advantages are that usually the reactions can be performed under aerobic atmosphere with wet solvents and the catalysts are inexpensive and often more stable than enzymes or other bioorganic molecules. These non-metallic organocatalysts have been recently demonstrated to make possible environmentally benign synthetic reaction processes; they have been used in the large-scale synthesis of useful compounds, in particular natural and unnatural aminoacids and peptides for pharmaceutical purposes, including L-Dopa, L-Azatyrosine, ACE- inhibitors which are hitherto difficult to obtain by previous industrial processes. These chiral organocatalysts, some of them highly active with a catalyst load of 0.01% mol, are already commercially available, and have attracted considerable attention from the industrial world, mainly because about 20% of the top 500 drugs contain amino acids and their derivatives. The opportunity for organocatalysts to be produced from sustainable biomass-derived chemicals (platform molecules) has been highlighted recently within the framework of the 'First International Symposium on Organocatalysis in Organic Synthesis' held in Glasgow, Scotland, on July 2006.

Besides the recent significant achievements of organocatalysis based on the use of fairly simple molecules, there is a considerable need to expand the research for the development of more complex organocatalysts that have multifunctional sites and elaborate stereochemistries. Although their initial syntheses can in some instances pose challenges, such catalysts can become economically viable if they can be recycled and if they are highly efficient. Relatively complex tailor-made macrocyclic compounds, molecular clefts and multi-component supramolecular assemblies, if they bind reagents and/or transition states, can offer a means to fine-tune reaction pathways leading from certain substrates to specific target compounds. For example, the complexation of anionic intermediates and/or transition states with appropriate molecular receptors could allow the action of natural enzymes such as aldolases to be mimicked. Indeed, the potential of synthetic molecular receptors designed to function as enzyme analogues, although pioneered by a number of researchers worldwide, is still vastly unexplored and mostly unexploited.

4.3.3.5 - Future issues in catalysis.

Further research is needed for the development of new catalysts and new ligands for asymmetric reactions of hydrogenation, oxidation, carbonylation, hydroformylation and in general of C-C coupling reactions to be applied not only to simple reactions but also to substrates of commercial interest. Also useful for synthetic applications are heterogeneous metallic catalysts modified with chiral auxiliaries, the use of chiral organic compounds (organocatalysis, see above) and biocatalysts (overlapping with industrial biotechnology). Another hot research topic in this sector refers to the catalytic activation/functionalization of the C-H bond both of the alkanes and of the aromatic molecules which could lead to a breakthrough in both bulk and fine chemistry. Examples are the direct oxidation of methane to methanol and of benzene to phenol or, in the absence of oxygen, the C-C coupling reactions. Also, the direct functionalization of the aromatic and hetero-aromatic rings with easily recoverable acid catalysts is of great importance for both bulk and fine chemistry.

Lastly, as far as the production of commodities is concerned, a new generation of more active and selective catalysts in milder conditions must be found. New techniques for a more dispersed catalyst preparation, a fast screening of the catalytic performances, and catalyst characterization are required. Progress is necessary for all kinds of heterogeneous catalysts, for example: both Brönsted and Lewis type acid-base catalysts , zeolite catalysts, redox catalysts based on the use of more dispersed transition metal oxides, semiconductor oxides, well-dispersed metal catalysts, and bi-functional or multi-functional catalysts. Computational approaches could be used with the aim of both explaining the reaction mechanism and improving the catalyst performance.

4.3.3.2 - Catalysis both for the production and management of sustainable energy and for sustainable transportation (mobility).

Great amounts of energy are consumed by the chemical industry (about 20% of the energy consumed by all the manufacturing industries). In Italy today, most of this energy is imported, often from politically unstable countries. Chemical industries are highly interested in the development of energy-saving technologies. Besides, these new technologies could be used also in other industries, and chemistry could play a leading role in a more rational production, storage and use of energy. Therefore, all the efforts aiming at reducing energy consumption and decreasing the dependence on oil and other non-renewable fossil sources of chemical production are strategic issues which will be substantiated by seeking alternative feedstock based on natural resources, in order to replace fossil fuels. Efforts are focusing on implementing the methods of biomass exploitation (bioethanol, vegetable oils, etc.).

In this respect critical points are:

Bio-Oil Upgrading - The pyrolysis of biomasses produces bio-oils, which must be upgraded in order to replace traditional diesel and gasoline fuels. Indeed, bio-oils have some negative properties (low heating value, incompatibility with conventional fuels, solid contents, high viscosity, incomplete volatility, and chemical instability) which need to be removed or reduced. Upgrading is necessary to eliminate the negative properties of bio-oils. Several procedures are available, the most promising of which are hydrodeoxygenation with hydrotreating

catalysts (e.g. CoMo or NiMo sulfides) and zeolite upgrading. Alternatively, bio-oils and chars can be converted into syn-gas by steam-reforming and, consequentely into hydrocarbon fuels through the Fischer-Tropsch process.

Syn-gas and Fischer-Tropsch synthesis - Fischer-Tropsch synthesis (FTS) is an industrial process for producing alkanes from syn-gas using Co-, Fe-, or Ru-based catalysts. This technology was first developed in the early 1900s and used by Germany during the 1930s and 1940s to produce liquid fuels from syn-gas derived from coal. FTS received much attention during periods of oil shortage (in the seventies) and several oil companies are currently using or building FTS units to produce liquid fuels (e.g. in South Africa and Malaysia). The products from FTS are a range of mostly straight-chain alkanes ranging from C1 to C50. The lack of selectivity remains a major limit, in spite of the continuous effort to modify the catalytic properties to tune the product selectivity. Organometallic di- and polynuclear complexes have offered interesting models for investigating the fundamental steps in FTS synthesis, but a homogeneous catalytic approach appears still far from being successful. The shift from oil to alternative sources, including biomasses, to produce liquid fuels requires substantial progress in the current FTS technologies, and the use of new and more efficient catalytic systems.

An important role is attributed to the replacement of oil with less costly and more abundant hydrocarbon sources, such as gas and coal. The more efficient and less polluting conversion of such fuels can be achieved through catalytic combustion. This process allows burning the hydrocarbons at much lower temperatures than with homogeneous combustion, thus decreasing or virtually eliminating NOx emissions. Moreover, the catalyst pushes the reaction towards complete oxidation, thus avoiding the emission of CO and partially unburnt hydrocarbons. This technology can be successfully applied in stationary power generation plants, where very high efficiency can be obtained through catalytic combustion in gas turbines with co-generation plant schemes; moreover, it can be applied in more restricted application areas, such as domestic heating, thus achieving a better control of noxious emissions.

The improvement of well- known processes such as the Fischer-Tropsch synthesis of a liquid fuel from syn-gas - which is similar to the diesel fuel from petroleum or the Mobil process to obtain gasoline from methanol, the latter easily obtainable from syn-gas - is fundamental for reducing the dependence on petroleum. Syn-gas represents the intermediate step for obtaining both hydrogen and methanol, which, in perspective, are considered the most important energy vectors.

Production of hydrogen and biofuels - Hydrogen can also be obtained from different procedures such as methanol/ethanol steam reforming, thermochemical processes based on the use of solar energy like solar-powered reforming natural gas, and thermochemical or photoelectrocatalytic water-splitting cycles. The photoelectrocatalytic splitting of water into hydrogen and oxygen is the most fundamental and important stoichiometric reaction in artificial photosynthesis, because it has great potential for the direct conversion of solar energy into chemical energy and provides a clean, renewable source of hydrogen fuel from water. Indeed, among the various methods of solar energy conversion, the best results were achieved with semiconductors as photosensitizers. The development of an efficient artificial photosynthesis system for energy conversion by irradiation is mandatory from the standpoint of efficient solar energy exploitation.

If successfully developed with economic viability, this would be the ultimate technology that could solve simultaneously both energy and environmental problems in the future.

The development of catalytic process technology for both on-site and large-scale centralized efficient production of hydrogen is one objective. Therefore, new materials for hydrogen production, storage and purification are required. In particular, the storage capabilities of gaseous molecules such as hydrogen must be improved by novel hybrid organic-inorganic materials, porous metal organic frameworks, and mesoporous oxides. Membranes with selective permeability to hydrogen must also be developed to reach high standards of gas purity compatible with its usage in stationary and mobile hydrogen fuel cells.

The relevant increase of the share of gasoil-driven vehicles in latest years, in Italy and all over Europe as well, has pushed the development of new technologies aimed at the production of gasoil from renewables sources. The production of biodiesel by means of the transterification of vegetable oils and animal fats requires new and more efficient catalysts and opens the way to the production of chemicals starting from the by-products that are obtained in these processes such as, for example, glycerol which is a by-product of biodiesel. An alternative approach for the production of Green Diesel includes the concomitant hydrodeoxygenation, decarboxylation and hydroisomerization of vegetable oils, to produce a high quality gasoil, readily blendable with the traditional diesel fuel, plus hydrogen at mild reaction conditions.

As already mentioned, efficient methods for the use of CO_2 as a building block for C1 chemistry have not yet been developed. This is a very important issue and efforts are being made to achieve an efficient reduction of carbon dioxide through catalytic or chemical looping-based processes.

Fuel Cells - Catalytic processes operating within fuel cells, especially concerning the conversion efficiency, fuel versatility, resistance to poisons, transport within the cell, lifetime of the device, and economics of fuel cell manufacture, must be strongly improved for a large-scale commercial availability of these devices to be achieved. This represents an essential part of the exploitation strategy for transport and portable applications of fuel cells. One of the largest hurdles encountered in the development and production of fuel cells is the shortage of platinum, which is a very rare and highly expensive noble metal used as an efficient electro-catalyst for the reduction of either hydrogen or alternative fuels in the cell. In the future, fuel cells will play an important role in

ensuring the mobility of vehicles and electrical devices (laptops, mobile phones, etc.) only if platinum will be completely (or almost completely) replaced by less expensive and more abundant metals. One of the main goals of this project is the replacement of platinum with nanostructured metal aggregates or alloys, mainly containing cheap and abundant metals like iron, cobalt or nickel. Research targets will also be the development of innovative membranes which may be used to selectively transport protons or anions between segments of the fuel cell. New catalysis processes should also be developed to further increase the removal efficiency of pollutants from vehicle exhaust. Such technologies are needed in order to match future emission regulations targeting a zero-emission goal.

4.4.3.3 - Catalysis and other strategies for environmental protection

One of the main purposes of "Sustainable Chemistry" is to minimize wastes and environmental impact. These objectives can be reached, first of all, by detecting more selective catalysts and devising "increasingly cleaner processes". However, new process technologies for the maximum removal of any possible pollutant from the waste streams, including waste process water (Advanced Oxidation Processes) and fuel gases, automobile exhausts and sewage effluents, are necessary, and they will include methods which combine catalytic and separation techniques. A valorization of waste streams that contain organic pollutants will also be attempted, for example through the development of photocatalytic processes which enable both the contemporary production of hydrogen and the removal of organic substances. Recalcitrant organic molecules such as azoic colorants that could be present in leather tanning waste waters, can be destroyed by deep oxidation processes performed - for example - with heterogeneous photocatalytic processes. Cold plasma techniques can also be improved for organic pollutant destruction.

4.4.3.3.1 - Advanced Oxidation Processes for water remediation

Water shortage and security are major worldwide issues due to water-intensive lifestyles, rapid industrialization, and agricultural intensification. The current state of the art in water remediation is represented by a group of Advanced Oxidation Processes (AOPs). All these processes exploit free radical-mediated reactions to decompose hazardous compounds, basing their action on the oxidant and kinetic properties of the OH radical. Applications count on an established know-how of the OH-initiated degradation of various pollutants (halo-compounds, phenols, polychlorinated biphenyls (PCBs), aromatics, azocompounds, etc.), conducted by means of both time-proven methods like pulse radiolysis and flash photolysis, and steady state electrochemical, sonochemical, plasma discharge, and Fenton-like methods. Further studies in this field should focus on a series of persistent organic pollutants (POPs), like dioxins and furans (PCDD/PCDF), PCBs, hydrochlorobenzene (HCB) and polyaromatic hydrocarbons (PAHs), as outlined by the UN Stockholm Convention. New pollutants, particularly those from the pharmaceutical industry, deserve careful consideration.

Among a variety of AOPs, the E-beam method represents the most efficient remediation process. In fact, a) it can accomplish the production of very high concentrations of oxidizing radicals in microseconds, b) it makes it possible to control the decomposition degree of organic compounds up to their complete mineralization, and c) it destroys bio-resistant pollutants, thus being the ideal pre-treatment for a conventional biodegradation. Additional benefits with respect to conventional treatments are: a) no need for chemical additives, b) minimization of the stock of chemicals, c) operation at room temperature, d) penetration into the bulk of water even in the case of turbidity (not possible with light irradiation), and e) disinfection. Therefore, it accomplishes several environmental tasks simultaneously: a) depollution (mineralization of organics, removal of odors and colors), b) water disinfection, c) destruction of endocrine disrupters, and d) rapid action. The E-beam remediation is economically advantageous for the treatment of medium-large volumes of effluents from dye, textile, and paper mill industries, hospitals, public utilities and animal-breeding plants. It aims at rehabilitating wastewaters to new uses, some of which are firefighting, street washing, park watering and horticultural irrigation, industrial cooling and washing cycles. Today, a full-scale plant in Korea confirms the feasibility and financial convenience of the method.

Therefore, both the process optimization and the development of rehabilitation plants implementing the AOPs - and particularly the E-beam for large effluent volumes - constitute one 21st-century challenge for environmental processing and engineering.

4.4.3.3.1 - Nanotechnology in pollution prevention and remediation

Nanoscale science offers great promises for the delivery of new and improved environmental technologies. Nanotechnology can substantially enhance environmental quality and sustainability through pollution prevention, treatment, and remediation.

Environmental technologies can greatly benefit from an understanding of chemical properties at the nanoscale level. In particular, two broad application areas can be taken into account:

Pollution prevention / Nanostructured catalysts, for example, can make chemical manufacturing more efficient by providing higher selectivity for desired reaction products. The assemblage of nanostructures from biopolymers or bio-inspired materials is an example of an environmentally benign approach to fabricating microelectronics. Nanotechnology applications could also help to create benign substances that replace currently used toxic materials. For example, nontoxic, energy-efficient computer monitors are replacing those made with cathode ray tubes (CRT), which contain many toxic materials.

Treatment and remediation / Nanoparticles of various oxidants, reductants, and nutrients have been suggested as useful for both promoting contaminant transformation and stimulating microbial growth. Nanoscale bimetallic particles essentially eliminate all the undesirable by-products given off by conventional methods (e.g., bioremediation and zero-valent iron) for the in situ remediation of chlorinated organic solvents. Nanoparticles that are activated by light, such as the large band-gap semiconductors titanium dioxide (TiO_2) and zinc oxide (ZnO) - which are readily available, inexpensive, and of low toxicity - remove organic contaminants from various media. Nanoparticles could provide enormous flexibility for in situ remediation as well. For example, nanoparticles are easily deployed in ex situ slurry reactors for the treatment of contaminated soils, sediments, and solid wastes. Alternatively, they can be anchored onto a solid matrix such as carbon, zeolite, or membrane for the enhanced treatment of water, wastewater, or gaseous process streams.

Methods - The new functionalities shown by nanomaterials originate from the fact that nanoscale materials have unique structures (large surface area, small size or shape, and intimate nanoscale connectivity). These structures cannot be extrapolated from our understanding of traditional bulk materials that have been routinely used in daily life.

The experimental search for new materials suffers from a slow feedback from theoretical models and computational simulations for understanding and improving nanomaterial synthesis. In other words, the potentials of theoretical and computational tools for the design of materials with enhanced nanoscale properties have not been explored thoroughly.

This exploration can be accomplished efficiently through the development of computational methods for the search for novel materials, thereby limiting the space for experimental research.

Therefore, synthesis is a key step in what should be a tightly connected loop of synthesis, characterization, theory/modelling/simulation and design. This loop can be repeated over and over until objectives have been reached.

4.3.4 - Synthesis and Characterization of Nanosystems

Over the past few years, an increasing interest has been focused on the fabrication and study of inorganic nanocrystals, namely semiconductor, oxide and metal nanoparticles. The physical properties of such crystalline nanoclusters appear to be intermediate between those of bulk matter and of molecular systems, which are composed of just a few atoms, and are strongly dependent on their size and shape. Inorganic nanocrystals possess unique optical, electronic and magnetic behaviour that can be potentially modulated by varying the size and shape of the nanocrystals. In this field there is a clear fundamental interest boosted by the understanding of basic physical processes, but there is also a growing awareness of the potential applications of such nanocrystals as active materials in optoelectronic devices and sensing materials for biomedical and environmental purposes.

The development of such novel materials designed for specific purposes requires:

1. Setting up of scientific protocols for the implementation of colloidal nanocrystal preparation in order to have access to different types of materials with great control over size and shape as well as for nanocrystal processing, in order to modify their surface by exchanging organic capping molecules and/or growing inorganic epitaxial layers (core-shell structures).
2. Theoretical/computational characterization of nanocrystals at the structural, spectroscopic and dynamic levels
3. Conversion of processed nanocrystals into functional nano-structured materials by organizing them as building blocks into higher ordered hierarchical systems.
4. Modelling of nanostructures

4.3.4.1 - Nanoparticle synthesis, functionalization and processing

Synthesis of semiconductors (CdSe, CdS, ZnS, ZnSe), oxides (ZnO, TiO_2), metals (Au, Ag), and magnetic material as metal transition and rare earth oxide nanocrystals will be performed by colloidal chemistry methods. The preparation of nanocrystals with core-shell structures can be also performed (CdSe@ZnS and CdS@SiO_2).

The possibility of manipulating prepared nanocrystals by properly engineering their surface through capping exchange is very significant. The prepared inorganic nanocrystals can be coated with a monolayer of surfactant, rendering the nanocrystal hydrophobic. The surfactant exchange makes it possible to tune the solubility and the reactivity of nanocrystal, and thus place them in almost any chemical environment. Moreover, it is possible to functionalize the nanocrystal surface through a suitable choice of the capping agent, thus conferring specific chemical reactivity to the nanocrystal. Nanocrystals are really a new class of chemical macromolecules, and the inorganic component of materials can be organized by using the well-established principles and techniques of synthetic organic chemistry and molecular biology. Different possible strategies need to be exploited to build 3D nanostructures while taking advantage of the combined directed nanoparticle self-organization and new surface patterning techniques.

In order to optimize the synthetic conditions in terms of shape and size distribution, models simulating nanocrystal formation in different experimental conditions will be designed.

4.3.4.2 - Modelling and design of building blocks for nanostructured materials

Combined expertise is needed in a wide range of theoretical approaches and computational techniques which are instrumental for providing insight into nanoscale experimental measurements, understanding functions, virtually characterizing new materials, quantifying transport mechanism (including electron transport) on the nanoscale, predicting self-assembly, and designing and virtually synthesizing new materials.

The basic goals for any significant in-silico activity in the field are:

- To bridge a wide range of length and time scales, so that the phenomena captured in atomistic simulations can be modelled on the nanoscale and beyond.
- To develop new force fields for molecular dynamics methods and other classical, particle-based methods, which are capable of describing nano-interfaces between dissimilar materials
- To develop rigorous methods for the inclusion of stochastic effects as well as more effective methods for the characterization and solution of stochastic differential equations which are necessary in the upscaling
- To extend theoretical approaches for the analysis of high-resolution and single-molecule spectroscopies used to probe the molecular-level mechanism of energy-producing and energy-using processes.
- To improve the quantitative reliability of electronic structure algorithms in order to handle ground and electronically excited states.
- To improve our understanding of both intermolecular interactions and how to model them efficiently, accurately, and realistically in large ensembles.
- To predict the self-assembly of nanoscale building blocks by evaluating the relative contributions of various interactions, including dispersion forces, hydrogen bonding.
- To discover strategies for dealing with the “inverse problem,” where the composition and structure of a new material are designed to express a desired property.

4.3.4.3 - Conversion of processed nanocrystals into functional nano-structured materials - Nanocomposites

Significant interest in material science is devoted to the development of novel materials based on polymer modification by means of nanoparticles. In fact, there is a real possibility to modify/add new peculiar properties to polymers (for example, electrical conductivity, photoactivity, luminescence, catalytic and magnetic properties), while maintaining and improving their processing capabilities and mechanical properties. Hybrid materials consisting of nanoparticles in polymer matrices represent a novel class of nanostructured systems that are potentially able to surpass the performances of classic materials, by accessing new properties and exploiting unique synergisms among substances. The combination of polymer and nanoparticle offers opportunities for tuning the physical properties of the final materials for electronic, photonic and biological issues which can be exploited in optoelectronic, sensing and biomedical domains. In addition to the incorporation process, the local deposition and positioning of NCs by means of block copolymer, 2/3D organization of NC in polymers can be exploited.

Inorganic/biological nanostructures

Metal and semiconductor nanoparticles are of great interest not only for their new and original properties which are generated by their reduced dimensions, but also for their dimensional affinity with biological macromolecules (peptides, proteins, nucleic acids, etc.) This affinity makes possible an integration between nanotechnology and biology, with consequent progress in new material assembling, which can find applications in the sensor, biological labelling, and medical diagnostics fields. Wate-soluble colloidal nanocrystals are essential in light of their bio-conjugation with proteins for biological applications. Colloidal nanocrystals have a number of peculiar advantages over the organic dyes that are conventionally used in optical bio-detection. Indeed, their wide absorption spectrum, coupled with their extinction cross-section, makes it possible to excite different luminescent nanoparticles with different sizes using a single excitation wavelength.

Nanocrystals for photocatalysis

The photocatalytic degradation of organic pollutants assisted by seminconductors (TiO_2 and ZnO) represents one of the most appealing techniques among the Advanced Oxidation Processes (AOPs). Improved charge separation and inhibition of charge carrier recombination is essential in enhancing the overall quantum efficiency of the photodegradation process. Nanocrystalline semiconductor photocatalysts offer an interesting way to increase the efficiency of a photocatalytic process by both increasing the charge separation and extending the energy range of photo-excitation for the system.

A significant advancement is provided by the possibility of synthetizing nanostructured materials with high photocatalytic activity and different chemical composition (TiO_2, TiO_2/CdS), which are effective in the degradation of organic pollutants. Supported systems can also be developed in order to set up degradation processes (e.g. deposition of nanostructured material onto glass, glass fibre, and alumina fibre), in order to overcome the technological and economic drawbacks connected with catalyst recovery in the case of slurries.

Nanocrystals for energy conversion

Hetero-junctions composed of nanostructured semiconductor/organic molecules can be prepared using TiO_2, ZnO semiconductor nanocrystals and organic pigments such as chlorophylls, porphyrins and phthalocyanines. These

large band-gap semiconductors need to be associated with molecules that absorb light in the visible range of the solar spectrum and give rise to a charge transfer on the surface. The reduced nanocrystal dimension results in a great surface extension of the nanosized semiconductor film, thus enhancing the energy transfer efficiency. The use of sensitizers modifies the surface of semiconductor materials, making them suitable for photoelectrochemical applications in the visible range.

4.3.4.4 - Modelling of nanostructures

The development of physical-chemical models suitable for interpreting the behaviour of the molecular and supramolecular systems and their transformation into silico procedures, by modifying and optimizing existing general processes, is a significant problem for the study of nanosystems in connection with environmental impact and energy conversion research efforts.

In principle, information concerning self-assembling processes and the resultant superlattices of nanoparticles is encoded in such molecular components as the nanocrystallite core, surfactant chain, solvent, and solid substrate. Simulated molecular dynamics can be used to investigate the energetics, dynamics, kinetics, and structural properties of nanoparticles and their self-assemblies under selected conditions representing different self-assembling stages.

Nanoparticles in polymer hosts are described by adapting coarse-grained simulation techniques to describe the translational dynamics of a semi-rigid core and chain conformational motions.

Suitable theoretical models can be developed with the aim of describing energy, geometrical structure and electronic properties of organic molecules adsorbed on crystals or nanocrystals. Few models exist that explicitly treat hybrid systems (molecules/surfaces), thus a new computational strategy is necessary in order to include the solvent effect in the calculations of energies, structures and properties, also extending this approach to spatially anisotropic solutions. Such an approach, for instance, is ideally suitable for describing large size molecules (e.g. derivatized porphyrins) in interfaces (liquid/solid surface), and also supramolecular systems.

4.3.5 - Process and Plant Design

In the near future, chemical productions will focus on completely new fields. New plants will be designed and operated to produce pharmaceuticals, nanoparticles, and food specialities; their design will involve knowledge and expertise in very specific areas. In this framework, multidisciplinary collaborations among chemical engineers, physicians, chemists and biologists will be unavoidable. Moreover, the processes of sustainable chemistry will produce minimum amounts of wastes or no waste at all; they will be safe and energy-saving in order to protect the environment and make up for the shortage of carbon-based fuel in the Western developed countries.

4.3.5.1 - New processes for alternative fuels and energy sources.

The interest in hydrogen as a clean fuel has been recently increasing. Hydrogen produces only water when it burns, and can be efficiently used in fuel cells; therefore, it has a great chance of being the replacement for carbon-based fuels in the near future. The anticipation of this transition has been so great that the future vision for hydrogen power has been labelled by the scientific community as the “hydrogen economy”.

Today, more than eighty percent of the industrial hydrogen produced is obtained from the steam reforming of hydrocarbons in syngas production. The traditional process may be greatly improved by adopting an integrated reactor module consisting of subsequent stages of catalytic reaction and H_2 removal by means of metal- or ceramic-based membranes. Thus, it is possible to achieve very high yields for the reaction process and a high purity of the hydrogen product. In the long term, the main target is the production of hydrogen from a clean, renewable chemical source using a clean, sustainable energy source. Solar water splitting can provide clean, renewable sources of hydrogen fuel; various approaches have been studied to achieve this important goal, including indirect or direct or thermochemical, photosynthetic or photo-electrochemical solar water splitting. The simplest thermo-chemical process for splitting water involves heating it to a high temperature and separating the hydrogen from the equilibrium mixture. Unfortunately, the decomposition of water does not proceed well until the temperature is very high and the overall process efficiency is poor, whereas at lower temperatures the efficiency of a solar array is quite high due to minimal radiation losses. In order to reduce the operating temperature, the direct water splitting reaction can be replaced by a set of chemical reactions that lead to the decomposition of water into hydrogen and oxygen. The most promising among these cycles is the sulfur-iodine cycle, originally studied in the mid-1970s by General Atomics with the aim of using the low-temperature waste heat of nuclear reactors. This technique requires the catalytic reduction of sulphur trioxide to sulphur dioxide at a temperature of around 800-1000 °C, and with a high heat absorption, which can be provided by solar energy.

Natural gas can be involved in many different innovative processes depending on the use of new catalytic systems. An example might be the development of novel bi-functional (noble metal/perovskite) monolith and foam catalysts with great thermal resistance and high performance, to be used in catalytic autothermal processes of partial oxidation of natural gas to syngas as an alternative to steam-cracking processes. Another example is the development of structured catalysts for the catalytic oxidation of methane/air mixtures under fuel-rich conditions as a preliminary conversion stage for gas turbine burners which use short-contact-time autothermal reactors, thus avoiding the noble metal catalyst thermal deactivation characteristic of traditional fuel-lean operation. Other examples are: i) the development of novel structured perovskite-type catalysts as alternatives to noble metals for

ethylene production from methane/ethane/oxygen mixtures under short-contact-time conditions, and ii) the development of an autothermal partial catalytic oxidation process which is an alternative to steam-cracking, but with a higher conversion and yield.

Gasification of biomass to produce syngas for gas turbines or fuel cells with a low tar content requires the development of new catalysts and new reactor design. Stable, durable and high mechanical strength in-bed catalysts for biomass tar and methane reforming in a fluidized bed reactor must be studied in order to eliminate the hot gas cleaning stage, thus reducing investment costs.

Further classes of alternative energy production processes are those concerning the production of liquid fuels such as bioethanol, biobutanol, dimethylether and biodiesel. To be competitive this production, relies on cheap and reliable sources of renewable raw material and efficient production processes. The most suitable source for bioalcohol comes from an efficient conversion of cellulosic, fibre- or wood-based, or cereal waste biomass into fermentable sugars. Biomass is first subjected to pre-treatment to solubilize hemicelluloses and to expose the cellulose for subsequent enzymatic degradation. The cellulose then undergoes enzymatic hydrolysis to produce glucose, which can be converted into bio-fuels and chemicals by fermentation. The reaction products must then be separated and purified. To purify the bioalcohols, hybrid purification processes based on the integration between azeotropic distillation, pervaporation, and molecular sieve adsorption could be implemented in the best configuration. Lastly, energy savings can also be regarded to as an alternative energy source: the optimization of energy uses in industrial processes is a task that can be easily pursued by tools such as pinch technology. This is usually known as process integration.

4.3.5.2 - Advanced product engineering

New advanced product technology requires innovation with regard to various aspects. First of all, new techniques for the production of nanoparticles, ionic liquids, pharmaceutical compounds, etc. must be developed. Then the formulation of active ingredients must be implemented to produce formulated products as nanostructured materials or systems for a quick release of pharmaceutical products. The equipment for performing the new processes in the most effective way will be very compact due to the intensification of mass and heat transfer. Moreover, in order to perform the process safely and efficiently, there is a need for equipment endowed with strict control systems based on advanced control algorithms (Archa Gambineri). Moreover, data will be monitored and analyzed by Multivariate Statistical Process Control.

Research based on close academic-industrial collaboration will focus on advanced product design, combining the industrial experience in product formulation and the academic knowledge in process simulation and control.

The major prospects for the development of new advanced products are as follows.

- New methods to carry out reaction-precipitation processes for the production of nano-scale materials. Chemical precipitations and co-precipitations in sol-gel material and in emulsion appear to be the most effective ways to control the crystal size and the crystalline nature of the products. To assure the required performance of the precipitation process, high intensification reactors – such as the rotating disc reactor – could be used. This apparatus has the great advantage of allowing an easy scale-up from the pilot to the industrial scale. Nanoparticles produced in sol-gel materials will be ready to be used for coatings either in new material applications (TiO_2) or in the healthcare area (hydroxyapatite for in situ human body implant).
- Application of hybrid systems based on the integration of more operations. Here the membrane processes may play a very important role. In fact, the combining of a membrane process with crystallization (to produce well-shaped proteins), distillation (for solvent recovery), and reactors (to improve the efficiency of chemical and bio-chemical reactions) is a meaningful example of effective hybrid processes. Some applications of membrane reactors are in the hydrogenation and oxidation reactions, the supply of high pure hydrogen, enantiomeric productions, etc. As a particular class of membrane reactors, bio-reactors are new devices for a wide range of applications. In these systems, the catalytic action of enzymes is extremely efficient and selective if compared with chemical catalysts: enzymes show higher reaction rates, milder reaction conditions, and greater stereo-specificity.
- Desublimation and money-intensive processes like the rapid expansion of supercritical solutions (RESS), supercritical antisolvent precipitation (SAS), particle from gas-saturated solutions (PGSS), and depressurization of an expanded liquid organic solution (DELOS). These processes exploit the unique properties of supercritical fluids to develop products with new properties and morphologies; they are extremely attractive for minimizing the use of organic solvents in fine chemistry, pharmaceuticals and the food industry, thus providing innovative technologies which are fully eco-sustainable.
- Advanced process control. The chemical process industry – once characterized by product variability, cheap energy, and production capacity – is now striving to obtain massive production while using minimum energy and creating little waste. This new prospect has generated the demand for more effective operational strategies for the production line. Hence, the process control has become increasingly important in the process industries, as an effective tool for dealing with global competition in today's rapidly changing economic environment, while complying with stringent environmental and safety regulations. Process control is the only way to achieve all the design objectives of a sustainable chemical process at the production line (minimum raw materials and energy; strict quality specifications for products and effluents; safety of personnel, equipment and site). Without a properly designed and implemented multivariate process control system, sustainable processes could only be conceived, but never be put into operation.

Lastly, it is important to assess the safety of new technologies by developing integrated approaches within the context of regulatory decision-making processes for emerging and breakthrough technologies. It is also important to evaluate how the gap between risk and perceived risk can be closed for new technologies, hence defining and characterizing (i) risk, (ii) perceived risk, (iii) risk management options, and (iv) risk communication options for meeting stakeholder concerns.

4.3.5.3 - Process Systems Engineering

Process systems engineering is a typical chemical engineering approach, which is able to address the production process "from cradle to grave": from the design of the molecules to the invention of the process, from process analysis, simulation and synthesis, to process scale-up, optimization and control, including life-cycle assessment and supply-chain management of the final products.

In particular, the theoretical modelling of complex homogeneous and heterogeneous steady-state and dynamic systems must be significantly improved by including more detailed molecular approaches. Molecular dynamics models will become much more sophisticated and include such things as salvation effects and transition state calculations. Chemical reactions will have to be studied in a much more rigorous way than today, in order to carefully establish reaction cycles and kinetic models.

In addition, process simulation programs also need to be improved, so that material and energy balances can be solved together with momentum balances and population balance equations, in order to provide a complete picture of the chemical and physical phenomena occurring within each piece of equipment. Therefore, appropriate simulation programs will be developed for each process and plant. The automation of all the regulation and control systems must be strongly improved as well, while following the progress of information technology and miniaturization of sensors, actuators and electronic devices, also in view of a more efficient and safer plant operation.

4.3.5.4 - Process intensification

Process integration and intensification are enabling factors for a significant improvement in process/plant efficiency. Process intensification can be achieved, for example, through the integration of reaction/separation, heat/mass transfer. In many cases, such integrations can be optimized by means of structured catalysts and reactors with well-defined properties at the macro- and micro-scale. The use of a membrane reactor to shift an equilibrium reaction is another example of process intensification. The chemical engineering approach must be changed. A broader range of production scales must be taken into account by focusing on completely integrated production systems rather than individual devices. An example of this approach is offered by the extension of processing options for continuous operation to small plants for the production of fine chemicals, possibly with a multi-production process. This latter concept can also be extended to large-scale processes. A novel energy source (electrochemical, photochemical, microwave device) could be locally supplied in order to promote a reaction pathway.

Plant miniaturization, conceived few years ago, is a promising research topic which is worth being further developed. In fact, microprocess technologies could achieve major breakthroughs in both fine and bulk chemical areas, as well as in energy-related technology. In this respect, chemical and biochemical reaction engineering will play a major role.

Reactor intensification means the integration of the mixing of reactants, reactions, and separation of products within a single piece of equipment of consistently reduced volume, with much lower hazardous potential due to the very low material holdup. Most of these new technologies are related to multiphase catalytic and non-catalytic reactors (gas-liquid, gas-solid, liquid-solid and gas-liquid-solid). Microfluidic techniques will provide a much better control of both mixing and heat exchange, thus resulting in astonishing improvements in yields and selectivity towards the desired products, as well as in the reduction of by-products. It is also noteworthy that, whenever a new catalyst is proposed, only a properly conceived and designed reactor is able to exploit and maximize its activity and selectivity characteristics. In summary, reactor design will benefit greatly by taking the above-mentioned issues into account, and the sustainability of chemical productions will be remarkably enhanced by following the new reactor design procedures.

4.3.5.5 – In-silico techniques.

The recent and accelerating developments in high performance computing (HPC), process system engineering (PSE), chemical sensing technology and distributed process control will ensure that *in-silico* techniques will have a revolutionary impact on the chemical industry operations over the next 20 years.

In-silico techniques will play an ever-increasing role in all aspects of the chemical industry with the growing requirements of data storage, retrieval, harvesting, and mining. The ultimate objective of *in-silico* techniques is the integration of molecular-scale theoretical chemistry, physical chemistry and hydrodynamics through to the full-scale operation of a catalyst in steady- and unsteady-state conditions. There is a broad range of time and length scales to be taken in consideration. However, the integration of currently existing and yet-to-be-developed modelling methodologies will yield powerful tools which make it possible to define an active site, quantify the surface chemistry, and determine the step rate through a rationally based rate equation. Only by linking all the modelling scales is it possible to achieve optimum process and plant configuration.

In particular, the theoretical modelling of complex homogeneous and heterogeneous systems must be significantly improved by including detailed molecular approaches. The models will have to become much more sophisticated and include such things as solvation effects and transition state calculations, etc. It will be necessary to study chemical reactions in a much more rigorous way than they are today, in order to carefully establish reaction cycles and kinetic models.

Therefore, more suitable simulation programs must be developed. The automation of all the regulation and control systems must be strongly improved following the progress in computer hardware and software and the miniaturization of sensors, actuators and electronic devices, with the aim of achieving a more efficient and safer plant operation. All these aspects are of paramount importance for scaling up the processes; therefore, the necessary theory, modelling, simulation and automation improvements must be studied using a multi-disciplinary team approach.