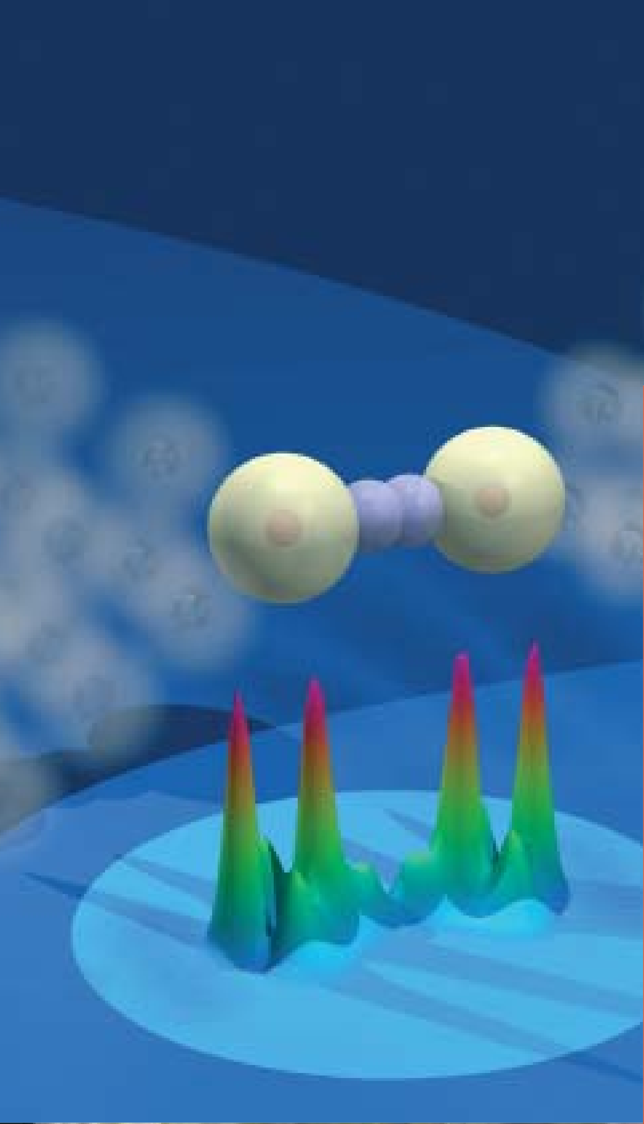

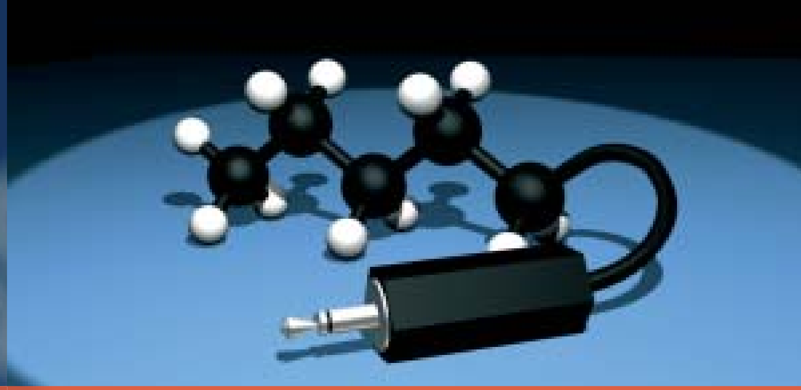

Towards a multidisciplinary national nanoscience programme

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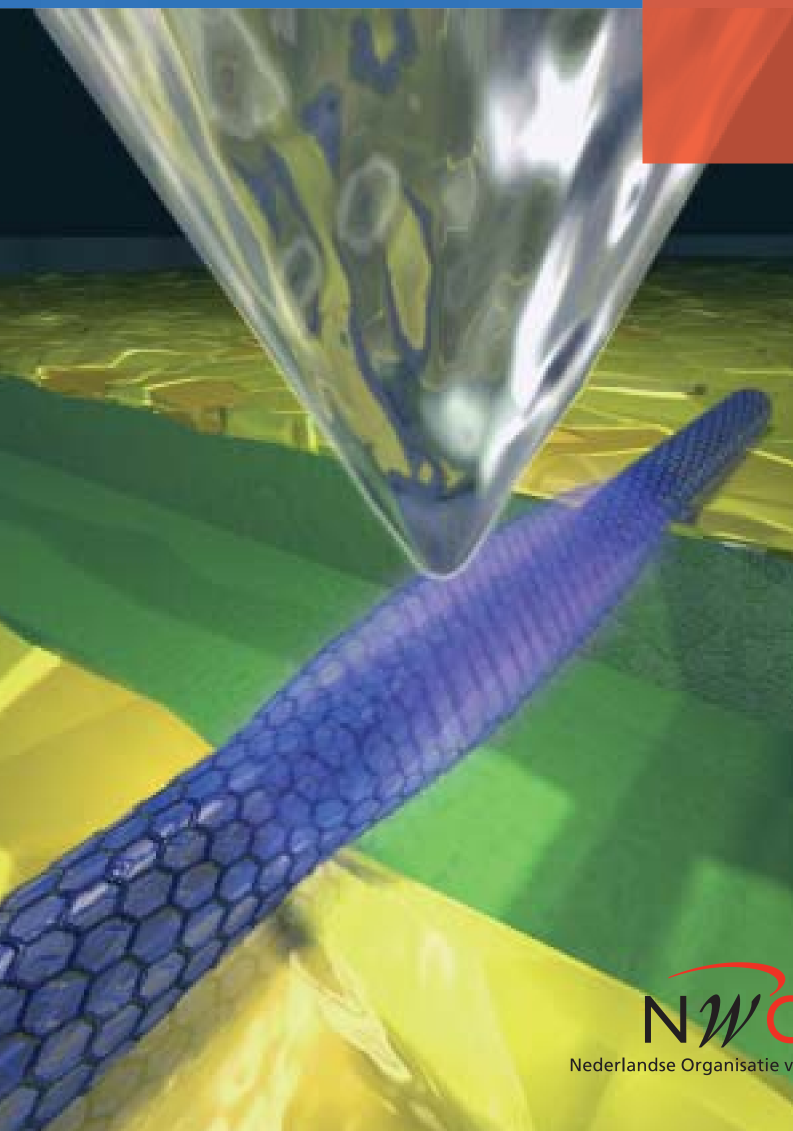

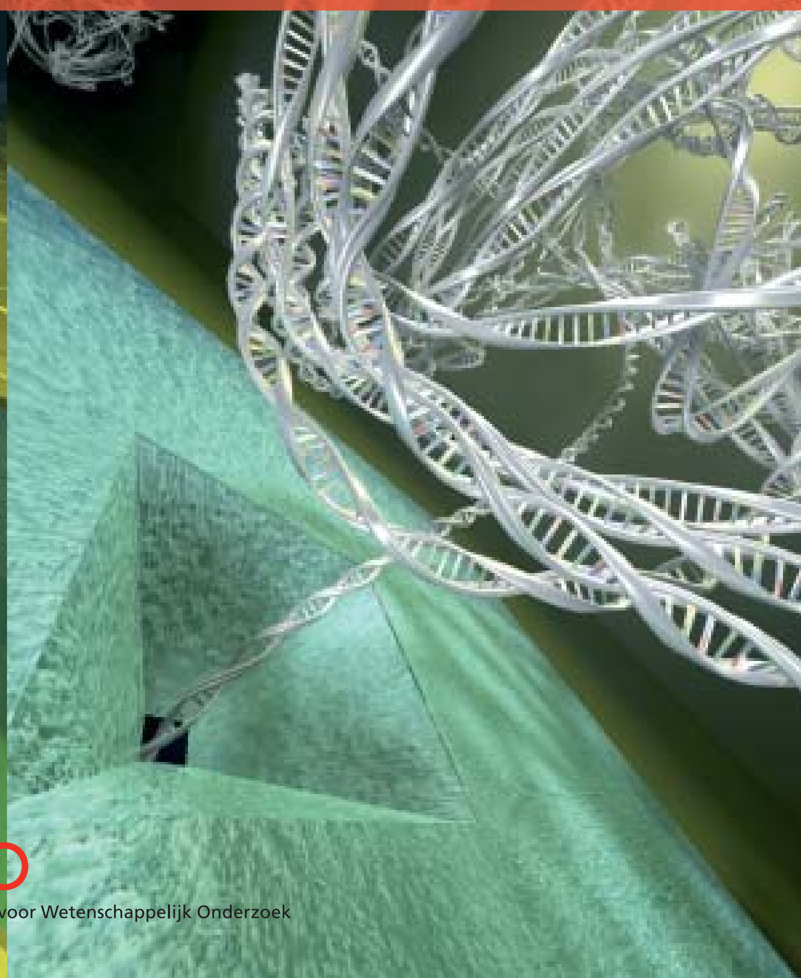

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OUTLINE

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Executive summary

Introduction

The importance of nanoscience and -technology for Dutch society has been recognized at an early stage. In the NWO Strategy Document 'Thema's met talent, 2002-2005' special attention has been paid to the development of nanoscience in The Netherlands, however, without explicit actions. From the Dutch state subsidy BSIK the national programme 'Nanoned' has been granted. Nanoned is a Dutch initiative on nanoscience and -technology in which both industry and academia participate. Aside from this temporary initiative, with a duration of 5 years, there is currently no structural funding for nanoscience in the form of a national programme. This worries the scientific community, because it is believed that, internationally, nanoscience and -technology will determine the agenda for developments in science, technology and society for the next decades. Nanoscience has everything to become an independent research field, with an impact comparable to that of silicon technology. It is a multidisciplinary field that will merge traditional fields such as chemistry, physics, biology and materials science. In this strategic pamphlet we provide an inventory of the strengths and opportunities of nanoscience and -technology in The Netherlands and define three major themes that are fundamentally challenging and have a strong application potential.

The study group

A study group has been instigated by the Foundation for Fundamental Research on Matter (FOM) and the Dutch Technology Foundation (STW) to prepare this report that could serve as input for the strategic discussion within NWO. The study group had the following members:

Prof.dr.ing. Dave Blank (University of Twente, chairman)
Prof.dr. Theo Rasing (Radboud University, Nijmegen)
Prof.dr. Albert Polman (FOM-Institute AMOLF, Amsterdam)
Prof.dr. Reinder Coehoorn (Philips Research/Technical University of Eindhoven)
Prof.dr. Huub Salemink (Delft University of Technology)
Prof.dr. Christoph Schmidt (Free University Amsterdam)

Secretarial support was provided by:
Dr. Paul Schuddeboom (programme officer STW, secretary)
Dr. Mijke Zachariasse (programme officer FOM, secretary)

Method employed

The study group started in January 2005 with an inquiry to get an overview of the research field. This inquiry has led to responses from a large number of the Dutch groups that are actively involved in the nanosciences. The research issues that came up were grouped into the following research topics: *quantum effects, functional materials, nano-organics, spintronics, nanofluidics, individual particles, nanophotonics, nanobioscience and -technology and nanomedicine.* Subsequently, the impact of nanoscience and -technology on Dutch industry is described.

Conclusions and recommendations

Considering both the strength of the Dutch (academic) research groups and the expected social and economic impact, the study group advises NWO to initiate a national multidisciplinary programme on nanoscience and -technology that focuses on three main research themes. On these three themes The Netherlands has the potential to develop real excellence. At the same time, these fundamentally challenging topics were chosen to have a clear relation with applications that are in development by Dutch and European industry. The three themes are:

1. **Nanomedicine**
   The focus of this theme is on nanoscale biomolecular, inorganic or hybrid structures and devices with the purpose of finding solutions towards the diagnosis, treatment and prevention of diseases and genetic deficiencies. On this theme The Netherlands has pockets of excellence in many universities and a dedicated national programme would bridge the gap between the technical and the general universities and University Medical Centres. A programme on nanomedicine has great possibilities for creating start-up companies and has a huge societal impact.

2. **'Beyond Moore'**
   This theme addresses fundamental scientific issues and applications in fields that have developed parallel to the steady development of technology that helps sustain 'Moore's law'. This includes e.g. novel nanoscale optical, electronic, and magnetic phenomena that can lead to novel light sources, displays, information storage, sensors and actuators.

3. **Functional nanoparticles and nano-patterned surfaces**
   This theme aims at combining the presently strong Dutch expertise on the manufacturing of functional nanoparticles and nano-patterned surfaces with the physico-chemical and medical properties thereof, in part through characterization – down to the sub-cellular level - of living cells with these surfaces. This field is a 'niche' with great industrial and societal potential (biomedical, storage, nano-electronics, coatings, food, etc.) for large as well as small (start-up) companies. The subject has societal impact (health). Options could be to start a focussed programme or the establishment of an institute.

This report

This report starts with a description of the three main themes in Chapter 2. In Chapter 3 the earlier mentioned main underlying topics that summarize the Dutch expertise are presented. Each of the three main topics described above builds on this expertise. An overview of the responses to the inquiry is given in Appendix A.

Dave Blank (chairman)
December 7, 2005

2.1 Strategic theme 1: NANOMEDICINE

2.1.1. General overview

Disease starts at the biomolecular and cellular level on the (sub)nanometre length scale. The holy grail of medicine is diagnostics and intervention on that scale. The molecular scale is now becoming accessible with rapid progress in molecular biology and medicine as well as experimental technology. It should be realized that many candidate drugs never reach the market because of their unfavourable biopharmaceutical characteristics. Nano-sized delivery vehicles are suitable system to deliver drugs specifically at their site of action. Also, the present generation of macromolecular therapeutics, such as proteins, peptides, DNA and si-RNA require delivery vehicles to become successful as drugs. *Nanomedicine* is the application of nanotechnology in medicine. It deals with nanoscale (1 to 100 nm) biomolecular, (in)organic or hybrid structures, devices, and technical or biological systems with novel properties that have potential applications in the prevention, diagnosis, and treatment of disease and genetic deficiencies. Examples are the use of nanoparticles as labels in intracellular imaging and molecular diagnostics or the use of nanoscale containers, such as viral shells and polymeric colloidal particles, as precisely targeted drug delivery vehicles. The functionality of fluorescence or MRI imaging can be enhanced dramatically. Single cancer cells could be eliminated in the earliest state of cancer. A next step, using more complex nanodevices, would be molecular diagnostics combined with therapy. Implants with nanoscale functional parts (such as electrodes) could be used for ultra sensitive biochemical analysis in the body, local and targeted drug delivery, and wireless reporting of progress. Mass-produced and inexpensive *in vitro* biosensors would enable family doctors, or patients themselves, to routinely detect extremely small concentrations of DNA, proteins, hormones, drugs, metabolites or pathogens in body fluids, or of gases in exhaled air. Nanosized particles loaded with drugs and imaging agents would enable the guided at triggered release of the therapeutic agents once the carrier arrived at its site of action. For all these applications the molecular characterization and manipulation of the interaction between living cells and animate and inanimate surfaces will be crucial. At the same time, studies of the health effects of nanoparticles in food and other consumer products and in outside and in-house air will be of emerging societal and industrial relevance.
Nanomedicine is clearly a highly interdisciplinary endeavour, including physical, chemical, biological and pharmaceutical sciences, engineering sciences and clinical medicine. An eventual success in nanomedicine will be inseparably connected to a quantitative understanding of the physical/chemical properties and engineering principles and biological function of the molecular building blocks and nanomachines in living cells. A crucial part of a nanomedicine initiative will therefore be concentrated on strong support for basic science elucidating the microscopic dynamics and functional properties of biomolecular nanomachines and assemblies in cells.

2.1.2. National context

Success in nanomedicine will particularly be based on the success of biophysicists and biochemists to achieve a fundamental understanding of the bio-nano-machinery of cells and of the chemical processes in cells (using genomics, proteomics, metabolomics, etc.), and of physicists, chemists and engineers to create novel nanostructures by top-down or bottom-up methods. In The Netherlands, *academic groups* that contribute to these developments are present in Leiden (Schmidt, Aartsma), Amsterdam (Schmidt, MacKintosh), AMOLF (Frenkel, Dogterom, Mulder, Tans, Ten Wolde), Delft (Dekker, Young), Eindhoven (Nicolaij, Meijer, Prins), Twente (Huskens, Van de Berg, Subramanian, Schasfoort, Lohse), Utrecht (Rodenburg, Hennink, Crommelin, Storm, De Kruijff), Rotterdam (De Jong), Groningen (Robillard, Verpoorte, Poolman, Driessen, Hoekstra,

Poelstra) and Nijmegen (Nolte, Van Hest, Speller, Figdor, Heerschap, Corstens). Expertise on nanoscale nutrient delivery processes in the body is present in Wageningen (Sudhölter, Cohen Stuart). Important enabling sciences and technologies are nanobiology and biophysics, nanofluidics, the physics and (bio)chemistry of functional nanoparticles, pharmaceutics and cell biology; these sub-areas are discussed separately in this document.
The largest *industrial company* in The Netherlands that is involved in medical technologies, i.e. Philips, is currently expanding from medical imaging and image-guided therapy to other phases in the 'disease management cycle' (prevention, early detection, therapy). Philips has advised that the Dutch nanoscience community aggressively should enter and develop the nanomedicine field. Recently, Philips Research, TU/e and Maastricht University and Academic Hospital have signed a letter of intent to found a Centre for Molecular Medicine (CMM, [1]), a unique Centre of Excellence. FEI, a leading company in electron beam imaging and focused ion beam nanostructuring methods, considers growth in biomedical applications as a top priority. Smaller enterprises in this field are Cytocentrics, Pamgene, Future Diagnostics, Syntharga, Encapson and Modiquest.

2.1.3. Future developments

The concrete achievements one could envisage as part of the technological (r)evolution in the next 15 years, given the research and industrial infrastructure in The Netherlands, are:

- an understanding of bio-molecular machines in physico-chemical terms of functions for crucial systems;
- a microscopic understanding of the physical and material properties of cells and their important structural machineries, including interaction with nano-patterned surfaces at sub-cellular level;
- the development of tagged nanoparticles for molecular imaging and therapy;
- the development of nanotechnological sensors for *in vitro* diagnosis;
- the development of self-assembled and self-organized smart nanomaterials from proteins or DNA;
- the development of nanosized particles capable to specifically deliver biologically active agents (low molecular weight drugs, proteins, DNA, siRNA) to their site of action.

A further future goal concerns multifunctional particles for transporting drugs or nucleic acids into e.g. tumour cells, while minimizing side effects by application in biocompatible housings, which are not attacked by the human immune system and which become only active upon reaching their destination. Ideally, the fate of these particles can be followed by imaging techniques and the release of the active substance can be triggered by an external stimulus (heat, UV-irradiation, magnetic field). An even further step will lead to integrated medical nanosystems (e.g. retina chips), which perform complex sensing or repair actions on a cellular level inside the body. It is important to keep a disease-oriented focus for nanomedicine development and application (for instance in cancer, cardiovascular disease, diabetes mellitus, neurodegenerative disorders).

The following concrete research topics can be distinguished:

1. <u>Knowledge for nanomedicine</u>. Research towards a quantitative microscopic understanding of processes at the molecular and (sub)cellular level.
2. <u>Materials for nanomedicine</u>. Examples are nanoparticles, nanostructures, bio-functionalization of nanoparticles or structures, artificial molecular receptors, biocompatible surface coatings, biodegradable materials, biosensor arrays. An entirely novel route to take would be 'active assembly'. In contrast to 'passive' self assembly, active assembly uses energy-consuming agents (molecular motors, polymerizing fibres, possibly entire bacteria) to build novel, highly complex structures that cannot form as an equilibrium phase. Smart materials are envisioned which use and/or mimic biomacromolecules, that

could find use as implants, biosensors, drug delivery vehicles, or even crystallization agents. DNA-coated colloids or DNA-tiles made from oligos are but two examples of systems that can be used to design multicomponent crystals with tailor-made unit cells. However, other nano-particles should also be considered: e.g. inorganic nano-colloids (Au, PbSe etc), organic nanoparticles (based on lipids or biodegradable polymers), proteins (possibly modified to form specific structures) and DNA constructs. Transport properties of these particles in organisms as well as targeting methodologies will be an important part of this research.

3. 'Functional nano-devices'. Nano-devices that aim to change the function of a biological system. Examples are nanostructures for improved human abilities (e.g. releasing oxygen or drugs) or for wound healing, nano-devices and artificial viruses for gene therapy, bioengineered viruses and bacteria, synthetic genomes and implantable devices.
4. Nanodevices loaded with drugs that can be followed with imaging techniques, and that can release their contents after an external trigger.
5. Nanodevices and nanosystems such as nanoneedles, femtolitre flow controllers/dosing systems, nanoelectrodes, picospray interfaces for MS-equipment as tools for biological/bioanalytical single cell studies ('lab-in-a-cell').
6. Research instrumentation and software for nanomedicine. Devices and systems based on nanomaterials or nanodevices, including software tools, aimed to study for example cell function, tissue properties or tissue processes, *in vitro* and/or *in vivo*. E.g. electron beam imaging, molecular modelling software, analysis tools for the study of biological model systems (e.g. isolated living cells), and molecular imaging systems for small biological model systems.
7. Devices and systems for the application of medical nanotechnology. This topic spans a wider range of length scale than the previous topics, namely from nano- to micro- to human scales. Examples are devices and systems for bio-molecular sensing using nanomaterials, devices and systems for analysis of biopsies, imaging devices and systems centred around the use of nano-materials. For example systems accessory on the use of nanotechnology biosensor arrays, molecular imaging systems based on nanoparticles.

Crosscutting through these the various topics is so-called translational research, i.e. the translation of promising laboratory results (newly developed nanodevices or nanomedicines) into application in patients. This includes: (1) preclinical research directed towards the safety and efficacy of new materials/devices using *in vitro* or *in vivo* (animal experiments) methods; and (2) clinical research: phase I and II studies in patients, including development of clinical protocols for the use of these new 'medicines' or diagnostics.
In The Netherlands various university medical centres have longstanding and extensive experience in designing and executing multicentre clinical research which is necessary for the testing and registration of the products of nanomedicine.

Societal and ethical impact, environmental, and health effects (e.g. of nanoparticles) should be studied as well as regulatory issues to facilitate the safe and fast introduction into clinical and preventive practice. Spin-offs would be in veterinary medicine, food science, environmental testing and in the biotechnology processing industry.
These developments should be accompanied by improvements in (nano)molecular platform technology for *in vitro* diagnostics and molecular imaging for diagnosis and therapy response monitoring.

2.1.4. Recommendations

Nanomedicine is an emerging but not yet established field of research. We recommend that NWO takes the following two steps in order to promote the development of this field:

A. National Nanomedicine Roadmap

We recommend that NWO takes the initiative towards the formulation of a national Nanomedicine Roadmap. Such an initiative should bring together the academic and industrial research communities, from the wide range of disciplines involved. A similar initiative in the US, started in 2004, has led to nanomedicine development plans, and will lead in mid 2005 to the establishment of several Nanomedicine Development Centres [2]. The European Science Foundation has recently developed a rather general 'Scientific Forward Look on Nanomedicine' [3]. The roadmap should be built on the specific strengths and ambitions of academic groups and industries in The Netherlands. Advantage should be taken of strong nuclei of collaboration already present in the form of the Centre for Molecular Medicine, which will work closely together with other Dutch universities, and with the research centres in Jülich and the RWTH Aachen, as well as new activities in several universities/institutes where ties have developed between (bio)physical and medical groups (e.g. Amsterdam: VU, AMOLF, ACTA, VUMC, SILS, AMC; Erasmus MC; Nijmegen: IMM, NCMLS; Groningen: BioMaDe/MSC+ en UMCG and Utrecht: UMC, UIPS and UU). This initiative, and the resulting collaborative structures (in which participation of groups from neighbouring countries should be actively sought), should provide the Dutch research community with a strong position in the EU 7th Framework Programme.
The following two themes are examples of concrete research areas within the roadmap that would find a strong existing base in The Netherlands and offer the prospect of securing an internationally prominent position for Dutch research in Nanomedicine:

(1) '*Nano-electronic biomedical devices*'
(2) '*Self-assembled and (actively) self-organized nanomaterials*'

Both themes have links to all research areas mentioned above. We recommend that, as a part of the roadmap initiative, NWO will promote that the opportunities towards the founding of (virtual) centre(s) on these themes are explored.

B. Nanomedicine 'seed' research programme

The potential of (Dutch) research and research collaborations in this new field is larger than reflected by the groups that are mentioned in section 2.1.2 and in the separate documents on enabling sciences, particularly in the medical field where many potentially interested groups have not invested in nanotechnology yet. Therefore, we recommend that NWO provides, already before a roadmap has been established, financial support to a 4-year nanomedicine 'seed' research programme, with the specific purpose to establish top-level interdisciplinary research that links physics, chemistry and technology with nanobiology, medicine and pharmacology, and that also links academic and industrial research.

References

[1] CMM: *www.hightechcampus.nl/press/letterofintentCMM/*
[2] US Nanomedicine roadmap initiative: *nihroadmap.nih.gov/nanomedicinelaunch*
[3] ESF Forward Look on Nanomedicine: *ftp.cordis.lu/pub/era/docs/3_nanomedicine_tp_en.pdf* and *www.esf.org/newsrelease/83/SPB23Nanomedicine.pdf* (February 2005).

2.2. Strategic theme 2: BEYOND MOORE

2.2.1. General overview

In the past 30 years, the ongoing miniaturization of electronic circuits has brought an enormous wealth to our daily lives. Integrated circuit and computer technology has changed the way we communicate, and has enabled the development of technologies that one did not even dream of 40 years ago. Key to this ongoing development is the steady decrease in the critical dimensions in electronic integrated circuits. This pace is surprisingly well described by Moore's 'law', that predicts a two-fold decrease in the dimension of a Si MOS transistor every 18 months. While Moore's law has been a key guideline in the development of industrial roadmaps in electronic technology for several decades, the end of its validity is approaching. This is because 'classical' fabrication technologies, such as optical lithography, reach their physical limitations. Also, power dissipation puts a limit to the compactness of complex integrated circuit designs. And most importantly, further shrinkage in integrated circuit design halts once the atomic limit is reached: a gate oxide can not be made thinner than a few atomic layers for it to be insulating, and a metal contact wire needs to be several atoms thick to conduct current. As a result, an increasing number of functional requirements and physical constraints are unaccounted for in the International Technology Roadmap for Semiconductors (i.e. do not scale with Moore's law) beyond 2010. Thus, it is likely that by that time the development of novel integrated circuit and device technologies will gradually come to a halt. As a consequence, the ongoing increase in speed, complexity, and functionality of integrated circuits and devices will stall, and the continuous stream of innovations based on the increase in these quantities, that we have become so use to in the past decades, will dry up.

Yet, in the past years, parallel to the steady development of 'Moore' technology, an entirely new world of nanotechnology is emerging that enables innovations in application areas that are distinct from the 'Moore'-related applications. They include use of light for signal processing and data storage, lasers based on nanowires, plasmonic LEDs, carbon nanotube-based displays, the use of single electronic charges, single spins or single molecules in memories or storage, the use of quantum entanglement in optical or electronic logic, use of unexplored frequency regimes (e.g. THz radiation), new nanoscale sensor and actuator concepts, etc. While these novel device concepts may in some cases still be linked with existing 'Moore' technology, e.g. as a back-end-process, they often require entirely new types of device architecture and fabrication technologies that are well beyond the 'Moore' technology.

2.2.2. National and international context

An innovative 'Beyond Moore' programme requires a truly multi-disciplinary approach, in which physicists, chemists, biologists, and materials scientists must collaborate on fundamental research towards applications 'Beyond Moore'. Several *academic consortia* exist in The Netherlands that can contribute specific expertise to this: Centre for Nanomaterials (TU/e), Centre for Nanophotonics (AMOLF), Debye Institute (UU), Kavli Centre for Nanoscience (TUD), Institute for Molecules and Materials (RU), Leiden Institute for Physics Research (LEI), Materials Science Centre (RuG), MESA+ (UT), Science Faculty University of Amsterdam. Large fabrication facilities are available at DIMES, MESA+, and Philips MiPlaza. Smaller facilities, often very efficient and specialized in particular nanofabrication areas, are available at many institutions.

The largest industrial company in The Netherlands that is highly dependent on 'Beyond Moore' technology is Philips, in its development of healthcare, optical storage, displays, lighting systems, and in enabling technologies (e.g. print technologies). ASML is the world's leading manufacturer of lithography systems, and develops novel lithographic techniques as options for realizing ever smaller feature sizes. FEI is a leading manufacturer of electron beam imaging systems

and focussed ion beam systems, which enable nanotechnology in industry and laboratories. FEI is committed to work with nanoscientists to develop instruments that will serve their needs in the area of nanocharacterization (metrology, imaging, chemical analysis, structural analysis, cryotech), nanomanipulation and modification (materials deposition and removal, local scale activation) and nanoprototyping.
On a European scale, industrial developments involving nanotechnology are coordinated within the MEDEA+ consortium [1]. Here the concept of 'Beyond Moore' technologies has been specifically defined, and it is expected that when capitalizing on European strengths in certain areas, it can directly lead to economic growth and fulfil important needs of individuals and societies. It is also expected that a key role will be played by 'innovation ecosystems', in which small and large industry collaborate with academic partners in an open innovation model.

2.2.3. Future developments

In a new 'Beyond Moore' roadmap, several application areas can be identified in which significant academic expertise exists in The Netherlands. Many of these have direct links with the needs of the Dutch companies listed above; several others can find applications on a European scale.

Lighting

- Development of new types of LEDs, e.g. based on semiconductor quantum wires, quantum dots or tubes. This will open up the possibility to realize polarized light emitters and efficient emitters in the green or in the UV wavelength regions;
- Integration of LEDs with photonic or plasmonic nanostructures to enhance the colour, out-coupling, brightness or directionality of light emission;
- New types of organic LEDs, in particular for large-area light sources, based on supra-molecular chemistry of novel emitting molecules. Printing and soft lithography may be used to structure the devices. Roll-to-roll coating may lead to breakthroughs in manufacturing technology;
- Single photon sources and detectors in communications and molecular diagnostic units.

Displays

- Carbon nanotube field emitter displays;
- Colour filters and out-coupling structures based on supramolecular chemistry;
- New types of active matrix displays based on polymer electronics or printable inorganic nanoparticle or nanotube thin-film transistors.

Storage

- High density optical storage based on deep UV radiation generated e.g. using semiconductor nanowires;
- Novel methods to increase storage density using near-field optics and/or plasmon optics, aiming for pit size well below 100 nm;
- Optical storage based on biomolecules;
- Optical or electronic storage in single quantum dots;
- Magnetic storage in single spins;
- Storage technologies based on nano-electromechanical systems;
- Entirely new organic or inorganic optical storage concepts.

Novel integrated circuit concepts, designs, and fabrication technologies

- Organic molecules as building blocks in electronic circuits: diodes, transistors or memory elements. Electrical connection of molecules. Combining molecular building blocks with existing semiconductor electronics. Developing reliable techniques for fabrication and characterization of molecule-metal interfaces at

the atomic scale; chemical methods for self-assembly of molecular structures, computer simulations;
- Bio-electronics: controlled modulation of electron transfer within biomolecules, tunnelling in protein assemblies, communication between electrode surfaces and active sites. Use of photosensitive enzymes and proteins in optical memories, optical bio-switches and electronic gates. Interfacing biomolecules to a suitable substrate or electronic interface is a central issue in bio-electronics (glass or semiconductor);
- Using spin-polarized transport in nanoscale organic and inorganic devices such as magnetic tunnel junctions;
- All-optical integrated circuits using passive and active optical nanoresonators, optics below the diffraction limit using surface plasmons, manipulation and storage of light in metal nanoparticle assemblies;
- Novel integrated circuit designs based on the direct generation of ultra-high carrier frequency, e.g. in the THz domain: THz lasers, FETs, diodes, in particular for space applications, computer industry, infrared (molecular fingerprint) detection and telecom;
- Nano-imprint and other soft lithographies, nano-embossing, plasmon printing, multiple emitter technology;
- Bottom-up molecular design, top-down self-assembly, novel ordered solution processes, atomic scale manipulation with scanning probes, ion-beam generated nanostructures, plasma-assisted nanoscale fabrication.

Sensors and actuators
- Using complex-chemistry and supramolecular chemistry to build up sensors;
- Dispersion control in photonic and plasmonic nanostructures to slow down light and thus enhance field intensity and sensing efficiency;
- Create value beyond Moore's law, by adding functionality to integrated circuits system in package solution approaches: sensor and actuator integrated with nano-electronic and nanophotonic devices, plasmonic sensors;
- Creation of integrated (UV) photonic excitation sources with single-molecule detection analysis sensors (miniature optical analyzers), including filtering/selection subunits based on fluidic/electronic separation.

The academic potential of these topics is immense, addressing e.g. exciton dynamics in confined organic and inorganic nanostructures, understanding and manipulating surface plasmons, nanoscale energy transfer, nanoscale spin transport, near-field and single-molecule optics, photon statistics, electronic processes in mesoscopic structures, high-frequency detection, quantum point contacts, optical and electronic interactions in biomolecules, nanomechanics, etc.
This selection of topics within the 'Beyond Moore' theme is unique in that it provides a direct link between a large number of fundamental questions and scientifically challenging issues, and a large array of applications. Some of these novel concepts can become the precursors to disruptive technologies that may emerge in applications that are fabricated from 2010 onwards. It is expected that these hybrid and converging technologies open up completely novel smart functional assemblies that are also of relevance to the field of life sciences.

2.2.4. Recommendations

We recommend that NWO starts a 'Beyond Moore' programme that addresses the topics described above within three main themes:

(1) <u>Nano-scale photonic/electronic phenomena with applications in lighting, displays, storage, lithography, sensors and actuators.</u> This theme capitalizes on existing strengths in fundamental studies on nano-photonics and nano-electronics. It also has an immediate link to industrial applications. This theme thus addresses fundamental research with an application horizon of 5-10 years. It can benefit from interaction with industrial partners in The

Netherlands (Philips, ASML, FEI) and in Europe, as represented in e.g. the European Photonics Industry Consortium (EPIC) [2].

(2) From organics to bio-electronics: novel molecular scale devices and integrated circuit concepts. This theme capitalizes on existing strengths of the Dutch organic electronics/photonics community. It may evolve from novel molecular scale memory concepts to more complex bio-electronic integration.

(3) GHz/THz electron and spin dynamics. This theme represents emerging fundamental research fields in which excellent Dutch groups are active. It brings together time scales in electronics and photonics. The application horizon is > 10 years, with many revolutionary fundamental and application aspects, like spin-electronics and quantum computing, waiting to be explored.

References

[1] *www.medeaplus.org/forum2004/2_AVP_close.pdf*

[2] *www.epic-assoc.com/index.html*

2.3. Strategic theme 3: FUNCTIONAL NANOPARTICLES and NANO-PATTERNED SURFACES

2.3.1. General overview

The materials and device industries, as well as numerous universities, laboratories and institutes, already have a large history of studying and utilizing a wide variety of nanoscale particles, surfaces and structures, ranging from metallic and semiconductor particles, colloids, carbon nanotubes, to supramolecular structures and bio-inspired DNA, protein architectures etc. Design tools and characterization capabilities at the nanoscale, for new material structures and function have only recently become possible. This substantial scientific breakthrough has opened a whole new frontier for the development of an unlimited range of new nanostructured materials and devices by design.

A definition of functional nanoparticles and nano-objects is architectures with a size range of 10-100 nm that have specific functionality such as reactivity, optical, electronic or magnetic properties, biological activity, and recognition. The emphasis is on *function and its relation* to the nanoscale size: from the single molecule and particle level to defined materials and new devices. A result of the small size and high surface area-to-volume ratio of nanoparticles is that they have novel and as yet much unexplored, properties such as unique mechanical, optical, electronic, electrical and mechanical properties. This includes reduced elastic modulus, improved strength, hardness, super plasticity, size dependent optical properties, higher electrical resistivity and lower thermal conductivities than bulk materials. Indeed, nanoparticles are already used in advanced composite materials, catalysts, batteries, automotive devices, optical devices, aerospace/aeroplane components.

A new and rapidly developing application of functional nanomaterials lies in the field of biological systems. Their usefulness of nanoparticles in biological systems lies in the fact that they match the size of typical functional biological assemblies, i.e. protein machines, chromosomes, viruses, and sub-cellular assemblies. Inorganic and defined organic particles can bring new functionalities, such as fluorescence or magnetism to these biological systems, and even alter the metabolic pathways by the addition of non-natural components, producing 'cyborg cells' that generate new bio-products. This hybrid approach has considerable potential for the future, not only for a better understanding of natural systems but also in numerous commercial areas. Nanoparticles made from biomolecules, can uniquely deliver a key property for many potential applications, both in nanomedicine (e.g. drug delivery, MRI contrast agents, biomaterials) and in bioengineering, namely extremely high specificity in targeting. Furthermore, the functional characterization of subcellular interactions with nano-patterned surfaces will allow the design of entirely new classes of devices.

2.3.2. National context

The Netherlands has a rich tradition in the research and applications of nanoparticles, especially in the fields of colloid science and supramolecular chemistry. This holds for the Debye Institute (UU, Lekkerkerker/Philipse, Van Blaaderen, Vanmaekelbergh/Meijerink) as well as Wageningen University on particle synthesis and model studies of colloids, systems of particles and macromolecules particle synthesis, and steered self organisation. Work on III-V nanorods with p-n junctions for LED application, or n-p-n transistors is performed at Philips (Bakkers).

A related field of photonic crystal research (photonic crystals using the self-organization of colloids) is studied by Vos and Polman (AMOLF) and Van Blaaderen (UU). Metal nanoparticles for catalysis, energy storage and nanophotonic applications are studied by Schropp (UU), Lefferts (UT), Kroesen (TU/e), Van Blaaderen (UU) and Polman (AMOLF). Magnetic nanoparticles for

magnetic data storage and biomedical applications (MRI, hyperthermic curing, drug delivery, biosensing) are made and studied at the IMM (RU), such as virus capsid applications, biohybrid nano architectures (Nolte), bioengineered systems (van Hest) and nanomotors and machines, single molecule studies and molecular materials (Rowan, Speller, Rasing). Quantum effects are studied by Erné (UU), De Jongh (LEI), Poelsema (UT), Kouwenhoven (TUD). Nanoparticles for hydrogen storage, fuel cells, PV cells by Schoonman (TUD) and Blank (UT), nanoparticle based medicines and agents for medical diagnostics and targeted drugs by Schmidt-Ott, Picken (TUD). Recently, NWO awarded an investment grant for an MeV ion beam facility to UU (Vredenberg), with which controlled nanoscale shape modification and engineering of colloidal nanoparticles becomes possible.
Research on the mechanics of biological nanoparticles and living cell-surface interactionsis done by Schmidt and MacKintosh (VU; mechanics of viruses, DNA nano-particle self-assembly), and Frenkel and Dogterom, Tans, Den Blauwen (AMOLF SILS; DNA-mediated colloid assembly, dynamics of microtubili, cell division machinery).
In the field of nanoparticles probing techniques are very important and here the groups of Frenken (LEI), Vancso, Bennink, Zandvliet (UT), Speller (RU), and Zandbergen (TUD) are active in it.
It is important to know that The Netherlands is viewed as one of the world leaders in the field of supramolecular chemistry and functional self-assembly, an area which has embraced the nanosciences. The group of Feringa (RuG) is active in the area of nanomotors, Meijer (TU/e) in the area of dendrimers, Nolte (RU) in the area of biohybrids, and Reinhoudt (UT) in organic assemblies, functional surfaces, and molecular printboards.
Most of the larger companies such as Philips, Unilever, AKZO, Shell and DSM have nano-particles research going on. In addition, smaller companies exist such as Aurion (Wageningen) that make nano-gold for labelling and ENCAPSON (Nijmegen), which makes polymer nanocontainers for medical and materials applications, have their entire business in the field of nano-particles.

2.3.3. Future developments

There is little doubt that nano-structured materials will be the key building blocks of many functional materials and devices, ranging from the presently largest application in cosmetics, to catalysts, paints, data storage, nano-electronics, biosensors, bio-probes, drug delivery. It is expected that they will be present throughout every aspect of life.
Several key issues need to be addressed in order to realize the potential of this field. These are: (a) what are the properties of the individual particles and what are the effects of and on the environment; (b) how can these nanoparticles be properly positioned and addressed in a well controlled way; (c) how can one design and construct nanoparticles and nano-architectures with the desired properties or functionalities; and (d) how can one understand and manipulate the interaction between living cells and such surfaces at the sub-cellular level. In addition, the environmental and health issues of these nanoparticles should be addressed.
Critical to the study and applications of functional nanoparticles are: the development of methods for large scale synthesis of well-defined, monodisperse nanoparticles; the development of flexible and versatile positioning tools and the development of sensitive probes. In order to make, manipulate and use nanoparticles with pre-defined functionality, one should be able to:

- *synthesize finite and pre-defined nanoparticles;*
- *control of their ordering at surfaces and in three dimensions;*
- *manipulate them and address them en masse and individually;*
- *control and manipulate their material properties;*
- *develop routes for large scale synthesis.*

The prime examples of functional nanoparticles are the viruses found in nature. These nano-sized containers have a tough protective shell of protein and in some cases lipid with recognition functions that allow them to target specific cells for the delivery of their genetic material. Intensive research is currently directed at understanding and modifying the structure, the assembly, the physical properties and the functional mechanisms of viruses. A thorough understanding of the engineering principles would make it possible to construct the ideal drug delivery vehicle. However, the potential application of the viral capsides goes far beyond biomedical applications. By the inclusion of synthetic components, such as magnetic, conductive and even catalytic systems within these spheres or dodecahedron containers, a new field of unique materials is rapidly developing (nanoreactors and nanocapsules).
Substantial research on the improvement of nanoparticle processing techniques is a pre-requisite for the future development of this area of nanoscience. Of primary importance is the development of new approaches for the controlled growth, e.g., nucleation and grain growth, particle agglomeration, size distribution and reproducibility. At the moment the best-defined (nano)-particles are made by wet chemical synthesis, which will remain the predominant route for the production of nanoparticles for the foreseeable future. However, despite considerable effort throughout the world, it is still difficult to produce monodispered objects and control in a desired way their subsequent self-assembly and organization to give functional materials and surfaces. Well-defined means not only that all particles have the same size, it also can refer to being of a pure single crystalline state, highly-ordered and with a defined shape of which can be controlled (rods, sphere, disks, platelets etc.). One of the most promising routes to self-assembled nanoparticles is the use of the 'code of life'-DNA. It has been shown in the last five years by *Seeman et al.* that DNA oligomers can be programmed to assemble with high yield into rings or cubes, tetrahedra or tiles that form building blocks for larger structures, sheets, tubes or more complex assemblies. These scaffolds can then be combined with proteins or enzymes, and even colloids or lipid vesicles to form unique composites. More recent, and potentially even more exciting, is the construction of similar architectures using the more easily attainable RNA. It is clear that considerable effort still needs to be focused on new molecules and systems which have encoded in their structure like DNA and RNA, the blueprints for their own architectural assembly.
The uniqueness of nanoparticles, and the subsequent materials they form is slowly being unearthed. They have special properties in the fields of: *Materials*: hardness, colour; *Electronics*: semiconductor elements; *Optics*: single dot lasers; storage, sensing, fluorescence enhancement; *Magnetic*: memory, spintronics, sensors; *Computation*: quantum computing; *Catalysts*: cascade reactions and lab-on-a chip; *DNA tagging:* detection; imaging; *Drug delivery*: virus capsid, smart nanocapsules.
Also the techniques for nano-patterning of bio-compatible surfaces will have to be improved, to develop new types of functional surfaces at which the interaction with living cells can be manipulated down to the sub-cellular level. In addition, facilities must be created to: (a) supply attached cells with nutrients; and (b) maintain attached cells in confined spaces so that force generation, originating because of growth and/or metabolic activity of the cells, can be analysed. Such materials will form the basis of an entire new generation of nano-biosensors and nano-force transducers.

The industrial potential in this area is huge and ranges from food, coatings, biomedical, nano-electronics storage, sensors, biosensors, drug delivery, catalysis, diagnostics, to fuel cells. However, it is important that NWO also takes a pivotal role in helping the development of small spin-off companies bringing the scientific idea from the university to commercialization. In this area the USA and Japan are more advanced.

The academic potential of this area is also huge as these nanoparticles and nano-patterned surfaces represent a new class of zero-dimensional materials. Each nanostructure represents a mesoscopic system that is neither totally microscopic nor totally macroscopic, but where micro- and macro-behaviour co-exist. Quantum behaviour controls the properties of the individual particles whereas their organization is often regulated by thermodynamics.
The study of the physical, chemical and biological properties of nano-particles and single molecules and their interactions is in itself an enormous scientific challenge, including quantum effects, bio-compatibility, toxicity, and chemical stability. In addition, their applications usually require a combination of different properties, making this a truly interdisciplinary science.

2.3.4. Recommendations

The research on functional nanostructures in The Netherlands is of high level and the joint knowledge is impressive and has the potential to grow into a well-recognized international centre of expertise. However, the synergy between the different research groups is to some extent weak. We therefore recommend a strong collaboration, for example by a virtual centre on science and technology of functional nanostructures. This centre must be the 'spokesperson' for this research field for The Netherlands in Europe and beyond. Important issues are:

- Exchange academic knowledge in preparation, properties and application of functional nanoparticles and nano-patterned surfaces (nano-structured materials);
- Making expertise available for the research groups;
- Synergy with the two other initiatives presented in this report (Nanomedicine and 'Beyond Moore');
- Give Dutch initiatives a strong position in Europe, e.g., the 7th Framework Programme;
- Explore field towards small business initiatives.

NWO could be a perfect podium in which this initiative could develop.

A national programme on *Functional Nanostructured Materials* should be directed into the following two areas:

A. Construction of finite nano-architectures and defined materials

With a focus on:

- <u>Bioinspired and biohybrid systems</u>. Application of proteins, DNA/RNA and virus capsids and cells as components in nanosystems and as nanoreactors. This is an area which has considerable potential and is, as yet, unexplored.
- <u>Self-assembled and self-organized systems</u> (see also Nanomedicine). For functional colloids, materials and surfaces only the first tentative steps have been taken on how to make materials with a defined molecular order and hierarchical self-organization. This development will be the foundation for much of the development of nanoscience.
- <u>Programmed assembly</u>. Development of new approaches using multiple interactions to steer the self-organization into the desires architecture or pattern. This is a vastly unexplored world at the interface between physics, chemistry and molecular cell biology, in which The Netherlands could excel.

B. Investigation of the properties of nanoparticles

- Study of individual nanoparticles. Effort should be addressed to the study of the mechanical, electronic and optical properties of individual nano-objects (including single molecule studies of quantum dots and enzymes).
- Nanocomposites and nanomaterials. In addition to the study of individual molecules funding should be directed towards the properties of molecular materials composed of nanoparticles.

By creating virtual Centres of Excellence and by stimulating joint projects at the relevant interfaces between physics, chemistry and biology, the abovementioned areas NWO can develop a new 'Nanoscience and -technology' programme that takes a lead in the European environment, positioning The Netherlands as leader in this field. It is also recommended that NWO initiates a new 'Gordon type' conference on an annual basis in this area of nanosciences. This conference series could establish The Netherlands credentials and act as platform for investment in this economically important area. A further possibility is to establish NWO scholarships for nanomasters study in The Netherlands, attracting top students from around the world.

3.1. Research topic: QUANTUM EFFECTS

Prof.dr.ir. L.P. Kouwenhoven (TUD)

3.1.1. General overview

Quantum mechanics automatically becomes important at nanometre length scales. Dimensions of order or less than 10 nm give rise to quantum effects already dominating many properties at room temperature. In fact, one could take quantum effects as a requirement in the definition of nanostructures. On the other hand, for the specific functionality of a certain nano-object, quantum effects may not always be so relevant. For example, molecules are obviously quantum objects, however, self-assembly in a monolayer is regulated rather by classical thermodynamics. In this section we limit ourselves to functionalities of nanostructures that have their origin in quantum mechanics.

Quantum effects can determine *electronic* properties (e.g. the conductance of a quantum conductor is quantized), *optical* properties (e.g. photons from quantum dots have tailored colours and their intensity correlation shows anti-bunching), and *mechanical* properties (e.g. vibration frequencies can become the dominating energy scale). Interesting new functionalities are often born from mixtures such as in *NEMS,* where electrical signals tune mechanical deformation and in electroluminescence with single photons being emitted on demand by electrical pulses. We wish to distinguish two entirely different classes of quantum functionalities. First, objects can be designed to have specific quantum properties (e.g. semiconductor nanocrystals like CdSe dots emit specific colours and are used as recognizable flags in bio-systems). Second, nano-objects as mentioned above are connected together quantum coherently and form a complex quantum circuit.

Scientific perspective

The control over size at the nanometre length scale allows for a new type of engineering. Nanostructures with previously unknown properties have been realized in the past decade. New phenomena that have been uncovered include: quantum interference (like the Aharonov-Bohm effect or quantum chaos), quantized electrical and thermal conductance, mesoscopic superconductivity, single-electron tunnelling based on Coulomb blockade, quantum confinement in quantum dots, anti-bunching in photon emission, quantized mechanical motion in molecular transistors, etcetera. Since recently the dynamics of single spins can be measured. Such new physical regimes will most likely yield new and yet unknown phenomena.

Application perspective

Virtually all applications require proper operation at room temperature. This severely limits the number of 'useful' quantum effects. Quantum confinement is one of the more robust phenomena and is used already successfully in several optical applications. One inspiring example is quantum dot probes in live cells. These semiconductor nanocrystals are used in bio-environments as stable (e.g. long lived) fluorescent objects and find applications in drug delivery and local medical diagnoses (see review in Science, 28 Jan 2005). Quantum confinement is also employed in new types of lasers (quantum wells/dots or THz cascade lasers).

The wide-spread belief for electronics is that silicon CMOS is unbeatable. Some specific applications are expected from carbon nanotube FETs (low leakage currents) and semiconductor nanowires (integration between III-Vs with silicon for opto-electronics).

In the rapidly developing area of quantum information processing, quantum effects are absolutely crucial. Secure cryptography based on quantum information is already being implemented in prototype secure intranet systems. Several highly desired nano-devices still need to be realized, such as efficient single

photon sources and quantum repeaters. Secure inter- or intranet could grow to a very large market.
The time scale for quantum computing is much longer. So far the concept revolutionized the theory of information. However, the requirements for quantum computing hardware are enormous. At present only some of the largest multinationals pay modest attention (e.g. IBM and NTT). Nevertheless, the expectation exists that this new type of quantum engineering provides an entirely new resource, which very likely will lead to new computational applications.

3.1.2. National context

Academia

Dutch academic groups with a focus on quantum effects in nanostructures are found in Groningen (van Wees/Blom, electronics; De Raedt/Knoester, spontaneous emission), AMOLF (Vos/Lagendijk/Polman, quantum emission in photonic crystals, quantum dots), Twente (Rogalla, Hilgenkamp, devices), Nijmegen (Rasing), Leiden (Woerdman, photon-plasmon entanglement; Beenakker, theory; Van Ruitenbeek, atomic-scale breakjunctions), Delft (Nazarov, theory; Mooij, superconducting devices; Kouwenhoven, quantum wires and dots).
A special programme on Solid State Quantum Information Processing is funded by FOM and located in Delft as a Concentration Group.

Industry

No serious investigation takes place within Dutch industry on quantum effects. Internationally, industrial research focuses on carbon nanotube electronics (IBM), quantum information (IBM, NTT, NEC) and quantum optical applications (Lucent).

3.1.3. Future developments

Scientific developments

The scientific direction will likely be the study of quantum behaviour in single atom/donor/molecule or other single nano-object devices. Importantly, an increased control over quantum effects will become the focus of research. Two ways to increase control is during synthesis and by fabricating control electrodes (e.g. gates that can couple to individual atoms or molecules) or environments (e.g. photonic crystals or single-photon sources with directional emission). Also in coherent quantum circuits the focus will be on increasing the control; here control over qubit dynamics and prolonging coherence.

Developments in applications

Quantum effects will most likely be found in optical applications, ranging from coherent or colour-tailored light sources to quantum dots in live cells. See 3.1.1.

3.1.4. Outlook and recommendation for future research

Much of the studies on quantum effects involve development of new or improved technology, ranging from growth via fabrication to measurement. It is central to stimulate further enhancement over the control over nano and quantum, i.e. both in size and in addressing carefully designed quantum states. Thus the keyword is CONTROL.
Concerning size control: there are several good Dutch groups in organic chemistry but very few (Vanmaekelbergh in Utrecht and Bakkers at Philips) working on the syntheses of inorganic nanostructures (e.g. semiconductor nanocrystals or wires).
Concerning quantum control: this is the focus of the FOM Concentration Group on solid state quantum information processing. It involves electronics (solid state qubits) as well as quantum optics (e.g. photon sources and crystals). Here the connection between nanophotonics and quantum optics can be strengthened (e.g. develop on-chip quantum cryptography circuits).

3.2. Research topic: FUNCTIONAL MATERIALS

Prof.dr.ing. D.H.A. Blank (UT)

3.2.1. General overview

Scientific perspective

Novel materials have always been a motor for further developments. Materials that exhibit unique properties if scaled down to nanometres are an essential key element in nanotechnology.

The recent development in functional materials, such as strongly correlated as well as organic materials, has brought on many new ideas on the use of these materials in novel devices. The completely new understanding of underlying physics of these materials is expected to open up many new possibilities for their application. However, as is usually the case of new class of materials, the actual adoption of these materials has been slow. Nevertheless, during the last decade a tremendous progress has been made in controlling these complicated materials. To name just a few: the epitaxial growth technique, understanding of their grain boundaries, atomic-level control of their layering, manipulating the oxygen contents and dopant densities in oxides, and so on. We believe that the next decade will show the development of new devices based on these materials with huge potentials.

In the latter part of the 20^{th} century metal and semiconductor based devices have dominated the scene. These devices were possible because of the new understanding based on the quantum mechanics established in the early 20^{th} century. Those devices based on semiconductors and metals have worked reliably well and ushered in the information revolution. There is no doubt that these devices will be further improved. However, they have limitations such as heat consumption, low spin polarization, no realistic ferro-electricity, and slow switching. The use of new classes of materials, organic as well as inorganic and the use of devices on nanoscale can defeat these limitations.

Application perspective

An important goal nowadays is to elucidate the effects of the size, structure, and interface of atomically controlled nanostructures on diverse properties such as conductivity, complete spin polarization, ferro-electricity, and optical nonlinearity. The exhibited phenomena are diverse but the elements that control these phenomena are common in these materials, such as carrier doping and strong correlation of the carriers. Structures made from these materials will serve as the prototype device that show surpassing performances or completely new functionalities, compared with those of devices based on conventional materials, such as semiconductors and metals. As stated before, novel materials are essential in the development of nanotechnology.

3.2.2. National context

Academia

Materials science is not an independent research field in The Netherlands, unlike in the USA and Japan. However, several Dutch university groups and institutes play a very important international role. This is the case for organics, inorganics, as well as theory. Because of the extensive theme 'materials science' for nano-electronic devices, there is a strong exchange between the different research groups. Roughly speaking the nano-materials science deals with growth studies and preparation of novel materials, characterisation and analyses, devices concepts, and theory. A (tentative) overview of the main activities in The Netherlands is given below.

- RuG (MSC+): Palstra (organic crystals, multiferroics), Rudolf (thin films), Blom/Hummelen (organic semiconducting devices);
- UT (MESA+): Blank (artificial thin films), Poelsema (low dimensional systems), Kelly (theory);

- TUD: Kouwenhoven (electronic materials), Bauer (theory);
- TU/e: Janssen (polymers);
- UU : Vanmaekelbergh (nano-wires and dots), Van Blaaderen (nano-particles);
- RU: Nolte (biohybrids), Rowan (molecular materials);
- LEI: Aarts (magnetic materials), Van den Brink (theory);
- Philips Research: Wolf, Coehoorn and several others.

Industry

There are several companies interested in novel materials. Although most applications are based on nanostructured materials, like nano-particles in host materials, an increasing interest is based on different properties in nano-sized structures.

Examples are: Philips Research Laboratories (electrical materials), ASML (diverse materials, including polymers), Océ Technologies (nanoparticles, piezo's), Shell Laboratories, DSM (nano-particles in polymers).

3.2.3. Future developments

Scientific developments

The development has to be on the controlled growth of the new materials and their implantation into nanoscale devices. In particular the fabrication of high quality organic molecular crystals and gate dielectrics, determination and explanation of their transport, optical and magnetic properties, and development of theoretical description of field induced electronic properties. Furthermore, the growth of high quality inorganic materials, like (complex) oxides as well as alternatives like sulfides and borides. Nanoscale devices toward field induced effects and non-volatile memories has to be worked on. The search after novel compounds for operation at room temperature is very important.

To relation between the chemical composition and atomic structure to various electronic properties including the polarizability, optical, magnetic, transport properties etc. has to be studied using ab-initio calculations, with model Hamiltonians. Furthermore, important is the search after and fabrication of insulating and semiconducting nanocrystals and wires that show strong quantum confinement effects for opto-electrical and logic devices. The characterization of these nanocrystals with advanced optical, opto-electrical and electrical spectroscopy is essential to apply these nanostructures in active devices.

3.2.4. Outlook and recommendations for future research

The introduction of new materials in electronic devices has rapidly decreased over the last years. The applicability of giant magnetoresistance in storage devices is a good example. In general one could say that the knowledge we obtain about the strong interaction between charge-carriers pave the way to new materials as well as new devices. Furthermore, the possibility to fabricate these materials on a controlled, even on compatible substrates, with standard semi-conducting industry way makes the introduction of these materials easier. New, high knowledge-content materials, providing new functionalities and improved performance, will be critical in the innovation of technologies and devices. Since these applications have a strong impact on individuals as well as on society, a new research area can be defined. RTD activities are expected to be high risk, inter and multidisciplinary, long term and generic, with potential benefits in material, maintenance and energy savings as well as on information technology, optical devices and technologies for the environment. Breakthroughs will come not only from the new materials developed but also from new processing and from the new approaches taken. Finally, this research topic will assure the strong Dutch position in this research area. Those groups working in the field of novel materials, based on charge carriers, optical responses, quantum confinement, has to be supported. Furthermore, those groups have to be supported that merge the gab between the integration of materials and manufacturing or processing by developing new tools and material systems for the implementation of devices based on nanotechnology.

3.3. Research topic: NANO-ORGANICS

Prof.dr. A. Rowan (RU)

3.3.1. General overview

The application of organics, organic molecules and polymers in the field of nano-materials, in particular nano-electronics and nano-composites, is an area of the nanoscience which has often been proclaimed as one of the futures for the nano-industry but has yet to reach its true potential and deliver on its promises. Among the top ten nanoproducts of 2003 were indestructible ski wax, breathable waterproof ski jackets, wrinkle- and stain-resistant slacks, anti-wrinkle skin cream, high-performance sunglasses, nanocrystalline sunscreen, and high-tech tennis balls and rackets.

One of the most successful nano-organics have been carbon based nanotubes which have found applications in the field of high strength nano-composites and in fire-retardant films, and their spherical cousins, the fullerenes with a diameter of ~2-3 nm which have found application in photovoltaics, as lubricants and as contrast agents in MRI. The application of the more established conductive polymers in the field of light emitting diodes and displays has proven very successful; applications in photovoltaic devices are also emerging The development of nano-organic circuitry has yet to be achieved, a main difficulty is ordering molecules or macromolecules between electrodes and their interface to the outside world. The link from basic research to technology development and process integration in the fields of optoelectronics, bioelectronics and organic/polymer electronics needs considerable attention.

An alternative approach to nano-circuitry or machinery is the construction of nano sized switches, based upon rotaxanes, cataenanes. These unique organic systems consisting of a thread over a ring shuttling between two positions has been developed by Stoddart and Heath at UCLA and incorporated in to chip circuitry with the help of Hewlett Packard. There still considerable scope for the future development of ordered molecular materials for applications in e.g. light emitting diodes and field-emitting transistors. The new area of nanomachines however is yet to be explored and these nano-objects may well be incorporated in future smart materials and sensors. Given the extraordinary ATP driven motors and machines found throughout nature there is little doubt that there is much to be discovered and applied.

An area of research which has considerable potential is BioMEMS. It is all but forgotten that digital circuits, designed in the 1950s and 1960s, were inspired by the understanding at that time of how the nervous system operates. The biological metaphor is simply too compelling to ignore, and that is perhaps the best argument for a bright future for the emerging technology of BioMEMS. A combination of silicon chip technology and the basic molecular processes of living organisms, BioMEMS promise to go beyond mere metaphor by actually merging organic processes with electronic circuitry. One example is research into how to attach metal and semiconducting nanoclusters to proteins. One could conceive of a bioarray that creates 3D protein clusters with intricate semi-conducting devices and circuits - the BioMEMS analog of a silicon wafer full of chips. More recently a redox-protein has been studied between two electrodes as a simple biotransistor. In addition groups at MIT and in Copenhagen (Belcher and Brown) have by phage screening discovered protein sequences that stick to CMOS circuitry. Integration of biological active proteins and enzymes into current CMOS electronics has enormous potential in the fields of biosensors and biomachines.

In addition to nano-electronics, bioelectronics and nanomachines, the area of *nano-catalyst* should not be neglected. Ranging from defined enzyme/catalyst arrays for cascade reactions to nanoreactors, there is still surprisingly little research on self-assembled nanometre sized catalysts arrays.

3.3.2. National research

There is considerable general research in nano-organics throughout The Netherlands. The University of Delft (Dekker, Morpurgo, Kouwenhoven, and Hadley etc.) has a world reputation in the study of nano-electronics. The groups of Nolte (functional self-assembled architectures) and Rowan (nanomachines) in collaboration with Maan and Rasing at the RU Nijmegen have been developing new nanowires and functional surfaces. In Eindhoven, Philips Research has refocused some of their research into the area of nanobiotechnology which will embrace the developing area of bioelectronics. At the TU/e, Meijer, Janssen and Scheenning study nanoscale electrical transport in self-organized molecular assemblies and new nano-organics for photovoltaic devices. In Groningen, the group of Hummel has an international reputation in the field of fullerenes, Palstra on organic crystals, and Van Wees on organic field effect devices. This holds in Twente for the group of Vancso on engineering and analysis of polymer surfaces and interfaces, Reinhoudt on functional surfaces, and Subramaniam on single-molecule techniques for DNA-protein interactions, and in Wageningen for Cohen Stuart on self-assembly of ionic amphiphilic copolymers. Furthermore, research activities on nano-organics are also embedded in the Dutch Polymer Institute (DPI).

3.3.3. Scientific prognosis

It is clear that CMOS technological will remain as the primary chip technology for the foreseeable future. However there is still considerable potential for new nanotechnology making hybrid CMOS and bioorganic system. Despite this new area, there is still considerable research to still be carried out in the area of novel photoactive, conductive materials and molecules for application in devices. This area should not be neglected. It is proposed that the following four areas should be spotlighted.

- <u>NanoDat</u> (datastorage at the nanolevel)
  In conventional memory cells a bit of information is either a zero or one. One way of increasing the areal density of data is by using single molecules as individual storage bits. In this way it may even be possible to store more than one bit in each memory cell. This is one goal of molecular electronics (or 'moletronics') where, for instance, one would like to store information in the form of parcels of charge placed at several active sites around a single molecule or biomolecules with hierarchical levels of information. To achieve this goal; (i) new molecules need to be developed which can adopt numerous specific states; (ii) new techniques need to be developed for positioning and addressing individual molecules.

- <u>Bio-electronics</u>
  There is little doubt that if BioMEMS research can reach the same level in proteomics that it has now achieved for DNA, a genuinely disruptive technology will emerge. But getting to that level will require a much more varied group of biotechnologies than is found in the typical BioMEMS lab. The combination of functional enzymes, alloesteric proteins at the CMOS interface offer unlimited potential for numerous research fields. An integrated multidisciplinary group needs to be assembled, aimed at tackle together specific problems. In particular attention should be given to the study of direct electron transfer to metalloproteins at surface engineered metallic and semiconductor electrodes and *in vivo* systems.

- <u>Nanocomposites and materials</u>
  There is little doubt that nanotechnology is a classic, general-purpose technology (GPT). Other GPTs, including steam engines, electricity, and railroads, have been the basis for major economic revolutions. GPTs typically

start as fairly crude technologies, with limited uses, but then rapidly spread into new applications. The convergence of the nanosciences, biotechnology, information-technology and cognitive science has led the US-Army to establish an Institute for Soldier Nanotechnologies at MIT and Cambridge England in 2002. This high-tech application of nanomaterials, for their strength and 'smartness' has also led NASA to also initiate a programme called nanotechnology in space. Both the above areas have been largely been neglected by the European research establishments and have left open a potential market. The application and incorporations of nano-objects with defined properties into the materials world has significant interest but still needs to be explored.

- Nanomachines

  The recent development of simple nanometre sized nanomachines which can move along stations like a 'molecular train' has already been tentatively incorporated into the electronic world as molecular switches. More recently the natural rotary nanomotor, ATPase, has been modified and a working *in vitro* motor constructed. This field is however still in its infancy and needs considerable nurturing to manipulate natural motors such as myosin (found in muscles) flagellar motors and to construct synthetic analogous of these systems which possess their own unique properties, such a unidirectional rotary motion (Feringa, RuG), shuttling and switching (Brouwer, UvA) and molecular machines which run along polymer carryout sequential reactions (Rowan, RU), mimicking DNA polymerase. All these systems are the first of their kind.

3.3.4. Recommendations

- The development of a nanomaterials institute in The Netherlands, or under the umbrella of NWO a nanomaterials initiative, aimed at the stimulation of nanocomposites and smart materials.
- A strong programme should be established in the area of bioelectronics toward BioMEMS. This would bring together the Dutch expertise in proteins and enzymes with the CMOS technology, generating numerous spin-offs in the areas of biosensors and nanomedicine.
- The area of nano-organics in the more traditional sense should still be stimulated in particular novel approaches toward the self-organization and programmed self-assembly of the respective components.
- The area of nanomachines and motors, a field for which The Netherlands already has a world reputation should be more strongly nurtured since the potential of such systems remains unexplored.

Finally, one must not forget the field of nanocatalyst and it is suggested that in combination with other CW initiatives such as NRSC-NIOK an emphasis is placed on catalysis in the nanoworld.

3.4. Research topic: SPINTRONICS

Prof.dr. Th.H.M. Rasing (RU)

3.4.1. General overview

Scientific perspective

Spintronics can loosely be defined as an emerging new technology that tries to exploit the fact that charge carriers (electrons and holes) have a spin as well as a charge. This field has emerged as a result of two parallel developments:

- the expected end (sooner or later) of the still ongoing miniaturization: what happens beyond Moore?
- spectacular discoveries in nanomagnetism, like giant magnetoresistance (GMR) and oscillating exchange coupling.

The area of spintronics is closely related to the information technology. Therefore, it is customary to include not only spin-based transport like phenomena, but also the very important and related area of information storage and manipulation.
Important and illustrative examples are GMR based sensors, magnetic random access memories (MRAMs), spin-transistor, and quantum computation based on coherent manipulation of spin-states.

Application perspective

Applications can be expected in many areas:

1) storage (MRAMs, Magneto Optical Recording)
2) Sensors (already widely applied in modern read heads, but having an enormous potential in automotive, robotic, household, bio-industry)
3) Quantum computing
4) Nano-electronics ('Beyond Moore')

The market potential in these areas is enormous: in data storage >25 billion Euro, in sensors 10-100 million Euro.

3.4.2. National context

The Dutch have quite a strong reputation in this field, going back to the first ideas for a spin-transistor (De Groot, Nijmegen), its realization (Lodder et al., Twente), the strong contribution of TU/e with Philips Eindhoven in the area of GMR in the nineties and the more recent development of ultrafast manipulation of spinstates (Rasing, Nijmegen).

Academia

Momentarily, the following strong academic groups can be identified:

- TU/e: Koopmans, De Jonge: materials (metals, semiconductors, oxides, organic) and devices, ultrafast dynamics;
- UT: Janssen: transport, storage; Blank: thin films; Kelly: theory;
- RU Nijmegen: Rasing, Kirilyuk: ultrafast dynamics, coherent control, magnetic clusters, local probing; De Groot, Katsnelson: theory, half-metals;
- TUD: Bauer, theory; Kouwenhoven: quantum computation;
- RuG: Van Wees: transport.

Industry

Though the major Dutch industry Philips, has moved its own research in the area of MRAMs abroad, its interest in the application of nanomagnetism and sensors (in particular bio-sensors) is still strong.
For the rest, there is no real 'spintronic' industry in The Netherlands, though there are of course important related industries like ASML, OnStream, Twente Solid State Technology.
It can be expected that, in particular in the area of biosensors, there will be room for spin-off companies in the coming decade.

3.4.3. Future developments

Scientific developments

Quantum magnetism: macroscopic quantum tunnelling of magnetization has been observed and studied; another process – magnetic quantum coherence – was never observed yet. This is a key point for the use of spins in quantum computing.

Very small magnetic particles/clusters: both phonon and magnon modes become discrete; the interaction between them changes character. This can lead to the increased stability of the spin configuration in specially designed magnetic clusters

To further develop spintronics that uses spins of both holes and electrons, thorough study of the time- and length scales of their coherence is essential.

Further research of the interaction between spins and intense laser pulses will explore the ultimate limits of ultrafast spin dynamics and may lead to the development of a new area of coherent opto-spintronics. The recent developments of current-induced spin dynamics may offer interesting new perspectives, e.g. for oscillators, but first a lot of research will have to be done.

In the area of storage, the stability of nanomagnetic elements, and the reading and writing of information in such devices will offer great fundamental and technical challenges: what are the fundamental and practical limits in density and speed?

A very different but on the other hand closely related area is that of biomagnetism: how does nature exploit nanomagnetism? This leads also to the very interesting class of oxidic magnetic materials, including the large group of antiferromagnetic materials, that start drawing a lot of attention recently.

Developments in applications

Most immediate area of applications will be in storage. This is still growing with close to 100% in capacity per year.

For a real development of spin-based electronics, the further development of room temperature semiconductor based spintronics will be essential.

A second strong growing area is that of sensors, from automotive to biosensors.

Long term application could be in quantum computation (Delft).

3.4.4. Outlook and recommendations

In the area of spintronics and nanomagnetism, The Netherlands have a very strong impact with groups that operate at and define the state of the art. Though short term payoffs for applications are not so clear, both the potential and the current impact on science by these Dutch groups make this an important area of future research.

There are a number of issues/topics that need to be addressed in particular:

1. novel magnetic materials and structures (oxides, clusters, antiferromagnets). This also includes a creation of stable, addressable nanostructure arrays on a large scale with high densities.
2. development of spin-based quantum computing schemes: wise to pursue, given strong Dutch involvement in this field.
3. coherent optics control of spin states and development of femtosecond-scale opto-spintronics.
4. semiconductor-based spintronics: novel ferromagnetic semiconductors, hybrid structures, time-scale properties, etc.

3.5. Research topic: NANOFLUIDICS

Prof.dr.ir. J. Westerweel (TUD)

3.5.1. General overview

Nanofluidics deals with the flow of liquids and gases in very small capillaries and very thin channels. The challenging aspect mainly deals with the scaling of flows in such very small geometries, i.e. the so-called *square-cube law*, where surface effects (proportional to the square of the typical geometric scale) become dominant over volume effects (which scales with the cube of the typical geometric scale). Although in general we do not expect 'new' physical phenomena, a new regime is entered in which the classical 'macroscopic' transport phenomena are considered under very extreme conditions (an example is 'thermal creep' in which a gas flows against a temperature gradient; another example is the visco-electric effect, due to surface charges, that increases the effective fluid viscosity). This opens new possibilities for many technical applications (see below). At the same time we observe interactions that generally insignificant at a macroscopic scale, but that dominate the fluid behaviour at very small scales (e.g., surface tension effects and electrical effects). More examples of the extreme conditions that exist in nanochannels are the negative liquid pressures (tensile stress) created by capillary forces and the strongly accelerated drying occurring in nanogrooves due to corner flow.

<u>Scientific perspectives</u>

The description of the transport phenomena (for momentum, heat and mass) at macroscopic scales are considered to be well-established descriptions that are valid in a continuum approach. These descriptions break down at molecular scales. For gases this will occur at fairly large scales (~micrometre) for low densities (Knudsen regime), and the description of rarefied gases is generally considered to be an established discipline. For liquids the continuum hypothesis breaks down at much smaller scales (~10s nanometres). A major scientific challenge lies in the description of the transport phenomena at such very small scales where the continuum approach is no longer valid. An example is the discussion on the validity of the 'no-slip' boundary condition based on observations in small capillaries. One approach is to combine the continuum approach with the molecular approach for the description of transport phenomena. The general problem is that most fluidic systems are too large for a representation in a molecular dynamics simulation, while a continuum approach cannot lead to a solution as the proper boundary conditions and constitutive relations are unknown. One approach is to combine *molecular dynamics* (or similar codes) and solutions of the continuum equations to describe the transport processes in nanofluidic devices. This combines the expertise from statistical physics and phenomenological physics.

When we consider flow geometries that are well below a micrometer, the confinement of a capillary or nano-channel is so small that individual (large) molecules (i.e., polymers, large proteins and DNA) are transported through these devices, which makes it possible to manipulate and analyze or synthesize these individual molecules. In classical fluid mechanics dissolved constituents, such as polymers, are generally considered to be uniformly distributed over the fluid, and the fluid properties are described by the (bulk) rheological constitutive relations. This approach is not valid in small confinements, where the local presence of large molecules is incongruent with the continuum concept of a 'fluid'. This requires a description of the behaviour and physical properties of individual (large) molecules, e.g. by means of molecular dynamics. Furthermore, even at the low volume flow rates for small channels, the shear rates at the interfaces can become several orders of magnitude higher than encountered in macroscopic applications. For certain fluids this means that non-Newtonian behaviour can become apparent.

Much is to be expected from the implementation of molecular interactions similar to those commonly found in biological organisms. Aquaporins e.g. allow water transport but block proton transport by a smart protein structure. Comparable structures could be implemented in nanofluidics devices to obtain selectivity. The implementation of active transport modes like occurring by kinesin could be considered as well.

Some of the other scientific challenges will lie in the development of measurement methods that can operate in such devices, e.g. for the detection of individual molecules.

<u>Application perspectives</u>
As mentioned before, the small scale of microfluidic and nanofluidic devices enhances the importance of surface-dominated effects. An obvious example is that the heat transfer rate will be much higher in these small devices as compared to their macroscopic counterparts. This makes it possible to design more efficient heat exchangers (e.g., for the purpose of cooling electronic components). Another advantage of the small scale of these devices is that it is possible to handle very small samples (e.g., in forensic analysis). This makes it possible to implement chemical analysis on a small microfluidic device, i.e. a Lab-on-a-Chip or μTAS. Similar approaches are used to implement chemical reactors as MEMS devices. The major advantages are the portability of such systems and the low costs per device for mass-production applications and disposable devices. An example is the blood analysis that can be done at the site of a hospital bed, rather than in a hospital laboratory.
One of the most promising aspects of nanofluidic devices with respect to applications is that the confinement of the device makes it possible to manipulate individual (large) molecules. This can be used to probe (parts of) individual DNA molecules, or to sort molecules based on their optical or chemical properties. Detection of individual molecules will make it possible to identify very low concentrations of pathogens.
In addition, the small dimensions of the devices imply that the fluid behaviour is completely dominated by viscosity, whereas most macroscopic fluid handling components rely on fluid inertia rather than fluid viscosity. Consequently, new concepts for pumps, valves, mixers, sieves and separators have to be invented, in addition to metering devices for measuring flow rates.
Micro- or nano heat pipes designed with nanogrooves will show strongly improved thermal transport.
For separation purposes very large regular 2D arrays e.g. of nanoposts can repeat the same separation step on single molecules many times in flow-through mode. This will both effect separations on a single molecular basis and solve detection issues by the flow-through mode.
For separation purposes nanomachined Brownian ratchets also show a promise, since their separation speed scales with distance squared.

3.5.2. National context
There are a number of groups active in areas that are closely related to fundamental and practical aspects of nanofluidics. The groups that deal with traditional fluid mechanics can be found within the FOM/Phenomenological Physics and the J.M. Burgers Centre. Research groups active in polymers and colloids are mainly found within FOM/Statistical Physics. The area of nanofluidics would benefit from a close collaboration between these two groups. Most of the research groups are involved in either Nanoned or Microned. In the MESA+ institute, four research groups (Lohse, Mugele, Elwenspoek, Van den Berg) with strong activities in nanofluidics can be found supported by excellent nanomachining facilities.

The main industries that have interest in microfluidic and nanofluidic applications can be found in the biomedical field (e.g., sample analysis), the food industry, and the drug industry. Companies that have expressed their interest are: Philips, DSM, Unilever, Organon, Océ Technologies. Smaller companies are Coberco, Pamgene, Micronit, Aquamarijn.

3.5.3. Future developments

The ability to create very small fluidic devices will be concurrent with the technology for the production of dedicated materials. The area of nanofluidics will mainly focus on the detailed interaction between solid surfaces and liquids, in relation to other physical phenomena (e.g., electric and magnetic interactions). As mentioned before, the very small confinement of nanofluidic devices makes it possible to manipulate individual molecules. This will simplify detection systems that can be used in the food and drug industry and in forensics. On a slightly larger scale, one can imagine the development of fluidic systems that, instead of molecules, manipulate and transport individual cells. This can be combined with suitable detection systems that characterize different properties of cells, after which cells can be sorted based on their properties. This can strongly impact the development of new medical diagnostics, and even be the basis of certain cell-based therapies. Evidently this clearly interacts with other nanoscience areas.

From engineering perspective much is to be expected from the merger of life sciences and nanomachining. Existing macromolecules from biological origin can be incorporated in nanostructures to include their functionality, but also new molecules can be designed and incorporated that exhibit the behaviour found in nature more strongly. Evidence of the effectiveness of this approach can be found e.g. in pharmacy by comparing the receptor binding strength of naturally occurring and specially designed neurotransmitters.

3.5.4. Outlook and recommendations for future research

The main future research will lie in an increase in the complexity of nanofluidic and microfluidic devices. Most devices developed so far have fairly simple geometries (i.e., straight channels), but the ability to create more complex structures with different materials makes it possible to consider more complex behaviour. A lot of attention is now on detection and characterization of molecules in nanochannels, but one can expect that the focus will shift to control and detection of molecules in (complex) nanofluidic devices. This involves both passive and active control mechanisms (actuators). Rather than 'mechanical' actuators, one can also think of molecular actuators, e.g. using antibodies to bind molecules to 'larger' structures (e.g., gold nanoparticles) that can be manipulated with optical tweezers.

There will also a development of numerical codes that describe the flows at these very small scales. This will combine a continuum approach and MD approach. The MD approach can be used to describe the phenomena, and to generate the proper boundary conditions that can be used to solve problems in a larger and more complex domain by means of a continuum approach.

It is expected that specific single-molecule interactions performed in a controlled fashion will play an increasingly important role. Examples of molecules that perform such operations can be found in nature (aquaporins, ion channels, kinesin and tubulin). In addition, there exists a lot of fragmented knowledge in widely varying disciplines such as sol-gel chemistry, membrane science, soil science, nano-engineering, biology and classical fluid mechanics. Intensive interaction between all of these disciplines is therefore necessary, and it is anticipated that nanomachining will deliver a variety of new tools that will enable exciting new research.

3.6. Research topic: INDIVIDUAL PARTICLES

Prof.dr. A. van Blaaderen (UU)

3.6.1. General overview & scientific/application perspective

Particles or (non-biological) macromolecules with one of their dimensions in the nano size range (arbitrarily defined as < 100 nm) are considered here as belonging to the theme covered, and will be referred to in what follows as (nano)particles. This of course includes so-called quantum dots or nanocrystals where already from their name it is clear that their specific properties are strongly related to the fact that their size is on the order of tens of nm or smaller. However, also particles with for instance a size of 500 nm, but a shell of gold with a thickness of 20 nm fall under the definition just given. The plasmon resonance which is confined in one dimension to the shell thickness of 20 nm gives such a particle indeed properties that are completely different from that of bulk gold. Another example is given by particles that are built up from nano-crystals, here again the (optical) properties are determined to large extent by the quantum mechanical properties of the quantum dots.

Dispersed in a liquid such 'individual (nano)particles' belong to a class of matter referred to as colloids. The upper size of colloids is several μm and particles that are larger are referred to as granular matter. The lower size is defined at a few nm such that the particles can be described to good approximation as being dispersed in a continuum. Thus the degrees of freedom of the solvent can be averaged out and replaced with constants characterizing the continuum (refractive index, density etc.). Einstein was the first to show that colloids have a well-defined thermodynamic temperature and thus can self-organize into for instance colloidal crystal phases which are completely analogous to atomic or molecular crystals. (A statistical mechanical description in which the free energy is lowered is not (yet) possible for granular matter.)

At the moment the best-defined (nano)-particles are made by wet chemical synthesis. With well defined is not only meant that all particles have the same size (are monodisperse), it also can refer to being of a pure single crystalline state, and even the shape of several of these systems can be controlled (rods, sphere, disks, platelets etc.). It is not only that the particle properties, be it photonic, electronic or magnetic are strongly size dependent, that make individual particles interesting for a lot of applications, their functionality can be strongly increased by chemical or physical surface coatings. This can even lead to very specific interactions if the surface coatings used are taken from biology (DNA complementarily, binding of antigens etc.). Individual nano-particles are therefore already successfully used in very diverse fields, such as *(bio)-labelling* (microscopy, NMRI, screening), *nano-electronics* (Coulomb blockade, single electron transistor), *(nano)-photonics* (photonic crystals, plasmonics, local field enhancements), *sensors*, *catalysis*, *displays*, *storage, lighting* and even in 'less advanced sounding' products like *paint*, *food* and *healthcare products*.

However, even although the theme is 'individual particles' self-organization is a third powerful way in which properties of materials made from these components can be changed in what sometimes is referred to as a 'bottom-up' approach. In self-organized structures, such as colloidal crystals, the nano-particles can interact and change their properties as dramatically as atoms in a crystal. Just one example for which such a change has been worked out already in detail is photonic crystals of metallo-dielectric nano-particles (e.g. small gold core of 30 nm with a thick silica shell). For certain crystal symmetries a complete band gap in the visible will result if they are made from such particles. One has just started exploring the possibilities of self-organization for making new nano-based materials, but it is clear from results on larger colloids that the use of external fields such as a flow field (shear), electric or magnetic field or light are very powerful ways to manipulate this self-organization in inexpensive ways. Especially as the collective effects are usually well developed with no more than ~10 lattice

constants, total feature sizes are still so small that almost all applications mentioned above for the single particles apply here as well (or actually some, like photonic crystals really doe not exist for single particles).
Having control over particle shape has just been started for some systems and also control over the particle interactions and possibilities of using core-shell geometries (mixing for instance properties such as in metallo-dielectric structures) leaves a lot of room for improvement. This is even more so for using (directed) self-organization to create new properties. Despite all this room for improvements there are a number of commercial applications available or close to becoming so in which nano-particles are used for their nano-properties. Next to the applied sides of having control over particle geometry, properties, interactions and self-organization there are also many fundamental issues of interest as well. The quantum mechanical properties of nano-particles allow for a tuning of wave-functions that is very hard or impossible to achieve with molecules and this ability is and will lead to new science.

3.6.2. National context: academia & industry

The Netherlands has been at the forefront of colloid science for a very long time. A world wide recognized centre both in particle synthesis and model studies of colloids is in Utrecht (Lekkerkerker/Philipse, Van Blaaderen), but also Wageningen University has a strong reputation. More recently, other Utrecht groups, also in the Debye Institute, have become involved in nano-particle research with a strong focus on the specific properties coming along with the nano-size (Vanmaekelbergh/Meijerink). In the closely related field of photonic crystal research, where one way of making photonic crystals is by using the self-organization of colloids, the group of Vos (AMOLF) belongs to the international research top.
Most of the larger companies like Philips, Unilever, AKZO, Shell and DSM have nano-particles research going on; many real products based on these systems are already on the market. A much smaller company like Aurion (Wageningen) that makes nano-gold for labelling has (virtually) its entire business in nanoparticles.

3.6.3. Future applications and scientific developments

Along the lines as sketched in 3.6.1. there is still a lot of improvement possible for many systems in particle geometry (core-shell) and interactions (more specific, tuneable by external fields or stimuli etc.). Many new possibilities will be realized by the additional control that (manipulated) self-organized nano-particles based materials will have as a result of the collective properties. Many synergies, such as for instance local field enhancements, may result from multi component systems. In addition, wet chemical synthesis in combination with already available fields known from polymer processing (such as spin coating, ink-jet printing) to manipulate 3D self-organization have the possibility leading to large-scale and low-cost applications. This combination has the potential to truly change applications such as displays, lighting, storage etc.

3.6.4. Outlook and recommendations for future research

The wet chemical 'bottom-up' approach of designing and studying the physical properties of individual nano-particles and the manipulation of their self-organization into materials for applications and fundamental science is truly multidisciplinary. Support will therefore only be effective if it addresses both the chemical and physical aspects. It is important that aside from more applied research with applications nearby, it is important tot support structured and longer-lasting fundamental support in The Netherlands on nano-particle based research. The Netherlands has the concentration of scientists to keep it a major player in the field of colloidal nanoscience, but is lacking a major multidisciplinary programme. (The 'individual nano-particles' theme is not well represented within the Nanoned consortium.) Such a research programme can best be focused on self-organization of soft condensed matter as a whole than on that of particles alone as in a more broader sense also several other strong 'bottom-up' approaches can be recognized in the total field of *soft matter science* (e.g., soft lithography, phase separation of block-copolymers etc.) and many issues follow a similar scientific approach and may benefit from each other.

3.7. Research topic: NANOPHOTONICS

Prof.dr. A. Polman (AMOLF)

3.7.1. General overview

Nanophotonics is the research field that studies the manipulation, storage, generation, detection, and amplification of light at length scales that are typically smaller than the wavelength of light. Examples are the optics of surface plasmons in nanostructures, semiconductor nanowires and quantum dots for generation of light, confinement of light in nanocavities, control of spontaneous emission in photonic crystals, near-field interactions, local field enhancement in metallic nanostructures, multiple scattering and localization of light, random lasing.

Within the nanosciences, nanophotonics is a research field that is relatively unexplored. But at the same time the field is rapidly growing worldwide. Today, nanophotonics is at the same stage as micro-electronics in the early 1980s, or nano-electronics in the 1990s. Yet, it is expected that within 10 years nanophotonic technology can have the same impact on our society as micro-electronics has today.

Fundamental research on nanophotonics can lead to novel applications in e.g. communications technology, lasers, solid-state lighting, data storage, lithography, (bio-) sensors, optical computers, quantum cryptography, solar cells, medical imaging, metrology, light-activated medical therapies, displays, navigation, automobile industry, surveillance and security, smart materials. Given the importance of these applications there is large interest from industry in fundamental research in the area of nanophotonics. Nanophotonics is a unique and extremely interesting field of research because it combines a wealth of scientific challenges with a large variety of near-term applications.

3.7.2. National context

Academia

The largest concentration of research on nanophotonics in The Netherlands is at the recently established Centre for Nanophotonics, at the FOM-Institute for Atomic and Molecular Physics (AMOLF) in Amsterdam (Kuipers, Lagendijk, Polman, Vos, Verhoeven, partly: Bonn, Herek). Nanophotonics is also an important topic at several general Dutch Universities, e.g. Van Blaaderen (UU), Dijkhuis (UU), Gregorkiewicz (UvA), Knoester (RuG), Lenstra (VU), Orrit (LEI), Rasing (RU), Vanmaekelbergh (UU), Woerdman (LEI). The technical universities generally focus on technological aspects of (nano)photonics: Driessen (UT), Salemink (TUD), Wolter/Smit (TU/e).

All Dutch researchers in nanophotonics are part of an active national photonics network. This has first been established by the National FOM research programme *Photon Physics in Optical Materials* (1999-2006). The international panel that evaluated the proposals concluded: '*Overall, it was felt that the quality of the proposals was very high, covering quite a large fraction of the field, an amazing feat given the size of The Netherlands, a unique testimony to the excellence of photonics research in the country, well-known by the international visibility of its leaders*'. In 2002, the national nanotechnology programme Nanoned declared Nanophotonics as one of the four key flagship themes that were granted within Nanoimpuls, the programme for pre-funding of the most urgent nanotechnology topics within Nanoned.

Industry

Several Dutch companies are partners in existing FOM and Nanoned research programmes, and thus take advantage of fundamental research in academia in nanophotonics: Philips, ThreeFive Photonics, Lionix, C2V, ASML, Alcatel, Phoenix, Shell Laboratories. Other Dutch companies that (can) profit from nanophotonics are: DSM, Océ Technologies, Unilever, Akzo Nobel, and a large number (> 20) of

small companies. The Centre for Nanophotonics (AMOLF) has stationed one of its research groups at Philips.
On a European scale, photonics companies are organized within the European Photonics Industry Consortium (EPIC). This network mediates transfer of knowledge between scientists at academia/institutes and European industrial partners. It also enables European research and development initiatives, and serves to develop roadmaps that can guide academic researchers in their research. In a recent report, EPIC says: *Photonics is one of the most important key technologies for markets in the 21st century. It influences all aspects of our lives and is essential to Europe's industrial competitiveness. The Photonics industry plays a vital role in securing the leadership in areas such as information and communication, lighting, manufacturing, security or life science and health. Photonics is a driver for technological innovation and has a tremendous leverage creating products that multiply by many times the value of initial photonics components and technologies.*

3.7.3. Future developments

Photonics thus is a key enabling technology for a broad range of applications, with a very large market potential. Yet, this technology can only be developed if key fundamental questions are solved. In fact, nanophotonics is a research field that is still in its infancy. Today, a critical opportunity exists to initiate a national fundamental research programme on nanophotonics. This may provide on a medium-term time scale (> 5 years, but in some cases even one a shorter time scale) the knowledge and innovation base that will enable Dutch and European industry to acquire a key strategic position in nanophotonics application areas.

Scientific developments

Scientifically challenging nanophotonics themes for which unique expertise exists within the fundamental research community in The Netherlands are (among others): photonic light sources, plasmonic light sources, controlled dispersion control of light, nanoscale energy transfer, nanoscale confinement of light, plasmonic photonic integrated circuits, light propagation and scattering at the nanoscale, single-molecule physics, photonic nanowires.

Developments in applications

Application areas with a strong Dutch industrial interest include: solid-state lighting, data storage, lithography, (bio-)sensors, quantum cryptography, solar cells, medical imaging, light-activated medical therapies, displays, smart materials.
A national nanophotonics research programme should be chosen around fundamental research themes that are scientifically challenging and, at the same time, have a clear relation with well-defined applications.

3.7.4. Outlook and recommendations for future research

A future nanophotonics programme can based on either:

1. Concentration: *a coherent well-selected research programme carried out on a single location*. This is presently the case at the Centre for Nanophotonics in Amsterdam, where 40-50 researchers collaborate in a common nanophotonics research programme.
2. Thematic focus: *combining expertise at different locations to achieve a single goal.*

The latter was the aim of the previous FOM and Nanoned programmes. These programmes have served to stimulate a very strong and active nanophotonics network in The Netherlands. At the same time, research projects in these programmes were sometimes carried out in a rather isolated way, and (in Nanoned), top-level groups were left out. A future thematic programme is most likely most successful if a limited number of well-chosen themes are addressed in which participants are then chosen based on quality and their openness towards contributing to innovation.

3.8. Research topic: NANO-BIOSCIENCE AND -TECHNOLOGY

Prof.dr. C.F. Schmidt (VU)

3.8.1. General overview

The 21st century will be the century of life sciences. Large challenges lie ahead in the basic understanding of living systems and in the application of such knowledge in human healthcare, nutrition and environmental protection. A growing world population, potential pandemics including viral and other infectious diseases, aging populations in large parts of the world with connected issues such as cancer, heart disease or neurodegenerative diseases all require major investments in healthcare and medicine. Meanwhile biology, biochemistry, biophysics, biotechnology and medicine are all progressing towards a molecular level of analysis and manipulation. The basic functional units in living systems are macromolecules, nanometres in size, and cells. There is thus a strongly growing need for nanoscale basic science, including the development of experimental technology and conceptual tools, as well as for devices that can interface with living systems on the sub-cellular level (or: the molecular scale). This includes diagnostic devices, implantable devices, and precisely targeted treatment devices. On the other hand, living systems are far ahead of human technology in terms of complex self-assembled materials and truly nanometre sized assemblies of high functional complexity. It is to be expected that much can be learned from biology to be applied in advanced technology, for example for synthetic nanoscale-designed materials. Nano-bioscience is therefore an immensely rich field of science with a very wide range of applications with primary societal and economic importance.

3.8.2. National context

Academia

Apart *from* purely medical and biological research on the molecular level, such as The Netherlands Genomic Initiative, there is a mostly recently established community of interdisciplinary research groups, focussing on dynamics and function on the nanometre scale, both in biological systems and in synthetic soft-condensed-matter systems. Research includes imaging technologies such as scanned probe methods (Van Hulst, Subramanian, UT; Schmidt, VU; Schmidt, Oosterkamp, LEI; Speller, RU; Dekker, TUD), or (single molecule) fluorescence microscopy (Schmidt, Peterman, VU; Schmidt, LEI), single-molecule manipulation methods (Dogterom, Tans, Mulder, AMOLF; Bennink, Subramanian, UT; Schmidt, MacKintosh, VU; Dekker, TUD; Den Blaauwen, Van Driel, UvA), microscopic manipulations of cells (Vink, UvA/AMC; Schmidt, VU; Schmidt, LEI; Figdor, RU; Tans, AMOLF), self assembly of complex materials (Frenkel, AMOLF; Schmidt, VU), and theory of soft matter and biological matter (MacKintosh, VU, Mulder, AMOLF). A large fraction of these groups is embedded in the FOM-subfield 'Physics of processes in living systems', but links to medical and cell biological groups are rapidly growing. Molecular cell biology is a science area with excellent groups at several Dutch universities.

Industry

Industry in The Netherlands in the bio-nano area is mainly focusing on medical technologies. Philips, is currently expanding from medical imaging and image-guided therapy to other phases in the 'disease management cycle' (prevention, early detection, therapy). Philips has advised that the Dutch nanoscience community aggressively enters and develops the nanomedicine field. Recently, Philips Research, TU/e and Maastricht University and Academic Hospital have signed a letter of intent to found a Centre for Molecular Medicine (CMM), a unique Centre of Excellence. FEI, a leading company in electron beam imaging and focussed ion beam nanostructuring methods, considers growth in biomedical applications as a top priority.

3.8.3. Future developments

The demand for basic research and technology development on and around the scale of biomolecules, i.e. 1-100 nm, is clearly immense. While much of the biochemistry is well advanced, the physics and the engineering on that scale is still in its infancy. The field is very large and within The Netherlands it will be wise to contribute through targeted areas of emphasis where critical mass and excellence exist.

Scientific developments

Areas with existing local expertise and with a promise to be pivotal in the future are: single molecule techniques, high resolution imaging techniques (scanned probe techniques), analysis and development of novel nanostructured materials, manipulation techniques for single cells, and design of new biosensor technology.

Developments in applications

Important applications include medical diagnostics and medical imaging, including the use of nanoparticles a s sensors and labels, as well as research on cells, including stem cells and tissue engineering.

3.8.4. Outlook and recommendations for future research

There is a clear need for continued support in this field. It should be emphasized that basic research is necessary to provide and support the platform on which technological developments can take place. Efficient connections to industry are necessary to guarantee fast technology transfer. This area is located at a critical interface of conventional nanotechnology with applications in the huge market of modern materials science, biotechnology and medicine.

3.9. Research topic: NANOMEDICINE

Prof.dr.ir W.E. Hennink (UU) and prof.dr. G. Storm (UU)

3.9.1. General overview and scientific / application perspective

Nanomedicine has been defined by the European Science Foundation [1] as 'the science and technology of diagnosing, treating, and preventing disease and traumatic injury, or relieving pain, and of preserving and improving human health, using molecular tools and molecular knowledge of the human body [2]'. This novel research area comprises applications of nanotechnology for treatment, diagnosis, monitoring, and control of biological systems. Nanomedicine is a large subject area. Originating from the visionary idea that tiny nanorobots and related machines could perform cellular repairs in the human body at the molecular level, nanomedicine today is now branching out in hundreds of different directions. Research into the rational delivery and targeting of therapeutics and diagnostic agents via nanosized particles administered by intravenous or local routes is at the forefront of projects in nanomedicine. These involve the identification of precise targets (cells and receptors) related to specific clinical conditions and choice of the appropriate nanocarriers to achieve the required responses while minimizing the side effects. These nanosized carriers can be loaded with drugs that have unfavourable biopharmaceutical properties. E.g., drugs are rapidly cleared form the circulation, are rapidly degraded, do not reach their target site at a sufficient level and exert toxic side effects due to accumulation in healthy tissues. In addition to low molecular weight compounds, also modern biopharmaceuticals like pharmaceutical proteins and nucleic acids (e.g. plasmid DNA, si-RNA) may benefit greatly form nanosized delivery systems. Particularly, nanosized drug delivery vehicles are of interest for the treatment of life-threatening diseases (e.g. cancer, cardiovascular), chronic inflammatory disorders (e.g. rheumotaoid arthritis, multiple sclerosis), and infectious diseases (e.g. HIV, tuberculosis). Several nanosized drug delivery systems are currently clinically applied. The first generation of systems is mainly based on lipids. These drug-loaded colloidal particles accumulate at their site of action (e.g tumor tissue or other sites of inflammation) by passive processes (EPR, enhanced permeation and retention) because the vasculature at these sites is more permeable than elsewhere in the body. Drug release from these particles is not well controlled and is dependent on destabilization and/or enzymatic degradation of the drug-loaded particles. Therefore, for the future there is a need for systems that are able to specifically interact with the target cell by molecular recognition and that are able to pass a number of biological barriers (e.g. cellular and nuclear membranes). Moreover, such targeted nanomedicines should be able to release their drug contents at the aimed site of action triggered by a certain physiological (pH, redox potential) or external stimulus e.g., heat, ultrasound, magnetism). There is also need for nanosized drug delivery vehicles that can be administered via another route than via injection, such as e.g. the pulmonary, nasal, and oral route of administration. Also, systems ('artificial viruses') are urgently needed that are able to efficiently deliver macromolecular therapeutics to their intracellular site of action, as for example siRNA to the cytosol and plasmid DNA to the nucleus. Such artificial viruses are hybrid structures composed of synthetic biodegradable polymers and/or lipids, and proteins/peptides or fully protein-based as those prepared by protein engineering technologies. A major challenge is the design of nanoparticles for 'imaging-guided drug delivery'. Here, targeted nanomedicines are loaded with a drug as well as an imaging agent (e.g. magnetic resonance imaging probe, or luminescing quantum dot) that reports on the *in vivo* target localization of the targeted nanoparticles. Release of the drugs can subsequently be triggered using an external stimulus (e.g. temperature, light, magnetism, ultrasound, etc). In addition to imaging of the location of the administered nanomedicine, the combination of drug targeting with molecular imaging also allows the acquisition of information on the drug release process,

specific biomarkers and therapeutic outcome. Delivery of drugs to the pathological tissue using (targeted) nanomedicines will lead to improved therapeutic activity, reduced side effects and more efficient drug use.
Applying nanotechnology to medicine could bring a revolution to healthcare. It is essential that benefits of genomics and proteomics research, and advances in drug delivery, are rapidly utilized to realize improvements in diagnosis and therapy. At the longer term, nanomedicine will embrace opportunities arising from stem cell research, tissue engineering research, and device miniaturization. Risks and benefits must be addressed carefully to yield useful and safe technologies.

3.9.2. National context

See section 2.1.2.

3.9.3. Future developments

Nanotechnology approaches to particle design and drug delivery are starting to yield more medical benefits and to form the basis for a highly profitable niche within the industry.
To realize the full medical potential of nanomedicine, nanocarriers have to get 'smarter'. Pertinent to realizing this, is a clear understanding of both physicochemical and physiological processes. These processes are at the basis of the interactions between the nanosized carrier systems and the biological (micro)environment. Examples include: (1) carrier stability, (2) extracellular and intracellular drug release rates in different pathologies, (3) interactions with the biological milieu including opsonization and other barriers (be it anatomical, physiological, immunological or biochemical) encountered during transport to the target site, (4) exploitation of opportunities offered by disease states (e.g. receptor overexpression, extravasation from the circulation into the disease site), and (5) intracellular trafficking of nanomedicine particles internalized by target cells. Inherently, design of appropriate nanocarriers and delivery strategies may vary in relation to the type, developmental stage, and location of the disease.
For the future of nanomedicines, it is important to develop imaging-guided drug delivery procedures to monitor nanoparticle localization, drug release, and the levels of drug and biomarkers at the site of pathology.
Strong attention should also be paid to the translation of preclinical findings to the clinical application. Industrial exploitation issues like scale-up, long-term stability, validation and regulation, and evaluation of safety and efficacy should be addressed.

3.9.4. Outlook and recommendation for future research

The future of nanomedicine will depend on rational design of nanotechnology materials and tools based on a thorough understanding of biological processes. The research in this field requires a multidisciplinary approach to ensure that the exciting potential of many nanomedicine technologies will become a practical reality in healthcare. Input from researchers with a background in chemistry, physics, biology, pharmaceutical sciences and medicine is essential. It is recommended to particularly focus in the near future on the endowment of nanomedicines with superior targeting and release properties, on the combination of therapeutics and molecular imaging by implementation of imaging-guided drug delivery *in vivo* applications, and on the development of 'intelligent' targeted nanomedicines from which drug release can be triggered by endogenous stimuli or 'on demand' by externally applied stimuli.

References

[1] *www.esf.org*
[2] *www.nanomedicine.com*

4. THE INDUSTRIAL IMPACT OF NANOSCIENCES

Prof.dr. R. Coehoorn (Philips Research, TU/e)

4.1. General overview

The nanosciences open the pathway towards the manufacturing of nanostructures with enhanced or even revolutionary functions. Presently, the leading economic driving force is the semiconductor industry, which has already entered the *nano-electronics* domain. The Moore's law evolution in the smallest feature size of a transistor enables fast progress in e.g. the computer, data storage and mobile telephone industries. These industries are by themselves drivers of other developments in nanotechnology (magnetic nanostructures, solid state lasers, nanophotonic structures, passive component integration, nano-electrical-mechanical systems (NEMS)). Moore's law evolution may come to a halt within maybe a decade, as a result of economic and/or technological limitations. However, that will stimulate more revolutionary developments ('more than Moore'): novel materials combined with silicon, and various chips combined as a 'system in package' (SIP).

An emerging future driving force is *nanomedicine*. This encompasses molecular imaging, molecular diagnostics, molecular therapy, all using nanoparticles as labels or as drug carrying agents, and implantables (drug delivery, neurostimulation, wireless sensors). *Ex vivo* sensors will enable home doctors or patients to routinely detect ever smaller concentrations of e.g. DNA, proteins, metabolites or pathogens in body fluids, and of gases in exhaled air. Studies of health effects of nanoparticles in food and other consumer products and in outside and in-house air will be of emerging societal and industrial relevance. Important partner and future consumer of nanomedicine is the Dutch 'zorgsector'.

4.2. National context

<u>Academia</u>

Academic research in The Netherlands presently has no leading position in the field of 'more of Moore' type nano-electronics. Excellent far-out research is carried out on quantum computing (TUD), molecular electronics (e.g. LEI, TUD), spintronics (TUs, RU, RuG), nanotube transistors and single electron tunnelling devices (TUD). However, in view of the focus of this fundamental physics work on concepts, rather than on integration aspects, the lack of industrial partnerships, and the disruptive nature, the application relevance of these highly speculative concepts is presently in most cases not evident. For organic/polymer electronics (RuG, TU/e) applications are now emerging.

For 'Beyond Moore' type SIP research The Netherlands has strong centres at Philips Research/High Tech Campus, DIMES and Mesa+, while for nanophotonics research the new Centre for Nanophotonics (AMOLF) has a good position.

Nanomedicine is, in The Netherlands and worldwide, an emerging field. Initiatives have been taken to build a unique Centre of Excellence in The Netherlands (Centre Molecular Medicine, collaboration TU/e – Maastricht – Philips). Several excellent academic research groups have focussed their efforts on fundamental questions in this field (TUD, UU, LEI) or nanoscale drug delivery systems (BioMaDe and UT). Strong academic activities are ongoing on enabling technologies, including research on the physics and materials science of nanoparticles (UU), plasma technologies (TU/e) and Extreme Ultraviolet mirrors (FOM Rijnhuizen).

<u>Industry</u>

In The Netherlands, Philips, ASML and FEI Company are the main industrial companies that use nanotechnology, and contribute to its development. Philips employs nanotechnology in nano-electronics, healthcare, optical storage, displays, lighting systems, and in enabling technologies (e.g. print technologies). ASML is the world's leading manufacturer of lithography systems, and develops Extreme

Ultraviolet, Liquid Immersion and nano-imprint lithography as options for realizing ever smaller features sizes. FEI is a leading manufacturer of electron beam imaging systems and focussed ion beam systems, which enable nanotechnology in industry, laboratories and hospitals (imaging of biological tissue). Start-up companies include e.g. Mapper (Delft, massively parallel e-beam lithography) and Fluxion (Eindhoven, nanosieves for food processing). Important in this context are the several small and medium sized companies, mostly spin-offs from universities and institutes.

4.3. Future developments

Relevant future application areas are:

– Nanomedicine: Philips has the ambition to aggressively enter this field, in most subfields mentioned in section 4.1.
– Nano-electronics: embedded solid state memory (scalable 'unified memory', special low power devices, nanofabrication methods for integrated circuits (Philips, ASML).
– Nano-instrumentation: tools that can be used for imaging and diagnostics, in particular related to the life sciences (Philips, FEI).
– Nanophotonics: new types of light generation devices (LEDs, lasers), light manipulation devices, and non-invasive or minimally invasive optical sensors (Philips).

The enabling scientific developments, to be carried out in interdisciplinary teams, are:

– Materials technologies: nanoparticle and nanomembrane technology, growth of III-V semiconductor wires on any substrate, surface modification, linker chemistry, biocompatible and biodegradable materials, (bio)organic/inorganic interfaces, 3D nanoporous materials, materials with switchable nanoporosity, and novel functional materials (such as nanotubes filled with other molecules).
– Nano-imprint and other soft lithographies: nano-embossing.
– Biomedical developments: genomics, proteomics, metabolomics, stem cell therapies and marker identification (characteristic for specific diseases).
– Micro and nanofluidics.
– Nano-optics: e.g. plasmonics and photonic crystals.

4.4. Outlook and recommendations for future research

The Netherlands should choose a few application areas, coupled to key technology areas, with the aim to develop real excellence. This will be the basis for an 'innovation ecosystem'. For 'More of Moore'-type nano-electronics, The Netherlands can only play a minor role in very specific applications and at the concept level. Device and process integration should be left to institutes such as IMEC. Instead, it is recommended:

– To focus aggressively on **nanomedicine**. The Netherlands has pockets of excellence in many universities. It would bridge the gap between technical and general universities. We could create start up companies. There is a huge societal impact.
– To stimulate '**Beyond Moore**' type work (sensors, actuators, nanophotonics). A linking of the Holst Centre to MESA+ and DIMES will create the required coupling between academia and industry.

We also recommend investigating how The Netherlands could capitalize on the presently distributed expertise on the manufacturing and the physical, chemical and biomedical properties of **functional nanoparticles**. This is a 'niche' with great industrial potential (biomedical, storage, nano-electronics, coatings, food, etc.), also for starting up companies. There are important open fundamental issues and the subject has societal impact (health). Options could be the start of a focussed programme or the establishment of an institute.

APPENDICES

Appendix A. The Dutch nanolandscape

Prof.dr. R. Coehoorn (Philips Research, TU/e)

The inquiry initiated for this report in January 2005 has led to responses from a large number of the Dutch groups that are actively involved in the nanosciences. The tables 1-3 give an overview of all responses, grouped along the three proposed main themes. The text in between quotes is in some cases a paraphrased version of the literal response. The respondent number refers to the overview of inquiry responses made by FOM/STW. In case no number is given in the first column, the information on 'expertise, applications and challenges' was obtained in another way.

Table 1. Nanomedicine and related subjects.

Respondent (affiliation)	**Expertise, applications, challenges**
Van Houten (Philips Research)	'In view of the strategic orientation of Philips, nanomedicine may be viewed as the most important subject..... For nanomedicine, we have the chance to build a unique centre of excellence in The Netherlands.... My recommendation is to aggressively focus on nanomedicine....there are additional chances in fields such as nutrogenomics, with interesting synergies with nanomedicine'
De Jong (FEI)	'One of the most prominent nano-market segments that FEI serve is nano-biology.... FEI is very interested to participate in joint R&D programmes with excellent nano-science groups'
Schmidt (LEI)	'Urgent issues are: molecular observation and manipulation technologies, organic/inorganic nanometer-sized surface structuring biomolecular material, integration of cellular/molecular biology with micro/nanostructured devices......The strength of the biomolecular science and biotechnology SMEs in The Netherlands is a great opportunity to the nanoscience community for a joined strategy'
Aartsma (LEI)	'We address questions with regard to biomolecule/metal interfaces .... which is a central issue in bionanoscience.....resulting technology for biosensors, bio-electronic logic device, PV cells....In Leiden the Bio-AFM consortium studies this using scanning probe techniques...The huge challenge is to combine biomolecules with solid state components'
Dekker (TUD)	'We work on bionanoscience and single-molecule biophysics....our holy grail is to build up understanding of the working of a living cell; what are the minimal elements of a living system.....How can we couple biomolecular elements to solid-state devices? ......we focus on biomedical applications and biosensors .... it will be crucial to build up good relationships with doctors and to be able to do *in vivo* experiments .....The Netherlands has a unique number of research nuclei in single molecule biophysics: use this human capital and focus on this subject!'
Young (TUD)	'We work on the quantitative imaging of molecules in cellular and sub-cellular structures, i.e. instrumentation development, down to the single molecule limit.... nanotechnology is for us an enabling factor ..... tagging of molecules with quantum dots or metallic nanobeads is one of our challenges.... is dynamics on a 10 ms scale measurable?....Are 10-100 nm scale fluidic processes controllable .... a great challenge is the study of single DNA as it interacts with proteins, and to develop instrumentation for that'
Siebbeles (TUD)	'Great challenges: .... (bio)molecular sensors and motors, nanocapsules'
Nicolai (TU/e)	'Recently, molecular MRI has emerged as a means to detect a disease in a very early stage.....also unique possibilities emerge for optimizing therapies.....a solution to the known restricted sensitivity of MRI is the use of targeted nanoparticles to which MRI contrast agents are coupled ....making such particles will be a big challenge..... imaging of biological processes that are key to cardiovascular and neurological diseases.....The Netherlands has great opportunities to contribute strongly to this field, because Philips is one

	of the world's leading manufacturers of MRI equipment'
Huskens (UT)	'Can we develop nanostructuring methods that are applicable to .... biomaterials? ..... A crucial novel technology is that of binding chemistry while retaining bioactivity and specificity....Applications of bionano are in biochips, high-throughput assays, biotechnology in nano/microchannels'
Rodenburg (UU)	'We study the physiology of metabolic processes, ... lipid transport, protein-lipid interaction..... focus on biomedical applications ... e.g. using lipoproteinstructures as drug transporting units..... after metabolomics and interactomics, we must also develop 'physiolomics', ...leading Dutch centres are BioMaDe/RuG and Kavli/TUD/LEI..... one great challenge is now the integration of the various 'omics' cultures'
Sudhölter (WUR)	'The application area for which we foresee for The Netherlands the brightest future is 'Food, food-safety and health'.... food processing, encapsulation and delivering, sensing systems, drug-delivery like nutrient delivery systems, sensors of food quality.... Risk of nanoproducts?'
Cohen Stuart (WUR)	'We focus on colloid science that is relevant to food products and pharmaceuticals, and on processes in living cells, such as transport, cell membrane formation and gene expression.....Crucial issues are the controlled modification of surfaces with bioactive components without loss of bioactivity, novel methods for immobilizing proteins, for encapsulating active components and for manipulating DNA, fabrication of novel biopolymers'
Knoester (RuG)	'Our research on nanomaterials within the MSC is, in collaboration with BioMaDe, increasingly focussed on (bio)organic materials.....In order to be viewed by Brussels as a key country in nanoscience/technology, the large Dutch centres should collaborate and speak with one voice'
Speller (RU)	'We carry out nanophysics using scanning probe microscopies..... chemically and biologically compatible microscopies, for *in vivo* SPM .... use of nanocrystals in biological detection .... important questions concern the physics of biochemical processes and biological/inorganic systems.... challenges are the physics of biology, with the purpose to programme a cell for a specific purpose, and in the interfaces with nano-objects'.
Dogterom (AMOLF)	*In vitro* experiments with sub-cellular biomolecular assemblies, biomolecules interacting with micromachined structures, active/non-equilibrium biomolecular assemblies, microscopy.
Tans (AMOLF)	Biochemical networks, single molecule experiments, transport processes in cells.
Mulder (AMOLF)	Theory of biomacromolecular assemblies, structure formation.
Frenkel (AMOLF)	Molecular simulation and modelling of biological structures and processes
Schmidt (VU)	Motor proteins, DNA enzymes, cytoskeletal mechanics, mechanosensitivity of cells, protein folding, single-molecule experiments, optical tweezers, single molecule fluorescence microscopy, atomic force microscopy.
MacKintosh (VU)	Theory, equilibrium and non-equilibrium biomolecular structures, cellular nanomechanics.
Vink (UvA-AMC)	Mechanics and molecular transport mechanisms in the endothelial cell glycocalyx, mechanosensing, nanomechanics of cellular biopolymer networks.
Smit (VU-VUMC)	Tissue engineering, biomechanics; biomaterials; spine; bone; materials testing; finite element analysis, mechanosensing in bone cells, tissue mechanics, stem cells.
Wyman (Erasmus MC)	DNA-enzyme interactions, DNA repair, molecular genetics, cell biology, atomic force microscopy.
Subramanian (UT)	Nanobioscience, elucidation of structure-function relationships at the single molecule level, advanced imaging of complex molecular organization, quantitative biology at the cellular level, and analytical and diagnostic imaging of functional tissue.

Table 2a. 'Beyond Moore' type nanotechnology, demonstration of applications expected on a medium (5 year) timescale.

Respondent (affiliation)	**Expertise, applications, challenges**
Van Houten (Philips Research)	'The Netherlands should chose a limited number areas where it wants to excel... besides nanomedicine, 'Beyond Moore' type work (sensors, actuators, linking the Holst Centre to MESA+ and DIMES and incl. nanophotonics) has a good chance'
De Jong (FEI)	'FEI is committed to work together with nano-scientists to develop instruments which will serve their needs in the areas of nano-characterization (metrology, imaging, chemical analysis, structural analysis, cryotech), nanomanipulation and modification (material deposition and removal, local scale activation) and nanoprototyping'
Bastein (TNO Industrie &Techniek)	'TNO works on instrumentation that makes mass fabrication of sub-30 nm structures possible. .... Replication, metrology and inspection technologies, lithography.... contamination control.... surviving the 'nano-hype' will be a big challenge....it will be a challenge to find the right balance between fundamental science and technology development that is recognized and used by industries.'
Huskens (UT)	'We work on .. nanotechnology and nanofabrication......How can we combine top-down and bottom-up structuring methods? Can we develop structuring methods that are compatible with many types of materials (organic, inorganic, polymer, bio)? Can we develop single molecule detection methods and manipulate structuring on a single molecule level? .... applications in nano-electronics, nanophotonics, bionano, nanofluidics'
Polman (AMOLF)	'We work on nanophotonics (photonic crystals, light scattering, manipulation and confinement of light, near field effects on spontaneous emission, near field probing, plasmonic materials, plasmonic photonic integrated circuits ...... communication technology, lasers, lighting, data-storage, lithography, optical computers, quantum cryptography, (bio)sensors, PV cells, medical therapies, displays.....AMOLF has recently started a Centre of Nanophotonics (40 researchers)...it will be a challenge to set up a Dutch programme that couples excellence in fundamental research with the creation of options for applications'
Klapwijk (TUD)	'Nano-objects must show their functional properties at ever higher frequencies, into the THz regime. We presently do not know how to handle that, but the field is now ripe, also in view of emerging novel apparatus (e.g. THz lasers)......FETs, diodes, space applications, computer industry .....integration of THz technologies with nano-device technology is crucial .....in the nanosciences control of materials and interfaces is key .....we should become strong in nanosciences at room temperature, not only at the mK scale'
Frijns (TU/e)	'Heat transfer on a micro and nano scale ..... cooling technologies ..... continuum methods no longer valid .... Monte Carlo approaches.... challenges are the efficient numerical simulation, development of pumps for micro and nanochannel cooling.... use electrowetting or electro-osmosis ..... applications in cooling of electronics, (medical) analysis apparatus, cooling fuel cells and micro-nano turbines in e.g. mobile telephones'
Van de Sanden (TU/e)	'We work on plasma physics, plasma etching and plasma deposition, which has a great potential for creating functional materials (plasma assisted atomic layer deposition)... plasma methods also make bottom-up approaches possible'

Table 2b. 'Beyond Moore' type nanotechnology, demonstration of applications expected on a long (> 5-10 year) timescale.

Respondent (affiliation)	**Expertise, applications, challenges**
Kes et al. (LEI)	'The research programme of LION (outside the themes mentioned in tables 1-3, RC) focusses on nanowires and nanomagnetism, scanning probe methods and nanotribology, nanofluidics with helium, superconductors, single molecule spectroscopy, (molecular) conduction on a nanoscale, quantum information processing'
Knoester (RuG)	'The research programme of the MSC focusses on novel functional materials with nanometre scale building blocks......electronic, optical, mechanical, ...manipulation of charge, energy and spin transport, energy conversion in PV cells, LEDs and molecular motors'
Poelsema (UT)	'Keywords in our programme are LEEM (a unique instrument), scanning probe techniques, molecular (nano)electronics, nanomagnetism, nanocolloidal films, selfassembly'
Dijkhuis (UU)	'anipulation of the interaction of light with THz acoustic and electromagnetic pulses in quantum dot systems ...... entangled states, optical computer, ... use of plasmons? ....heat management?'
Maan (RU)	'Nano-research in the High Magnetic Field Laboratory focusses (i) on the properties of top-down made semiconductor nanostructures (2-DEGs; magnetospectroscopy, transport, electron-electron interactions), and (ii) on research of bottom-up made nanostructures as made using self-organisation and with chemical methods, under conditions such that diamagnetic forces dominate thermal movement so that ordering and selforganisation are influenced'
Giessen (TUD)	'Micro- and nanomechanics of materials, on a nanoscale and on larger scales (but based on mechanics at smaller scales) .....micromechanics of biological materials are our new line or research ....active materials such as ferro-electric and memory materials ..... tissue engineering .....constructional science via e.g. selfassembly will be an important new technology and challenge.'
Janssen (TUD)	'Hard, wear-resistant and low-friction coatings .... Making strain-free cubic BN is a great challenge.'
Kelly (UT)	'Computational physics ......interfaces'
Koopmans et al. (TU/e)	Research programme of the Centre of Nanomaterials: - optical studies of magnetic precession processes, experiment and theory of carrier transport in organic nanolayers, spin-polarized transport in organic and inorganic nanodevices such as magnetic tunnel junctions, photonic processes in organic layers containing inorganic nanoparticles, atomic-scale tribology, persistent currents in nanorings, - applications in organic LEDs, PV cells, transistors, magnetic field sensors and memories
Bauer (TUD)	'Theory electron transport in nano-scale devices and circuits, ... conceiving next generation electronics.....nanoscale magnetoelectronics .....interfacing with conventional electronics.... maybe also biosystems.... heterostructures and interfaces will be urgent subjects ...... becoming at par with developments in US, Japan, Korea is a great challenge.'
Salemink (TUD)	Target is the development of nanophotonic concepts and technologies for future optical light sources and switches. Of critical importance is the development of GaN based optical sources, if possible combined with silicon processing. Such hybrid materials research will be used for converging technologies in cell diagnosis, molecular drug delivery and miniaturized molecular analyzers, combining: photonics, fluidics, and silicon-like technology.
Kouwenhoven (TUD)	Quantum Information processing.
Rasing (RU)	Ultrafast manipulation of ferromagnetic and antiferromagnetic metallic and semiconductor structures for studying changes in the magnetization and spin-injection..... coherent control of spins, finding and exploring magnetic

	semiconductors at room temperature and making nanostructures smaller than 50 nm are the most important research questions,....many challenges, in particular at the physics/biology boundary..... nanoscience research in The Netherlands should become recognized as being more than the sum of parts

Table 3. Fabrication and study of nanoparticles.

Respondent (affiliation)	**Expertise, applications, challenges**
Van Blaaderen (UU)	'Our work on colloidal model systems of particles and macromolecules is of an experimental and theoretical nature...... particle synthesis, steered self organisation,......enormous progress is possible..... many commercially attractive applications (data storage, sensors, labelling, PV cells, electro/magnetic rheological liquids, optoelectronics, displays).....Hazardous effects of nanoparticles should get proper attention..... Utrecht is a world-wide recognized top location'
Schropp (UU)	'One of the focus areas of the Debye Institute will be metal nanorods for catalysis, energy storage and nanophotonic applications..... key technological developments should be nanoprocessing of nanoparticles (manipulation, modification, functionalization) and the development of self-organizing nanoparticles and/or substrates (templates) for large-scale applications.......economic high-volume production of nanoparticle deserves much attention'
Erné (UU)	'Research of magnetic nanoparticles .... for magnetic data storage, but maybe more importantly for biomedical applications (MRI, hyperthermic curing, drug delivery, biosensing......there is a lack of knowledge on the surface chemistry of nanoparticles.....'
De Jongh (LEI)	'We work on metallic nanoparticles, nanowires and magnetic cluster molecules...... quantum size, surface, mesoscopic, superconducting effects.....magnetic nanoparticles are model systems for qubits ...... See also ch. 3 in the STT report Nanotechnology, ed. by A. ten Wolde (1998)'.
Schmidt-Ott (TUD)	'At DelftChemTech we produce and characterize nanoparticles ...... doping, mixing, metastable compositions by fast quenching, fast on line screening, development of particle sensors that give health relevant signals ...... catalysts, magnetic materials, chemical sensors, fillers for polymers, hydrogen storage, fuel cells and batteries, nanoparticle based medicines and agents for medical diagnostics and targeted drugs.......a key novel technology would be the aerodynamic/electrostatic focusing of nanoparticles to nanoscale areas or surfaces ...... research in The Netherlands should take up a more high-risk approach to create more original results, and should team up with the best in class in Europe'.
Picken (TUD)	'A key development will be the large scale synthesis of well-defined nanoparticles for a fair prize. This will give the entire field a firm basis. There are indications that companies are entering this field.'
Kroesen (TU/e)	'Fabrication of nanoparticles and tubes with low energy density plasmas ......application in optically and chemically active areas (PV cells, catalysts)'
Frenkel (AMOLF)	Theory, simulations, protein crystallization, colloidal systems, DNA linked nanoparticles, self-assembly.
Schmidt (VU)	Biomolecular nanoparticles (virus shells, protein tubes, self-assembled DNA structures, chaperonins/ protein folding), fluorescent quantum dots, surface chemistry for bio-inorganic interface, single-molecule experiments, optical tweezers, single molecule fluorescence microscopy, atomic force microscopy.
MacKintosh (VU)	Theory, equilibrium and non-equilibrium biomolecular structures, virus shells, protein tubes, colloidal systems, granular systems.
Vredenberg (UU)	MeV ion irradiation to control the shape of single colloids and colloidal assemblies
KNAW	'More research should be carried out on the possible toxical properties of nanoparticles and their kinetics in organisms and in the outdoor and indoor environment. It may be necessary to develop novel toxicity models'

Appendix B. List of respondents

Bastein, Ton	TNO
Bauer, Gerrit	TUD
Van den Berg, Albert	UT
Van Blaaderen, Alfons	UU
Blank, Dave	UT
Burger, Joost	UU
Coehoorn, Reinder	Philips Research & TU/e
Cohen Stuart, Martien	WUR
Debye Institute	UU
Dijkhuis, Jaap	UU
Erné, Ben	UU
Figdor, Carl	RU
Frijns, Arjan	TU/e
Griessen, Ronald	VU
Hellingwerf, Klaas	UvA
Van Houten, Henk	Philips Research
Van der Horst, Dick J.	UU
Huskens, Jurriaan	UT
Janssen, Guido	TUD
De Jong, Frank	FEI
De Jongh, Jos	LEI
Kampers, Frans	WUR
Kelly, Paul	UT
Kes, Peter	LEI
Klapwijk, Teun	TUD
Knoester, Jasper	RuG
Burger, Koert	UU
Koopmans, Bert	TU/e
Kouwenhoven, Leo	TUD
Kuipers, Kobus	AMOLF
Kroesen, Gerrit	TU/e
Lenstra, Daan	VU
Luiken, Joost	UU
Maan, Jan Kees	LEI
Nicolaij, Klaas	TU/e
Orrit, Michel	LEI
Picken, Stephen	TUD
Poelsema, Bene	UT
Polman, Albert	AMOLF
Rasing, Theo	RU
Reek, Joost	UvA
Rodenburg, Kees	UU
Rudolf, Petra	RuG
Van Ruitenbeek, Jan	LEI
Salemink, Huub	TUD
Schmidt, Christoph	VU
Schmidt-Ott, Andreas	TUD
Schropp, Ruud	UU
Siebbeles, Laurens	TUD
Speller, Sylvia	RU
Van Steenhoven, Anton	TU/e
Sudhölter, Ernst	WUR
Vredenberg, Arjen	UU
Westerweel, Jerry	TUD
Zsom, Rob	UvA

Appendix C. List of affiliations

AMOLF	FOM-Institute for Atomic and molecular physics (Amsterdam)
LEI	University of Leiden
TUD	University of Delft
TU/e	University of Eindhoven
UT	University of Twente
UU	University of Utrecht
UvA	University of Amsterdam
VU	Free University (Amsterdam)
RU	Radboud University (Nijmegen)
WUR	Wageningen University and Research Centre
RuG	University of Groningen