NanoNextNL

Netherlands micro/nanotechnology research and innovation programme

Updated research appendix to End Term Report

2010-2016

nanonextnl

innovating with micro and nanotechnology

NanoNextNL
June 2017

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1 Mission and vision

1.1 Mission

From 2010-2016 academic and industrial participants collaborated in the Dutch research and technology programme NanoNextNL with the following mission:

> *“To accelerate the creation of durable economic and societal value by developing and commercialising innovative nano and microtechnology, and by forming a sustainable ecosystem of researchers, entrepreneurs and policy makers.”*

NanoNextNL aimed to fulfil this mission in the following ways:

1. **Top science: the basis of a strong innovation programme**
   conducting top-quality research in the field of nano/microtechnology, as evidenced by scientific publications, conference presentations and outreach activities;
2. **Innovation: creating business from technology**
   by developing key new innovations, technologies and products, as evidenced by the filing of patents and the development of prototype and demonstrator devices in which nano/microtechnology plays a key role;
   by initiating new start-up companies that develop products based on nano/microtechnology;
3. **Responsible research and innovation**
   by devoting specific attention to risk analysis and technology assessment (RATA) aspects of nano/microtechnology;
4. **Education: training highly skilled innovators**
   by training highly skilled scientific and technical specialists and innovators in the field of nano/microtechnology who will find jobs in the Dutch nano/microtechnology industry;
5. **Added value of the NanoNextNL approach**
   by bringing together and connecting academic researchers and industrial technology developers and aligning their research and development agenda’s;
   by becoming the leading national organisation in nano/microtechnology, initiating new research and development activities both in the Netherlands and in Europe and contribute to the development of national and international nano/microtechnology roadmaps;
   by combining all the above aspects to generate a nano/microtechnology ‘ecosystem’ that guarantees a long-term integration of academic research and industrial innovations in nano/microtechnology in order to create economic value and scientific strength for the Netherlands and Europe.

1.2 NanoNextNL programme

The NanoNextNL programme was drafted in 2010 by the participating academic and industrial partners and comprises of 28 research programmes within 10 themes. Each research programme consisted of multiple projects that are carried out by academic and industrial partners. These projects were selected to lead to strong synergy and collaboration within the programme, and academic and industrial partners worked together towards closely coordinated common targets. An overview of all programmes and themes is given in Table I.

The total budget of NanoNextNL is 251 M€ for the period 2010-2016. A subsidy of 125 M€ was awarded by the Dutch Government from the ‘Fonds Economische Structuurversterking (FES)’. Matching funds were contributed by academic (69 M€) and industrial (57 M€) partners of NanoNextNL. Overall, over 1100 PhD students, post-docs and other research staff at 13 universities, 8 medical centers, 12 knowledge institutes and 110 companies contributed to NanoNextNL. A list of all partners in NanoNextNL is provided in Appendix B.

Table I NanoNextNL Themes and Programmes with names and affiliations of Theme Coordinators and Programme Directors.

Themes *and* Programmes	Theme Coordinator/ Programme Director[1]	Affiliation of TC/PD
Theme 1 Risk Analysis and Technology Assessment	**Adriënne Sips**	**RIVM**
1A Human health risks	Hans Bouwmeester *Han van de Sandt*	Wageningen University & Research Centre , TNO, FOM Instituut AMOLF, TNO
1B Environmental risks	Annemarie van Wezel	KWR Watercycle Research Institute
1C Technology assessment	Harro van Lente	Maastricht University
Theme 2 Energy	**Erwin Kessels,** ***GertJan Jongerden***	**Technische Universiteit Eindhoven**
2A Efficient generation of sustainable energy	Erwin Kessels *Wim Sinke*	Technische Universiteit Eindhoven, ECN
2B Efficient energy utilisation by secondary conversion of energy and separation	Freek Kapteijn	Delft University of Technology
Theme 3 Nanomedicine	**Hans Hofstraat**	**Philips Research**
3A Nanoscale biomolecular interactions in disease	Vinod Subramaniam	VU University Amsterdam
3B Nanofluidics for lab-on-a-chip	Albert van den Berg	University of Twente
3C Molecular imaging	Michel Versluis, *Klaas Nicolay*	University of Twente Eindhoven University of Technology
3D Drug delivery	Gert Storm	Utrecht University & University of Twente
3E Integrated microsystems for biosensing	Han Zuilhof	Wageningen University & Research Centre
Theme 4 Clean Water	**Bert Hamelers,** ***GertJan Euverink***	**Wetsus**
4A Nanotechnology in water applications	Rob Lammertink	University of Twente
Theme 5 Food	**Erik van der Linden**	**Top Institute Food & Nutrition**
5A Food process monitoring and product quality assessment	Maarten Jongsma	Wageningen University & Research Centre
5B Molecular structure of food	Krassimir Velikov	Unilever Research & Development
5C Food products and processes	Karin Schroën, *Remko Boom*	Wageningen University & Research Centre
5D Microdevices for structuring and isolation	Karin Schroën	Wageningen University & Research Centre
Theme 6 Beyond Moore	**Hans Huiberts,** ***Dirk Reefman***	**Philips Research**
6A Advanced nanoElectronics devices	Bert Koopmans	Eindhoven University of Technology
6B Functional nanophotonics	Kobus Kuipers	FOM Institute AMOLF
6C Nano-bio interfaces & devices	Serge Lemay	University of Twente
6D Active nanophotonic devices	Paul Koenraad	Eindhoven University of Technology
Theme 7 Nanomaterials	**Ardi Dortmans**	**TNO**
7A Supramolecular and bio-inspired materials	Alan Rowan	Radboud University Nijmegen
7B Multilayered and artificial materials	Guus Rijnders	University of Twente
Theme 8 Bio-nano	**Menno Prins**	**Eindhoven University of Technology**
8A Nanomolecular machines in cellular force-transduction	Marileen Dogterom	Delft University of Technology
8B Bionano interactions for biosensing	Gijs Wuite	VU University Amsterdam
Theme 9 Nanofabrication	**Wim van der Zande,** ***Vadim Banine***	**ASML**
9A Nano-inspection and characterisation	Bram Koster	Leiden University Medical Center
9B Nano patterning	Pieter Kruit	Delft University of Technology
Theme 10 Sensors and actuators	**Machteld de Kroon,** ***Jan van Eijk***	**TNO, Mice BV**
10A Systems and packaging	Urs Staufer	Delft University of Technology
10B Micro nozzles	Herman Wijshoff	Océ Technologies
10C Microdevices for chemical processing	Marko Blom	Micronit Microfluidics

[1] Former theme coordinators and programme directors are presented in italic font.

1.3 Programme organisation

Governance

Executive Board

NanoNextNL is led by an Executive Board (EB) consisting of seven members, four of which are from knowledge institutes and three from industry. The Board oversees the general progress of the programme, finance, initiates knowledge transfer and Risk analysis and technology assessment (RATA) activities, maintains links with external stakeholders and holds progress meetings with Programme Directors and Theme Coordinators. The EB meets once a month and holds a yearly full-day strategic planning meeting.

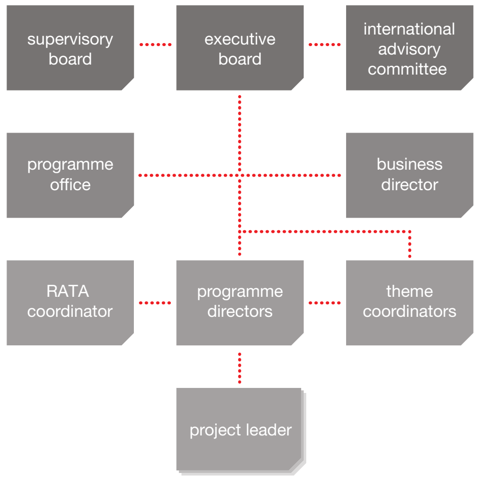


Fig. 1 NanoNextNL organisation

Programme Office and Business Director

The programme office (PO) carries out all administrative, financial and organisational tasks related to the NanoNextNL programme and reports to the EB. The PO is composed of 4-fte programme officers including a PO director, 2-fte management assistants and 1,5-fte financial, communication and legal expertise. The business director (BD, 0,8 fte) initiates cooperation with external parties and identifies opportunities to enhance innovation. Coordination between all management activities occurs in the Daily Management Committee (DMC) which consists of the chair and vice-chair of the EB, the PO director and the BD. The DMC holds a weekly teleconference.

RATA Coordinator

In order to stimulate and coordinate overarching risk research within NanoNextNL, a RATA coordinator is appointed through a collaboration agreement between NanoNextNL and the National Institute for Public Health and the Environment (RIVM).

Supervisory Board

The Supervisory Board (SB) is composed of 18 stakeholders from knowledge institutes, related research programmes, Small and Medium Enterprises (SMEs) and large industry in the nano/microtechnology field. The SB oversees the general progress of the NanoNextNL programme and gives advice to the EB. The SB meets twice a year.

International Advisory Council

The International Advisory Council (IAC) comprises internationally renowned specialists in the nano/microtechnology field and gives advice to the EB. The IAC carried out a mid-term review of the NanoNextNL programme in 2013 and the final review in 2016.

Programme Directors, Theme Coordinators

Each NanoNextNL programme is led by a Programme Director (PD). The majority of PDs is from academia. The PD is responsible for the general progress of the programme and stimulates collaboration and innovation activities. The Theme Coordinators (TCs) oversee the activities of the programmes within each theme. The majority of TCs have a background in industry and their task is to help stimulate interaction between programmes and between academia and industry. A plenary PD/TC meeting with the EB is held twice a year, in which the general progress of the NanoNextNL programme is discussed.

Fig. 1 gives a schematic representation of the NanoNextNL organisation. Appendix C lists the names of the members of all NanoNextNL governing committees described above.

2 NanoNextNL results for each programme

In the following sections, each NanoNextNL programme presents a 2-page summary of research and business-related highlights for the period 2010-2016 as well as lessons learned provided by the programme director. The programmes are ordered by theme, and a general introduction is provided for each theme. An overview of the Key Performance Indicators is presented in Appendix A. The NanoNextNL budget is detailed in Appendix D.

1. Risk analysis and technology assessment
2. Energy
3. Nano-medicine
4. Clean water
5. Food
6. Beyond Moore
7. Nano materials
8. Bio-nano
9. Nano fabrication
10. Sensors and actuators

2.1 Theme 1

Risk analysis & technology assessment

Theme coordinator: Adriënne Sips
(RIVM National Institute for Public Health and the Environment)

Introduction

Innovation is an important driver of societal prosperity and is indispensable for sustainable development and economic growth. Nanotechnology is seen as one of the strengths of the Dutch knowledge economy. Various themes in NanoNextNL have shown the potential of this technology to contribute to solutions for addressing grand societal challenges like reducing energy consumption or improved health care applications. At the same time, the potential of nanotechnology is hampered by 'unknowns' about human, environmental and societal risks. Attempts to address these 'unknowns' are generally carried out in the privacy of discussions about risks. However, a way out of the situation of too high uncertainties about the risks needs a strong interaction between innovators and risk researchers. Authorities and industry are in need of insight into which information is pivotal to address the question whether a nanomaterial or nanotech application is safe. This requires smart approaches to reduce these uncertainties to acceptable levels as quickly as possible. Meanwhile, the interaction between innovators and those dealing with RATA issues should be improved in order to allow safety and societal discussions to keep better pace with innovation processes.

Development of the theme through the years

At the start of NanoNextNL there was a huge demand to quickly gain insight into health risks of nanomaterials and its products, but at the same time nanotoxicology was in its infancy. In order to investigate this multitude of issues (investigations demanded by Dutch Parliament), 15% of the total NanoNextNL budget was invested in risk analysis and technology assessment (RATA). Moreover, the organisational architecture of NanoNextNL intended to support optimal interaction between innovation and RATA. This architecture is in line with goals of the EU Horizon2020 strategy, in which the core values are excellent science, industrial leadership and addressing the grand societal issues. The starting point of the theme was the ambition to support sound regulation of especially nanomaterials with excellent science. Dutch research groups with excellent embedding in both international scientific and regulatory arenas regarding safety of nanotechnology were included as partners in this theme. The Dutch RATA community holds a strong position in the worldwide debate about efficiently addressing 'unknowns' about human and environmental health safety. This was put into practice by strong involvement in EU H2020 projects, input into European roadmaps and participation in international fora like Scienfic Committees of the European Commission, ISO, OECD Working Party on Manufactured NanoMaterials, etc.

Beside this starting point the ambition was to bridge the gap between innovation and safety, by facilitating interaction between RATA and other themes. Although an intention shared by partners from all themes from the start of NanoNextNL, it was difficult to translate into a structural relationship. Now, it is seen that we first needed an exploratory phase like in other themes. Nanotoxicology was in its infancy and the integration between RATA and innovation already in early phases of innovation appeared to be a unique approach. Scientific knowledge developed in RATA had to meet the demands from a regulatory context whereas the RATA needed to discover its new supportive role in early innovations. The projects in the RATA theme have produced knowledge and insights that are in support of questions on how to regulate nanomaterials and their products, thereby not only facilitating questions and needs from regulators but also giving clarity on regulatory demands to industry.

As RATA in nanotechnology is a highly dynamic field, input form the Mid Term Review has been taken to evolve RATA from a theme merely addressing gaps in knowledge into a theme transforming a conventional role for RATA into an integrated and supportive role for innovation. Experiences from the first two years were used to give shape to collaborative activities with other themes, whereas at first instance RATA only participated in meetings of other themes to explore their needs.

Highlights of these collaborative activities:

- **In support of business cases:** RATA considerations were included in the Lean Business Canvas and the Golden Egg Check, an initiative for a societal incubator as an added value for a business incubator was developed, reflections of investors towards the role of safety information in early stages of innovation were gathered.
- **Raising awareness and training:** a RATA course for PhD's was established and successfully attended by a large number of PhD's, initiatives for addressing RATA issues in thesis were taken and supportive activities for further implementation were defined.
- **Safe Innovation Approach:** RIVM developed on the basis of experiences in NanoNextNL a Safe Innovation Approach based on frequently applied innovation models like the stage gate model of Cooper and facilitating an integrated role for safety information in the various stages of an innovation process. In connection to the EU Flagship NanoReg project (coordinated by the Dutch Ministry of Infrastructure and Environment) a safety screening strategy was developed for the early stages of innovation.

Added value of NanoNextNL consortium and ecosystem

The impact of NanoNextNL on the supportive role of RATA to innovation is high. Interaction between RATA and the other themes was pivotal to raise awareness that discussions on RATA should take place from the perspective of innovation processes and not the other way around. Moreover, the combination of risk analysis and technology assessment activities created added value as technology analysis gave insight into perceived risks whereas risk analysis gave insight into human and environmental health risks.

Like other themes, NanoNextNL provides inroads into new programmes like the Nationale Wetenschaps Agenda (National Science Agenda). Exploration for the potential role and support RATA can give in this NWA was only possible by direct participation of RATA in the NanoNextNL ecosystem. The knowledge and insights gathered were in turn further given shape in the Valorisation Programme by e.g. TA providing additional support to identify bottlenecks in next steps in the challenge to bring an original idea to a product. RA partners became more aware of the benefits to formulate their needs in terms of required innovations thereby in turn expanding the business potential for an innovation. For example, the business potential of organ-on-a-chip was explored to extent to toxicity testing and to identify the route needed to make this application regulatory accepted as an alternative to animal testing (rather than only applicable for in-house testing).
NanoNextNL has been essential for the partners in RATA to keep its status as a forefront runner in the field of risk research and responsible research and innovation. Experiences in NanoNextNL, offering view on a combination of technological innovation, business awareness, social sciences and toxicological research appeared to be key to meet the needs on Safe-by-Design and Responsible Innovation in e.g. the H2020 programme of the European Commission. This knowledge formed a solid basis for participation and coordinator ship in around 30 EU-projects. The Dutch RATA community has, based on the experiences in NanoNextNL, developed innovative ideas to make RATA an integrated part of innovation thereby intensifying interaction between innovators and regulators, between innovators and RATA researchers. These innovative ideas are seen as a blueprint for responsible research and innovation for other emerging technologies.
In November 2016 a Safe-by-Design workshop was organized attended amongst others by policymakers, and researchers from institutes, industry and academia. The concept of Safe-by-Design aims to integrate safe manufacturing, safe production and responsible waste management in the research and technical development during the innovation process at the earliest possible. The participants of the workshop agreed on the importance of Safe-by-Design whereby a timely dialogue between relevant stakeholders is started early on in the innovation process.

2.1.1 Programme 1A

Human health risks

Programme director: Hans Bouwmeester (DLO and Wageningen University; from 1-10-2014) before that Han van de Sandt (University of Amsterdam & TNO)

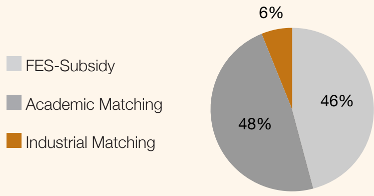
Partners

Academic Medical Center Amsterdam (AMC), BECO Group, Delft University of Technology, IVAM, Philips Electronics Nederland, RIVM, DLO, TNO, University of Twente, Utrecht University, Wageningen University, Zuyd University of Applied Sciences

Projects

5

Budget 1A: € 7.707.407



Output

33	Journal articles
2	Patent filings
	Valorisation programme
6	Business case
1	Granted
	Researchers
9	PhD student
4	Postdoc
16	Company
21	Master student

Ambition & Realisation

The ambition of this programme is to help industry develop new nano-based products which can be used safely, and to provide public policy makers with tools for evaluation and regulation of nanomaterial

Research ambition

- To develop effective tools and approaches to assess potential human health risks of nano objects.

Research realisation

- Exposure to nanomaterials at the workplace (Bekker – TNO, Utrecht University). This project investigates the exposure of people who work professionally with commercially available nanomaterials, e.g. in construction, electronics or in manufacturing. New methodology is being developed, such as measurement strategies and improved statistical analysis of data. Together with information on toxicological properties, this research provides insight into potential health risks.
- Bioavailability of nanomaterials (Bouwmeester, Braakhuis, Riejtens, Kezic, Bellmann – RIKILT, RIVM, Wageningen University, AMC, TNO). Intestinal, lung and dermal penetration of model nanoparticles has been studies aiming to setup in vitro models to study the potential bioavailability of nanoparticles. Experimental papers have been published as well as review papers describing the applicability of the developed in vitro models for risk assessment. Lastly data that can be used for risk assessment has been delivered while evaluating the in vitro models. Limited in vivo work has been performed to benchmark the in vitro models.
- Characterisation of nanoparticles for toxicological and kinetic research (Rietjens, Bouwmeester, Kuper - Wageningen University and Research Centre, RIKILT, TNO). It was shown that the surrounding matrix in which a nanoparticle is embedded has a large effect on its characteristics. Therefore, measurements in this field need to be analysed with utmost care. The results imply that the classical dose-response relationships may not be applicable to many nanoparticles.
- A device to measure airborne nanoparticles is being developed by the TU Delft.
- Develop a Decision Support System (DSS) (Marvin, Kroese, Bakker, Lokers, RIKILT, DLO, RIVM, ALTERRA) to prioritise engineered nanoparticles for risk assessment. This system (or model) applies novel Bayesian network approaches. This makes it possible to integrate various types of data and to manage knowledge gaps in datasets. As the field of nanotechnology and its applications evolve rapidly innovative approaches need to be developed that can be implemented in risk prioritisation and assessment ("keeping pace with innovation"). Therefore it is an advantage that desicsion support systems based on Bayesian networks are flexibile and can integrate new data as it appears. This projects integrated with programme 1B: Environmental risks.
- Contributions to EU-funded projects awarded: NanoStair, FutureNanoNeeds, GuideNano, SUN, Nanodata. Active participation in the preparation of EU Horizon2020 calls and projects (NanoFase).

Business ambition

- To interact with industrial partners within NanoNextNL working on improving product functionalities.

Business realisation

- Programme 1A consists of five projects. Three are engaged in developing tools and approaches focusing on the public domain (in line with the general aim of the programme), and two projects work on methodology that may be suitable for commercialisation.
- A toolbox is being developed in order to assess risks to man and the environment. The possibilities of commercially presenting this to the market will be evaluated.
- A device to measure airborne nanoparticles is being developed by Delft University of Technology that incorporates features not present in currently available tools. The business initiators are Andreas Schmidt-Ott (Delft University of Technology), Han van de Sandt and Rens Vandeberg.

Other ambition

- To interact with national and international authorities in order to develop and implement effective guidance and legislation.

Other realisation

- In the autumn of 2012 NNNL and TNO organised the workshop 'Safe Design of nanomaterials' in which both industry and authorities participated. The participants exchanged views and experiences and formulated 10 action points in order to enhance aspects of safe design internationally.

All project partners actively contributed in NanoCity (and other NNNL events).

2.1.2 Programme 1B

Environmental risks

Programme director: Annemarie van Wezel
(KWR Watercycle Research Institute)

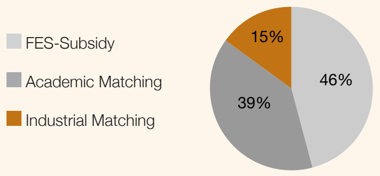
Partners

Deltares, KWR Watercycle Research institute, Philips Electronics Nederland, Radboud University Nijmegen, RIVM, DLO, TNO, University of Amsterdam, Utrecht University, VU University Amsterdam, Wageningen University

Projects

5

Budget 1B: € 7.474.860



Output

56 Journal articles
0 Patent filings

Valorisation programme
5 Business case
0 Granted

Researchers
9 PhD student
5 Postdoc
15 Company
13 Master student

Ambition & Realisation

Research ambition

The added value generated by the programme on environmental risks is an improved understanding on the factors that govern potential environmental risks of manufactured nanoparticles, and guidelines for risk assessment for nanomaterials as compared to 'normal' chemicals.

Research realisation

The programme performed higher than set by the KPI goals.

- Analytical methods were developed and optimised for the analysis of both inorganic and organic nanoparticles in water, sediment, soils, air and biota. Both the composition and size of various organic and inorganic nanoparticles can be measured. Surveys were carried out to evaluate the occurrence of nanoparticles in environmental compartments and sewage treatment plants (STP).
- Imaging method tracing and scanning metal environmental nano ENPs in whole organisms showed the spatial distribution of ENPs in the organisms. In vivo accumulation and effects on earthworms using systematically engineered nanomaterials are studied, including gene profiling.
- A surface structural (SD) model using state of the art surface complexation modelling resulting in realistic predictions of the adsorption of many elements over a wide range of environmental conditions.
- Models (i.e. NanoDUFLOW) were developed that describe the fate of nanoparticles in rivers, to be used as tools for prospective exposure assessment. Chemical exposure assessment modeling is made 'fit for nano'. Probabilistic environmental risk assessment of nanochemicals is made possible.

- The programme is linked to many international collaborations such as IWA (International Water Association, a specialist group on Nano and Water - Application of Nanoparticles, Nanoengineered Materials and Nanotechnology), SETAC (Society of Toxicology and Chemistry, global advisory group on nanotechnology), COST action ES 1205 (Engineered nanomaterials in the environment: analysis, occurrence and impacts), NORMAN (working group on Engineered nanomaterials in the environment). Programme 1B explicitly strengthens the international dissipation of the unique RATA combined with technological development within NanoNextNL.
- The subject is of interest to the general public, and many requests have been made to our researchers to give presentations to the broader public.
- The work resulted in over 50 papers being published in generally high-impact journals thusfar, and more papers will be coming out. Several of these papers are with industrial partners, and the majority is with multi-party co-authorship.

Business ambition

Besides excellent science, the programme generates;

- better understanding by technology developers on environmental risks, stimulating that nano-development includes both functionality and societal acceptability.
- tools for policy-makers for evaluation, regulation and safe use of nanochemicals.
- tools for analysis, modelling and assessment that are of interest to industry and consultancy.

Business realisation

- The research has strongly contributed to the general understanding of the behavior of natural, incidental, and manufactured inorganic nanoparticles in laboratory and natural settings. The NanoDUFLOW model and analytical developments will be further developed and applied in the scientific field of microplastic research. SimpleBox for nano is offered to European Commission's Chemicals Agency ECHA as instrument for environmental risk assessment of nano chemicals for inclusion in REACH regulation.
- The 1B researchers actively participate in RATA events throughout the programme, e.g. the courses.

Business case

The parties involved participate in a number of follow-up projects, with their experience in NanonextNL as a basis.

2.1.3 Programme 1C

Technology assessment

Programme director: Harro van Lente (Maastricht University)

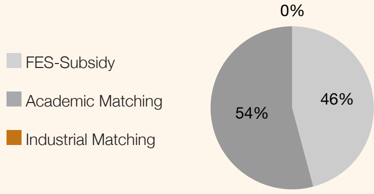
Partners

Delft University of Technology, Maastricht University, DLO, University of Twente, Utrecht University, Wageningen University

Projects

15

Budget 1C: € 6.029.179



Output

48	Journal articles
0	Patent filings
	Valorisation programme
0	Business case
0	Granted
	Researchers
11	PhD student
8	Postdoc
0	Company
3	Master student

Ambition & Realisation

This programme investigates how the societal embedment of nanotechnology can be anticipated. In this way it aims to bridge the gap between the world of science and innovation on the one hand and societal (including broader economic) aspects on the other.

Research ambition

Performing in-depth studies of current development in nanosciences and nanotechnology, to deepen insight into dynamics and governance of nanotechnology, to understand conditions of responsible innovation of nanotechnology and to interact better with society.

Research realisation

- Many publications have investigated the dynamics of various nanotechnological developments and studied the changing conditions of regulations (EU and national), including responsible innovation.
- Special issue of the academic journal NanoEthics, with 5 NanoNextNL Technology assessment (TA) contributions.
- Active contribution to the International Society for Nanoscience and Emerging Technologies (S.NET) and their conferences in 2012, 2013, 2014, 2015 and 2016.
- Contributions to international Volume on TA in Nanoscience (AKA Verlag), in 2012, 2013, 2014, 2015 and 2016). In each year both as editor and contributor.

Business ambition

- To ensure that TA is supportive in defining business ambitions of NanoNextNL research in other themes.
- To ensure central ideas and concepts of TA are taken up by other parties in business and society.

Business realisation

- Further development of methods and tools, such as sociotechnical scenarios, roadmapping and impact pathways.
- At PhD level: close interaction with researchers in themes 3, 5 and 10.
- Organisation of Joint NNNL workshops on TA in food, water, energy and medicine with NNNL researchers and societal/industrial stakeholders.
- Additional Joint Postdoc project together with theme 3. The first NNNL PhD graduate Verena Stimberg has made bridges between the two themes.
- Development of the notion of a “societal incubator” to allow experimentation and collective learning in areas of nanotechnology. It is the analogue of a business incubator where a research finding is guided towards a commercial product. Here a range of applications in a pre-commercial phase is collectively investigated and supported. The idea has been taken up by NanoNextNL board. The Rathenau Institute (The Hague) was commissioned to develop the approach further and published the report 'van draagvlak naar meer - ontwerp van een maatschappelijke incubator voor beloftevolle (nano)technologieën' about its merits.

Social valorisation ambition

- To achieve general progress in interactions between science and society and the development of tools to facilitate assessment of the societal implications of technology.

Social valorisation realisation

- The organisation of a series of RATA courses for NanoNextNL researchers in other themes. First held on 4/5 July 2013 and 26/27 September 2013. In total 7 courses have been organized.
- Intensive contact with the Center for Nanotechnology and Society in USA (Arizona and California) to exchange insights, methods and reinforce collaboration.
- TA researchers are frequently invited as experts in scientific and policy meetings.
- In August 2012 a 3-day nano & society stand at Lowlands, the biggest Dutch pop festival (Llowlab) resulting in thousands of contacts with young people.
- The development of an elective course on nanotechnology at Utrecht University (including scenarios and technology roadmapping). More than 100 students have participated.
- Contribution to the National Science Agenda workshops and National Science Festival (2015).

2.0 Theme 2

Energy

Theme coordinator: Erwin Kessels (Eindhoven University of Technology)
By programme directors Erwin Kessels (Eindhoven University of Technology) and Freek Kapteijn (Delft University of Technology)

Introduction

The world is in great need of a rapid transition to a (more) sustainable energy system. This requires the development of scalable renewable energy technologies for efficient energy generation, storage and utilisation. In this theme nanomaterials and nano-based systems are investigated to assist in this development. The focus is especially on advanced light management options in photovoltaics (programma 2A) and chemical conversion processes by photo- and electrocatalysis (programme 2B) as prompted by the Dutch world-class position in basic and applied research in these areas. Cost, performance and overall sustainability of the technologies considered are the key.

Development of the theme through the years

The projects in programma 2A all had an early start and currently most projects have ended. The PhD students have defended their thesis or will do so in the near future. One student was awarded the PhD degree cum laude at the University of Amsterdam. Also as much as 12 MSc students were involved in the research. The programme itself faced some challenges due to strongly dropping solar panel prices, consolidation in the solar industry and the relocation of solar cell manufacturing from Europe to Asia. This has had some consequences on the industrial involvement in the programme and industrial partners stepped out and embarked on the programme (two new partners within the programme are Levitech and Morphotonics). Overall, the programme has been able to react quickly and adequately on the changes and the programme has been able to become truly succesful.

The projects in programme 2B developed along the original planning, and most projects are still running depending on the starting date. Six PhD students have successfully defended their thesis, one was even awarded the cum laude degree at TU Delft (only for the top 5%). The participation of the industrial partners shifted due to changing focus within companies or ending start-up SMEs. Fortunately in most cases this could be taken over by new companies.

The publication numbers for theme 2 are very high and still increasing now most projects approach their end. Focus on obtaining IP was much less, especially due to changes in the industry involvement and the underlying dynamics in the associated markets as addressed above. However very interesting scientific and technical developments can certainly be reported. On the basis of the work within the project on ultra-thin plasmonic and quantum dot solar cells, a proposal related to optical external light trapping was submitted to the NanoNextNL Valorisation Programme although it was not granted in the end. The electrocatalytic CO2 fixation project resulted in a patent application by UTwente on porous metal hollow fibre electrodes. In a follow-up project they aim at valorisation within 3-5 years.

Many meetings were organised between the theme partners including programme meetings and public events and seminars. An international symposium on light management for solar cells organised by AMOLF was a true highlight for knowledge exchange.

Participation in the NanonextNL courses was high, especially in the IP & Valorisation awareness course. Furthermore considerable attention was given to risk analysis & technology assessment.

2.2.1 Programme 2A

Efficient generation of sustainable energy

Programme director: Erwin Kessels
(Eindhoven University of Technology)

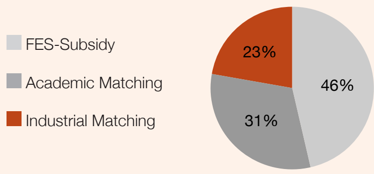
Partners

FOM Institute AMOLF, Delft University of Technology, Eindhoven University of Technology, Netherlands Energy Research Centre (ECN), Morphotonics, Meyer Burger, Philips Electronics Nederland, Levitech, University of Amsterdam, Utrecht University

Projects

5

Budget 2A: € 8.560.608



Output

79 Journal articles
3 Patent filings
Valorisation programme
1 Business case
0 Granted
Researchers
8 PhD student
5 Postdoc
2 Company
10 Master student

Ambition & Realisation

This programme aims at the investigation and development of new applications of nanomaterials and nanostructures to achieve higher energy conversion efficiencies for solar cells at lower cost. The research focus is especially on advanced light management options with the aim to develop these in proof-of-principle cells in laboratory settings such that they can subsequently be applied in pilot production facilities.

Science ambition

The application of nanomaterials and nanostructures to thin-film and thin-wafer solar cells will be studied with the aim of enhancing the absorption of sunlight in these cells beyond the level as obtained in conventional device architectures. More specifically the science ambition is to:

- Develop nanopatterned and plasmonic surface structures to enhance the coupling and trapping of light in solar cells. The aim is to provide fundamental understanding of the light scattering by the surface structures;
- Employ novel processing technologies for the development of Si quantum dot layers for efficient spectral converters. The aim is to identify efficiency limiting steps for emission from the quantum dots;
- Understand the impact of the surface texture on the deposition of thin film semiconductor materials (amorphous and nanocrystalline Si and SiGe films, transparent conductive oxides, etc.) to optimise solar cells with ultrathin absorbers;
- Study novel nanostructures (e.g., those based on periodic arrays of metallic nanoparticles) to enhance the emission from luminescent materials for application in luminescent solar concentrators;
- Investigate a new generation of solar modules based on coated glass spheres (diameter 200 μm) instead of planar thin films as well as to optimise the device configuration through advanced optical modelling.

In the last phase of the programme, one new project was installed complementing the other research activities; the aim was to investigate nanolayers prepared by atomic layer deposition for their application as passivating contacts in crystalline silicon solar cells.

Business ambition

The outcome of this research will lead to new or improved processes and equipment by implementing nanotechnology in building blocks for new or improved solar cells and modules while reducing the amount of material needed without compromising the production throughput of the solar cells. More specifically, the business ambitions are to:

- Transfer the fundamental knowledge and know-how on the design and production of nanopatterned and plasmonic surface structures to applications in solar cells or other relevant fields;
- Exploit the synthesis of silicon nanocrystals for use as quantum dot layers in photovoltaic devices or advanced batteries;
- Implement the results by developing large-area nano-imprinting equipment that can produce textures on glass or other surfaces for solar cell modules;
- Integrate luminescent materials in luminescent solar concentrators as well as in solid-state lighting for energy-efficient light management;
- Develop low weight and flexible CIGS glass–bead-based modules that have improved light absorption.
  In the last phase of the programme, one new project was installed complementing the other research activities; the aim was to implement nanolayers for applications as passivating contacts in crystalline silicon solar cells.

Science realisation

Even before the end of the programme, the research has led to many journal publications (far exceeding the number projected initially) and it included many publications in high-impact journals. Many publications had multi-party authorship including authors from industry. A selection of the scientific achievements is:

- AMOLF, Utrecht University and ECN combined their expertise to produce an ultra-thin silicon solar cell employing light-trapping nanopatterns. Using an array of silicon nanoparticles the average reflection (i.e. loss) was reduced to a value of 1%, well below current industry standards;
- Proof-of-principle experiments at the University of Amsterdam demonstrated the use of silicon nanocrystals for spectral shaping while the efficiency limiting steps for emission where identified and aspects with respect to exciton diffusion were clarified;
- By the Eindhoven University of Technology in collaboration with OM&T and Morphotonics, detailed insight was obtained into several aspects related to the deposition of semiconductor thin films on textured surfaces, including those related to conformal growth and to plasma-surface interaction;
- By Philips Research and the Delft University of Technology the key physics behind the use of luminescent layers in solar cells and in solid-state lighting was unravelled.
- In 2016 Levitech and Morphotonics joint programme 02A in order to explore interesting avenues for the application of alternative materials in solar cells. In the first case, the material turned out not to be suited for solar cell integration although it will have other applications. In the second case, the results were promising and need now to be verified in real solar cells.

Business realisation

Although industrial implementation of research outcomes in photovoltaics takes considerable time, it is anticipated that industry will benefit significantly from the research. A selection of the business achievements is:

- Optical external light trapping structures have triggered interest from industry and were discussed with DSM.
- Many device demonstrators were made with nanopattered surface structures. The technology was transferred to ECN and application to commercial solar cell fabrication is currently being explored. Together with ASML a roadmap was developed for the use of nanopatterning technology in photovoltaics.
- In collaboration with ECN, a first demonstrator of a spectral conversion layer based on silicon nanocrystals was realised by integrating the spectral conversion layer in solar cells.
- Luminescent solar concentrators were demonstrated by realising a record 4.2% efficiency and it was shown that related light management techniques also have applications outside the field of energy generation, e.g. in solid-state lighting. Philips has been developing techniques in this direction.
- Glass-bead-based solar cell modules have been developed and can be brought to the market in due time.

Lessons learned

- During the course of NanoNextNL programme, the solar research landscape has undergone major changes due to a strong price reduction of solar panels and the related move of solar cell production to China and South-East Asia. This has lead to changes in the industrial partners and to an adjustment of the research lines in order to stay at the forefront of photovoltaics research. The new partners (Levitech and Morphotonics) will strengthen the position of solar research in NL through their focus on surface passivation and light-trapping textures. The lesson learned is that a research programme should allow for some flexibility due to dynamics in industry and in the application domain (especially in the very dynamic domain of photovoltaics).
- Industry can highly benefit from research efforts even when no IP is generated. Success in valorisation should therefore be judged on the basis of many factors and not only from business and IP generated.

2.2.2 Programme 2B

Efficient energy utilisation by secondary conversion of energy and separation

Programme director: Freek Kapteijn (Delft University of Technology)

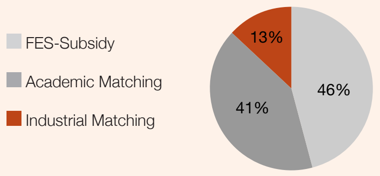
Partners

Delft University of Technology, DENS solutions, Eindhoven University of Technology, Van Dijk FEM Engineering, HyET, Leiden University, NXP Semiconductors, Philips Electronics Nederland, TNO, University of Twente

Projects

10

Budget 2B: € 6.732.388



Output

28 Journal articles
0 Patent filings
Valorisation programme
1 Business case
0 Granted
Researchers
10 PhD student
2 Postdoc
0 Company
18 Master student

Ambition & Realisation

This programme addresses the need for new carriers and sources of energy in combination with the efficient use of energy and feedstock. Development of nanomaterials and -based systems for efficient energy storage and energy utilisation are key.

Science ambition

- The programme addresses three subjects relevant for the global energy challenge and the transition to sustainable energy.
- CO2 fixation by photo- and electrocatalytic conversion into hydrocarbons as energy carrier. Fundamental insight in the surface processes is essential to develop new nanostructured materials and catalysts for selective and intensified processes. Development of high-pressure system and electrochemical cell elements are integral elements;
- Sensing, separation, and design: selective sensors for monitoring, controlling and optimising reactions and reactors. New sensors are being developed that can be applied by the participating industry partners. New topology optimisation methods are being developed that allow for improved design of (nano)structured materials and reactors;
- Structured nanomaterials for energy conversion (electro catalysis): development of non-noble metal electrodes for use in fuel cells for instance. These can replace traditional noble metal electrodes and will be cheaper and/or more efficient. Large-scale use of energy conversion requires these new kinds of electrodes and use of non-critical elements.

Business ambition

- There is a direct link between the research performed at the knowledge institutes and industrial partners in each project. Results from the projects are of direct interest to the companies, as shown by their close collaboration and active participation in the projects.

Science realisation

Although most projects are still running and evolving successfully in their last stage a selection of most appealing results is:

- In the NAMECOSH project (TUDelft, Delmes, followed up by DENS Solutions) world record graphene stretching (>10%) was achieved with a developed micro-tensile stretcher based on MEMS technology. Commercial CVD graphene evaluation reveals its poor quality regarding this application.
- A scaleable method for the production of core-shell particles for application in fuel cell technology ('Non-Noble': TUDelft, Hyet), potentially reducing the use of noble metals.
- Direct growth of metal-organic frameworks (MOFs) or spin coating of polymer-MOF composites successfully detects selectively components reversibly and enhances the overall response of CMOS sensors ('MOFCMOS': TUD, NXP). MOF addition allows tuning selectivity. Electrografting MOF growth on copper surfaces suppresses the formation of interpenetrated structures when using long linkers.
- The 'TOCAS' project (TUDelft, Van Dijk FEM Engineering) developed a topology based methodology to generate microreactors tailored for specific chemical and catalytic reactions, optimising degree of mixing and hence productivity and selectivity.
- In the CO_2 fixation programme 'CO_2-Fix2' (UTwente, TNO) several achievements can be mentioned. Over copper electrodes mass transport limitations determine the local pH, controlling selectivity towards methane or ethylene formation. High pressures favour the CO dimerisation and ethylene production, thereby suppressing deactivation.
- Porous copper hollow fibre electrodes were developed that resulted in CO formation at one order of magnitude higher rates than currently available and Faraday efficiencies of 85% 'CO_2-Fix2' (UTwente)
- On the basis of the reversible catalyst principle nanoparticle alloy electrocatalysts of Pd-Pt were developed that effectively reduce CO_2 to formic acid at low overpotentials, minimizing energy loss ('CO_2-Fix3': Leiden University, Hyet). Alloys of Au-Pd lead to C1-C5 hydrocarbon production.

Business realisation

- The NAMECOSH project development led to reduced interest of the SME Delmes, and SME DENS Solutions took over the participation in the project and is developing applications of the graphene stretching capabilities techniques, e.g. in TEM.
- A first step towards a new activity on the NXP CMOS sensors was proven to be successful via a feasibility proof of detection of relevant volatile organics with MOF-polymer films.
- Through the TOCAS project business contacts between Van Dijk FEM Engineering and DENS Solutions were initialized. TOCAS developed through the NanoNextNL Valorisation Programme a business canvas and business plan for a design/consultancy activity built on the project results.
- UTwente applied for patent on porous metal hollow fibres for electrocatalytic CO production from CO_2. A business case is being developed.

Lessons learned

Overall programme:

- Industry can benefit from research efforts even when no IP is generated; some have the policy not to do this. Success in valorisation should therefore be judged on the basis of more factors than on business and IP generated.
- Most projects turned out to act as seed for follow-up projects and or applications.

Follow-up programme:

- The involvement of start-up companies is a challenge as they may have a limited lifetime, although adequate solutions could be worked out. Changing focus within companies reduces the industrial involvement during the programme execution, something beyond control within a programme. Large companies often need a long lead-time before concrete participation decisions are made. Timely availability of programme information is essential for involvement of new companies.

2.3 Theme 3

NanoMedicine

Theme coordinator: Hans Hofstraat (Philips Research)

Introduction

The growing number of elderly people, and the concomitant overall growth of the world population drives a strongly-growing demand for healthcare. The constant struggle to control the exploding costs of the healthcare system, while satisfying the increasing demand and at the same time improving the quality of care poses an insurmountable problem to the future of healthcare. Transformations in the healthcare system are required to address the global grand challenges, leveraging the opportunities offered by ICT, 'big data'. But ICT solutions cannot deliver without having robust systems that deliver trustworthy and sound data where they are needed, based on deep medical insights. Nanomedicine is a key enabler for achieving this goal, by providing the required and right information at the right time, and at the right place.

Development of the theme through the years

The core of Nanomedicine is bringing together science and technology to realise meaningful medical applications. The starting point of the theme was the ambition to bring together the country's excellent research groups that have a good reputation across the field of nanomedicine and integrated microsystems for healthcare. The good position of the Netherlands in the field of Nanomedicine is demonstrated by the participation of several Spinoza and Stevin laureates, and by a number of VICI laureates participating in the theme. A second important element is providing the required technological elements, provided by participating groups from the Technical Universities, but also by activite participation of numerous companies. The private partners are mainly SMEs (above 20 SME partners actively participate). Participants from large, multinational, industry are Philips, a global leader in medical technology with a strong internal research programme in this field, and NXP. Obviously, the companies also play a key role in bringing innovations to market. Of particular relevance and unique for the Dutch approach to public-private partnerships is the participation of a number of teams from university medical centres, and major research institutes in the medical domain such as NKI (Dutch Cancer Institute), the Royal Tropical Institute, and the Hubrecht Institute of the Royal Dutch Academy of Sciences (KNAW), that add specific and highly pertinent know-how and competences. The joining of forces of this wide range of partners helps to accelerate the path from concept to clinic and market.

Input from the Mid Term Review has been explicitly taken into account. Concrete examples on the actions taken can be found in the reports of the individual programmes.
Specific action has been taken to bring the 'in-vitro diagnostic' programs (3A, 3B and 3E) together, which have clear programmatic overlap. A number of joint initiatives have been taken to strengthen the benefits of being together in the Nanomedicine programme, leveraging the support of NanoNextNL. The joint initiatives are not only limited to the present program, but have a further impact beyond, e.g. the organ-on-chip initiatives (see further). The synergy in the 'in-body' programs 3C and 3D was already strong from the beginning, with a focus on image-guided drug delivery in both programmes, and with joint activities in EU projects on Molecular imaging (led by the Programme Director Gert Storm). In addition also here new collaborations were started, mainly on image-guided drug delivery.
Engagement with pharma (in addition to the already intensitive collaboration with the health-tech industry) has been on the agenda, but has so far been relatively limited. The Netherlands does not have its 'own' pharma industry, and therefore lacks major local research efforts. To be of interest for 'big pharma' projects would need to provide more evidence of outcomes than we can realise with available resources. Some steps in the right direction have been made by Mimetas, offering a platform for organ-on-chip, and Enceladus, that has started a collaboration with Sun Pharma. The hDMT initiative aims for links to big pharma, with the help of Galapagos.

Explicit attention has been paid to Risk assessment and technology assessment (RATA) aspects, taking into account that the RATA aspects are quite different for the in vitro programmes 3A, 3B and 3E, and for the in vivo programs 3C and 3D. RATA has been a main point of attention at the Nanomedicine theme days. Refining and replacing animal experiments is the aim of the organ-on-chip initiatives. Furthermore RATA has been a specific topic addressed in every thesis resulting from Nanomedicine theme. On a regular basis Theme 1 took the initiative to organise Nanomedicine RATA meetings at RIVM, which were well attended, with updates on important developments in Theme 1, and where individual projects could get advice.
Outreach to the wider community has been taken up by, for instance, organising the Nano World Cancer Day, together with other Nanomedicine initiatives across Europe. Presentations were provided by participants of the Nanomedicine theme. Attendance also included representatives of patient organisations, and broader representation from the medical/clinical domain.
Finally, several promising projects in NanoMedicine have received additional funding from NanoNextNL to explore business and application potential in the Valorisation Programme.

Added value of NanoNextNL consortium and ecosystem

The impact of NanoNextNL on innovations in healthcare is strongly boosted through interaction with other themes; examples being the Bionanotechnology theme, particularly the 'Bionano interactions for biosensing' programme, the Nanomaterials theme, and the Beyond Moore theme, in particular the 'Nano-bio interfaces & devices' programme, all of which are linked to the diagnostic projects in Nanomedicine. Furthermore, valuable contributions have been and are received from the RATA theme, which is relevant for the whole theme, but is of particular importance for the in vivo NanoMedicine programmes. The combined activities within the Nanotechnology area form a major contribution to the development of innovative healthcare solutions for Dutch patients and industry. Concrete results from Nanomedicine are in the form of new start-ups, the generation of IP and ideas for novel products and solutions.
Another important factor is the fact that NanoNextNL facilitates interactions in a wider Dutch ecosystem. The Nanomedicine theme has quite clear and mutually synergistic links to the Top Sectors HighTech Systems & Materials (HTS&M) and Life Sciences & Health (LS&H) in particular. Both Top Sectors are significantly active in the field of healthcare. Important elements in the innovation of medical technologies are to be found in the Top Sector Hightech Nanotechnology and Nanotechnology-enabled microsystems. Nanomedicine is also at the core of multiple roadmaps in LS&H. Specific attention has been devoted to synergy with the Top Institutes (CTMM, BMM, TI Pharma, and with DTL). Interaction with CTMM is the most intensive. The active involvement of researchers in the theme, who are also engaged in the Top Institutes contributes to the effective transfer of new technology-based insights.
The Valorisation Programme helps to provide additional support to take the next step in the challenging path from original idea to product. A number of projects in Nanomedicine have benefited from this opportunity.
NanoNextNL, finally, provides inroads into new programmes, like the ongoing discussion on the "Nationale Wetenschapsagenda" (National Science Agenda). Nanomedicine, in particular, is a key element in addressing the questions addressed by the Routes 1-3, on Personalised Medicine, Regenerative Medicine and on Prevention and Care. Relevant new initiatives, for instance on human disease models, based on organ-on-chip technologies, have been taken in hDMT, and in STW (gut-on-a-chip and cancer-on-a-chip projects).

2.3.1 Programme 3A

Nanoscale biomolecular interactions in disease

Programme director: Vinod Subramaniam (Vrije Universiteit Amsterdam)

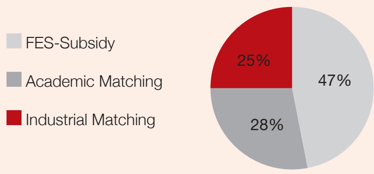
Partners

Dannalab, Delft University of Technology, Erasmus University Medical Center, Hubrecht Institute, University of Twente, Philips Electronics Nederland

Projects

5

Budget 3A: € 5.971.925



Output

49 Journal articles
7 Patent filings

Valorisation programme
3 Business case
1 Granted

Researchers
2 PhD student
6 Postdoc
5 Company
5 Master student

Ambition & Realisation

We aim to use the nanotechnology toolbox to unravel molecular mechanisms in disease, potentially leading to improved diagnostics or treatment

Science ambition

- The goal of all projects is to understand molecular mechanisms underlying disease processes in cancer and neurogenerative disorders, and to develop new diagnostic capabilities.
- To develop a microfluidic platform to perform drug screening on membrane proteins (University of Twente).
- To conduct fundamental studies on, and the development of dedicated X-ray scattering methodologies for characterising the structural and functional properties of nano-scale protein aggregates in neurodegenerative diseases, e.g. alpha-synuclein in Parkinson's disease (Dannalab & University of Twente).
- To obtain insights into the repair mechanism of double strand breaks of DNA (Erasmus University Medical Center & Delft University of Technology).
- To detect genomic rearrangements as novel biomarkers for tumour metastasis (Hubrecht and Philips).

Business ambition

This fundamental programme foresees two aspects involved in generating added value for business. (1) In collaboration with others, understanding the relevant molecular mechanisms will pave the way to identifying novel drug targets and to develop novel drugs which target the actual biology of the disease. (2) We will develop commercialisable nanotechnology-based diagnostic tools and characterisation methods.

Science realisation

- An integrated microfluidic platform for experiments on lipid bilayer membranes and ion channels was developed. Main achievements: (1) Multiplex device, (2) combined electrophysiological measurement and high-resolution imaging. Applications to unravel nanoscale interactions in neurodegenerative disease include (1) investigating protein-lipid interactions, (2) characterise nanoparticle membrane interactions and (3) determine ion channel function (publications in Small (cover article) and Lab on a Chip).
- Insights into the role of protein-membrane interactions on the aggregation of the Parkinson's disease related protein alpha-synuclein (multiple publications); Insights into the role of key amino acids in determining human alpha-synuclein conformation when bound to membranes and in modulating aggregation (published as Rapid Report in ACS Biochemistry); Quantitative analysis of a systematic set of measurements of the dependence of alpha-synuclein fibril growth rate on the concentrations of monomers and seeds (publication in Journal of Physical Chemistry); Characterisation of significant structural differences in alpha-synuclein fibrils formed at different ionic strengths (published in Scientific Reports); New information on the internal architecture and chemical microenvironment of elusive oligomeric aggregation intermediates of alpha-synuclein (in preparation).
- Techniques combining fluorescent and scanning force microscopy to determine the localisation of different proteins participating in DNA double strand break repair with nm precision have been developed, opening novel and exciting possibilities for understanding the molecular mechanism of cancer (published in PNAS 2013).
- Applied the techniques developed in combined SFM-fluorescence to reveal new functional details of the BRCA2 tumor suppressor protein and developed image analysis tools for efficient and robust quantification. The results open the door to understanding the molecular defects in this nanomachine of DNA break repair identified as disease associated but with currently unknown significance. These results lead to new collaborative project proposals with other NNNL project partners and medical researchers (article in Nucleic Acids Research, methods article BMC Bioinformatics 2015, related review DNA Repair 2014).
- Insight into the mechanism of action of HepA related proteins (HARP) which are believed to have an important role in DNA damage response (published in Biophysical Journal and PLoS).
- Computational models for several crucial oncogenic signal transduction pathways to be used as companion diagnostic tools with mRNA levels of a dedicated set of genes as patient sample input have been developed. Initial validation in clinical samples from the Erasmus University Medical Center partner has shown very good and dependable performance. Hi-C technology developed by Hubrecht Lab has been compared with paired end sequencing of tumour genome and is ready to be used on patient samples, supplied by Erasmus University Medical Center. Established genome-wide 3C (called Hi-C) as a reliable diagnostic tool for the detection of chromosomal rearrangements; A modified 4C strategy has been established, called Targeted Locus Amplification, or TLA, for the mapping of rearrangement breakpoints at single base-pair resolution.

Business realisation

- The identification of DNA rearrangements in an individual patient's cancer enables the development of a blood-based therapy response monitoring test which is expected to enable detection of drug resistance within weeks instead of months; this allows a timely switch to a potentially more effective therapy. These commercial applications are being worked out at Philips.
- Cancer tissue-based tools for the identification of tumour-driving signalling pathway on an individual patient basis are expected to enable a great improvement in targeted therapy efficacy thanks to more reliable patient stratification (Philips/van de Stolpe). Based partly on progress from this program Wyman/Kanaar group projects with Philips to develop new prognostic/diagnostic tools for personalised cancer treatment (Kanaar-van de Stolpe targeting DNA repair defects for cancer treatment); based directly on progress from this programme Wyman-Wuite project proposal to test models of tumor suppressor protein BRCA2 function as new application of the instruments made by Lumicks company.
- Dannalab (partner in 2 projects): commercialise SAXS methodology and devices for protein aggregation studies for e.g. the pharmaceutical and food industries. Dannalab has explored as a business case the development of a SAXS device as an alternative for synchrotron experiments.
- New technologies developed (but not yet commercialized): SFM-TIRF instrument and analysis tools, microfluidics BLM platforms, multiplex magnetic tweezers, combined MT-fluorescence instrument for studying DNA repair machinery.

Societal impact

- Therapy response monitoring test has potential to significantly impact patient treatment strategies.
- Understanding molecular bases of disease is fundamentally relevant for medical diagnostics and treatment of important diseases.

Lessons learned

- The area of nanomedicine is witnessing a move away from the lab bench towards translational research. The fundamental insights from this program, such as how these molecular machines interact with DNA, or how proteins aggregate in disease, will inform future work.

2.3.2 Programme 3B

Nanofluidics for lab-on-a-chip

Programme director: Albert van den Berg (University of Twente)

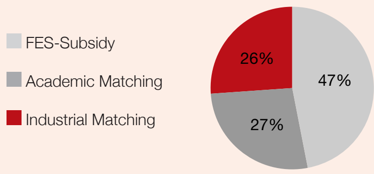
Partners

Delft University of Technology, LioniX, PamGene International, Philips Electronics Nederland, University of Amsterdam, University of Twente

Projects

7

Budget 3B: € 8.951.615



Output

37 Journal articles
3 Patent filings
Valorisation programme
0 Business case
0 Granted
Researchers
7 PhD student
1 Postdoc
11 Company
1 Master student

Ambition & Realisation

Top level micro/nanofluidics research is coupled to industrial efforts

Science ambition

- To perform cutting edge research on single cells using micro-/ nanofluidics for diagnostics purposes combined with more applied research towards cell analysis in body fluids.
- To discover new (optical) sensing principles for ultrasensitive biomolecule detection.
- To find and characterise nanofluidics phenomena for the separation and manipulation of biomolecules.

Science realisation

- Combined with antibiotic treatments, our new platform lead to large-scale quantitative studies on the pattern formation and genome organisation, which are essential for cell division of bacteria. This includes several publications in high-impact journals such as Nature Nanotechnology (cover: http://www.nature.com/nnano/journal/v10/n8/index.html).
- The findings are of fundamental importance for understanding how the internal structure of bacteria are organised, which is essential for understanding the mechanism of antibiotic killing and antibiotic resistance.
- Work realised in programme 3B has lead to a variety of new research activities. Worth mentioning are the ERC Adv program VESCEL (total 2.2 MEuro), H2020 program Cancer-ID (5.8 MEuro) and significant participation in the "Zwaartekracht" programme MCEC (total 32 MEuro) as well as several FOM and STW projects.
- As a result of the NanoNextNL activities members of the NanoNextNL program 3B are actively involved in the creation of the hDMT Institute (Human Organ and Disease Model Technologies), a collaborative action between 5 universities and three companies.
- Preparation of a national "Zwaartekracht" programme Netherlands Organ on Chip Institute (NOCI) programme.
- An innovative technology to filter excitation light in an integrated optical waveguide platform for fluorescence detection has been developed. This technique is applicable in integrated optics-based fluorescence detection systems and will be applied in a later stage on cells.
- A new size selective detection method for integrated optical interferometric biosensors which strongly enhance their performance (published in Optics Express). It is anticipated that this detection method will be suitable for the detection of viruses in complex media.
- Separation of macromolecules by miniaturised asymmetrical flow field fractionation for application in LDL/HDL cholesterol test.
- The design of a novel method to sort ultrasound contrast agents' microbubbles acoustically using a microfluidic sorting chip. The bubbles are not sorted by size but by their acoustic properties.

Business ambition

The directly participating companies (Philips, PamGene, LioniX) will profit from scientific and technical innovations generated in the programme as well as new start-ups indirectly originating from this programme (Cellanyzer, Organ on Chip Institute) and create new business value for the Netherlands. Examples are the sensitive optical detection concept for LioniX and the microdroplet platform for drug development purposes for the Organ on Chip Institute.

Business realisation

- In programme 3B Philips focuses on the feasibility of technological modules for sensing and fluidics with the perspective of integrating these modules with other technology components, in particular those related to the use of magnetic nanoparticles. The feasibility of miniaturisation of a high-resolution optical imaging system has been investigated, resulting in a system with sequential illumination of fluidic chambers and a total device volume of about 1 dm^3. A miniaturised electrochemical sensing module has been investigated, and the limitations of integrated calibration have been quantified. Also, a foil-based fluidic cartridge concept with an integrated filtering function suited for blood sampling by capillary forces has been studied.
- Filtering of the excitation light in fluorescence detection is a necessity that is conventionally solved by bulk (filter) optics which brings about system complexity and costs. The integrated approach taken by LioniX is unique, cost-effective and promises very high performance.
- A research project at UTwente aiming at developing Organs on Chip financed by the leading company in this field Emulate is about to be signed.
- Collaborative project with Bracco in STW or TTT (Twente Top Technology) framework.
- The company Cellanyzer is started partly based on insights and expertise obtained in programme 3B.
- A new company aiming at sperm cell sorting (Semen Refinement Technologies) will be founded partly based on results of Nanonext 3B programme.

2.3.3 Programme 3C

Molecular imaging

Programme director: Michel Versluis (University of Twente)

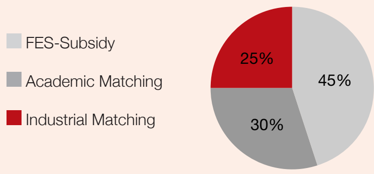
Partners

University of Twente, LioniX, Nanomi, Erasmus MC Medical Center, Mimetas, Eindhoven University of Technology, Leiden University Medical Center, SyMO-Chem, Tagworks Pharmaceuticals

Projects

3

Budget 3C: € 6.127.049



Output

29 Journal articles
7 Patent filings
Valorisation programme
2 Business case
1 Granted
Researchers
5 PhD student
4 Postdoc
0 Company
5 Master student

Ambition & Realisation

Overall aim: to develop novel formulations of nanoconstructs to improve the detection of disease biomarkers on a molecular level and to make therapeutic interventions more effective.

Science ambition

- To assess and improve the use of contrast agents for molecular imaging with ultrasound. This will be achieved by the applications of novel formulations combined with a size reduction, which prolongs circulation time and may increase targeting efficiency through enhanced permeability and retention.
- To improve the efficacy of photodynamic therapy (PDT). The combination of (thermosensitive) nanoparticles with MRI guidance will increase the selectivity of PDT and result in a more effective anti-cancer therapy.
- To develop a pre-targeting platform based on bio-orthogonal chemistry and to prepare tunable self-assembling nanoparticles, which in combination will lead to enhanced uptake for improved tumour imaging and to a more effective anti-tumour therapy.

Business ambition

- All three projects in the programme constitute a highly effective setting for business development especially by SMEs that are active in the domain of molecular imaging for nanomedicine.
- The programme provides the platform through which LioniX and Nanomi, in direct interaction with the academic users of their technologies, develop nanosieves and nanoparticles, respectively, in an iterative product optimisation scheme to enhance ultrasound-based molecular imaging.
- Two SMEs, Tagworks Pharmaceuticals and SyMO-Chem, are jointly developing platform technologies for pre-targeted cancer imaging and therapy.

Science realisation

- The University of Twente and Erasmus MC have achieved precision control of the activation of gas-filled polymeric microcapsules through a detailed understanding of the underlying physical phenomena. This has led to new insights that are published in high-impact journals, including Biomaterials and Nature Communications. The subsequent therapeutic response has been tested in various biological platforms including cell monolayers, in vitro 3D cell cultures on chip (Mimetas) and chicken-egg embryo (CAM) models and have shown direct implications for guiding localised and controlled drug delivery using ultrasound.
- Leiden University Medical Center has developed vitally important tools to optimise the efficacy of photodynamic therapy in mouse tumour models, which will be exploited in joint studies by Leiden University Medical Center and Eindhoven University of Technology to develop nanoparticle-enhanced image-guided PDT.
- Tagworks Pharmaceuticals, together with SymoChem, has discovered that the fastest and highly selective click reaction can be modified to achieve controlled and selective bioorthogonal release. This is a very promising tool for advanced drug delivery and in vivo diagnostics and imaging (published in Angewandte Chemie).

Business Realisation

- Tagworks Pharmaceuticals was created (www.tagworkspharma.com).
- Five patents filed (all by Tagworks Pharmaceuticals).
- Licensable nanosieve and nanoparticle production technologies are expected to result from the activities at LioniX and Nanomi.
- Nano-sized ultrasound-responsive particles will reshape the field of ultrasound-based molecular imaging and therefore technologies to reduce particle size have a high market potential. Customers are companies that produce diagnostic imaging agents, while medical institutions will be the end-users.
- The impact of photodynamic cancer therapy is withheld by limited delivery of photosensitiser to the tumour site and unwanted delivery to non-target sites in the body. Photosensitiser encapsulation in thermo-sensitive nanoparticles in combination with technologies for image-guided delivery to the tumour site will strongly improve PDT efficacy. Whereas the main customers are pharmaceutical companies, the technologies for image guidance may find their way to imaging instrument companies.
- Tagworks Pharmaceuticals is establishing a platform technology based on bio-orthogonal linkage for drug delivery, radio immunotherapy, sensing and imaging. Based on the different applications, different, as yet unmet medical needs will be addressed. The main customers will be pharmaceutical companies and manufacturers of diagnostic imaging agents.
- Mimetas is developing a new platform to port their 96 Transwell cell culture Organoplate technology to an optically and acoustically accessible system, which will open a new market for preclinical laboratory tools for ultrasound-mediated therapies, including tumour, thrombus and blood-brain barrier models.

Lessons learned

- The multidisciplinary projects and the environment of business and science incorporated in an integrative project structure was very rewarding both in terms of scientific output as well as porting the scientific ideas to the industry to be further developed into a device or product

2.3.4 Programme 3D

Drug delivery

Programme director: Prof. Dr. Gert Storm (University of Utrecht)

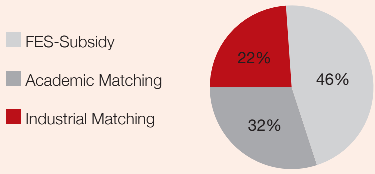
Partners

Academic Medical Center, Amsterdam BioTherapeutics Unit, BiOrion Technologies, Cambridge Major Laboratories, DC4U, Eindhoven University of Technology, Encapson, Enceladus Pharmaceuticals, Erasmus University Medical Center, Leiden University Medical Center, LinXis, PamGene International, Philips Electronics Nederland, Phytogenix, Podiceps, PolyVation, Radboud University Medical Center, Radboud University Nijmegen, Slotervaart Hospital, Syncom, Synvolux Therapeutics, Netherlands Cancer Institute, University Medical Center Groningen, University of Groningen, University of Twente, U-Protein Express, Utrecht University, Utrecht University Medical Centre, VU University Medical Center

Projects

12

Budget 3D: € 10.937.695



Output

- **52** Journal articles
- **10** Patent filings

Valorisation programme

- **5** Business case
- **3** Granted

Researchers

- **11** PhD student
- **9** Postdoc
- **0** Company
- **18** Master student

Ambition & Realisation

The ambition of this programme was to push new concepts and innovative academic research in the field of nanomedicine towards clinical and commercial application. To this end, patient- and disease-oriented nanomedicine projects were carried out within a structural collaboration between academic, clinical and/or industrial scientists.

Science ambition

In the nanomedicinal drug delivery field, there is an increasing need to push drug carrier systems from the academic lab towards the demonstration of clinical value. Important steps to be made in this translational process are 1) optimisation of these systems pharmaceutically and preclinically regarding safety and efficacy, 2) production, charactisation and upscaling of clinical grade batches according to Good Manufacturing Practice (GMP), and 3) performance of clinicial proof-of-concept studies in patients. While pharmaceutical drug development is a very costly activity, it has nevertheless been decided to utilise the limited programme budget for facilitating 12 promising translational projects - developing a variety of different types of nanomedicine systems - with smaller financial stimuli rather than supporting a few selected ones with larger amounts. To date, most research in this field has been directed towards solid tumours. One of the ambitions of the present programme is to reach out to other diseases as well. The challenge to 'shape' novel nanocarrier materials for drug delivery applications was addressed as well.

Business ambition

The scientific results produced during the execution of this programme are not only of academic interest but additionally of direct interest to the industrial partners participating in this programme. In most projects, companies participated bringing considerable amount of background Intellectual Property (IP) to the programme. While new IP may also be generated during the programme's lifetime, it is likely that most of the projects mature based on the already existing patents. In addition, if the project has reached stages of industrial exploitation and clinical evaluation, this will increase the company's commercial value. Also new spin-off companies may be created on the basis of convincing pharmaceutical and preclinical results obtained.

Science realisation

The majority of nanomedicines investigated in this project are based on established carrier materials with already a good track record in the clinic as they are composed of natural components: liposomes and albumin. Anti-inflammatory drugs, anticancer drugs, antifibrotic drugs, antibiotics, and anticancer antigens were associated with these carrier systems. The use of all these different drugs already indicates that the programme reached out to a variety of diseases (cancer, rheumatoid artritis, atherosclerosis, kidney and liver fibrosis, and tuberculosis). The resulting nanomedicines were occasionally modified at their surface with hydrophilic polymer and/or specific targeting ligands to confer superior targeting capability. A few novel polymeric nanocarrier materials were also taken into investigation. Regarding the RATA aspect, it should be realised that it is already mandatory for pharmaceutical drug development that promising nanomedicines, which are selected for clinical testing, are evaluated with respect to their preclinical safety profile. This was performed by the partners according to their fields of expertise and on the basis of exisiting safety testing methods. The results will either be used to optimise the formulations and/or to decide whether the selected formulations will be further evaluated as candidates for the development of pharmaceutical products.

Two projects dealt with 'smart' targeted nanomedicines from which drug release can be triggered after accumulation in tumour tissue by exposure to either ultrasound-induced heating or infrared light, this to strongly improve the therapeutic efficacy. Design of efficient preparation protocols, pharmaceutical characterisation, quality control, and determination of efficacy and toxicity in in vitro and in vivo models of disease were prominent activities. In the context of a project on improving the chemotherapeutic treatment of prostate cancer, also the GMP protocol to produce clinical batches of liposomal dexamethasone (Oncocort) was established. Based on this industrial exploitation outcome and a series of in vivo experiments with favourable anticancer effects, the project team was awarded a NanoNextNL Valorisation grant which provides funding to realise a clinical study in prostate cancer patients (at the LUMC). The clinical trial is now ongoing. The same team evaluated novel polymeric micelles for the targeted delivery of docetaxel to bone metastatses in the same patient population. Based on the convincing academic results, the plan is to start a spin-off company in 2017. The GMP step was also taken to produce an antibiotic inhalation powder formulation.

In several projects, an imaging (PET, CT, SPECT, MRI)-guided drug delivery approach was adopted for the purpose of monitoring drug delivery processes in vivo, nanomedicine optimisation and selection of the proper patients expected to benefit from the nanomedicinal treatment (personalised nanomedicine). Currently, one project team is currently preparing for a clinical imaging-guided nanomedicine study in whch patients with rheumatoid arthritis will be treated with Indium-radiolabelled corticosteroid-containing liposomes to study the correlation between the degree of accumulation of liposomes in sites of inflamed disease with the severity of the inflammation in these sites and the therapeutic outcome (at the Radboud UMC).

Lastly, as crowning glory of this programme, two clinical studies in atherosclerosis and tuberculosis patients were performed and already completed. Liposomal corticosteroid targeting (Nanocort) to inflamed and instable atherosclerotic plaques was demonstrated (AMC). Nanocort was well tolerated by the patients. However, as assessed by PET/CT and DCE-MRI, anti-inflammatory effects were not observed. Several factors (dose, time of observation, type of inflammation) are being addressed right now experimentally to come to an improved formulation. The second completed clinical study has been conducted in South-Africa. This study involved inhaled antibiotics for the treatment of tuberculosis. The inhalative treament was tolerated well but the dosing was slightly too low and requires further optimisation.

Business realisation

A series of patents have emerged from this programme and a few are still pending. One spin-off company was initiated in 2013 (Excytex BV). The positioning of participating companies is consolidated, increasing their value.

Societal impact

The development of superior medicines to treat diseases burdening our society does not need any further comments here.

Lessons learned

In conclusion, this programme has met its ambition to support the progression of nanomedicines towards clinical application. At the start, the choice was made to disperse the limited funding for this programme over 12 projects. As the programme has successfully produced its deliverables, this choice has proven to be a proper one to achieve these. The positioning of participating industrial partners has been strengthened. Those projects with outcome most promising to reach the clinic and the market will require substantial further support and investment (e.g. by obtaining applied funding and/or co-development with larger pharma).

2.3.5 Programme 3E

Integrated microsystems for biosensing

Programme director: Han Zuilhof (Wageningen University)

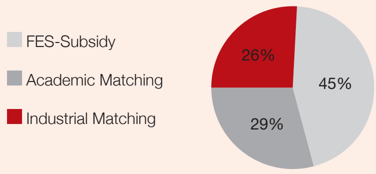
Partners

Universitair Medisch Centrum St. Radboud,NXP, Wageningen University, Lionix BV, Radboud University Nijmegen, Innosieve Diagnostics, Royal Institute 'Tropen', Aquamarijn Microfiltration B.V., Podiceps, Ostendum, University of Amsterdam, CCM Centre for Concepts in Mechatronics, Surfix, Stichting DLO, ATAS GL International BV, Microdish B.V., Concept to Volume (C2V/ThermoFisher)

Projects

Two clusters of projects were defined, and within these clusters informal groups of often 2-3 projects formed to reach goals.

Budget 3E: € 8.274.619



Output

41 Journal articles
5 Patent filings

Valorisation programme
6 Business case
3 Granted

Researchers
5 PhD student
6 Postdoc
11 Company
13 Master student

Ambition & Realisation

Overall aim: to develop novel detection platforms for a range of infectious bacterial diseases, with a focus to push improved molecular bases of detection to construction of working prototypes.
Science ambitions

Science ambitions

- Insight in the genetic factors (mRNA level) that determine the severity of infectious lung diseases
- Stable antifouling functionalisation of a range of materials
- Development of more specific sensing of bacteria causing tuberculosis and urine tract infections
- Establishing receptomics technology for medical diagnostics and discovery: a new "omics" technology based on large cell arrays.

Business ambition

- Investment in the R&D of several small companies (Innosieve, Aquamarijn, ATAS, Podiceps, Ostendum, Surfix and Microdish) in a truly cooperative manner with other industries and academia. This should lead to:
  - Development of biofunctionalised detection devices based on ring resonators and interferometry for the detection of biomarkers related to infectious lung diseases.
  - Gas chromatography-based device for the detection of (diseases like) tuberculosis
  - Porous devices for the selective capture and detection of pathogenic microbes.

Science realisation

A proof-of-principle of covalently attached antibodies to large pore microsieves and microbial detection has been demonstrated (Aquamarijn, Innosieve and WUR). Dedicated protocols for antibody coupling to microsieves (WUR and Aquamarijn) and microbial detection of four target pathogens (Innosieve) have been developed. The resulting microbial detection platform has resulted into the rapid and sensitive diagnosis of the causative agents of urinary tract infections. Wageningen University has been able to wrap up ongoing work on cholera toxin detection with a paper in Acc Chem Res (IF = 22).

- A method for the biofunctionalisation of porous aluminum has been developed, which has been used for the covalent attachment of specific sugars. Such a sugar-modified surface has been used for the specific capture and selective growth of Lactobacillus Plantarum (WUR).

- A set of 20 biomarkers was found that, combined in a chemometric model, can be used to differentiate between Mycobacterium tuberculosis (MTB) bacteria and non-tuberculous mycobacteria (NTM) in culture (UvA/KIT), as well as to determine MTB's resistance to antimicrobial compounds (antibiotics).
- KIT, MicroDish and CCM, now Sioux, have developed an automated integrated microscope/culture system.
- A miniaturised gas chromatograph (GC) inlet port was developed for coupling to portable micro-GC. The inlet can also act as chemical reactor unit providing rapid heating and cooling between ambient and 600 °C.

Business realisation

- Qmicro is busy with the commercialisation of the microGC technology (up to 180°C) towards an analyser instrument for fast gas analysis applications. Qmicro won a NanonextNL Valorisation grant to further develop this instrument.
- Surfix has developed a novel approach to quickly pattern glass slides with highly defined (super)hydrophobic/hydrophilic areas, and won a NanonextNL Valorisation grant to further develop this technique.

Societal impact

Several technologies have either been developed or improved that will contribute to the faster or more efficient/sensitive detection of infectious diseases in a clinical setting. Several companies that really struggled businesswise in the economic crisis around 2010-2012 have indicated to have been really been helped by the NanoNextNL subsidies – neither of these (with in total > 50 FTE) currently hinges for their business development on further subsidies, which shows an additional advantage of such 'economic lubricants'. One SME (Ostendum) finished their business partially based on research performed withing NanonextNL: they could prove their biomarkers of interest could not possibly be detected at the required low concentrations by the class of sensors under development. While surely disappointing, this is actually a success of the programme: they efficiently discovered the limits of what was feasible, preventing wasting further money into this direction.

Lessons learned

- The multidisciplinary projects and close integration of business and science is very stimulating – minimal critical mass within a programme needed to accomplish truly innovative results – industrial partners had strong and highly constructive impetus on direction of 'fundamental' research, and open atmosphere allowed landing of many 'wild/purely academic' ideas within commercial environments for further development.
- Assignment of small fraction of total budget (i.e.,10%) only half-way the project over already participating partners would have been highly preferable. This would have given the Programme Director/Theme Coordinator the chance to remedy errors made and especially stimulate the most promising initial successes. Within the programme several new conglomerates of groups and projects arose over the years (partners discovering interests and skills of others), which have led to several business cases and patent applications.

2.4 Theme 4

Clean water

Theme coordinator: Bert Hamelers
(Wetsus – Centre of Excellence for Sustainable Water Technology)

Introduction

Access to sufficient water of good quality is needed worldwide to ensure public health, food production and economic growth. Available water sources are under pressure due to increasing demand and pollution.
Currently applied technologies cannot keep up with these rising challenges, especially the upcoming presence of micropollutants. The theme's main ambition was to tackle the newly emerging challenges with nanotechnology based solutions. This should be done in concord with both tech and water companies, reflecting business opportunities.

Development of the theme through the years

The recommendations of the IAC were in line with the theme and strengthened the scope of the theme as described above. The action points have been followed up.

Added value of NanoNextNL consortium and ecosystem

By combining renowned science players in the field of nanotechnology and connecting them to new application fields like water is the major added value. Water technology encompasses many technology fields and there are many relative small company players, both aspects making it difficult for the sector to assess the appropriateness of a complety new technology like nanotechnology. NanoNextNL has provided the platform to do this. Within the Wetsus network nanotechnology is now well accepted and several projects have started especially in the field of membrane technology.

2.4.1 Programme 4A

Nanotechnology in water applications

Programme director: Rob Lammertink (University of Twente)

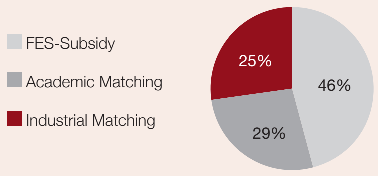
Partners

KWR Water recycle institute, LioniX, Pentair X-Flow, Philips Electronics Nederland, Phycom, Stork Veco, Wageningen University, University of Twente

Projects

4

Budget 4A: € 6.734.645



Output

22 Journal articles
1 Patent filings

Valorisation programme
3 Business case
0 Granted

Researchers
11 PhD student
1 Postdoc
0 Company
12 Master student

Ambition & Realisation

To develop nanotechnologies for the purpose of water purification and understand the behaviour of contaminants on a nanoscale. Nanotechnological fabrication methods will be applied to face the challenge concerning the analysis and removal of new water contaminations.

Science ambition

The investigation of catalytic routes regarding water treatment. Fundamental understanding regarding nanoparticle behaviour in aqueous environments and their corresponding isolation. Development of novel separation technologies using isoporous membranes.

Business ambition

Development of novel water treatment methods. A new generation of contaminants that are difficult to remove by conventional techniques is an increasing threat. Such contaminants, including pharmaceutical and nanoscopic materials, can already be harmful at very low concentrations.

Science realisation

- Extremely fast photocatalysis was reported and explained in terms of the importance of the electron-hole transporting substrate.
- High selectivity regarding catalytic nitrite reduction was observed via the control of species transport.
- Well defined porous membranes were fabricated via top-down and bottom-up methods.
- Functionalisation of isoporous membranes is demonstrated to increase functionality.
- Fouling behaviour during nanoparticle filtration was successfully studied.
- Already at least 21 peer reviewed papers with more to come.

Business realisation

- Joint patent application (Philips and UT) regarding catalytic reduction in aqueous media.
- Selective continuation concerning research activities.

Societal impact

- Implementation of fundamental understanding gained regarding membrane filtration. Close collaboration between theme 4 and theme 1 resulted in thesis of Roberto Flores (UT).
- Awareness generated regarding risks related to aqueous contaminations.

Lessons learned

Nanotechnology and science provide many opportunities for water treatment.

2.5 Theme 5

Food

Theme coordinator: Erik van der Linden (Top Institute Food & Nutrition)

Introduction

The theme aims to interrelate molecular scale properties with product properties and safety as a function of processing conditions, in order to better design high quality and healthy foods using sustainable routes.
The scope extends into four dimensions. The first focusses on more precise monitoring of food pathogens and specific food quality parameters. The second explores molecules and their interactions to control and design the sub-micron scale structures. The third relates to conditions during the processing of the food with the resulting food product quality properties. The fourth explores foodprocessing with devices acting on a micron scale.

Development of the theme through the years

The original focus has not been adjusted during the years. The nature of the projects has been user-inspired with a large amount of curiosity driven research as well. As a consequence, the development of each of the projects and their sub-projects have had a self-organisational character.

Added value of NanoNextNL consortium and ecosystem

- Some good courses have been organised (RATA and Effective communication) that were followed by various PhDs.
- The results are sometimes also relevant for other industries, and being part of NanoNextNL allows to efficiently reach these other industries, which are not part of the project at hand.
- Being part of NanoNextNL allows to send messages on new findings readily to a broad audience and it helps to deliver a convincing message.
- Sometimes invited lectures were given based on the fact it was based on a NanoNextNL project.
- The nanofield has clearly moved forward due to the concerted actions within NanoNextNL, including the overarching meetings between the themes including the EB.

2.5.1 Programme 5A

Food process monitoring and product quality assessment

Programme director: Maarten Jongsma (Wageningen UR)

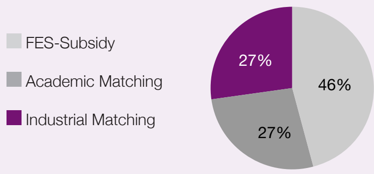
Partners

BLGG Research, Check-Points, Environmental Monitoring Systems, Enza Zaden Research and Development (no subsidy), Leiden University, LioniX, Micronit Microfluidics, Nanosens, Nikon Instruments Europe, Ostendum R&D, Phycom, DLO, Surfix,
Syngenta Seeds, TNO, University of Amsterdam, Wageningen University

Projects

3

Budget 5A: € 7.088.743



Output

22 Journal articles
2 Patent filings

Valorisation programme

3 Business case
1 Granted

Researchers

4 PhD student
3 Postdoc
2 Company
11 Master student

Ambition & Realisation

This programme is designed to investigate the possibilities of micro- and nanotechnologies to monitor specific parameters of a food product that are well correlated to the quality and safety of the end product.

Science ambition

- 5A1: To detect food pathogens and quality parameters at higher sensitivities using optical waveguide technology-based micro-ring resonator and (Young, Mach-Zehnder) interferometry, and capillary electrophoresis. This will enable on site monitoring of food pathogens at production locations.
- 5A2: To detect the ripening of stored and transported foods using miniature printable devices with wireless read-outs using transition metal complexes. This will enable consumers and producers to track freshness, optimising food and food products' lifetime.
- 5A3: To optically measure the sensory quality (flavour and aroma) of foods using human sensory receptors expressed in cell lines and arranged in cell arrays inside microfluidic flow cells. The results will enable food companies and plant breeders to optimise their products and cultivars.

Business ambition

- To realise novel technologies that allow the agro-food business to improve product quality & safety and add to a more sustainable society by reducing food borne incidents and product waste.
- To obtain participation of the complete knowledge chain (from hardware suppliers via specialised scientists to end users), this will warrant a continuous focus on business value.
- Several commercial spin-offs will be initiated in the field of food process monitoring and quality assessment. Foreseen examples based upon IP output are:
  - novel lab-on-a-chip devices to detect food pathogens and quality;
  - a printable ethylene sensor to assess and control ripening processes;
  - an optofluidic tongue/nose predicting and directing better sensorial quality of products.

Science Realisation

5A1

- Stable llama antibody fragments (DLO) to capture food pathogen-specific molecules (flagella proteins, DLO) have been developed. Protein targets / candidates have been identified for spores of food spoilage organisms (UvA).
- New sample pretreatment and DNA primer/probes for specific pathogen (Campylobacter, plant pathogen) detection via an isothermal DNA amplification procedure has been developed (TNO) and NALFIA (BLGG).
- Novel detection devices (microring resonators), including proprietary surface modification, have been constructed (LioniX, Surfix).

5A2

- Copper-containing molecules were produced that bind ethylene with high affinity and specificity and formed the sensitizers of a novel ethylene sensor (UL)
- Prototype sensors (nanotubes on electrodes) were produced, activated with copper molecules and cross reactivity with carbon monoxide (CO) and nitric oxide (NOx) was studied (UL, Nanosens)
- Increased stability was achieved with graphene based materials and cross reactivity with CO and NOx was tackled through different coating materials. Influence of humidity and air on the sensor lifetime was investigated (EMS, UL, Nanosens, DLO)
- A model describing the effect of ethylene on flowers and vegetables was produced to estimate the impact on quality of the measured ethylene readings (DLO)
- An electronic design for data collection / measurement and data transfer was developed (EMS)
- A patent on the new sensor concept was filed (UL)

5A3

- A microfluidic flowcell with cell lines expressing GPCRs and ion channels (flavour receptors) has been developed capable of measuring analytes at the 30 pM level using only a 5 microlitre sample (DLO-PRI, Micronit).
- Methodology has been developed to work with extracts from vegetables and algae, but also with drinks like undiluted coffee and milk and even blood plasma and serum.
- The receptor repertoire has been extended to include all major tastes and a few smells (DLO, UvA). For sweet and umami special cell lines were developed (DLO-FBR) because these receptors are under patent in NL and alternative methods were needed to give the industry freedom to operate.
- Software and statistical analysis has been developed for rapid analysis of receptomics data including baseline correction for coloured samples and peak shift measurements and statistical analysis in case of background responses (DLO).
- UvA: Novel biosensor development strategies have been developed. Improved biosensors for cAMP, a key messenger in olfactory transduction have been created and reported. Strategies for realtime optical detection of receptor activation have been evaluated and optimized. Several steps towards increasing the activation of odorant receptors in heterologous cell systems have been taken.

Business realisation

- 5A1: TNO (J. van der Vossen) is committed to market a campylobacter detection test based on isothermal DNA amplification for Campylobacter infections in slaughterhouses (multiple customers).
- 5A1: LioniX/Surfix (technology providers) - BLGG Research and Checkpoints (customers) are committed to market detectors for pathogens/ quality parameters/ DNA targets in horticulture and food samples.
- 5A1: Lionix licensed microringresonator (MRR) technology to BioVolt
- 5A2: EMS (Jan Kees Boerman) is committed to market an ethylene sensor for use in greenhouses, food storage and/or container transport on the basis of a patent that was submitted (multiple customers).
- 5A3: DLO participated in the NanoNextNL Valorisation Programme for a spin out (ReceptomX) of the optofluidic tongue/nose technology with customers in food and pharma. The launch was postponed to allow further development of the technology first within the institute

Societal impact

Follow up programmes have been realised working on applications of the sensing systems developed under this programme in the order of several million euro exceeding the initial investment.

Lessons learned

A follow up programme should be more interdependent and projects should be based on a strong central concept which has passed peer review. Project plans should be much more detailed than the executive summary which now constituted the entire application. Project reporting should be more extensive and regular. Project meetings should be organised by the partners and not the central office to create better ownership of the programme and projects.

2.5.2 Programme 5B

Molecular structure of food

Programme director: Krassimir Velikov (Unilever)

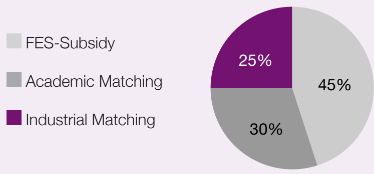
Partners

Danone Research, Delft University of Technology, FOM Institute AMOLF, Maastricht University, Unilever R&D Vlaardingen, University of Amsterdam, Wageningen University, MPI Mainz

Projects

3

Budget 5B: € 6.958.347



Output

100	Journal articles
8	Patent filings
	Valorisation programme
0	Business case
0	Granted
	Researchers
4	PhD student
10	Postdoc
0	Company
6	Master student

Ambition & Realisation

The programme aims to reveal the role of interactions between key molecular building blocks in food and to use these to create (novel) nano- and micro-scale structures, which allow control on product stability, texture, appearance, flavour and (micro)nutrients bioavailability. These scientific insights are used for design high quality healthy food product from sustainable materials and control their properties.

Science ambition

- To build key knowledge about the role of interactions in molecular building blocks (e.g. lipids, proteins, carbohydrates) to control nano- and micro-scale structures in food products.
- To translate fundamental knowledge into application insights to design superior (novel) food structures with increased health benefits and excellent quality.
- To build a sustainable ecosystem of outstanding academic research groups and world class industries that brings complementary expertise in various aspects related to food science and technology.

Business ambition

- To convert the newly developed structuring/delivery technologies into food systems.
- To establish strategic long-term partnerships between academic and industrial partners.
- To nurture a new generation of world class scientists to work effectively in both academic and industrial environments; to bridge the gap between the two and enhance future joint innovations.
- To support industrial partners in maintaining leading position in innovation by creating IP protected technologies and generating scientific insights for communication to consumers and regulatory bodies.

Science realisation

We have published 38 articles to date and 62 are in preparation. Four papers have been published in journals with an impact factor higher than 8 (*JACS, Adv. Func. Mat., Small*). Our research was featured in six journal covers, two press releases and in more than 10 invited talks. Three postdocs accepted academic positions in leading universities (Wageningen University, Gent University) and companies (Danone).

Using a diverse set of techniques and methods, we generated important knowledge in several areas:

- Strong molecular interactions between various molecular systems (e.g. whey proteins, polyphenols, biopolymers) and how to use these to create various novel nano- and microstructures;
- How to create and control nano- and microstructure using water insoluble proteins (prolamins) and carbohydrates (cellulose), which allows effective use of these renewable natural materials;
- Microstructure-rheology relationship in complex microfibril-polymer/protein networks, which is important for understanding and control of complex food systems;
- Lipid droplet morphology directly in human skeletal muscle with high resolution;
- Effect of small sugar molecules the reorientation dynamics of water molecules, which is important for processing of food (e.g. freezing) and many biological processes.

We have demonstrated several links between molecular building blocks of food and health related aspects:

- We developed a method to investigate the origin of altered composition cellular lipid droplets in excessive lipid accumulations in skeletal muscle that are associated with Type 2 diabetes;
- We showed that Type 2 diabetes mellitus is characterised by the pathological deposition of fibrillised protein (amyloids);
- We discovered important difference in inhibition of amyloid formation (by tea polyphenols EGCG), which differs strongly in efficiency and mechanism at lipid interfaces and aqueous bulk media;
- We identified lipid droplets in biological samples and classify their content with respect to lipid saturation level, esterification and packing density;
- We demonstrated a link between obesity and circadium rhythm. This has direct impact by showing how purely behavioural – not nutritional – changes lead to distinct chemical composition in lipid droplets.

Business realisation

The programme successfully delivered against the ambition to create relevant knowledge and IP protected technologies.
Various nano- and microstructures suitable for food applications were developed:

- Microcapsules structured with low-molecular-weight gelator for the encapsulation of lipids;
- Surfactant-free emulsions with pH responsive switchable behaviour for texture control;
- Temperature-responsive surfactant-free foamulsions with a high oil-volume fraction that enable cream-like structures without using hard fat (i.e. low in saturated fat formulations);
- All-natural microcapsules from water insoluble biopolymers for delivery lipophilic substances, control lipid digestion, and various biorelated applications;
- Structured solids with water insoluble plant proteins with less solid fat (*1 patent filed*);
- Colloidal colourants for acid stable green colour (*1 patent filed*, business case was written);
- Novel infant milk formula concept mimicking the structure and composition of human milk fat globule;
- We demonstrated that fibrils are promising structuring agents for liquid and semifluid products due to their elastic and shear-thinning properties already at low volume fractions (*6 patents filed*).

We successfully build talent in a stimulating long term partnership between the industrial and academic partners. Two postdocs are now permanently employed by the industrial partners.

Societal impact

We have seen extensive added value in the close interaction of academia across sectors (physics, chemistry, food science, engineering) and interested industrial partners. These interactions can inspire and help guide ongoing research projects, and provide a strong basis of mutual trust to build new collaborations.
We established fruitful interactions between industrial and academic partners, which are continuing beyond the NanoNextNL programme. PhDs and Postdocs are very successful in finding jobs in both academia and industry.

Lessons learned

The programme successfully delivered against our scientific and business objectives. We have delivered all and exceeded many KPIs. We established several new EU and Dutch government funded collaborations. Together with the other NanoNexNL food programmes, we proposed a follow up programme on food-body interactions which will oversee the interactions of nano-and microstructured edible products with the human body covering both sensory (e.g. taste, mouthfeel) and nutrition/health aspects. Our key messages for future programs are:

- Due to the edible, biocompatible and natural origin of the structures developed in the programme, these can be applied in other industrial sectors (e.g. drug delivery, personal care, agriculture).
- The combination of advanced physical-chemical analytical methods, unique soft matter materials, and biological questions revealed a deeper-than-expected synergy.
- The mix between food and non-food experts in various scientific disciplines is very fruitful, creating novel bottom up approaches to study and control new edible structures.
- A major body of publications based on the results from several PhD students and many publications from the in kind contribution of the industrial partners are still expected. Interdependencies between the projects have emerged at the end of the programme. These interdependencies perhaps would have been already more apparent during the past years when it would have been required to include their exploration in a more detailed grant application for the entire theme upfront, with an external review process that explicitly addresses this aspect.

2.5.3 Programme 5C

Food products and processes

Programme director: Karin Schroën (Wageningen University)

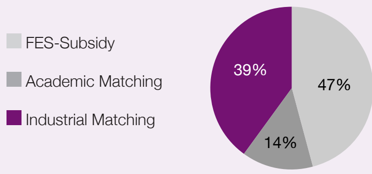
Partners

Radboud University Nijmegen, Encapson, FrieslandCampina Nederland, Pentair X-Flow, Unilever R&D Vlaardingen, University of Amsterdam, University of Twente, VION, Wageningen University

Projects

6

Budget 5C: € 6.394.951



Output

10 Journal articles
7 Patent filings

Valorisation programme

0 Business case
0 Granted

Researchers

4 PhD student
2 Postdoc
2 Company
27 Master student

Ambition & Realisation

This programme aims to achieve the development of sustainable food products and processes for the Dutch food industry, focusing on significant new functionality in products (aimed at combining better nutrition and better taste) by bringing together partners from various stages of the development and production chain.

Science ambition

The programme is based on two scientific challenges:

- Multi-scale structure down to the colloidal scale.
- (Dynamic behaviour of) complex, concentrated systems.
- The programme combines expertise on self-assembly and other phase behaviour of dispersed systems under flow, and characterisation of the structure via imaging and investigation of the properties. This approach will lead to novel foods with new functionalities. Examples are low-fat cheese with full, rich texture, and dairy products with prolonged shelf-life.

Business ambition

The partners strive to bring healthier (better nutrition, just as well as good taste) products to the market that still taste as good as conventional products; this will improve the quality of the consumers' food intake and will result in a healthier society.

Science realisation

- Fourty six peer-reviewed articles and conference contributions have been achieved, and it is expected that this will even increase in spite of the fact that the programme has finished.
- Exchange of ideas on bubbles and droplets were exchanged with other programmes within NanoNextNL, through a one day work shop held at Wageningen University. Many participated and appreciated the content of the day, that was spread out over 3 different programmes.
- The number of patents (7) also indicates that not only cutting edge science was performed, but that this also resulted in generation of IP.
- Various microfluidic tools have been developed that have attracted attention in various fields in science and in industry alike.

Business realisation

- The combination of partners represents the entire development chain: from basic components to final product to be introduced on the consumer market. This optimises the likelihood that innovations will find their way into the consumer market.
- The first results was in (bio)polymersomes with controlled release profile during digestion (Radboud University Nijmegen). The controlled release profile ensures that the contents of the polymersome (e.g. a medicine) will only be delivered at a specific location. As polymerosomes are pH sensitive they shrink during passage through the stomach, and subsequently open up when in a more basic environment releasing their content. This provides unique opportunities for targeted delivery.
- New methods for the preparation of low-fat cheese and meat products, which will have a similar texture to 'full fat' cheese and meat products have been patented (FrieslandCampina and VION Ingredients).
- The development of an emulsion stability test (Wageningen University), has attracted considerable attention, because it allows *ab initio* prediction of which emulsion formulation is going to result in a stable emulsion given certain process conditions.

Societal impact

- Being part of the NanoNextNL allows us to send our message much more readily to an interested audience, both within and outside NanoNextNL.
- There have been invites for lectures that specifically were based on the fact that we were part of NanoNextNL.
- The current results are e.g. also of interest for other science and industrial fields. For example the work done with emulsions is also relevant to the oil and gas, pharma, personal care etc, and we spin the technology toward these fields, also through a demonstrator project that was granted within 5D. At the moment this is still an academic collaboration based on exchange of people, but we expect that the impact within the scientific community will be much greater, also due to the specific requests we obtained from various application fields to write a special contribution to a magazine relevant for a specific group of professionals.

Lessons learned

Since NanoNextNL is a very large consortium with people collaborating from very different backgrounds, it takes serious effort to get this to work. Many complements to the programme office who carried out the massive task of getting things to run smoothly, and in the process also created a real community that was dedicated to the task of advancing the nanotechnology field. Even after the official ending of the programme, the community knows where to find each other and that implies that the efforts done within NanoNextNL have led to lasting connections, and network formation.

[12] See business case 5C-a (separate document).

2.5.4 Programme 5D

Microdevices for structuring and isolation

Programme director: Karin Schroën (Wageningen University)

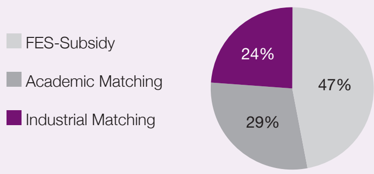
Partners

Aquamarijn Micro Filtration, FrieslandCampina Nederland, LioniX, MicroNext, Nanomi, Vietnam National University, Wageningen University

Projects

2

Budget 5D: € 6.124.502



Output

10 Journal articles
1 Patent filings

Valorisation programme
0 Business case
0 Granted

Researchers
10 PhD student
1 Postdoc
0 Company
10 Master student

Ambition & Realisation

The parties involved in this programme wish to achieve the development of sustainable food products and processes for the Dutch Food industry while developing significant new functionality in products (aimed at combining better nutrition and better taste). This programme aims at realising very new processing concepts, novel products and mild isolation of ingredients. This will result in a reduction in the use of energy and other utilities. In addition to novel foods and novel food production processes, the newly developed technology is expected to have a much wider range of applications.

Research ambition

The programme will:

- Generate better insight into the dynamics of multiphase fluidics in microsystems;
- Enable larger scale application, making use of those new insights;
- Generate knowledge of the behaviour of mesophase forming components in microchannels.
- The partners will specifically explore emulsification and separation techniques with microsystems.
- Microsystem emulsification can yield monodisperse emulsions under extremely mild conditions at low energy-consumption levels. Attention will be given to the dynamics of spontaneous droplet formation and the interaction between numerous nozzles when scaling out.
- For separation, new engineering approaches are being explored to make and apply membranes with complex inner and outer geometries and incorporating other driving forces in microstructures.

Research realisation

- The premix emulsification system had extremely high throughput (up to 1000 cubic meter per square meter per hour). Use of this technology may decrease emulsification production costs as it requires far less energy than classic emulsification technology. Industrial interest has been expressed;
- It has also been demonstrated that extremely monodisperse emulsion droplets can be generated by various generations of microfluidic devices using the EDGE mechanism. The throughput of these chips has very systematically been increased, now reaching values that make it interesting for larger scale application. This was further investigated within a demonstrator project.
- Work in another project has demonstrated the feasibility of spinning microstructured capillary ultrafiltration membranes featuring an enlarged membrane surface and a prolonged operation time.
  - Our Vietnamese PhD student working at the Nanolab at Ho Chi Minh University and has given a proof of principle using coconutwater and humic acid contaminated surface water.

Business ambition

- The partners aim to develop new emulsification process technologies and new emulsion products for the food market. The combination of partners represents the entire development chain: from basic components to final product to be introduced on the consumer market.
- Newly developed production processes will have a wider range of application that might be interesting in various fields including oil and gas, pharma, and personal care.

Business realisation

- Demonstration of ultrafiltration of water with microstructured capillary membranes. This technology provides a filtration membrane with a functional filtration surface that is nearly doubled compared with conventional membrane manufacturing technology. This will reduce costs. Application areas are potable water, beverages, healthcare and fluid processing. To be further developed in a business case.
- Premix emulsification technique is a successful approach for scaling up of small particle size emulsion production as it gives high fluxes. Industry has shown interest in this technique. The technology has a wide range of applications (food, pharma, personal care, coatings).
- The productivity of paralellised EDGE chips has been increased > 100 times to now reach levels that make the technology industrially interesting.

2.6 Theme 6

Beyond Moore

Theme coordinator: Hans Huiberts (Philips Research)

Introduction

The four research programmes that are part of the Beyond Moore theme focus on micro and nanometre scale science and technology innovation. They address innovation on electronics, spintronics, photonics, light generation and biological interfaces. In Beyond Moore we aim to bridge often very new and fundamental scientifc concepts with industrial application needs. Application areas under investigation comprise gas sensing, new memory and high frequency components, optical communication, drug screening and personal healthcare tools, diagnostic tools and light sources (OLEDs and LASERs).

Development of the theme through the years

Creating a bridge between fundamental science and industrial innovation has been a running theme throughout the lifetime of this NanoNextNL theme. Already in 2008 during the definition stage for the programmes it was difficult to align scientifically relevant activities and industrial application needs in combined programmes. Subsequently, timelines in industry and academia turned out to be very different and finally in some cases industrial activities disappeared completely from the radar leaving topics without an industrial outlet. Still, the collaboration, be it certainly open for improvement, did result in some excellent scientific and business results. Breakthroughs in nano-scale optics and potentially the onset of quantum communication, new spin-Hall based device concepts, new stable lipid anti-fouling layers, the Topo Chip that enables a high throughput screening platform for cell growth and finally new nanolaser concepts and plasmonic crystals for improved optical interconnects. But it was not only scientific highlights also direct business opportunities were created: new gas sensor solutions were developed for industry (Holst, Philips), the spin-off nanoPHAB was based on the electromechanical tuning of photonic crystals developed in 6B, the industrialisation of the Cytostretch platform at Philips innovation services and the new start-up LipoCoat in 6C and finally a new OLED start-up Simbeyond and the creation of valuable LED IP (taken over by LumiLEDs) in 6D.

Based on the input from the MidTerm Review, collaboration between programme 6A and 7B has been strengthened also via a joint progress meeting on 5 March 2015. This collaboration focused on alternative manufacturing methods also resulting in a new activity between the TU/e and Philips. In general it has not been easy to stimulate new cross programme/theme initiatives this late in the process although collaborations existed at individual level (example between programme 6C and theme 8). Still it was decided that formal joint events beyond the very successful NanoCity meetings would not create additional value. An inventory of valorisation opportunities has been made also for theme 6. We used four of the identified opportunities in a Dragons' Den event that was organised at Oudaen in Utrecht on the 28 May 2015. The topics were pitched by four specially trained innovators from our programmes to an expert panel. The audience consisted of innovation staff active in theme 6. This was both a learning experience for the topic owners and the audience. For the people present, the tension between a good scientific concept and a relevant commercial proposition became much clearer and the bridge between fundamental science and industrial innovation was at times visible in the pitches.

Added value of NanoNextNL consortium and ecosystem

Creating value from nanotechnology-based innovation is not easy, the conceptual distance between the scientific topic and the application can be huge and this is especially so for theme 6. Value creation is difficult to predict and even more difficult to programme. Cultures in academic institutes, start-ups and industry are often far apart. Still, the programmes in this theme resulted in a combination of strong scientific and business results, the Dragons' Den opened up a new world for people and new start-ups developed. The NanoNextNL approach certainly contributed to that result with a strong focus on collaboration, IP creation and valorisation.

The NanoNextNL consortium forced many of us beyond the boundaries of our own interest. To openly discuss how to improve and also how to understand and accept our differences. Academic and industrial innovation do address different stages in the innovation hype curve, these stages come with other challenges, rules and timings and collaboration will only work in an optimal way when it respects these differences and when it can start from an up-front understanding of the diverse interests. NanoNextNL created that awareness in the coordinating team for theme 6 and we should take that as a learning for a next collaboration.

The NanoNextNL ecosystem also helped to understand that differences can be overcome. It created a place where a very diverse community could come together to explore new opportunities and synergies. The NanoCity events were a powerful display of that collective diversity. Top notch science combined with start-up storytelling and early businesses on display. A tapestry of innovation journeys creating a rich inspirational setting for our young and old researchers.

2.6.1 Programme 6A

Advanced nanoelectronics devices

Programme director: Bert Koopmans
(Eindhoven University of Technology)

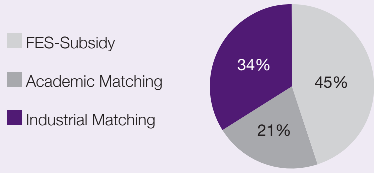
Partners

Delft University of Technology, Eindhoven University of Technology (including collaboration with IBM), Holst Centre, IMEC Leuven, NXP Semiconductors, Philips Electronics Nederland, University of Groningen

Projects

8

Budget 6A: € 8.285.958



Output

33 Journal articles
1 Patent filings

Valorisation programme
1 Business case
0 Granted

Researchers
7 PhD student
3 Postdoc
0 Company
8 Master student

Ambition & Realisation

The programme aims at demonstrating electronic devices with alternative operating principles and enhanced or novel functionality, enabling new applications particularly in hybrid electronic or smart embedded systems. Research focus is on sensors for gas sensing and magnetic field sensing as well scenarios for memory and logic devices, implementing nanowires as well as spintronics concepts.

Science ambition

The science ambition of this programme is to

- explore and demonstrate novel concepts for chemical sensing, including resonating clamped beams and semiconductor nanowire-based electrical sensing,
- explore and demonstrate techniques to fabricate (3D) nanowire architectures for nanoelectronic applications, addressing semiconductor nanowires grown by MOCVD as well as ferromagnetic nanowires grown by beam-induced deposition,
- explore and demonstrate novel spintronic concepts for non-volatile memory, logic, and sensors, in particular focusing on exploiting spin-orbit phenomena (such as the recently discovered spin-Hall effect) and nanomagnetic logic – both routes envisioned to provide a route towards highly energy-efficient devices.

Business ambition

This programme intents making steps towards creating new business by

- developing technology for an 'electronic nose' for the detection of volatile compounds and clear-air monitoring (with Holst Centre and Philips Research),
- improving nanowire production tools for future nanoelectronic devices (with FEI company; NB: not an official partner in this programme),
- demonstrating energy efficient and scalable scenarios for future nanoelectrics, including memory (such as magnetic random access memory, MRAM) and logic – routes that should pave the way towards 'green ICT' (with IMEC and IBM).
- In the last phase of the programme, two new projects were installed on key positions bridging different research activities; their aim was
- to improve production of enhanced atomically controlled thin film systems for gas sensing devices (industrial partner Philips Research, started November 2014), and
- to develop thermally robust magnetic field sensors for automotive applications with superior characteristics (to meet requirements for 'green driving') exploiting spintronic concepts (industrial partner NXP semiconductors, started October 2015).

Science realisation

Already just after completion, research in this programme has led to over thirty journal articles, many of them in high-impact journals including Advanced Materials (1 x, impact factor 17.5), Nano letters (1x, 13.6), and Nature Communications (1x, 11.9), as well as major (applied) physics journals such as Applied Physics Letters (6x), Physical Review B (9x) and Nanotechnology (2x). A selection of achievements that matched the programme's science ambition:

- Fundamental properties of doubly-clamped beam resonators and atomically-thin membrane resonators on graphene and MoS2 have been investigated, for which an interferometer set-up has been built that is now routinely used to test different resonators.
- 3D (hybrid) feromagnetic nanostructures have been fabricated using beam-induced deposition, and led to demonstrations of prototype superconducting- ferromagnetic devices and 'perpendicular' nanomagnetic logic, as well as high-purity antiferromagnetic deposits.
- Proof of principle demonstration of several device geometries exploiting the spin Hall effect (SHE), including SHE-assisted spin-transfer torque switching of MRAM, and field-free switching of MRAM by the SHE (envisioned to be a breakthrough for application of the SHE to non-volatile memory).
- Discovery of a new magnetoresistive effect, called the spin-Hall magnetoresistance (SMR) in YIG/Pt bilayers. The latter allows electrical magnetometry on an insulating ferromagnet, and was also detected simultaneously with the spin-Seebeck effect, a thermal effect, where spin-currents are generated by the presence of a temperature gradient.
- Several novel ideas were proposed and tested for combining elements from nanomagnetic logic with magnetic-domain wall devices, including the exploration of an in-line spin-torque nano-oscillator, which could provide efficient, tunable RF sources.

Business realisation

The collaboration between academic and industrial partners led to the several business opportunities in line with the ambition of the programme. Among them:

- Research activities on the chemical nose led to a very fruitful collaboration between academic partner (TUD) and the Holst Centre ending up in a patent application for a novel sensing device. The open innovation program of the Holst Centre provided a gateway to other programs within NanoNextNL as well as links to other external industrial partners.
- Within the project on top-down fabricated Si nanowire sensors, a business case was worked out on clean air monitoring. Discussion with NanoNextNL partners provided new insights, helping understanding the problem. Although this did not lead to a final solution yet, it did indicate a direction for future application in Philips Air purifier business.
- Novel spintronic concepts as discovered by academic partners TU/e and RUG have triggered renewed interest by the IMEC program on MRAM, and the collaboration will be intensified beyond the scope of NanoNextNL.
- Outcome of research has helped one of the academic collaborators in the project on resonance based biosensing to start his own company. Furthermore, it triggered the appointment of Dr. Steeneken as a part-time professor at TUD.
- Through the NanoNextNL programme several participating groups have established a stronger focus on sensors (both gas sensing as well as magnetic field sensors for automotive), which fuelled several follow-up projects in this direction.
- Input from our industrial partners provided an attractive learning environment for our young academic researchers. As an example, one of the projects was embedded in the Research group of Prof. Parkin at the IBM Almaden Research Centre (San Jose, CA); Parkin delivered an inspiring keynote lecture at the 2014 Nano City event.

Lessons learned

- The long incubation time and time over which NanoNextNL has run, together with the organisation in clusters with separate agreements, made changes in scope with changing business interests somewhat complex.
- In combination with dynamics of industrial research, it led to many unpredictable changes in partners and the scope of industrial research, which was not always easy to respond to by the academic research bound by 4 years PhD programmes. On the other hand, it led to some opportunities during the course of the programme, where a number of new (or modified) projects could be started to bridge other activities.
- Applied research can be highly successful without directly generating business or IP.

2.6.2 Programme 6B

Functional nanophotonics

Programme director Kobus Kuipers (FOM Institute AMOLF)

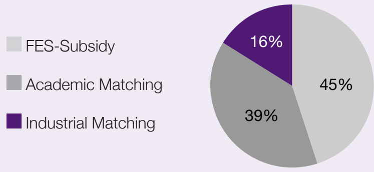
Partners

Delft University of Technology, Eindhoven University of Technology, FOM Institute AMOLF, Holst Centre, LioniX, Philips Electronics Nederland, PhoeniX, Radboud University Nijmegen, University of Groningen, University of Twente, XIO Photonics

Projects

13

Budget 6B: € 6.361.471



Output

60 Journal articles
10 Patent filings
Valorisation programme
1 Business case
1 Granted
Researchers
9 PhD student
8 Postdoc
2 Company
7 Master student

Ambition & Realisation

This programme aims to exploit nanophotonic structures to actively control light. These structures exhibit a high sensitivity to external stimuli mainly due to the high light confinement that can be used to detect ultra-small amounts of contaminants or to route optical information on ultrafast timescales on photonic chips.

Science ambition

The central scientific aim of this programme is to explore novel mechanisms to control, enhance and harness light-matter interactions with photonic nanostructures. Thus, new ways to control light with matter, light with light and matter with light will be investigated.

Business ambition

Within this programme the enhanced nanoscale light control is intended for use in telecommunications, data storage and sensing. The programme brought together academic and industrial partners to investigate both platforms that are close to or already on the market and platforms that are still mainly "in the lab". Example for high TRL are TriPleX® and SPR and were investigated for telecommunications and optical sensing, respectively. Photonic crystals and plasmonic nanowires could be considered as having a lower TRL. By combining a spectrum of TRL's and partners from both industry and academia the goal is to achieve cross fertilisation.

Science realisation

Many scientific breakthroughs were achieved and published in international journals. Six were published in a journal of the Nature family. Below a few highlights are presented.

- Electromechanical actuation was used to tune the resonance frequency of photonic crystal cavities. Such optomechanical actuation provides a highly energy efficient way of switching optical information and at high modulation frequencies facilitated by the small displacements of nanoscale objects.
- It was shown that light can, counterintuitively, be guided through the use of absorbing nanolayers. Similar to surface plasmon modes the resulting guided modes provide a route towards novel sensors.
- Numerical modelling has shown that thin layers can be added to the TriPleX® platform to achieve superior optical modulation rates, e.g., through the use of surface acoustic waves.
- It was shown that Fano resonances in periodic arrays of plasmonic nanoparticles can improve the sensitivity of plasmon sensors by more than an order of magnitude with respect to disordered arrays. A universal scaling relation was developed to evaluate the FoM for plasmonic sensors.
- Plasmonic nanowires were shown to outperform dielectric waveguides for ultrahigh bandwidth applications. Although these nanowires have high Ohmic losses, their modal dispersion is much flatter and they don't exhibit the losses of dielectric waveguides occurring due to mode cut offs.
- Unanticipated was the observation of rogue waves in chaotic photonic crystal cavities. These localised, high intensity waves may have use in photovoltaics or sensing. (cover Nature Physics)
- Slow light in photonic crystal waveguides was shown to provide effectively enhanced light-matter interactions that enable all-optical switching. By modifying the refractive index of the silicon backbone on a 100 fs timescale the frequency of the propagating light was changed by more than a single telecom channel (0.4 THz). This was used to control the ps-timing of optical information.
- By all-optically switching one of two coupled photonic crystal cavities, spontaneous emission of quantum dots in the second cavity could be manipulated. This forms a breakthrough in nanoscale quantum optics with implications for future telecom or even quantum communications. (Nature Nanotech.)
- Commercial TriPleX® waveguides together with a suitable pump were shown to exhibit supercontinuum generation over a 400 THz bandwidth. This white-light generation will facilitate on-chip spectroscopy.
- Nanostructures were used to reduce the spatial 'bit size' of all-optical magnetic recording on sub-ps timescales. It was shown that the resolution of the magnetisation reversal could be improved to 5 nm and isolated bits of only 40 nm could be switched through the use of plasmonic antennas. It was discovered that the range of materials in which this all-optical switching can be achieved is broader than previously expected.
- New nanoparticles (TiO_2 cylinders) were developed and successfully fabricated to improve the conventional Optical Torque Wrench. This increased the dynamic range of optical torques and angular frequencies that can be applied.

Business realisation

- Thin layers of various materials were added to the TriPleX® platform to provide new means of optical actuation. It was shown that this addition can be achieved without detrimental effects with respect to losses or the size of the transparency window. A business plan to exploit the new potential of this optical actuation was developed in collaboration with the NanoNextNL programme office.
- Proof of principle experiments have shown that strain-induced refractive index changes are a viable route to optical modulation even though the experimental realisation of the theoretically most efficient configuration may be challenging to realise.
- The electromechanical tuning of photonic crystals have become a core technology of the TU/e spin-off nanoPHAB.
- Waveguiding technology has been expanded to use water layers as a means to achieve the optical mirror symmetry required for the occurrence of surface plasmon lattice resonances, which are useful for sensing. The water layer can be used in an integrated microfluidic system.
- Several plasmonic sensing concepts have been taken up by the Holst Center for gas sensing.
- Interestingly, the optical sensing is now being used by Holst to complement electrical measurements in their wearable health programme.
- The fact the industry had already adopted heat-assisted magnetic recording greatly facilitates the implementation of the all-optical recording. New projects are currently underway to explore this possibility.
- An unanticipated spin-off of the programme was the implementation of the angle-resolved Stokes parameter polarimetry instrumentation -developed for the investigation of emission for nanostructures- into the "ARCIS" (Angle-Resolved Cathodoluminescence Imaging Spectroscopy) instrumentation. This polarisation mode is now integrated as part of the DELMIC product SPARC.

Lessons learned

- All programme meetings were held jointly with programme 6D. This provided additional opportunities for cross fertilisation, in particular because of the greater number of attendees from industry. Informal contacts allowed knowledge of light absorption in thin layers and light management through nanophotonics to feed into programme 2. Similar informal contact led to the implementation of the polarimetry instrument in a nanocharacterisation product (programme 9).
- The close interaction between industrial and academic partners was appreciated by both. Having said that, the long timescale of NanoNextNL, with the organisational structure in clusters with separate agreements made changes in scope and the flow of information (both ways) complex, particularly when business interests shifted and/or breakthroughs led to course adjustments.
- Within the programme the interaction between academy and industry varied in intensity.

2.6.3 Programme 6C

Nano-bio interfaces & devices

Programme director: Serge Lemay (University of Twente)

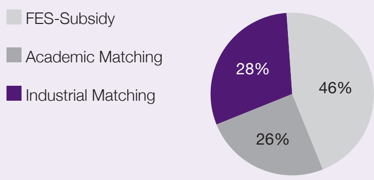
Partners

CellCoTec, Delft University of Technology, Erasmus University Medical Centre, Holst Centre, Nanosens, NXP Semiconductors, Percuros, Philips Electronics Nederland, Polyvation (access to NanonNextNL in progress), DLO, SmartTip, Surfix, University of Twente, VyCAP, Wageningen University

Projects

15

Budget 6C: € 9.098.118



Output

79 Journal articles
6 Patent filings

Valorisation programme
10 Business case
6 Granted

Researchers
7 PhD student
5 Postdoc
2 Company
12 Master student

Ambition & Realisation

The broad ambition of the programme was to explore the limits of electrical signal transduction and associated nanotechnologies for the interface biosystems and modern electronics so as to harness the economies of scale provided by semiconductor electronics to achieve advanced tools for environmental monitoring and medicine.

Science ambition

- To incorporate advanced (bio)chemistry into NXP's nanocapacitor array platform so as to permit the development of broadly applicable cell-level assays (cluster 1).
- To develop field-effect transducers for the sensing of environmental gases and analytes in aqueous solution, consistent with the strategy of Philips/Holst (cluster 2).
- To develop platforms for electronically monitoring in real time the response of living cells, and enabling application of these devices in drug screening and/or risk analysis (cluster 3).
- To develop advanced atomic force microscopy probes incorporating fluidic control and local electrical detection, further extending the scope of scanning probe technology for cell-level manipulation and analysis (cluster 4).

Business ambition

Two main groupings of projects aimed at further developing and validating large-scale, broadly applicable silicon-based sensing platforms being developed by industrial partners, namely, nanocapacitor arrays (cluster 1 anchored on NXP) and nanowire field-effect transducers (cluster 2 anchored on Philips/Host). Clusters 3 (interfaces to living cells) and 4 (multifunctional scanning probes) instead focused on smaller projects targeted at SME-level activities aimed at creating new product prototypes; these projects were generally characterised by a 1-to-1 coupling between an academic group and a SME.

Science realisation

- Surface modification and functionalisation methods were developed to tune selectivity of chemical sensors based on FETs (both nanowires and planar). The main application area pursued was sensing of NO_2 and CO_2 gases for environmental monitoring.
- A quantitative understanding of the performance of silicon nanowires for sensing in liquid was developed. These insights allowed partners to re-assess their development strategies.
- An 'artificial heart' organ-on-a-chip platform – coined Cytostretch – was developed that allows exposing cultured human heart muscle tissue on a mechanically actuated stretchable membrane. The platform continues to be developed by the Institute for Human Organ and Disease Model technologies (hDMT).
- The preparation of air-stable biomaterial-supported lipid bilayer coatings that possess superior non-fouling characteristics and the capacity to include bioactive ligands to steer mesenchymal stem cell differentiation was demonstrated.
- A high-throughput-screening device for biologically active surface topographies on biomaterials, the TopoChip, was established, and was employed to screen for topographies favoring the proliferation and functional performance of various cell types including stem cells and kidney epithelial cells.
- High-frequency detection and imaging of synthetic micro/nanoparticles and living (cancer) cells under physiological conditions was demonstrated using large-scale CMOS nanocapacitor arrays (*Nature Nanotechnology 2015*).
- Fluidic-enabled AFM cantilevers incorporating a readout electrode were developed for the FluidFM platform. A new "tip-on-a-chip" concept for single-cell analysis for use in combination with FluidFM cell manipulation was realized and validated using isotachophoresis readout.

Business realisation

- Over the years that NanoNextNL has run, Holst Centre has had a very active open innovation programme on chemical, and more specifically gas, sensing. Surface modification and functionalisation has been an enabling capability, applied to a range of transducer platforms, to tune selectivity of such sensors to analytes indicated by its industrial partners as relevant for applications. Partners in this program that have actively participated and co-financied the activities have included NXP, Philips, Panasonic, National Semi, ADI and others.
- The Cytostretch platform is now being industrialised by Philips Innovation Services in cooperation with partners and end-users in the context of the European ECSEL project "InForMed."
- Project PhD student J. van Weerd founded LipoCoat, a startup company aimed at exploring the full financial potential of the technology developed in the program. The initial focus of LipoCoat is to provide a bioinspired coating of contact lens surface, similar to what is found on the cornea provided by the tear film. LipoCoat will enable prolonged and comfortable wear of contact lenses. Lipocoat attracted several awards and start up funding, e.g. ERC Proof of Concept and NanoNextNL valorisation grants.
- Improved implant performance through surface topography implies value creation for medical device companies and therewith for Materiomics, a spin-off company of the University of Twente now centered in Maastricht, that aims to gain significant value through licensing hit-topographies.

Lessons learned

- The relatively long incubation time and overall duration of the programme proved challenging to reconcile with the short business cycles experienced by the (larger) industrial partners. Nevertheless the partners identified realistic projects of mutual interest and adjusted the initial research plans accordingly.
- Although it is not trivial to motivate participants to attend cross-theme activities on top of programme meetings and other national and international scientific meetings, several theme and cross programme meetings were organised. In addition, the courses organised by NanoNextNL were very well attended by researchers from this programme.
- Another challenge is to reconcile the demands of academic excellence (PhDs and postdocs need high-profile papers to propel their careers) with the type of development work (achieving reliability, manufacturability, etc.) needed to create business. The quality of the scientific output and the business activities that have arisen from this programme indicate that this challenge can be met, but that this is far from automatic.
- Additional partners such as Panasonic, National Semi and ADI have actively contributed and co-financed activities of this programme thereby extending the ecosystem and increasing exploitation of generated knowledge.

2.6.4 Programme 6D

Active nanophotonic devices

Programme director: Paul Koenraad
(Eindhoven University of Technology)

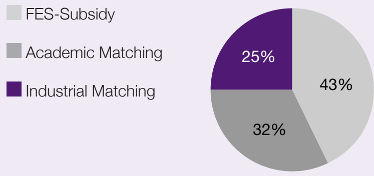
Partners

ASML Netherlands, Delft University of Technology, Eindhoven University of Technology, FOM Institute AMOLF, Holst Centre, Leiden University, Philips Electronics Nederland, Utrecht University

Projects

13

Budget 6D: € 8.971.379



Output

85 Journal articles
13 Patent filings

Valorisation programme
3 Business case
2 Granted

Researchers
12 PhD student
5 Postdoc
0 Company
4 Master student

Ambition & Realisation

In the Active Nanophotonic Devices programme we focus on the efficient generation and detection of photons in nanostructured materials and devices.

Science Ambition

We have brought together 3 coherent clusters aimed at specific photonic challenges in science and industry.

- Cluster 1 focuses on the efficient light generation in organic materials. This part aims at understanding the processes that occur on a nanoscale in a recent type of lighting device (OLEDs). It involved the close collaboration with strong industrial partners (Philips, Holst). The resulting insights were used to improve OLED efficiency and lifetime.
- Cluster 2 has a focus on nanolasers. This cluster explores the potential of two different types: plasmonic lasers and nanowire lasers. Special emphasis is given to the efficiency of these devices, which will be a major advantage for their integration in large numbers on integrated photonic devices. Nanolasers might also replace conventional lasers for a substantial number of applications, such as in ultra fast low-power signal processing and sensing.
- Cluster 3 investigates nanostructured photon sources and detectors. The principles for light sources and detectors with increased efficiency, speed and functionality were developed in this cluster. These devices represent an enabling technology.

Business ambition

Cluster 1 is very close to the market with strong participation of industry partners such as Philips and Holst, whereas in cluster 2 we mainly aimed for a demonstrator of nanolasers to assess its prospects for real applications, and finally in cluster 3 we aimed at developing new basic scientific knowledge.

Science realisation

An extremely large number over 200 scientific papers and conference contributions have been produced in theme 6D up to this moment. About 100 of these papers involved the collaboration between different groups and about 60 of them were based on an academic-industrial collaboration. Below a number of the highlights in each cluster are described in some detail.
In cluster 1 we focused on OLEDs that are regarded as the light sources of the future. Important progress has been achieved. In such organic light-emitting diodes, developed for display and lighting applications, a complex interplay takes place between the electronic and excitonic processes. Conventionally, simulation methods for developing understanding of this interplay are based on phenomenological parameters describing the separate processes and interactions. Such approaches are known to be often only descriptive, but not predictive. In this cluster a fully mechanistic simulation method has been developed, which for the first time also includes all relevant excitonic processes. The work demonstrates in a clear manner that this provides a powerful method for predictively simulating the luminous efficacy roll-off at high brightness, the emission colour and device lifetime. The work has been presented in several high-profile publications such Nature Materials.

The activities represent an excellent example of industrial and academic collaboration that spans the full knowledge chain from basic science to product engineering for upscaling in the industry.

Business realisation

- Up to now 13 patents have been filed in the theme 6D where 4 involved both an academic and industrial partner. Some highlights are indicated below.
- In cluster 1 a computer code has been developed to model current and emission in OLEDs. This has led to the foundation of a start-up company (Simbeyond) of which dr. van Eersel (former PhD student appointed in this programme) is one of the co-founders and the CTO
- The activities in cluster 1 have led to an intensive collaboration agreement between BASF, TU/e and Philips, which have made it possible to financially extend the activities in this cluster.
- In cluster 2 the research has contributed to the development of future optical interconnects that require efficient, low-power optical sources integrated on silicon and a novel type of plasmonic laser.
- In cluster 3 one of the teams filed 5 patents together with Philips Research that allowed for a more efficient operation of LEDs. These patents have been taken over by Lumileds.
- Several other companies such as Facebook and NDF have shown interest for the plasmonic antenna research in this cluster.

Lessons learned

- Interaction with industry has been very intense in some of the projects in cluster 1 and also, somewhat surprisingly, in the most fundamental cluster 3 where especially Philips research has respected the fundamental character of the research. This has led to a very good synergy with a significant output in terms of publication and patents. This dual character made that sub programme very successful.
- Although some very nice examples of joint academic and industrial interest have resulted in excellent fundamental science and patents within the same collaboration we also experienced that it was often very difficult to close the gap between academic and (potential) industrial partners.
- The timescale of the NanoNextNL programme was too long with respect to the dynamics of the major industrial partners and in several cases also too long with respect to the science interests in the academic groups.
- In a next round more attention should be given to close the gap between academic institutions and the “big” industrial partners by creating, supporting and developing start-up companies right from the start of the programme.
- It was very fruitful to have all progress meetings together with theme 6B on Functional nanophotonics.

2.7 Theme 7

Nanomaterials

Theme coordinator: Ardi Dortmans (TNO)

Introduction

Materials are commonly regarded as a prerequisite to solve grand challenges such as health, energy, etc. Advanced materials play this crucial role in many industrial domains because they create new options throughout the entire production chain. This results not only in new end products (e.g. a solar panel) but new materials also result in required new high tech production, processing and characterisation equipment. For the Netherlands both aspects are important given the presence of both a strong material manufacturing as well as a high tech equipment industry. The theme Nanomaterials develops new nanomaterials in 2 sub programmes on supramolecular and bio-inspired materials (7A) and multilayered and artificial materials (7B).

Development of the theme through the years

At the start of the 2 sub programmes in 2011, it was already quite clear that they cover quite different material and application areas and from that perspective limited cross-fertilisation would be possible. This has turned out to be the case, except for the common need of inspection technology for the materials and structures produced. As part of the MidTerm Review advice in February 2015 this has resulted in a common workshop with Theme 1 and Theme 9 on inspection technologies for nanomaterials. The different focus of the two programmes certainly also has contributed to the excellent progress in both areas, despite the unavoidable changes with respect to the initially defined project goals over a period of 5 years. It is also true that within the sub programmes it was difficult to come to new collaborations between the initially defined activities because of different time horizons and/or lack of resources. This also applied to collaboration with Theme 1 RATA despite the joint efforts made. On the other hand, a significant amount of collaboration has been initiated with existing and new partners in new initiatives outside of NanoNextNL. Some highlights of the results achieved in Theme 7 are: the high quality research on biomedical hydrogels and its direct transfer to new industrial activities, the significant progress made on the scientific and experimental basis to manufacture multilayer materials by Atomic Layer Deposition for electronic and semicon applications and the realisation thereof in mirrors, displays and transistors.

Added value of NanoNextNL consortium and ecosystem

Significant added value of being part of NanoNextNL is obtained through joint RATA, IP-awareness and valorisation courses because they provide a larger perspective than usually found in the settings of own work. Another advantage is found in the ease of access of high quality research infrastructure for particular experiments or simulations. The joint NanoCity events have certainly provided an excellent platform to present, discuss and follow-up research activities in a diverse community providing inspiration for new platforms and synergies.

2.7.1 Programme 7A

Supramolecular and bio-inspired materials

Programme director: Alan Rowan (Radboud University)

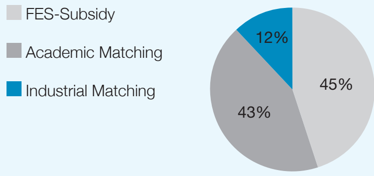
Partners

Encapson, Artecs, Bruker Nano, Delft University of Technology, DSM Advanced Surfaces, Eindhoven University of Technology, FEI Electron Optics, Nano Fiber Matrices, Radboud University Nijmegen, University of Groningen, University of Twente, Wageningen University

Projects

12

Budget 7A: € 8.020.925



Output

1 Nobel Prize
71 Journal articles
7 Patent filings

Valorisation programme
5 Business case
1 Granted

Researchers
14 PhD student
5 Postdoc
1 Company
8 Master student

Ambition & Realisation

Science ambition

Nature often uses soft materials in her design. The difference with man-made soft matter is that Nature developed many approaches to define the structure of these soft materials at all different length scales, which has a pronounced effect on the microscopic and macroscopic properties. In addition, Nature's materials are commonly responsive and dynamic ("smart"), i.e. their properties change upon application of an external stimulus.
In this programme, we aimed to study self-organised and self-assembled soft materials. The key questions in the programme are centred on the formation of novel (multi)responsive materials well-defined architectures at multiple length scales, the effect of these architectures on the properties and the use of these architectures either in biomedical applications or as a scaffold to create other three-dimensionally ordered functional nanomaterials.

Business ambition

With two groups active in the commercialisation of different soft polymer and self-assembling hydrogels for cell culture applications, our primary business ambition was to develop this field and generate materials that could be brought to the market. But our ambitions reached further. Also, we aimed to investigate the commercialisation perspective of approaches to generate smart materials, approaches for the generation of multi-length scale spatial order as well as the templating approaches to create new functional nanomaterials.

Science realisation

As the programme was running, many of the projects came together and formed strongly complementary focus groups around different challenges in bio-inspired soft materials:

- A central theme in the programme is the development of responsive hydrogels for biomedical applications. With these applications in mind, the topic has been addressed from multiple angles ranging from materials development to actual product development. On the materials side, we developed gels with complementary responsiveness to a range of stimuli, including redox (Vancso, UT), pH (de Wolf, WUR), temperature and ionic strength (Rowan, Kouwer, RU). On the preparative end, the use of biotechnology highlighted the opportunities for large scale preparation of specifically functionalised materials (de Wolf, WUR). Hydrogel composites with components from different partners (TUe/NanoFM/WUR/RU) were studied in Nijmegen and the structural and biological characterisation of different materials was carried out at RU and NanoFM. Diffusion-controlled synthesis has been used to prepare precisely-defined structures (van Esch, TUD), which are the first step towards materials with micrometre-scale spatially-controlled properties. In addition, this programme afforded a much deeper insight in the structure-property relations of biomimetic gels, benefitting the RU, TUD, NanoFM and WUR groups, and the effects found in these gels are currently tested in cell studies (Rowan, Kouwer, RU).
- A second major goal in the programme is to achieve order over multiple length scales, which is a currently outstanding challenge that needs to be addressed before many functional, self-assembled materials can enter the market. Excellence at the fundaments within the programme is exemplified by the Nobel Prize award to Feringa, RuG. Approaches based on liquid crystals (Broer, TUe and Kouwer, RU) and block-copolymers (ten Brinke, RuG) were developed to realise hierarchy in the structures. As a highlight, it was found that spatial and directional control could be achieved from hundreds of nanometre scale to the device dimensions, larger than centimetres (collaboration TUe/RU).
- Templating is a great tool to create order in material that is difficult to realise in other ways. The supramolecular and bio-inspired materials programme actively used templating to realise new nanomaterials, either nanoparticles (Subramanian, UT and Sommerdijk, TUe), nanowires (Kouwer, RU) or even more complex structures (Dekker, TUD). Interaction with (biological) macromolecules or liquid crystalline templates affords additional scaffolds to further organise and assemble such nanomaterials into higher ordered structures (Subramanian, UT and Kouwer, RU).

Business realisation

- Despite the reluctant business participation at the start of the programme, many of the opportunities that developed during the past years have been studied for commercialization.
- The most pronounced examples are in the hydrogel area. Furthest in the commercialization process are the cell culture matrices developed by NanoFM (de Jong) that are currently evaluated by a major US Life Science company for bulk synthesis and distribution.
- Next to these successes, a start-up company, Secmatix, was initiated to develop the gels from Nijmegen (Rowan) into commercial products for wound healing and regenerative medicine. For both applications patents were filed.
- Also UTwente (Vancso) is working with Artecs BV to develop a redox-active polymer foam, based on the results obtained within NanoNextNL.
- In addition, a patent was filed on one of the templating processes, developed in Nijmegen (Kouwer), that improves sensitivity and stability of liquid crystal based biosensors. This patent is an example how fundamental research in an application-driven environment such as NanoNextNL can readily develop into commercial activities.
- Business opportunities from Eindhoven (Sommerdijk) are currently developed together with their partner Ioniqa.

Societal impact

Direct societal impact of the research within the Supramolecular and bioinspired materials programme is concentrated in the hydrogel studies. The fact that start-up companies now take the lead to develop their health-care application also shows that the society can expect these materials to be in place in the near future. Some of the other topics in the programme are geared towards (bio)sensory materials in a very broad application range. Although the societal impact of such materials is beyond any doubt, the road towards their application will be much longer. The RATA and valorisation courses offered within the NanoNextNL programme are very important to introduce commercial awareness under the young scientists, which, for the future, will shape their research ambitions and prospects.

Lessons learned

- Research activities within the focus groups of this programme quickly streamlined and benefited from the complementary expertises and infrastructure that the groups offered. Cross-fertilisation between the focus groups and, on a higher level, cross-fertilisation with other programmes started much more towards the end of the NanoNextNL programme. To truly benefit from the foundations laid out in this programme, one needs such a programme to be continued.
- Commercialisation of (fundamental) research is greatly helped by offering RATA, IP-awareness and valorisation courses. These courses make researchers (from PhD student to supervisor) aware of factors like risk evaluation, technology assessment and valorisation in the settings of their own work. Although commonly not found as part of the standard PhD training, these topics should be an imperative part of an academic training to ensure a sustainable Dutch research landscape.

2.7.2 Programme 7B

Multilayered and artificial materials

Programme director: Guus Rijnders (University of Twente)

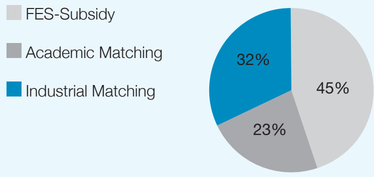
Partners

ASM Europe, ASM Belgium, Carl Zeiss SMT, Cosine Research, Delft University of Technology, Eindhoven University of Technology, FOM Institute DIFFER, Holst Centre, LioniX, Philips Electronics Nederland, Phoenix, SolMateS, Twente Solid State Technology, University of Groningen, University of Twente

Projects

14

Budget 7B: € 13.579.810



Output

44 Journal articles
4 Patent filings

Valorisation programme

3 Business case
1 Granted

Researchers

12 PhD student
6 Postdoc
16 Company
3 Master student

Ambition & Realisation

Research ambition

- This programme focuses on the development of nano-materials and relevant applications in emerging fields. In general, it can be stated that perfect control of the crystalline structure, chemical bonding and the phase formed are prerequisite to fully exploit functional properties of materials. Within the programme the research is concentrated in three areas:
  - The development of functional piezo and ferroelectric oxide layers on semiconductor substrates. The application areas investigated are: sensors and actuators in MEMS technology, photonics and (power) electronics.
  - The development of Atomically Engineered Nanostructures for semiconductors and the Atomic Layer Deposition Technique: specifically the fabrication of thin oxide/nitride materials layers for the semiconductor industry as well as for novel gas sensor applications and coated micro/nanoparticle catalysts.
  - The development of (large scale) fabrication techniques for multilayer for EUV applications in lithography (end consumer is ASML) and X-ray telescope (space research, Cosine) and techniques to study the growth of these layers in situ, to optimise the growth process.

Major research realisation

- The criteria for successful room temperature ALD growth of conformal thin film oxides and nitrides using an energy-enhanced process have been identified and experimentally verified. Such a process is of great interest for industries such as ASM and IMEC/Holst Centre in e.g. applications using temperature sensitive substrates (in flexible electronics). There was cooperation between ASM and the academic groups of Kessels (TUe) and van Ommen (TUD), which resulted in several publications.
- Devices with ALD layers were investigated as gas and chemical sensors by the Holst Centre.
- It was shown by modelling that strain engineering of transistor devices by using piezoelectric active layers can increase the sub threshold current-voltage slope, thus significantly enhancing the electronic performance of the FinFET transistor. These results suggest that strain modulation can open a new road to a new generation of devices. FinFET devices with a piezoelectric layer where realised in cooperation with Solmates showing experimentally the predicted effects.
- The integration of PZT with III-V materials (specifically on Si-based GaN) was realised experimentally. This potentially allows for actively controlled strain in the GaN. Secondly the very high dielectric constant of the PZT can be used in GaN-based High-Power FET devices. These results raised much interest from several industries (NXP, ASMi, Ommic).
- Piezoelectric layers were integrated in a photonics platform in the cooperation between Lionix, Solmates and Phoenix, demonstrating the active control of light transmission through waveguides.
- Piezoelectric layers were used in devices showing the properties needed for neuromorphic computing, which may constitute an alternative route for CMOS logic.
- Significant progress has been made in the development of adaptive EUV optics for lithography (active wave front correction) using thin film piezo-elements.
- PhDs and PostDocs have been trained in science and development. A new generation of scientists has been come aware and knowledgeable of the possibilities of (thin-film) piezoelectrics, which may have a noticible impact on further developments in this field.

Business ambition

The ambition is that the aforementioned material systems will be integrated in functional devices within the next few years. The ultimate goal of this programme is to increase the competitiveness of Dutch Industry by developing new materials and deposition techniques early in the adoption lifecycle, mainly concentrating on (multi-layered) nanomaterials deposited by Atomic Layer Deposition (ALD) and Pulsed Laser Deposition (PLD).

Business realisation

- The development of EUV-optics by the group of Bijkerk (first at FOM Institute DIFFER, now UT) in association with Carl Zeiss. ASML (as end-customer) has expressed strong interest (DIFFER/UT/Carl Zeiss). EUV optics are an essential part of present and new generation lithography equipment. Adaptive optics with multilayers with enhanced lifetime and reflectivity properties may create a competitive edge for ASML.
- The development of new ALD processes (ASM Europe, Eindhoven University of Technology and Delft University of Technology) – very thin conformal coatings are prerequisite for new 3d structured devices in the electronic industry (ASM). Also the possibility to deposit at low (room) temperature opens new opportunities in, for example, flexible electronics (Eindhoven University of Technology). ASM develops and produces equipment for the electronics industry worldwide.
- The advance in the technology of depositing high quality piezoelectric layers on Si and III-V and the knowledge of the material properties thereof has evoked much interest from various industries/companies and led to (the initiation of) new projects: development of piezoMEMS devices for sensing (AMC/Achmea/Philips/University of Manchester) and research into the lifetime/reliability of piezomaterial/device in piezodriven inkjet printheads (Oce) ; generic project into the further development of piezoeletrics on III-V materials (ASM/NXP/Ommic).

Lessons learned

- During the execution of the projects, some new collaborations have been established. However, the experience is that, in many cases, industries tend to follow their (short(er)-term) goals or shift goals during the runtime of the NanoNexNL project. As a result, establishing new cooperations between industrial and academic groups was found to be difficult, since the latter have longterm objectives defined for the runtime of their projects.
- To realise a more fruitful cooperation with (large) industries it appears more effective to spend the budget on industry initiated problems in jointly defined industry/academia projects in which the PD or PhD employed in the project is reporting to both an industrial and academic supervisor. It is expected that this format ensures focus of the research on a shared long-term goal and embedding of the project in the wider research of both parties.
- It was experienced that some of the end-users had a strong influence on the projects running in the supplying industries participating in the NanoNextNL projects. This caused large shifts in the research goals of the NanoNextNL projects of these industries and with that frustrated cooperation with academic groups as mentioned above.
- Cooperation with the RATA theme was challenging. In our view this was because there were no joint projects defined upfront between a 'RATA' group and an academic ((in our case materials research) group. Since there were no common research goals defined in a common project there was no incentive nor resources to seek such cooperation.
- The emphasis within the program on both ALD and the development and application of thin-film piezoelectrics has created a significant momentum in these fields and has led to important followup in new, related projects supported/initiated by various industries.

2.8 Theme 8

Bio-nano

Theme coordinator: Menno Prins
(Philips Research and Eindhoven University of Technology)

Introduction

The Bio-nano field deals with the interdisciplinary area between nanotechnology and biotechnology, at the crossroads where biology and biological materials meet with the miniaturisation and control provided by nanotechnology. The ambitions of the Bio-nano programme are to quantitatively investigate and control the function of nanoscale amounts of biological materials, to integrate scientific progress on the fundamental understanding of biological molecules (and their operational principles in living cells) with the development of novel commercial technologies to study the molecules, and furthermore to provide insights that can be used in novel generations of biosensing technologies and future strategies for tissue engineering materials design.

Development of the theme through the years

The programmes in the Bio-nano theme have focused on research that reveals how biological molecules and biological cells function and interact, as well as on developing technologies to measure and manipulate these interactions, along two lines:

- The 'Bionano interactions for biosensing' programme (Gijs Wuite – VU): The study of affinity interactions for biosensing in complex biological samples, with the aim to detect extremely low concentrations of biological molecules and measure their function with single-molecule resolution.
- The 'Nanomolecular machines in cellular force generation' programme (Marileen Dogterom – TUD): The study of single nanomolecular machines, their collective behaviour in functional cellular units, and the consequent ability of cells to transduce forces to their environment, with applications in tissue engineering and novel research tools.

Originally, the research overview meetings were organised per programme. To improve synergies, since 2013 joint theme meetings were organized with participation of both programmes. These meetings were very fruitful and involved pitch sessions, poster sessions, plenary discussion meetings, and RATA and business case sessions. The latter have led to several valorisation explorations and to a funded NanoNextNL valorisation project. Interactions with other NanoNextNL programmes have mainly taken place by PI involvement in programme overview meetings, and via the annual NanoCity conference.

One of the key developments in the Bio-nano field has been the move from the study of molecules in clean and isolated systems to the development of tools for studies of complex biomolecular and celluar systems. The Bio-nano theme has significantly contributed to these developments, as can be seen in the programme reports. The trend toward increasing complexity will continue in the coming years. Therefore discussions have taken place in order to develop a vision on how the NanoNextNL-nurtured Bio-nano field could develop beyond 2016. This has led to a continuation proposal entitled Biological NanoDevices. It proposes to focus on bio-sensory and bio-actuation functionalities that are based on adaptive molecular systems and devices that could function with and within live biological systems. The programme will build on academic and industrial strengths in bionano-technology, chemical biology, and medical device technologies. The proposal is presently being discussed with relevant stakeholders.

Added value of NanoNextNL consortium and ecosystem

The added value for Bio-nano being part of the NanoNextNL consortium has been the large national-scale network of academic and industrial partners that formed a basis for collaborative projects and for new initiatives. The consortium has enabled that academic research was done while new valorisation projects could be developed. Numerous collaborations were developed between academics, collaborations were developed between academics and companies with a series of business evaluations on selected technologies (e.g. with Nikon, FEI, NT-MDT, Lumicks, Philips, Xeltis) and initiatives were developed toward collaborations beyond NNNL (e.g. continuation plan Biological NanoDevices, NWO programs, EU projects).

The NanoNextNL research programme and corresponding ecosystem have had an impact on the companies in the Bio-nano programme: For Philips, the NanoNextNL studies have led to an improvement of the sensitivity and stability of the Philips Minicare system. For Xeltis, the insights have led to in-line process controls. For Nikon and FEI, the research has led to evaluated product options. For Lumicks, a new measurement modality (acoustic force spectrocopy) was further developed toward a commercial product. And for NT-MDT, a high-end flow cell prototype was realised for force microscopy in variable biological conditions.

2.8.1 Programme 8A

Nanomolecular machines in cellular force-transduction

Programme director: Marileen Dogterom
(TU Delft/FOM Institute AMOLF

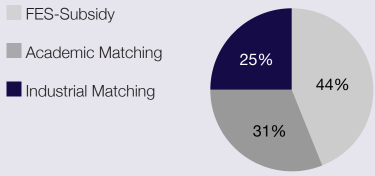
Partners

Eindhoven University of Technology, FEI Electron Optics, FOM Institute AMOLF/TU Delft, Leiden University, Netherlands Cancer Institute/Maastricht University, Nikon Instruments Europe, NT-MDT Europe, University of Twente, VU University Amsterdam, Xeltis (formally QTIS/e)

Projects

12

Budget 8A: € 6.794.277



Output

15 Journal articles
1 Patent filings

Valorisation programme

2 Business case
0 Granted

Researchers

3 PhD student
13 Postdoc
0 Company
13 Master student

Ambition & Realisation

The ambition of this programme is to integrate scientific progress on the fundamental understanding of biological nanomachines (and their operational principles in living cells) with development of novel commercial technologies to study these machines, and to provide insight that can be used in future strategies for tissue engineering materials design.

Science ambition

To understand, at a fundamental level, what the working principles are of cellular biomolecular nanomachines, how they collectively operate in functional units, how this affects the material properties of active cellular materials, and how, within tissue, this allows cells to transduce forces to their environment. We apply both experimental and theoretical techniques.
To bring together leading expertise in the biophysical investigation of cytoskeletal motors, experience gained in the study of active bionanomaterials, (industrial) expertise in tissue engineering (Xeltis), and (industrial) expertise in advanced measurement techniques (FEI, Nikon, NT-MDT).

Business ambition

To develop and apply new advanced imaging and force-measurement techniques for the study of biological systems (on the nano and microscale), and to commercialise these techniques where possible.
Knowledge obtained in this programme will be of immediate value to companies specialising in developing novel strategies and materials for tissue engineering. It furthermore holds the potential to lead to the molecular understanding of certain (motor-related) diseases.

Science realisation

- New imaging techniques have been developed in the context of the research projects, which has led to a patent. This patent relates to a new optical microscopy technique to follow in real time the dynamics of single proteins in living cells in three dimensions, which is used in the programme to better understand the collective behaviour of motors in cells.
- The interaction of molecular motors with a dynamic cytoskeleton was reconstituted in the context of mitotic spindle formation. The nanoscale imaging of this interaction will continue to be explored using novel cryo-EM sample preparation strategies developed during the programme.
- Several experimental and theoretical results were obtained in the understanding of how molecular motors operate collectively in various contexts (e.g. transport in cilia and the extraction of membrane tubes).
- Several motor and force-related biophysical processes were studied in the context of diseases (cancer, Parkinson's disease).
- Joint experimental and theoretical results were obtained on the ability of molecular motors to connect cytoskeletal networks over microscopic length scales. This is important to understand how these nanomotors can transmit forces over cellular length scales in tissues.
- Results were obtained showing that cellular traction forces exerted by cells embedded in fibrin gels cause significant gel stiffening by driving the networks into the strain-stiffening regime, but only when the cells are able to spread well within the network pores. Cell-driven gel stiffening provides a convenient global measure of cellular traction force generation.

Business realisation

- Patent: a new technique for optical imaging was developed that improves the possibilities to follow, in real time and in three dimensions, single proteins in living cells. Possibilities for commercialisation were explored (but not pursued) with Nikon.
- New AFM technology (hardware/software) was developed for local measurements of visco-elastic properties of biological material. This still has to find it's way to a commercial product by NT-MDT.
- New sample preparation strategies were developed for cryo-EM. This still has to find it's way to a commercial product by FEI.
- Knowledge about forces generated by cells embedded in matrices was developed that will be essential for future smart design of materials for tissue engineering.
- Xeltis has investigated in depth what the impact is of scaffold microstructure on the Endogenous Tissue Restoration (ETR) process that is the basis for Xeltis' technology platform. The outcome of these studies translated into product specifications that are still applicable today in the products that Xeltis is bringing to patients and commercialisation. Xeltis also developed in vitro characterization assays as part of the NanoNextNL programme. These assays were instrumental in selecting the right polymer and scaffold configuration leading to clinical trials as well as the current Pulmonary Valve design. Some of these assays are now being used as part of the in process controls during production in our cleanroom.

Lessons learned

- There is an enormous added value in the creation of a national-scale network of academic and industrial partners that forms a basis for future collaborative projects.
- The ecosystem that was created by NanoNextNL led to industrial collaborations that might otherwise not have been explored. It led to a better appreciation of the research needs and habits in industry that will have a lasting impact on the mind-set of the academic groups, and facilitate the crossing of barriers in future contacts with industry.
- Scientists learned that business value creation is not equal to filing a patent.
- For the SMEs in this programme, the programme has led to much improved contacts with the biophysics scientific community in the Netherlands. Also the courses offered by NNNL were much appreciated by the SMEs.
- Several pilot technologies were developed during this program that in the future may leed to commercial products for the industrial partners involved. However, it is clear that more than 5 years are needed to come to a full circle.

2.8.2 Programme 8B

Bionano interactions for biosensing

Programme director: Gijs Wuite (VU University Amsterdam)

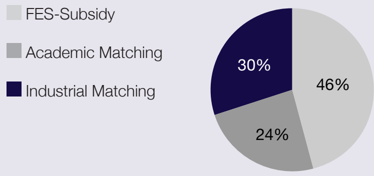
Partners

Delft University of Technology, Eindhoven University of Technology, Leiden University, NT-MDT Europe, Philips Electronics Nederland, Radboud University Nijmegen, VU University Amsterdam

Projects

9

Budget 8B: € 8.486.033



Output

21	Journal articles
1	Patent filings
	Valorisation programme
2	Business case
1	Granted
	Researchers
8	PhD student
5	Postdoc
10	Company
10	Master student

Ambition & Realisation

The aims of this programme are:

- to quantify biological systems;
- to solidify the international leading position of the Dutch single-molecule biophysics community;
- to build the basis for novel generations of biosensing technologies.

Research ambition

- To build novel biosensing technologies based on biomolecular interactions in order to enable the sensitive, accurate and rapid measurement of the concentration and function of biological molecules in complex biological matrices. This is relevant for personalised healthcare as well as for scientific research.
- This programme, particularly because of the close collaboration between industry and academia, will enhance the development of new biosensing technologies. The use of these technologies will in turn lead to discoveries in the understanding of biological systems and related research areas, resulting in a flywheel effect for both academia and industry.

Research realisation

The studies by Dame and co-workers are a highlight of the programme. In these studies the use of a paramagnetic bead assay was established to probe DNA-DNA interactions mediated by proteins. Using this assay the effects of changes in physicochemical conditions and interaction with natural protein partners on DNA-DNA interactions were evaluated. A structural switch underlying a functional switch in the activity of a protein involved in shaping genomes of bacterial was discovered. Targeting this protein and altering its functionality in live bacteria could be an effective strategy to combat bacterial infections. In this light the assay can be applied for systematic screening of effectors of this protein, as well as for functional screening of other proteins or ligands mediating DNA-DNA interactions.

In a study by van Vliembergen, van IJzendoorn and Prins, a new concept was investigated for point of care biosensing. Magnetic particles are used to accelerate and control the formation of two particle clusters by capturing an analyte and forming a sandwich immunoassay. Although the concentration of two-particle clusters was measured previously by detecting the frequency selective light scattering in a rotating magnetic field, this study revealed for the first time that by investigating various scattering geometries and analysing higher Fourier components of the scattered light also the distance between the particles can be measured. This provides the exciting opportunity to distinguish between different populations of two-particle clusters and thereby increase the specificity of the assay in a geometry that can be applied in a relatively simple device concept.

Business ambition

- To develop new biosensing technologies which will find use both inside and outside the academic setting.

Business realisation

- For the contribution of Philips research it is important to understand the detection of molecules by using magnetic particles. This is driven by complex processes that have so far mainly been described in a phenomenological way. In this project, an improved theoretical model of mechanisms at the molecular scale and their influence on sensing performance has been developed. The model is used for targeted improvement of crucial aspects of the detection process. Next, to visualise the behaviour of magnetic particles at the detection surface, a dedicated microscope setup has been built. The setup enables a new view on processes that were previously not directly observable. As a result, existing magnetic actuation protocols could be improved to enhance the sensitivity of the detection system. A theoretical model has been developed to describe the stability of the measurement as a function of temperature changes. The insights obtained from the model has been used to improve the existing temperature control and has led to improved sensitivity of the Philips Minicare system.
- Two new public private collaborations have been set up:
  - Acoustic Force Spectroscopy (AFS) is a technique that enables the characterisation of the mechanical properties of individual biomolecules. This technique is very promising as an academic research instrument and may become useful for medical bio-sensing in the further future. A key unique selling point of the AFS technique is the ability to perform a high number of measurements in parallel, which enables statistical analysis that is required for many applications in research and essential for sensitive medical bio-sensing.

    The goal of the NanoNextNL programme is to develop the AFS instrument to exploit this potential fully and concurrently commercialising these developments.

    The second development is the “resealable AFS flow-cell” that enables the user to combine AFS with a wide variety of biochemical surface treatments. This approach will broaden the amount of applications of AFS dramatically and increase experimental throughput. In 2015 the flow-cell has been designed and manufactured. The system works and will soon be available for commercial use.
  - High-end flow cell systems (NT-MDT and VU). The work within the programme has demonstrated that high-end flow cells will be essential for a profound investigation of the impact of varying buffer conditions on biomaterials. However, they did not yet exist and therefore we set-up an effort to produce them. For this we contacted the Enschede-based company Micronit, a company who focuses on microfluidics for life sciences applications. Micronit Microfluidics is a SME with 65 employees. The mission of Micronit Microfluidics is to design, develop and manufacture custom made microfluidic components for applications in micro- and nanotechnology. Therefore it is the ideal partner for the highly technical and precise requirements of the advanced flow-cell that needs to be built. Combining their knowledge and experience in microfluidics with the knowledge of NT-MDT in AFM and our knowledge in manipulation of biomolecules we have a perfect partnership to built this High-end flow cell and we already have the first proto-type ready which we are testing now.

2.9 Theme 9

Nano fabrication

Theme coordinator: Wim van der Zande (ASML Netherlands)

Introduction

Theme 9 dealt with the challenge around nanofabrication. The theme was subdivided in two parts. The first part with as theme coordinator Bram Koster, who succeeded Joost Frenken, concentrated on developing technologies for observing the nanoworld, in particular deriving knowledge on the living world. The second part with as theme coordinator Pieter Kruit, aimed at creating a functional nanoworld, devising and working on processes that make it possible to continue the minituarisation that accompanies the trend that was recognised already 50 years ago and is known as Moore's law. The themes consisted of 15 and 17 projects, respectively, which were cross linked in programme and theme related meetings.

Development of the theme through the years

The strategy and connection within Nano fabrication (theme 9) was established in the beginning. In view of the size of the programmess it was difficult and also unwise to keep all projects completely parallel. This is illustrated by the realisation that many qualified PhD students were needed for the execution of theme 9. Both programmes initially had a strong connection that was fortified in theme meetings where projects presented their progress. Of note, this interaction did not result in active project changes or new collaborations based on shared experiences during meetings.

One of the objectives of NanoNextNL which has been very successful was to train a new generation of researchers at a higher level with a broader scope. The intense interaction within each programme between industry, academics and knowledge institutes has additionally given rise to high quality and high impact papers, an example of which is mentioned in the subsequent pages of this report.

Finally, the NanoNextNL MidTerm Review resulted to strategic changes for the consortium. It was realised that defining themes created a separation between them resulting in (scientific) gaps. In the second half of the NanoNextNL programme a number of cross sectional meetings were organised to actively close these gaps.

Added value of NanoNextNL consortium and ecosystem

NanoNextNL theme 9 Nano fabrication has trained more than 24 PhD students, postdocs and researchers in academic research and also many others in industry. In their projects, they have achieved their objectives and actively converted their ideas into techniques, products and services.

For example at ASML, NanoNextNL contributed to understanding of contamination at the nanometer level and helped creating films with sizes of more than 10x10 cm^2 having sub-50 nm thicknesses. These films implied an important step for introduction of extreme ultraviolet (EUV) lithography. The development of microscopy, especially electron microscopy technology has further fortified the position of the Netherlands where a concentration of high level technology exists at industrial, for example FEI, and at an academic level. The understanding of nanosize physics has also increased awareness on generation, prevention in cases where ´nano´ is perceived as contamination. The availability of concentrated funds has no doubt assisted in increasing the quality and breadth of the technologies, such as multi-electron-beam writing, for the Netherlands and has directly and indirectly created benefits for the Dutch society.

2.9.1 Programme 9A

Nano-inspection and characterisation

Programme director: Bram Koster (Leiden University))

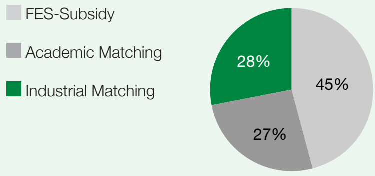
Partners

ASML Netherlands, Bruker Nano, Delft University of Technology, Eindhoven University of Technology, FEI Electron Optics, FOM Institute AMOLF, Leiden Probe Microscopy, Leiden University, Leiden University Medical Center, Nanonics Imaging, NT-MDT Europe, PANalytical, Philips Electronics Nederland,

Projects

15

Budget 9A: € 11.976.225



Output

85 Journal articles
6 Patent filings
Valorisation programme
0 Business case
0 Granted
Researchers
10 PhD student
3 Postdoc
5 Company
4 Master student

Ambition & Realisation

Ambition

- To develop a next generation of techniques and methodologies to image and locally characterise geometrical, electronic, magnetic, optical, mechanical, etc., properties of structures and materials on the nanoscale. The programme generates enabling technology for application in other nanotechnology areas.

Research

- The three main families of techniques in the programme are electron microscopy, scanning probe microscopy and optical microscopy/spectroscopy. New instrumentation has been developed with improved resolution, image contrast, imaging rate and the range of special conditions under which the microscopies can be applied. The latter enables live imaging during actual processes, such as catalysis and pulsed laser deposition. In addition, correlative microscopies were developed, e.g. electron and optical, that merge the strengths of different techniques into a single instrument. Moreover, fundamental knowledge has been obtained showing a better understanding of fundamental properties of materials that is essential for the next generation of instrumentation and tools.

Business

- This programme has led to a range of new products: new light and electron microscopes, new enhanced scanning probes microscopes, microscope combinations, auxiliary tools and software. Several has led to new companies, of which some are developed into mature companies (e.g. Delmic). The developed tools enabled new application areas to be explored, notably the live observations of active catalysts under realistic conditions, high-resolution imaging of fragile biological structures and high-resolution spectroscopic imaging of materials and nanostructures. The demonstrated experiments led to novel fundamental knowledge related to these new applications in other research domains.

Research realisation

A large number of peer-reviewed publications were realized, more than ten in journals with an impact factor higher than ten, several aimed at obtaining very specific new knowledge in a narrow specialised area of science, and several with academic and industrial co-authorships. They cover all three clusters (electrons, scanning probes and light) and in part combine these into single instruments and different application areas, namely catalysis, materials science and biophysics. Examples are:

- Catalytic processes monitored at the nanoscale with tip-enhanced Raman spectroscopy, E. M. van Schrojenstein Lantman, Deckert-Gaudig, A. J. G. Mank, V. Deckert and B. M. Weckhuysen, Nature Nanotechnology 7, 583 (2012)
- Deep-subwavelength imaging of the modal dispersion of light. R. Sapienza, T. Coenen, J. Renger, M. Kuttge, N. F. van Hulst and A. Polman, Nature Materials 11, 781 (2012)
- High-speed AFM reveals the dynamics of single biomolecules at the nanometer scale, A. Katan and C. Dekker, Cell 147, 979 (2011)
- Nanoscale spatial coherent control over the modal excitation of a coupled plasmonic resonator system. T. Coenen, D.T. Schoen, S.A. Mann, S.R.K. Rodriguez, B.J.M. Brenny, A. Polman, and M.L. Brongersma, Nano Lett., 15, 7666 (2015)
- Phase contrast STEM for thin samples: Integrated differential phase contrast. Lazić I, Bosch EG, Lazar S. Ultramicroscopy, 160, 265 (2016).

Business realisation

Several new instruments and methods have been developed, each of which serves as a basis for novel commercial products. Highlights:

- A scanning electron microscope (SECOM) within an integrated fluorescence light microscope has been realised and is commercially available. With it, one can routinely overlay the images from both microscopes without any sample manipulation enabling quantitative correlative imaging with inspiring new applications in materials and life sciences. A new company has been founded, DELMIC (www.delmic.com) that commercialises this new development. The company presently employs about 15 people. Three other types of instruments, all combining multi-model signals (photonic, electrons) are also commercialised by DELMIC.
- A strongly improved contrast in SEM analysis of nanoparticles and fragile samples (e.g. biological specimens) has been achieved by FEI Company. Important was the acquisition of novel knowledge - derived from theory, simulations and practical experiments- of electron-specimen interactions and the detection of back-scattered electrons through the SEM lens by two detectors sensitive to different energies. This has led to a commercial system (Verios) that is part of FEI's palette of instruments.
- SmartTip has developed a collection of new scanning probe tip and cantilever structures (e.g. sharp tripod probe tips, 'blade'-shaped AFM probe tips that can be easily combined with cantilever fabrication, AFM probes for >1 MHz imaging) that are used on commercially available platforms.
- Panalytical has developed new laboratory X-ray scattering instrumentation for the investigation of (1-100 nm) nanoparticles and nanostructures. The hardware was realised by the end of 2012 and now forms a commercial product (ScatterX[78]) an analytical size range from 0.03 nm to 1700 nm.

Lessons learned

- Important to exchange knowledge between different working groups. In NanoNextNL one could obtain an overview of state-of-the art technologies as well as the technological limitations, in different fields.
- The development of high-end hardware to a level where practical application to industrial processes is possible required close cooperation between university and industrial partners and created a clear goal and focus that helped to keep all parties active and involved.
- Working in the context of NanoNextNL, programme meetings and NanoNextNL-congresses, helped greatly to establish new contacts and in the generation of new ideas. Different kind of program meetings were organised. The 12 min talks were fruitful for understanding the work of other researchers of the programme, while poster pitches of a single slide were too short. It was valuable to have the possibility to learn and have discussions on the state-of-the-art methods and instrumentation by visiting other NanoNextNL partners.
- It was valuable to learn about planning and risk management in a PhD project, e.g. in collaboration with LPM BV, visits were planned to actively discuss design, testing and realisation of the instrumentation.
- Discussions with researchers from other disciplines (e.g. biomedicine) allowed manufacturers to test their instruments on relevant samples, provided direct customer-feedback and faster market introduction. It also allowed to attract further funding from other (biomedical) research areas.
- Annual meetings like NanoCity were well appreciated. It helped to maintain contacts within the network, in particular also those contacts that you do not see within this particular project itself.
- The practical evaluation of technology on realistic questions required often a faster adaptation of technology than anticipated. Implementations of new technologies on the cross-road between fields of research should anticipate multiple rounds of adaptation of technology and requires sufficient critical mass in terms of manpower and funding to realise these adaptations.
- An overall successful programme with high scientific and economic impact that needs to have some form of follow-up to keep NL positioned well in this field.

2.9.2 Programme 9B

Nano patterning

Programme director: Pieter Kruit (Delft University of Technology)

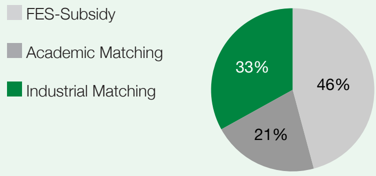
Partners

ASML Netherlands, Delft University of Technology, Eindhoven University of Technology, FEI Electron Optics, FOM Institute DIFFER, Holst Centre, MAPPER Lithography, PANalytical, TNO, University of Twente

Projects

17

Budget 9B: € 13.932.434



Output

41 Journal articles
16 Patent filings

Valorisation programme

2 Business case
2 Granted

Researchers

8 PhD student
6 Postdoc
11 Company
2 Master student

Ambition & Realisation

The general ambition of this programme is to involve excellent academic groups in solving major potential show-stoppers in the progress towards further miniaturisation in nanopatterning. The programme focuses on technologies in which Dutch industry has a leading position: high-tech systems for photolithography, e-beam lithography and direct-write prototyping.

Science ambition

Compared to the nano patterning possibilities of today, there are three major challenges for the future:

- To write structures smaller: Either extremely small or extremely accurate (0.5 – 10 nm).
- To produce patterns faster: For the semiconductor industry sub 22 nm at many wafers per hour.
- To be more flexible: Fast prototyping, especially for “More than Moore” or “beyond Moore” technologies, and patterning directly in the material of choice, especially for research.

In order to address these challenges, a new generation of patterning instruments and patterning processes needs to be developed. These patterning instruments are based on the precise understanding of the physics and chemistry that is in the machines. There are still large gaps in this understanding, such as the interaction of EUV and electrons with resist at the nanometer scale, or the processes through which high power EUV or dense electron beams interact with the optical elements. The science ambition of the programme is to fill the gaps in understanding the physics and chemistry of creating nano patterns.

Business ambition

The Netherlands is in the unique situation that it harbours the world market leaders in high tech systems for nanopatterning: ASML, FEI and MAPPER. Together, these companies employ thousands of engineers and scientists; spend 10-15% of their revenue in R&D (ASML has the Netherlands’ second largest R&D effort) and maintain an important eco-system of associated suppliers as well as academic partners. The business ambition of the programme is to strengthen the scientific infrastructure for the existing industry such that their international competitive advantage is enhanced.

Science realisation

- **Cluster A: EUV-induced optics contamination and cleaning processes at nanometer accuracies and surface topographies.**
  The feasibility studies on EUV mask inspection were completed and led to the conclusion that a pellicle would be highly desirable. The use of large area (80mm), ultra-thin (25nm) free-standing membranes was tested and the knowledge has already been transferred to the development department. Invited lecture on the subject in SPIE conference, 4 patent filings.
- **Cluster B: Direct write nano-prototyping with nm precision.**
  FEI is world market leader in dual beam (SEM/FIB) tools. The programme has contributed greatly to the possibility of making structures with predictable properties by a much deeper understanding of the interaction between beams, precursors and surfaces. In addition, the direct-write technique has been combined with in-situ annealing or deposition techniques for new possibilities in one-tool processes. In one project, a process in which the patterning capabilities of electron beam induced deposition (EBID) are combined with the purity of atomic layer deposition (ALD) was developed resulting in metallic patterns on a surface with superior purity and speed compared to EBID alone.
  This cluster has a record number of scientific publications, both from the industrial and the academic partners, and more in the pipeline to publication
- **Cluster C: Electron beam lithography with nm placement control.**
  MAPPER develops high throughput electron beam lithography with massive parallelism. The programme has to a large part solved the issue of contamination of the micro lens elements by understanding the exact mechanism of the cleaning process. Individual beam alignment was improved after an academic study on the optics of alignment deflectors and the implementation of an individual beam aligner in the MAPPER tool. An in-depth understanding and subsequent simulation of the interaction between electrons and resist resulted in a series of scientific papers on shot noise effects both in metrology and lithography.
- **Cluster D: Industrial scale nano patterning by nano-imprint.**
  This programme addressed current scientific and technological challenges in the fabrication of templates, large-area patterning, patterning on flexible substrates, and the fabrication of self-aligned structures. The technology was developed further and applications in many fields were explored. However, none were found to be sufficiently promising. The direction of the research was subsequently changed to industrial scale contact mask nanoprinting.

Business realisation

- **Cluster A:** The in-depth understanding of the physics involved has led to an improved methodology to keep EUV mirrors clean. The programme has also contributed to the early research into the introduction of pellicles for the protection of EUV masks, now a major development programme at ASML and its partners. TNO has established an international center for contamination control.
- **Cluster B:** Electron Beam Induced Deposition as a nano patterning technique has gotten closer to the point where well defined patterns of predictable composition can be produced. In itself this is already useful for nanotechnology and prototyping, but it also enhances the value of dual beam machines even if the new process control has not resulted in a new product.
- **Cluster C:** Massively parallel electron beam lithography has come very close to market introduction and this programme has helped in overcoming some of the potential show-stoppers. The business opportunities are not restricted to the lithography machines itself, but extend to the new applications of low volume electronics.
- **Cluster D:** The Holst Center where this project runs is based on the philosophy of realizing business from research.

Lessons learned

The programme was a great success in the sense that the infrastructure for the scientific support of an important economic activity in the Netherlands was strengthened: academic and industrial scientists worked together, new groups in academia got involved in research that is relevant for the industry and young researchers got their education in the field of nano patterning. The scientific results have been implemented in the designs of commercial nano-patterning instruments soon to be used in chip production. The Netherlands has maintained its leading position in the field.

A lesson learned is that the participants should have teamed up to secure European funding for their research in this field right from the beginning. The subject is highly relevant and the industry partners have the manpower to pull large projects. There is an opportunity to start a follow-up programme “3D nanomanufacturing & metrology” which involves a broader application field including some of the subjects in other NanoNextNL programmes.

2.10 Theme 10

Sensors and actuators

Theme coordinator: Machteld de Kroon (TNO)

Introduction

Global challenges

Over the last years sensor and actuator concepts have evolved rapidly. This has been driven by a need for gathering information and automation of intervention. This especially holds for high-tech systems, which is extremely important for the Dutch economic landscape. Further innovation of components, such as sensors and actuators, and their integration into larger systems will lead to an increasing level of functionality and more efficient production. Despite the availability of sensors and actuators, their application is still limited due to the difficulties to apply them on industrial scale, where:

- more devices applied in parallel and intelligent integration into networked systems are needed.
- manufacturability and packaging are of key importance.
- the specificity of each sensor or actuator is dependent on the actual working environment.
- extreme operating conditions may apply, i.e. extreme heat load.

Sensors and actuators in the Netherlands

The development of technologies for sensors and actuators is widespread across Dutch academia, knowledge institutes and industry. Examples are: world leading position and years of experience in high tech applications in lithography (ASML), microscopy (FEI), inkjet technology (OCE), sensor development for satellites (TNO and Dutch Space), radar technology for remote sensing (Thales).

Development of the theme through the years

Due to the involvement of industry, theme 10 already had a strong connection to applied research. During the execution of the programs and following the conclusions of the NanoNextNL MidTerm Review, additional attention to connection between programmes and also to other themes is seen as being important. Such a connection also offers the possibility for aligning technology developments. Several events took place to enhance interaction, among which we highlight:

- Microbubble workshop, Wageningen
- Theme-10 event, on 30 September 2014

During the theme 10 event special attention was given to the alignment of technology developments in two workshops, one on ''fluid-solid mechanics" and the other one on 'thermal control", with involvement from both Industry and Academia. Also several PhD students from other themes were invited.
For enhancing the innovation strength, next to in-depth research, an overall system approach is highly relevant. Therefore also a workshop on systems engineering was held, led by Prof. Gerrit Muller (Buskerud and Vestfold University College, Kongsberg, Norway and TNO Embedded Systems Innovation) during the theme 10 event.
In order to further enhance involvement of SME's it was proposed to organise a fair for SME during the next NanoNextNL conference. To this end both the NanoCity editions of 2015 and 2016 featured so-called demonstrators displaying tangible results from the NanoNextNL programme. In addition a dedicated NanoBusiness session and a matchmaking event was organized in the 2015 edition of NanoCity.

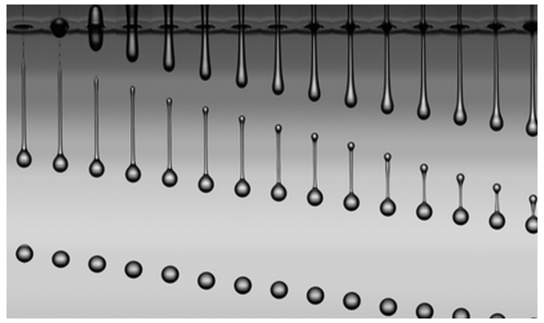
Added value of NanoNextNL consortium and ecosystem

High added value from the NanoNextNL consortium and ecosystem is experienced in the cross-over of technology between projects and programmes, meaning that specific fundamental research done with an initial main application in mind, also appears to be relevant for other applications.

In addition, due to the involvement from industry and applied research organisations, the NanoNextNL research resulted in ideas for new products, that are now being further developed by industry.

Cross-over developments

A nice example of cross-over application is the development of drop formation technologies. Knowledge and numerical tooling from the inkjet printing process of Océ is used for the design of the light source in the new generation EUV lithography machines of ASML. Strobe recordings (iLIF) by Twente University show highest details of the dynamics of drop formation process and enabled the measurement of liquid properties at very short time scale. The strobe recording was selected by Nature as one of the pictures of the year 2014.



Strobe recording by Twente University, published in Nature 2014

Another example of cross-over is the development of the Indoor localisation system by dr. ir. Chris Verhoeven, which results from research about navigation and localisation of nano satellites.

New products initiation

Due to the theme's 10 research, also several new products were initiated. E.g. Chemtrix initiated two main products, Labtrix Start Flex/UltraFlex and KiloFlow pumps. Both products represented an increase in functionality and specification for Chemtrix. The products have been sold both locally and globally to users in the fine chemical and pharmaceutical industry. In a military application, Chemtrix would not have had a suitable product without the NanoNextNL developments.

Another example of new product initiation is the extension of the FlowID modular flow chemistry product line: FlowFlex. FlowID developed and upgraded several new modules. Most important new module is the 'gas liquid separator'. Which can be used downstream of gas liquid reactors for phase separation and pressure regulation. FlowID is now able to offer services based on multi-channel reactors and other scaled up devices. Experience is gained and several designs are tested.
The company FutureChemistry could add the gas module to their product portfolio. With the gas module, controlled gas/liquid reactions can be carried out on a small laboratory scale. In this way, only small amounts of gas are required for experiments. For some expensive gases this is an important benefit in R&D environments. In addition, by being able to control the gas flows very well, the ratio of chemical compounds are known and thus a gas/liquid process can be developed better.
Another development enabled FutureChemistry to apply a new process for the creation of submicron particles from natural polymers (such as gelatin). FutureChemistry will be able to launch a new range of products based on these submicron particles. By using continuous flow technology, the process is scalable and economically feasible. Market segments in medical devices and cosmetics are now targeted and partnering is being set up for product development. FutureChemistry's subsidiary Element Orange B.V. will further develop this technology.

These examples illustrate the benefit of the NanoNextNL consortium, in which industry, applied research institutes and universities are joining forces in order to develop cutting edge technology and translate these technologies to relevant industrial applications.

2.10.1 Programme 10A

Systems and packaging

Programme director: Urs Staufer (Delft University of Technology)

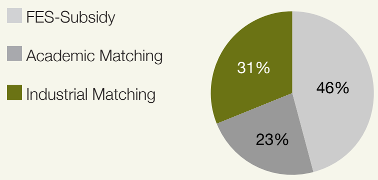
Partners

AEMICS, ASTRON, Boschman Technologies, Bronkhorst High-Tech, Coöperatie DevLab Development Laboratories, Delft University of Technology, Demcon Advanced Mechatronics, Dutch Space, Eindhoven University of Technology, Holst Centre, Innovative Solutions In Space, LioniX, Micronit Microfluidics, Nanosens, NXP Semiconductors Netherlands, Philips Electronics Nederland, SystematIC design, University of Groningen, University of Twente, Wageningen University

Projects

6

Budget 10A: € 11.964.664



Output

49 Journal articles
4 Patent filings

Valorisation programme

6 Business case
2 Granted

Researchers

10 PhD student
2 Postdoc
8 Company
6 Master student

Ambition & Realisation

Sensing devices must measure multiple parameters and freely interact with their environment while simultaneously being protected and robust enough to ensure error-free, long-living operation. Architecture, heterogeneous integration, innovative packaging technology, and manufacturability were key elements of our application-oriented research, which led to several demonstrators with relevance in health, environment and energy.

Science ambition

Create understanding of the architecture of sensor systems, and of heterogeneous integration, assembly and packaging technology to enable faster developments with less iteration, less energy consumption and less waste; thus contributing to a more efficient and sustainable economy. Exploit mechanical and nano-scale sensing as robust transduction principle. Develop showcases to demonstrate the advantages that can be gained by systems architecture and smart packaging.

Business ambition

- To provide the participating industrial partners with a leading edge by reaching at least Technology Readiness Level (TRL) 6 for at least 2 of the 6 projects.

Science realisation

- Studies in Systems Architecture resulted in:
  - Enhanced ground communication of distributed space systems led to robust sensing systems and has resulted in a better understanding of the following systems aspects:
    - scaling trends identifying optimal components and configurations of distributed systems;
    - scenarios (phased arrays) to extend the communication capability of distributed networks.
    - a novel concurrent GPS-Galileo receiver front-end has been designed, which includes compatibility of Chinese and Russion navigation systems.
  - In single-chip flow sensing systems, the dynamic flow range was increased to more than 5 orders of magnitude by co-engineering a thermal and a micro-Coriolis flow sensor with partially overlapping measurement ranges. Furthermore it was demonstrated that sensors for other parameters like pressure and thermal conductivity and a flow control valve can be integrated on the same chip.
- Studies in heterogeneous integration technology achieved/demonstrated:
  - a two stepped air cavity over-moulded package with floating leads by using Film-Assisted Molding (FAM) to be used for Radio Frequency (RF) packages including tests on prototypes;
  - a fast micro/nanosystem prototyping FAM method for advanced packages, like MEMS & Sensors, including wafer level molding; the dynamic insert technology was optimised by designing a new software, by improving the speed and pressure of the control unit (up to 55 bar/second), by fabricating new experimental sensor to achieve a better pressure control;
  - integration of light emitting diodes [LED] on flexible polyethylene teraphtalate [PET] foil substrates; bare LED bonded to copper–PET foil using conducting adhesives; excellent stability during flexing and accelerated humidity and temperature shock tests; an 8 × 8 array of blue LEDs with luminous flux of 22.5 lm and efficacy of 5.8 lm/W;
  - customised on-chip cooling solutions based on vertically aligned carbon nanotubes (CNTs); the augmentation of the surface area with CNT micropins results in a temperature reduction of a local hot-spot of up to 66 °C in free air;
  - increased thermal conductivity and mechanical strength by conformal coating of CNT based cooling elements;
  - cooling of ultrasonic actuators for minimally invasive cancer treatment.
  - that finite element modelling in system design and integration render the assembly of miniature permanent magnets in μ-sensing-systems error tolerant, while at the same time reduce unwanted magnetic fields outside the sensing area. New, smaller size magnets allowed a reduction in the sensor chip footprint by a factor of 3, reducing fabrication costs and consumption of precious/scares materials.
- A generic μ-fluidic platform technology demonstrated faster turnaround in device development.
- The demonstration that channel capillary intake of sweat into a flexible foil system is a reliable building block in the architecture for designing smart patch-devices for portable/bedside/wearable medical analysis applications.
- The development of a field-effect transistor [FET] Acetone sensor system based on functionalized Si-nanorods for diabetes monitoring.
- The development of a new type of nanogap-IDE (Inter Digitated Electrode) with a 50-fold increase in capacitance sensitivity with respect to thin aceton film sensing layers; applicable to different sensing functionality.

Business realisation

- The Coriolis based mass flow sensor is currently evaluated by beta testers of the industrial partner Bronkhorst. It has passed the level of demonstrator (TRL6) and is currently tested in operational environment at beta-clients. The integration of flow and density sensing due to improved systems-architecture technology proofed to be most valuable for the clients of the business partners.
- The indoor localisation system developed by ElpaNav BV and project partners demonstrated operation in a relevant environment (TRL6). Its commercialisation has been prepared through a NanoNextNL valorisation grant.
- Proof of concept of a flexible sweat sensor for continuous health monitoring (TRL 4).
- Proof of concept of an aceton breath analyzer (TRL 4).
- 3 Spin-off companies: Elpasys (smartphone applications), Hyperion (nano-satelites), ElpaNav (localisation systems).

Societal impact

As an evident example, sensor systems for easy, patient-friendly health monitoring will enable low-cost medical care for the aging society. Other sensors affect the everyday life, making it more energy efficient, safer and more comfortable.

Lessons learned

- Different workshops with all programme members present were an effective instrument to share knowledge and make use of the vast expertise to promote progress of our community of innovation and of individual members of that community. The size of a programme like 10A is already at the limit to make such workshops effective. When expanding to the theme level, the organisation became more involved, the character turned more into a conference with plenary presentation and in parallel smaller workshops (the size of a programme).
- The thematic workshops represent a useful tool to promote cooperation among the theme members. Moreover, collective actions are vital to tackle problems and to approach them from different point of view.

2.10.2 Programme 10B

Micro nozzles

Programme director: Herman Wijshoff (Océ Technologies)

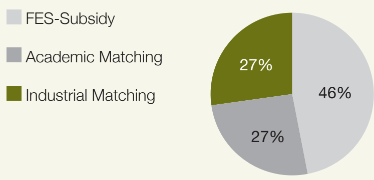
Partners

ASML Netherlands, Delft University of Technology, Eindhoven University of Technology, MA3 Solutions, Medspray, Nanomi, Océ Technologies, Purac Corbion, Tytonis, University of Twente, Utrecht University

Projects

8

Budget 10B: € 7.875.131



Output

36 Journal articles
0 Patent filings
Valorisation programme
1 Business case
0 Granted
Researchers
7 PhD student
6 Postdoc
0 Company
10 Master student

Ambition & Realisation

Research ambition

- The behaviour of fluids on micro scales differs greatly from that on large scales, offering both new technological opportunities and new scientific challenges. The ambition of this programme is to develop and apply knowledge on the formation and precise control of large numbers of miniature fluid volumes such as droplets, bubbles and films. The programme connects expert scientific knowledge of microfluidic phenomena and modelling and simulation techniques to device and process development, and focuses on a selection of applications with direct relevance for the Dutch high-tech industry.

Research highlights

- Control of sessile drop movement with wetting gradients and lattice-Boltzmann as a numerical platform by the University of Twente as the first steps towards self-cleaning inkjet printheads for Océ.
- New modulation mechanism for the break-up of a continuous jet of liquid tin by the University of Twente and the impact behaviour of a stream of drops as a crucial part of a new light source for EUV lithography of ASML and a shorter break-up length of a continuous jet of aqueous solutions with non-axi-symmetric nozzles by the University of Twente to create better inhalers for Medspray.
- Strobe recordings (iLIF) by Twente University show highest details of the dynamics of drop formation process (selected by Nature as one of the pictures of the year 2014) and enabled the measurements of liquid properties at very short time scale.
- Detailed high speed camera recordings (>100 k fps) of pl drop impact on moving substrates by the University of Twente show how drops make first contact showing the effect of substrate properties (cover of J. Fluid mech. 779) and enabled the measurement of evaporation rates of pl-droplets.
- A new simulation framework has been developed for droplet formation and impact with a new paradigm for elasto-capillarity and multi-scale flow in porous media.
- Knowledge and numerical tooling from the inkjet printing process of Océ is used for the design of the light source in the new generation EUV lithography machines of ASML.

Business ambition

The formation and precise control of large numbers of miniature fluid volumes enables the production of highly-uniform microspheres for drug delivery, precisely controlled sprayed and atomised pharmaceuticals and aerosols, deposition of minute amounts of biofluids for medical analyses, high-throughput high-resolution inkjet printing, new generation photolithographic machines, etc.

The three projects with SME involvement (Mespray, Nanomi and MA3 solutions) have the ambition to implement new droplet formation technology in next generation products.

The five projects in cooperation with large industry (ASML and Océ) focus on fundamental challenges in EUV light sources, topographical wafer-design optimisation, development of anti-wetting coatings, droplet formation and dynamics. Results contribute to (more cost-effective) product development.

Business highlights

- Inhalers that produce more homogeneous droplets of a controlled size for the optimised uptake of medicine by Medspray and the University of Twente.
- New pharmaceutical formulations based on highly purified polymers and mono-disperse spheres for a faster release and options to extend the release by Nanomi, Utrecht University, Purac and Tytonis resulted in pharmaceutical formulations which have been commercialised into new products. Because of confidelity reasons no further details are given in this report.
- Development of a dispensing and aspiration platform based on a modified AFM probe to deposit extremely small amounts of liquid (≤1pl) in micro-array assays for DNA analysis by MA3 Solutions and Delft University of Technology. Other applications are nano-batteries, cryo electron microscopy, soft colloidal chemistry, nanographene research etc.
- Development of an open source software platform to enable the use of the newly developed numerical tooling (www.nutils.org) to simulate material interactions by Eindhoven University of Technology.

2.10.3 Programme 10C

Microdevices for chemical processing

Programme director: Marko Blom (Micronit Microfluidics)

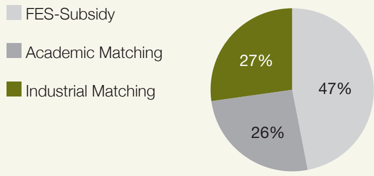
Partners

Chemtrix, Culgi, Delft University of Technology, Eindhoven University of Technology, Flowid, FutureChemistry Holding, Leiden University, LioniX, Micronit Microfluidics, University of Twente, Wageningen University

Projects

2

Budget 10C: € 6.856.201



Output

18 Journal articles
2 Patent filings

Valorisation programme

1 Business case
0 Granted

Researchers

4 PhD student
6 Postdoc
1 Company
6 Master student

Ambition & Realisation

The programme's ambition is to prove the technical and commercial relevance (essential for the uptake of this technology by industry) of the use of micro devices in chemical processing by achieving the following.

Science ambition

- Obtain a thorough understanding of the influence of the scaling of microreactors (from 10um to millimetres) on the reaction itself and on the reactor performance.
- Create new and improved functionalisation procedures.
- Model and simulate catalytic coatings in microreactors.
- Generate new technology to characterise coatings and catalysts and to monitor catalytic reactions.

Business ambitions

- New platform technologies for microreactors:
  - Manufacturability of micro devices:
    - Cost price efficient new fabrication processes of glass-based microreactors (Micronit, LioniX).
    - Increased pressure resistance of reactors and interfacing (Micronit).
  - Improved understanding through the modelling of catalysis in micro devices (Culgi).
- New functionalities:
  - Enabling integration of catalytic sites by various means, thereby enabling use in various reaction schemes (Chemtrix).
  - Optical detection, which can be applied broader than for the monitoring of catalytic activity only (LioniX, Flowid).
  - New technologies for gas-liquid contacting (FutureChemistry).
  - Scalable technologies for continuous flow processes (Flowid, Micronit, FutureChemistry).
- Marketing value of SMEs through association with high ranking publications in the field.
- Enlarged customer base of SMEs via contact with academic institutions.

Science realisation

- Development of technology for evanescent field sensing in microfluidic channels by Lionix enabled inline spectroscopical analysis of microreactor products on one or multiple positions. TU/e, TUD and FlowiD have been exploring and experimenting with the different prototypes of developed devices trying to determine concepts as chemical composition, reaction and kinetics studies. These have led to multiple outputs in public and journals. (Lionix, TU/e, TUD, Flowid)
- Implementation of computational modelling algorithms and techniques that were tested on catalytic reactions in microfluidic channels. (Culgi)
- Polymer brushes have proven to be a robust platform to immobilise various catalysts on the interior of a microchannel for performing supported catalysis. (UT)
- Designing new micro-fluidic devices for enhancing mixing and reaction intensification (TUD)
- Case-study on improved thermal Management in microfluidics: PCR reaction in droplets (with EMS-group of prof. Ter Brake of University of Twente).
- Testing of microchip designs that hold structures for channel parallisation in collaboration with Micronit Microfluidics (TU/e).
- Knowledge (theory and modelling) on use of gas mixtures in sorption compressor and in Joule-Thomson cold stages (UT).

Business realisation

- New product offerings
  - Chemtrix: pumps, screening platform
  - FutureChemistry:
    - Gas-liquid contacting module, also used by Flowid
    - New materials under the tradename Element-Orange: www.element-orange.com
  - Flowid's FlowFlex product platform: new modules of pumps, reactors and separators.
  - Micronit: parallel droplet generators
- The developed methods were applied to study by computational means chemical enhanced oil recovery, which is a major technique in the petroleum industry to get residuel (crude) oil out of a reservoir (Culgi).
- Platform technologies:
  - Evanescent field sensing using integrated optics (Lionix)
  - Various high pressure interfacing solutions (UT, Micronit)

Societal impact

At a high level, microdevices for chemical processing enable a more "lean and green" chemistry. Moreover, with the chemical industry one of the major export drivers in The Netherlands, the NanoNextNL investments in this technology have promoted a wider international use of these new chemistry tools.

Lessons learned

- Flowid: Inspiring collaboration with Micronit, FutureChemistry, Chemtrix, Eindhoven University of Technology and start up companies like TreeScaling. Working together on potential technology evaluation, exchange of hardware and discussions.
- The added value of being part of a larger programme is the access of a high diversity of the knowledge. For FutureChemistry, it has been an added value to learn about the problems and opportunities within different area's and how to apply our technology.
- NanoNextNL was suffering somewhat from the national focus whereas most companies have a very international customer base.
- Integration of evanescent field sensing in microfluidic devices and having the technology ready in an early stage of the project, allowed multiple project partnerts to explore the possibilities of such devices to a good extend. In turn their findings led to the development of new protytypes and output into publicity resulted in new development projects (Lionix).
- We learned that customisation of products is needed to address the needs of many researchers and customers. This project allowed us to develop technical solutions and options that are now commercially available for new Customers to buy (Chemtrix).

Appendix A: Key Performance Indicators

As of mid-March 2017

KPI Description	KPI status	target 2016	% of target 2016
Peer-reviewed papers and conference contributions			
Papers in peer-reviewed journals	1253	1200	104%
Conference contributions	2006		
Peer reviewed papers and conference contributions	3261	1200	272%
• with multi-party co-authorship	1303	500	261%
• with industrial and academic co-authorship	588	200	294%
• with alignment and interweaving of application themes and their matching programmes outside FES-HTS&M	99	100	99%
Joint publications with researchers from theme 1 and 2-10	190	30	633%
Newly established collaborations between generic and application themes	140	10	1400%
EU projects			
EU funded projects submitted and awarded	95	15	633%
Researchers			
PhDs	217		
Post-doctoral researchers	137		
PhDs and post-doctoral researchers	354	300	118%
Researchers that have followed an IPR awareness and or entrepreneurial course	213	300	71%
Patent filings			
Patent filings (first filings)	127	115	110%
• of which jointly filed between industry and academia	20	25	80%
• of which with programmes outside NanoNextNL	1	10	10%
Licenses			
Licenses to parties not participation in the license programme	16	12	133%
Demonstrators, prototypes or products			
Demonstrators, prototypes or products	86	-	-
Start-ups or spin-offs			
New start-ups or spin-off companies exploiting IPR created in this programme and predecessors	24	15	160%
Activities with programmes outside FES-HTSM			
Public seminars with programmes outside FES-HTSM	10	10	100%
Public events with matching programmes outside FES-HTS&M	9	10	90%
RATA events			
TA/Risk public events	52	5	1040%
Activities for non-specialists			
Publications for non-specialists	156	34	459%
Seminars and lectures for non-specialists	200	50	400%
Public events for non-specialists	74	10	740%
Workshops			
Within programmes	291	270	197%
Between programmes	78	60	130%
For the NanoNextNL ecosystem	4	4	100%
On alignment and interweaving of application themes and matching programmes outside NanoNextNL	10	40	25%

Appendix B: Partner overview

This appendix shows an overview of all NanoNextNL partners from 13 universities, 8 medical centers, 12 knowledge institutes and 110 companies.

Universities and medical centers

Universities

Delft University of Technology
Eindhoven University of Technology
Leiden University
Maastricht University
Radboud University Nijmegen
University of Amsterdam
University of Groningen
University of Twente
Utrecht University
Vietnam National University
VU University Amsterdam
Wageningen University
Zuyd University of Applied Sciences

Medical centers

Academic Medical Center Amsterdam
Erasmus University Medical Center Rotterdam
Leiden University Medical Center
Radboud University Medical Center Nijmegen
Slotervaart Hospital Amsterdam
University Medical Center Groningen
University Medical Center Utrecht
VU University Medical Center Amsterdam

Other knowledge institutes

AMOLF - FOM Institute AMOLF
ASTRON - Netherlands Institute for Radio Astronomy
DLO (Service Agricultural Sciences)
FOM Institute DIFFER - Dutch Institute for Fundamental Energy Research
Hubrecht Institute
IMEC Leuven
KWR Watercycle Research Institute
Netherlands Cancer Insitute
Energy Research Centre of the Netherlands (ECN)
RIVM National Institute for Public Health and the Environment
Royal Tropical Institute
TNO Netherlands Organisation for applied scientific research

Companies (A-E)

AEMICS
Amsterdam BioTherapeutics Unit
Aquamarijn Microfiltration
Artecs Polymer Research & Technology
ASM Europe
ASML Netherlands
ATAS GL International
Basic Membranes*
BECO Groep
BiOrion Technologies
BLGG Research
Boschman Technologies
Bronkhorst High-Tech
Bruker Nano (formally Veeco)
Cambridge Major Laboratories
Carl Zeiss SMT
Centre for Concepts in Mechatronics
CellCoTec
Check-Points
Chemtrix
Concept to Volume
Coöperatie DevLab, Development Laboratories
Cosine Research
Culgi
DANNALAB
Danone Research
DC4U
Delmes*
Deltares
Demcon Advanced Mechatronics
DENS solutions
DSM Advanced Surfaces
Dutch Space
Encapson (will withdraw)
Enceladus Pharmaceuticals
Environmental Monitoring Systems
Enza Zaden Research and Development

Companies (F-N)

FEI Electron Optics
Femto Engineering*
Flowid
FrieslandCampina Nederland
FutureChemistry Holding
Holst Centre
HyET
Innosieve Diagnostics
Innovative Solutions In Space
IVAM UVA
Leiden Probe Microscopy
Levitech
LinXis*
LioniX
MA3 Solutions
MAPPER Lithography
Medspray
Meyer Burger
MicroDish
MicroNext
Micronit Microfluidics
Mimetas
Minus9*
Morphotonics
MPI Mainz
Nano Fiber Matrices
Nanomi
Nanonics Imaging
Nanosens
Nikon Instruments Europe
NT-MDT Europe
NXP Semiconductors

Companies (O-Z)

Océ Technologies
OM&T*
Ostendum R&D
PamGene International
PANalytical
X-Flow (formerly Pentair X-Flow)
Percuros
Philips
PhoeniX
Phycom
PhytoGeniX
Podiceps
PolyVation
Purac Corbion
Qmicro
Scheuten Glass*
Shell Global Solutions International*
SmartTip
Solland Solar Cells*
SolMateS
Stork Veco
Surfix
SyMO-Chem
Syncom
Syngenta Seeds
Synvolux Therapeutics
SystematIC Design
Tagsworks Pharmaceuticals (formerly Bait Pharmaceuticals)
Thermo Fisher Scientific
Twente Solid State Technology
Tytonis
Unilever Research & Development Vlaardingen
U-Protein Express
Van Dijk FEM Engineering
VibSpec
VION Ingredients
Vitens NV
VyCAP
Xeltis (formerly QTIS/e)
XiO Photonics

* Former partner

Appendix C: Composition of governing bodies

Executive Board

Members	Affiliation
Chair	
Prof. Dave Blank	University of Twente
Knowledge institutes	
Prof. Fred van Keulen	Delft University of Technology
Dr. Frans Kampers	Wageningen University & Research Centre
Prof. Albert Polman	FOM Institute AMOLF
Industry	
Prof. Reinder Coehoorn	Philips Research, Eindhoven University of Technology
Dr. Frank de Jong	FEI Electron Optics
Jaap Lombaers, MSc	Holst Centre

Supervisory Board

Members	Affiliation
Knowledge institutes	
Prof. Karel Luyben, Chairman	Delft University of Technology
Prof. Frank Baaijens	Eindhoven University of Technology
Prof. Raoul Bino	Wageningen University & Research Centre
Prof. Ed Brinksma	University of Twente
Prof. Jasper Knoester	University of Groningen
Prof. Egbert Jan Sol*	Netherlands Organisation for applied scientific research (TNO)
Prof. Martin Kropff*	Wageningen University & Research Centre
Prof. Hans van Duijn*	Eindhoven University of Technology
Prof. Theo Rasing*	Radboud University Nijmegen
Industry	
Prof. Marco Beijersbergen	Cosine Research
Casper Garos, MSc	Philips Healthcare
Olivier Heyning, MSc	Lumicks
Ronnie van 't Oever, MSc	Micronit Microfluidics
Dr. Frank Schuurmans	ASML
Dr. Ger Willems	FrieslandCampina
Gerard Beenker, MSc*	NXP Semiconductors Netherlands
Adjacent programmes/institutes	
Dr. Johannes Boonstra	Centre of Excellence for Sustainable Water Technology (Wetsus)
Peter van Dijken	TNO Zeist, Kwaliteit van Leven

* Former member

Members	Affiliation
Adjacent programmes/institutes	
Dr. Rinie van Est	Rathenau Institute
Mw. Marian Geluk	TI Food and Nutrition (TIFN)
Dr. ir. Johannes Boonstra	Wetsus
Dr. Marc Hendrikse	Topteam HTSM
Prof. Peter Luijten	Lygature (former Center for Translational Molecular Medicine)
Drs. Mario van Wingerde	Materials innovation institute (M2i)
Prof. Cees Buisman*	Centre of Excellence for Sustainable Water Technology (Wetsus)
Dr. Sibbe Hoekstra*	Materials Innovation Institute
Dr. Jan Maat*	Top Institute Food & Nutrition
Mr. Jan Staman*	Rathenau Institute

International Advisory Council

Members	Affiliation
Prof. Martin Schuurmans, Chair	European Institute of Innovation and Technology
Prof. Gilbert J. Declerck	Interuniversitair Micro-Elektronica Centrum (IMEC), Belgium
Dr. Karel van der Mast	Solveigh Corporate Development, the Netherlands
Prof. Pingfan Rao	Fuzhou University, China

Programme office

Members	Tasks and responsibilities
Programme Director	
Dr. Léon Gielgens	Executive Board, Supervisory Board, Governance
Programme Officers	
Dr. Margot Beukers	Theme 1, 2, 6 and 7
Dr. Melvin Kasanrokijat	Theme 4, 5 and 10
Dr. Gerdine Stout	Theme 3, 8 and 9
Dr. Rens Vandeberg*	
Dr. Floor Paauw*	
Dr. Titia Plantinga*	
Dr. Marjan Fretz*	
Dr. Jeroen van Houwelingen*	
Dr. Freya Senf*	
Business Development Manager	
drs. Raoul Oostenbrink	
Management Assistants	
Sylvia van Mildert	
Anke Roerdinkholder	
Tanja Wesseling*	
Stephanie Dijkstra*	
Sharda Parmanand*	
Sishem Badal*	

Support	Affiliation
Mike van Altena	Finance
Gaby van Caulil	Public Relations and Communication
Jörgen de Gooijer	Finance
Leon van de Laarschot	Legal Affairs
Sandra Oudejans, LL.M*	Legal Affairs
Martie Vervoort	Finance
Sabrina Vredenberg	Public Relations and Communication
Erwin Woord, MA*	Public relations
Marja Berendsen, PhD*	Communication

Business Director

Name	Tasks and responsibilities
Dick Koster, MSc	Business objectives & (inter)national collaboration

RATA Coordinator

Name	Tasks and responsibilities
Dr. Adriënne Sips	Coordination of the risk analysis research within NanoNextNL

Management Committee

Members	Position
Prof. Dave Blank	Chair
Prof. Fred van Keulen	Vice Chair
Dick Koster, MSc	Business Director
Dr. Léon Gielgens	Programme Director

* Former member

Appendix D: NanoNextNL budgets

NanoNextNL FES-subsidy (2010-2016)[1]	
Total research programmes	€ 106.216.866
Post-Doc Valorisation Programme	€ 2.606.885
NanoInside	€ 181.588
Valorisation, Education and PR	€ 4.230.333
Management costs	€ 8.905.751
VAT partners	€ 2.758.578
Total	**€ 124.900.000**

Budget NanoNextNL Research Programmes[1]

Progr	Total budget	FES-Subsidy	Academic matching	Industrial matching	Costs made 2010-2015 (% of total budget)	Cost prognosis 2010-2016 (% of total budget)
1A	€ 7.707.407	€ 3.580.071	€ 3.672.638	€ 454.698	91%	100%
1B	€ 7.474.860	€ 3.459.411	€ 2.900.509	€ 1.114.940	104%	110%
1C	€ 6.029.179	€ 2.789.908	€ 3.239.271	€ -	99%	105%
2A	€ 8.560.608	€ 3.906.932	€ 2.641.400	€ 2.012.275	90%	102%
2B	€ 6.732.388	€ 3.130.432	€ 2.727.387	€ 874.569	96%	109%
3A	€ 5.971.925	€ 2.776.050	€ 1.697.675	€ 1.498.200	99%	107%
3B	€ 8.951.615	€ 4.157.102	€ 2.445.865	€ 2.348.648	103%	106%
3C	€ 6.127.049	€ 2.766.752	€ 1.835.549	€ 1.524.748	100%	107%
3D	€ 10.937.695	€ 4.995.429	€ 3.506.130	€ 2.436.136	96%	106%
3E	€ 8.274.619	€ 3.736.691	€ 2.404.889	€ 2.133.040	101%	108%
4A	€ 6.734.645	€ 3.123.170	€ 1.916.761	€ 1.694.714	104%	112%
5A	€ 7.088.743	€ 3.283.555	€ 1.933.073	€ 1.872.115	92%	102%
5B	€ 6.958.347	€ 3.162.000	€ 2.080.184	€ 1.716.163	129%	136%
5C	€ 6.394.951	€ 2.969.052	€ 905.214	€ 2.520.685	122%	130%
5D	€ 6.124.502	€ 2.847.932	€ 1.794.145	€ 1.482.425	78%	91%
6A	€ 8.285.958	€ 3.757.485	€ 1.741.612	€ 2.786.861	87%	103%
6B	€ 6.361.471	€ 2.887.252	€ 2.451.822	€ 1.022.397	99%	108%
6C	€ 9.098.118	€ 4.211.866	€ 2.354.581	€ 2.531.670	94%	106%
6D	€ 8.971.379	€ 3.871.377	€ 2.899.002	€ 2.201.000	84%	105%
7A	€ 8.020.925	€ 3.584.400	€ 3.441.805	€ 994.720	103%	110%
7B	€ 13.579.810	€ 6.104.135	€ 3.149.922	€ 4.325.753	100%	111%
8A	€ 6.794.277	€ 2.960.716	€ 2.108.286	€ 1.725.275	100%	107%
8B	€ 8.486.033	€ 3.944.902	€ 2.038.160	€ 2.502.971	100%	104%
9A	€ 11.976.225	€ 5.465.772	€ 3.197.727	€ 3.312.726	119%	127%
9B	€ 13.932.434	€ 6.363.959	€ 3.016.965	€ 4.551.510	96%	110%
10A	€ 11.964.664	€ 5.536.900	€ 2.773.978	€ 3.653.786	92%	108%
10B	€ 7.875.131	€ 3.661.798	€ 2.099.869	€ 2.113.464	97%	111%
10C	€ 6.856.201	€ 3.188.104	€ 1.794.036	€ 1.874.061	104%	106%
TOTAL	**€ 232.257.637**	**€ 106.216.866**	**€ 68.761.221**	**€ 57.279.550**	**99%**	**109%**

[1] Status 1 March 2017

Appendix E: Publications in high-impact journals

A total of 1253 papers in peer-reviewed journals have appeared from NanoNextNL research so far. Publications in journals with an impact factor IF>10 are reported below (data as of mid-March, 2017).

Nature (IF=41,5)

03A Topology of mammalian developmental enhancers and their regulatory landscapes, De Laat, W; Duboule, D, Nature 502, 499-506, 2013

07A Responsive biomimetic networks from polyisocyanopeptide hydrogels, Kouwer, P. H. J.; Koepf, M.; Le Sage, V. A. A.; Jaspers, M.; Van Buul, A. M.; Eksteen-Akeroyd, Z. H.; Woltinge, T.; Schwartz, E.; Kitto, H. J.; Hoogenboom, R.; Picken, S. J.; Nolte, R. J. M.; Mendes, E.; Rowan, A. E., Nature 493, 651-656, 2013

Nature Materials (IF=38,5)

02A Photonic design principles for ultrahigh-efficiency photovoltaics, A. Polman and H.A. Atwater, Nature Materials 11, 174-177, 2012

06D Molecular-Scale Simulation of Electroluminescence in a Multilayer White OLED, Mesta M., Carvelli M., de Vries J. R., van Eersel H., van der Holst J. J. M., Schober M., Furno M., Lüssem B., Leo K., Loebl P., Coehoorn R., Bobbert P. A., Nature Materials 12, 652-658, 2013

09A Deep-subwavelength imaging of the modal dispersion of light, R. Sapienza, T. Coenen, J. Renger, M. Kuttge, N.F. van Hulst and A. Polman, Nature Materials 11, 781–787 , 2012

Chemical Reviews (IF=37.4)

08B Torque Spectroscopy for the Study of Rotary Motion in Biological Systems, J, Lipfer, M.M. van Oene, M. Lee, F. Pedaci, and N.H. Dekker, Chemical Reviews, 115, 1449–1474, 2015

Nature Nanotechnology (IF=34,1)

02A/06D Nanoscale optical tomography with cathodoluminescence spectroscopy , A. Atre, B.J.M. Brenny, T. Coenen, A. Polman and J.A. Dionne, Nature Nanotechnology 10, 429-436, 2015

03B Symmetry and scale orient Min protein patterns in shaped bacterial sculptures, Wu, F., van Schie, B.G.C., Keymer, J. E., Dekker, C., Nature Nanotechnology 10, 719-726, 2015

06B Ultrafast non-local control of spontaneous emission, C.-Y. Jin, R. Johne, M.Y. Swinkels, T.B. Hoang, L. Midolo, P.J. van Veldhoven and A. Fiore, Nature Nanotechnology 9, 886-890, 2014

06C Real-time imaging of microparticles and living cells with CMOS nanocapacitor arrays, Laborde C, Pittino F, Verhoeven HA, Lemay SG, Selmi L, Jongsma MA, Widdershoven FP, Nature Nanotechnology 10, 791-795, 2015

07A In vitro measurements of transport across a single biomimetic nuclear pore complex, Kowalczyk, SW, Kapinos, L, Magelhaes, T, Nies, P van, Lim RYH, Dekker, C, Nature Nanotechnology 6, 433-438, 2011

07A Single-molecule transport across an individual biomimetic nuclear pore complex, Kowalczyk, SW, Kapinos, L, Magelhaes, T, Nies, PYB van, Lim, RYH, Dekker, C, Nature Nanotechnology 6, 433-438, 2012

09A Catalytic processes monitored at the nanoscale with tip-enhanced Raman spectroscopy, van Schrojenstein Lantman, E.M., Deckert-Gaudig, T., Mank, A.J.G., Deckert, V., Weckhuysen, B.M., Nature Nanotechnology 7, 583-586, 2012

Chemical Society Reviews (IF=34.1)

03B Nanofabricated structures and microfluidic devices for bacteria: from techniques to biology, Wu, F., Dekker, C., Chemical Society Reviews, 45, 268-80, 2016

Science (IF=33,6)

02A Plasmoelectric potentials in metal nanostructures, M.T. Sheldon, J. van de Groep, A.M. Brown, A. Polman and H.A. Atwater, Science 346, 828-831, 2014

02A Nanophotonics: shrinking light-based technology, A.F. Koenderink, A. Alù, and A. Polman, Science 348, 516-521, 2015

02A Photovoltaic materials : Present efficiencies and future challenges, A. Polman, M.W. Knight, E.C. Garnett, B. Ehrler and W.C. Sinke, Science, 6283: 307 + aad4424: 1-10, 2016

02A Photon recycling in lead iodide perovskite solar cells, L.M. Pazos-Outón, M. Szumilo, R. Lamboll, J.M. Richter, M. Crespo-Quesada, M. Abdi-Jalebi, H.J. Beeson, H.J. Snaith, B. Ehrler, R.H. Friend and F. Deschler, Science 351, 1430-1433, 2016

03B Treadmilling by FtsZ filaments drives peptidoglycan synthesis and bacterial cell division, A.W. Bisson-Filho, Y.-P. Hsu, G.R. Squyres, E. Kuru, F. Wu, C. Jukes, C. Dekker, S. Holden, M.S. VanNieuwenhze, Y.V. Brun, E.C. Garner, Science 355, 739-743, 2017

Nature Photonics (IF=32,9)

02A Direct generation of multiple excitons in adjacent silicon nanocrystals revealed by induced absorption, Trinh, M. T; Limpens, R; De Boer, W. D. A. M; Schins, J. M; Siebbeles, L. D. A; Gregorkiewicz, T., Nature Photonics 6, 316-321, 2012

06B Mapping nanoscale light fields, Rotenberg, N.; Kuipers, L., Nature Photonics 8, 919-926, 2014

Cell (IF=32,2)

03A For Genomes to Stay in Shape, Insulators Must Be up to PAR, Wijchers P, de Laat W., Cell 155, 15-16, 2013

09A High-Speed AFM Reveals the Dynamics of Single Biomolecules at the Nanometer Scale, Katan AJ, Dekker C, Cell 147, 979-982, 2011

Nature Methods (IF=32,1)

08A Acoustic Force Spectroscopy, Sitters, G., Kamsma, D. Thalhammer, G., Ritsch-Marte, M., Peterman E.J.G. & Wuite, G.J.L., Nature Methods 12, 47–50, 2015

09A Correlated Light and Electron Microscopy: Ultrastructure lights up!, de Boer, P; Hoogenboom, J. P.; Giepmans, B. N. G., Nature Methods 12, 503-513, 2015

Nature Chemistry (IF=27,9)

09A In situ observation of self-assembled hydrocarbon Fischer-Tropsch products on a cobalt catalyst, Navaro, V., Spronsen M.A. van, Frenken, J.W.M, 8, 929–934, 2016

Energy and Environmental Sciences (IF=25,4)

02A Indirect to direct bandgap transition in methylammonium lead halide perovskite, Tianyi Wang, Benjamin Daiber, Jarvist M Frost, Sander A Mann, Erik C Garnett, Aron Walsh, Bruno Ehrler, Energy and Environmental Sciences, 10, 509-515, 2017

Cell Stem Cell (IF=22,4)

03A Cell-of-origin specific 3D genome structure acquired during somatic cell reprogramming, Krijger PHL, Di Stefano B, de Wit E, Limone F, van Oevelen C, de Laat W, Graf T, Cell Stem Cell, 18, 597-610, 2016

Nature Physics (IF=20,2)

06B Triggering extreme events at the nanoscale in photonic seas, Liu, C.; Wel, R.E.C. van der; Rotenberg, N.; Kuipers, L.; Krauss, T.F.; Di Falco, A.; Fratalocchi, A., Nature Physics 11, 358-363, 2015

08A Molecular motors robustly drive active gels to a critically connected state, J Alvarado, M Sheinman, A Sharma, FC MacKintosh, GH Koenderink, Nature Physics 9, 591-597, 2013

08B Excitable Particles in an Optical Torque Wrench, F. Pedaci, Z. Huang, M. van Oene, S. Barland, and N.H. Dekker, Nature Physics, 7, 259–264, 2011

Nature Cell Biology (IF=19,7)

08A Functional differentiation of cooperating kinesin-2 motors orchestrates cargo import and transport in C. elegans cilia, Prevo, B., Mangeol, P., Oswald, F. , Scholey J.M. & Petermna E.J.G., Nature Cell Biology 17, 1536–1545, 2015

Advanced Materials Interfaces (IF=17,5)

03B A microfluidic device with continuous ligand gradients in supported lipid bilayers to probe effects of ligand surface density and solution shear stress on pathogen adhesion, van Weerd, J.; Sankaran, S.; Roling, O.; Sukas, S.; Krabbenborg, S.; Huskens, J.; Le Gac, S.; Ravoo, B. J.; Karperien, M.; Jonkheijm, P., Advanced Materials Interfaces 3, 1600055, 2016

03E Flow-Through Microbial Capture by Antibody-Coated Microsieves, Nguyen, AT; Van Doorn, R;Baggerman, J; Paulusse, JMJ; Zuilhof, H; Van Rijn, CJM, Advanced Materials Interfaces 2, 201400292, 2015

06C Highly Polymer-Repellent yet Atomically Flat Surfaces Based on Organic Monolayers with a Single Fluorine Atom, Zhanhua Wang, Sidharam P Pujari, Barend van Lagen, Maarten MJ Smulders, Han Zuilhof, Advanced Materials Interfaces 3, 1500514 1-10, 2016

06D Origin of Work Function Modification by Ionic and Amine-Based Interface Layers, van Reenen, S; Kouijzer, S; Janssen, R.A.J.; Wienk, M.M.; Kemerink, M., Advanced Materials Interfaces 1, 1400189 1-11, 2014

07A Selective Absorption of Hydrophobic Cations in Nanostructured Porous Materials from Crosslinked Hydrogen-Bonded Columnar Liquid Crystals, Bögels, G.M.; Kuringen, H.P.C. van; Shishmanova, I.K.; Voets, I.K.; Schenning, A.P.H.J.; Sijbesma, R.P. , Advanced Materials Interfaces 2, 1500022 1-10, 2015

10C Clickable Mesoporous Silica via Functionalization with 1,ω-Alkenes , van den Berg, S.A.; Tu, J.; Sliedregt, K.M; Kros, A.; Wennekes, T.; Zuilhof, H., Advanced Materials Interfaces 1, 1300061 1-5, 2014

Advanced Materials (IF=17,5)

02A Solution-grown silver nanowire ordered arrays as transparent electrodes, B. Sciacca, J. van de Groep, A. Polman and E.C. Garnett, Advanced Materials 27, 905-909, 2015

04A Spatioselective Electrochemical and Photoelectrochemical Functionalization of Silicon Microwires with Axial p/n Junctions, Alexander Milbrat, Rick Elbersen, Recep Kas, Roald M. Tiggelaar, Han Gardeniers, Guido Mul, Jurriaan Huskens, Advanced Materials 28, 1400–1405, 2016

06A Single-Layer MoS2 Mechanical Resonators, Castellanos Gomez, A, Leeuwen, R van, Buscema, M, Zant, HSJ van der, Steele, G & Venstra, WJ , Advanced Materials 25, 6719 – 6723, 2013

06D Efficient Small Bandgap Polymer Solar Cells with High Fill Factors for 300 nm Thick Films, W Li, KH Hendriks, WSC Roelofs, Y Kim, MM Wienk, RAJ Janssen, Advanced materials 25, 3182-3186, 2013

06D Effect of the Fibrillar Microstructure on the Efficiency of High Molecular Weight Diketopyrrolopyrrole-Based Polymer Solar Cells, Weiwei Li, Koen H. Hendriks, Alice Furlan, W. S. C. Roelofs, Stefan C. J. Meskers, Martijn M. Wienk and René A. J. Janssen, Advanced Materials 26, 1565-1570, 2014

06D Fundamental Limitations for Electroluminescence in Organic Dual-Gate Field-Effect Transistors, W. S. Christian Roelofs, Mark-Jan Spijkman, Simon G. J. Mathijssen, René A. J. Janssen, Dago M. de Leeuw andMartijn Kemerink, Advanced Materials 26, 4450-4455, 2014

06D Polymer Solar Cells with Diketopyrrolopyrrole Conjugated Polymers as the Electron Donor and Electron Acceptor, Weiwei Li, W. S. Christian Roelofs, Mathieu Turbiez, Martijn M. Wienk and René A. J. Janssen, Advanced Materials 26, 3304-3309, 2014

07A Self-Assembled Organic Microfibers for Nonlinear Optics, Xu, J. L. Semin, S. Niedzialek, D. Kouwer, P. H. J. Fron, E. Coutino, E. Savoini, M. Li, Y. L. Hofkens, J. Uji-I, H. Beljonne, D. Rasing, T. Rowan, A. E., Advanced Materials 25, 2084-2089, 2013

08B DNA responsive polyisocyanopeptide hydrogels with stress stiffening capacity, S.R. Deshpande, R. Hammink, R.K. Das, F.H.T. Nelissen, K.G. Blank, A.E. Rowan, H.A. Heus, Advanced Materials 26, 9075–9082, 2016

Light, Science and Applications (IF=14,6)

02A Highly efficient GaAs solar cells by limiting light emission angle, E.D. Kosten, J.H. Atwater, J. Parsons, A. Polman and H.A. Atwater, Light, Science and Applications 2, e45 1-6, 2013

06D Plasmonics for solid-state lighting: enhanced excitation and directional emission of highly efficient light sources, Gabriel Lozano, Davy J. Louwers, Said R.K. Rodriguez, Shunsuke Murai, Olaf T.A. Jansen, Marc A. Verschuuren and Jaime Gomez Rivas, Light, Science and Applications 2, e66 1-7, 2013

06D Metallic nanostructures for efficient LED lighting, Lozano, G.; Rodriguez, S. R. K.; Verschuuren, M. A.; Gómez Rivas, J., Light, Science and Applications 10.1038/lsa.2016.80, 5, e16080, 2016

Nature reviews Gastroenterol Hepatol (IF=14.4)

03D Liver fibrosis in 2015: Crucial steps towards an effective treatment., Poelstra, K, Nature Reviews Gastroenterol Hepatol 13, 67–68, 2016

Molecular Cell (IF=14.0)

03A CTCF binding polarity determines chromatin looping, de Wit E, Vos ESM, Holwerda SJB, Valdes-Quezada C, Verstegen MJAM, Teunissen H, Splinter E, Wijchers PJ, Krijger PHL, de Laat W, Molecular Cell, 60, 676-84, 2015

03A Cause and consequence of tethering a sub-TAD to different nuclear compartments, Wijchers PJ, Krijger PHL Geeven G, Zhu Y, Denker A, Verstegen MJAM, Valdes-Quezada C, Vermeulen C, Janssen M, Teunissen H, Anink-Groenen LCM, Verschure PJ, de Laat W, Molecular Cell, 61, 461-473, 2016

Nano Letters (IF=13,6)

02A Optical impedance matching using coupled metal nanoparticle arrays, P. Spinelli, M. Hebbink, R. de Waele, L. Black, F. Lenzmann and A. Polman, Nano Letters 11, 1760-1765, 2011

02A Optimized spatial correlations for broadband light trapping in ultra-thin a-Si:H solar cells, V.E. Ferry, M.A. Verschuuren, C. van Lare, R.J. Walters, R.E.I. Schropp, H.A. Atwater, and A. Polman, Nano Letters 11, 4239-4245, 2011

02A Transparent conducting silver nanowire networks, J. van de Groep, P. Spinelli, and A. Polman, Nano Letters 12, 3138-3144, 2012

02A Evolution of light-induced vapor generation at a liquid-immersed metallic nanoparticle, Z. Fang, Y.-R. Zhen, O. Neumann, A. Polman, F.J. García de Abajo, P. Nordlander, and N.J. Halas, Nano Letters 13, 1736-1742, 2013

02A/09A Nanoscale spatial coherent control over the modal excitation of a coupled plasmonic resonator system, T. Coenen, D.T. Schoen, S.A. Mann, S.R.K. Rodriguez, B.J.M. Brenny, A. Polman, and M.L. Brongersma, Nano Letters 15, 7666-7670, 2015

02A Single-step soft-imprinted large-area nanopatterned anti-reflection coating, J. van de Groep, P. Spinelli, and A. Polman, Nano Letters 15, 4223-4228, 2015

02A Solution-Processable Singlet Fission Photovoltaic Devices, Le Yang, M. Tabachnyk, S.L. Bayliss, M.L. Böhm, K. Broch, N.C. Greenham, R.H. Friend and B. Ehrler, Nano Letters 15, 354–358, 2015.

02A Lead Telluride Quantum Dot Solar Cells Displaying External Quantum Efficiencies Exceeding 120%, M.L. Böhm, T.C. Jellicoe, M. Tabachnyk, N.J.L.K. Davis, F. Wisnivesky, R. Rivarola, B. Ehrler, A.A. Bakulin and N.C. Greenham, Nano Letters, 15, 7987–7993, 2015

02B Controlled, reversible, and nondestructive generation of uniaxial extreme strains (>10%) in graphene, Perez Garza, H H; Kievit, EW; Schneider, G F; Staufer, U, Nano Letters, 14, 4107–4113, 2014

02B Metal–Organic Polyhedra-Coated Si Nanowires for the Sensitive Detection of Trace Explosives, Anping Cao, Wei Zhu, Jin Shang, Johan H. Klootwijk, Ernst J. R. Sudhölter, Jurriaan Huskens, Louis C. P. M. de Smet, Nano Letters 17, 1–7, 2017

03B Nanopore Fabrication by Heating Au Particles on Ceramic Substrates, de Vreede, LJ, van den Berg, A, Eijkel JCT, Nano Letters 15, 727-731, 2015

06A Gas Detection with Vertical InAs Nanowire Arrays, Offermans, P et al, Nano Letters 10, 2412-2415, 2010

06B Optical Nanoantennas with Tunable Radiation Patterns, Munarriz, J; Malyshev, A.V.; Malyshev, V.A.; Knoester, J;, Nano Letters 13, 444-450, 2013

06B Resonant coupling from a new angle: coherent control through geometry, Rotenberg, N.; Beggs, D.M.; Sipe, J.E.; Kuipers, L., Nano Letters 13, 5858-5865, 2013

06B Experimental realization of a polarization-independent ultraviolet/visible coaxial plasmonic metamaterial, M.A. van de Haar, R. Maas, H. Schokker and A. Polman, Nano Letters 14, 6356-6360 , 2014

06B Nanoscale Confinement of All-Optical Magnetic Switching in TbFeCo - Competition with Nanoscale Heterogeneity, Tian-Min Liu, Tianhan Wang, Alexander H. Reid, Matteo Savoini, Xiaofei Wu, Benny Koene, Patrick Granitzka, Catherine E. Graves, Daniel J. Higley, Zhao Chen, Gary Razinskas, Markus Hantschmann, Andreas Scherz, Joachim Stöhr,, Nano Letters 15, 6862-6868, 2015

06D Controlling a Nanowire Quantum Dot Band Gap Using a Straining Dielectric Envelope, Maaike Bouwes Bavinck, Michal Zieliński, Barbara J. Witek , Tilman Zehender, Erik P. A. M. Bakkers, and Val Zwiller , Nano Letters 12, 6206-6211, 2012

06D Nanowire Waveguides Launching Single Photons in a Gaussian Mode for Ideal Fiber Coupling, Gabriele

Bulgarini,Michael E. Reimer, Maaike Bouwes Bavinck, Klaus D. Jöns, Dan Dalacu, Philip J. Poole, Erik P. A. M. Bakkers and Val Zwiller, Nano Letters 14, 4102-4106, 2014

06D Nanoscale spatial coherent control over the modal excitation of a coupled plasmonic resonator system, T. Coenen, D.T. Schoen, S. Mann, S.R.K. Rodriguez, B.J.M. Brenny, A. Polman and M.L. Brongersma, Nano Letters 15, 7666-7670, 2015

07A Measurement of the docking time of a DNA molecule onto a solid-state nanopore, Kowalczyk, SW, Dekker, C, Nano Letters 12, 4159-4163, 2012

07A Slowing down DNA translocation through a nanopore in lithium chloride, Kowalczyk, SW, Wells, DB, Aksimentiev, A, Dekker, C, Nano Letters 12, 1038-1044, 2012

07A Fast translocation of proteins through solid state nanopores, Plesa, C., Kowalczyk, S.W., Zinsmeester, R. Grosberg, A.Y., Rabin, Y, Dekker, C., Nano Letters 13, 3445-3445, 2013

07A DNA Translocations through solid-state plasmonic nanopores, Nicoli, F, Verschueren, DV, Klein, M, Dekker, C, Jonsson, PM, Nano Letters 14, 6917-6925, 2014

07A Photoresistance switching of plasmonic nanopores, li, Y, Nicoli, F, Chen, C, Lagae, L, Groeseneken, G, Stakenborg, T, Dekker, C, Dorpe, P, Jonsson, PM, Nano Letters 15, 776-782, 2015

09A Directional emission from plasmonic Yagi-Uda antennas probed by angle-resolved cathodoluminescence, Coenen, T. Vesseur, E. J. Polman, A. Koenderink, A. F., Nano Letters 11, 3779-3784, 2011

09A Highly parallel magnetic tweezers by targeted DNA tethering, Vlaminck, I de, Henighan, TC, Loenhout, MTJ van, Pfeiffer, I, Huijts, J. Kerssemakers, JWJ, Katan, AJ, Langen-Suurling, AK van, Drift, EWJM van der, Wyman, C, Dekker, C, Nano Letters 11, 5489-5493, 2011

09A Imaging of hidden modes in ultra-thin plasmonic strip antennas by cathodoluminescence, Barnard, E. S. Coenen, T. Vesseur, E. J. Polman, A. Brongersma, M. L., Nano Letters 11, 4265-4269, 2011

09A Planar parabolic optical antennas, D.T. Schoen, T. Coenen, F.J. García de Abajo, M.L. Brongersma and A. Polman, Nano Letters 13, 188–193, 2013

ACS Nano (IF=12,9)

02A Solar steam nanobubbles, A. Polman, ACS Nano 7, 15-18, 2013

02A/06D Gallium plasmonics: deep-subwavelength spectroscopic imaging of single and interacting gallium nanoparticles , M. Knight, T. Coenen, Y. Yang, B.J.M. Brenny, M. Losurdo, A.S. Brown, H.O. Everitt, and A. Polman, ACS Nano 9, 2049-2060, 2015

02A Light coupling and trapping in ultra-thin Cu(Ga,In)Se2 solar cells using dielectric scattering patterns, M.C. van Lare, G. Yin, A. Polman, and M. Schmid, , ACS Nano 9, 9603-9613, 2015

03B One-Step Homogeneous Magnetic Nanoparticle Immunoassay for Biomarker Detection Directly in Blood Plasma, A. Ranzoni, G. Sabatte, L.J. van IJzendoorn, M.W.J. Prins, ACS Nano 6, 3134–3141, 2012

03D Atherosclerotic plaque targeting mechanism of long-circulating nanoparticles established by multimodal imaging, Lobatto ME, Calcagno C, Millon A, Senders ML, Fay F, Robson PM, Ramachandran S, Binderup T, Paridaans MP, Sensarn S, Rogalla S, Gordon RE, Cardoso L, Storm G, Metselaar JM, Contag CH, Stroes ES, Fayad ZA, Mulder WJ, ACS Nano 9, 1837-47, 2015

06B Active Control of the Strong Coupling Regime between Porphyrin Excitons and Surface Plasmon Polaritons, Berrier, A et al, ACS Nano 5, 6226-6232, 2011

06B Universal Scaling of the Figure of Merit of Plasmonic Sensors, Offermans, P, ACS Nano 5, 5151-5157, 2011

06B Plasmonic antennas hybridized with dielectric waveguides, Felipe Bernal Arango, Andrej Kwadrin and A.Femius Koenderink, ACS Nano 6, 10156-10167, 2012

06B Coherent and broadband enhanced optical absorption in graphene, G. Pirruccio, L. Martin-Moreno, G. Lozano, and J. Gómez Rivas, ACS Nano 7, 4810-4817, 2013

06B/06D Plasmonic band structure controls single-molecule fluorescence, Lutz Langguth, Deep Punj, Jerome Wenger and A.Femius Koenderink, ACS Nano 7, 8840-8848 , 2013

06D Coherent and Broadband Enhanced Optical Absorption in Graphene, Pirruccio, G; Martin Moreno, L; Lozano, G; Gomez Rivas, J, ACS Nano 7, 4810–4817, 2013

06D Shape-Dependent Multiexcitation Emission and Whispering Gallery Modes in Supraparticles of CdSe/Multishell Quantum Dots, Vanmaekelbergh D., van Vugt L.K., Bakker H.E., Rabouw F.T., de Nijs B., van Dijk-Moes R.J.A., van Huis M.A., Baesjou P.J., van Blaaderen A., Vanmaekelbergh D., et al., Acs Nano 9, 33942-3950, 2015

07A/09A Ionic permeability and mechanical properties of DNA origami nanoplates on silid-state nanopores, Plesa, C, Ananth, AN, Linko, V, Gulcher, C, Katan, AJ, Dietz, H, Dekker, C, ACS Nano 8, 35-43, 2014

08B Electron beam fabrication of birefringent cylinders for optical torque tweezers, Zhuangxiong Huang, Francesco Pedaci, Maarten van Oene, Matthew Wiggin, and Nynke H. Dekker, 5, ACS Nano, 1418–1427 (2011)

08B Mechanical Unfolding of an Autotransporter Passenger Protein Reveals the Secretion Starting Point and Processive Transport Intermediates, Marian Baclayon, Peter van Ulsen, Halima Mouhib, Timo Verzijden, Sanne Abeln, Wouter Roos, Gijs Wuite, ACS Nano, 10, 5710–5719, 2016

09A Deep-subwavelength spatial characterization of angular emission from single-crystal Au plasmonic ridge nanoantennas, T. Coenen, E.J.R. Vesseur and A. Polman, ACS Nano 6, 1742–1750, 2012

09A Dispersive ground plane core shell type optical monopole antennas fabricated with electron beam induced deposition, H. Acar, T. Coenen, A. Polman and L. Kuipers, ACS Nano 6, 8226–8232 , 2012

09A Resonant Mie modes of single silicon nanocavities excited by electron irradiation, Coenen, T. van de Groep, J. Polman, A., ACS Nano 7, 1689-1698, 2013

09A Optical Properties of Single Plasmonic Holes Probed with Local Electron Beam Excitation, Coenen, T. Polman, A., ACS Nano 8, 7350-7358, 2014

09A Electron microscopy of living cells during in-situ fluorescence microscopy, Liv, N.; van Oosten Slingeland, D. S. B.; Baudoin, J. P.; Kruit, P.; Piston, D. W.; Hoogenboom, J. P., ACS Nano 10, 256-273, 2016

10A Shedding Light on Axial Stress Effect on Resonance Frequencies of Nanocantilevers, Pini, V; Tamayo, J; Gil-Santos, E; Ramos, D; Kosaka, P; Tong, HD; van Rijn, C; Calleja, M, ACS Nano 5, 4269–4275, 2011

Journal of the American Chemical Society (IF=12,1)

05B The polyphenol EGCG inhibits amyloid formation less efficiently at phospholipid interfaces than in bulk solution, Maarten F.M. Engel, Corianne C. vandenAkker, Michael Schleeger, Krassimir P. Velikov, Gijsje H. Koenderink, Mischa Bonn, Journal of the American Chemical Society 134, 14781-14788, 2012

06C A Supramolecular Host–Guest Carrier System for Growth Factors Employing VHH Fragments, Cabanas-Danés, J: Rodrigues, E.D.: Landman, E: van Weerd, J: van Blitterswijk, C: Verrips, T: Huskens, J: Karperien, H.B.J.: Jonkheijm, P, Journal of the American Chemical Society 136, 12675–12681, 2014

06C On-Chip Electrophoresis in Supported Lipid Bilayer Membranes Achieved Using Low Potentials, van Weerd, J: Krabbenborg, S.O.: Eijkel, J: Karperien, H.B.J.: Huskens, J: Jonkheijm, P, Journal of the American Chemical Society 136, 100-103, 2014

06D Enhancing the Photocurrent in Diketopyrrolopyrrole Based Polymer Solar Cells via Energy Level Control, W Li, WSC Roelofs, MM Wienk, RAJ Janssen, Journal of the American Chemical Society 134, 13787–13795, 2012

06D Universal Transients in Polymer and Ionic Transition Metal Complex Light-Emitting Electrochemical Cells, van Reenen, S.; Akatsuka, T.; Tordera, D.; Kemerink, M.; Bolink, H., Journal of the American Chemical Society 135, 886-891, 2013

07A Cooperative conformational transitions keep RecA filament active during ATPase cycle, Kim, SH, Ragunathan, K, Park, J., Kim, D & Ha, T , Journal of the American Chemical Society 136, 14796-14800, 2014

Advanced Functional Materials (IF=11,8)

02A Dramatic Enhancement of Photoluminescence Quantum Yields for Surface-Engineered Si Nanocrystals within the Solar Spectrum, Svrcek, V., Dohnalova, K., Mariotti, D., Trinh, M.T., Limpens, R., Mitra, S., Gregorkiewicz, T., Matsubara, K., Kondo, M., Advanced Functional Materials 23, 6051-6058, 2013

03B Desalination by Electrodialysis Using a Stack of Patterned Ion-Selective Hydrogels on a Microfluidic Device, Gumuscu, B; Haase, A.S.; Benneker, A.M. Hempenius, M.A.; van den Berg, A.; Lammertink, R.G.H.; Eijkel, J.C.T., Advanced Functional Materials 26, 8685-8693, 2016

05B Novel All-Natural Microcapsules from Gelatin and Shellac for Biorelated Applications, Patel, A.R., Remijn, C., Cabero, A-i, M., Heussen, P.C.M., Seijen ten Hoorn, J.W.M., Velikov, K.P. , Advanced Functional Materials 23, 4710-4718 , 2013

05B All Natural Oil Filled Microcapsules from Water Insoluble Proteins, E. Filippidi, A. R. Patel, E.C.M. Bouwens, P. Voudouris, K. P. Velikov, Advanced Functional Materials 24, 5962 - 5968, 2014

05C Fabrication of Gelatin Microgels by a 'Cast' Strategy for Controlled Drug Release, Wang, A., Cui,Y., Li, J., van Hest, J.C.M., Advanced Functional Materials 22, 2673-2681, 2012

06D Salt concentration effects in planar light-emitting electrochemical cells, S. van Reenen, P. Matyba, A.W. Dzwilewski, R.A.J. Janssen, L. Edman, and M. Kemerink, Advanced Functional Materials 21, 1795-1802, 2011

06D Dynamic Processes in Sandwich Polymer Light-Emitting, van Reenen, S; Janssen, R.A.J.; Kemerink, M., Advanced Functional Materials 22, 4547-4556 , 2012

06D Mechanism for efficient photoinduced charge separation at disordered organic heterointerfaces, van Eersel, H.; Janssen, R.A.J.; Kemerink, M., Advanced Functional Materials 22, 2700–2708, 2012

06D Dynamic Doping in Planar Ionic Transition Metal Complex-Based Light-Emitting Electrochemical Cells, Meier, S.B.; van Reenen, S.; Lefevre, B.; Hartmann, D.; Bolink, H.J.; Winnacker, A.; Sarfert, W.; Kemerink, M., Advanced Functional Materials 23, 3531-3538, 2013

06D Light Emission in the Unipolar Regime of Ambipolar Organic Field-Effect Transistors, WSC Roelofs, WH Adriaans, RAJ Janssen, M Kemerink, DM de Leeuw, Advanced functional materials 23, 4133-4139, 2013

06D Kinetic Monte Carlo study of the sensitivity of OLED efficiency and lifetime to materials parameters, Coehoorn, R.; Eersel, H. van; Bobbert, P.A.; Janssen, R.A.J., Advanced Functional Materials 25, 2024-2037, 2015

07A Bioinspired Magnetite Crystallization Directed by Random Copolypeptides, Lenders, J.J.M.; Zope, H.R.; Yamagishi, A.; Bomans, P.H.H.; Arakaki, A.; Kros, A.; de With, G.; Sommerdijk, N.A.J.M., Advanced Functional Materials 25, 711-719, 2015

07A Tuning Hydrogel Mechanics Using the Hofmeister Effect, Jaspers, M.; Rowan, A. E.; Kouwer, P. H. J., Advanced Functional Materials 25, 6503-6510, 2015

07A Order at Extreme Dilution, Alvarez Fernandez, A.; Hammink, R.; Kragt, S.; Cattaneo, L.; Savoini, M.; van der Velden, J.; Rasing, T.; Rowan, A. E.; Collings, P. J.; Kouwer, P. H. J., Advanced Functional Materials 26, 9009–9016, 2016

07A Size-Selective Binding of Sodium and Potassium Ions in Nanoporous Thin Films of Polymerized Liquid Crystals, GM Bögels, JAM Lugger, OJGM Goor, RP Sijbesma, Advanced Functional Materials 26, 8023–8030, 2016

07B Long-Range Domain Structure and Symmetry Engineering by Interfacial Oxygen Octahedral Coupling at Heterostructure Interface, Liao, Z., Green, R.J., Gauquelin, N., Macke, S., Li, L., Gonnissen, J., Sutarto, R., Houwman, E.P., Zhong, Z., Aert, S. van, Verbeeck, J., Sawatzky, G.A., Huijben, M., Koster, G. & Rijnders, A.J.H.M., Advanced Functional Materials, 26, 6627–6634, 2016

07B Multistability in Bistable Ferroelectric Materials toward Adaptive Applications, Ghosh, A., Koster, G. and Rijnders, A.J.H.M., Advanced Functional Materials, 26, 5748–5756, 2016

Blood (IF=11,8)

09A Content delivery to newly forming Weibel-Palade bodies is facilitated by multiple connections with the Golgi apparatus, Mourik, M.J.; Faas, F.G.A.; Zimmerman, H.; Voorberg, J.; Koster A.J.; Eikenboom J., 125, 3509-3516, 2015

Nature Communications (IF=11,5)

02A Broadband omnidirectional antireflection coating based on subwavelength surface Mie resonators, P. Spinelli, M.A. Verschuuren, and A. Polman, Nature Communications 3, 692 1-5, 2012

02A Multiple-exciton generation in lead selenide nanorod solar cells with external quantum efficiencies exceeding 120%, N.J.L.K. Davis, M.L. Böhm, M. Tabachnyk, F. Wisnivesky, T.C. Jellicoe, Caterina Ducati, B. Ehrler and N.C. Greenham, Nature Communications, 1-7, 2015

02B Electrocatalytic reduction of carbon dioxide to carbon monoxide and methane at an immobilized cobalt protoporphyrin, Shen, J. Kortlever, R., Kas, R., Birdja, Y.Y., Diaz-Morales, O., Kwon, Y., Ledezma-Yanez, I. Schouten, K.J.P., Mul, G., Koper, M.T.M, Nature Communications 6, 8177 1-8, 2015

02B Three-dimensional Q1 porous hollow fibre copper electrodes for efficient and high-rate electrochemical carbon dioxide reduction, Kas R., Hummadi K.K. , Kortlever R , de Wit P. , Milbrat Alexander , Luiten-Olieman M. , Benes N , Koper M.T.M.,Mul G., Nature Communications 7, 10748 1-7, 2016

03C Ultrafast vaporization dynamics of laser-activated polymeric microcapsules, Guillaume Lajoinie, Erik Gelderblom, Ceciel Chlon, Marcel Böhmer, Wiendelt Steenbergen, Nico de Jong, Srirang Manohar, and Michel Versluis, Nature Communications 5, 3671 1-8, 2014

04A Electrocatalytic reduction of carbon dioxide to carbon monoxide and methane at an immobilized cobalt protoporphyrin, Jing Shen, Ruud Kortlever, Recep Kas, Yuvraj Y. Birdja, Oscar Diaz-Morales, Younkook Kwon, Isis Ledezma-Yanez, Klaas Jan P. Schouten, Guido Mul, Marc Koper
6, 8177, 2015

06A Field-free magnetization reversal by spin-Hall effect and exchange bias, van den Brink, A.; Vermijs, G.; Solignac, A.; Koo, J.; Kohlhepp, J.T.; Swagten, H.J.M.; Koopmans, B., Nature Communications 7, 10854 1-6, 2016

06B/09A Directional emission from a single plasmonic scatterer , Toon Coenen, Felipe Bernal Arango, A.Femius Koenderink and Albert Polman, Nature Communications 5, 3250 1-8, 2014

06B Nanophotonic control of circular dipole emission, le Feber, B.; Rotenberg, N.; Kuipers, L., Nature Communications 6, 6695 1-6, 2015

06B Nanoscale sub-100 picosecond all-optical magnetization switching in GdFeCo microstructures, L. Le Guyader, M. Savoini, S. El Moussaoui, M. Buzzi, A. Tsukamoto, A. Itoh, A. Kirilyuk, T. Rasing, A. V. Kimel & F. Nolting, Nature Communications 6, 5839 1-6, 2015

06D Bright single-photon sources in bottom-up tailored nanowires, Michael E. Reimer, Gabriele Bulgarini, Nika Akopian, Moïra Hocevar, Maaike Bouwes Bavinck, Marcel A. Verheijen, Erik P.A.M. Bakkers, Leo P. Kouwenhoven & Val Zwiller, Nature Communications 3, 737 1-6, 2012

07A Ultra-responsive soft matter from strain-stiffening hydrogels, Jaspers, Maarten Dennison, Matthew Mabesoone, Mathijs F. J. MacKintosh, Frederick C. Rowan, Alan E. Kouwer, Paul H. J., Nature Communications 5, 5808 1-8, 2014

07B Superswitching and control of in-plane ferroelectric nanodomains in strained thin films, Matzen, S., Nesterov, O., Rispens G. , Heuver J.A., Biegalski M., Christen H.M. and Noheda B., Nature Communications 5, 4415 1-8, 2014

08A Ensemble and single-molecule dynamics of IFT dynein in Caenorhabditis elegans cilia, Mijalkovic, J; Prevo, B.; Oswald, F.; Mangeol, P.; Peterman, E.J.G., Nature Communications 8, 14591, 2017

09A Asymmetric cryo-EM reconstruction of phage MS2 reveals genome structure in situ, Roman I Koning;Josue Gomez-Blanco;Inara Akopjana;Javier Vargas;Andris Kazaks;Kaspars Tars;José María Carazo;Abraham J. Koster; Nature Communications 7,12524, 2016

Angewandte Chemie (IF=11,2)

02B Polymer-Induced Surface Modifications of Pd-based Thin Films Leading to Improved Kinetics in Hydrogen Sensing and Energy Storage Applications, Ngene, P.; Westerwaal, R.J.; Sachdeva, S.; Haije, W.;de Smet L.C.P.M.; Dam B., Angewandte Chemie 53, 12081-12085, 2014

06C Kovalente Oberflächenmodifikationen von Oxiden, SP Pujari, L Scheres, A Marcelis, H Zuilhof, Angewandte Chemie 126, 6438-6474, 2014

07A Templated hierarchical self-assembly of poly(p-aryltriazole) foldamers, Pfukwa, R.; Kouwer, P.H.J.; Rowan, A.E.; Klumperman, B., Angewandte Chemie 52, 1104-11044, 2013

08B Antibody activation using DNA-based logic gates, Janssen, BMG: Van Rosmalen, M: Van Beek, L: Merkx, M, Angewandte Chemie 54, 2530-2533, 2015

Angewandte Chemie International Edition (IF=11,2)

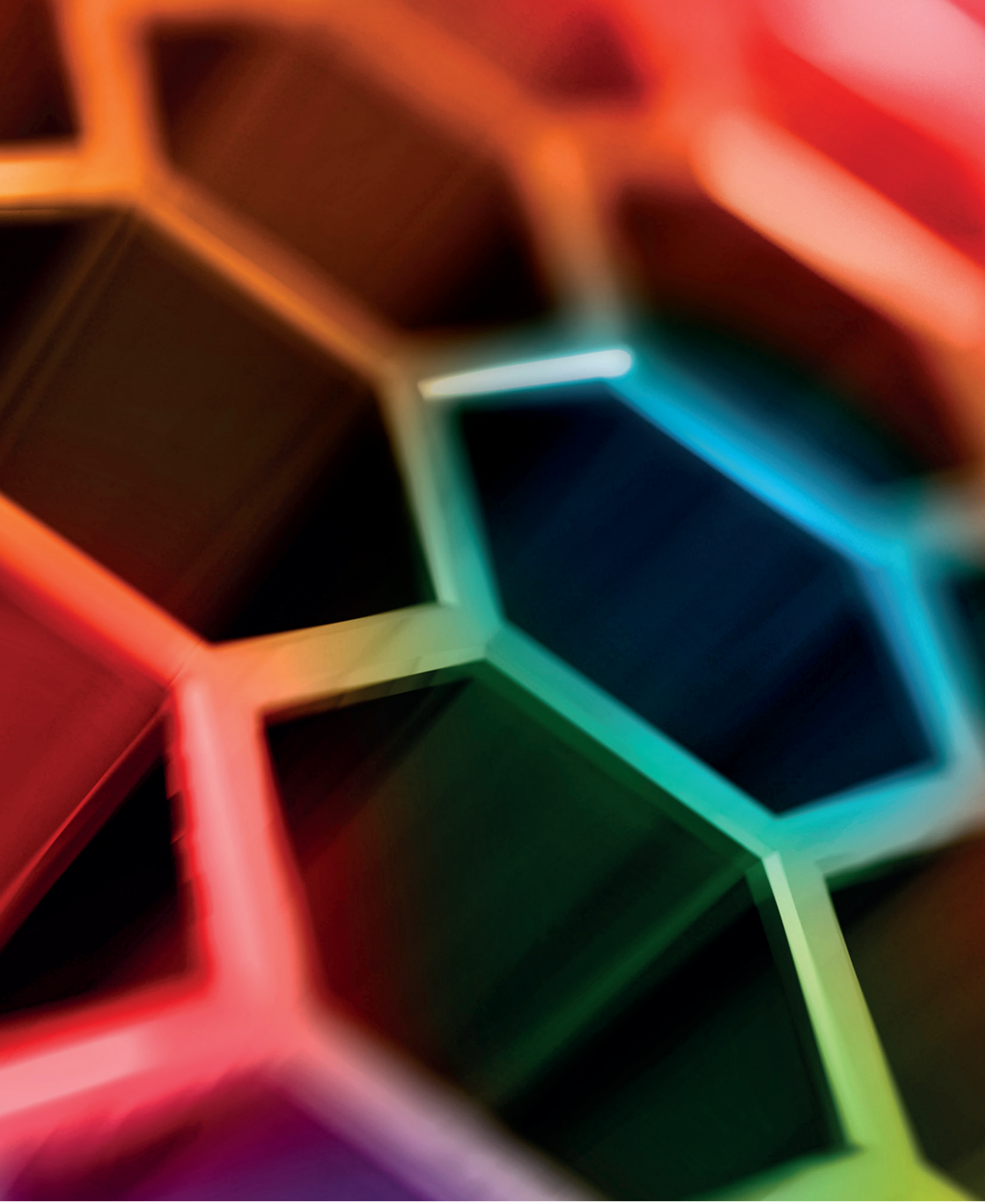
03C Click to Release: Instantaneous Doxorubicin Elimination upon Tetrazine Ligation, Versteegen, RM; Rossin, R; ten Hoeve, W; Janssen, HM; Robillard, MS, Angewandte Chemie International Edition 52, 14112 -14116, 2013

06C Covalent Surface Modification of Oxide Surfaces, Sidharam P Pujari, Luc Scheres, Antonius Marcelis, Han Zuilhof, Angewandte Chemie International Edition 53, 6322-6356, 2014

07A Hierarchical Layer Engineering Using Supramolecular Double-Comb Diblock Copolymers, Hofman, A.H., Reza,M., Ruokolainen, J., ten Brinke, G., Loos, K., Angewandte Chemie International 55, 13081-13085, 2016

Hepatology (IF=11,1)

03D Novel engineered targeted interferon-gamma blocks hepatic fibrogenesis in mice, Bansal R, Prakash J, Post E, Beljaars L, Schuppan D, Poelstra K, Hepatology 54, 586-596, 2011



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