Roadmap Route:

NANOTECHNOLOGY AND DUTCH OPPORTUNITIES

This roadmap covers the whole of planned activities in the field of nanotechnology in relation to activities within the HTSM roadmaps and other top sectors for the period of 2012-2020 and is part of the Innovationcontract of the top sector HTSM. The proposed innovations items have been determined in close consultation between industry concerned, knowledge institutes, government and social institutions.

1.1 Societal and economic relevance

Nanotechnology plays an important role in the Dutch innovation landscape. The Netherlands has invested heavily in nanotechnology over the last ten years. Even at an early stage the Netherlands adopted a pro-active stance in relation to nanotechnology by initiating various national programmes. As a result, it has acquired a high level of knowledge and an excellent position in the international field of nanoscience and nanotechnology. Despite the small size of the Netherlands, Dutch Nanotechnology publications are very frequently cited, and in terms of filed patents on nanotechnology the Netherlands takes seventh place globally.

Opportunities for the Netherlands in the different areas of nanoscience and technology are focus on several generic and application areas. Generic research themes in the field of nanotechnology important for the Netherlands are nanoelectronics nanomaterial science, sensors and actuators, nanofabrication and bionanotechnology. The most important application areas are life sciences, food & nutrition, energy, and water. Nanotechnology can help solve societal challenges such as the ageing population, climate change, food for a growing population and clean water.

Within the nine defined top sectors, nanotechnology is mainly positioned in the 'High Tech Systems & Materials' (HTSM) top sector. Due to the multidisciplinary character of nanotechnology, the top sectors 'Agro-Food', 'Energy', 'Life-Sciences', 'Chemistry' and 'Water' are of interest as well. The cross connections with other top sectors gives the social embedding and contribution to the societal challenges. In table 3 the cross connections between the several top sectors are given for the presented items and priorities in this roadmap.

Competitive position of Dutch Industry

Nanotechnology is important to Dutch industry. At least 13 of the top 20 companies intensely involved in R&D perform research in the field of nanotechnology. Furthermore, the number of companies actively engaged in the nanotechnology sector is growing.

The high tech systems sector, including Philips, NXP (semiconducting components), ASML (equipment for lithography), ASM International N.V. (leading supplier of semiconductor process equipment) and FEI (high-resolution microscopy) are the biggest industrial players. In addition, DSM and Akzo Nobel are active on the market of nanomaterials and *coatings*. In addition to these companies, the role of the Holst Centre, interacting between industry and academia, have to be mentioned.

The number of nano-related projects in industry is growing fast by approximately 10% per year (2007-2010 indication Agentschap NL). Also, since 1998 MESA+ (the nanotechnology institute in Twente) alone has to date over 45 spin-offs in the domain of nanotechnology. Examples of starters (including the *spin-offs* of knowledge institutes) are Mapper Lithography (semi-conductor equipment), Micronit Microfluidics ('lab-on-a-chip devices') and Aquamarijn and Fluxxion (nanosieves for foodprocessing), Medimate (lithium detection in blood), LioniX (devices based on MEMs) and SolMateS (large area functional materials and nanostructures).

Global Market size addressed

The global position of Dutch nanotechnology activities and development is difficult to quantify. Leading countries in nanotechnology are the US, Germany, and Japan. Figure 1 shows a 9th position on government funding of nanotechnology. The Netherlands, being a small nation, is not comparable to the large nations in terms of absolute numbers, but can still be specified as an important player. As is often the case, the Netherlands is the largest player among the smaller nations. On nanoscience the Netherlands belongs to the top three worldwide, together with Switzerland and USA.

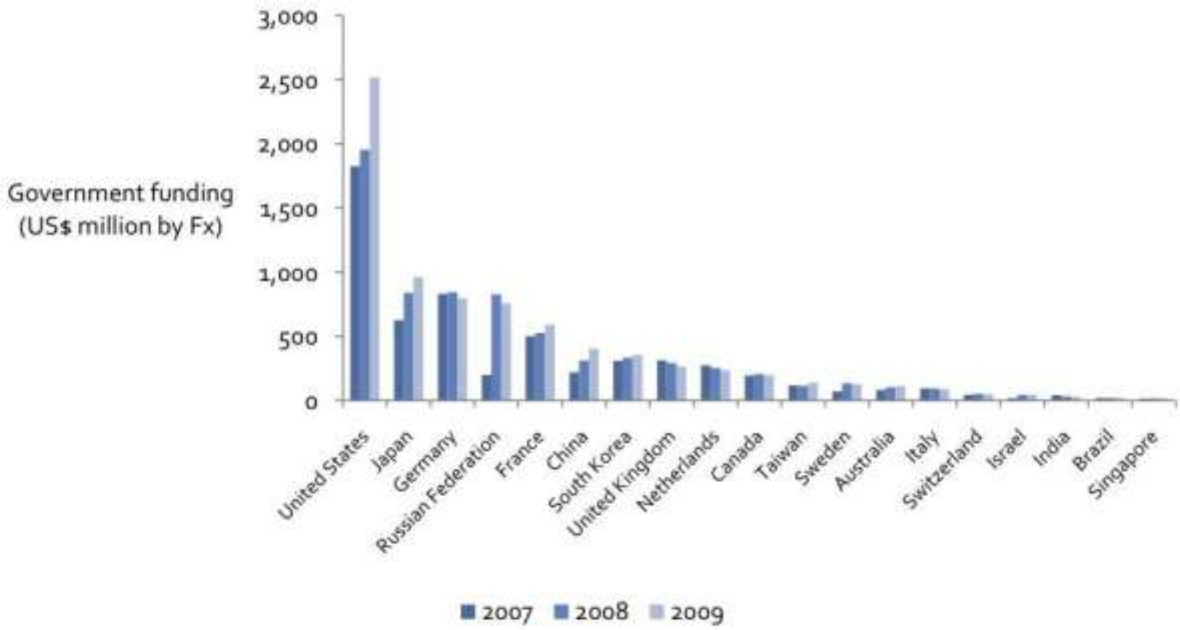


Fig. 1 Government funding of nanotechnology (source: LUX Research 2010)

A recent study carried out by LUX Research 'Ranking the Nations on Nanotech' (2010) shows that Dutch nanotech activity is high. At the same time, the report concludes that the Netherlands scores low on technology development capacity and strength. As a result, the research agenda of NanoNextNL shows a stronger link with industry, aiming to significantly improve this position (LUX Research 2010).

1.2 Application and technology challenges

The Netherlands is at the forefront on the science and technology on nanotechnology. Thanks to the proactive activities in industry as well as in academic institutes and science foundation's (NWO) the Dutch position worldwide is outstanding. The challenges in nanotechnology are set out below. Starting with the strength of the industry, as well as the academic and infrastructure position a overview is given of the nanotechnology highlights in the various top sectors. This results in the top priorities for the Netherlands in the different items that are indicated as most important for the innovation of nanotechnology in the next 15 years.

State of the art for industry and science

The first-class position of the Netherlands in nanoscience and nanotechnology was achieved by investing in the best Dutch research groups and simultaneously providing excellent laboratory facilities within NanoLabNL.

Bibliometric research about the scientific output on nanotechnology over the period 1997-2008, commissioned by Technology Foundation STW, shows worldwide first rate scientific quality of nanotechnology research in the Netherlands. The number of Dutch publications on nanotechnology increased from 700 per year in 2005 to above 950 per year in 2010. The number of citations increased in the same period from 18,000 to 38,000 in 2010 (ISI, Web of Science).

The number of personal grants (Spinoza, Simon Stevin Meester, ERC Advanced Grants, VICI) in the field of Nanotechnology is remarkably high.

The first tranche of NanoNed-funded PhD students has been very successful in finding employment in industries in the Netherlands (ASML, FEI, Holst, Philips, NXP, etc.), with 45% going into industry and 45% continuing at knowledge institutes, thus showing the importance of Nanotechnology as part of the Human Capital Agenda.

More than 100 companies, of which 80 are SMEs, are participating in NanoNextNL, both in cash and in kind.

Infrastructure and open innovation

By combining research in the area of nanotechnology within the NanoNed, MicroNed and NanoNextNL consortia, a strong basis has been laid for nanotechnological research in the Netherlands, as well as its practical application and the dissemination of knowledge. NanoLabNL is a high-quality nanotechnology infrastructure, comprising four centres: the MESA+ Institute for Nanotechnology (in Twente), the Kavli Institute of Nanoscience Delft and TNO (both situated in Delft), the Zernike Institute for Advanced Materials (in Groningen) and Nanolab@TU/e (in Eindhoven). NanoLabNL belongs in the roadmap of large Dutch infrastructures.

The availability of excellent national laboratory facilities is necessary to attract, educate and keep hold of excellent scientists for ground-breaking research.

Valorisation initiatives, such as the High Tech Factory in Twente, promote a shared production facility that aims to establish a pilot production infrastructure and organisation for nanotechnology-based products. A shared production facility is essential in order to guarantee continued growth and to retain these companies.

In addition to NanoLabNL, the knowledge infrastructure in the Netherlands is formed by academic research laboratories and private research facilities.

The European Nano landscape

The European Union budget of €3.48 billion reserved for nanotechnology research in the 'Seventh Framework Programme' (FP7) for the period 2007 to 2013. FP7 bundles all high tech research initiatives together with the objective of increasing growth, competitiveness and employment. The programme is one of the key pillars of the European Research Area (ERA) and is coordinated by the European Commission. For nanotechnology, the European Technology Platforms (ETPs) and the Joint Technology Initiatives (JTIs) covered by the FP7 are of great importance. In 2009, €17.9 million (5.8%) of the FP7 funding was allocated to the Netherlands.

The first call for proposals for the next Research and Innovation programme (HORIZON 2020) will be published in 2013. In general terms, there will be 3 main blocks under HORIZON 2020:

- Excellent science (27.8 billion), including nano-science
- Industrial leadership (20.3 billion), including nanotechnology
- Societal challenges (35.9 billion)

1.3 Priorities and programmes

This roadmap *Nanotechnology in the top sectors* gives an overview of the challenges of nanotechnology in knowledge and innovation in the Netherlands. The roadmap is based on the strategic research agenda of the Netherlands Nano Initiative (NNI) that was drawn up at the request of the Dutch Government. It identifies the generic research themes and application areas that are crucially important for the Netherlands as a knowledge economy and for its global position. It describes the Dutch research scene in the area of nanotechnology and sets out the research programmes that can give the Netherlands an advantage over other countries. Furthermore, it outlines the options for attaining valorisation by setting up communication channels between knowledge institutes and companies. The proposed innovation items have been determined in close consultation between the industry concerned, knowledge institutes, government and social institutions. For a list of all participating industries as well as institutes see Appendix 2. For this, the industrial partners known to be active in nanotechnology (>80) were consulted together with the theme coordinators (representatives of industry involved with the application areas in NanoNextNL), leading scientists and the captains of science in the top sectors. Note that the items are complementary to the programmes that run in, e.g., NanoNextNL and NWO-NANO. The items and priorities presented are the technology challenges for the period 2012 to 2020.

Table 1: Items and priorities identified for the period 2012-2020

Items	priorities
Nano-materials	nanostructured materials and structures with novel functions/applications
Nano-sensors	dynamic systems, packaging, reliability, selectivity, sensitivity
Nano-actuators	position and motion control, placement of nano-objects, up-scaling and integration
Nano-biology	biological functions from molecule to cell
Nano-mechanics	mechanics of nanostructured materials and their interaction with molecules, optics and electronics
Nano-fluidics	towards single-molecule control and manipulation and sustainable technologies
Nano-electronics	quantum- and nanodevices of functional materials
Nano-tools	detection and visualization of (dynamic) processes in a wide range of the electromagnetic spectrum and in a variety of environments at the nanoscale
Nano-optics	control, understanding and application of light at the nanoscale
Chemistry of nano-architectures	self-assembly, nano-assemblages, interfacing with nanoparticles, functional properties
Solar energy	heat generation, fuel production, quantum dot structures
Wind energy	self-healing, self-cleaning materials
Energy storage	hydrogen storage, batteries
Nanomedicine	disease diagnostics, targeted medicine, drug delivery
Molecular imaging	disease-related biomarkers, nanoparticles for MRI or MPI
Biosensing & diagnostics	lab-on-a-chip, point of care, nanofluidics,
Clean water	sensoring, catalytic methods, fouling reduction, re-use of salt water, desalination
Food & nutrition	nano-emulsions, nanostructering of proteins, filtering & separation
Food & detection	nano-sensors, RFID

Cross connections

The priorities mentioned above are cross connections with the following top sectors and their societal relevance. This table also shows the connection with risk-analysis & technology assessment.

Table 2. The cross connections of the identified items that have priority in the nanotechnology roadmap.

	HTSM	Food	Life Science	Energy	Chem	Water	Risk & TA
Nano-materials	■	■	■	■	■	■	■
Nano-sensors	■	■	■			■	
Nano-actuators	■		■				
Nano-biology		■	■	■	■		■
Nano-mechanics	■			■			
Nano-fluidics		■	■		■	■	
Nano-electronics	■	■	■				
Nano-tools	■	■				■	
Nano-optics	■		■	■			
nano-architectures	■			■	■		
Solar energy	■			■			
Wind energy	■			■			
Energy storage	■			■		■	
Nanomedicine		■	■		■		■
Molecular imaging	■	■	■		■		■
Biosensing		■	■		■	■	■
Clean water		■			■	■	
Food & nutrition		■	■		■		■
Food & detection	■	■	■				■
NanolabNL	■	■	■	■	■	■	■

1.4 Investments

Especially industrial stakeholders are an important part of the 'triple helix' between government, industry, and academia. Industrial partners have the ability to capture knowledge, execute commercialisation and reinvest revenues. The number of companies within the field of nanotechnology has grown significantly since 2000. Over 10 new spin-offs are started annually in the area of nanotechnology.

The following PPS programmes are active in nanotechnology.

NanoNextNL

NanoNextNL covers most R&D activities in the Netherlands in the field of nanotechnology. NanoNextNL is a consortium of more than a hundred companies, nine knowledge intensive institutes, six academic medical centres and thirteen universities. Various stakeholders collaborate in fundamental as well as applied research in research projects. NanoNextNL is expected to grow into an open-innovation ecosystem, with new partners joining the consortium. Industry commits to continue its support to NanoNextNL after 2015.

The total investment in NanoNextNL for the period between 2011 and 2015 is approximately €250 million. €125 million is funded by the consortium; the other €125 million consists of public investments from Dutch natural gas revenues. Founded in 2011, NanoNextNL is the largest nanotechnology programme in monetary terms and number of contributors in the Netherlands.

NanoLabNL

The NanoLabNL programme provides the necessary knowledge infrastructure to conduct high tech nanotechnology research. The state-of-the-art facilities (cleanrooms, equipment, offices, etc.) and the close proximity of research hubs in the Netherlands, makes NanoLabNL a unique platform for collaborative nanotechnology research. The total (BSiK + FES) budget of NanoLabNL was €74 million apart from the investments by host institutions/knowledge institutes.

The nanotechnology facilities are open for use by external organisations. On average, 100 companies spend an annual €2.5 million in cash and over €10 million in kind on nanotechnology in NanoLabNL.

Point One

The Point One programme was launched in June 2006 with the main ambition to expand the Dutch high tech industry by 50% from 2005 to 2013. (NL Agency, 2010) Research within this programme is strongly focused on applications and product development.

This integral public-private financial and organisational programme consists of collaborative projects by companies and research institutes that cover the research fields of nanoelectronics, embedded systems and mechatronics.

The Point One programme activities were funded by the industrial partners, the Dutch Government (NL Agency in particular) and the European Commission (EC). The total public-private investment in the Point-One programme reaches €800 million up to 2011. The programme includes the Dutch participation of industry and knowledge institutes in international R&D consortia under the European Eureka clusters Catrene and Itea2, and the European Joint Technology Initiatives (JTIs) Eniac en Artemis. The estimated share of nanotechnology research in these R&D consortia is 50%.

The following scientific programmes and associated grants, that are relevant for nanotechnology, are:

NWO/STW

STW has the following nanotechnology programmes: Open Technology Programme (OTP), Perspective, Partnerschip and Valorisation Grant (a total of €10 million/year). Most financed projects have industrial partnership, typically 25%. In the Partnership Programme this is 50%.

NWO/FOM

FOM has the following programmes on nanotechnology: Projectruimte, Industrial Partnership programme. In addition FOM has research institutes that make investments in nanotechnology (institute Rhijnhuizen, Amolf) (a total of €15 million/year).

NWO

Till 2014 the NWO-Nano programme ‘fundamentals on nanotechnology’ runs with an annual budget of €2.5 million. Researchers within the nanotechnology domain are very successful in the ‘vernieuwingsimpuls’ (VENI, VIDI, VICI). Furthermore, since 2000, 8 Spinoza awards are in the field of nanotechnology.

EU

The companies, universities and research institutes taking part in 7th framework EU-programmes, of which some programmes are managed by the Dutch partners. Dutch researcher on nanotechnology are very successful in the starting and advanced ERC grants (on average 4 starting and 2 advanced ERC grants/year).

In 2013 the first calls for proposals for the next Research and Innovation programme (HORIZON 2020) will be published. In general terms, there will be 3 main blocks under HORIZON 2020: Excellent science, Industrial leadership, and Societal challenges. Nanotechnology is included in all three blocks.

The EU will start with 10-year flagship programmes with an annual budget of €100 milion. Within nanotechnology a flagships on "Graphene science and technology for ICT" is proposed. A bidbook has been published about graphene opportunities in the Netherlands, in order to obtain national support and commitment for Dutch participation in this Future and Emerging Technologies flagship.

Topconsortium voor Kennis en Innovatie (TKI)

It is proposed that the 'roadmap nanotechnology in the Top sector' will be formulised in a TKI. Because most parties are already organized within NanoNextNL, and the aim of this initiative to set up an eco-system in nanotechnology for the Netherlands, this governance structure will form the basis for the TKI-Nano. As a consequence, the existing foundation NanoNextNL will be extended with new parties that joined in this roadmap.

Table 3: The annual budget for nanotechnology. Blue stands for cash, orange for in-kind contributions. The budget includes FES-NanoNextN. The total for nanotechnology is given as well as the part that will be linked to TKI-NANO. For a detail description, see annex 3.

Finance → **↓ Execution**	Comp (incl NNL)	State /TNO+	State /NWO	State /other	Univ	EU
Univ /TKI	**20**		**30**	**5**	**60**	**15**
University	**30**				**50**	
TNO+ /TKI	**4**	**15**				
TNO+NLR						
Comp /TKI	**50**					**5**
Comp						
Int'l R&D						
Total M€/yr **Nano**	**104**	**15**	**30**	**5**	**110**	**20**
Total M€/yr **TKI**	**74**	**15**	**30**	**5**	**60**	**20**

In addition, the different regions of the Netherlands are to invest in nanotechnology in the coming period (2012-2020) as well. Most of these investments are for the purpose of supporting local industry, including R&D for institutes.

ROADMAP NANOTECHNOLOGY IN THE TOP SECTORS

Nanotechnology is considered to be the main technology of the 21st century. This is based on the - as yet - unknown opportunities created by nanotechnology, but mainly because the expectation is that nanotechnology will provide a major contribution to resolving several global problems, such as the energy issue and worldwide public health.

In the early years, the semiconductor sector was the main driving force behind nanotechnology. Microelectronics is experiencing a progressive process of miniaturisation. It has become possible by means of lithographic techniques to create constantly smaller structures for the production of computer chips. Over the past thirty years the density of transistors on a chip has doubled every eighteen months. This is known as *Moore's law*. This principle will come to an end sooner or later, increasing the need for new ideas and technologies. This new era in electronics is what we call 'beyond Moore'. Nanoelectronics will use energy much more efficiently by applying light as an information carrier or by using plastic electronics. Nanotechnology will be *the* technology in the near future that will give *High Tech Systems & Materials* new impulses. Starting with the semiconducting industry, such as equipment to produce chips based on nanostructures (ASML, ASM International), microscopes to visualise and manipulate nanostructures (FEI) as well as consumer electronics (NXP).

In the previous decade, nanotechnology and biology have become increasingly closer bed partners. Living cells are full of 'machines' constructed of protein molecules and other nanometre-sized structures. Physicians, biologists and technicians are therefore increasingly seeking inspiration in biotic systems for their research and for designing applications. On the other hand, nanotechnological developments can utilise new research methods, techniques and instrumentation to provide impetus to biomedical and medical research. For example, through a 'lab-on-a-chip' which can easily analyse the composition of minute quantities of bodily tissue in a fraction of the time: the basis for molecular medicine. Further possibilities include the development of new medicines, the early detection of viruses, the control and administration of medication, and intelligent surgical equipment. For that reason, this roadmap will include both public and private sector participants from the medical and healthcare sectors.

Recently, mankind has been more able to manufacture materials with absolute minute proportions. It is therefore becoming possible to exploit the special properties of nanomaterials. Materials that have been modified with the help of nanotechnology lead to more efficient solar cells, fuel cells and batteries. There are also environmental applications (catalytic convertors, membranes), applications in data storage (quantum dots, multiferroics) and data transport (photonic crystals). The use of low-energy nanomaterials will help to resolve the major global problem of energy consumption. Examples are low-energy data processing (computers, mobile phones, the Internet). The Netherlands has already established an international reputation in this area and many Dutch companies (multinationals, SMEs) are focusing on these new materials.

Nanotechnology is making an entrance in various application areas, ranging from food, health and energy to water purification, for example. The application of nanotechnology will help to resolve various social problems, the creation of high-quality employment and the performance of innovative scientific research.

This is the reason why nanotechnology is important in different top sectors and special attention has been given in this roadmap to showing the possibilities of nanotechnology in the short term as well as the medium and long term.

Top sector High Tech Systems & Materials

The Netherlands is renowned for its excellent expertise in the area of fundamental and strategic technologically-relevant research into device-oriented phenomena at nanometre scale. The Netherlands has a history of ground-breaking high-tech research and industrial activities (e.g. Philips, NXP, ASML, ASM International NV), which are now also being implemented in innovation programmes like Point-One. This roadmap takes up the challenge to realise medium to long-term innovation within nanoelectronics. The guidelines that apply are as follows:

- Ground-breaking research into specifically chosen *enabling technologies* will ensure the creation of generic knowledge, guaranteeing a continuous stream of ideas for achieving innovative applications.
- Programme lines conceived on the basis of specific *application areas* ensure the development of new applications, motivated by social and economic boundary conditions, confronting fundamental research activities with new long-term challenges.

Nanotechnology will play an important role in almost all roadmaps within the top sector HTSM. In some cases nanotechnology will be even essential. We can divide HTSM into three main subjects: materials, devices & components, and systems & equipment.

Materials (advanced nanomaterials)

Materials technology is a crucial enabler for many of the required innovations to challenge the problems facing mankind over the next 50 years: health, energy, environment, food and mobility. The successful development of new solutions mostly depends on cost-efficient functional/structural properties and cost-efficient processing technologies. The materials used in all cases critically influence the cost of processing and the resulting properties. Ultimately, new products will require new materials as the options to improve properties or reduce costs become exhausted. New materials can bring forward new options for processing and properties, and thus can lead to paradigm shifts. The necessity to produce materials that allow paradigm shifts is the key challenge in materials technologytoday . The evolution of materials technology has arrived at a point where we are beginning to be able to build materials starting from particles, molecules and atoms. This sometimes leads to unexpected and unpredictable properties, but will always create a wealth of options for innovative products in all domains.

The tasks to be completed in order to fulfil the above challenge are still numerous. It is essential to come to new technologies to better organise the material structure, while it is also essential to much better understand the development of the relation between material structure and properties during the entire production chain. This is fully in line with 'The Roadmap of the European Technology Platform for Advanced Engineering Materials and Technologies' which states that "Materials technology shall be a major success factor for European industry influencing the competitiveness of not just material technological industry but practically all industrial sectors. Investments in materials provide possibilities to succeed in global markets and to create new spearhead technologies and products thus improving the employment in Europe". Part of this section coincides with the nanomaterials mentioned in the roadmap of M2i.

Recent developments in the field of the fabrication and characterisation of objects at the nano-scale make it possible to design and realise new materials with special functional properties. For example, materials can be strengthened or, conversely, made more flexible, or materials can be given greater electrical resistance and lower thermal resistance. The possibilities are virtually endless, particularly in relation to the coupling between living cells and specific functional nanoparticles, nanosurfaces or nanostructures. Artificially inserted (an)organic particles or surfaces can influence a cell to the extent that it takes on an entirely new functionality, such as fluorescence or magnetism. Insertion of these particles or surfaces in cells may even result in the production of new biomaterials. Conversely, proteins, viruses or cells can be processed into nanosystems. These couplings open up many new scientific and commercial avenues.

It will be obvious from these examples that the field of 'nanomaterials' is extremely broad and that it is set to reoccur in all other subjects, particularly as a part of integrated activities aimed at the realisation of specific applications, for example, in devices. Yet, it is still important to pinpoint nanomaterials as a separate subject. It is precisely this concentration of research into materials on the one hand and the multidisciplinary approach on the other hand that has resulted in new applications in which nanomaterials play an essential role. Building new materials at the atomic scale and structuring or combining existing materials (*metamaterials*), resulting in entirely new characteristics of these materials, make the application area virtually limitless. The scientific/technological challenge ensuing from the frequently large number of requirements that devices are expected to meet, demonstrates that this type of material research occupies an important position within NNI.

In addition to nanoparticles, nanostructured surfaces are also playing an increasingly important role in nanotechnology. Treated surfaces can adopt various properties, such as becoming hydrophilic or precisely hydrophobic. The interaction with (living) cells and viruses also has applications, for example in lab-on-a-chip, i.e. a device that integrates one or several laboratory functions on a single chip.

Devices & Components (nanoelectronics)

Moore's Law has dominated developments within information and communication technology (ICT) for several decades. Technological roadmaps anticipate that the number of transistors that can be fitted on a silicon chip surface will double every two years. This development has changed our society in an unprecedented fashion. Our life is now inconceivable without mobile communication, intelligent consumer electronics and the Internet. It is anticipated that the exponential growth of semiconductor technology will grind to a halt within a decade. The reason is that the production technologies are confronted with fundamental boundaries whereas circuits will be so small within the foreseeable future that the current principles will no longer apply.

Further to the advancing miniaturisation in the ICT industry, requirements exist for new functions as well as for the integration of various functions on the surface of a single chip. New concepts within nanotechnology lend themselves extremely well to contribute to this future development. By implementing new optical, electrical and magnetic phenomena at nanometre scale, as well as the engineering of structures on an atomic and molecular scale, new applications will become available of great social and economic significance. This revolutionary development is coined with the phrase *'Beyond Moore'.* This will serve to redefine not only the possibilities of the hardware itself, but also the interaction between man and technology and the social implications. To achieve future breakthroughs it is essential to provide evenly balanced support for ground-breaking scientific research, as well as for application-oriented activities; the two can work closely together and remain in tune with the social and economic context. A good example is the discovery of graphene, which is considered as a new building block for the next generation of nanoelectronics.

A great challenge of the era 'Beyond Moore' is the manufacture of complex new structures using cheap methods, such as replication through stamping techniques, using the self-assembly of molecules.

The 'nanoelectronics' roadmap is in keeping with the research agendas of ongoing initiatives in the Netherlands and in Europe. With ENIAC, the European Technology platform. The 'More than Moore' activities are also given prime billing on the Point-One research agenda. The European platform on 'Smart Systems' (EPoSS) targets 'More than Moore', which is the integration of various complementary technologies for the realisation of 'Systems in Package'. The 'Beyond Moore' research mentioned in this roadmap generates fundamental building blocks for the aforementioned agendas. It is therefore sure to link up to industrial initiatives in the region and with any project opportunities at European level.

The coming decennia will see an increase in specific, targeted data collection to facilitate knowledge-founded decisions and operations in industrial production, food processing, healthcare, or environmental protection alike. Sensors are the essential first elements in this data collection and information-processing chain because they detect the primary information about the status of an object or situation in a specific measurement and transduce it into a processable signal. Sensors are therefore of uttermost importance for society and for maintaining and facilitating innovation in Dutch industry. Robust systems will be able to utilise these benefits even in harsh environments and field applications in remote areas. Easy-to-use systems will enable personalised healthcare, which increases the efficiency of medical treatments and helps to reduce costs. Moreover, they also give underprivileged people in remote areas access to modern medicine. (E.g. low-cost AIDS diagnosis in Africa).

The recently developed and experimentally established, fundamental understanding of phenomena taking place between different entities at the nanoscale enables collecting new, up to now unavailable information about these entities and their immediate environment. This fundamental understanding will become a major driver for the development of new types of sensors that will show unprecedented performance in terms of robustness, reliability, costs, and breadth of information. A typical example for healthcare is the detection of minute amounts of biomarkers for certain illnesses at an early stage; while highly selective gas sensors are essential for environmental monitoring, or nano-mechanical measurements in process control, to give just a few examples.

The sensor selectivity will excel through very specific interactions among molecules like in antigen-antibody type of reactions, or direct interactions between fields or molecules and nanoparticles, -wires, -membranes or -pores, which together form the primary transducer element. Surfaces and interfaces will need to be treated, i.e. structured, chemically functionalised and organised at the corresponding length scale to host and facilitate the primary transducers. Special attention will be needed to translate these interfacial processes into a measurable signal. One possible path is for example that the interfacial process changes the conductivity of an underlying or imbedded electron channel.

A typical measuring system will comprise many different sensors, have a large degree of autonomy, local intelligence, and communication means. This is achieved for instance with energy harvesting, wireless power delivery, and maintenance-free decentralised systems.

The sensors will be integrated into systems that will react on the measurements. For this functionality different kinds of micro- and nano-actuators will be needed. These actuators, for example, have to open and close gateways, valves, and direct small mirrors in adaptive optical systems, or remove (cut or drill into, chemically dissolve) material in remote operations.

Next to the actuation as reaction on sensor information (feedback) micro-actuators will also be applied in feedforward situations where the action is based on indirect information and reliable models. Once it comes to settings that are different from switching type of operations, power and efficiencies become important issues. Think of locomotion and pumping through, for which nano-actuators will provide mobility at the micrometre and nanometre scale. This will become a key competence, also in processing. For example, precise and small amounts of materials (solids, liquids or gases) must be transported to/through sensor columns, injected into reactors or deposited on surfaces. Transporter devices equipped with functionalised cargo-bays transfer material with high selectivity across an otherwise leak-tight barrier or membrane, which allows active, highly efficient separations or process intensification. Energy consumption, speed of throughput, controllability, and longevity will be important performance parameters.

Besides the primary task of sensing and actuating, systems architecture and integration needs to fulfil demands on compactness and simplicity in order to increase reliability. The packages for sensors/actuators often already form more than 50% of the component costs. Hence, the capability of integrating the active elements into full, packaged systems that can be economically manufactured, will be decisive for the leading edge in the exploitation of this aspect of nanoscience.

Systems & Equipment (nano-patterning & nano-inspection)

As nano- and microtechnologies are playing an ever more important role in products serving a wide variety of markets and applications, nanofabrication is an essential part of the innovation chain from ‘concept’ to ‘economic activity’. Especially in nanotechnology, it is almost impossible to design a product or process without taking nanofabrication, patterning, inspection and characterisation possibilities into account. Nanofabrication is one of the few thematic areas which is really strongly coupled to the flourishing high tech equipment industry in the Netherlands. This sector of the Dutch economy has in recent years exhibited a strong growth and a strong ambition to grow even further. The strength of the high tech equipment industry in the Netherlands is based on a combination of outstanding scientific excellence of a number of academic groups, several (large) corporate players who are market leader in their field, and a group of smaller (start-up or spin-out) companies.

Technical challenges in the field of nanofabrication are large and numerous. Making and characterising structures with sub-100nm dimensions, the scale on which fabrication and inspection has to be controlled, is nearing 3D atomic dimensions. The development and use of the equipment requires more and more scientific understanding at the atomic scale as well. The main technology challenge can be formulated as follows: *How can we understand and control the physics and chemistry of fabrication and inspection within the enabling equipment at atomic dimensions.* Two general research topics can be distinguished: modelling of beam/material interactions for both patterning (electron or photon-induced) and inspection; and using nano-technologies to make critical equipment parts such as (nanostructured) multi-layer UV mirrors for use in future highly advanced X-ray spectrometers, multi-beam electron lenses or SPM tips.

For the semiconductor industry it is important that the new nano-inspection methods have a sufficient throughput to play a role in manufacturing. This challenge in itself yields interesting scientific questions

Beyond the drivers in this field coming from the semiconductor industry, there is a great scientific interest to find new methods for making individual nanostructures, or small series: ‘nanoprototyping’. There are both process challenges (the use of He and electron beams, dip-pen technologies, imprint, etc.) and equipment challenges.

Application and technology challenges on cross connections

Nanotechnology will be at the very basis of many future products. Examples can be found in future computing and data handling, which will benefit from advances in nano-electronics as well as new quantum computing and information processing techniques and optical data transfer. The latter will be facilitated by a profound understanding of nano-optics. New nanosensor systems which combine fundamental knowledge on nanomechanics, nano-optics, nanoelectronics, nanobiology, and their interactions will penetrate in daily healthcare and health monitoring. New pharmaceuticals can be developed by virtue of future nano-imaging systems and cell-on-a-chip technology. These pharmaceuticals will be nano-engineered faster and, ultimately, without animal tests. These are just a few examples that illustrate how a comprehensive fundamental understanding enables new, innovative nanoproducts. Hence, new nano-technological knowledge paves the route towards an extremely wide spectrum of applications with tremendous social, environmental and economic impact. Due to the complexity of nano-technology, fundamental research typically requires 10-15 years before it translates into real products. Integration of these new nano-technological functions into products will greatly benefit from already well-established technological platforms, e.g. for microfluidics and integrated optics.

Besides the multi-disciplinary character of nanotechnology, the fundamentals of nanotechnology encompass the profound understanding of quantum effects and the manipulation of quantum systems such as single charges, spins, photons, phonons, and plasmons. At larger scales, the fundamental aspects of nano-sized particles, nano-structured surfaces, interfaces and materials need to be unravelled. Interactions between mechanical motion, magnetic, optical and electric fields need to be understood at the nano-scale. At this scale interactions cause structures, electromagnetic fields and fluids to exhibit completely different behaviour as compared to their microscopic and macroscopic counterparts. Interfaces between engineered materials and living materials impose major fundamental scientific challenges which need to be addressed.

At the nano-scale one faces the challenge to manipulate nano-sized entities, e.g. the manipulation and testing of individual, atoms molecules or particles and their interactions. Moreover, nano-sized entities must be manufactured. Nano-scale manipulation, testing and manufacturing rely on a solid understanding of physics, chemistry and biology and the knowledge on how to combine and unleash this knowledge for manipulation at the nanoscale.

Nanotechnological research will rely more and more on analytical and computational models. The fundamentals of the nanotechnology are the starting point for new computational modelling and engineering tools which will help cost-effectively designing future nanodevices and systems. The development of these computational tools requires substantial fundamental research.

Top sector Chemistry

Chemistry is one of the basic disciplines of nanotechnology. In addition, chemistry is a strong industrial sector where new nanotechnological applications find their way and applications in the other top sectors are supported. The recent developments in the field of the manufacture and characterisation of nano-scale objects allow the design and synthesis of all sorts of new molecules and materials with special functional properties. The possibilities are virtually unlimited, especially when it comes to links between biological materials (molecules, cells, tissue) and nanoparticles, nano-surfaces or nanodevices. Nanotechnological materials can achieve selective links with biological material, focusing on biological detection and/or biological influence. The chemistry plays an essential role, in particular the supramolecular chemistry and biochemistry.

Applications include the detection of diseases at an early stage, healing, or producing of new biomaterials. Vice versa, proteins, viruses or cells in nano-systems can be processed. These links offer many scientific and commercial points.

In addition to research on macromolecules such as DNA, research is increasingly taking place on peptide and protein-based nanomaterials. Nanomaterials built from proteins can be used for surface modification and the covalently attaching of specific ligands or medications. Also, such materials are biodegradable and metabolically active. Nature has found ways to create biological nanostructures from molecules such as proteins and lipides. Mimicking nature delivers nano-machines that can be used, for example, for biological detection technology and/or influencing biological systems.

The value of new nano-architectures follows from the technological features that can realise the materials. That is why the development of new molecules and nanomaterials goes hand in hand with the development of methods for studying the nanotechnological functionality of the molecules and materials. The nanotechnological methods are highly developed, for example in single-molecule techniques, single-cell techniques and super-resolution microscopy. One of the major challenges in the field of nanotechnological research methods is the ability to determine in detail the functionality in complex biological systems, such as in blood plasma, in living cells, or tissues.

It is important to have an integrated research approach focused on both the development of new nano-materials and new methods to quantify the nano-functionality in complex samples. An integrated approach will provide the basis for applications in molecular diagnostics, Molecular Pathology, regenerative medicine and targeted drug delivery for example.

Top sector Energy

Never before has humanity faced such a challenging outlook for energy and the planet. This can be summarised in just 5 words: "More energy, less carbon dioxide". In meeting this challenge we can no longer avoid three 'truths' about energy supply and demand:

1. A step change in energy use. Developing nations such as China and India are entering their most energy intensive phase of economic growth as they have started to industrialise on a major scale, build their infrastructure and increase their use of transportation. Demand pressures stimulate alternative supply and more efficiency in energy use – these are necessary but not sufficient to offset growing demand tensions completely.
2. Supply will struggle to keep up the pace. By 2015, growth in the production of easily accessible oil and gas will not match the projected growth in the rate of demand. While energy from coal is an option for India and China (as well as the US), transportation difficulties and environmental degradation will put stringent limits on its use. Alternatives, like bio-fuels may become a significant part of the energy mix, but there will be no silver bullet that will solve the demand challenge.
3. Environmental stresses are increasing. Even if the current dominant role of fossil fuels remains in the energy mix, the impact it has on carbon dioxide emissions would pose a serious threat to human well-being – globally. This of course in the context of the fact that energy availability is at the basis of all economic and societal activities, be it food production, water purification, healthcare, or other activities.

It is generally accepted that these 'truths' will remain valid for a significant time to come, even despite a temporary relative slowdown in the current economic climate. Up to now, world economic growth has been strongly coupled to (the ability) to increase the use of fossil fuels. Indeed, the underlying key technical challenge may be to achieve a transition to a world in which economic growth is uncoupled from fossil fuels. Such would be a world "more of electrons than of molecules". For example it would provide transport by electric vehicles, power generation by more renewable energy sources (e.g. solar and wind) or coal plants implemented with affordable carbon dioxide capture and storage technologies as well as increased efficiency in energy use. To realise this, breakthroughs are required in energy generation and storage capabilities, efficient energy conversion processes, and carbon dioxide separation technologies.

The development and application of nano-based technology in the energy sector is a relatively new but rapidly emerging development. This field is much more in an explorative stage than most other developments in nanotechnology, including the areas addressed in the 'Strategische Research Agenda Nanotechnologie'. This is mainly due to the complexity and scale of the technical challenge inherent to the energy transformation alluded to above. Indeed, among leading politicians and industry decision makers the 'Energy Access, Supply and Usage question' will play a significant if not dominant role on the agenda of national technology innovation and development programmes in many economies around the globe. For example the new US Administration has allocated funds of several tens of billions USD to stimulate technology development addressing specifically the 'energy question' and it has asked Nobel prize winner - and now also Secretary of Energy Dr. Stephen Chu - to give this top priority.

Indeed it has become clear that a transition towards a world that is less dependent on fossil fuels is an unparalleled scientific challenge. Even at this early stage it has become clear from scientific and technology developments achieved so far that nanoscience and nanotechnologies will play an important role in all these aspects. Indeed one could argue that such technologies hold the unique promise to play a pivotal role in achieving higher and more efficient energy storage and supply – crucial for e.g. electric means of transport to become attractive on a mass scale, as well as for more efficient energy storage and conversion of renewable sources of energy. Also the role of nano-technology in affordable carbon dioxide capture and separation processes that would allow for example the retrofitting of conventional power plants, will play a key role in future power supply processes.

One application in which the role of nanotechnology is steadily growing is energy provision. Both through the development and improvement of conversions, such as natural gas converted into diesel, and sunlight converted into electricity or hydrogen; such as through the miniaturisation of electronic control systems for an intelligent Energy Internet.

The storage of electricity in batteries or in hydrogen has much to gain from developments in nanotechnology (particularly catalysis, ion conduction and hydrides). In addition, nanotechnology can contribute to a more economical use of energy. For example, by developing lighter materials and LEDs (light emitting diodes). The main economic growth market of nanotechnology in this field lies in energy-saving technologies by using more advanced materials, added to the more obvious points of new materials for energy storage via battery technology, hydrogen storage and fuel cells.

Important progress is expected from solar energy in the longer run, for example by quantum-dot structures that can greatly improve the yield. Research is taking place in the area of the Grätzel solar cell, a cell based on nanoparticles, and into organic solar cells. New colourants, such as biodyes, will need to be found in order to increase the yield.

Nanostructured materials, such as membranes, find their application in the separation of gases (for example, carbon dioxide and pervaporation) or the influencing of bacteria in biomass processes.

Applications of nanotechnology in the realm of energy provision often involve material sciences. One example is the research into intelligent (or energy-generating) windows, for which applications are envisaged in solar energy. The development of materials that can absorb hydrogen for storage, or materials with oxygen permeability for fuel cells. Reinforced and/or lighter-weight materials can be applied in turbines and vanes used for wind energy. Wear-resistant materials will contribute to the durability of moving parts and hence will also be accommodated within the energy-saving theme.

The transition to sustainable energy management is a particularly long-term process, requiring the application and improvement of existing technologies for energy generation (more precisely: energy conversion), distribution, storage and use, as well as the development and implementation of new technologies. Nanotechnology will play an important role in both categories by improving the performance or reducing the costs of existing technologies. Furthermore, it will also form the basis of entirely new systems, with the promise of excellent performance and/or very low costs. In addition, nanotechnology can create new application possibilities and improve durability.

Top sector Life Sciences

The growing number of elderly people – not only in the affluent countries of North America, Europe and Asia, but also in upcoming economies, like China, India, Russia, and Brazil, as well as the continuing overall growth of the world population drives a strongly growing demand for healthcare. At the same time, our lifestyle habits, unhealthy diets and less and less exercise, lead to a more than proportional growth in chronic diseases. Driven by obesity, Type II Diabetes, for instance, is reaching epidemic proportions in some countries. Improvements in therapeutic drugs, which are able to contain previously incurable cancers and neurological disorders, also drive the growth of the chronically ill. The constant struggle to control the exploding costs of the healthcare system, while satisfying the increasing demand, and at the same time improving the quality of care poses an insurmountable problem to the future of healthcare. Moreover, many countries experience difficulties in making available sufficient and qualified hands. At the same time patients become more vocal and demand more information on and insight into their condition so that they can participate in their own cure and care process, and a higher level of treatment, and – in some countries – are willing to pay for that.

A recent analysis of the US Institute for Health Improvement concludes that "Many healthcare systems around the world will become unsustainable by 2015. The only way to avoid this critical situation is to implement radical changes…". Nanomedicine is an important gateway to radical change, and as such provides both a tremendous economic opportunity *and* addresses an answer to one of the main societal challenges.

Nanotechnology allows the characterisation, manufacturing and manipulation of matter at basically any scale, ranging from single atoms and molecules to micrometre-sized objects. Since diseases typically originate at the biomolecular and cellular level, at the length scale of 1-100 nm, nanotechnology precisely addresses the 'holy grail' of healthcare – early diagnosis and effective treatment, tailored to the patient with minimal side effects. At the nanoscale, man-made structures match typical sizes of natural functional units in living organisms, facilitating their interaction with the biology of these organisms, enabling novel opportunities for (targeted) therapy and diagnosis. Furthermore, nanometre-sized materials and devices often show novel properties, e.g. as a result of quantum size effects, which may lead to unexpected applications. Finally, nanotechnology enables the miniaturisation of many current devices, resulting in increased sensitivity, faster operation, the integration of several functions, and the potential for high-throughput approaches, enabling operation at decentralised locations. The integration of devices and structures built with nano-sized building blocks in microsystems facilitates interaction with the macroscopic world. The resulting products, which take advances from both nanotechnology and microsystems technology, hold the promise to provide breakthroughs in healthcare, leading to paradigm shifts in clinical approaches within the areas of preventive medicine, diagnosis, therapy and follow-up.

For example, in the case of neurodegenerative diseases the burning scientific question is to understand the role of early-stage nanoscale supramolecular aggregates in neuronal death. Which species in a heterogeneous spectrum of aggregates is involved in disease pathways, and how do they exercise their toxic effects? Similarly, in cancer, which of the multiply redundant signal transduction pathways is the most suited for signalling pathway-targeted therapy? Answering these questions requires a detailed understanding of biomolecular interactions at the nanoscale, a challenge uniquely suited for the nanotechnology toolbox. Successfully addressing these questions will undoubtedly require new technical advances and additions to the nanotechnology arsenal, be it in ultrasensitive detection approaches, in the platform technologies used for visualisation, or in the generation of new nano-probes and tools for sensing and probing specific interactions.

The societal relevance of the theme Nanomedicine and Integrated Microsystems for Healthcare is primarily determined by the tremendous anticipated impact of the products, which may be created as a result of the projects. The changing demography of the Dutch population as a result of the double ageing process and the baby boomers, which are starting to reach retirement age, put a significant strain on the healthcare system. The topics addressed in the theme offer breakthrough solutions to alleviate these strains through technologies enabling prevention and early diagnosis of disease, personalised and more effective targeted treatment and inroads into regenerative medicine. The focus on important diseases is strengthened and focused by the active involvement of researchers in academic medical centres. The theme both includes projects involving broadly applicable technology-driven projects and a large number of projects dedicated to important clinical questions in cancer, cardiovascular diseases, neurodegenerative diseases, inflammatory and infectious diseases,

Nanomedicine not only provides an answer to the challenges in healthcare, it also offers a tremendous commercial opportunity. Healthcare represents the largest global service 'industry', with annual revenues in the order of 4 T$, with a number of area's showing large growth rates, far beyond a single digit, and 'recession-proof'. These 'granules of growth' in the healthcare industry coincide very well with the subjects covered by the theme Nanomedicine and Integrated Microsystems. Molecular diagnostics, for instance, shows a healthy 15% cumulative annual growth rate, CAGR, with a present global revenue of about 4 B$. Dutch industry is in a very good position to benefit from the research programme, and, subsequently, to bring products to market. Particularly Philips is a leader in medical technology with a global footprint, and core R&D and production facilities in the Netherlands. NXP is a leading semiconductor company, Dutch-based, but also with world-wide activities. A large number of SMEs are involved in all aspects of the science and technology related to Nanomedicine and provide a fertile ground for the generation of economic and knowledge capital.

Top sector Water

Currently, over 1 billion people worldwide do not have access to reliable water sources. This has overwhelming consequences that demand technology-driven solutions. Nanotechnology can contribute to water-related challenges in roughly three areas: separation processes, catalytic processes, and sensoring.

Separation processes that exploit nanotechnology can be developed for water cleaning strategies. Membranes remove particles, micro-organisms and organic matter from water. Using nanotechnology, ultraprecise membranes can be fabricated with even more accuracy, increasing their selectivity. The tunability of pore size allows one to discriminate on retention behaviour. Nanoscale fabrication provides access to exploit charge-based interactions very effectively. Related to ionic separation processes, major advancements are still required in connection with increasing the productivity of drinking water. Especially the purification of water in regions lacking adequate drinking water should be considered. This means that the technology should be based on economic processes. Detailed fundamental insight into charge-based separations are nevertheless crucial in order to design these technologies. Next to membrane-based separations, the use of nanoparticles or coatings for selective adsorption can be exploited for water cleaning. Adsorption capacity and kinetics benefit from small characteristic length scales. Further use of functional particles, e.g. magnetic or electronic, allow for novel separation processes.

Catalytic processes for water cleaning exploit the activity of nanomaterials for selective conversions. Components that are challenging to remove but are harmful at already low concentrations include pharmaceuticals and hormone residues, pesticides, and endocrine disruptors. Chemical routes to remove these unwanted components are currently inadequate due to unwanted by-products and limited selectivity. Heterogeneous catalysis exploits the unique properties of nanoparticles to convert harmful components completely into harmless species.

Sensoring is another area where nanotechnology contributes to clean water. The measurement and monitoring of water quality is an important research and development activity. Guarding water quality by fast detection of pathogens and toxic components is a societally-important and relevant requirement. Current detection strategies do not provide adequate methods at this moment to meet this need. Nanotechnology is extremely efficient for fast and selective detection of even the smallest amounts of contamination.

Top sector Agrofood

A significant number of research topics in the Agri-Food sector are depending on the understanding of material properties in terms of the ingredients, which become specific on molecular (nano-) scale. Since the conditions that are relevant to food and nutrition vary from making, transporting, storing, consuming to digesting, the aforementioned understanding is required in terms of ingredient composition and concentration, energy input, temperature and time. The connecting link is the structure that exists between the macroscopic and nano-scale.

Health

The composition of our daily food intake has a great impact on our personal health and well-being. The reality is that our modern food consumption has led to overweight, obesity and various related chronic diseases like diabetes. On the one hand, it is responsible for the rapidly growing costs in the healthcare sector, on the other hand, this offers opportunities for innovative companies to produce smarter food by making products that contribute to the support of specific bodily functions.

Demographic ageing will be a fact in the coming decades. Also in this respect is it clear that companies at the interface of nutrition and care have new challenges to come up with products that meet the latest insights in the field of healthy nutrition. This means that such foods at the same time have to meet the stringent requirements that the consumer requires, in the areas of taste, convenience and food safety. Together, this constitutes an enormous technological challenge. Nanotechnology can help in a number of areas to meet this challenge.

Encapsulation of nutrients is an application which uses nanotechnology to create capsule walls that offer new opportunities for releasing the capsule's contents. With this technique it is possible to encapsulate certain ingredients in micro-or nano capsules. These capsules ensure that there is no reaction with the environment or that the substances remain in the product and thus prevent unpleasant taste, and that the substances are released where they have the most effect. Nanomedicine is a clear link here, where the use of medications can be applied much more accurately and faster, for example not through digestion or injection, but through the lungs or the skin.

Safety

The safety of food has never been so superior in industrialised countries as it is now. However, there is always room for improvement. Data on doctors visits and hospital admissions show that people can eat the wrong or contaminated food. Nanotechnology enables us to faster, more sensitive and more specific measure and determine whether there is a safety problem with certain food products. Nanotechnology will definitely play a role in the packaging industry. The objectives in this respect are longer storage times of food products and more information about the quality of the packaged food. The application of RFID tags (Radio Frequency IDentification labels) will be extended with direct information about the product or outlining the route from the production site to the consumer. Nano-structured membranes can be used for the measured administration of liquids, gases and medicines, among other things, or for filtering bacteria or enzymes from liquids.

Nanotechnology brings an innovation wave in the processes required to produce foodstuffs, far beyond incremental improvements. One example is the use of sieves for removing bacteria from products and to pasteurise them in a chilled condition. In the long term, nanotechnology may even be able to make a contribution to better meat substitutes based on vegetable proteins.

There are many applications of nanotechnology in agriculture. Examples are: sensors for greenhouses, reflection coatings in greenhouses and encapsulation of pesticides and fertilizers for optimal issue. In wider (High Tech) perspective, there are various interfaces between the Top sectoren agriculture and High Tech, such as Robotics, embedded systems, high throughput systems, measurement and control systems, etc. Sensors that can measure volatile substances or viruses and therefore have the possibility to detect much faster.

The Netherlands scientific community and the food industry are at the forefront of the research and developments with respect to the application of the micro- and nanoscale scientific results to food products and processes.

The application of nanotechnology in food and health offers clear advantages, also for the individual consumer. Cold sterilizing food with sensitive ingredients, programmed and in the time phased issuance of taste-and odor substances, advanced local preparation of food, are just a few examples of the possibilities that should be studied and developed in the future.

NanoLabNL

NanoLabNL is the national facility for nanotechnological research and development. It provides an open-access and full-service infrastructure for R&D in nanotechnology. NanoLabNL offers the use of its facilities and expertise at attractive rates to universities, research institutes, start-ups and industry at four locations in the Netherlands. Each of the NanoLabNL locations offers a range of basic and expert techniques. The basic techniques provide a general infrastructure suitable for routine nanofabrication activities with the lowest possible geographical barrier, while expert techniques are unique facilities and/or expertise you are unlikely to find elsewhere in the country.

The NanoLabNL consortium partners are MESA+ NanoLab Twente (Enschede), Kavli NanoLab Delft (Delft), NanoLab@TU/e (Eindhoven) and Zernike NanoLab Groningen (Groningen). TNO is a NanoLabNL partner, investing and collaborating with the Kavli NanoLab at the Delft location. Philips Innovation Services is an associate partner, participating in NanoLabNL in terms of content. All NanoLabNL facilities are open to all NanoNextNL partners, as well as external users.

NanoLabNL is a valued and valuable national nanotechnology infrastructure. The decision to make use of only a limited number of research laboratories and to make them accessible to all researchers, both public as well as private, has proven extremely effective. NanoLabNL creates, maintains and provides access to a coherent, high-level, state-of-the-art infrastructure for nanotechnology research and innovation in the Netherlands. NanoLabNL brings about coherence in national infrastructure, access, and tariff structure. Alongside the various open innovation initiatives, the Netherlands offers a unique infrastructure which needs to be kept up-to-date.

Governance

The NanoLabNL organisation consists of the board/foundation, steering committee and programme office. The NanoLabNL programme office is managed by STW. The NanoLabNL foundation will be established in 2011. The foundation's goals are:

- to realise the micro and nano research facility ambitions;
- to facilitate and stimulate current and future nano-related research;
- to stimulate the open access character of the high tech nanolabs;
- to connect up with national and international research programmes; and
- to increase external use by companies.

The board consists of at least five members, four representatives of the NanoLabNL locations, and a seat for a representative from industry.
The NanoLabNL steering committee is continued, including its tasks:

- implementing the infrastructural investment;
- carrying out the agreements reached between the parties on access and pricing;
- managing PR strategy;
- ensuring a sound account of the policy and the resources spent on the management of NanoLabNL;
- the optimisation of cooperating with other industrial facilities in the Netherlands.

In order to keep a competitive advantage and a worldwide leading position additional funding will be required in the near future. A rough estimate of the total investment and operating costs for about 10 years (2013-2022) is in the region of 210 M€.

NanoLabNL is part of the Dutch Infrastructure on Large Facilities and a request for continuation has been submitted.

PRIORITIES AND PROGRAMMES

A more detailed description of the priorities on nanotechnology within the different top sectors is given below.

Materials (advanced nanomaterials)

Nanomaterials - Nanomaterials and nanotechnology is assumed to reveal many opportunities in almost any (industrial) domain. Further development of this technology will bring many new applications and functionalities to benefit from in our society. One main research issue however is the safety aspect of nanomaterials and nanotechnology. This has also been recognised by the European Commission. Examples include nanostructured materials for nanocatalysis and photocatalysis, plasmonics for PV, graded thin films for SSL, and phase change materials for energy storage.

Smart materials - Smart or intelligent materials, like nanomaterials, show a great development in new applications. All kinds of smart functionalities can be added to materials on different length scales (nano, micro, meso, macro) in order to create special properties. Examples are drug delivery on demand, selective measuring and sensor techniques in the personal healthcare domain (e.g. lab-on-a-chip technology), photonic sensor materials for process control and the monitoring of ageing, self-healing and debond-on-command materials, flexible foils for electronic devices such as OLED and PV, printable electronics, and switchable optical materials.

Surface modification - Many surface modification techniques are available to give products or moulds and dies special properties. Apart from coating, cladding and thin film techniques, surfaces can also be modified by direct laser treatment (e.g. 3D micromachining) or the implantation of nano particles. A variety of these surface modification techniques are included in the various sub-roadmaps.

Technical textiles - Nanotechnology is one of the drivers for improved technical textiles. Nano fibres, nano particles and nano surface engineering will add new functionalities to many applications. This calls for the further development of advanced production technologies. For example plasma and laser treatment, pick and place robotics and inkjet technology will play a key role in the introduction of new products to the market. MEMS and conductive polymers are another example in this respect.

Graphene - Graphene is pre-eminently an enabling material and has numerous potential applications, such as electrodes for flat panel displays, touch screens, RF devices, MEMS, photo-electronic sensors, flexible electronics and CMOS replacement. It is a relevant topic for multiple Top sectors: High Tech Systems and Materials (HTSM), Energy, Life sciences en Health, Water and Chemistry. The Top sector HTSM covers most of the topics for which graphene can be an enabling material and/or of which graphene is an integral part. A special 'Graphene Flagship' bidbook has been published about the possibilities for graphene in the Netherlands.

Devices & Components (nanoelectronics)

Autonomous sensors and sensor systems - Interfacing: wireless powering of and data-transfer from/to large systems, energy harvesting; systems architecture, system control and reliability; local signal and data processing; maintenance and regeneration; packaging, fabrication and deployment;

Degree of freedom and dynamic range - Large multi-parameter systems for fingerprinting;

Materials and fabrication technology for sensing - Graphene, carbon nanotubes, diamond and other nanowires and their functionalisation and integration; low cost, printable sensors; large (waver) scale / high volume sensor production;

Packaging - Wafer-level packaging of complete systems; new packaging materials and processes, (accelerated) testing;

New Sensors and Sensing Principles - For measuring in nanofluidic systems: flow-rates, concentrations of chemical or nanoparticle or nanobeads, electrical, magnetic or optical properties, or fluorescence; THz detection and imaging; magnetic sensing and steering at the nanoscale; noise processes at the nanoscale; Quantitative measurements at the zepto-molar level; the whole transduction chain needs to be considered, which requires systems engineering and integration;

Reliability, Robustness, and Recovery, Regeneration - Stabilisation of functional surfaces and protection against poisoning and other environmental influences, self-cleaning and self-healing of sensor surfaces; applicability in highly complex biological environment (in vitro/in vivo); long-term stability and its accelerated testing, self-testing, self-calibration; CMOS-sensors and sensors integrated on CMOS electronics for harsh environments, packaging; very specific binding events often have a strong k-on but a weak k-off, hence the recovery of the sensor is an issue which needs to be investigated for the continuous operation of sensors;

Selectivity - Exploiting lock-key type molecular interaction, local functionalisation of surfaces by organic or polymeric monolayers, by peptides (antibodies), by biomolecular receptors, by (inorganic) material contrasts; nano-porous selector devices, functionalised zeolites;

Sensitivity - Single particle (molecule, photon, nanoparticle,...) detection at very low concentrations or intensities; up-concentration and 'fishing' concepts; quantitative and traceable measurements; interfaces to electronic signal processing;

Mobility at the Micro/Nanoscale: Transporter, Conveyor - Study and control of the carrier-cargo interaction, release of the cargo; requires research on interfaces especially when mobility is extended to an area outside a confined, protected environment; integration of the transporter into a frame or infrastructure, for example a micro- and nanofluidic system; pumping of fluids and propulsion of objects in micro- and nanochannels;

Transduction of Electrical Signals and Energy Supply into Motion / Placement / Change in Position - At nanometre scale classical actuators based on magnetic fields are no longer efficient. In that case, electric field or thermally sensitive materials take over the task of motion with piezoelectric, electrostatic, molecular and phase change actuation. These actuators exhibit quite different properties that have to be well understood in order to be able to design a well-balanced integrated system.

Wireless energy transfer at nanometre scale differs from large-scale systems and concepts using (bio-) chemical fuelling may offer advantages.

The forces of the transducing field relative to the mass of the objects can become problematic and add to other physics-oriented forces like van der Waals and Casimir forces. Utilising extremely high frequencies and balanced capacitive transfer could tackle these problems;

Position and Motion Control - Local integrated control is the only way to be efficient when controlling motion at the nanometre scale. New control principles are needed to provide this functionality with a minimum of added complexity and power consumption. The related high bandwidth may require pure analogue control, which gives an additional constraint on sensitivity;

Placement of Nano-Objects - Inkjet printing is well established at the millimetre to micron scale, where it will become the de-facto standard for high-speed flexible creation of both two and three-dimensional objects. Since fluids are attractive carriers for nano-objects, inkjet inspired/derived techniques have to be studied for accurate placement of nano-objects. The ever-increasing requirements on diversity, complexity and density may be addressed by electrospraying;

Up-scaling and integration - Integration of nanoscale and molecular actuators in an infrastructure, accessibility and controllability from the macro world; macro scale effect of up-scaled nanoactuators.

Systems & Equipment (nano-patterning & nano-inspection)

Nano-patterning - Main drivers continue to be the fabrication of ever smaller structures at an ever increasing speed. 'Smaller' now means sub-20 nm however with precision and accuracy down to 0.5 nm. In addition, the need has arisen for much more flexibility as many more types of substrates, materials and processes are being explored in very different nanotechnology domains. This means that besides extreme UV lithography-based processes, also direct-write technologies will play a larger role. Beam / matter interactions have to be modelled extensively to anticipate the desired resulting structure. in the area of macromolecules we can use stamping techniques to manufacture nanostructures efficiently and cheaply. For applying lab-on-a-chip, instruments are also needed that are capable of working with either minute volumes or extremely small signals.

Double and multi-exposure techniques must also be mentioned. With plasma enhanced atomic layer deposition (PEALD) high quality layers can be produced at significantly lower temperatures.

Nano-inspection - The major challenge is not only to probe at atomic resolution (which can be done by electron microscopy or scanning-probe microscopy tools), but to achieve that in realistic conditions. This will mean adding capabilities for e.g. very fast or near real-time imaging, 3D structure determination, adding property-measurement to mere structure and composition, and probing under conditions relevant to the user, for instance in liquid or atmospheric pressure rather than in vacuum.

As an example, small-angle X-ray scattering (SAXS) is a technique that is used for the structural characterisation of solid and fluid materials in the nanometre (nm) range. This probes inhomogeneities of the electron density on a length scale of typically 1-100 nm, thus yielding complementary structural information to XRD (WAXS - wide angle X-ray scattering) data. It is applicable to crystalline and amorphous materials alike. Some typical applications comprise the determination of nanoparticle and pore size distributions of specific surface areas and the structure analysis in inhomogeneous (e.g. core-shell) particles. The technique may also yield information with respect to the aggregation behaviour of nanoparticles.

Nanobiology: biological functions from molecule to cell

Nano biomaterials - Controlled assembly of molecular, lipid-based and polymer networks with new functional and mechanical properties. Creation of artificial vesicles or cells.

Bioelectronics - Electronic interactions on chip surfaces with living biomaterials, biomembranes or even living cells, under the influence of controlled environments. Bioelectronics as a building block for future organ-on-a-chip research.

Nanobiology - Achieving a molecular basis for complex biological functions (incl. cause and development of illnesses): from molecule to cell using nanoscale tools such as atomic force microscopy, optical and magnetic tweezers, fluorescence microscopy. Mechanical properties of cells.

Biochips – Nanofluidic systems with integrated sensor arrays for medical diagnostics. Nanofluidic sampling and storing for off-line analysis, nanofluidic systems for studying organ-on-chip interactions.

Bionanoimaging – Using sub-wavelength super-resolution microscopy to map out molecular structures and interactions within living cell.

Nanomechanics: mechanics of nanostructured materials and their interaction with molecules, optics and electronics

Nanomechanics - The interaction between nano structural motion and electrical, optical and magnetic fields. On-chip integration in nanomechanical systems.

Nanomechanics of materials - Experimental investigation and modelling of the mechanical aspects of nano-structured materials and interfaces.

Nanoprecipitates in a crystalline matrix - Improvements of the mechanical and chemical properties of alloys by optimisation of nanoprecipitates.

Nanotribology- Friction and wear phenomena between surfaces at the atomic scale. Origin of energy dissipation, role of coatings and novel lubricating nanostructures to reduce friction and/or wear, but also the opposite: Nanoglues.

Nanofluidics: towards single-molecule control and manipulation and sustainable technologies

Nanopore/nanogap/nanowire sensing - Label-free detection of molecules and their reaction in solution using nanostructures (protein-protein interaction and DNA) in combination with (near-field) optical spectroscopy.

Zeptolitre reactor - Preparation of extreme small volumina (droplets) containing a few molecules (single molecule) to study their reactions when combined with other droplets.

Nanopipette - Local deposition of small (Zepto to attolitre) droplets of reagents on surfaces to initiate local chemical reactions, material deposition for 3D nanostructuring or injecting them into cells, cell-nuclei, micelles to initiate (bio-)chemical reactions.

Nanopumps, -valves and sensors - Means to propel (pump), stop, switch directions of fluid streams, and measure their volumina, mass, flow speeds, molecular composition in nanochannels.

Nanofluidics for energy - Streaming current in nanochannels, transport through nanoporous membranes

Nanofluidics and high surface area materials - Capacitive desalination, electrochemistry at nanoscale, study of nanostructures for batteries/supercapacitors/water desalination

Nanomaterials: nanostructured materials and structures with novel functions/applications

Theory of nanomaterials - Development of new concepts and prediction of new phenomena in nano-structured materials.

Quantum Matter - Exotic states in nanostructured solids, such as topological insulators, nano-structured superconductors and nanomagnets.

3D Nanostructures - Realisation and behaviour of complex, 3D nano structures (e.g. by folding graphene and DNA origami). Control of their (electronic, optical, mechanical, catalytic) properties and interactions. Biomimetics.

Self-assembled nanostructured material and structures – Nano-structured materials, particles and structures as a building block towards nano devices and systems with unique electrical, optical, magnetic, mechanical and thermal properties.

Layered and single-layer 2D materials - The mechanical, optical and electric properties of coatings, interfaces, layered and single-layer 2D materials, for example, graphene, molybdenum sulphide, polymeric layers and organic/inorganic hybrids.

Nanoporous/reticular materials - Design, modelling, construction, synthesis, characterisation of nanoporous/reticular materials for application in separation, sensing and cascade (bio)catalytic conversions.

Surface modification in (bio)materials - Precision and control of thickness, patterning and structuring of surfaces using (bio)molecular and (bio)polymeric monolayers for biocompatibility control, multi-array sensing, affinity, etc.

Synthesis of nanoparticles - Controlled synthesis and up-scaling of inorganic, organic, polymeric and hybrid nanoparticles via gas phase and liquid phase chemistry (e.g. CVD, ALD, MLD, plasma decomposition, spark discharge, controlled precipitation, controlled reduction in nanospace (reversed micelles).

Synthesis of reporters and actuators for use in living cells – Controlled synthesis of synthetic dyes or particles with tailored properties (fluorescence, magnetic properties, etc.) that can be readily introduced into living cells to act as reporters or actuators.

Controlled hierarchical assembly of nanoparticles - Making highly organised complex structures in 2D and 3D from nanoparticles to achieve functional systems (e.g. batteries, fuel cell membranes, photo-catalytic systems, sensors, etc.).

Nano-electronics: quantum- and nanodevices of functional materials

(rather than functional nanodevices of common materials)

Quantum information processing - Use of entanglement and quantum super positions for safe information transport and computing.

Quantum Devices - Manipulation and control of the quantum state of systems using single spins, electrons, photons, plasmons, phonons; Quantum sensors - sensitivity enhanced by entanglement.

Spintronics and Magnetism - Manipulation of spin by electrical/optical/mechanical means. Magnetic particles and nano-structured materials with unique (e.g. thermal) properties. Multiferroics.

Molecular and organic electronics - Translation of molecular and organic electronic concepts into new functional electronic components.

Theory of nano devices - Development, exploration and simulation of novel devices.

High-frequency nanodevices - Electrical components operating at MHz to THz frequencies (also for remote control of nanodevices).

Nanofabrication - Patterning on the true nm scale (e.g. He-ion microscope) as well as development of large-scale processes for structures with nanometre dimensions.

Light nanoparticle interactions - Excitation, emission and charge transfer in combined nanoparticle systems.

Nano-Tools

Detection and visualisation of (dynamic) processes in a wide range of the electromagnetic spectrum and in a variety of environments at the nanoscale

Nano-imaging - Novel techniques for high resolution (spatial and temporal) microscopy in a wide range of environments, ranging from biological to UHV environments. Techniques may rely on tunnelling effects, nano-mechanical interactions, novel nanoprobes, optical spectroscopy using electron beam excitation, etc. Super-resolution microscopy (X-rays, advanced optical microscopy,...).

Particle beam-induced nanostructuring - sub-nm (Helium, Neon) particle beams with appropriate precursor gases, nano-growth and nano-etching, prototyping in the sub-5nm area, direct application in areas such as nano-bio, nanophotonics (plasmonics, metamaterials), EUV mask technology, ...

Computational Physics & Engineering - Adaptive modelling techniques bridging different length scales using *ab initio*, discrete models (e.g. molecular dynamics) and (enhanced) continuum models, among others, to study and predict nano-scale phenomena in nano devices and nanosystems. Modelling techniques are at the very basis of future computational nano-engineering tools. Complex simulations require advanced data enhancement and visualisation.

Fluctuations and noise - Effects and use of fluctuations (heat) and noise at nano scale. Applications may range from sensing to energy harvesting.

Nanosensors and actuators - Conversion of one type of signal into another at the nanoscale. Biodegradable sensors and actuators.

Nanomotors – Creation of motion at the nanoscale, e.g. on the basis of chemical energy carriers.

Nanomanipulation - Novel techniques to directly address and modify materials and structures on the nanometre length scale.

Nano-optics

Control, understanding and application of light at the nanoscale

Sub-wavelength control of light - Optics using surface plasmons to achieve deep sub-wavelength control of light. Nanoscale opto-electronic integration on a chip using surface plasmons.

Single-photon detection - Development of efficient detectors in a broad spectrum ranging from THz, IR, optical to the UV range. Applications in optical imaging, security (THz) and space research.

Nanoscale light harvesting - Controlled nanoscale confinement, guiding and conversion of light for novel LEDs, lasers and solar cells (organic, inorganic and hybrids)

Optical magnetism - Exploring the magnetic field of light at the nanoscale. Optical metamaterials.

Quantum nano-optics - Exploring quantum phenomena in e.g. light scattering in nanoscale complex media.

Light structuring - Controlling light using sub-wavelength control over the phase and intensity of light.

Chemistry

Chemistry for the construct of nano-architectures - For a further development of this area new supramolecular methods need to be created and new design principles are called for: development of nano-assemblies, functional interfacing of nanostructures with surfaces and nanoparticles, control over position, specificity, orientation and function of nano structures, the development of multivalent ligands for organic detection and for influencing cell growth, the development of probes for monitoring cellular processes, etc. Methods must also be developed to fabricate the new materials in a controlled way. In this context, it is a major challenge in supramolecular chemistry to develop a better understanding of the complex processes of hierarchical self-organisation.

Functional properties of nano-architectures studies - The development of methods for investigating the functional properties of new nanomaterials is a significant focus. Functions at the molecular scale, dynamic properties, mechanical properties, optical properties, etc. can be measured on both nano-level (individual particles and molecules) and micro-level (ensembles of molecules, particles, and cells). Quantitatively determining the functionality of new nanomaterials is a great challenge especially for supramolecular nanomaterials with a biological functionality. Examples include research into the specificity, affinity and orientation of nanostructures to molecular interactions, research on nano-probes to molecular processes of cells to quantify, and research on the function of supramolecular nano-architectures to affect biological cells.

Perspectives and New initiatives - Research on new nano-architectures and their functional effects will be a basis for applications in the following areas: early detection of diseases will be possible by Biomolecular Diagnostics with biomarker, specific supramolecular ligands producing biological materials for pharmaceutical research or for regenerative medicine will be possible by nano, architectures that specific cell growth stimulate the place, time-dependant and dosing of medicines will be possible through the development of nano-architectures for medication delivery. Molecular tissue Diagnostics (Molecular Pathology) with new nano-probes will allow cancer treatment by identifying and quantifying cellular processes.

Energy

The efficient generation of sustainable energy - Improved and entirely new types of solar cells will need to be developed for the efficient generation of electricity through photovoltaic conversion. Possible avenues for nanotechnology are quantum dot structures providing an improvement of the conversion yield by shaping the solar spectrum, the improved use of high-tech light, optimised absorption properties, etc. Moreover , nanostructured (hybrid) materials will make it possible to use very cheap (and in some cases, low-quality) materials by minimising the transport distances in the cell and through improved light housekeeping, etc.

Solar energy for generating heat - Solar collectors can be improved by applying spectral selective layers (extremely high light absorption in combination with low heat emission) or heat transferring layers (excellent transfer of heat between different media).

Solar energy production of fuels - Hydrogen is a good case in point. Nanotechnology plays a role by applying catalytically active, nanostructured materials. These materials will suppress the degradation of catalysts and improve the yield. Naturally, the trend is increasingly in favour of applying microreactors.

An important new development is the conversion of sunlight to fuel by means of integrated nanosystems based on efficient multi-electron catalysis processes derived from the photosynthesis processes in real-life nature. The fundamental challenge is to find the scales for energy, time and length in which the catalysis works efficiently, and which can be applied for making photo-anodes for separating water and photocathodes for the synthesis of hydrogen and methanol from carbon dioxide. This is dubbed 'The Artificial Leaf'. The low efficiency of biomass conversion can be improved by the direct conversion of sunlight to fuel *in vivo*. To that effect, it will be necessary to achieve an engineering platform for quantitative system biology as a foundation for the continuous improvement with synthetic biology, biobricks and hybrid systems, based on life as well as on artificial systems. This is about fundamental breakthroughs which are also extremely important for the provision of food and the reduction of water consumption in the future.

Wind energy - With this form of energy we can expect developments in 'self-healing' and self-cleaning materials ensuring a longer economic life and improved behaviour. For example, corrosion sensors will become important in sea-based wind parks.

Efficient energy consumption through the secondary conversion of energy and the separation of substances - An essential component within this topic is the study and application of nanostructured materials for separation applications, including carbon dioxide recovery and pervaporation (separation of mixtures). Nanostructured materials also form the basis for new catalysts for fuel extraction from biomass. Nanomaterials will be applied for the upgrading of cellulose (biomass from woody plants) and for biocatalysis, for the preparation of products from biomass and the influencing of bacteria to improve ethanol synthesis.

Nanotechnology for energy storage - Nanostructures that can absorb and release large quantities of heat quickly and efficiently. Nanostructures for lithium-ion batteries: extension of economic life and increase of storage capacity. Nanostructured materials for hydrogen storage as well as catalytically active materials for hydrogen production.

Anorganic and organic LEDS with extremely high efficiency - LEDS are nanostructures within which electronic power is converted into light. Nanotechnology offers opportunities to further increase the efficiency of LEDs, using economically attractive production methods.

Life sciences

Nanomedicine: from fundamental studies to advanced applications - At the most fundamental level, Nanomedicine investigates the molecular origins of disease using the nanotechnology and nanobioscience toolboxes. At a more applied level, nanomedicine explores new technologies and devices for disease diagnosis and therapy, and new approaches and materials based on nanotechnology for medical applications. Integration of the technologies and devices in microsystems is the key to connecting the products, which takes advantage of nanotechnology, to the macroscopic world.

Nanoscale studies of the molecular origins of disease - The goal of this area is to use the nanotechnology toolbox to unravel molecular mechanisms in disease, devoting specific attention to biomolecular interactions at the nanometre scale. Nanoscale imaging, including recent advances in optical super-resolution imaging and high-speed atomic force microscopy, nanomanipulation, and nanoscience and nanotechnology-based technology platforms for measuring molecular interactions play a crucial role in understanding specific molecular mechanisms involved in disease.

Molecular Imaging - Molecular imaging is a rapidly growing field that has enormous potential in many areas, including biomedical and pharmaceutical research as well as clinical management of patients suffering from major disorders. Molecular imaging is a broad term; the precise meaning depends on the context in which it is applied. In relation to nanomedicine, molecular imaging predominantly signifies the use of nano-sized objects for the in vivo visualisation and localisation of disease-related biomarkers. Nanostructures offer several advantages as they can be equipped with a high payload of contrast agent to facilitate detection and visualisation of biomarkers present in very low concentrations. Alternatively, the nanoparticles themselves can be directly visualised, such as nanobubbles with ultrasound or iron-oxide nanoparticles with MRI or MPI. The majority of the nanostructures can be loaded with therapeutic agents, enabling monitoring of the delivery of medication in the tissue of interest, or stimulus-induced drug release under image guidance. Thus, nanostructures offer many applications in molecular imaging, ranging from early detection to image-guided therapy.

Nano- and Microfluidics for Biosensing and Diagnostics - The total in-vitro diagnostic (IVD) market will grow to nearly 56 billion USD in 2012, and is rapidly changing thanks to advances in areas such as functional genomics, bioinformatics, improved surface chemistries, microelectronics, test device miniaturisation and wireless capacities. The projected fast growing worldwide market for cartridge-based near-patient testing using biosensors is expected to amount to about $4.3 B in 2012. The trend towards a demand for new, chip-based, technologies to allow point-of-care testing is demonstrated by several market analyses. Recent developments in micro/nanofluidics and their integration in Lab-on-a-Chip systems have great potential for point-of-care medical diagnostics. On the one hand, they enable the realisation of portable analytical instruments that can be used at the point-of-care, while on the other hand new micro/nanofluidics phenomena and techniques enable the analysis of all components in biofluids, ranging from various biomolecules to subcellular fragments and whole cells at extremely low concentrations.

The challenges include tailoring biomedical assays and diagnostics for compatibility with a nano- or microfluidic platform, developing widely applicable microfluidic tools and bio-sensors platforms for the realisation of lab-on-a-chip based (bio)sensors, and achieving unprecedented low limits of detection and high-speed, high-throughput parallel detection of multiple analytes, down to the single molecule level. Innovative solutions and rapid advances can be expected not only in the (nano/micro)-fluidics technologies, but also in new ultrasensitive sensing principles and detection modalities, and the ancillary processing steps, such as surface-oriented chemical biology for the immobilisation and capture of analytes.

Nano- and microfluidics technologies not only lend themselves for the detection of biomolecular analytes, but also for the study of entire cells, leading to the 'Cells-on-a-chip' concept, where cutting edge scientific research on (single) cells using micro/nanofluidics for diagnostic purposes can be combined with more applied research towards cell-analysis in biofluids.

Drug Delivery/Targeted Therapeutics - Many candidate and established drugs developed for the treatment of life-threatening and serious chronic diseases have inferior properties with consequently unfavourable therapeutic implications. Nanomedicines (i.e. advanced drug delivery systems) of a particulate or macromolecular nature are being designed to improve the therapeutic behaviour of such drugs. Nanotechnology-inspired approaches to system design and formulation, an improved understanding of (patho)physiological processes and biological barriers to drug delivery, as well as the lack of new chemical entities (NCEs) in the 'pipeline' of large pharmaceutical companies, indicate that there is a bright future for nanomedicines as pharmaceuticals. In principle, nanomedicines are comprised of a DRUG associated with a CARRIER system. The *carrier* system serves to modulate the pharmacokinetics, tissue distribution and/or target site accumulation of the drug in a beneficial way, i.e. to enhance therapeutic activity (by 'site-specific' delivery) and/or to decrease side effects (by 'site-avoidance' delivery). Novel carrier materials will need to be developed, and proof of drug delivery capability will have to be properly demonstrated. These novel materials are expected to have beneficial properties for application in patients as compared to currently used materials, for example in terms of interaction with target cells or safety profile. The challenge is to 'shape' these new carrier materials for drug delivery applications.

It is mandatory that promising nanomedicines, which are selected for clinical testing, are evaluated with respect to their preclinical safety profile. This requires close interactions with pharmaceutical and clinical scientists, pharmaceutical SMEs and majors, and toxicologists. The results will either be used to optimise the formulations and/or to decide whether the selected formulations will be further evaluated as candidates for the development of pharmaceutical products. These non-clinical safety studies are a prerequisite to obtain permission to conduct human clinical trials.

Societal and Economic Relevance - The societal relevance of the theme Nanomedicine and Integrated Microsystems for Healthcare primarily is determined by the tremendous anticipated impact of the products, which may be created as a result of the projects. The changing demography of the Dutch population as a result of the double ageing process and the baby boomers, which are starting to reach retirement age, cause significant strain in the healthcare system. The topics addressed in the theme offer breakthrough solutions to alleviate these strains through technologies enabling prevention and early diagnosis of disease, personalised and more effective targeted treatment and inroads into regenerative medicine. The focus on important diseases is strengthened and focused by the active involvement of researchers of academic medical centres. The theme includes both projects involving broadly applicable technology-driven projects, and also a large number of projects dedicated to important clinical questions in cancer, cardiovascular diseases, neurodegenerative diseases, inflammatory and infectious diseases.

Nanomedicine not only provides an answer to the challenges in healthcare, it also offers a tremendous commercial opportunity. Healthcare represents the largest global service 'industry', with annual revenues in the order of $4 T, with a number of areas showing large growth rates, far beyond a single digit, and 'recession-proof'. These 'granules of growth' in the healthcare industry coincide very well with the subjects covered by the theme Nanomedicine and Integrated Microsystems. Molecular diagnostics, for instance, shows a healthy 15% cumulative annual growth rate, CAGR, with a present global revenue of about $4 B. Dutch industry is in a very good position to benefit from the research programme, and subsequently to bring products to market. Particularly Philips is a leader in medical technology with a global footprint, and core R&D and production facilities in the Netherlands. NXP is a leading semiconductor company, Dutch-based but also with worldwide activities. A large number of SMEs are involved in all aspects of the science and technology related to Nanomedicine and provides a fertile ground for the generation of economic and knowledge capital.

Clean water

Sensoring and monitoring during process- and drinking water purification - Remote monitoring is necessary as well as the development of efficient and economic sensing equipment for the re-use of slightly contaminated domestic water.

Catalytic water cleaning strategies - In addition to separation processes, catalytic methods can be developed for reactive purification of water. Nanoparticles and coatings that display selective adsorption and catalytic activity towards removal of harmful components are foreseen as next generation cleaning strategies.

Nanofluidics for transport phenomena - In order to improve water cleaning processes in terms of reduced energy requirements, increased productivity, and reduced fouling, better understanding of the underlying fundamental principles is required.

Fouling reduction strategies in water purification processes - This includes the development of methods to measure (in situ) the accumulation of matter, the chemical en physical cleaning strategies, as well as modification strategies (e.g. coatings) to reduce fouling.

Energy from water - Contaminated water can be regenerated while simultaneously producing energy (electrical or chemical). Further development of biocompatible electrodes, selective membranes, and activated electrodes are subjects where nanotechnology can contribute greatly.

Re-use of salt water - The treatment by bioconversion under high salt concentrations, in order to re-use clean salt water or safely dispose clean salt water. Nanotechnology can provide corrosion resistant materials and surfaces that are required for these processes.

Desalination - The development of selective membranes for ion selective processes. Here, additional fundamental insight is required to understand charge selective separation processes better. Alternative desalination processes, including adsorption processes that exploit functionalised nanoparticles and coatings, are also considered.

Agro-food

Filtration and fractionation - The development of process technology components in the form of sieves and filters. Possible applications include the purification and filtration of raw materials and semi-manufactured products, fractional separation and cold sterilisation. Another possible application is equipment that replaces unhealthy components (such as saturated fats) by healthier components (unsaturated fats or fat substitutes).

Sensor/detection systems and processing - The development of sensors and diagnostic kits able to measure the quality of food faster and cheaper than existing methods, to monitor the production process and to detect microbial and other types of contamination in time. Secondly, the field engages in the *downscaling* of the production and preparation of food. This can be done in the form of devices that are operating locally, on the farm or at the consumer’s home (filtering, mixing, emulsifying, individualised food). Installing those units in parallel allows upscaling, creating flexible central production units.

Emulsions, texture and delivery systems - The manufacture of foodstuffs with a different texture and/or composition. It may be done through double emulsions (water-in-fat-in-water). It thus becomes possible to prepare ingredients with a very low fat content. Delivery systems are applied for which functional ingredients such as vitamins are released in carefully controlled doses, under control of a programme, for example during eating (aromatic substances) or in the body (delicate nutrients). In addition, improving the solubility of nutrients or medicines through nano-encapsulation can boost their effectiveness.

Nano-emulsions - Traditional emulsions have a droplet size of around 1 – 100 μm; they are – literally – milk-fed. If the drops created are smaller than approximately 100 nm, the emulsion is completely transparent, while the properties become different. The stabilisation of such an emulsion has different requirements than those of conventional emulsions: the strong curvature of the surface plays a major role. In this example, very poorly soluble components (e.g. vitamins) can be solved in concentrations many times higher than their maximum solubility in oil, and have a very high bio-availability.

Nano structuring of protein products - Dense aggregates of proteins, for example, with a specific size smaller than 1 μm can be merged to macroscopic structures via deformation (shear banding). By interaction of these aggregates accurately, a variety of granular materials can be obtained: fibrillair, solid or fluid. Mono-disperse particles will be prepared and their behaviour studied under flow, particularly in highly concentrated suspensions (> 20% overall protein content).

Packaging & Logistics - This topic is approached in two different ways. The first approach focuses on ingredients for the improved wrapping of food, for example to protect it against oxidation or light. The second one couples the packaging to sensors and/or RFIDs. Sensors can point out the status of the product in the packaging and, where possible, even correct it in combination with actuators. RFIDs can carry data about the composition, origin and/or actual status of the food (such as vitamin content or hardness of fruit).

RISK ANALYSIS AND TECHNOLOGY ASSESSMENT

Nanotechnology is a typical example of a new technology in which technological innovation is progressing so fast that it is leaving information on safety too far behind. This leads to uncertainties regarding the potential risks for humans and the environment. There is no specific approach for how to best deal with these uncertainties. Recently, in a letter to the Lower House, the Dutch Cabinet stressed that it attaches great importance to the development of nanotechnology because of the opportunities it presents for economic growth and the response to societal issues. In this respect the Cabinet strives to realise an integral approach towards nanotechnology policy in which the developments must be in balance with risk control. Doing this could utilise the opportunities in a responsible fashion.

Dutch position

Meanwhile, the Netherlands has gained itself a prominent position in Europe in the field of research into the risks of nanotechnology and the societal impact. Even in the early stages the Netherlands recognised that the number of research questions were many and urgent. In addition to our own research attention has therefore been focused on (inter)national harmonisation and collaboration such as in the OECD context or in the 7th Framework Programme of the EU.

Reducing the uncertainties concerning the risks in the most efficient way is achieved through collaboration and/or coordination between stakeholders, trade and industry and science.

Whereas discussions among stakeholders often focus on uncertainties regarding the risks of nanomaterials, attention is also given to the possible consequences of nanotechnology in the field of privacy for instance, the manipulability of human beings and shifts in the markets. If we are to achieve responsible development it is important that we anticipate the societal impact. Otherwise the danger can arise that unforeseen consequences of nanotechnology could stand in the way of development.
A responsible development of and the ultimate entry into the market for nanotechnological products can only be realised if the potential risks for humans and the environment have been sufficiently examined. These potential risks arise as an effect of exposure to nanoparticles or as a result of using such products.

Current bottlenecks and future-proof

When researching the risks we can differentiate between three significant themes:

1) how can sufficient insight into the risks of nanomaterials be obtained as efficiently as possible within the present regulatory frameworks. This is of particular importance with regard to products that are already on the market or are close to being launched;

2) how can the acquisition of such insight be accelerated and

3) how can the pace of research into the risks be brought more into line with the speed of innovation?

With regard to the first theme it is important to know what the validity and applicability of existing testing methods are for nanomaterials. Investigations must also be carried out into how the current risk assessment methods can be optimised for nanomaterials within the existing frameworks.

The second theme is chiefly driven by the fact that risk assessments still have to be made on a case-by-case basis because of the lack of extrapolation possibilities between files. It is in the interests of all stakeholders that meta-analyses with extensive databases are used as much as possible in order to gain insight and thus expand the extrapolation potential.
The third theme mainly relates to the fact that the pace of innovation has constantly increased, and is consequently widening the gap between that and the speed at which information on the risks involved can be gathered. Solutions will need to be sought to

bring these two rates of speed closer together without making any unacceptable compromises in terms of risk assessment quality.

However, there are still some significant bottlenecks that make risk research and the assessment of the results of that research problematic. For instance, there is a great need for simple, inexpensive and reliable methods to demonstrate the presence of nanomaterials in various matrices. The recently published recommendation for a definition of nanomaterials calls in the short term for a method that allows particle sizes to be measured.

As yet there has been relatively little attention given to research into the risks of nanoparticles vis-à-vis the budgets for technology development. In conformity with the dynamism of new technologies, attention – both national and international – has mainly been focused on developing the technology. Considering today's wide range of fields of application, plus the fact that there are numerous products now being developed as well as products that are already on the market, it is essential that we have an insight into the risks for workers, public health and the environment. Uncertainties about the risks will stand in the way of the valorisation and implementation of this technology. Moreover, it can lead to (unnecessary) social unrest and consequently a lower acceptance of this technology among consumers.

The research questions at hand are many, and selecting those to be taken up in the Netherlands can be done via different routes. Considering the multitude of questions involved, investments must be made in both substantiating research and exploratory research and should therefore be put on the research agenda. Furthermore, the starting point taken should be that opportunities must be present for expanding those expertises for which the Netherlands has a good/excellent basis and including research into the risks of nanoparticles.

The impact that nanotechnology will have on society is difficult to forecast exactly but it is certainly quite possible to anticipate the potential consequences. With the further development of nanotechnology new economic opportunities could evolve in the future, new political interests could emerge and new moral dilemmas could arise. Especially in the cross-areas of generic themes and application areas is such anticipation essential and will need to become an integral part of research programmes. Assessment and scenario studies are of the essence here; studies in which researchers, entrepreneurs and social scientists work together.

As stated earlier, broadly-based fundamental research should be made use of in the first instance. However, the research programme must provide opportunities - on the basis of progressing developments - to tighten up the programme in terms of specific application areas and to obtain a higher forecasting value. The following research lines are prioritised on the basis of importance as well as on the presence of outstanding expertise in the Netherlands:

Measuring methods and measuring equipment – There is a great deal of uncertainty regarding the exposure of individuals (exposure at work, consumers) and the environment to nanoparticles. This means that equipment will need to be developed to measure emissions and exposure at the individual level for instance. Measuring methods will also need to be set up in order to determine those particle properties of relevance for defining the relationship between dosage and (eco-)toxic effects. It is absolutely essential to establish norms and the certification of equipment for measuring exposure to nanoparticles. Interaction between risk-researchers and the developers of measuring equipment will contribute to products that are expected to be easy to market.

Dosimetry – It is still not possible to determine the units to be used to best describe the dose. To achieve this, studies must be conducted into which particle properties best define the dose. A strong multidisciplinary approach between chemists, mathematicians and (eco-)toxicologists is essential in this respect.

Toxicokinetics/behaviour of materials – Information about the behaviour of nanomaterials is apparently of major importance to make a sound assessment of the risks for humans and the environment. To what extent are the particles absorbed, in what part of the body do they end up in, how long do they remain there? Research must focus on gaining insight into how the various particle properties influence the actual behaviour of those particles in humans and the environment. This type of research however also demands that particles can be measured in a variety of tissues and matrices. Development of measuring methods must be given attention.

Dosage-effect relations for humans and the environment – There is an increasing number of indications that nanomaterials have the potential to accumulate in different tissues. This implies that so-called repeated dose testing is necessary, but it also implies that in vitro tests must be examined critically as to their applicability for nanomaterials.

Risk assessment and implementation in regulatory measures – Can the available methods and assessment strategies also be used on nanoparticles? Extrapolation of data on particles of an average 50 nm, for instance, to a different size is out of the question for the time being. In practice this means that each particle size of a substance should be regarded by the regulatory bodies as a new substance with an accompanying toxicological file. It would also imply that a separate standard would need to be set up for each particle size. This is an undesirable scenario for any stakeholder. Moreover, research focusing on the possibilities for extrapolation contribute to a faster and more efficient acquisition of insight into the risks of nanomaterials. For instance, from its involvement in various activities in REACH, the Netherlands already has a good basis.

Risk-benefit analyses – Transparent methods for weighing up the risks and the benefits will be crucially important in order to get consumers to accept nanotechnology products in the long term.

Safe by design – Within the framework of sustainable development, possibilities are more frequently being sought to distinguish particles with a relatively high level of toxicity at an early stage of development. By doing this an attempt is made to innovate along the line of functional, low-toxic materials in order to prevent risk-reducing measures as much as possible.

Annex 1: Participated partners

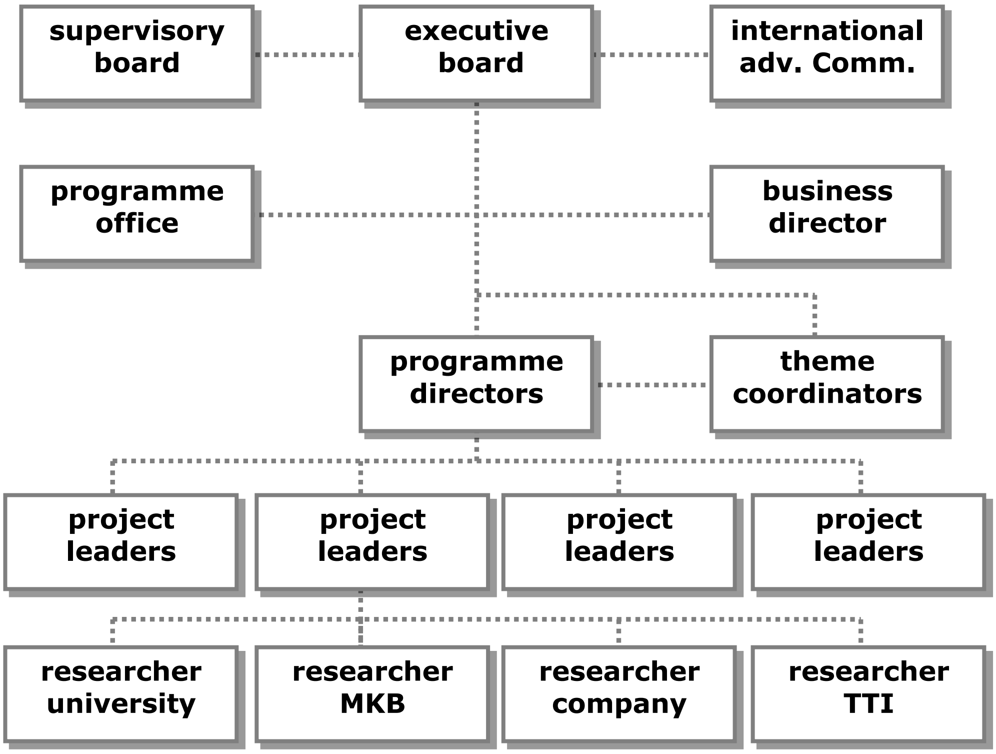
Academisch Medisch Centrum	AEMICS B.V.
Andor Technology	Aquamarijn Microfiltration BV
ASM International NV	ASML Netherlands B.V.
ASTRON	ATAS GL International B.V.
AVEBE UA	Basic Membranes
BECO Milieumanagement en Advies B.V.	BioConnection
BiOrion Technologies BV	Boschman Technologies BV
Bronkhorst High-Tech BV	Cambridge Major Laboratories Europe B.V
Carl Zeiss SMT AG	CellCoTec BV
Centre for Concepts in Mechatronics	Check-Points B.V.
Chemtrix BV	Cosine Research BV
Culgi B.V.	DANNALAB
Danone Research B.V.	DC4U B.V.
Delmes b.v.	Deltares
Demcon Twente b.v.	DevLab
DSM Ahead B.V.	DSM Chemical Technology R&D BV
Dutch Space B.V.	Encapson BV
Enceladus Pharmaceuticals BV	Energieonderzoek Centrum Nederland
Environmental Monitoring Systems (EMS)	Enza Zaden BV
Erasmus MC	FEI Company
Femto Engineering B.V.	Flowid B.V.
FOM-AMOLF	FrieslandCampina
FrieslandCampina	FutureChemistry Holding BV
Galapagos Genomics NV	Helianthos B.V.
Hogeschool Zuyd	Holst Centre
Hubrecht Instituut	HyET B.V.
IMEC	Innosieve Diagnostics B.V.
Instituto of Microelectronics-(IMM, CSIC)	ISA Pharmaceuticals BV
ISIS - Innovative Solutions In Space BV	IVAM Environmental Research UVA BV
JPK-instruments	Keygene N.V.
Koninklijk Instituut voor de Tropen	Kreatech Diagnostics
KWR Watercycle Research Institute	Leiden Probe Microscopy BV
Leids Universitair Medisch Centrum	LioniX BV
MA3 Solutions B.V.	MAPPER Lithography
Medspray XMEMS BV	MicroDish BV
Micronit Microfluidics BV	Minus9 B.V.
Monsanto Holland BV	Mosaic Systems BV
Nano-FM B.V.	Nanomi B.V.
Nanonics Imaging	Nanosens
Nederlands Kanker Instituut	Nikon Instruments Europe B.V.
NSure BV	NT-MDT Europe BV
NXP Semiconductors	Océ Technologies NV
OM&T B.V.	OTB Solar BV
Oxford Nanopore technologies	PamGene International B.V.
PANalytical BV	Philips Electronics Nederland B.V.
Philips Research	PhoeniX BV
Phycom B.V.	PhytoGeniX BV
PicoTwist	PodiCeps BV
Polyganics bv	Polyvation BV
Princeton University	Purac Biochem BV
QTIS/e BV	R&R Mechatronics B.V.
Radboud Universiteit Nijmegen	Rijksinstituut Volksgezondheid en Milieu
Rijksuniversiteit Groningen	Slotervaart Ziekenhuis

SmartTip BV	Solland Solar Cells B.V.
SolMateS BV	Stichting Amsterdam Biotherapeutics Unit
Stork Veco BV	SyMo-Chem BV
Syncom BV	Syngenta
Synvolux therapeutics BV	SystematIC Design BV
Technische Universiteit Delft	Technische Universiteit Eindhoven
Tembo Momentum Technologies B.V.	Thermo Fisher Scientific
TNO	TNO Kwaliteit van Leven
To-BBB	Twente Solid State Technology BV
Tytonis b.v.	Unilever R & D
Universitair Medisch Centrum Groningen	Universitair Medisch Centrum St. Radboud
Universitair Medisch Centrum Utrecht	Universiteit Leiden
Universiteit Maastricht	Universiteit Twente
Universiteit Utrecht	Universiteit van Amsterdam
U-Protein Express B.V.	Vertex Pharmaceuticals LLC
VibSpec-Training	VION Food Nederland
Vitens	Vrije Universiteit Amsterdam
VU Medisch Centrum Amsterdam	Wageningen Universiteit
X-Flow B.V.	

Annex 2: Structure and Governance

Topconsortium voor Kennis en Innovatie (TKI)

It is proposed that the 'roadmap nanotechnology in the Top sector' will be formulised in a TKI. Because most parties are already organized within NanoNextNL, and the aim of this initiative to set up an eco-system in nanotechnology for the Netherlands, this governance structure will form the basis for the TKI-NANO. As a consequence, the existing foundation NanoNextNL will be extended with new parties that joined in this roadmap.



Executive Board:
Eindverantwoordelijk voor het programma en de afstemming en communicatie met aanpalende top sectoren. Monitoring van status en voortgang.
Supervisory Board:
Board bestaande uit vertegenwoordigers vanuit industrie, top sectoren en kennisinstellingen.
Theme Coordinator:
Adviseur afkomstig uit bedrijfsleven met kennis van zaken vanuit de top sectoren.
International Advisory Committee
Commissie bestaande uit internationale wetenschappers en leden afkomstig vanuit bedrijfsleven. Belangrijke rol bij reviews van het programma.
Programme director:
Verantwoordelijk voor de uitvoering van het door de EB geaccordeerde programma. Organisatie van samenwerking, kennisuitwisseling en communicatie. Indien nodig bijsturing binnen het betreffende deelprogramma.
Project leader:
Verantwoordelijk voor de uitwerking van het project. Organisatie van kennisuitwisseling en interactie op "de werkvloer".
Programme Office and Business Director
Zorgen voor de ondersteuning van het programma, inclusief leveren van programma begeleiders en communicatiemiddelen.

Annex 3: Investments

The investments in nanotechnology covered in this roadmap have the following background:

Annual budgets:

Industry in NanoNextNL (committed): M€ 15 (25% cash)

Industry in HTSM-nano related programmes (estimation): M€ 25 (25% cash)

University (1st money stream on nano): M€ 110 (NNNL: M€ 15)

University (2nd money stream on nano): M€ 50 (NNNL: M€ 15, NWO: 30)

University (3rd money stream on nano): M€ 50 (including M€ 15 EU)

Exec.↓ / finance ->	1st	2nd	3rd	NWO	TNO	Industry
Industry (NNNL)						**15**
Industry (HTSM)						**25**
Universities	**110**	**50**	**50**			
Universities (NNNL)	**15**	**15**	**0**			
STW				**10**		**3**
FOM				**15**		**4**
NWO (VIDI/VICI)				**5**		
EU			**15**			**5**
TNO					**15**	
NanoLabNL (cash)						**2,5**
NanoLabNL (in kind)						**12**

The above results in the following table in HTSM format (in integers M€'s):

Finance → **↓ Execution**	Comp (incl NNL)	State /TNO+	State /NWO	State /other	Univ	EU
Univ /TKI	**20**		**30**	**5**	**60**	**15**
University	**30**				**50**	
TNO+ /TKI	**4**	**15**				
TNO+NLR						
Comp /TKI	**50**					**5**
Comp						
Int'l R&D						
Total M€/yr **Nano**	**104**	**15**	**30**	**5**	**110**	**20**
Total M€/yr **TKI**	**74**	**15**	**30**	**5**	**60**	**20**