ROADMAPS AT 2015 ON NANOTECHNOLOGY APPLICATION
IN THE SECTORS OF:
MATERIALS, HEALTH & MEDICAL SYSTEMS, ENERGY

All roadmaps reports are under revision of the European Commission, final approval from the EC is pending.

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SYNTHESIS REPORT

Project Partners:

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VDI/VDE (DE)

Istitute of Nanotechnology (UK)

MATIMOP (IL)

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Foreword

The past years have seen a unprecedented growth of R&D activity in the field of nanotechnology propelled by the belief that nanotechnology represents a radically new approach to manufacturing which is bound to revolutionise practically all the industrial sectors and everyday life in this beginning of 21st Century. Knowing how nanotechnology will develop in the coming years and which will be its more relevant applications, will be of considerable value to devise future planning.

Preparing roadmaps about the evolution and future applications of a technology is always difficult and even more so when dealing with an emerging one like nanotechnology. No forecast can reflect all the views of all the experts nor encompass all possible outcomes. At best it can reflect a consensus on most of the views. There is no guarantee that the predictions will materialise, but roadmaps can nevertheless be of great help to better address the efforts and work towards predicted targets thus increasing the chances of success.

The aim of the Nanoroadmap (NRM) Project has been a long term (10 years) forecasting exercise on the application of nanotechnology in the fields of material, health and medical systems, energy with the objective of preparing roadmaps that monitor progress and discuss tendencies which can allow the evaluation of opportunities and problems of nanotechnology in these sectors and act accordingly. Quite many nanotechnology experts participated at this exercise, both from academia and industry, to give a rather comprehensive view of today situation and forecasts. The result has been condensed in 12 roadmaps (4 for each sector) prepared by three of the project partners, each having the responsibility for the roadmapping of a given sector. In particular:

- *Materials* - Willems & van den Wildenberg (W&W);
- *Health and Medical Systems* - VDE/VDI IT;
- *Energy* - The Institute of Nanotechnology (IoN).

The 12 roadmaps have been grouped as possible by the said project partners in three specific sectoral roadmap reports which can be downloaded from www.nanoroadmap.it.

The present document is synthesis of the above reports and all information, data and figures presented in it originate from them.

AIRI/Nanotec IT, Project Co-ordinator
January 2006

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Introduction

Background & Objectives

Nanoroadmap (NRM) is a project co-funded by the European Commisssion (EC) within FP6 whose objective is the preparation of technology roadmaps about nanotechnology application in three different areas:

- Materials
- Health & Medical Systems
- Energy

An International Consortium, consisting of partners coming from eight European countries and Israel, has joined forces to cover the time-frame for technological development in this field up to the year 2015 with the primary objective to provide coherent scenarios that could help the European players to optimise the positive impact of nanotechnology, giving the necessary knowledge on its future development and when technologies and applications will become operational to a higher extent. To avoid that the roadmaps become too general as a consequence of the width of the sectors taken into account, it has been decided to focus on a restricted number of themes (4 for every sector) considered of major relevance (especially for Europe) within the time-horizon considered to produce for each of them a roadmap, for a total of 12.

The European industry, the research organisations (public and private), public bodies within the European countries, the EC, the financial community, are the expected key users of these roadmaps to address R&D strategies and/or plans taking into consideration the impact of nanotechnology. Even though a special focus is put on SMEs, these roadmaps are also meant to be useful for larger corporations. (For additional information on the NRM project initiatives, please refer to www.nanoroadmap.it)

Methodology

A specific feature of the project is its two phases approach. The first one consisting in the collection and analysis of relevant available information about nanotechnology and its applications to assess situation and trends to start from and identify a number of themes representative of nanotechnology application.
The second essentially devoted to the preparation of the roadmaps and the dissemination of information. The latter activity had a relevant role in the project economy and its highlights have been two International NRM Conferences, one in Rome (Italy) at the end of the first phase (4th-5th of November 2004) and one In Cologne (Germany) close the end of the project (8th-10th of November 2005), and 8 National NRM Conferences held in each of the partners countries between the end of October 2005 and the end of November 2005 (details of the events can be found in www.nanoroadmap.it). Comments and feedbacks originated from these events have been incorporated into the roadmaps.

Collection of information and selection of topics to roadmap

To assess current situation and trends of nanotechnology, the project partners set out to collect all available information on the subject from all over the world (national programmes/initiatives, position papers, existing roadmaps, technology and market forecasts, etc.). The survey covered 35 countries (see below) and the results of this survey, together with the themes from which to choose those to roadmap, have been synthesised in three sectoral reports (Materials, by W&W, Health & Medical Systems by VDE/VDI IT, Energy by VTT). (The reports can be downloaded for free on the project web site).

Australia	France	Korea	Slovakia
Austria	Germany	Latvia	Slovenia
Belgium	Greece	Lithuania	Spain
Canada	Hungary	Netherlands	Sweden
China	India	Norway	Switzerland
Czech Republic	Ireland	Poland	Taiwan
Denmark	Israel	Portugal	UK
Estonia	Italy	Russia	USA
Finland	Japan	Singapore	

Countries covered by the NRM survey

The reports, which highlight R&D activities, give indication about current and future markets and applications, identify the leading countries in the sector, have been presented at the 1st NRM International Conference held in Rome (Italy) the 4th – 5th of November 2004 where a preliminary selection of topics to roadmap was also discussed. The definitive choice of the four topics for each sector was made according to selection criteria agreed upon by the consortium partners (such as the degree of innovation, expected technological improvement, relevance of the sectors of possible application, positive impact on human life) and thorough discussions which involved international experts. The final selection was eventually validated in dialogue with the European Commission.

Roadmaps elaboration

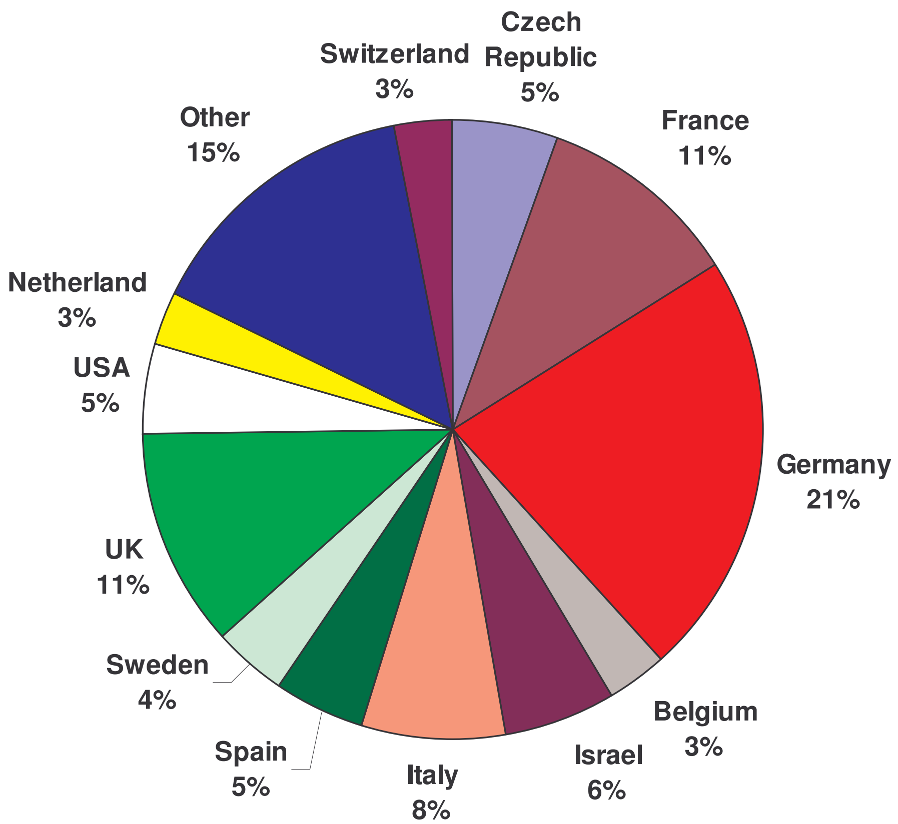
A two cycle Delphi-like approach was used for the roadmap exercise. The methodology has been the same for all the topics and consisted in:

- Selecting top international experts on the field;
- Preparing a dedicated on-line questionnaire to each of the topics to be roadmapped;
- Circulating the questionnaires among the experts and gathering of their responses (1st cycle);
- Preparing a first summary/draft roadmap document based on answers received from the experts and, occasionally, personal interviews with some of them;

- Circulating the document asking for feedback and reflection (2nd cycle);
- Elaborating the final version of the roadmap taking into consideration aspects raised in the 2nd cycle and feedback from the NRM conferences.

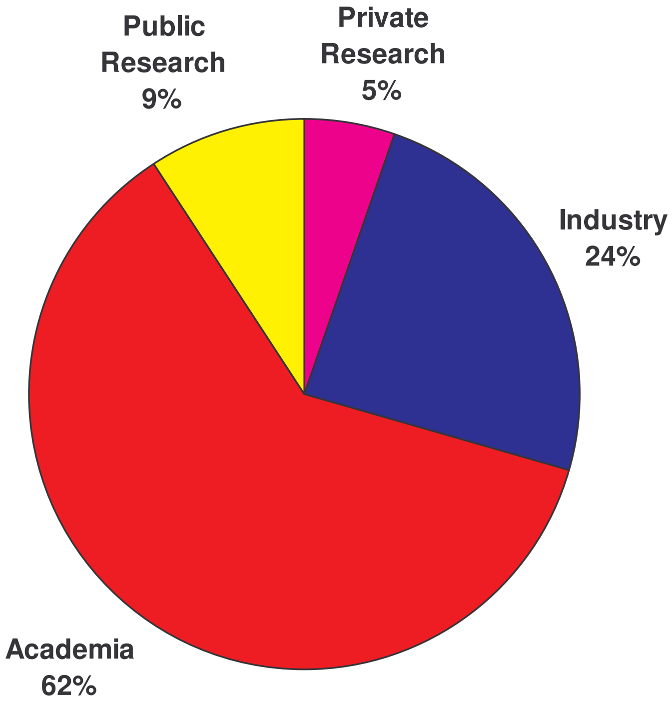
The structure of dedicated questionnaires was simultaneously aimed at being highly selective, covering the topics considered in a sufficiently distinct manner, comparable to a high extend, concise as well as manageable by the experts. Based on the appraisal of the present state of the art room was given for perspective views on future applications and opinions on technical and non-technical barriers and possible means to overcome them.

All partners contributed to the identification of the experts to be part of the Delphi panel and some gave also a strong help to solicit their answers. In the end a total of about 350 experts were contacted and some 65% (230) completed the Delphi exercise. The spectrum of the countries of origin of the experts was very ample (see figure), but Europe, with roughly 80% of the total, had by large the major share.



Experts by country *(Other - below 3% - includes :Austria, Australia, Finland, Ireland, Slovenia, Slovak Republic, Poland, Japan, Portugal, South Africa, Taiwan, Russia, Estonia, Turkey)*

Considering the background, it turns out that academia, with more than 60%, provided the largest number of experts, but industry and private research organisations, which accounted for almost 30% of the total, was also well represented.



Experts by organization type

The roadmaps have been first presented at the 2nd International NRM Conference and the eight National Conferences which have taken place, as said, between the end of October and the end of November 2005.

Structure of the reports

Aim of this report is to give a unified overview of the three sectoral roadmaps reports to give a comprehensive (albeit synthetic) vision of the potentialities of nanotechnology in three very relevant sectors and stimulate communication and cross-fertilization among the different sectors.

Properties, advantages, current and future applications, are presented and analysed before going into the detail of the timeline for applications development in the next 10 years.

Forecast for the next decade are presented in terms of potential applications, giving a qualitative picture of their stage of development (timeline). Challenges, barriers and bottleneck, both technical and economical, are also discussed.

Non-technological aspects (European competitive position, HSE issues, access to infrastructures, survey on the need of more multidisciplinary centres) and recommendations are treated at the end of each of the three sectors.

Throughout the roadmaps and hence in this report, the following definitions have been used to indicate the various stage of development of the considered applications:

Basic R&D phase: applications in this phase have received the interest of one or more researchers in the world. Some applications might still be in early development, while others are tough to develop and need a lot of basic research to be understood. The object of basic R&D is to validate the original hypothesis. Various applications are currently in this phase.

Applied R&D phase: after the hypothesis is validated, research typically (but not necessarily) moves from pure research labs to more commercial labs and companies. Applied R&D will eventually result in a proof of concept, a successful demonstration model. While the production issues might not have been solved yet, a successful prototype/model has been validated.

Product R&D phase (**first applications**): after demonstrator models and prototypes, initial, usually prohibitively expensive, small numbers of products may be produced. If these prove successful, companies will seek to enhance production to gain market share. Generally at some point, demand increases sufficiently to offset the investment needed to start production. This phase ends at a point when feasibility is proven and production starts.

Production level and incremental research (**mainstream applications**): the final development phase, when production has reached significant numbers and research focuses on incrementally improving the products.

1. MATERIALS ROADMAPS

Background

Nanomaterials have been described as "*novel materials whose size of elemental structure has been engineered at the nanometre scale*". At this dimension materials exhibit greatly improved or totally new behaviours and properties and because of this it is possible the creation of materials and devices with enhanced or completely new characteristics and functionalities.

To call them "nanomaterials" at least one of their dimensions must be in the range between 0.1-100nm (nanometres). This means, clusters of atoms or grains less than 100 nm in size, fibres less than 100nm in diameters and films with thickness less than 100 nm.

The forecasts about the future development (and market) of nanotechnology, indicate nanomaterials as the largest segment of all, being their applications ubiquitous, and research in this sector has a pivotal role in the activity in nanotechnology.

12 topics, even not being completely homogenous in terms of scope or classification, which adequately represent the field of nanomaterials have been identified. The roadmap exercise focused on the 4 indicated below.

1) Nanostructured materials
2) Nanoparticles / nanocomposites
3) Nanocapsules
4) Nanoporous materials
5) Nanofibres
6) Fullerenes
7) Nanowires
8) Single-Walled & Multi-Walled (Carbon) Nanotubes
9) Dendrimers
10) Molecular Electrics
11) Quantum Dots
12) Thin Films

1) Nanoporous materials
2) Nanoparticles/nanocomposites
3) Dendrimers
4) Thin Films & coatings

Following are the results of the roadmap exercise.

1.1 Nanoporous materials

1.1.1 Topic description

Nanoporous materials are natural or synthetic, organic or inorganic, hybrid materials, with holes less than 100 nm in diameter (are called mesopores those with a diameter of 2 to 50 nm and macropores those with a 50 to 100 nm diameter). Nanoporous materials can have open (interconnected) or closed pores and amorphous, semi-crystalline or crystalline frameworks. These two characteristics determine the applications a given nanoporous material is suitable for.

Nanoporous materials are usually divided into bulk nanoporous materials and membranes. Examples of materials considered suitable for bulk materials and membranes are carbon, silicon, silicates, polymers, metal oxides, organic/metals, organic/Silicon, while specific for membranes are zeolites or the so called schwartzites. Zeolites are the material with which the experts are most familiar with, followed by ceramics (silica, alumina, zirconia) and polymers.

Nanoporous materials combine the advantages of the porous structure with the physic-chemical-biological functionality of the material itself whose properties can be enhanced or inhibited by the nano scale dimension. The most remarkable characteristics of nanoporous materials, both bulk materials and membranes, are:

- *Increased specific surface area* (together with control over pores' size and distribution this feature enhances adsorption properties and the possibilities for surface chemistry);
- *Improved sieving* (including selectivity);
- *Reduced weight*;
- *Thermal insulation*;
- *Photonic properties* (nanoporous materials can be tailored to exhibit photonic crystals properties).

1.1.2 Nanoporous materials preparation & applications

The nanoporous materials pipeline could include *template preparations*, *synthesis*, *functionalisation* and *final application*. Often some of the steps prior of application are combined or skipped.

1.1.2.1 Template preparation

The production of nanoporous structures with controlled pores' size, morphology and size distribution or crystalline framework usually involves the use of tailored templates which provide the conditions for raw materials' self-assembling in the desired way. When the template is removed the porous material is obtained.

Templates preparation can follow two routes: use of substrates whose pattern and/or structure is reproduced in the nanoporous material (e.g. mesoporous structures for carbon nanoporous materials) or use of colloidal suspension of particle (which may contain surfactants) acting as precursors of the pores and around which the nanoporous materials is formed.

1.1.2.2 Synthesis

A broad range of methods can be used for the synthesis of nanoporous materials, but most of the attention is focused on few of them. In particular:

- *Solution precipitation routes* (incl. sol-gel);
- *Self-assembling*;
- *Liquid crystal routes*.

The solution precipitation routes could be used to produce a wide range of material structures such as nanoporous membranes and aerogels. The fact that the process works at room temperature enables its use in bio-encapsulation related applications. Self-assembling is a bottom up approach and its main advantage is that it doesn't require scaling down the manufacturing tools (as in all top down productions), uses less raw material and produces less wastes. Finally, liquid crystal phases (at high enough concentrations) can replicate their liquid crystalline structures.

1.1.2.3 Functionalisation

The functionalisation step provides nanoporous materials with special characteristics (notably on the pores surface) that couldn't be achieved with the standard processes. Post-treatment processes are also intended to remove solvents and precursors used in the process.

There are two principal approaches for providing the required functionality: post modification (so called grafting method) and direct synthesis (co-condensation of the functional groups). The latter is mostly applied to the sol gel process and basically consists on adding functional groups to the sol gel so they undergo the normal production process. It allows a high load of functional groups though it has a negative impact on the long range order of the mesoporous structure.

1.1.2.4 Applications

In general, nanoporous materials can find application in quite a variety of markets their use spanning from catalysis to membranes for fuel cells or for the chemical/petroleum industry, to gas separation, to medical application.

The timing for these applications to occur could vary rather much. Also market volumes and risk associated to each of these developments might be substantially different, as well as the technical requirements. No clear "winners" emerge from the answers of the experts, although some viewed as more promising than others.

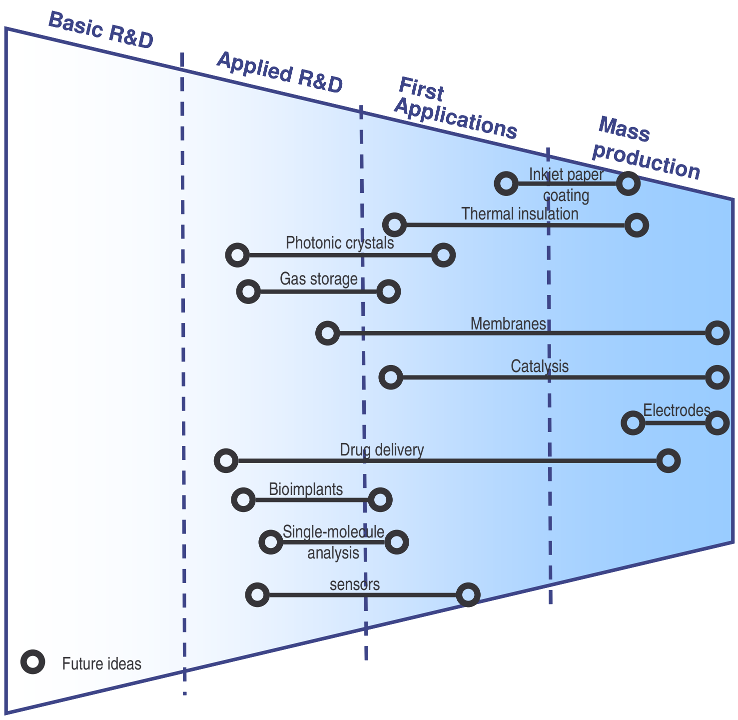
Catalysis seems to offer great opportunities to nanoporous materials and is a field of intense research activity. Some catalytic applications can be enormously important such as, for example, those aimed to make new liquid fuels from various fossil and non-fossil sources, or those that aid production of hydrogen from water. Amongst the other most developed applications, thermal insulating windows are already in the market, although applications combining thermal insulation properties with mechanical properties (e.g. for space applications) are still in their infancy. Gas storage (and in first place hydrogen storage) has also attracted over the last years a lot of attention, but it must be pointed out that nanoporous materials are in this case in competition with other solutions under investigation and this raise the risk of not getting to the market. Other examples of applications include fields as diverse as photonic crystals, electrodes, tissue engineering, bio-implants and sensors.

1.1.3 Timeline for applications development

Although some application of nanoporous materials has already reached the market, such as catalysis, in first place, and then thermal insulation and membranes, according to the experts, the majority of the activity on nanoporous materials is presently still at the basic and/or applied R&D stage. An intense basic research is underway also in the case of the applications most advanced.

The situation shouldn't be much different in 2010 while what is expected in 2015 is illustrated in the figure below which indicate the position of just the fore runners (the tip) of a large field of related applications. Basic research will be important also at that time to support the applications on development and as a source for new ideas.

For some applications foreseen at early first application stage in 2015, such as photonic crystals, there are great expectations.



***Overview of possible nanoporus materials applications at 2015**. (Origin: Material Roadmap)*

1.1.4 Challenges, barriers, bottlenecks

There are several barriers to overcome on the way of the application of nanoporous materials. They are both economical and technical.

Price has been highlighted as one of the main bottlenecks for many of the steps of the nanoporous materials pipeline, from template preparation to material synthesis, to functionalisation. A bottleneck is considered also a certain lack of suitable templates.

The poor understanding of industrial requirements pointed out by the experts is especially worrisome. A large part of the research is devoted, in fact, to get a better understanding of structure-properties relations, which is of course essential, but not much on processes development. This poses the risk that the production processes developed may not align with the industrial requirements. A particular effort must be made to close this gap favouring the contact between academia and industry.

On the scientific/technical side various challenges have been pointed out. Those considered most important are both general and application specific. In particular:

- A better understanding (basic research) on how materials work at a molecular atomic/scale, necessary to improve the ability to tailor made the material characteristics and properties.
- The lack of suitable modelling/simulation and software tools. (This fact is linked to the said insufficient understanding of the structure-properties relationships).
- The availability of suitable raw materials (namely templates) both in quality and price.
- The lack of equipments for meaningful and quick characterisation at nanoscale.
- Development of environmentally friendly materials.
- For membranes related applications: control over pores' characteristics and pores' functionalisation as well as (thermal) stability over time.
- For applications as bulk materials: pores' framework. In many cases pores' collapse after template removal is an issue of crucial importance.

1.2 Nanoparticles/Nanocomposites

1.2.1 Topic description

Nanoparticles are usually referred to as particles with a size up to 100 nm. Below this size the physical properties of the material do not just scale down or up, but change to completely new or greatly improved properties. Even though nanoparticles can be made of a wide range of materials, the most common are metal oxide ceramics, metals, silicates and non-oxide ceramics.

Nanoparticles can present several different morphologies (flakes, spheres, dendritic shapes, etc.). However, metal and metal oxide nanoparticles are typically spherical, while silicate nanoparticles have usually flaky shapes. Nanocomposites are obtained incorporating nanoparticles into a matrix (in this report polymeric) which then show properties influenced/depending from the properties of the nanoparticles.

According to the experts that have participated in the Delphi panel, the most potentially exploitable properties of nanoparticles are related to:

- *High specific surface area* (very high surface to volume ratio);
- *Magnetic and Electric properties* (improved/specific magnetic and electric properties);
- *Optical properties:* (absorption or emission wavelengths can be controlled by size selection, interaction with ligands and external perturbation.);
- *Chemical properties* (enhanced chemical reactivity).

1.2.2 Nanoparticle/nanocomposites preparation & applications

The nanoparticles pipeline could include *production, functionalisation, incorporation into nanocomposites* and *final application*. Not always this linear approach, with sequential independent steps before final application, is followed.

1.2.2.1 Nanoparticles production

Production of nanoparticles can be achieved through various approaches the most common being:

- *Solid state methods* (grinding, milling, mechanical alloying techniques*)*;
- *Vapour methods* (Physical Vapour Deposition – PVD*,* Chemical Vapour Deposition – CVD *;*
- *Chemical synthesis /solution methods* (sol gel, colloidal chemistry);
- *Gas-phase methods* (flame pyrolysis, electro-explosion, laser ablation, plasma synthesis).

According to the experts, chemical approaches are presently the most popular methods for producing nanoparticles.

1.2.2.2 Nanoparticles functionalisation

Once produced (and purified to a satisfactory level) it might be necessary to functionalize nanoparticles to improve or modify their properties and facilitate/enlarge their application. Metallic nanoparticles, for instance, which are highly oxidisable, can be stabilised by surface passivation, while adding chemical functional groups on the surface can be obtained useful hydrophilic or hydrophobic properties or favoured the interaction with a polymeric matrix.

Functionalisation can be achieved with many different methods, but the most commonly used are coating and chemical modification. This step, according to the experts, could add to an increase between 10-50% to the final cost of nanoparticles.

1.2.2.3 Nanocomposites incorporation

The addition of nanoparticles to a polymeric matrix to obtain (nano)composites plays a relevant role in the use of nanoparticles. The nanocomposites so obtained show specific new properties such as improved mechanical, electrical and optical characteristics or better barrier and flame retardant behaviour.

There are several methods for incorporating nanoparticles into the polymer, but the most commons are incorporation by melt compounding or during polymerisation. Functionalisation of the nanoparticles has often a necessary step to improve their incorporation into the polymer matrix.

1.2.2.4 Nanoparticles applications

The potential applications of nanoparticles are almost endless and their use includes fields such as:

- *Engineering*
- *Electronics*
- *Healthcare/medical*
- *Environment*
- *Consumer goods*
- *Energy*

With respect to final applications, bulk structural materials are, according to the experts, by far the largest potential market for nanoparticles. Nanocomposites will contribute substantially to this result.

Improved strength can be of value in countless applications. Nanoclays polymer composites represent so far the most advanced application in this area but they suffer from pricing problem. As a consequence, notwithstanding the reasonably advanced state of development of such composites, commercialisation has till now only be seen in limited areas (e.g. high-wear components in cars) and a threat for the future of this material is the great potential of composites based on carbon nanotubes.

A request of nanoparticles for composites, albeit with lower volumes, is likely to be driven also by the demand for non-structural composites having special properties as for example gas barrier or flame resistance.

Reasonably high nanoparticle volumes can be expected in areas such that of abrasives, currently the largest segment of application of this sort, cosmetics, pesticides, environmental remediation, catalysts, lubricants, sealants, adhesives, coatings.

The conclusion is that a wide variety of niche applications could generate significant demand and therefore, the most profitable scenario for nanoparticle-based products considers also relatively low-volume, specialised materials. This fact makes the field open to small operators such as start-ups and SMEs.

Many nanoparticulate formulations used as catalysts derive their value, notably increased catalytic activity, simply from the increased surface area. However, nanotechnology can go beyond that for some materials only exhibit catalytic activity when have nano dimensions, which open up a new range of applications or alternative reaction pathways.

Coatings obtained by using nanoparticles deserve a special mention as a class of significant current and near-future applications. With these coatings peculiar characteristics can be imparted to the surface which go from scratch resistance to optical properties (ex. modulated transparency or reflectance), self-cleaning (a deeper insight of this topic can be found in the following specific roadmap on *Thin films & coatings)*.

The medical sector is also expected to provide a remarkable opportunity for nanoparticles and examples include molecular imaging, alternative drug delivery, targeted delivery of drugs. (The field is thoroughly investigated in the *Health & Medical Systems Roadmap*)

Nanoparticles for these applications are generally required to be within a certain specific size range, often need a specific finer nanostructure and frequently need to be functionalised.

Raw materials production costs are generally of little relevance in medical applications since the quantities used are generally very small and the capability achieved, often totally novel, outstrip the costs. Nanoparticles are simply a component in a system that is dependent on many factors for success.

1.2.3 Timeline for applications development

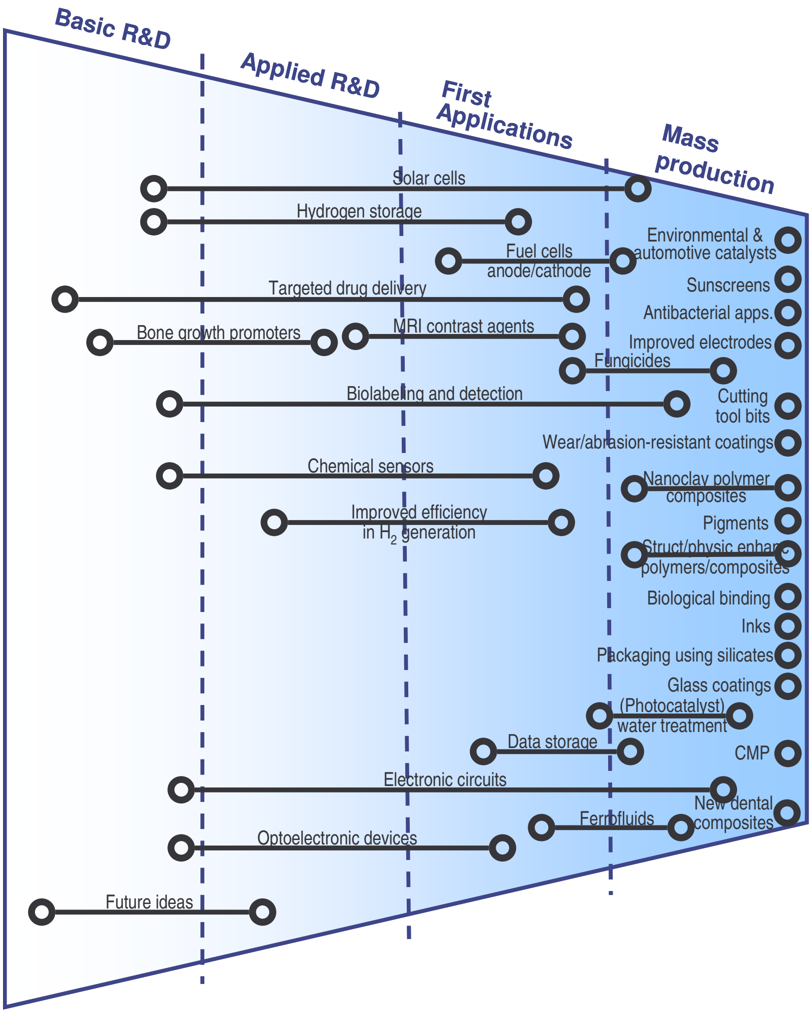
According to the experts, the principal fields in terms of (high) revenues for nanoparticles applications are, in perspective, those related to the (opto)electronics/magnetic sector, followed by biotech/pharma, energy/catalysis, engineering/ mechanical.

At present many of these applications are generally still at the basic/applied R&D stage and many hurdles have to be overcome before reaching the market. In 2015, some applications could be at first commercial stage.

A significant number of applications of nanoparticles are already on the market. These include slurries to polish Si wafers (CMP), several pigments (as sunscreen), coatings (for scratch resistance), catalysts, biomarkers.

Nanoparticles reinforcement of polymers is presently attracting a strong attention and automotive and packaging industries have been identified as the major growth markets for plastic nanocomposites.

The already mentioned nanoclays polymer composites are already at the stage of first application and by 2010 they could be in mass production (bar the mentioned competition from other nanomaterials). By 2010 also other applications could by in mass production. Among them there can be cited glass coatings, automotive catalysts, composites for packaging, antibacterial foams. In 2015 the number of possible applications in mass production could be quite high and the following figure illustrates the projected situation of possible nanoparticles applications at that date.



Overview of possible nanoparticle/nanocomposites applications at 2015 *(Origin: Material Roadmaps)*

1.2.4 Challenges, barriers, bottlenecks

With respect to major technical barriers associated with nanoparticles, the accurate control of size and morphology is a principal issue for many applications. In some cases adequate functionalisation also represents a barrier. In both cases scaling these capabilities to reliable, quality-controlled, industrial production, represents a challenge.

Improvement of the production yield, which would help to lower products cost is also considered a challenge and yields could be increased by preventing agglomeration and unwanted chemical reactions on highly reactive particles during the production process.

Since size and size distribution are important for the activity of nanoparticles, understanding the optimum ranges of these characteristics is an essential first step.

Development of on-line instrumentation capable of measuring size and size distribution at nano scale would be beneficial in overcoming this barrier and would improve product consistency and performance.

Other barriers and bottlenecks can be on the way of nanoparticles utilisation.

For certain health-related applications as, for example, drug delivery, they will also face the lengthy, arduous approval process by regulatory bodies (e.g. FDA) which will surely lengthen the time to market, but which could also forbid altogether certain application. Also in other field, such as for cosmetic applications, there could be in the future stricter regulations to pass before commercialisation.

An early assessment of the health and environmental impact of the nanoparticles and of the processes used to prepare them, must be a priority. Legislation in this sector is expected to be quite severe.

1.3 Dendrimers

1.3.1 Topic description

A dendrimer is generally described as a macromolecule which is characterized by its highly branched 3D structure that provides a high degree of surface functionality and versatility. Its structure is always built around a central multi-functional *core molecule*, with *branches* and *end-groups*. Dendrimers can be made out of virtually anything that can branch (metal atoms, organometallic groups, or purely organic materials) and can have a variety of functionalities depending on what they are built of and how. They are synthesised in a stepwise manner through a hierarchical self-assembly process in which additional iterations lead to higher-generation dendrimers. The principal difference between a dendrimer and other hyperbranched polymers is that each of the monomer units in the dendrimer has at least one functional unit that allows further branching.

Practically all the experts contacted (90%) agreed in considering dendrimers as the most versatile, compositionally and structurally controlled synthetic nanoscale building block available today. Their most remarkable properties include:

- *polyvalency* (easy surface functionalisation with different ligands);
- *defined architecture, size and shape control*;
- *monodispersity* (consistency of shape and form between molecules);
- *loading capacity*,
- *biocompatibility / low toxicity* (some);
- *transfection properties* (transporting genetic material into cell interiors).

Exploiting these properties, singularly or in combination, make it possible to use dendrimers in a very large variety of fields.

1.3.2 Dendrimers preparation & applications

The dendrimers pipeline includes three distinct steps (*synthesis, functionalisation, application*) which are strictly interconnected. Following their synthesis, dendrimers are in fact typically functionalised in accordance to the features the researcher wants them to display and the application they are intended for.

1.3.2.1 Preparation and functionalisation

There are different methods to synthesise dendrimers. However two, the so called divergent and convergent synthesis, are the most common and extended ones. In general, it could be said that the convergent approach is appropriate for obtaining small dendrimers while the divergent approach is good for obtaining the large ones. For both the main technical challenges are found in establishing process control methods, high purity and well defined products, specifications and final product analytical methods.

Dendrimers can be (relatively easily) functionalised to display features that are useful for the application they are intended for and the functionalisation methods most commonly used are filling the dendrimer cavities, modification of the dendrimer core and modification of the dendrimer surface. According to the experts contacted, modification of the dendrimers surface is the method they mostly use, after which dendrimers may display a novel range of functionalities such as:

- *polyvalency*
- *flexible charge and solubility properties*
- *flexible binding properties*
- *transfection*

1.3.2.2 Dendrimers application

As anticipated above, the spectrum of the fields of potential applications of dendrimers is very ample and it includes sectors such as:

- *health care/medical* (for ex. diagnostics or targeted drug delivery);
- *engineering* (for ex. carbon fibres coatings and ultra thin films or polymers/plastics additives);
- *consumer/industrial goods* (for ex. inkjet inks-printing toners or dyes and paints);
- *environment* (for ex. decontamination agents);
- *electronics/optoelectonics* (for ex. data storage or OLEDs);
- *energy* (for ex. catalysts).

Inkjet inks and toners, dyes and paints, industrial adhesives, additives for composites, are presently the applications of dendrimers most advanced on the way of commercialisation, although it must be said that they have to confront themselves with other competing alternatives.

This treat is common in almost all the areas in which dendrimers show promise. Nevertheless dendrimers are poated high in the agenda and, according to the experts, the areas where dendrimers will most likely achieve sustained commercial success will be those where the application strongly depends on the unique characteristics of dendrimers, like polivalency.

The field of medical applications is presently at an earlier stage but it is considered the one offering the greatest potential (and with less competing technologies) for the use of dendrimers. In this field also the high costs associated with them can be considered a less limiting factor.

Applications of dendrimers as transfection reagents, MRI contrast agents, diagnostics and analysis are at or close to application stage.

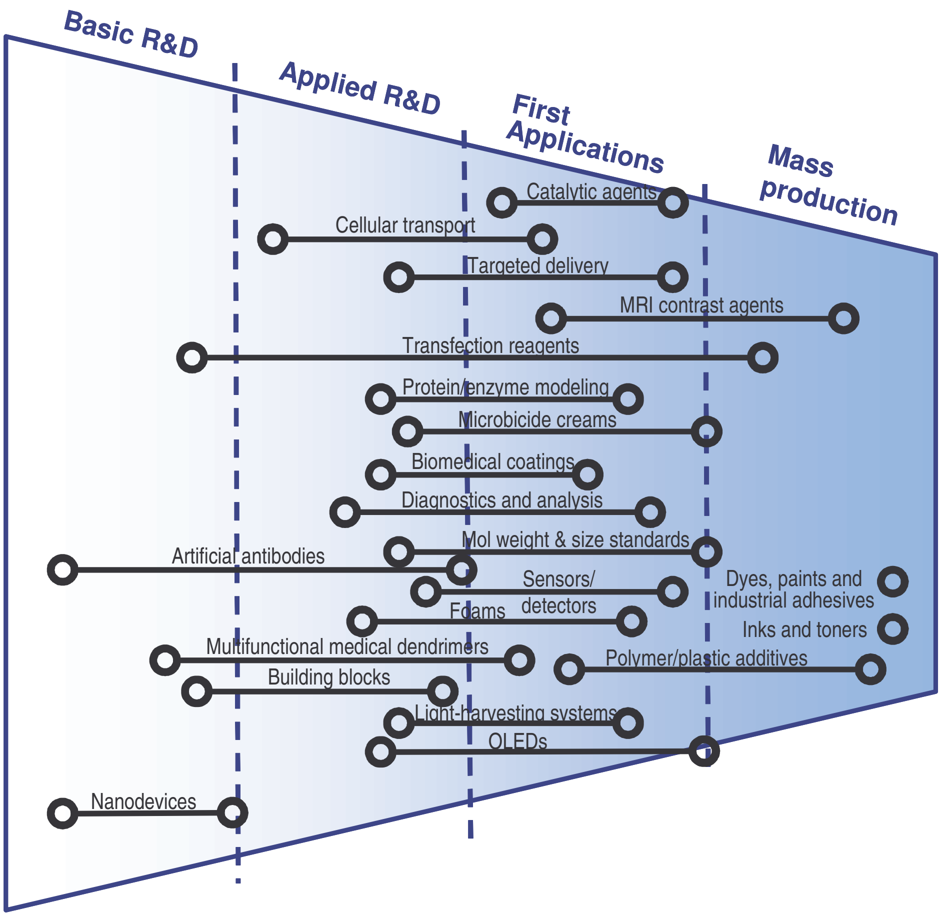
Investigations of dendrimers as carriers for imaging contrast agents (an expected early medical application of dendrimers) have demonstrated excellent potential. A key advantage in this application is their ability to bind to multiple contrast agents and bind them tightly, which improves contrast. Dendrimer-based reagents are also being researched in order to create a more efficient and versatile delivery agent with low toxicity levels.

Other biomedical applications, such as targeted drug delivery or cellular transport, are also actively investigated. The high level of control over the dendrimers architecture makes them ideal carriers for the delivery of active pharmaceutical ingredients.

Electronics is another area of possible application of dendrimers which is attracting strong attention and very good work is being done also for the development of light-harvesting or light-emitting systems. Research is under way to exploit the tree-dimensional shape of dendrimers in generating porosity in highly-insulating dielectric materials.

1.3.3 Timeline for applications development

Except for MRI contrast agents, transfection agents, inkjet inks-printing toners, dyes/paints, additives for polymers/plastics, the majority of possible applications of dendrimers are currently in the basic and/or applied R&D phases and it will be practically so also in 2010. At that date (2010), inkjet inks-printing toners, dyes/paints, additives for polymers/plastics, should be, according to the experts, well in mass production. By 2015 also MRI contrast agents and transfection agents should be at this stage, as indicated by the following figure which gives an overall picture of the situation at 2015 of some of the possible application of dendrimers actively investigated.



***Overview of possible dendrimers applications at 2015**. (Origin: Material Roadmap)*

Certain specific electronic and medical applications, however, might take even further time to develop. In particular, in the case of health-related applications, this might be due also to the need to carry on lengthy clinical trials and approval procedures.

1.3.4 Challenges, barriers, bottlenecks

According to the experts, price and process/reproducibility control are indicated among the most important challenges in the production and commercialisation of dendrimer related products although it must be said that price is likely to be not a major barrier when considering medical applications where the quantities involved are low and the unique capabilities/properties of dendrimers offer a premium.

Nevertheless, if dendrimers are to be competitive against other materials/technologies in a number of applications, substantial efforts should be made to reduce dendrimers price. Through research, for novel synthesis methods, or through the reduction of steps in the existing ones (combined convergent/divergent synthesis approaches could achieve this goal).
Up-scaling of production (which not necessarily means very large quantities) is also a key field of research. It may be an appropriate time for the production of dendrimers for many applications to come out of the labs and move to the pilot plants.

Although in terms of reproducibility, dendrimers do far better than many other nanomaterials, this aspect is another major barrier. In particular, for medical, electronic or optical applications.

In these fields it is key to work with high purity and well-defined products with reproducible properties. Regular and consistent nanoscale organisation are vitally important and this area of research would greatly benefit from improved modelling capabilities and of the theoretical knowledge that feeds them.

Another barrier or, better, a bottleneck, for the applications of dendrimers in the medical sector is the necessity to overcome lengthy clinical trials before getting approval for commercialisation and this step can delay the time to market.

Finally, in evaluating application/technology of dendrimers, the patent situation must carefully be revised. The world of dendrimers is controlled by fundamental patents in the hands of a few groups and individuals. These patents could block the way for some applications and recently there have been established patents agreements among some of the patents holders to avoid this type of obstacle.

1.4 Thin film & coatings

1.4.1 Topic description

Thin films and coatings are material structures resulting from the deposition of one or more layers of material onto a surface. In the case of this report, the thickness of the thin film considered is below 100 nm. Materials used include, amongst others, Si films (crystalline or amorphous), Fe_3O_4 (magnetite) and other metals and metal-oxides, diamond, metal sulfides, polymers.

The main advantage of thin films (or any other coating for that matter) is that the properties of the materials deposited can be acquired by the surface. The substrate and the thin film become a material system where each of them provides the required functionality. In general, nanotechnology provide the tools for better controlling three key parameters of the surface deposit: chemical composition (and crystalline nano structure), thickness and topography.

The possibility of transferring specific or otherwise expensive properties to a nanometer-sized coating makes the list of potential applications almost endless with an impact in almost every industrial sector.

According to the experts of the Delphi panel, the most remarkable properties associated which could be associated to thin films and coatings are:

- *Chemical* (ex. chemical reactivity, chemical inertness/barrier);
- *Optical* (ex. light trapping, transmission, opaqueness);
- *Mechanical* (ex. wear/abrasion resistance, dry lubrication);
- *Electrical* (ex. energy potentials, conductivity/ insulation):
- *Magnetic* (ex. data storage);
- *Thermal* (ex. thermal barriers).

1.4.2 Thin films & coating preparation and application

The thin films pipeline includes *production and deposition* onto a surface, *post-treatment* and *patterning, application*. Thin films production, however, does not always follows this linear approach and for many applications, such as in the semiconductors industry, only the first 2 steps are normally implemented.

1.4.2.1 Thin films & coating production and deposition

The list of the methods for the production and deposition of thin films and coatings is quite long and includes:

- *Chemical Vapour Deposition (CVD);*
- *Physical Vapour Deposition (PVD);*

- *Sol gel ;*
- *Electrodeposition/electroplating ;*
- *Spin coating ;*
- *Spray coating ;*
- *Self – assembly;*
- *Positional assembly.*

These processes can work rather differently. There are, in fact, processes which provide the raw materials (i.e. sol gel) subsequently applied using another technique (i.e. spin-coating) and there are processes, like PVD or CVD, which provide both the chemical composition as well as the application of the thin film.

Substrate pre-treatment (i.e. cleaning, etching) is not indispensable for many of the materials considered (e.g. carbon, metals), however, it can be essential in some cases to make possible the adhesion of the thin film. The highly sophisticated clean rooms used in the semiconductor industry, which deals with some of these processes, show how critical this step can be.

1.4.2.2 Thin films & coating post treatments

Post-treatment processes are sometimes required for consolidating the thin film obtained by other (wet) methods like sol-gel or spin coating. In other cases, thin film post-treatment is used as a subsequent production step (e.g. thermal oxidation to obtain SiO_2 thin film or UV curing to improve thin film adhesion by creating cross-links). In general, many post-treatment processes considered have been used for many years by many industries and include in first place:

- *Annealing;*
- *Thermal oxidation;*
- *UV curing.*

Within the experts contacted, annealing is at present the most used post-treatment process.

1.4.2.3 Patterning methods

Patterning methods are intended to provide the coated substrate with the required pattern and they involve techniques for both removing or adding material. They have been widely used for the applications in the semiconductors industry and many other applications could benefit from them. Among the methods which are more familiar within the expert contacted are:

- *Optical lithography;*
- *Plasma etching;*
- *Nanoimprint lithography (NIL);*
- *Electron beam nanolithography;*
- *Ion beam lithography*
- *Ion milling;*
- *DipPen nanolithography;*
- *Inkjet.*

Optical lithography (the main mass-production patterning method used by the semiconductor industry) and plasma etching are the two methods the experts said they are most familiar with.

1.4.2.4 Applications

With regard to thin films and coatings applications, some are already in the market (e.g. thermal insulating or self-cleaning windows) or on their way out of R&D labs to first application (e.g. chips or M-RAM). However, for many other (e.g. planar waveguides for optical components integration), several years will be required to get to a similar stage of development (and investment).

In general, most of thin film applications are linked to developments in the semiconductors industry such as:

- *Thin films transistors (TFT);*
- *Large area displays (LCD, OLED);*
- *NEMS/MEMS;*
- *Planar waveguides;*
- *Magnetic RAM;*

Any development in each one of these fields could be beneficially shared with the others. The above sectors are foreseen to be the most relevant applications for the future in terms of commercial impact and enabling new applications, nevertheless the fact that these applications are related to capital-intensive sectors, could slow down the adoption of the new technologies developed and limit the role of SMEs.

One area that is less capital intensive (and therefore more attractive for SMEs) is the creation of cheap, flexible, disposable electronic devices. The key application most quoted at the moment is RFID tags, but also smart packaging represents another very promising application.

Besides the semiconductor-related applications, coatings providing certain mechanical or other specific functional properties is also a sector which is attracting strong interest and research activity.

The success depends essentially on the achievement of a favourable cost to benefit ratio. The possibilities are the most diverse, In particular:

- Glass coatings could become ubiquitous (non-scratch coatings in spectacles are already widespread, for example);

- Coatings could significantly improve the quality of certain treatments in the medical sector. For example significantly extend the life of implants;

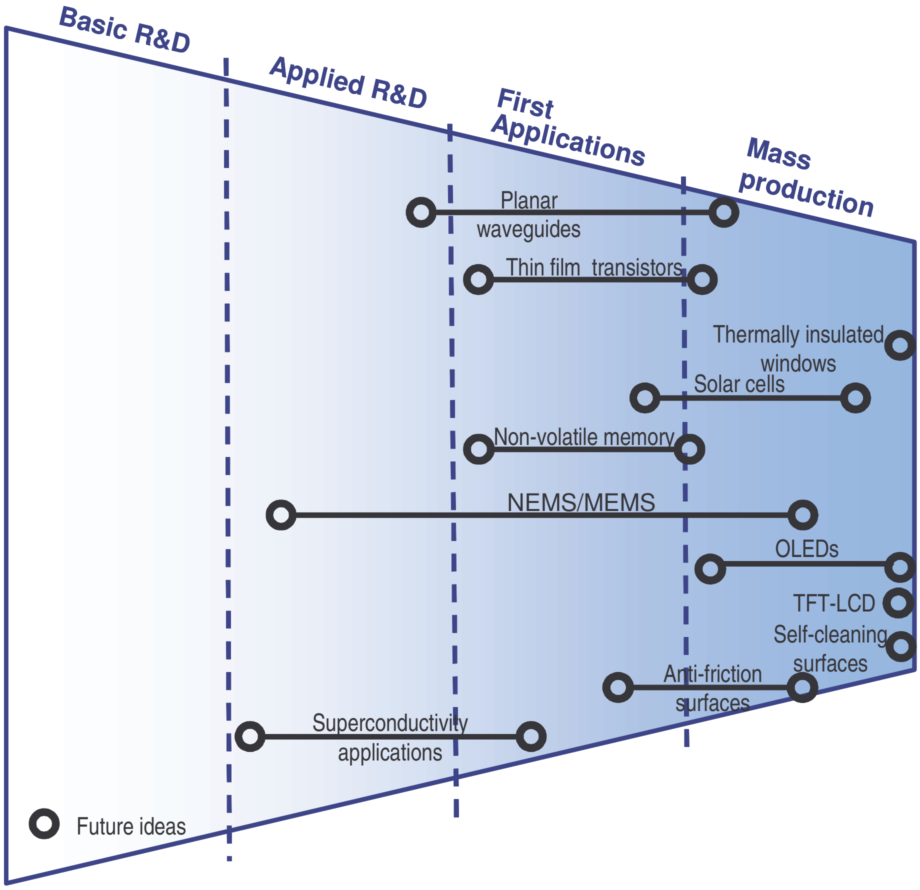
- Low-friction or wear resistance coatings have almost endless applications which can span from engine parts to mechanical or drilling tools;

- Solar cells can be an area where nano-thin films could have a strong impact, and large returns (see *Energy Roadmap*).

Some more futuristic applications can be envisioned beyond 2015, with the quality and cost of thin films being just one part of the challenge. For example, wall-sized displays, doubling as lighting and also interactive, are featured in many visions of the future.

1.4.3 Timeline for applications development

Although many of the possible applications of thin films & coatings are at the moment at the basic and applied R&D stage, some, as the mentioned thermally insulated and self cleaning glasses for windows, are already in the market, albeit at the stage of first commercial application. By 2010 these products should be, according to the experts, in mass production while others, such as for example planar wave guide, OLEDs, TFT or solar cells, should be at first application and/or R&D stages. The situation expected at 2015, according to the experts of the Delphi panel, is illustrated in the following figure.



Overview of thin films&coatings at 2015 *(Origin: Material Roadmap)*

For applications such as thermally insulated windows or self cleaning surfaces, a significant market already exist, so the forecast seems quite safe. In other cases, such as TFT or NEMS/MEMS, which could mean big growth, the market has yet to materialise and this add an uncertainty to the projection.

1.4.4 Challenges, barriers, bottlenecks

According to the experts, several are the obstacles standing on the way of applications of nano thin films & coatings.

Two of the most important are certainly price and production volumes.

But various other barriers also exist even if thin films & coatings have been around since quite some time. Nanotechnology is posing new opportunities , but also new challenges.

In general, most coating processes are intrinsically difficult to control (spray coating, PVD, spin coating etc.) and if really precise control is needed there are probably limits to what can be obtained with these techniques. These drawbacks refer both to the size and (3D) shape of the substrates to be coated. Self-assembling techniques which intrinsically starts at the molecular level can help to overcome these problems and the expanding of this approach may allow the replacements of less precise processes in some application.

Lack of a full understanding of the adhesion mechanisms between substrate and the coating as well as among multi-layers is another barrier together with the understanding of the basic principles behind tribology at the nano scale.

Bottlenecks are considered also the lack of equipment for meaningful and quick characterisation (crucial in industrial environments) and the lack of understanding of industrial requirements, essential if thin films are to be integrated into material systems and their production processes. For capital-intensive industries this may hinder the deployment of new technologies.

Many of the experts have also highlighted the need for improved computer modelling as critical.

For applications where large volumes are required or in medium-tech applications for which the technologies have been demonstrated (i.e. PVD, CVD) R&D efforts should focus more toward production up scaling.

On the contrary, in more high-tech applications such as OLEDs or NEMS/MEMS, a strong commitment on basic and applied research is advocated to better understand behaviour and properties at the nano scale.

1.5 Non-technological aspects conclusions & recommendations

1.5.1 European competitive position

The potential economic and societal contribution of nanomaterial make them an important factor which Europe has to reckon with in today worldwide competition.

According to the opinion of the experts participating at the Delphi panel, the European competitive position in the 4 areas considered in this report is overall generally good in academia, while there are differences when looking at the industrial camp. A more detailed description is given below.

In nanoporus material most of the experts consider European academia good or even excellent, although it must be said that some 20% qualified EU science as poor. On the industrial side the scene is dominated by big large global companies which at the moment are considered the key players, mainly referring to typical large industrial sectors, like electronics, chemical and pharmaceutical products (catalysis is the current largest application).

In the case of nanoparticles, academic research is perceived as of good quality while the situation in industry varies considerably depending on the type of organisation. Big industry is the best positioned (in particular for mass markets of these products) and also some medium size companies contribute to this perception. Innovative SMEs, including some start-ups, are also well positioned, but traditional SMEs get a low rating, with more than 45% of the experts defining their position as poor.

In the field of dendrimers, where also academic research is rated of good quality, only the big industry, which can count in large international companies, is considered in a satisfactory position by over 80% of the experts.
Both traditional and innovative SMEs and start-ups, on the contrary, are considered, by more than 40% of the experts to be in a poor position. From a EU RTD policy point of view, this diagnosis leads to a clear suggestion to focus RTD policy instruments above all on improving the link between excellence in academia with industrial applications and competitiveness. Industrialization could be considered as the key missing ingredient in EU dendrimer research and development.

With regard to thin films & coatings the relative position of the European research is considered good by almost 60% of the experts, excellent by 14% and satisfactory by another 14%. Industry, both large and SMEs, is also well placed, but there is a fierce world wide competition, especially in applications related to semiconductors. Countries such as Taiwan and South Korea are heavily investing in this area together with, of course, USA and Japan. Europe may need to focalise in some specific field to reach the critical mass required for global competition.

1.5.2 Health, Safety and Environmental (HSE) issues

Preparation, handling and use of nanomaterials put to the front the need for a strong attention at the possible risks for the health and the environment associated with these actions. Most part of the experts consider absolutely important to undertake early studies and research on HSE issues to reduce at a minimum the potential hazards possibly arising from preparation and use of nanomaterials.

Production and handling of nanoparticles is attracting at the moment the greatest concerns. All the experts agree that special equipments and/or facilities, as well as handling guidelines, should be adopted in order to protect researchers and workers dealing with nanoparticles and particular attention must be devoted to the disposal and treatment of the large quantities of waste foreseen which would contain nanoparticles in a free state capable of interfering with human and animal life and the environment. The timely assessment of human health and environmental impact is considered a priority. The increasing of applications which bring nanoparticles in direct contact with the skin (cosmetics), or for medical use, add to the concern and ask for a close scrutiny also in this direction.

For nanoporous materials, experts suggest to take particular care of the recovery /recycling of either the solvents or structure directing agents and also in thin films, environmental concern can arise namely from the utilisation of different solvents, as is case of two well established methods such as sol gel or the electrodeposition.

Dendrimers are considered to be less bound to present unexpected HSE hazards since they are likely to be developed by companies with good experience of bringing novel chemicals (as dendrimers are) to market and their synthesis lends itself to established methods of risk evaluation and should be covered by existing safety legislation for chemicals.

1.5.3 Conclusion and recommendations

Nanomaterials represent a tremendous opportunity for practically all the industrial sectors for they can make it possible to introduce new products which can revitalise existing industries or create entirely new business able to generate new opportunities for employment and economic growth.

With reference at the 4 topics roadmapped the European situation is, as just said above, rather good from the scientific point of view and also at industrial level there are positions of strength, but to make real the applications envisaged specific actions and initiatives must be taken over the next ten years and beyond.

The issues (and priorities) to consider are often the same for the 4 themes. In particular:

Reduction of production costs is a need pointed out by the experts for all the 4 fields considered and so is the up-scaling of the relevant production processes, in first place for nanoporous materials, nanoparticles and dendrimers, to have processes in line with the industrial requirements. Particular attention must be placed on production yields of specific active sizes and size distribution.

Many would be the consequence of an effective process up-scaling:

- A reduction in production costs;
- An increased reproducibility between batches, which will help to meet strict standards of most demanding application fields;
- Improvement of production volume/throughput.

The market of these nanomaterials is going to be large. However, the wide spectrum of possible applications envisaged, referring to very different markets, makes it difficult to estimate with a reasonable accuracy the dimension of the market.

Characterization methods, on line instrumentation for process monitoring and control, metrology are areas which also demand a strong commitment since they will benefit both research and production activities.

Fundamental research for understanding structure-property-processing relationship at the molecular level, and also discovering and designing new molecular complexes - effectively the discipline of molecular engineering - is surely needed to assist in improving many new process or designing new materials (especially in conjunction with self-assembly).

Computer modelling and simulation is another vital tool to support research and applications.

Access to suitable infrastructures/equipments to favour knowledge sharing is considered essential. Most of the experts stated that they have an adequate access to infrastructures/equipments required to perform typical nanotechnology-related activities, including both own & external facilities. Nevertheless, the great majority of them considered essential for taking nanotechnology-related products to the final market, access to newly created multidisciplinary centres with advanced knowledge on materials development and their own pilot production facilities.

Both industry and academia will take advantage from them and the existence of pilot production plants in (or nearby) would be an important factor to help production up-scaling, facilitate technology transfer, provide skills and training.

SMEs could greatly benefits from these structures and this would not only contribute to the identification (and potential exploitation) of the appropriate nanotech-related opportunities by such companies, but will also help the consolidation of a firm nanotechnology base in Europe, given the number and relevance of such companies in the European economy.

The role for start-ups and SMEs in general will most likely be:

- As niche suppliers to end markets.
- As technology providers (new approaches) to major corporations (intellectual property strategies are vital here).
- As intermediate suppliers for incorporation into the final product.

Finally, a proactive approach to timely tackle HSE issues related to nanomaterials and an open communication on this matter are deemed mandatory to gain the public consensus, necessary for the acceptance and success of nanotechnology related products.

2. HEALTH AND MEDICAL SYSTEMS ROADMAPS

Background

The impact that nanotechnology will have on the medical sector is expected to be impressive for it can lead to improved medical devices, more specific acting drugs, better diagnostic systems.

Due to quantum phenomena occurring at the scale of single atoms and small molecules, nanotechnology will bring up new materials with improved and novel physical, chemical and biological properties.

Specifically functionalised nanomaterials will form the interface between living matter and the technical devices. The discovery of new markers for the detection of certain diseases as well as molecular and metabolic disorders will accelerate. A quantum leap is expected to occur in medical therapies and diagnostics, being the latter shifted from the currently pursued symptom based approach to an early state diagnostics.

By means of nanotechnology, in combination with other basic sciences and technologies, it will be possible to better understand and map the complex cellular machinery and to diagnose and treat diseases by the aid of appropriate drugs.

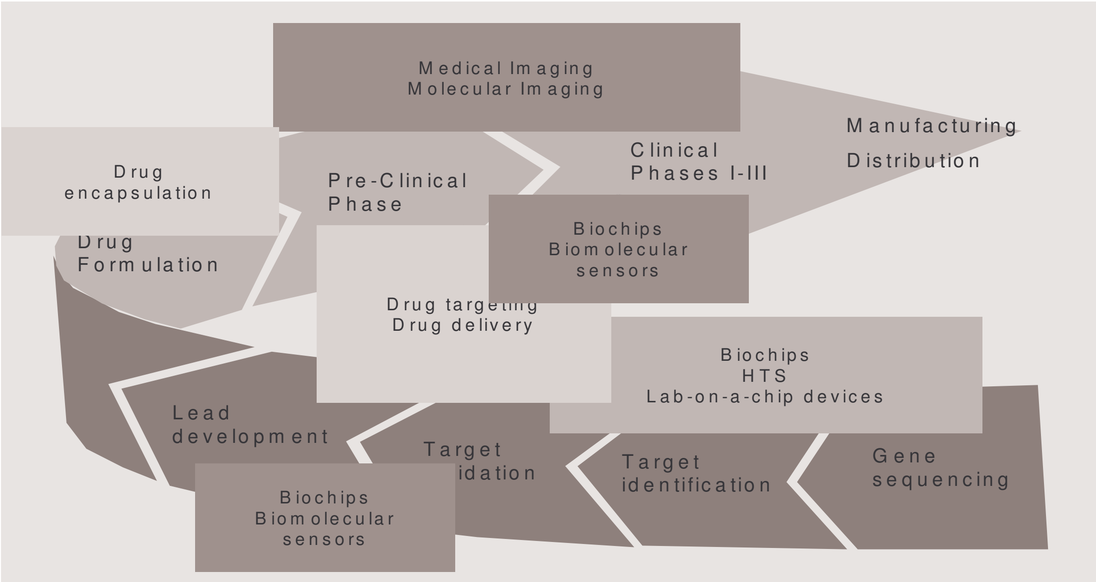
Eleven topics have been identified as representative of the application of nanotechnology in the biomedical sector and the roadmap exercise has been focused on the 4 indicated at right below.

1) Tissue Engineering/ Regenerative Medicine
2) Bio Nano Structures
3) Drug Encapsulation / Drug Delivery / Drug Targeting
4) Molecular Imaging
5) Biophotonics
6) Biocompatible implants
7) Biomimetic Membranes
8) Biomolecular sensors
9) Biochips/ High Throughput Screening
10) Lab-on-a-chip
11) Functional Molecules: Switches, pumps, means of transportation

→

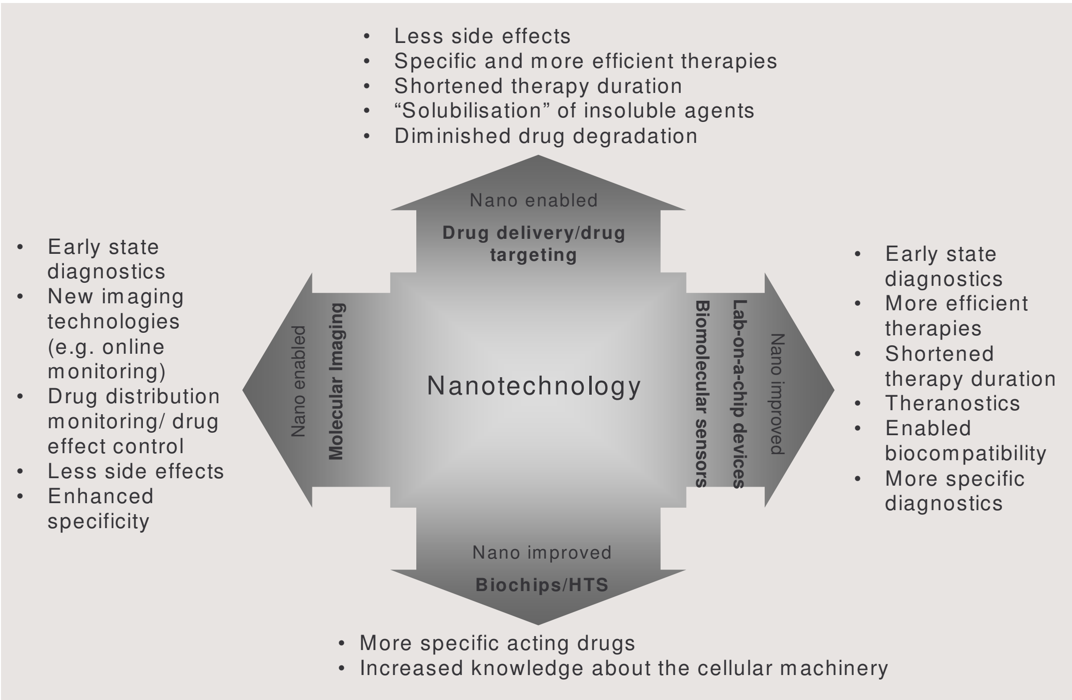
1) Drug encapsulation/ Drug delivery/ Drug targeting
2) Molecular Imaging/ Biophotonics/ Medical Imaging
3) Biochips/ High Throughput Screening/ Lab-on-a-chip devices
4) Biomolecular Sensors

The focusing process was application oriented and although the chosen narrow areas are considered to be distinct they do interface to a varying degrees with each other. They must be regarded in a holistic way, as visualised by the following figure, which illustrates how the topics are involved and can affect the pharmaceutical value chain.



Origin: Health and Medical Systems Roadmaps

As illustrated in the following figure, the impact that nanotechnology might have in the four application areas may either be enabling or improving and this justify the expectations pinned on them.



Origin: Health and Medical Systems Roadmaps

2.1 Drug encapsulation / Drug delivery / Drug targeting

2.1.1 Topic description

The demand for more specific and efficient drugs and diagnostic agents for the cure and the detection of a large spectrum of serious diseases is raising in order to improve the quality and the effectiveness of the medical treatments.

Research into the rational delivery and targeting of therapeutic and diagnostic agents is at the forefront and nanotechnology will be increasingly used to create systems which can allow to deliver drugs to distinct area within the body, using targeted, specifically interacting drugs which could be released in a controlled and well-dosed manner, so providing a better and more effective way of administration.

The progress in nanomedicine which combine molecular tools and a deepened understanding of the cellular architectures and biochemical processes will thus give reason to hope for more effectively acting drugs and less side-effects and/or adverse drug reaction.

All participants of the Delphi panel were of the opinion that nanotechnology will provide pharmaceuticals with suitable properties which cannot be achieved utilizing other concepts. Therapeutics, diagnostics and theranostics will benefit from nano-related drug encapsulation/drug delivery/drug targeting.

2.1.2 Properties and applications

Nanoparticles to be used as drugs or carriers of drugs will play one of the most important roles in future drug based therapy, due to their unique biological, chemical and physical properties which derive from their nanoscale dimensions.

Nanoparticles are usually defined as particles with a size up to 100 nm, but the medical sector builds an exception because even particles, being bigger than 100 nm can have biological relevance. In drug delivery, particles up to 400 nm and more show characteristics that will revolutionise the drug sector.

Nevertheless is below 100 nm that biological, chemical and physical properties and behaviour are unique. Particles smaller than 50 nanometres, for instance, can enter most cells very well, while those smaller than 20 nanometres can move through the walls of blood vessels. As a result, drugs at nanoscale can easily interact with molecules on both the cell surface and within the cell, often in ways that do not alter the behaviour of those molecules.

The spectrum of nanoparticles employed in nanomedicine is quite wide. Are used in fact:

- *inorganic nanoparticles* (i.e.gold, silicates, magnetic nanoparticles);
- *polymer nanoparticles* (i.e. polysaccaides, polylactic acid, polyacrilates) ;
- *polymers therapeutics* (i.e. polymers drugs, polymer micelles) ;
- *nano-crystals* (i.e. nano-sized milled drugs);
- lyposomes.

In spite of this variety, however, about 81% of the participating experts stated that investigation of further nanoparticles is needed because the range of currently available nanoparticles is insufficient to fulfil all presently needed therapeutic functions.

Drugs and pharmaceuticals can either be encapsulated into nanoparticles or prepared as a nanoparticle themselves and there are range of applications which can be related to the function/functionalisation of the nanoparticles.

The nanoparticle/s surface can in fact be treated with coating, layers or linkers to provide or improve their characteristics as for example biocompatibility, targeting and detection properties, shape recognition, biological interaction.

When used as “nanoscale ferries” nanoparticles can offer many advantages:

- “Insoluble” drugs become in a way “soluble”, being transported by the "ferries";
- The drugs can be protected against decomposition during transport to its destination;
- Nanoparticles may accumulate actively or passively within target tissues and release the transported drugs in a controlled time-dose profile;
- They can be used as contrast agents for diagnostic systems.

The increase of the surface/volume ratio due to the nanoscale size of pharmaceuticals may results in an enhanced therapeutic activity while the magnetic/thermal behaviour of certain types of nanoparticles, combined with other specific properties, open a wider spectrum of therapeutic methods.

Nanotechnology is regarded as a general enabling platform to drug delivery, giving advantages at many levels. It can, in fact, offer new ways to deliver pharmaceuticals, it can be supportive in individualized therapies, making them more efficient thus leading to a decrease in effective drug dosage and a reduced drug toxicity which enhances patient acceptability and lowers health-care costs.

The discovery of further in vivo cellular uptake targets for drugs will improve existing therapy approaches, inter alia DNA delivery vehicles for gene therapy and the delivery of therapeutic proteins to their site of action.

Nanotechnology, in combination with other technologies and tools such as microtechnologies, combinatorial chemistry, computational biology, computer-aided drug design, data mining, and data processing will lead also to the discovery and development of new personalised drugs. Within the next 10 – 15 years the number of designed drugs, based on a person’s genotype is expected to raise.

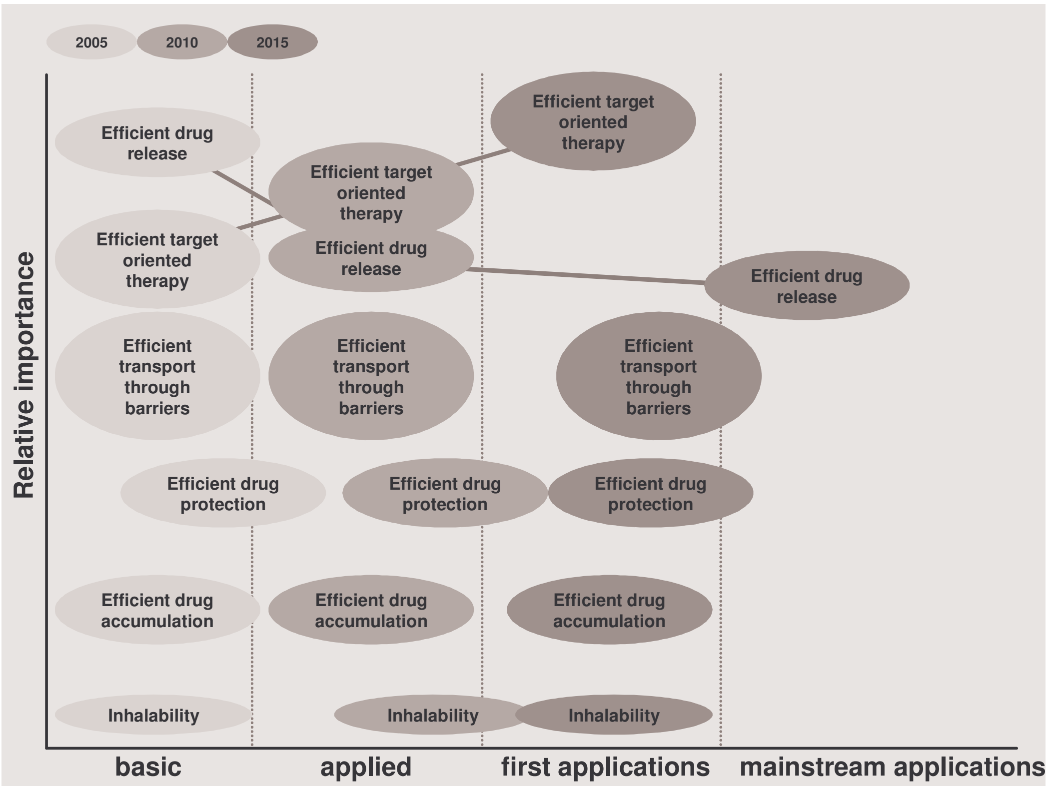
2.1.3 Time line for applications development

Drug delivery and targeted drug delivery are expected to be the applications which gain most from nanotechnology in the biomedical sector within the next decade and beyond with a slightly different time scale for main stream applications.

As is shown in the figure below, which indicates the various steps of development of nanoparticles based therapies within the next decade, only efficient drug release is supposed to be in 2015 well established and in mainstream applications.

Efficient target oriented therapy, which of course implies the effective drug release and which would certainly be of much more advantage, in 2015 will likely be still at the stage of first (commercial) application.

The inhalability of certain drugs, which would enlarge the range of pharmaceutical forms, also improved by nanotechnology, was stated to be of lower importance because this is considered to be not one of the properties which makes the difference of nanobased therapies when compared to the conventional ones.



***Average technology stage of specific technical challenges of drug delivery**/..(Origin: Health & Medical System Roadmap)*

The number of diseases which could benefit from nanoparticles based therapies is large, but the experts of the Delphi panel emphasised (almost 70 % of them) that cancer therapy should be the field where this approach will be most effective allowing a large variety of ways for treatment.

2.1.4 Challenges, barriers, bottlenecks

Despite the huge expectation on nanoparticles for medical applications, the technology is still at its early stage and there are many problems to solve or circumvent to attain the results expected within the 10 years horizon considered.

The interaction between nanoparticles and intracorporeal targets need still to be intensively explored to better understand the complex biological basic principles of the impact of the specific applications.

According to the experts, one of the most important challenges is linked to the assessment of the possible (harmful) side effects of available nanoparticles (e.g. general cell toxicity), to be sure that these effects do not could prevail over the therapeutic effects of the drug.

Scalability of nanoparticle production is another challenge, especially in manufacturing three-dimensional nanostructures. Manufacturing standards for nanomaterials and components are yet to evolve and there is also an urgent need for a standardisation for nanoparticles characterisation and analysis that can provide chemical (molecular) characterisation at the nanoscale.

Insufficient targeting and unsatisfactory drug release, together with efficient transport through barriers, efficient drug protection and accumulation, are also considered fields in which research is mostly needed.

The development of a broader scale of nanomaterials with specific properties is certainly a trend within the next decade.

According to most of the experts there is a need for the investigation for further nanoparticles because, as anticipated, the range of existing nanoparticles is not considered satisfactory.

According to the experts, an important economical barrier (and a bottleneck) is also clinical evaluation, especially for pharmaceutical applications. The lengthy approval processes means that both health benefits for the patients and the economic return for companies take longer to materialise than in other sectors.

Research in this field is expensive and risky therefore the drugs developed must be kind of “blockbusters” to regain the invested money for the long and complex development of the drug.

On the contrary, also with the help of nanotechnology, the future medicine is going toward more individualised treatments and therefore smaller will be the relevant target group and market, thus reducing the economic return. Public support of the early stages of the research is therefore fundamental and an attempt to somehow simplify the approval processes (without of course any loss of quality and security of the process itself) should be considered.

2.2 Molecular Imaging / Biophotonics / Medical Imaging

2.2.1 Topic description

Medical imaging has increasingly gained room in the past years as a fundamental in vivo diagnostic tool. There are various imaging technologies for the detection, characterization and diagnosis of diseases (X-rays, Magnetic Resonance Imaging - MRI, nuclear and ultrasonic imaging) and there is a strong demand in technology advancement to improve speed, efficiency and functionality of the instrumentation, lower costs and hence, increase accessibility, expand their use for therapeutic applications.

Advances in cell biology, biochemical agents, instrumentation, computer analysis, have in recent years offered the tools to improve the efficiency and reliability of detection systems.

Molecular imaging and biophotonics are two emerging technologies to support this effort and nanotechnology will be critical in supplying the above mentioned demands.

2.2.2 Properties and applications

Molecular imaging refers to the visual representation, characterization, and quantification of biological processes at the cellular and sub-cellular levels within intact living organisms.

In molecular imaging, molecular probes which possesses a targeting unit (e.g. special receptors, ligands or peptides) are used as the source of image contrast. When the molecular marker is specific of a certain disease the contrast medium accumulates within the sick tissue.

This approach, which is being developed for the above said imaging diagnostic procedures, promises new insights into disease processes in the laboratory, but since the said imaging modalities are applicable clinically, they can be used to translate this knowledge into new diagnostics and clinical treatments, with a change in emphasis from a non-specific to a specific approach.

A real paradigm shift for imaging which can now provide the potential for the understanding of integrative biology, earlier detection and characterization of diseases, clinical treatment.

This is reflected in the experts estimations which stress that more emphasis in the future has to be placed on individualisation of therapies, followed by specific acting pharmaceuticals and theranostics, which means targeted integration of diagnostics and therapeutics.

Two thirds of the experts involved consider nanotechnology to be unique in providing a variety of highly sensitive and specific imaging agents with the properties needed for their more efficient use and consider the ability of the nanoparticles to be specifically guided to a target as a winning property in the pharmaceutical sector respect to existing or alternative technologies

Biophotonics uses light beams and other forms of energy and it can be described as the science of generating and using light (photons) to image, detect and manipulate biological materials. One example is the Photo Dynamic Therapy (PDT) in which drugs (photosensitizing agents) and particular types of light are used to delete pathogenic tissues in a specific manner. Nanotechnology, by facilitating the targeting of the photosensitizers, is going to promote biophotonics and consequently PDT.

However, since the light needed to activate most photosensitizers presently available cannot penetrate much into the tissues, to exploit this possibility to the full, there is the need for photosensitizers that are activated by light which penetrate deeper. In crucial fields, such as anti-cancer therapy, the availability of these photosensitizers will expand very much the potentialities of biophotonics.

There are no clear preferences when indicating the most appropriate types of nanoparticles for Molecular Imaging. The experts participating in the Delphi exercise named in first place dendrimers, linear polymers, filled phospholipids, microbubbles, but also a variety of “other” materials. These, were nano-caged compounds, multimeric (or unimeric) micellular assemblies as well as inorganic nanoparticles with tuneable physical properties.

The contrast enhancing media mainly used by the participating experts are gadolinium and superparamagnetic iron oxides. Perfluorocarbon nanoparticles, quantum dots, chromophore-coupled target molecules as well as near infrared fluorophores, radionuclides and proteins are more rarely used for this purpose.

A very interesting (and promising) example of a modular platform are quantum dots, they allow for efficient multicolour imaging of biological samples and should be especially useful for fluorescence imaging in living tissues, where signals can be obscured by scattering and competing intrinsic emissions. Coated with biocompatible layers or proteins they may not be recognised by living cells as toxic. Quantum dots could possibly be used to repair damaged neural pathways or to deliver drugs by activating the dots with light.

Molecular imaging permits both the temporal and the spatial biodistribution of a molecular probe and related biological processes to be determined in a more meaningful manner throughout an intact living subject. For example, in drug discovery processes it offers the advantage of being able to study and monitor the location and possibly the action of a potential drug in an animal model, before phenotypic changes become obvious (thanks to temporal and spatial control) and afterwards start to move into human studies.

By improving the possibilities of medical imaging and moving deeper and deeper into the molecular level, it is likely that preclinical trials prior to human studies can be accelerated.

2.2.3 Time line for applications development

Molecular imaging/biophotonics will profoundly change the medical sector by enabling within the next decade novel methods of diagnosis and the treatment of various diseases. Nanoparticles will serve as modular platforms, from which a wide variety of highly sensitive and specific targeting agents can be created which could lead to revolutionary changes in sector of great social importance such as chronic pain, dementia, depression, diabetes, autoimmune diseases, neurodegenerative diseases. However, cancer, in particular, and then vascular/ cardiovascular diseases and viral infections, are considered to be those better placed to benefit from these technologies.

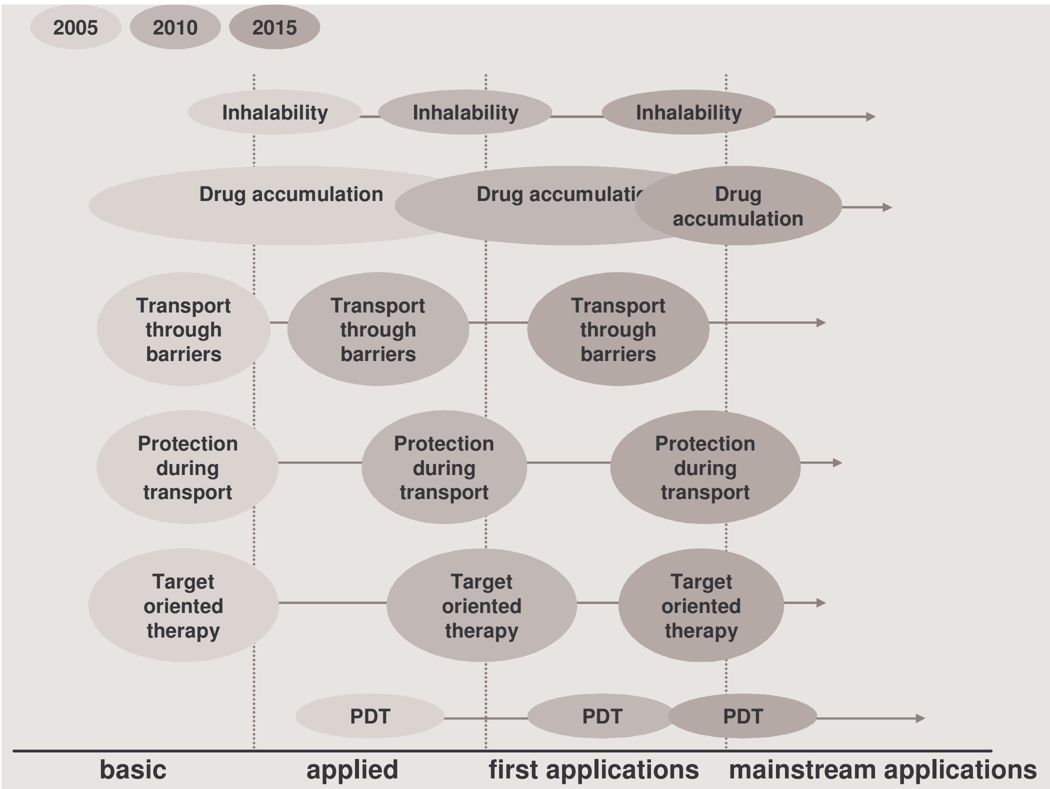
According to the experts within the Delphi panel, the targeting of nanoparticles and hence, molecular imaging and biophotonics in 2015 will be sufficiently investigated so that the Photo Dynamic Therapy (PDT), which is regarded to be at present in an applied R&D status, at that date should enter mainstream application.

Directed transport through biological barriers is expected to be, at that time, at the stage of first applications. Since transport happens more or less passively, obviously much more effort has to be put in improved active and well targeted transport processes.

Inhalability, which can enlarges the usage of available pharmaceutical forms (but where nanotechnology has lower edge respect to other approaches) in 2015 will be slightly behind.

Drug accumulation and drug protection during transport are posing a though problem, but in 2015 this feature will be close to mainstream application together with target oriented therapy, as also indicated in the previous roadmap.

The following diagram reflects the relative importance of nanoparticle properties in molecular imaging and photonic and their evolution from now to 2015 to give an integrated view of the various stages of development.



***Average technology stage of nanoparticles in the medical imaging sector**. (Origin: Health & Medical Systems Roadmap)*

2.2.4 Challenges, barriers, bottlenecks

Nanotechnology applied to molecular imaging is a relatively young technology which means that there are a lot of challenges to meet within the next decade.

Some have already been indicated in the previous paragraph, but the list is longer.

The development of non-invasive, high resolution in vivo imaging technologies is posing several challenges. Nanotechnology in molecular imaging within living subjects, in fact, offers more theoretical and practical problems than in vitro or cell culture detection. The probes need, In first place, to be biocompatible, but additional barriers have to be overcome to have a correct delivery. Special in vivo amplification strategies need to be developed.

The sensitivity of measuring and thus of imaging has to be enhanced to detect minimal concentrations (in the pico - to nanomolecular range) and specific acting probes, transporting drugs and contrast enhancing media have to be developed.

Both, a bottleneck and a challenge, has been indicated by the experts the possible negative side effects of available nanoparticles (e.g. general cell toxic effects) which is followed by the lack of suitable nanoparticles, to solve existing contrast media distribution problems, and that of suitable imaging agents.

Low profitability of molecular imaging and subsequent therapy due to expensive and extended R&D is also considered a problem to overcame while other important economical challenges are considered the need of shortened production processes and more simplified approval procedures.

Existing regulations, in fact, demand a totally new production permissions also if known and well characterised basic components (i.e. nanoparticles, used as contrast media) are functionalised.

This means that the whole process, including every single step, has to run a long and time-consuming approval process, even if manufacturing doesn't change up to the functionalisation step. The European Medicines Evaluation Agency (EMEA) has been asked to simplify approval processes.

2.3 Biochips / High-throughput screening / Lab-on-a-chip devices

2.3.1 Topic description

Biochips, as broadly defined, are a technology platform that consists of the miniaturization of a variety of biological substrates and their deposition onto computer chip-like substrates for automated, high throughput analysis. Their preparation relays both on traditional techniques of microlithography and new microarraying (spotting and *in situ* synthesis) technologies.

Up to now, microarray technology has been most valued in the basic research arena as a technique to generate hypothesis. Studies using microarrays have served to advance the understanding of disease processes and to accelerate knowledge gains about fundamental biochemical processes. With the evolving of the knowledge, these technologies will become an essential tool for clinical medicine for diagnostics of a large spectrum of diseases, offering reproducibility, low cost and speed.

They also promise to open new areas for screening in drug development. Examples of this application represent already actual sales of products and this sector is expected to have a very significant business future.

Nanotechnology will lead to improved biochip devices, such as lab-on-a-chip devices with built-in nano-optical, mechanical and electronic intelligence, capable of performing reactions, separation and detection on a single platform.

The use of nanotechnology will enable totally new production processes with integrated bottom-up assembly of structures at a molecular level to realize highly miniaturised diagnostic systems.

2.3.2 Properties and applications

Most of the presently used systems in biomedical research cannot be classified as nanobiotechnological devices since they neither have a nanoscale structure nor is nanotechnology applied in their detection systems. However, there are several approaches to improve present chip platforms or to supplement distinct functions via nanotechnology.

Nanotechnology is expected to be critical in improving biochips technology, offering novel ways to design and create biochip architectures, to coat surfaces, and produce building blocks for small devices as well as nanoscale optics to allow the study of individual and collective properties of luminescent particles (e.g. molecules, quantum particles). The advantages offered by nanotechnology when compared to existing or alternative technologies will be lower costs, improved device performance and reliability, extreme miniaturisation.

Other advantages include the ability to enhance sensitivity, improve equipment compatibility, reduce energy consumption and allow reactions, detections and identifications not otherwise available.

New nanomaterials, among them programmable adaptive protein-based materials, will form the base for new forms of sensitive measurements of very small amounts of important molecules, such as neurotransmitters, carbohydrates, pollutants, or proteins.

Thin films, layers and surfaces, followed by biopolymers and nanoparticles have been indicated by the experts to be the nanomaterials mostly used in their devices while dendrimers, carbon nanotubes, nanocomposites, nanoporous materials as well as nano-sized electrode structures, are applied to a lesser extent.

The great majority of the experts (two-thirds) indicated that the future demand in this sector will ask for more emphasis in implantable biosensors, and the individualisation of therapies. Both implies a maturation and improvement of existing biochip devices to become biocompatible, more precise, more reliable.

Future medicine will need to be more predictive. Besides the deepened knowledge about the complex cellular processes this could imply genetic testing of individuals to forecast a genetic susceptibility to future diseases.

Nanotechnology is expected to offer the solution to these problems and the tremendous variety of biochips, which derives also from the wide range of possible detection methods such as, for example, field effect transistors, microelectromechanical systems (MEMS), optical or thermal devices/methods, radio labelling or mass spectrometry, will expand the range of applications.

2.3.3 Time line for applications development

Diagnostic systems, together with drug delivery, are considered by the experts of the Delphi Panel to be the main applications of nanotechnology in the medical sector within the next decade and biochips/high-throughput screening/lab-on-a-chip devices will be at the forefront.

The fields in which nanotechnologically improved biochips can play an important role within the next 10 years are many and diverse. Among them are:

- Gene identification, gene-sequencing
- Identification of suitable drug candidates
- Basic research
- Choice of suitable therapies/doses
- Point-of-Care diagnostics
- Medical diagnostic
- Predictive medicine
- Toxicology screening
- Food production /food safety
- Theranostics

According to the experts estimations there are three mainstream applications which should emerge in the next ten years:

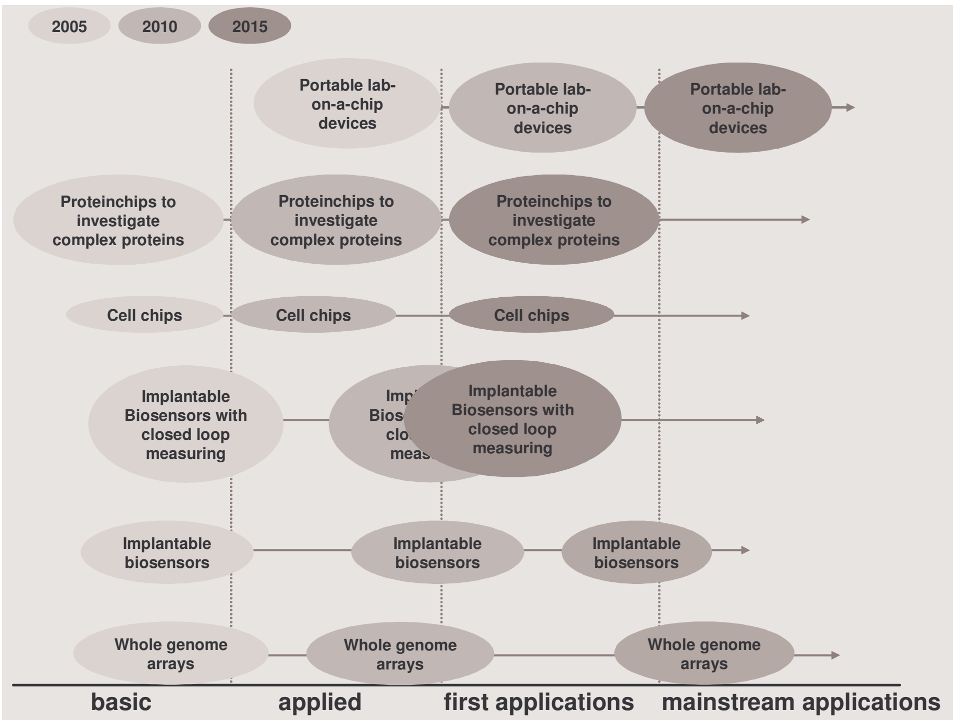
- Sophisticated portable lab-on-a-chip devices;
- Implantable biosensors;
- Cheap whole genome arrays.

The figure below illustrate the expected timeline for the above applications. It indicates that the development of portable lab-on-a-chip devices is expected to proceed in a linear manner, the progression in implantable sensors and whole genome arrays is supposed to take discontinuous courses.

Portable lab-on-a-chip devices should be in first commercial application by 2010 and main stream application in 2015. Non invasive devices are considered much more attractive than the invasive ones since they can simplify maintenance and avoid contact with body fluids. Non invasive measurement devices, however, need highly sensitive sensors and nanotechnology can help in this direction.

Implantable biosensors should enter mainstream applications by 2015 while protein chips to investigate complex proteins and cell chips are supposed to be at that date one step behind and to be still at the stage of first application.

The fact that whole genome arrays are expected to be in 2015 mainstream application assumes that there is a market for these devices. Presently, due to reproducibility and standardisation problems as well as high costs, they are predominantly used for research.



Average technology stage of specific technical challenges in the biochip sector *(Origin: Health and Medical Systems Roadmap).*

2.3.4 Challenges, barriers, bottlenecks

Nanotechnology related biochips is still at its early stage and there are numerous problems and challenges still to overcome.

A very important one is cost. Biochips, in fact, began as high-end, expensive products, aimed exclusively at genetic research and pharmaceutical development while the medical practice demands for cheaper manufacture costs and increased throughput to reach the commercial standards as well as chips with broader applications.

Standardisation of the assays themselves and of the ancillary instrumentation is also key, together with accuracy and reliability. This is particularly important when genetic diagnostic applications are at stake and important clinical decisions are to be based on the interpretation of gene chip readouts.

Sample handling and delivery as well as the interfacing of the nanosensor with the macroworld is also a crucial bottleneck to overcome.

In implantable biochips, biocompatibility, the stability of biomolecules which are linked to the sensors and thus the lifetime of such an implant, are high in the list and suitable solutions must be found.

As far as regards cell-based biochips the realization of cell compatible surfaces and of tools for cell manipulation an characterization are challenges that may be overcome thanks to nanotechnology.

2.4 Biomolecular sensors

2.4.1 Topic description

There is an urgent need to develop rapid, simple, cost-effective and more specific medical devices, capable of performing screening of multiple medical diseases simultaneously and monitor infectious pathogens.

This require new sensors, with improved biocampatibiliy and sensitivity, to monitor in vivo processes within living cells leading to new information on the inner workings of the entire cell which enables early medical diagnosis of diseases, more individualized therapies and improved theranostic.

Biosensors are increasingly seen as medically desirable for the control and effective treatment of a range of chronic conditions. Easing the patient experience, improving the functionality and reducing the cost of these devices is critical to assure their widespread success.

Nanotechnology, which allows to operate at the scale of atoms and molecules may have a dramatic impact on sensor design and capabilities.

The combination of nanotechnology, biology, microtechnology and advanced materials will offer, in fact, new devices which will be able to detect and manipulate atoms and molecules. The small size of these sensors will lead to reduced weight, low power requirements, greater sensitivity and thus, to a totally new medical diagnosis at the cellular/ molecular level.

2.4.2 Properties and applications

Biosensors are highly integrated analytical devices, incorporating a biological or bio-mimetic sensing element (receptor or recognition system), a signal converter or transducer and an amplifier. In a way they act like noses by specifically detecting certain molecules with recognition units that are based on biological components. The integration of a biochemical recognition element and a transducer is the main aspect which distinguish biosensors from other bioanalytical configurations.

Two basic sensor types can be distinguished, termed after the respective recognition reaction: affinity sensors and catalytic sensors.

Affinity sensors are based on the specific bonding capacity of biological molecules and subsequent modifications of electron densities, light absorption, layer thickness, surface stress or refraction index can be detected by the appropriate methodology. Catalytic biosensors, on the other hand, are based on the molecular recognition of substrates by biocatalysts and their subsequent conversion into products which are detected via an enzyme electrode.

Biosensors must have stringent features such as high specificity, stability over a large number of assays and minimal probe pre-treatment. For invasive use, the probe must be tiny and biocompatible, have no toxic or antigenic effects and be steriliseable.

All the experts involved predict nanotechnology to be unique in providing biomolecular sensors with the properties which are needed for their more efficient use. Like in biochips, nanostructuring will offer, for example, novel ways to structure and coat surfaces to provide them with several new functions.

The potential to tailor nanomaterials with desired mechanical, electrical, magnetic or optical properties will enlarge the possibilities of application, could have a positive environmental impact and lead to cost-reduced processes. Nanotechnology will enable the realization of highly integrated, complex biosystem devices, useful for combined diagnosis and therapy (theranostics).

The possible abolition of a necessary internal calibration, due to an enhanced sensitivity and an improved accuracy and precision, will involve the development of faster, cheaper and smaller biomolecular sensors.

The experts indicated thin films and nanoparticles as the materials (nanotechnology) they mostly use in their devices, followed by biopolymers, carbon nanotubes, nanoporous materials and molecular imaging. Dendrimers, nanocomposites and polymeric nanogels result applied to a lesser degree.

The main advantage of thin films is that they can exhibit a large variety of properties (optical, mechanic, magnetic, chemical, electrical, thermal) which can allows a great flexibility in their use and application. A similar flexibility is offered also by nanoparticles.

Advanced biosensors are increasingly seen as desirable for the control and effective treatment of a range of diseases which mirrors the indications of the experts pointing to the raising demand for predictive medicine, need for implantable biosensors, individualisation of therapies, closed loop control systems, theranostics.

The experts ranking of the impact of nanotechnologically improved biosensors in the diagnostic and therapeutic sector, select a range of applications for which an high or medium impact is forecasted at 2015. In vitro and in vivo diagnostics looks as the application of choice.

For in vitro diagnostics the impact of biomolecular sensors is expected to derive from miniaturisation and new, highly sensitive and selective biosensor arrays, which could be integrated as multiple components in single, manageable devices to be used in clinical laboratories and home self-diagnostics (point of care diagnostics).

Nanobased biosensors are expected to find their way also in food production to improve quality control in production processes and hence food chain management as well as consumer protection, providing confidence in the products quality.

2.4.3 Time line for applications development

Thanks to biomolecular sensor integrated in portable lab-on-a-chip devices, advanced tools for self-diagnosis (e.g. low-cost blood screening tests) for faster and more specific clinical diagnostic will be available, while implantable biosensor will increase knowledge about the cellular machinery and the capability to monitor and prevent diseases.

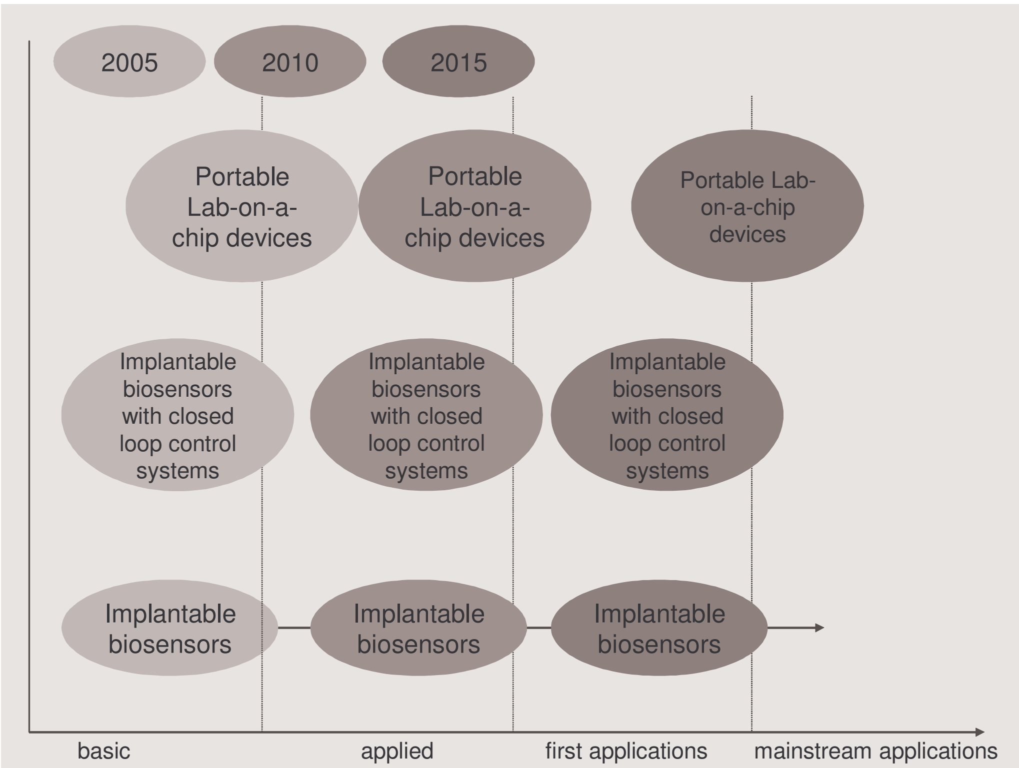
As indicated in the figure below portable lab-on-a-chip devices, implantable biosensors and implantable biosensors with closed loop control are at present at the basic/applied research stage.

In 2010 the above applications are expected to have moved in, or close to, first commercial application, but according to the experts, in 2015, only portable lab-on-a-chip devices are predicted to be in the mainstream application stage.

Implantable biosensors and implantable biosensors with closed loop systems are stated to lag in 2015 a little behind.

This result partly differs from the indication given in biochips (see previous chapter 4), in which sophisticated portable lab-on-a-chip devices and implantable biosensors were predicted to be firmly established as mainstream applications.

The differences among the fields could explain these differences, but it could just indicate that time to market, based on the technical evolution is hardly to predict.



***Average technology stage of specific technical challenges in the biochip sector**.*
(Origin :Health and Medical Systems Roadmap)

2.4.4 Challenges, barriers, bottlenecks

The barriers on the way of biochips development are both of technological and economic character (often linked together) and the research must aim to overcome them.

Biomolecular sensors are still novel products with high production costs, combined with relatively low volumes and limited market penetration. The reduction of production costs is considered a prerequisite to enlarge their use and nanotechnology, which promises to have a dramatic impact in improving sensor design and capabilities, is expected to be able to lower their price too.

Technological challenges and bottlenecks refer to various aspects of biomolecular sensors features, preparation and use.

Stability of bio components over a large number of assays, for instance, is still an issue for applications other than glucose monitoring, but a major problem is also in the interaction of biorecognition layers with biological environment on a molecular level. The development of biorecognition layers with minimum non-specific adsorption of biological molecules is a prerequisite for the detection in biological media and the application in medical diagnostic. Thus, technologies for a controlled preparation of biorecognition layers, for the design of sensor architectures at nano scale, are necessary.

Other important barriers are the immobilisation and compartmentalisation of different biomolecules and cofactors/coenzymes, to allow for manageable devices with multiplex detection, new functionalized nano-bio interface to increase sensitivity and selectivity, the integration of processing and telecomunication systems into the sensors to manage sensors data and improve diagnostic and theranostics.

Scarcity (lack) of suitable nanoparticles and their biocompatibility as well as homogeneity and specificity of thin films are also considered bottlenecks to clear.

Essential is considered by the experts the availability of analytical methods that can provide chemical (molecular) characterisation and standardisation at the nano scale.

Concerns over the collection and use of the vast amount of data that could be compiled may also be a restraining factor to the wide-spread adoption of sensors in health care. Data protection schemes are, however, already in place to overcome these reservations.

2.5 Non technological aspects conclusions & recommendations

2.5.1 European competitive position

According to the opinion of the experts participating at the Delphi panel, the European competitive position in the above 4 areas is mixed.

The scientific side is the best placed being, in fact, rated generally good, sometimes excellent in all the 4 areas, while some differences exist when looking at the industrial camp. Across the 4 areas, as well as when comparing big industry and SMEs.

In more detail the situation is the following.

Big companies are generally considered by the experts in good or even excellent position and to have a good international standard on three of the areas. Only in the field of biomolecular sensors they seem to be less competitive. When considering SMEs it turns out that:

- Start-up companies mostly get a rating from good to satisfactory, with a slight move to excellent. Traditional SME's get a similar rating, although in the case of drug delivery and biochips, about 20% of experts consider their position poor;

- Innovative SME's are generally considered in a good or even excellent position by the majority of experts.

2.5.2 Economic aspects

Besides the beneficial effect on the medical practice, the economic impact of nanomedicine is also expected to be relevant. However, due to its early stage of development and the broad spectrum of potential applications, makes it difficult to estimate market penetration of future novel or improved products deriving from the use of nanotechnology.

Nevertheless, although it is not easy to find homogeneous figures valid worldwide for the 4 topics roadmapped, an analysis of their market and the expected evolution can give an indication of the possible economic relevance of nanotechnology in the medical field in the coming years.

In 2004, the world market of pharmaceuticals was of about $ 506 billion (Global Pharma Forecasts and IMS). This market has been growing at an average rate of roughly 8% a year, albeit with variations depending on the country and market segments. The US market for drug delivery systems in 2002 was $38.8 billion, and is expected to grow at an average 11 % annual rate to reach $74.5 billion by 2008 (BCC, 2003: Advanced Drug Delivery Systems: New Developments, New Technologies)

In US sales of medical imaging contrast media have reached in 2003 a value of $1.41 billion and are expected to rise to $2.58 billion by 2010. Contrast media sales grew 7% in 2003. The annual growth rate of this market is expected to step up to a 9-10% per year between 2004-2006 and rise to 11-12% per year from 2006-2010.

Market growth in the contrast media field should also benefit from higher prices for new products in all modalities. In addition, more products will incorporate targeting capabilities, expanding the range of imaging procedures. This technical influx will help all segments of the contrast media field as imaging and therapy move closer together.

Biochips, and diagnostic systems in general, are expected to gain market share in a slightly shorter time enabling miniaturization and high-throughput screening. Many of them represent an improvement of existing systems, and thus have reduced time for approval procedures and moreover they can be accepted by stakeholders more easily and faster.

In the biochip sector, the faster-growing markets are point-of-care, clinical diagnostics and point-of-need. The potential for increased efficiency, lower cost and faster response time is driving the growth in these markets.

This market is very volatile and thus difficult to estimate. However there is a general consensus on the fact that the need for biochips is going to increase in the following decade and so is the market size. Only the magnitude of it differs when considering different forecasts.

According to BCC, the total market for DNA microarrays and materials is rising at an average annual growth rate of 13.4% and is expected to exceed $1 billion in 2007. By 2007, the total revenues of protein array technologies will approach $336 million (BCC, 2003: Protein Chips: Where To?).

Due to their importance in drug research, protein chips are expected to become tools of outstanding impact for the pharmaceutical industry, and in the long run protein chips are expected to attain much higher total revenues than DNA-chips.

According to the experts, lab-on-a-chip and microarray technologies are expected to gain from 25% to 50% of the market in the next decade, with DNA-chip and protein-chip being among the most important applications.

Biosensors represent another rapidly expanding field, with an estimated 60% annual growth rate. The major thrust is coming from the health-care industry (e.g. 6% of the western world people suffers of diabetes and it would greatly benefit from the availability of a rapid, accurate and simple biosensor for glucose), but areas, such as food industry and environmental monitoring will benefit from the development of novel sensors.

According to a report from Business Communications Company, Inc, the global market for biosensors is projected to grow from $6.1 billion in 2004 to $8.0 billion in 2009, at an AAGR (average annual growth rate) of 5.8%.

2.5.3 Health, Safety and Environmental (HSE) issues

The understanding of the hazards for the human health and the ecosystem associated with nanomaterials, in particular nanoparticles is a key factor for their safe implementation in standard production processes and this has been stressed before in the nanomaterials roadmap. In the clinical context the issue is even more stringent

Although most of the participants excluded a potentially HSE hazard in the nanotechnological processes they are being involved into, all of them advocate HSE impact studies on certain types of functionalised nanomaterials.

Nanoparticles unique characteristic makes them both technologically interesting and potentially risky for the human health.

Nanoparticles, used as drug vehicle or as drugs by themselves, have an active and large surface that can potentially interact with many targets in the body. Due to their size and surface properties, they are badly recognised by the immune system and can even enhance response to antigens.

Being in the range of size of proteins they can interfere with normal cellular signalling pathways and also the interactions of nanoparticles that have entered cells opens a wide field of potential effects resulting from the interaction with cell structures such as ribosomes and DNA.

The specific properties of nanoparticles, differing from that of bulk materials of the same composition, leads to the fact that they represent a new category of substances and the experts agreed on the need of evaluating their potential toxic/adverse effects since these cannot be derived with sufficient reliability from those of the bulk material.

Even if the details are not yet clear, it is evident that the interaction with the human body will depend on various parameters such as, for example, chemical composition, particle size, surface area and surface coatings, bio-persistency.

Therefore, until a theory of the impact of nanoparticles on human health has been established, each nanomaterial should be treated individually when health hazards are evaluated. A systematic risk screening will be helpful to establish the basic know-how to understand the interaction with the human body and the environment and to establish the theoretical framework needed.

2.5.4 Conclusion and recommendations

There are great expectations on the nanotechnology ability to bring forward unprecedented tools for health care which can greatly improve the medical practice. The future diagnostic systems and advanced medical devices made possible by nanotechnology will, in fact, help foremost to learn more about the complex biomolecular processes that control life and this will allow to treat diseases in a much more specific, precise and well defined way than today.

As stated above, Europe holds in this field a strong position in science, and a good worldwide position of industry, particularly with big enterprises. However, the science of nanotechnology applied to the medical system (i.e. nanomedicine) is now moving its first steps. Many are the challenges and hurdles to overcome to bring the maturity this field and, in the end, to the efficient and effective use of the many important applications envisioned.

The first step should be the reduction of the present fragmentation of the organisation and funding of the research which hinder the effectiveness of the efforts made and the transfer of the excellence in science practical applications.

A better coordination and networking of research activities and the development of funding mechanisms with sufficient scale and scope and longer term budget cycles were indicated by the experts as fundamental.

To support this effort, most of the experts emphasised the necessity for the creation of multidisciplinary centres of excellence (analogously to what it's advocated in the other two sectors considered in this reports) which can foster cooperation, carry out baseline programmes of R&D, offer unique technical facilities and support staff. Both academia and industry, most of all SMEs, will take advantage from them.

The improvement of the understanding of all HSE implications associated with nanomedicine must be a priority and a transparent discussion about benefits and risks (and the efforts to keep them under control) is necessary since it will help people reach a considered, balanced view, necessary to get public trust and acceptance.

Another important topic to be addressed is the need for simplified product approval processes for nanorelated drugs and medical systems. This is considered a necessity to speed up application, but in order to not contradict what just said above, a right balance between the demand of shortening of the approval process and the need for more specific and detailed regulations dedicated to nanomaterials have to be found.

The establishment of an European Health Institute (comparable to NIH) is advocated to bundle and streamline biomedical research, reduce bureaucratic burden in funding and to learn from best practice, but it is also fundamental also to address correctly public perception to gain public acceptance.

3. ENERGY ROADMAPS

Background

Modern society is heavily depending on energy and any progress in this field is affecting a very large spectrum of sectors which are important for the EU policy as, for example, security and diversification of energy supply, climate changes and pollution, industrial competitiveness and sustainable growth.

The development of alternative energy sources, environmentally friendly and capable of reducing the dependence from fossil fuels, becomes more and more urgent. The increasing number of equipments and devices energy hungry demands efficient and compact energy sources with reduced heath production.

Nanotechnology is considered to have very promising potentials all along the energy pipeline, from production to transmission, to distribution, conversion and utilization for it can offer alternative ways of energy generation, storage and saving.

10 topics which adequately represent the field of energy in which nanotechnology could have an important impact be have been identified. For the the roadmap exercise have been selected he 4 at the right side of the figure below.

1) Solar cells
2) Fuel cells
3) Thermoelectricity
4) Rechargeable batteries
5) Supercapacitors
6) Hydrogen storage
7) Insulation
8) Glazing Technology for Insulation
9) More efficient lighting
10) Combustion

1) Solar cells
2) Thermoelectricity
3) Rechargeable Batteries and Supercapacitors
4) Heat Insulation and Conduction

Following are the results of the roadmap exercise.

3.1 Solar cells

3.1.1 Topic description

Photovoltaic is the only technology to transform sun light directly in electricity. Photovoltaic solar cells consist of a diode made of semiconducting materials sandwiched between two electrical contact layers and when sunlight is absorbed in the semiconductor it generates electrons and holes, separated by the diode, which diffuse to the different contacts to generate a current.

In theory all parts of the visible spectrum, from near-infrared to ultraviolet, can be harnessed and the spectrum of light which can be successfully transformed in electricity by the solar cell depends on the type and configuration of the material(s) used.

Solar cell are already competitive for electricity production in specific situations, such as homes in remote areas or gadgets, but they have grave draw backs which hamper a much larger diffusion. High cost and limited efficiency to transform sun energy in electricity is, essentially, the main limitation.

The principal drivers in solar cell technology are, therefore, reducing cost and increasing efficiency. Nanotechnology advances can offer solution to both problems either by improving the existing technologies or helping to replace them with alternative solutions.

3.1.2 Properties and applications

Reducing cost of solar cells can be achieved both through the use of cheaper materials and by designing cheaper manufacturing processes, while efficiency depends by the ability of the solar cell to harness and transform as much of the incident light as possible. The contribution of nanotechnology to the latter requirement is related in first place to the large surface to volume area which could be offered by the use of nanoparticles.

Silicon (crystalline) solar cells, which presently account for around 90% of photovoltaic market, are of two types, monocrystalline and multicrystalline (or polycrystalline). The former shows the highest efficiency (typically about 15% for commercial products and almost 25% in the lab), but they are, as said, expensive, mostly because require pure semiconductor material, the same used for computer chips. The latter are cheaper, but due to the irregularities in the crystal matrix their efficiency is lower respect to crystalline silicon..

Other inorganic and organic materials are being developed to overcome the above problems and a list of different types of solar cells technologies available or in development, and their related properties, are briefly described below.

Amorphous/thin films. Active coatings of thin films are applied to different substrates (both stiff or flexible). Amorphous silicon is the material presently most used and these solar cells are much cheaper respect to crystalline solar cells due chiefly to the smaller amount of active material required. The efficiency (currently 8% for silicon), however is quite low. Other materials used for thin films are copper indium diselenide (CIS or, with gallium added, CIGS) and cadmium telluride (CdTe). Thin film solar cell commercially available have a share of the market of about 6% (in 2003).

Dye sensitised (Grätzel) solar cells. These cells convert sun light to energy with a mechanism similar to plants and are made with cheap, low purity materials and low cost procedures. Electrons are produced by light absorption in a dye and subsequent transfer to nanostructured Ti2O. The efficiencies are quite low (10% in experimental models), and there are issues with robustness as electron transfer requires the presence of an electrolyte. Their cost is however around 60% lower than silicon based cells and a growing market for them is expected.

Polymer cells. Particular organic polymers (such as polyphenylene vinylene) that have semiconductor characteristics are used for these cells as ultrathin layers. These cells are cheap to manufacture, but suffer from low efficiencies and are sensitive to air and moisture.

Multi-junction solar cells. Cell with a multi-layers structure formed by growing successive layers of different semiconductor materials (with different bandgap) on the same substrate which enable absorption at different wavelengths. In laboratory, a triple junction solar cell has reached an efficiency of 34%. These solar cells are relatively expensive and can find use for niche applications (ex. powering space satellite systems).

Quantum dots, quantum wells, carbon nanotubes and fullerenes, nanowires and dendrimers are also attracting attention as materials for solar cells.

Nanotechnology has at present a limited use in solar cells, and most of the activity is at the basic research stage. However, according to the experts, nanotechnology is expected to play an increasing role in the coming years. Its contribution will be through:

- Development of thin films, layers and surfaces;
- Use of nanoparticles to increase surface area;
- Use of nanocrystalline materials
- Development of new materials.

Thin films layers and surfaces (nano) are the most extensively used technology for solar cells applications, followed by nanocrystalline materials and nanoparticles. The experts expressed the opinion that these three technologies should be the leaders within the next 10 years, followed by the dye sensitised solar cells.

Quantum dots, quantum wells, carbon nanotubes and fullerenes are considered of strong interest, but around one third of experts believe that it is still too early to predict which technologies will be most influential.

However, quantum dots are believed to deserve a special attention since they are predicted to be the in the first place in terms of efficiency. By arranging multiple layers of quantum dots, tuned to absorb different wavelengths, an overall efficiency of about 86% could in theory be achieved.

Quantum dots have also the advantage of being able to be placed on rigid matrices as well as on, for example, electrically conducting polymer supports, to provide flexible solar cells.

Solar cells can find use in various market sectors, from ubiquitous and cheap low-power devices (e.g. RFID tags) to high power applications suitable for more demanding energy needs. The degree of their success depends most of all from the overcoming of the two above said limits, cost and efficiency. All R&D research in this field is aimed to these two objectives.

3.1.3 Timeline for applications development

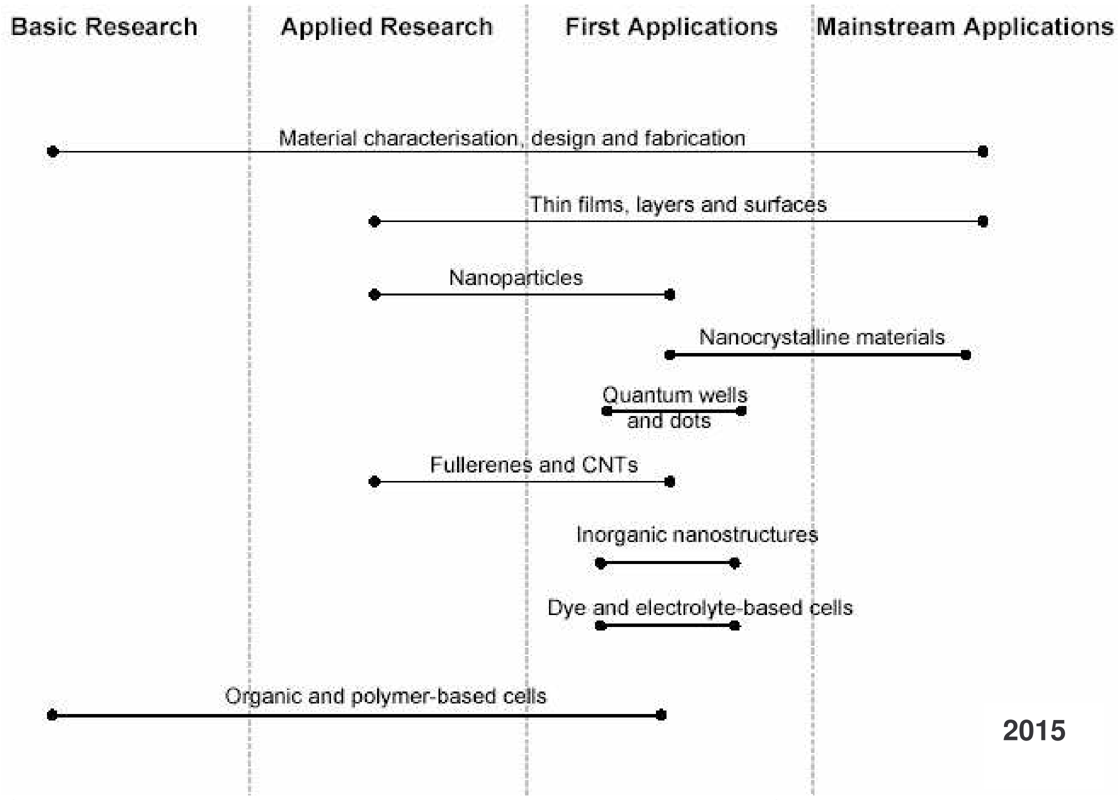
Material characterisation, design and fabrication will be a fundamental area of research which will concern all the stages of development up to 2015 to improve photovoltaic efficiencies, in first place, and stability. At present, the activity on nanotechnology-related solar cell is essentially at the basic or applied research stage, except than for thin films and dye and electrolyte based cells which see already first commercial application.

By 2010 practically all the cells considered are predicted to have moved to applied R&D and first commercial application, with thin-films solar cells expected to be as the earliest mainstream application. In 2015 cells incorporating nanocrystalline materials will follow thin films in main stream application.

Dye and electrolyte based cells, which are seen as early entrant into the market place with small-scale applications already in 2005, in 2015 are expected to be not yet at the stage of main stream applications.

Quantum dot-based solar cells will be in 2015 perhaps lagging further behind in commercial application, however as described earlier, they promise the highest theoretical efficiency and can be manufactured to absorb specific wavelengths of light. The interest on them is strong.

The overall picture of situation at 2015 for application development of solar cells technology is reported in the following figure.



***Stage of development of solar cells nanotechnology at 2015**. (Origin: Energy Roadmap)*

3.1.4 Challenges, barriers, bottlenecks

As mentioned already many times, major challenges for solar cell technologies are reduction of manufacturing costs, which must be associated with environmentally friendly processes, and the increase of the efficiency of energy conversion. To these it should be added also the need of improving reliability and lifetime. Nanotechnology, as said, is expected to be essential to reach these goals.

Increasing efficiency and decreasing cost, are likely to develop as separate R&D strands at least in the near future, with certain materials offering cheaper manufacturing costs and novel applications, but at the price of a lower efficiency to current state-of-the-art, and other materials, expensive but with higher efficiency, dedicated to particular applications.

According to the experts, the R&D efforts within the next ten years should mainly aim to:

- Develop materials which can absorb more of the available incident light and convert it to electricity through the integration in a cell of a series of photoacceptors with different bandgaps or absorption spectra (quantum dots, new dyes, multilayer of ultrathin nanocrystalline materials are good candidates)

- Maximise charge transfer. For thin films or multilayered cells this is achieved with a regular crystalline structure, enhanced by using nanocristalline materials. For dye-based and polymer cells this require an electrolyte to transfer the charge from the photo-acceptor to the electrodes. For nanoparticle-based cells is necessary the presence of an electrolyte or that particles are sufficiently close to one another so that they can transfer charge directly.

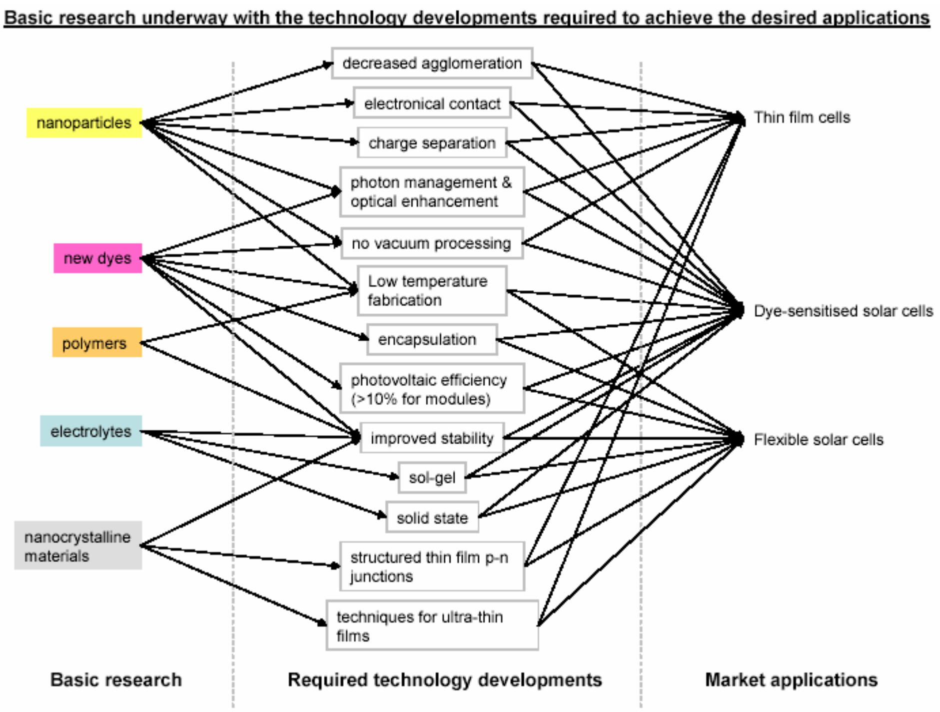
- Guarantee a cost-effective lifetime (reliability) through the right integration of photoacceptor, charge transfer structures and electrodes within the bulk of the solar cell.

- Assure that the technological steps for the creation of these integrated structures may be easily and cost-effectively scaled-up to industrial processes.

Regarding flexible solar cells, realized with the deposition of a thin film onto flexible polymering supports, there are problems related to the printing or deposition methods. High temperature processes, the best methods to have reproducibility, damage the polymer, while alternative technologies, utilising lower temperatures, such as chemical vapour deposition (CVD) or Spray CVD, still suffer of draw backs which must be overcome.

Dye and electrolyte based cells may not compete with multijunction solar cells in terms of efficiency, however, as said, they are cheaper and simpler to implement also on flexible support . The main driver in this case is improving the environmental stability of cells (i.e. to temperature changes, moisture etc). Identification and development of new dye molecules are other R&D objectives.

In the figure below are summarised the basic research necessary to develop the solar cell that are expected to have the larger application in the next decade.



Origin: Energy Road Map

3.2 Thermoelectricity

3.2.1 Topic description

Thermoelectricity is the conversion of heat to electricity or vice versa and it is also known as the Peltier-Siebeck effect. The simplest thermoelectric (TE) device generally consists of a junction of two materials possessing different thermal conductivity properties. When the two junctions are kept at a different temperature an electrical current flows from one material to the other. Conversely, passing a current through the junctions can result in cooling. Such devices could be used as power generators to reuse waste heath or as refrigerators.

A good thermoelectric material (TE) must have a large Seebeck coefficient (or thermopower), to produce the required voltage, a high electrical conductivity, to reduce irreversible heat losses (joule heating), and a low thermal conductivity to decrease thermal losses from the thermocouple junctions.

The dependence of device efficiency, related to the material properties, is expressed by the dimensionless thermoelectric figure of merit, ZT, where T is the operating temperature and Z is proportional to the Seebeck coefficient.

The most efficient thermoelectric materials are semiconductors, and this ability depends largely on a material possessing a high electrical conductivity, but low thermal conductivity.

The present best materials have ZT values of approximately 1, which is seen as the necessary limit for practical applications.

3.2.2 Properties and applications

Thermoelectric materials are being used since quite some time, nevertheless, even though they are reliable, their low efficiency, due to the low ZT values of the presently available materials, has so far limited a more widespread use.

Since ZT values vary with temperature, different types of materials must be considered depending from the operative temperature range of the specific application.

Some materials will be better candidates for power generation at high temperatures (since their ZT values are high only at higher operating temperatures), others for medium temperature generators and yet others will be more suited to refrigeration (high ZT values at room temperature).

Examples of such materials include bismuth antimony and tellurium selenide alloys for refrigeration, lead telluride alloys for medium temperature generators, and skutterudites and silicon germanium alloys for high temperature generators.

All the experts of the Delphi panel agreed that in the coming years nanotechnology will be important for TE development and application because nanotechnology shows promises for providing materials with high ZT and hence higher efficiencies for thermoelectric generators and cooling devices.

Nanostructured systems with ZTs as high as 3 to 4 seem to be achievable.

The main advantages in TE expected from nanotechnology, when compared to existing technologies, are:

- Decrease of thermal conductivity (according to 48% of the experts)
- Increase of thermopower (according to 31% of the experts)

Different types of nanostructures have applications in thermoelectricity. According to the experts the winning categories are:

- Thin films
- Nanocrystalline materials
- Nanoparticles
- Superlattices

Nanowires, quantum wells, quantum dots, inorganic nanotubes, carbon nanotubes, nanocomposites are also used in thermoelectricity, primarily through decreasing thermal conduction.

The particular lattice structures of these nanomaterials, often in the form of thin or ultrathin layers, may affect heat and electrons flow so enabling the optimization of both thermal and electrical conductivity. However, generally, thermal conductivity is decreased without modifying the electrical conductivity of the material.

At present there are limited market applications of TE materials, but relevant business opportunities are envisaged to materialise within the next ten years.

The field attracting more interest, on which R&D of the experts of the Delphi panel mainly is focused on are:

- Management of “waste” heat to generate electrical current;
- Applications where a local cooling is needed;
- Generation of electricity under restrictive conditions.

Examples of possible applications are:

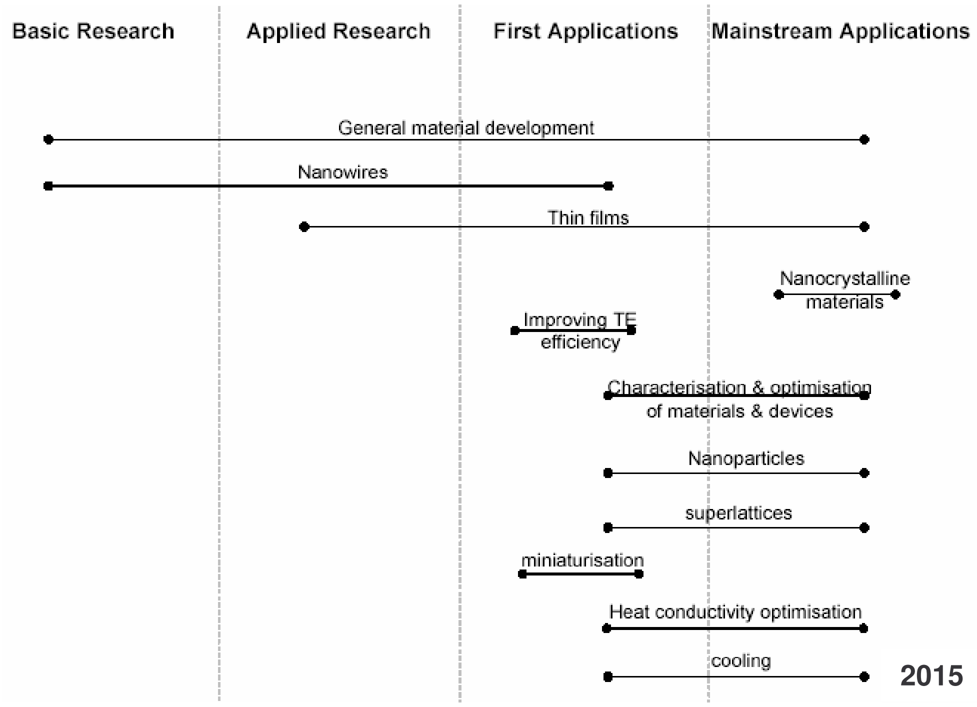
- TE generators converting the waste heat from automobile engines in electricity;
- Microdevices using tiny dots of TE materials applied to the surface of microprocessor chips to aid localised cooling;
- Microgenerators and generators for space applications.

3.2.3 Timeline for applications development

As stated above, at present market applications of TE are limited, and the technologies highlighted by the experts are still mostly in the basic or applied research phase. The main efforts are devoted to development of novel materials, understanding of their properties and developing the tools and fabrication processes for their routine manufacturing.

By 2010, this research is expected to be applied in specific devices, with first applications (ex. energy generation from waste heat in vehicles) as early as 2015. At that date, also other applications, such as temperature stabilisation and cooling for electronics and telecommunications, are seen as early market entrants to manage waste heat, thus allowing faster and more powerful devices to be developed.

The nanostructures of choice for TE applications are expected to be thin-films, nanocrystalline materials, nanoparticles, nanowires and also superlattices, with thin films and nanocrystalline materials. The stage of their development forecasted at 2015 is illustrated in more derail in the figure below.



***Development TE nanoechnology at 2015**. Origin: Energy Roadmap*

3.2.4 Challenges, barriers, bottlenecks

At present, the main challenge in the field of thermoelectricity is the identification and development of new materials, rather than their integration into devices.

The objective is to have materials with high ZT and the optimum goal would be a ZT of bout 3 at both room and high temperature. Good stability performances and reduced manufacturing costs are the other features sought.

As far as the latter point is concerned, however, about 30% of the experts believe that cost could be not necessarily an issue, because the benefit associated with the novel products may overcome the cost barrier.

One of the most important bottlenecks is the bulk synthesis of nanostructured materials and in particular their application in thin films. At present materials with the highest TE values are produced at the laboratory scale, and even at this level there can be structural variations (e.g. grain size, even dispersion etc).

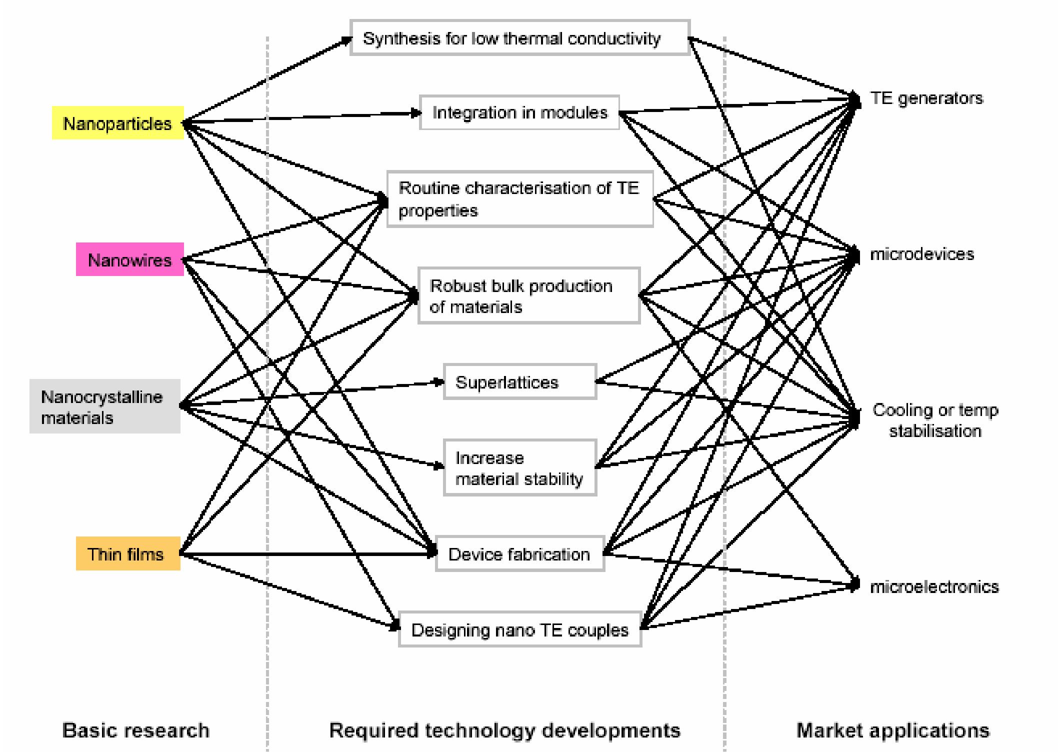
Eliminating this variability will be essential if TE generators are to be mass-produced. This demands both tools to accurately measure physical properties of new materials at the nanoscale (both structural and thermoelectric properties)) and robust and economical means to mass produce these materials in a form suitable for incorporation into TE devices.

Equipment like Scanning Thermoelectric Microscopy (SThEM) will be essential to validate nanoscale thermocouples at the junction between ultrathin layers.

A non-technological barrier indicated by the experts, more tightening than in other energy topics, is the access to infrastructure and the rising costs of equipment.

Following are in synthesis are indicated the R&D requirements for nanorelated thermoelectricity.

Basic research underway with the technology developments required to achieve the desired applications



Origin: Energy Roadmap

3.3 Rechargeable batteries and Supercapacitors

3.3.1 Topic description

Energy storage is a necessity when demand doesn't match production or when dealing with intermittent energy sources. With renewable energies, for example, this capability is essential. Energy storage, however, is also fundamental when there is the need of energy for movable or portable machines and devices.

The research for ever more efficient, reliable and affordable energy storage systems is flourishing due to the increasing demand of "portable" energy, the need of energy recovery, the urge to use alternative/renewable energies.

Rechargeable batteries and supercapacitors are both form of portable energy supply which can be replenished and reused.

Batteries store energy in a chemical form. They are charged when undergo an internal chemical reaction under a potential applied to its terminals and deliver electricity when the chemical reaction is reversed. Capacitors store electrical energy (rather than chemical energy) as a charge or concentration of electrons in electrochemical double layer on the surface of a material.

The lead-acid battery used in cars represents the most known example of rechargeable battery, but the largest market and interest concerns at present the smaller, portable batteries used in the plethora of modern-day electronic devices.

Nanotechnology is expected to have an important role to improve the performances and characteristics of both rechargeable batteries and capacitors.

3.3.2 Properties and applications

Energy storage devices are broadly characterized by following properties:

- Energy density (energy stored per unit volume or mass)
- Power density (it indicates how fast energy is delivered or absorbed, it affects charge/discharge time)
- Lifetime (number of charge/discharge cycles)
- Temperature dependence

Respect to the these characteristics batteries and capacitors show quite distinct features, which determine also their use. In particular, batteries can store lot of energy but have low power density (it takes a long time to be charged or discharged), have low lifetime and high temperature dependence. Traditional capacitors, at the contrary, exhibit considerable power density, but very low energy density, have long lifetime, low temperature dependence.

There has been a natural development of the battery technology and from the first compact rechargeable NiCd batteries, the top end of the market is now dominated by Lithium-Ion (Li-ion) and Lithium-polymer batteries. Lithium is the most electropositive and also the lightest metal, making it the element of choice for rechargeable batteries. At present the cathode materials include oxides of manganese, nickel, and cobalt, the anode is generally made in graphite. Another area of research refers to metal hydrides based batteries, at present Nickel-Metal-Hydride (NiMH).

This progress has lead to improved power outputs and faster charge/discharge cycles, but it is still not enough for many power-hungry, modern devices.

In lithium batteries, R&D activity now focuses on how to deliver Li in the rechargeable battery to maximize power output, charge/discharge time, and the number of charge/discharge cycles. This demands research on both electrodes and electrolytes.

The principal limitation of capacitors is the said very low energy density and supercapacitors, which exhibit moderately high energy density, offer a solution to this problem thus combining the advantages of their intrinsic high power density with an energy storage capability not much different from that of batteries.

The main determining factor for the increase of power density and maximum power output of supercapacitors, compared to the traditional ones, is the surface area of each electrode that makes up the capacitor.

Supercapacitors utilize nanostructured materials, like porous carbon, instead of standard metal plates, which dramatically increase the surface area. Typically, a supercapacitor will reach full charge in a matter of seconds (compared with minutes or hours for rechargeable batteries). As there are no electrochemical processes, supercapacitors are more stable than rechargeable batteries and have a virtually unlimited lifetime.

Current portable power supplies are still struggling to meet the demand of many applications (mainly latest generation electronic portable devices) as they still suffer from limited energy reserves, maximum power output and slow charge/discharge rates.

According to the experts, nanotechnology, which has already found application, as said, in supercapacitors, can play a very important role to overcome the limitations of the present energy storage devices.

Current technologies are limited, in fact, not so much by the materials but by the active surface area (it is estimated that only 25% of the volume of a rechargeable batteries is actively used) and the use of nanomaterials, with their high surface to volume ratio, tailored interfaces and in general special morphology will help to improve:

- Power density
- Energy density
- Charge/discharge rates

Lifetime is also expected to improve.

R&D activity is concentrated in first place on electrodes development and then on electrolytes. There are several different electrode platforms, based on nanotechnology, that are being explored and which can be implemented both in batteries and supercapacitors.

Among the winning category of nanotechnology for energy storage, the experts indicated:

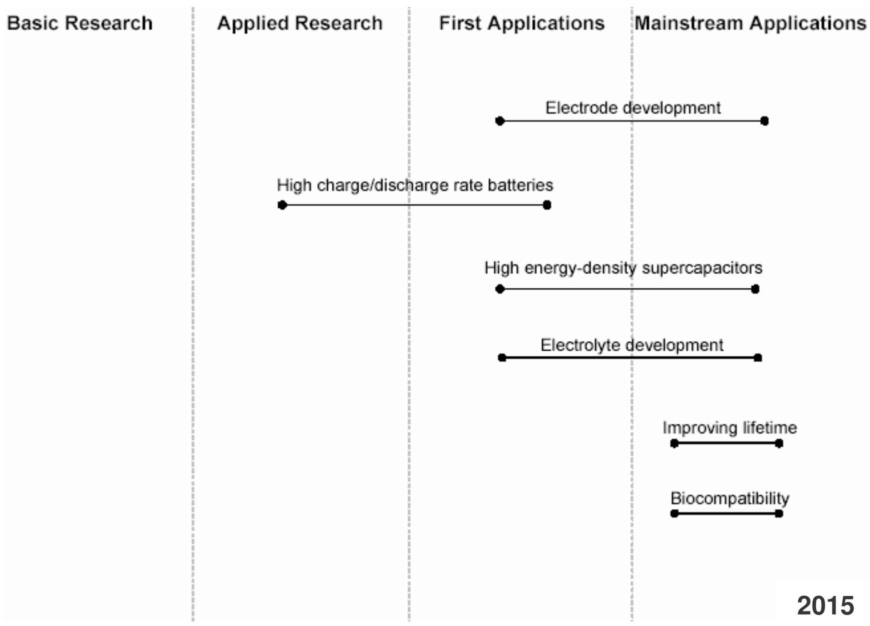
- Nanoparticles /nanocrystalline materials
- Thin films, layers and surfaces
- Carbon and inorganic nanotubes
- Nanowires

Nanocomposites and nanoparticles were the top choices.

The development of safe and environmentally friendly material is also object of particular attention.

3.3.3 Timeline for applications development

Much of the research in the field of nanotechnology-related batteries and supercapacitors is comparably more advanced respect to the research other energy fields, but it still mostly at the basic/applied R&D stage. Nevertheless, nanotechnology is expected to play an important role in batteries and supercapacitors markets as early as 2010, with many of advancements already at first commercial application stage.
In 2015 practically all the present goals: advancement in electrodes and electrolytes, improvement of batteries lifetime, new safer materials should have been achieved



Stage of development of nanotechnology-related energy storage at 2015.
Origin: Energy Roadmap

By 2015 high energy density supercapacitors are expected to be in main stream application while high charge/discharge rate batteries should still be at the first commercial application stage.

According to the experts, given the large demand for enhanced portable power supplies, a relatively high increase in cost, accompanying the improvements of the performance offered by nanotechnology, is expected to be tolerated by the markets.

3.3.4 Challenges, barriers, bottlenecks

As already mentioned, the rationale behind the development of new energy storage systems is the increase of energy and power density and lifetime under real operating conditions of an application.

As stated above, R&D efforts are mainly devoted to improve electrodes and electrolytes technologies.

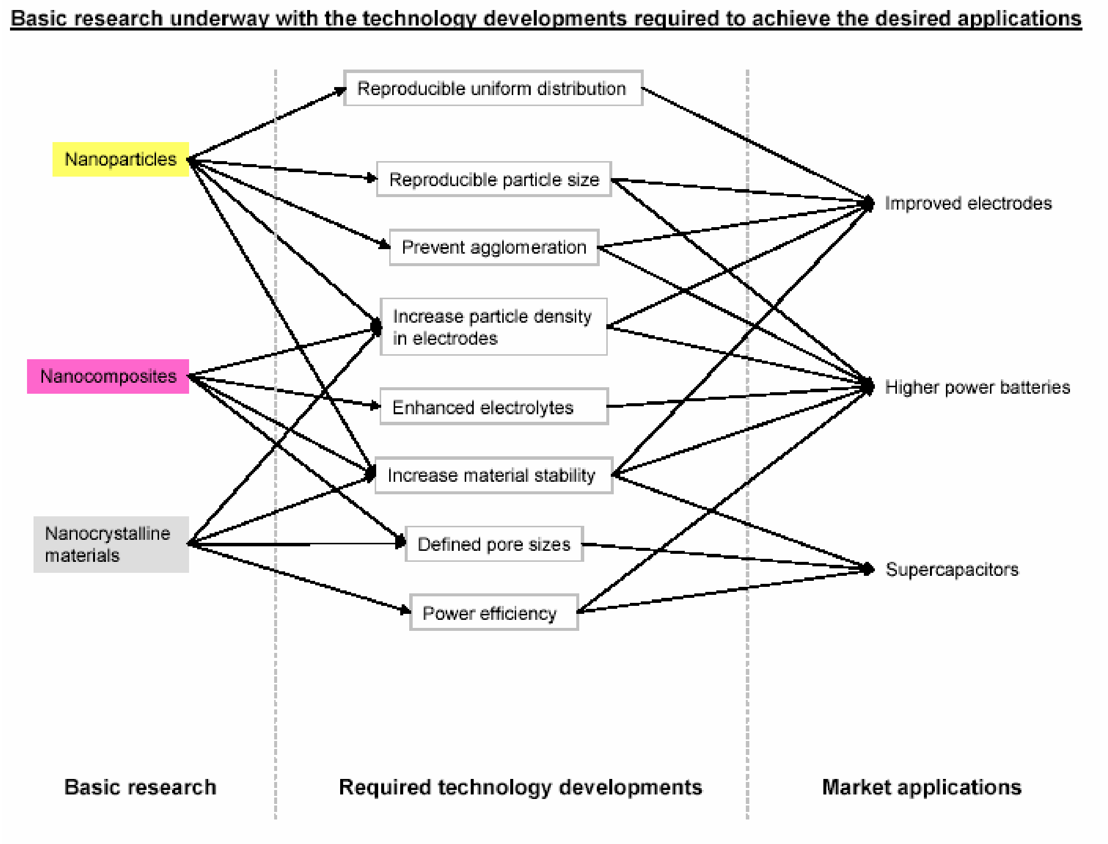
For batteries electrode the efforts are focusing on several factors:

- increased surface area (i.e. nanoporosity) to accommodate more lithium and hence higher power density;
- development of materials that can withstand volume changes due to lithium migration between electrodes;
- use of environmentally safer materials for the cathodes;
- decrease passivation of electrodes;
- ensure uniform distribution of nanoparticles within cathodes (preventing their agglomeration) and ensure that conductance is maximised;
- ensure regular crystallinity (robustness to cycling over time);
- take into account all the above and apply it in industrial manufacturing processes.

Electrolyte development must proceed in combination with this research to ensure that the final batteries are robust and safe.

For supercapacitors, the electrode porosity must be controlled: to maximise electrolyte interaction and hence charge density, and to ensure that both cations and anions interact efficiently with the respective electrodes (which entails manufacturing the same material for both electrodes, but with different sized pores). This becomes even more an issue with the use of organic electrolytes (which increases the maximum voltage output) as the anions and cations can have quite different sizes.

The research concerns nanoparticles, nanocomposites and nancrystalline materials. In the following figure are synthetically outlined the research goals.



Origin: Energy Roadmap

3.4 Heat insulation and conductance

3.4.1 Topic description

Insulating materials are used to keep the temperature constant in an enclosed space such as a building or a vessel and advances in insulation will help reducing energy waste, especially in homes and industry. The consequent decrease in energy demand would be beneficial for the environment and will help to counteract the increase of energy costs.

The basic requirement for thermal insulation is that it must reduce the rate of heat transfer by conduction, convection, radiation, or any combination of these mechanisms.

There are two principal methods of achieving this:

- Using a porous material which traps and immobilises air or another gas, thus decreasing convection.
- Applying a coating to reflect heat (such coatings can be used on glazing, and can be transparent to visible light).

As far as it regards the latter method the term “smart glazing” has been coined for glass that reacts and responds to its environment primarily by altering its transparency and translucency. This alteration in opacity can have great energy saving effects.

3.4.2 Properties and applications

Materials currently used for insulation include fibreglass, rockwool and slag wool. Although arrived more recently on the scene, also aereogels are now established as one of the most efficient materials for insulation, although, up to now, their high cost make them suitable essentially for specialized applications. Only the fast increase in energy costs has recently made their use more widespread, with some applications in glazing and pipelines (for natural gas).

With a decrease of costs and the development of transparent aerogels (examples already exists), these materials may find use in the most diverse applications, as for example temperature-resistant windows.

Nanotechnology will probably be fundamental for the future development of aereogels. These materials are, in fact, highly porous matrices usually of carbon, but also of silica, which can be up to 99.8% air with pores and particles that are smaller than the wavelength of light.

Given their porous structure, nanotechnology could be used to control pores size to tailor the material’s response to incident radiation, thus helping to control optical properties.

Regarding glazing technology, the biggest breakthrough over the last 25 years has been the development and widespread use of large area, low cost, multilayer thin films. Recent developments with respect to quality, cost and reproducibility have allowed for their application in the construction industry. Architectural glazing surfaces showing a microstructure with the shape of venetian blinds have been used to improve reflectivity.

There are already several marketed products which utilise tungsten oxide as the electrochromic material, with voltage supplied through indium tin oxide (ITO) electrodes (which are transparent). However, these products are expensive (due to the ITO) and therefore there is the need to develop cheaper alternatives.

Traditional insulating technologies can be bulky and/or heavy, and therefore even if they offer relatively high insulating efficiency, they can be inadequate for specific tasks. In terms of coatings for glazing, there is no effective traditional technology that provides effective insulation while remaining transparent.

Nanotechnology is supposed to be critical also in this case in supplying the mentioned demand.

In synthesis, according to the experts of the Delphi panel, the most relevant property of nanomaterials in heat insulation when compared to existing alternatives, is their capability in reducing the rate of heat transfer by various mechanism, but in particular conduction. Besides this, however, other advantages which can derive from nanomaterials must be taken into consideration. In particular: improved rate of heat transfer (the reverse of the above property), tailored materials' absorption, increased lifetime, reduction of costs.

The research is focusing in particular on development of:

- Thermochromic, photochromic, electrochromic "smart glazing";
- Developing alternatives to Indium-Tin-Oxide (ITO)
- Microstructured surfaces;
- Porous materials with immobilised air or other gases

With reference to the most suitable nanotechnologies for the heat insulation and conductance the experts named:

- Thin films, layers and surfaces
- Nanoparticles/ nanocomposites
- Aerogels
- Sef-assemble structure
- Mesoporous materials
- Carbon nanotubes (CNT)

In the case of aerogels, attention has been drawn also to the development of aerogel composites, including polymers and carbon black. These could reduce the overall cost of the material while retaining or enhancing thermal properties.

3.4.3 Timeline for applications development

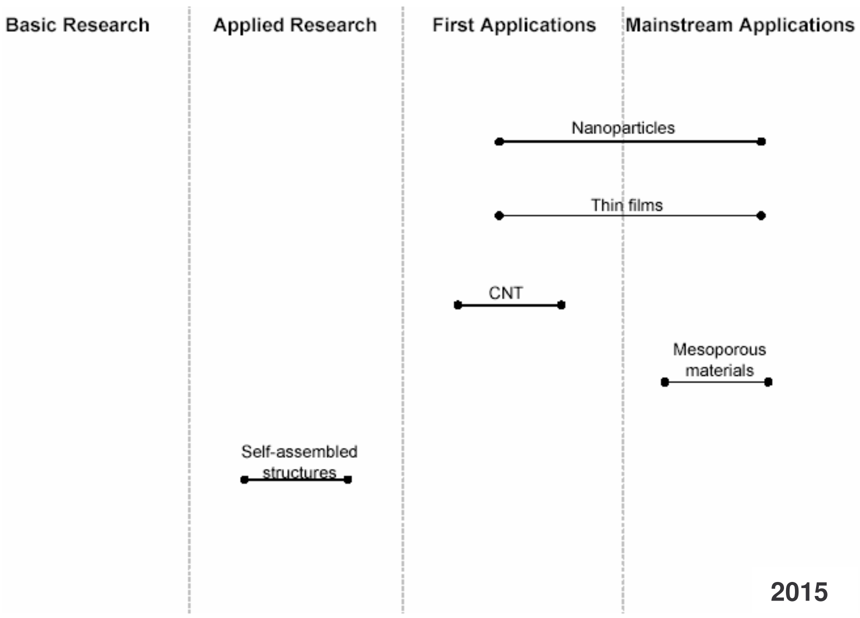
According to the large majority of the experts involved in the Dephi panel, within the next ten years nanotechnology is expected to play a role indicated as high or very high in heat insulation and conductance .

Nanoparticles and thin films are considered to be the major contributor to this, with applications in areas, for example, such coatings for glazing products with switchable chromic properties, which is expected to develop into applications over the next 10 years.

Except than for aerogels, which presently are already in full commercial application, the rest of the nanomaterials for heat insulation mentioned above are practically all at the basic research stage.

In 2010 they are expected to have moved all at the stage of first commercial application with main stream application generally attained in 2015, as indicated in figure below.

There is no clear indication of the focus of basic R&D in 2010 and 2015. This may be because many of the materials undergoing basic development just now are expected to address current limitations and thus have significant impacts on products within the next decade. It is still unclear what the next demand will be. Solving current material limitations means that these new materials can expect to command a medium to high price increase compared with existing technologies.



Development of nanotechnology-related heat insulation/conductance at 2015.
Origin: EnergyRoadmap

3.4.4 Challenges, barriers, bottlenecks

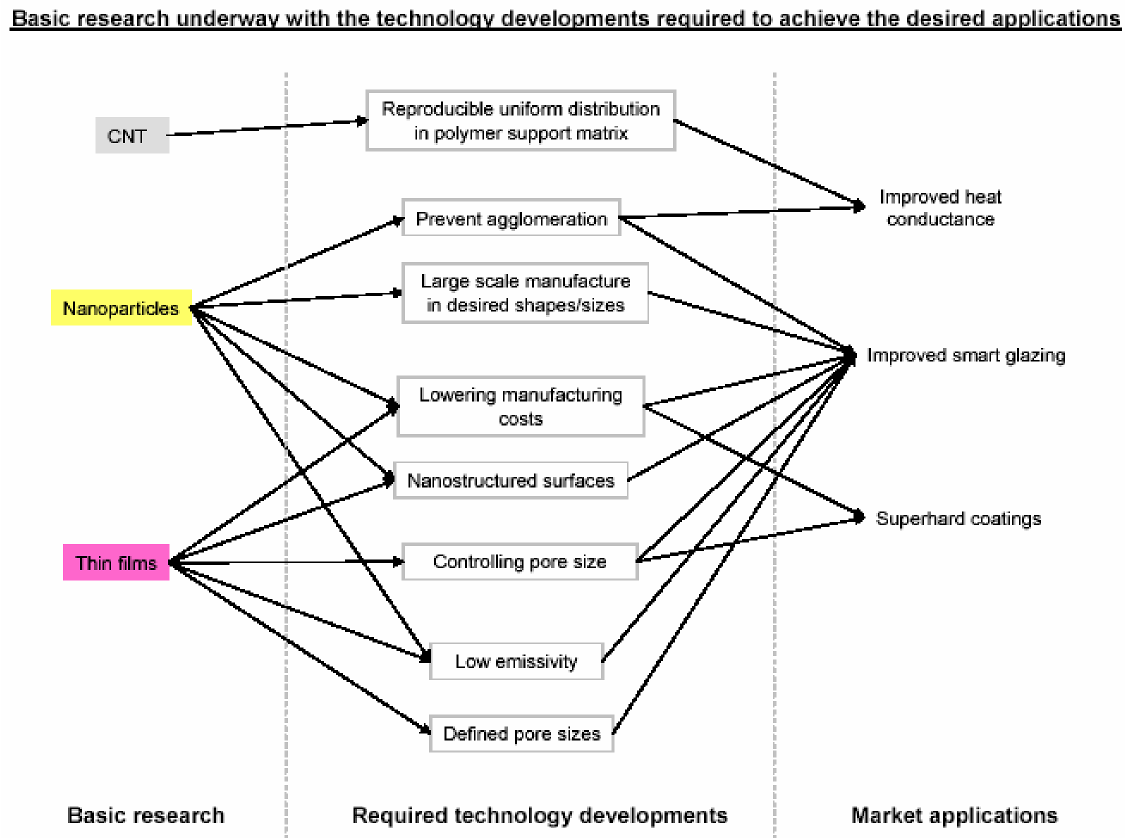
As said, nanotechnology is expected to play a major role in heat insulation as early as 2010 and this will be mainly due to novel, higher, properties rather than decreasing costs compared with existing technologies.

The major challenges in nanotechnology-related heat insulation/conductance R&D within the next ten years include:

- Stabilizing electrochromic systems;
- Preparing photoelectrochromic windows;
- Routine uniform incorporation of nanoparticles in support matrices;
- Large scale manufacture of specific nanoparticles in specific shapes (e.g. for reflective coatings);
- Lowering of the costs of aerogel;
- Controlling nanoporosity;
- Developing smart environment-responsive glazing;
- Developing superhard materials for heat-insulation coatings.

Already much of the R&D is in the applied phase with the main challenges, for the coming decade, in the further development of coating materials in terms of stabilisation and their mass-production (rather than identifying new materials).

The diagram below summarises the major areas of research.



Origin:Energy Roadmap

3.5 Non-technological aspects conclusions & recommendations

3.5.1 European competitive position

According the experts of the Delphi panel, European nanoscience, in all the 4 topics considered by the Energy Roadmap, is performing well when compared with the other world regions. Only in thermoelectricity a significant 40% of the experts rate the European position as poor.

In contrast to the good opinion on European nanoscience, the judgement is not so favourable when evaluating the competitive position of the EU industry and varies passing from one topic to another and with the type of industry considered (large enterprises or SMEs). Only a mere 15% of the experts considered the European big industry in these 4 sectors good although, it must be said, some European champions do exist.

In general, European industry is thought to be somehow lagging behind respect to USA and SE Asia. In the case of thermoelectricity, the vast majority of companies cited by experts as contributing the most to advancing nanotechnology in this field are based in the USA (sixteen out of twenty-four).

There are, nevertheless, some brighter spots. In nanotechnology-related heat insulation and conductance, for example, the position of the European industry is thought to be good or excellent by most of the experts of this topic. In solar cells, there are big companies and some start-ups which the experts consider in a quite good position. Also in rechargeable batteries and supercapacitors the position of European SMEs is rated from satisfactory to good.

3.5.2 Economic aspects

The present very early stage of development of nanotechnology in the energy sector, makes it difficult to exactly determine the economic impact deriving by the extensive use of nanomaterials, or nanotechnology processing.

For this reason only some predictions of the market of already existing products are reported to give an indication of the possible economic dimension of the nanotechnology relate products.

In the case of solar cell the growth of the market is accelerating fast, with 64% increase in installations from 2003 to 2004 compared with a 32% increase the preceding year (Market Buzz 2005: Annual world solar photovoltaic market report). This means a doubling of the market between 2000 and 2003, which is equivalent to approximately

5% of the global energy market in 2003. The market leaders in terms of megawatts of installation are Germany, followed by Japan and then the US. Globally the revenues from solar energy are estimated at 3 to 4 billion USD. The market leaders in manufacturing solar cells are Sharp, Kyocera, BP Solar and Shell Solar, and take over 50% of the market share (Gans: Spektrum der Wissenschaft, April 2002, 90-91)

Also the rechargeable battery market is growing fast year after year. The turnover for all batteries in Europe, which was almost €3 billion in 1999, is expected to reach a value of more than €4.6 billion in 2006 (Gans: Spektrum der Wissenschaft, April 2002, 90-91).

Supercapacitors are an emerging technology for portable products and other sectors, they are very promising for markets where high power is needed.

Power back-up in electronic devices, weatherproof power source (thanks to supercapacitors low temperature dependence), regenerative braking and catalyst preheating for the automotive sectors, power supply for mobile telephones, are just few examples of applications where supercapacitors properties may represent a real breakthrough.

The insulation and conductance material industry is well established, so new technologies must primarily address increased efficiency per unit mass of material, or completely new applications such as smart glazing. The worldwide insulation market is estimated to be of about US$ 20 billion (Aspen2003).

Nanotechnology is expected to have a profound impact on all these sectors, but its too early to exactly determine the level of the performances of the nano-related products and the difference in price compared to existing products. Thus market penetration is difficult to estimate. For all the applications considered the experts said that if the expected improvements are reached an increase in price of 5-15% should be accepted.

3.5.3 Conclusion and recommendations

It is undeniable that the demand of new and improved energy systems is necessarily going to increase within the next 10 years.

Many technologies are facing this competition, looking for cost effective, efficient and sustainable methods of producing, storing and saving energy.

Nanotechnology, at least regarding the partial view of this project, is not going to be a completely new solution or method but, instead, a very effective leverage for many already existing technologies.

In many example, as new highly efficient solar cells (e.g. based on quantum dots) or supercapacitors, nanotechnology may completely change the figure of merit of these applications, making them competitive among existing alternatives.

Absorption and reflection of radiation, thermal and electrical conductivity, charge transport, conduction and convection of heat are all properties that can be accurately tuned acting on materials at molecular level. And this is what nanotechnology is supposed to do.

In all the topics considered there are many products already on the market, but development of applications using nanotechnology is presently mainly at a basic or applied research phase.

A strong commitment is needed to maintain and support the well-respected position of European basic research (in nanotechnology) in the energy field and translate it in a strengthened position of the European industry.

An higher support from the EU and national governments is considered to be fundamental by about 30/40% of the experts involved in the Delphi Panel.

A certain lack of an effective industrial application of the important research activities undertaken by European science is a critical point resulted from the Nanoroadmap survey. There is a real danger that Europe could be left behind in what could be lucrative markets.

Adequate access to infrastructure/equipment for the performance of typical nanotechnology-related activities (including the use of both internal and external facilities through existing collaboration), does not appear to be an issue for R&D in these fields.

Nevertheless a closer collaboration of academic science (which is most often seen as the driver of innovation) with industry is thus fundamental to allow manufacturing processes to be developed in parallel with the identification of new materials.

According to the experts, this collaboration could be achieved through the provision of more and smaller collaborative projects (allowing a larger number of R&D topics to be pursued, and better collaborative links to be established between partners), rather than larger, but fewer projects.

In many situations there simply is not the appropriate technology to manufacture materials on the large scale, e.g. ensuring that nanoparticles are produced of similar size, shape and uniformly distributed.

This may be an important bottleneck, if scaled-up production of the raw materials must be accomplished before starting the manufacture of the final product.

The scale-up of laboratory to industrial processes is, in fact, a main challenge, overall considering that, as stated above, the future improved products will have to enter well-established market and there must be special attention that the processes are safe and environmentally friendly.

3.6 General conclusions

There is practically unanimous consensus on the fact that nanotechnology is among the emerging technologies which will dictate the future technological development and trend of growth.

The roadmap exercise has given an insight about the current situation and the perspectives of future development of nanotechnology application in three fundamental sectors such as materials, health and medical systems, energy, which have (will) a crucial impact at both economic and social level. The roadmaps prepared are based on the view of a rather ample number of experts, coming from many countries around the world, both from academia and industry and give a thorough insight of progresses and tendencies about a quite ample number of application of nanotechnology.

Those dealing with the fields considered and, more in general, with innovation, know that many novel ideas and predictions with emerging technologies do not survive critical examination about their applicability on an industrial scale.

Nevertheless, the 12 topics roadmapped, which were chosen among more than 30 identified with a preliminary selection, can be considered representative of the priority themes of research in the above said sectors for the next ten years. The indications which emerged from the roadmaps and synthesised in this document, represent a common wisdom shared among experts working in these fields about the applications of nanotechnology that could eventually make it to utilisation in this time span.

The roadmaps have put forward also the strong correlation and potential cross fertilization among the three sectors surveyed which advocates the promotion of an exchange of information to share knowledge and speed up the transfer of the research results to application.

One thing has become, however, clear from the work done. For the benefits of nanotechnology to be fully exploited there are quite few more years to go and many things have to be done in the right direction.

In all the three sectors surveyed, in fact, the use of nanotechnology results at present generally still at an early stage of development. The majority of the most advanced applications (for example catalysis, semiconductors, thin films) are still relaying on the processes of microtechnology to go at the nano scale, while the newest concepts see an intense activity of basic or applied research and just a few examples at an early stage of first applications (biochips, solar cells, inks/toners, contrast agents and drug delivery, nanocomposites).

Ten years, the period taken into account by the project, seems the time span necessary for bringing the applications considered to the market, although, for many of them, even this time could be not enough to attain full maturity, especially in the medical field.

In this case many questions must in fact be answered before nanorelated treatments are fully accepted. The study of toxicity/citotoxicity of nanoparticles or of their degradation products as well as biocompatibility deserves a strong commitment and also the stability of nanoparticles in the biological environment or their interaction with cellular barriers require still intense research. The lengthy procedures for the approval of pharmaceuticals could add a further delay. Nevertheless the rewards could be huge and nanomedicine, as indicated by the intense activity going on, is considered one of the winning card of nanotechnology,

The concern for the lack of a full understanding of the interaction of nanomaterials with the human body and the environment is, however, not limited to medical applications, but it refers as well to their preparation, handling and widespread utilization. The great majority of the experts acknowledged the rising awareness for the potential hazards associated with nanomaterials and highlighted the need of a thorough investigation on this matter because it is a shared opinion that a slack approach of this problem could hinder (or even jeopardise) the success of nanotechnology.

The research in this field is thought to be a priority, together with a transparent discussion and information about benefits and risks (and the actions to keep them under control), in order get public acceptance.

A continuous effort on basic research is considered also pivotal. The understanding of the relationships linking structure, properties, behaviour and processing at nanoscale is essential to guide research and the development of applications.

According to the experts participating in the Delphi panel, when science/research (i.e. academia) is taken into consideration, the competitive position of European nanotechnology in the three above sectors is considered generally good, in some cases also excellent, respect to the rest of the world.

With industry, on the contrary, the opinion is less straightforward and depends from the type of enterprise or sector considered. Big enterprises are generally perceived to compete rather well with other countries in all sectors but energy where except, may be, solar cells, both big industries and SME's get a lower rating.

Innovative SME's and start-ups in the medical sector are generally considered in good or satisfactory position, with cases of excellence, while in the material sector the situation turns out more mixed.

The roadmap exercise has also pointed out that the good or excellent position of European science has difficulties to be translated into a comparable position of the European industry. A gap between the very well-positioned European research and the European industry is what most of the experts perceived, regardless of the specific topic considered.

An improvement of the cooperation between the two world is considered essential as well as an improvement of the process of technology transfer.

The vast majority of the experts agree on the need, in principle common to the three sectors, of the creation of multidisciplinary centres with advanced knowledge on materials development/application and their own pilot production facilities. These centres will favour cooperation, make it possible the access to needed sophisticated equipments, help to transfer research results into products, scale up production processes in line with industry requirements and safe, train people. Both academia and industry, most of all SMEs, will benefit.

A strengthened support from the EU and national governments, both through coordination efforts and promotion of collaborative projects is another fundamental requirement for a competitive development of European nanotechnology which is pointed out from the roadmaps.

In conclusion, many challenges and bottlenecks, most of them common to the three sectors, have to be overcome within the next ten years to bring to the market successfully the applications envisaged.

They are both technical and economic and the **PRIORITY REQUIREMENTS** are summarized below:

1) Fundamental research for understanding structure-property-processing relationship at the molecular level;

2) Computer modelling and simulation at the nanoscale;

3) On-line tools for characterization, process monitoring and control; metrology;

4) Developing a standard regulatory framework and common approval procedures;

5) Identify and pre-develop materials, applications and capabilities that respond to the stringent needs of mass production, thus reducing the risk associated with their development;

6) Production up-scaling;

7) Improving collaboration between academia and industry and technology transfer;

8) Provide education and skills both for young researchers and co-workers;

9) Answer to the increasing concerns regarding HSE issue;

10) Foster transparent discussion and information with all the stakeholders about benefit and risks of nanotechnology.