Corporate Staff
Stieltjesweg 1
2628 CK Delft
P.O. Box 155
2600 AD Delft
The Netherlands

www.tno.nl

T +31 88 866 20 00
F +31 88 866 06 30

TNO report

TNO Early Research Program 2015-2018 Annual report 2016

Date	27 February 2017
Editor	Dr. K.E.D. Wapenaar
Copy no	
No. of copies	
Number of pages	63 (incl. appendices)
Number of appendices	
Sponsor	
Project name	
Project number	

Contents

1 Introduction

In this report we present the progress made during the second year of TNO's Early Research Program 2015-2018[1]. For the 2016 program we further developed 10 research topics that are at the heart of societal and economical grand challenges where we believe a concerted effort of applied research, fundamental research and future private development will have great impact. We therefore continued use case inspired research with equal emphasis on generating cutting edge knowledge and technology, together with research partners from academia, and building research ecosystems with stakeholders and sponsors from industry and public organizations. The Table below presents the 10 topics and the TNO contact persons.

nr	ERP	Research	Ecosystem
1.	Quantum Computer / Quantum Internet	Richard Versluis richard.versluis@tno.nl	Rogier Verberk rogier.verberk@tno.nl
2.	Complexity	Ardi Dortmans ardi.dortmans@tno.nl	Paul van den Avoort paul.vandenavoort@tno.nl
3.	Personalised Lifestyle for Health	Frank Schuren frank.schuren@tno.nl	Peter van Dijken peter.vandijken@tno.nl
4.	Energy Storage and Conversion	Ardi Dortmans ardi.dortmans@tno.nl	René Hooiveld rene.hooiveld@tno.nl
5.	3D Nanomanufacturing	Hamed Sadeghian hamed.sadeghian@tno.nl	Rogier Verberk rogier.verberk@tno.nl
6.	Structural integrity	Henk Miedema henk.miedema@tno.nl	Peter Paul van 't Veen peter_paul.vantveen@tno.nl
7.	Human Enhancement	Mark Neerincx mark.neerincx@tno.nl	Myra van Esch-Bussemakers myra.vanesch@tno.nl
8.	Sense Making of Big Data	Wessel Kraaij wessel.kraaij@tno.nl	Henk-Jan Vink henk-jan.vink@tno.nl
9.	Organ Function on a Chip	Evita van de Steeg evita.vandesteeg@tno.nl	Cyrille Krul cyrille.krul@tno.nl
10.	Submicron Composite Materials	Pascal Buskens pascal.buskens@tno.nl	Jaap Lombaers Jaap.Lombaers@tno.nl

In addition to these 10 topics we conducted a seed project on: *Interaction Robotics (i-Botics)*, taking the 2015 exploration in this area a large step further. Progress is reported in chapter 12.

Three new topics were selected for a first exploration of their potential to strengthen TNO's future knowledge base:
- Artificial Intelligence; an enabling technology for many domains (e.g. robotics)
- Bio-nano devices; focusing on cooperation with the TU Delft biophysics group of prof. Cees Dekker
- Chemical sensing; focusing on joining forces with TI-Coast

These explorations are ongoing and will be evaluated later in 2017.

[1] TNO Early Research Program 2015-2018; Annual plan 2015, September 2014; TNO Early Research Program 2015-2018; Annual plan 2016, September 2015

The ERP program is focused on building the future knowledge base of TNO. At the same time we constantly look for opportunities to leverage our research with the efforts of others, to gain mass and jointly generate a higher pace of development. We shared our plans and results in 2016 with many potential partners and stakeholders. Some examples and highlights:

- On TNO.nl, see links TNO ERP and e.g. the White paper Organ-on-a-Chip link
- On YouTube (human enhancement: https://youtu.be/MH0Vj-rChrM)
- Via dissemination events (Organ on Chip, 3D Nano, Big Data, Human Enhancement, i-Botics)
- At Topsector gatherings (LSH, Organ-on-chip, Personalized Lifestyle for Health)
- At the TO2 Enabling Technology Event (January 2017)
- By sharing results in scientific publications, and at conferences

TNO's CSO Jos Keurentjes presented the ERP approach and topics to the Topsector Captains of Science (in March). The ERP program director Koen Wapenaar presented the same to the TKI directors (in May).

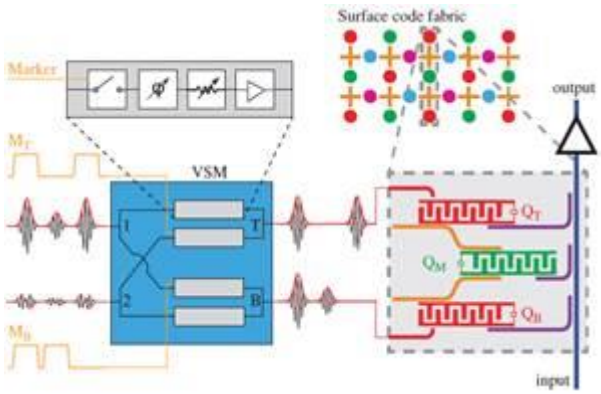
In the next chapters the progress in the ten projects is described in a concise format agreed with the ministry of Economic Affairs, explaining the setting of the research in national and international context, some highlights of results obtained, the cooperation in ecosystems pursued, the use cases, and program dynamics. The plans for 2017 and beyond are described elsewhere[2].

[2] TNO Early Research Program 2015 – 2018; Annual Plan 2017, September 2016

2 Quantum computing and Quantum internet

General data	
Title	ERP Quantum Computer / Quantum Internet
'Topsectors'/Societal Themes	HTSM Nanotechnology
Contact person TNO	Rogier Verberk, Richard Versluis, Garrelt Alberts
Contact person government	Michiel Ottolander
Progress 2016	
Abstract	An increasing number of companies and institutes share the motivation to develop quantum computing and quantum internet. Driving forces are (1) future applications of the unprecedented computing power for sciences and Grand Challenges (including, e.g., development of high-temperature superconductivity for the energy challenges, and in the long run faster developments of drugs for the aging society), (2) computing power for industrial applications (big data search, logistical tasks), (3) being among the front-runners in the development of quantum communication (for national security as well as commercial applications), and (4) to develop a new industry based on Europe's leading scientific position in this field. QuTech, the quantum technologies research center by TU Delft and TNO, has made significant progress in 2016. Besides the cooperation with Microsoft and Intel, IARPA granted a large project to a consortium led by QuTech. In May QuTech, the European Commission and the Dutch Ministry of Economic Affairs hosted a large Quantum Europe conference in Amsterdam for scientists, policy makers, and representatives from industry. At this conference European Commissioner Oettinger announced the initiative for a European Flagship on quantum technologies. For further information on the ambition and people of QuTech, an introduction to quantum computing, and breaking news, please visit www.qutech.nl.
Short description	The TUD hosts a team of world class scientists in solid state quantum technology. Four out of the ten most-cited scientists of the Netherlands (all fields of expertise) work in Delft in this field . This is the scientific foundation of QuTech. On the other hand the Netherlands has a large ecosystem of high-tech / high-precision equipment manufacturing companies including an extended supply chain. This sector has developed and successfully commercialized tube technology for radio and television, transistor and chip technology, lighting and medical equipment, and wafer steppers. Each wave of innovation has led to a new wave of employment. And like ASML and FEI started as spin-off companies from Philips, it is now time to create the new seed for the next high-tech business. World class science and this infrastructure of high-tech industry will accelerate the development of the quantum computer. In future quantum technology will be a new unique selling point of Dutch high-tech industry. TNO is experienced in multiple technologies which are critical for the development of the quantum computer, and complementary to the knowledge of the TUD. Secondly, TNO brings to QuTech its experience in prototyping, system architecture, mission oriented project execution, and contacts to the industry. By building prototypes and demonstrators, TNO/QuTech shall be positioned as a pioneer in

quantum technology. Moreover, TNO/QuTech will invite industrial partners to participate in the development of the demonstrators to strengthen the relationships and have some of this work funded by industry and European projects.
On the other hand TNO has to develop some of its existing technologies further to meet the requirements of the quantum computer (e.g. RF-technology, nanofabrication, multiscale physics simulations). This will also improve the competitive position of TNO in the existing (non-quantum technology) markets like nano-technology/semicon and RF-technology/Radar. These markets are already very important to TNO.
Finally, the further development of existing and new technologies generate possibilities for unforeseen spin-off.

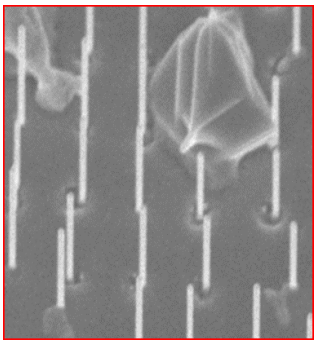


Caption: The electronics to broadcast microwave signals to multiple qubits as developed by TNO in 2015, has been used by scientific experiments by QuTech/TU Delft on transmon qubits in 2016. The results were published in a joint paper in a journal related to Nature.

Topologically protected quantum computing roadmap

Highlights

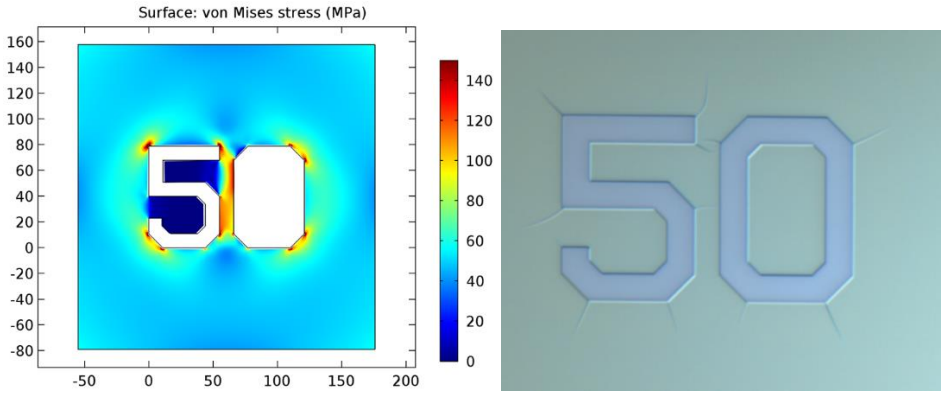
In 2015 a new and very advanced system for material deposition (MBE/ALD) was installed in the VLL cleanroom in Delft. In 2016 the system has been successfully used for the growth of InAs semiconductor nanowires. Such nanowires form a critical component of quantum computers based on Majorana quasi particles.



The work on devices for mobility measurements was continued. Devices have been grown with perfectly flat (<1nm rms) dielectrics with conductive gates underneath. Colleagues of TUD will perform mobility measurements on nanowires laid on top of these devices. One colleague has focussed on 3D lithography to enable growth of nanowire crosses.
Two colleagues have simulated the effects of stress, induced in nanowires upon cooling down from room temperature to 15 mK, on electron mobility.

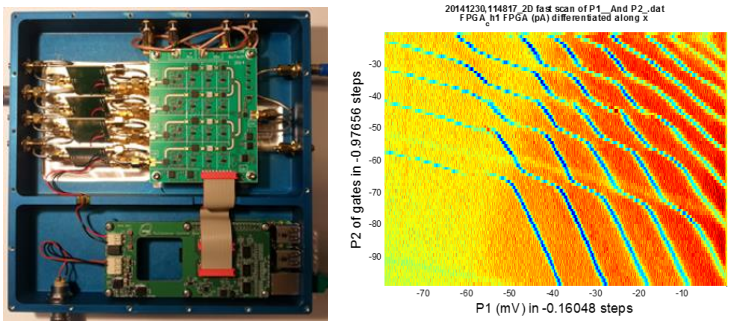
Figuur 1 First nanowires grown in the MBE/ALD facility at VLL

Two more colleagues have focussed on nanowire characterisation and process control for extremely well defined thin layers of superconductive material (NbTiN).
One colleague has supervised these activities and developed the long term strategy: the requirements and design of the device ultimately to be used for braiding, in which all these technologies have to work together.



Figuur 2 Stress Calculation results vs crack observations

Program dynamics	QuTech is still growing. New scientists and engineers are participating every month. This roadmap has some specific dynamics due to the fact that it's Roadmap Leader (Leo Kouwenhoven) has moved to Microsoft. Furthermore, one other professor (Erik Bakkers) has decided to focus his activities to the TUE. Unclear at this point of time is what the consequences will be for the roadmap.
Fault- tolerant quantum computing roadmap:	
Highlights	Several colleagues have worked on the challenges related to the 17 or 49 transom qubits devices: The next generation of the successful vector switch matrix will be designed and built to be used for qubit control by frequency re-use. The FPGA-based feedback loop electronics, designed and built in 2015, have been tested, implemented, and used in quantum measurements. The feasibility of (coax) connections from the third dimension to the 2x7mm small device have been investigated.



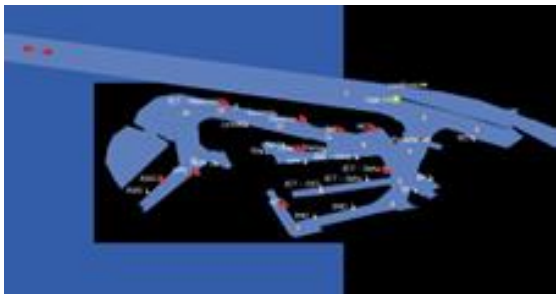
Figuur 3 Vector Switch Matrix & automated qubit tuning

For the first small size demonstrator of the quantum computer (17 and 49 qubits) the functional architecture has been defined to support full use of this system. This includes error correction functionality and automated control of simple qubit algorithms. Support has been given to the development of a quantum emulator, aimed at emulating small scale quantum systems at a very detailed level, up to 40 qubits,
Support has been given to the development of a cryo CMOS control system for spin qubits. This system is essential to allow upscaling of quantum computers to larger numbers of qubits (>50 qubits).
The successful computer-assisted tuning of double spin qubits will be extended for tuning of devices with larger numbers of qubits.

	A consortium of TUD, TNO, ETH, and ZI was granted a funding from IARPA for the development of the first logical qubit. TNO engineers delivered or contributed to: • Sample holder design and production for surface-7 quantum chip, BGA (ball grid array) style • Quantum Wave Generator (QWG) for RF control of SC and spin qubits • Single SideBand (SSB) mixer prototype and first series production • Flip-chip process for spin qubits • Video-mode tuning: Real-time feedback of the status of the quantum dots. • Development of QCoDes, data acquisition modules • Automated tuning, continued from 2015: New algorithms to automate the tuning of the spin qubits, e.g. the tunneling rate. • Database for fabrication (processes flow written down, common library of processes, fast and easy way to share info, continuity facilitated, process monitoring) • Fast turnover fabrication introducing the Else Kooi Lab capabilities.
Program dynamics	With the start of the IARPA and the Intel projects, this roadmap has gained extra momentum. This has led to an increased involvement of TNO.
Quantum Internet and Networked Computing	
Highlights	Wavelength conversion, as demonstrated in 2015, has been extended to the single-photon level. Difference frequency generation (DFG) setup upgraded with new crystal and very narrow-frequency pump laser, and improved overall conversion efficiency. Design and assembly of extremely stable unbalanced (with large Optical Path Difference) fiber interferometer system for the telecom (1588nm) wavelength, with an option of active piezo-stretcher assisted stabilization of the Optical Path Difference (OPD). Assembly of unbalanced interferometer for the visible (637nm) wavelength. Contributed to demonstrating frequency conversion of single photons from an NV-center to telecommunication wavelength. Contributed to experiments showing that the single-photon nature of the converted photons is preserved. Achieved better than 2% phase stabilization with the unbalanced fiber interferometer with an in-fiber OPD of ~40 m by accurate compensation for both thermal and mechanical instabilities, with a piezo-based feedback loop. This interferometer is a crucial component for the planned experimental demonstration of spin-photon entanglement.
Program dynamics	The roadmap has been steadily growing in 2016. The move of Leo Kouwenhoven to Microsoft has resulted in the promotion of Ronald Hanson as Scientific Director of QuTech. This will have an effect on his availability as QINC roadmap leader.
Shared development roadmap	
Highlights	TNO scientists and engineers established a new concept to reach Fault Tolerance in quantum computers and new applications of quantum technologies. TNO submitted to ESA a proposal for a scientific experiment on quantum technologies at low gravitational fields, together with TUD, Leiden University, and satellite manufacturer OHB. TNO scientists contributed to a new RVO research proposal, roadmap Human Effectiveness, on quantum effects, and a new KI research proposal, roadmap Networked Information on Quantum Computing, on Quantum Communication and (post-) Quantum cryptography.
Program dynamics	The development of QuTech organization continued in 2016. The interaction between the QuTech partners has been improved. New TNO personnel on management level (Jorrit van Wakeren, Garrelt Alberts) was introduced to further improve TNO and TU Delft cooperation in the fast growing organization and to professionalize the interaction with partners..

3 Complexity

General data	
Title	Complexity
'Topsectors'/Societal Themes	Water, Logistics, Life Sciences & Health, Horticulture and Starting Materials, Chemical Industry, Creative Industries, Agriculture and Food
Contact person TNO	Ardi Dortmans; Paul van den Avoort; Esther Zondervan
Contact person government	Michiel Ottolander (EZ)
Progress 2016	
Abstract	In the Early Research Program (ERP) Complexity, TNO combines beta and gamma sciences to be able to develop technical and social innovations, especially system transitions. Modelling approaches in which a variety of qualitative and quantitative models are used and combined are most valuable to achieve this. Examples of relevant models are (heterogeneous) agent based models, Bayesian belief models, business models etc. as developed in the academic world under the umbrella of complexity science. The primary aspects investigated are fundamental dynamics of complex systems: the emergence of collective behaviour; the transition from one system state or phase to another, resilience to external shocks or disruptions. TNO works on the growth of the eco-system along three parallel lines: together with NWO[3] and industrial partners, through the Netherlands Platform Complexity Science (NCPS) and by setting-up PPS activities for valorisation of the more fundamental research with NWO. As a good example of the relevance of this ERP, the figure shows the essential geometry of part of the Port of Rotterdam. The spatial scope of the ECT terminal is used and visualized. A basic model for port nautical processes has been developed. It captures operations of the deep sea vessels visiting the port, operations of the support services such as piloting and tugging, terminal handling. The model represents physical and information exchange interactions between the agents. Special attention has been paid to modelling of piloting activities (pilots are experienced seamen who help captains navigating ships in the harbour). The modelling of pilots goes beyond basic agent based modelling: the piloting company faces an operational issue of an optimal use of the human pilots. Therefore, the planning, scheduling and assignment of the pilots to the ships needs to be done in a normative sub-model, which solves a planning problem similar to the traveling salesman problem. Such developments are part of the joint NWO program granted in the NWO call Complexity in Transport and Logistics as a 4 year collaboration between TNO, TU Delft, University Maastricht, InterTransIS, Smart Port, ECT, Rotterdam Port Authority and Topsector Logistics.
Short description	Complexity is commonly briefly described as the science that deals with "the study of the phenomena which emerge from a collection of interacting objects". The primary aspects



[3] http://www.nwo.nl/en/about-nwo/media/publications/ew/paper-grip-on-complexity.html, September 2014

	investigated are fundamental dynamics of complex systems. The NWO position paper "Grip on Complexity" has identified 3 important areas where knowledge gaps exist and research is required: • the emergence of collective behaviour • the transition from one system state or phase to another • resilience to external shocks or disruptions A small list of examples where complexity plays a role: traffic jams, epidemics, criminal and terrorist organisations, industrial value chains, energy and material transitions etc. In 2015 TNO started its activities in this ERP in a number of research projects. By the end of 2015 the topics for the project calls with NWO for 2016 were identified and this was the basis for focussing and shaping the activities in 2016. The relevant project calls for 2016 are: • NWO call Complexity in Transport and Logistics with involvement of NWO MAGW, NWO EW, TNO, Topsector Logistics[4,5] • NWO call Complexity in Health and Nutrition[6] with involvement of NWO EW, TNO, Topsector Agri&Food • NWO call Closed Cycles[7] with involvement of NWO ALW, TO2, Topsectors Agri&Food, Water, Horticulture and source materials, Logistics. In all of these TNO has actively participated in defining the scope of the call, organisation of expert meetings, initiation and formulation of proposals. The formulation of adequate proposals is supported by carrying out preliminary research in TNO to identify bottlenecks and research questions for the project submitted in the call. This is always done in close discussion with external stakeholders (industry, topsectors, government).
Circular Economy and Resource Efficiency	
Highlights	The involvement of TNO in the NWO call Closed Cycles was initiated by our role as coordinator of the NWA route Circular Economy and Resource Efficiency[8] and subsequent contacts with a variety of players in the circular economy area including NWO ALW. The research questions and key solutions ("man-on-the-moon") in this NWA route are good examples of Complexity as playing a key role in shaping our future. In the NWO call Closed Cycles the model for cooperation with TNO was extended to TO2 and Hogescholen. The need for new business models leads to a joint project call on Duurzame Business Modellen II, together with NWO MAGW, prof. Jonker (RU) and drs. Heideveld (Groene Brein), to be executed in 2017 following a workshop on Januari 24 2017. 

[4] http://www.nwo.nl/financiering/onze-financieringsinstrumenten/magw/complexity-in-transport-and-logistics/complexity-in-transport-and-logistics.html
[5] http://www.nwo.nl/en/news-and-events/news/2016/magw/seven-consortia-complexity-in-transport--logistics-granted.html
[6] http://www.nwo.nl/financiering/onze-financieringsinstrumenten/ew/complexity-in-health--nutrition/complexity-in-health--nutrition.html
[7] http://www.nwo.nl/en/funding/our-funding-instruments/alw/closed-cycles---transition-to-a-circular-economy/closed-cycles---transition-to-a-circular-economy.html
[8] http://www.wetenschapsagenda.nl/circulaire-economie-en-grondstoffenefficientie/

	Sustainable circular impact from a systems perspective *In its essence, the transition to a sustainable circular economy involves our adaptation to complete value networks, from product design to new business and market models and new forms of consumer behaviour. It requires an understanding of the structures and institutions, behaviour, policies and technological advances that can impede a sustainable circular economy – or drive it forward. What changes are possible and necessary? What barriers need to be removed? And what incentives to encourage the relevant stakeholders to adopt the right behaviour are effective and acceptable?* The activities in the NWA route Circular Economy and Resource Efficiency also led to contacts with the NWA route Measurement and Detection and the exploration of possibilities to set up a new ERP on Chemical Sensing in close collaboration with this NWA route and TI Coast (outcome expected Q1 2017). The topic for the next joint NWO EW-TNO call in 2017 will be "self-organisation" for which the topsectors Chemistry and Logistics have shown their interest. Self-organisation of materials for chemical sensing could be a relevant TNO topic in this call in view of the above possible new ERP, while also self-organisation for cooperative driving is an interesting research area.
Building the Ecosystem	
Highlights	In the NWO calls mentioned above TNO has actively participated in defining the scope of the call, organisation of expert meetings, initiation and formulation of proposals. The formulation of adequate proposals is supported by carrying out preliminary research in TNO to identify bottlenecks and research questions for the project submitted in the call. This is always done in close discussion with external stakeholders (industry, topsectors, government). Because the projects for the latter 2 calls are in the final stage of formulation or evaluation and in view of briefness below first 2 example projects from the NWO call on Transport and Logistics are highlighted to show the research questions and to answer the question why complexity helps to solve those research questions. In this call 15 projects were submitted, 7 were granted of which 4 with TNO involvement. *Example project: SWARMPORT* The goal of the project is to develop a prototype simulation model for deep sea ports. The model will enable: 1. To improve our understanding of the self-organizational properties of the chain of nautical handling processes directed at maritime ships around seaports, from arrival to departure. 2. To develop valid and practicable methods for modelling port operational processes, implementing agent based modelling from a self-organizational, complex system perspective. 3. To design strategies based on self-organizational properties of port processes to increase the resilience, reliability and flexibility of services of individual actors and of the aggregate service chain. This project is a 4 year collaboration between TNO, TU Delft, University Maastricht, InterTransIS, Smart Port, ECT, Rotterdam Port Authority and Topsector Logistics. *Example project: COMET-PS* Synchromodality is a highly powerful and promising concept for boosting the efficiency of freight transportation, based on combining multiple transportation modes (barges, trucks, trains) in a smart way. This makes a transition possible from the delivery of plain logistic services to integrated services by exploiting the complementary nature of available transportation modes.

This project is a 4 year collaboration between TNO, UvA, UT, TU Delft, Port of Amsterdam, Tata Steel IJmuiden, Combi-Terminal Twente, Air Cargo Netherlands and Topsector Logistics.

In May 2015 TNO and NWO took the initiative to come to the formation of the Netherlands Platform Complex Systems (NPCS). The Platform took several initiatives in 2016, e.g. a one-day satellite session on the topic security during CCS'16, in order to bring together security practitioners and complexity scientists.

The table below gives a concise overview of the active and developing network of stakeholders of this ERP Complexity:

TNO research activities in ERP Complexity in 2016

Research topic	Stakeholders		
	Industry, government	Academia, Applied Research	TNO Theme
Transport and Logistics	InterTransIS, Smart Port, ECT, Rotterdam Port Authority, Port of Amsterdam, Tata Steel IJmuiden, Combi-Terminal Twente, Air Cargo Netherlands and Topsector Logistics (a.o.)	TU Delft, UvA, UT, University Maastricht	Urbanisation
Grip on health	Almery City, de Vogellanden, Isala hospital, PON, Informens, NOC-NSF, Diabetes, Alzheimer, HartStichting, MaagleverDarm Stichting, Friesland Campina, Danone, DSM, Philips, IBM, Arbodienst Beter, Topsector Agri&Food	Shanghai Institute of Systems Biology, UU, WUR, DLO, LU, UvA, CWI	Healthy Living
Sustainable business models	Alliander, Topsector Energy	EUR, RU	Energy
Closed cycles	Topsector Agri&Food, Water, Horticulture, Logistics	WUR, DLO	Urbanisation, Industry

Program dynamics	Overall the ERP follows the ideas described in multiannual plan 2015-2018 and as illustrated above. The cooperation with NWO and industry is being shaped by the various NWO calls and initiatives like the NWA routes. For 2017 the relevant calls and topics have been identified and will be pursued. For 2018 the situation will evolve in 2017 as part of the TNO Strategic Plan 2018-20201.

4 Personalized Lifestyle for Health

General data	
Title	Personalized Lifestyle for Health (PLH)
'Topsectors'/Societal Themes	LSH, Agri&Food
Contact person TNO	Peter van Dijken, Frank Schuren, Nynke van Berkum
Contact person government	Michiel Ottolander (EZ)
Progress 2016	
Abstract	The ERP Personalized Lifestyle for Health aims at changing the vision on healthcare by developing new approaches in diagnostics, personalized food and lifestyle advice, motivational tools and personal empowerment to choose the optimal lifestyle for personal health during different phases in life. The need for such a change was demonstrated in 2016 by the results of the study on the drivers of change: funding and economy. The cost evaluation of the current diabetes healthcare was accurately calculated and found to be 13x higher than a lifestyle based sustainable cure program. This clearly demonstrates the economic benefit when the current system will shift from care to cure and offers the motivation to continue development and implementation of the technologies of this program. In 2015 the focus was on development of individual tools and technologies. Further development and integration of these tools within the Lifestyle as Medicine project was accomplished in 2016. Importantly, we chose to start testing implementation of these services in a specific region (Leiden-Den Haag-Rotterdam) to concentrate multiple aspects of healthcare and health economy that together strongly increase compliance. In this process, a strategic collaboration is constructed with the LUMC, spanning fundamental research, applied research and implementation in healthcare of all aspects of a healthCURE program for type 2 diabetes. Within Early Life, the first Do-It-Yourself study with healthy and obese pregnant women resulted in valuable lessons learned. Moreover, the development of an online Advice tool for parents of toddlers ("OpVoedWijzer") has been started in 2016 and will be continued and tested in the next year. This is done in close collaboration with multiple academic partners. Finally, the experimental platforms of the program support the identification and validation of novel interventions and treatments on disease development. These platforms are applicable both from a pharmaceutical and nutritional point of view and offer TNO the ability to build a strong position in this area. The major development for 2017 within the program is that both use cases will adopt a joint concept: the systems flexibility approach will be applied from early life to ageing related disorders. In the Early Life program a specific emphasis will be given towards the knowledge and application gaps which separate early life from the adult situation, both from a knowledge perspective and a practical perspective. In the Lifestyle as Medicine program, first steps towards implementation will be made in 2017. After two years of "building the parts", the technologies are now brought to actual implementation in the Leiden-Den Haag-Rotterdam region. This will bring the program closer to its main objective: Implement a science based Lifestyle as Medicine program focusing on cure of type 2 diabetes patients in the Dutch Healthcare system, changing the current disease management into a real and sustainable cure for type 2 diabetics.

Short description	Lifestyle related diseases such as type 2 diabetes, cardiovascular diseases, cancer, obesity, allergies, asthma/COPD, autism, dementia and so on are rapidly increasing. Typically, these diseases are treated from a medical and pharmacological perspective. However, changing diet and lifestyle offer alternative remedies, since we now know that an unhealthy diet and lifestyle are the major causes of most of these diseases. The ERP Personalized Lifestyle for Health aims at changing the view on healthcare by developing new approaches in diagnostics, personalized food and lifestyle advice, motivational tools and personal empowerment for choosing the optimal lifestyle for personal health during different phases in life. The fields of expertise are all present within TNO and integrated application of these technologies will result in impact in society, healthcare and economy. A key factor in health is the ability to adapt to many different stresses and changes, in other words, being a flexible and resilient system. Most lifestyle related diseases are characterized by a loss in flexibility of some sort. The concept of resilience has been extensively applied by TNO in investigating health in adults and elderly: stabilization of an existing healthy and flexible system or preventing a system from losing its flexibility (or even reverting to a more flexible system) plays a key role in staying healthy. The element of resilience, either in shaping or restoring, comes back in all three projects within this ERP. 1. Lifestyle as Medicine The major goal of this part of the program is on one hand to implement a cure-based healthcare for lifestyle related diseases, facilitating citizens / consumers / patients to choose exactly those services and products they need for a healthy and active life and on the other hand to create a new focus in the health and food industry to supply these services and products in dedicated and integrated ways. The main activities are setting up a program “Lifestyle as Medicine” aiming at curing type 2 diabetes, building a knowledge base containing information on food solutions for optimal health and developing strategies for health empowerment. 2. Early Life Main driver for our work in this field is the development of a system to make a healthy development in early life measurable, quantifiable and predictable. This system allows not only for a diagnostic approach but also forms the basis for determining the efficacy of interventions in the areas of metabolic health, cognitive development and infection control. 3. Lifestyle Interventions and its Impact on Health This project focuses on the development of experimental platforms, which allow for measuring the effects of various interventions on health/disease status in vitro and in vivo. Interventions can either be of nutritional or pharmacological origin or combinations thereof. The main goal is to develop platforms that are experimentally robust and that are able to mimic both healthy and disease states. Three platforms under development are the Intestinal Microbiome platform, the Intestinal Organoid platform and an Early Life Mouse Model.
Lifestyle as Medicine	
Highlights	This TNO program develops and implements a comprehensive toolkit for first line healthcare aimed at curing type 2 diabetes patients. It includes personalized diagnosis, tailored nutritional and physical activity programs, a “data democracy” infrastructure that helps citizens to fully self-empower themselves based on their own health data, an e-health component and an extensive behavioral change program. It connects to a training and education program within the partnership of the Medical Delta (UL and EUR). Importantly, we chose to start testing implementation of these services in a specific region (Leiden-Den Haag-Rotterdam) to concentrate multiple aspects of healthcare and health economy that together strongly increase compliance. These include the involvement of the regional healthcare partners, local health insurance, employer health programs, local innovative

	lifestyle service providers, knowledge and technology partners and funding mechanisms. The aim is to generate a completely new, economically viable and sustainable healthcare system for type 2 diabetes that can later be both exported to other regions or nations and expanded to other lifestyle related diseases. In this process, a strategic collaboration is constructed with the LUMC, spanning fundamental research, applied research and implementation in healthcare of all aspects of a healthCURE program for type 2 diabetes. The fundamental research focuses on mechanisms of type 2 diabetes reversal, subgroup diagnosis and interventions, and behavioral change technologies. The applied research deals with data ownership and valorization according to the Health Data Cooperative model, experimenting with subject personal health empowerment mechanisms in the “Health Café” settings. A pilot implementation program is created with a primary care center in Rotterdam-Zuid (“Lijn 2”), while scientific support is provided for healthcare programs specifically aiming for type 2 diabetes cure (“Voeding Leeft”).  Figure 1: Screenshots of the Health Cafe Application Importantly, the program has also focused on the drivers of change: funding and economy. The cost evaluation of the current diabetes health was accurately calculated and found to be 13x higher than a lifestyle based sustainable cure program. Interestingly, these convincing values have met a relatively inert reaction from current stakeholders (insurance, healthcare, regulators, economical establishment), implying the need for the creation of a new basis for a healthcare industry, which focuses on cure instead of care. This was addressed by the program by aligning with the H2020 project SHINE, which aims at creating and stimulating a new health economy in this area.
Early Life	
Highlights	Lifestyle as Medicine targets older people in which the resilient system has been disrupted which makes that these people are developing or have already developed disease. Early Life however targets newborns and infants which still have to develop a resilient system. This also means in most cases these infants have not developed a (specific) disease. However, the inability to develop a resilient system will significantly increase the chance of developing disease later in life. The differences in resilience state between elderly and infants mean that although the tools used in Lifestyle as Medicine and Early Life resemble each other, the way these tools are used is clearly different. As an example, Do-It-Yourself (DIY) design studies are more complex in Early Life. Such a study for the analysis of a healthy development of healthy and obese pregnant women has been performed, but was strongly limited by the inability to include sufficient obese pregnant women. The study has resulted in a list of lessons learned, that will be used in future DIY studies. It was concluded that studying early delivered (preterm) low-birth weight children should be a focus for the follow up of this work package, because the parents are expected to be

highly motivated for such a study and because this is commercially of high interest. As preparation for a DIY study in early life, an overview was made of tools available for measuring health in young children and systems knowledge of a healthy early development was collected. By combining data driven search tools with expert input in the areas of metabolic health, cognitive development and infection control in early life a knowledge base has been constructed which makes health related scientific knowledge in early life and ways to influence an early life healthy development readily accessible. This system both allows for the development of science based advice systems as well as for supporting health claims and effects of interventions. Furthermore, the d-score, a tool for determining cognitive and motoric development in early life and used by Dutch health practitioners, was translated into a DIY app, which is under evaluation now with a large group of parents.
The microbiome development was analyzed in cohorts of children, in a study of children from Uganda (in collaboration with a groups in Oslo, Norway and Kenia) and the Dr. Snuit study (in collaboration with the RIVM and UMC Utrecht). It was shown that there is a strong relation between age and the microbiome composition. However, it is shown to be hard to connect the microbiome data to health parameters, first because we do not have access to all meta-data and second because there is a large variance in the microbiome data. Recently, we were able to get access to relevant meta-data of the Dr. Snuit study which will be further explored.
A start was made with a framework for 'personalized nutritional advices' for toddlers from 4-6 years with overweight / obesity as well as parental guidance, to create a decision aid for parents to enable them to make healthy nutritional choices in daily life. Within the personalized nutritional advice for toddlers framework it was decided to map parental distresses/worries beyond overweight/obesity into more detail so that it can also be included into the Advice System (such as sleep, crying, behavior problems, do not like the food etc.). For the relations between nutrition and emotions / psychosocial stress; nutrition and cognition/behavior; nutrition and metabolic development; nutrition and infection control / allergies; and nutrition and sleep the knowledge was used that was collected in the knowledge base. In 2017, this online Advice tool for parents of toddlers ("OpVoedWijzer") will be further developed and tested.
Current academic partners in this area include UMCU, EUR, LUMC, UvA, RUG, Spaarne Gasthuis, ZGV and RIVM with which different collaborations on better understanding Early Life development are underway.

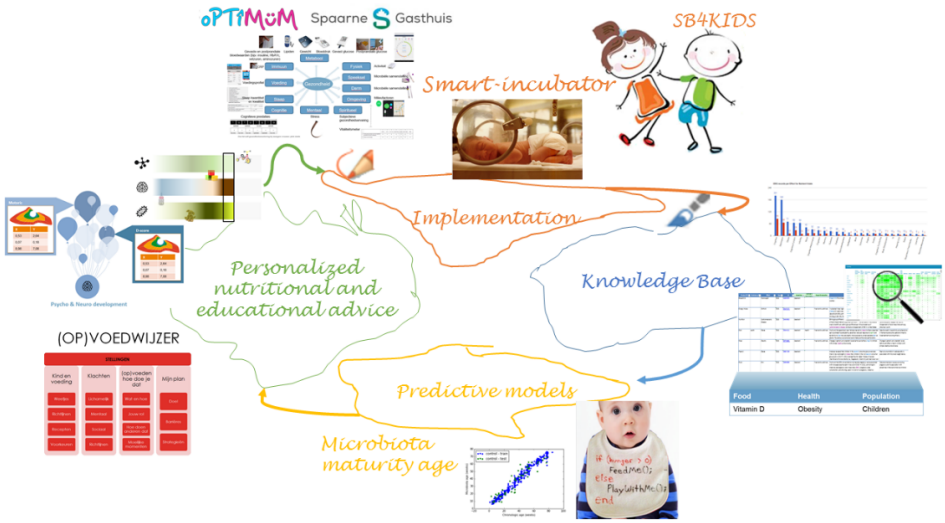


Figure 2: Schematic overview of the achievements and their interplay in 2016.

Lifestyle Interventions and its Impact on Health	
Highlights	Early changes in resilience are represented by changes in microbiome composition (dysbiosis),

intestinal permeability (leaky gut) and local inflammation. These changes have been shown to occur in many different human diseases, especially those with a more chronic character. The platforms in the interventions project target different aspects of this process.
The intestinal microbiome platform focuses on the microbiome composition aspect (dysbiosis) which can be triggered by using antibiotics. The effects of antibiotics on microbiome samples of different age groups was analyzed as well as the effect of food derived fibers. It was shown that different antibiotics have clearly different effects on the same microbiota, that different microbiota samples representing different age groups respond clearly different to the same antibiotic and that dietary fibers can positively influence microbiota composition after antibiotic treatment. This represents a clear example of personalized health effects, both in a negative (antibiotics) and a positive (dietary fibers) way with the availability of a unique tool for in vitro analyzing and predicting in vivo effects of interventions.
The second platform targets the intestinal epithelium. For this the intestinal organoid platform was used and developed into a medium throughput exposure and read-out system based on RNAseq technology, allowing for analyzing the responses of all intestinal genes at once. Organoids were exposed to multiple short chain fatty acids (including butyrate) which are produced by intestinal microbiota and have been related to numerous health effects in humans. However, mechanistic understanding is still limited and this platform allows for obtaining better insight in the processes occurring in the intestinal epithelium.
The third platform combines the dysbiotic and leaky gut features in a new mouse model. First evidence for a model showing disturbed intestinal permeability was obtained in 2015. In 2016 this was further supported by a study starting early in life with exposure to either a normal diet or three different westernized diets (high sugar, high fat). It was shown that all three westernized diets have clear and severe effects on intestinal permeability and microbiome composition (causing dysbiosis), albeit all with a different timing, severity and end points. In this study, many different health related aspects were included allowing for a systems biology based approach for further interpretation of all data. This is a very promising platform for evaluating potential health effects of both dietary and pharmacological interventions.
Together these platforms allow to study early stage disease development, but they especially support the identification and validation of novel interventions and treatments on disease development. These platforms are applicable both from a pharmaceutical and nutritional point of view and offer TNO the ability to build a strong position in this area.
Current academic collaborations in this area are numerous and usually involve specific aspects of either the platforms or specific application fields. They include Donders Institute (RU), ACTA (VU/UvA), EMC, AMC, UMCU.

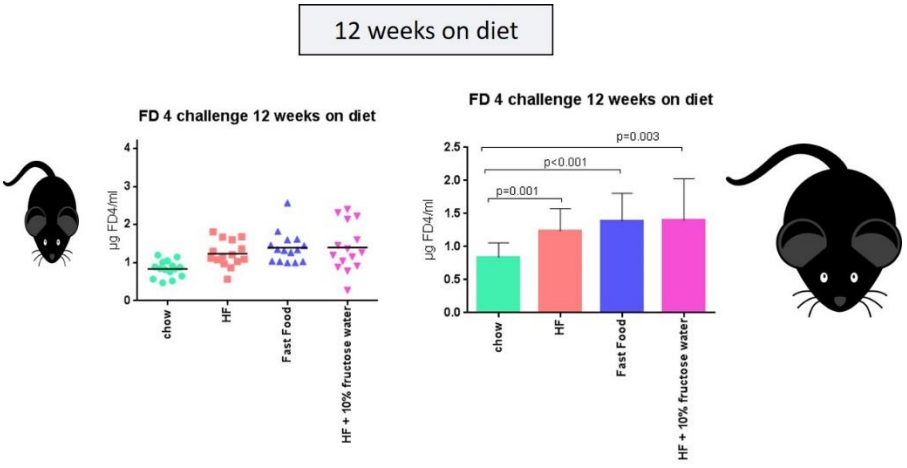


Figure 3: Rapid development of elevated gut permeability in FastFood treated mice in childhood

Program dynamics	The third year of the program is characterized by expansion, integration and implementation. Though food is one of the variables affecting health, lifestyle is prevailing as a health determining factor and has therefore broadened the focus of this program. Hence the name of the program has been changed into Personalized Lifestyle for Health. With the broadened scope collaborations with other programs will be essential. Within TNO this means that various activities contributing to the Lifestyle as Medicine concept will be streamlined into a pipeline of fundamental / applied / implementation / valorization strategy. In addition, external research programs will be contacted to fortify the toolbox and pipeline as mentioned above. The broadened focus of this program has been discussed with the Top sector Agri and Food (by Peter van Dijken, director of innovation Food & Nutrition) and with the Top sector Life Science and Health (By Cyrille Krul, director of innovation Predictive Health Technologies). The major development within the program is that both use cases will adopt a joint concept: the systems flexibility approach will be applied from early life to ageing related disorders. In the Early Life program a specific emphasis will be given towards the knowledge and application gaps which separate early life from the adult situation, both from a knowledge perspective and a practical perspective. Activities will be centered around systems biology knowledge, modelling development and advice systems with a main focus on metabolic development. Because of this joint concept, the tools that were developed in the first two years in the various TNO-departments, will be even more intrinsically connected in their application. These tools, encompassing diagnostics, lifestyle interventions, advice systems and coaching, are fundamental building blocks of a cure program aimed at promoting resilience and health. In the Lifestyle as Medicine program, first steps towards implementation will be made in 2017, bringing it closer to its main objective: Implement a science based Lifestyle as Medicine program focusing on cure of type 2 diabetes patients in the Dutch Healthcare system, changing the current disease management into a real and sustainable cure for type 2 diabetics. After two years of “building the parts”, the technologies are now brought to actual implementation in the Leiden-Den Haag-Rotterdam region. Finally, because of budget cuts in the overall ERP program and the need for focus, “Lifestyle Interventions and its Impact on Health” unfortunately will not be continued in 2017. We strive to continue the development of these platform in other research programs and projects.

5 Energy Storage and Conversion

General data	
Title	ERP Energy Conversion and Storage
'Topsectors'/Societal Themes	TKI Chemie TKI Urban Energy
Contact persons TNO	Pascal Buskens (2016) / Ardi Dortmans / René Hooiveld
Contact person government	Michiel Ottolander (EZ)
Progress 2016	
Abstract	Energy Conversion and Storage becomes more and more important to achieve an increased use of durable energy. In 2015 and 2016 we made good progress in our search for new conversion and storage processes as well as software tools for improved balancing between supply and demand of energy on the electricity grid.
Short description	One of the grand challenges for Europe in the coming decades will be to guarantee a sustainable supply of energy, while at the same time keeping the system reliable and affordable. Amongst others, energy storage and conversion solutions will be needed to achieve this. Within this ERP, our mission is to provide new solutions for large scale, central and small scale, decentral (local) energy conversion and storage to increase the necessary flexibility of the energy system. We aim to provide solutions for both industrial and domestic users. We will primarily focus on three different technology concepts for energy conversion and storage and on a management control systems for balancing energy supply and demand: • Development of an electrocatalytic process that uses (green) electricity to produce fine chemicals and fuels. • Studying the feasibility of a process that directly uses sunlight for the production of fine chemicals. • Studying and development of new material combinations for efficient and safe storage of heat, generated with sun collectors. • Development of additional functionality of a software tool aiming at optimal matching of energy supply and demand by using market mechanisms. ("Powermatcher")
Electrons to Chemicals	
Highlights	The goal of this research line is to build the infrastructure and capability of assessing the technical feasibility of an electrochemically induced transformation, the knowhow on the design of the total system and the possibility to assess economic feasibility. In the past year, the main aim of TNO was to establish suitable knowledge and infrastructure to develop and asses electrochemical transformation towards organic molecules and to demonstrate an integrated electrochemical process including purification / separation at laboratory scale. ***WP1: CO2 Reduction structured electrodes*** Cu and copper alloys have been prepared and tested for electrochemical CO_2 reduction. Based on voltammetry studies the materials seem to be active for the electrochemical reduction of the CO_2. However a low Faradaic efficiency towards CH_4 and C_2H_4, <5%, was observed during electrolysis experiments. The rest of the products were liquid products of the CO_2 reduction, such as formic acid, ethanol and methanol (up to 50-60% FE). The major product of the electrolysis is H_2.It has been clear that using bimetallic systems the selectivity can be changed compared to Copper. Future research will be done into other electrode materials. For example materials such as

CuAu, CuIn alloys need to be further investigated. Also, the measurements on CuSn, CuMn and Cu need to be repeated and the results reconfirmed. However, because of the fundamental and labor intensive research needed it was decided that TNO will not further continue this research. In the meantime, the NWO solar fuel project on CO2 conversion has been granted in which the universities of Leiden, Utrecht and Twente will continue the research on CO2 reduction. TNO will participate as a sponsor, will take an active role in steering the research and will have access to all knowledge generated.

WP2A: System development butanol oxidation

In 2016, this work was continued from the previous year. The pH effect on conversion was researched with respect to reaction rates (pH10-14). Oxidation was done on a Ni-foam electrode. However, after consultation of industry and the advisory board, it became apparent that the showcase of electrochemical oxidation of butanol to butyric acid is very interesting and successful from a scientific point of view but less interesting from an economic point of view. Therefore, it was decided to stop this showcase and move to the more attractive showcase of converting HMF to FDCA, a case with high interest from industry.

WP2B: System development: hydroxymethylfurfural (HMF) to 2,5-Furandicarboxylic acid (FDCA)

Within an accompanying project of the VoltaChem program (the “EZ-Transitie” project) an integrated continuous bench scale setup has been designed and built for electrochemical conversion of HMF to FDCA based on results obtained in small scale and a lab scale electrolysers. (see figure below). The work in 2016 focused on scaling up towards more industrially relevant conditions such as increased HMF concentrations, utilization of an industrial type of plate-and-frame cell together with the construction of a bench-scale system which includes integrated product separation.

In parallel downstream activities were performed using a twostep crystallization approach for isolation of the product, FDCA. The developed method for two step FDCA precipitation has been experimentally proven and optimized, and the maximum FDCA separation yield of ~80% has been achieved when the selectivity of the HMF to FDCA electrolysis selectivity is ~90 % at a feed concentration of HMF of 10wt. Because of the innovative concept with possible industry application, a patent application has been filed. The results of this work and the setup have attracted attention from market parties resulting in a possible follow-up research project in 2017 sponsored by industry.

WP3: System development – Electrochemical H_2O_2

The research in this work package focused on validation of an innovative concept for the electrochemical production of hydrogen peroxide. In order to avoid production of hydrogen peroxide in a salt containing solution it is suggested to utilize so-called solid polymer electrolyte (SPE). Findings from experimental work in combination with lower energy usage is considered as validation of our proposed concept. In addition, we demonstrated the viability of the continuous production of hydrogen peroxide with our laboratory set-up which shows continuous production during a period of almost 100 hours. A patent application has been filed for the proposed concepts.

Photons to Chemicals

Highlights

In 2016 we optimized and up-scaled the procedures, the system, and the experimental reaction catalytic test, for synthesizing the required Au-Pd nanoparticles. In order to test the conversion efficiency and selectivity of the developed catalyst in the Suzuki reaction, a complete reactor has been designed and manufactured. This reactor is equipped with a laser as monochromatic light energy source and a cuvette. With this reactor we are now able to perform catalytic experiments and to test the activity of the different catalysts. During the lasts months we have validated the experimental methodology and we are able to close the mass balance. Under thermal heating the yield achieved is lower than under laser irradiation, using a commercial catalyst.

Table 1. Results of conversion an molar balance of the Suzuki reaction of Bromobenzene and m-TolylboronicAcid in the presence of commercial Au-Pd Nanoestructures (Nanoseedz)

Under the laser illumination[a,b]			Under heating[a]		
Conversion (%)	Molar balance (%)	End temp (^oC)	Conversion (%)	Molar balance (%)	Difference (%)
90.5	96	58	74	98	16.5

a H_2O MilliQ 2 ml; CTAB 36 mg; NaOH 5 mg; 0.08 mmol Bromobenzene; 0.08 mmol m-Totylboronic acid; reaction time 20 min; environmental temperature 25^{o}C catalyst Pd-Au. Reaction product is extracted with diethyl ether 10 ml; Hexadecane as standard.
b Laser power 1.7 W

We succeeded in preparing the catalyst ourselves, being aqueous gold nanorods dispersions. Unfortunately in some cases spherical nano particles were formed during the reaction as a side-product. Also deposition of Pd onto gold nanorods was successful, depending on the Pd content different morphologies can be obtained. Upscaling and reproducibility of the AuNR synthesis will be further improved in 2017.

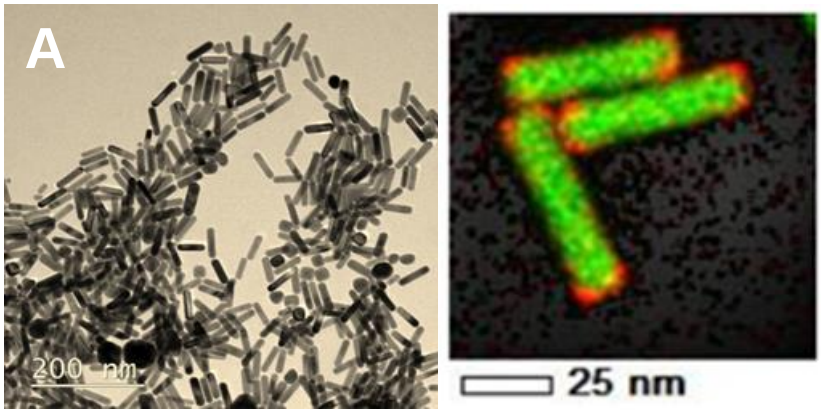


Figure: TEM and TEM-EDX images of two representative large batches **A.** Au nanorod and **B.** Au-Pd nanorods prepared in our laboratory at TNO

Thermochemical storage

Highlights

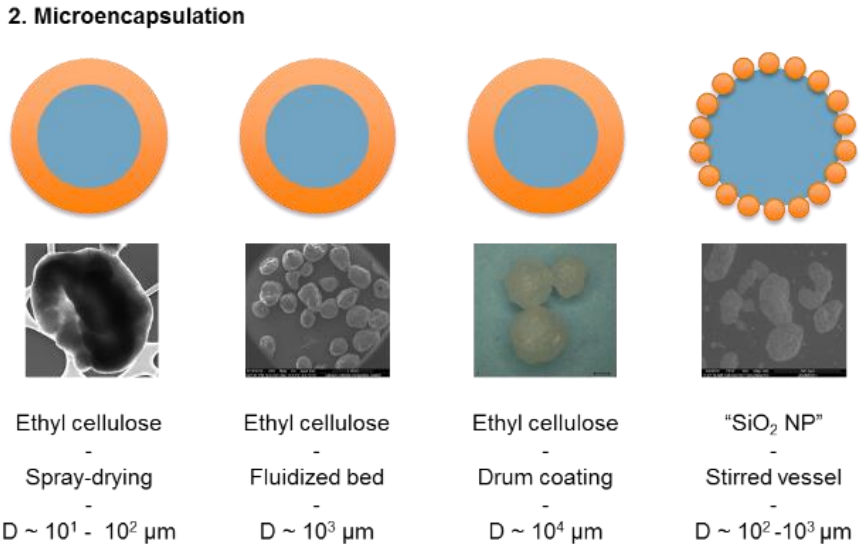
Stable, high energy density storage material with appropriate power has been identified as the weakest element in the chain until now. The ultimate goal is to identify engineering principles for creating competitive heat storage materials based on the solid-solid transitions involving

hydration and dehydration of salts.
The first milestone in reaching this general objective concerns the stabilization of selected heat storage material, whereas optimizing its effective energy density and considering the synthesis methods for upscaling it to competitive industrial production. This formed the starting point of the work in 2015, which is continued in 2016. The use case is a heat battery in an existing building, consisting of a compact thermal storage module that is connected to either a solar thermal panel (use case 1) or to a heat pump driven by renewable electricity (use case 2).

Main results of the work performed in 2016:
• WP1. Basic salt-sorbate selection
For all the alternatives investigated, it had to be concluded that not one salt is ideal in meeting all the requirements. For stability tests CaCl2 has been selected and so far, K2CO3 seems most promising for use case 1. Furthermore, other sorbates were evaluated like NH3, methanol and ethanol.

- WP2. Salt stabilization

At the beginning of this year, it was decided to focus on two potential stabilization strategies, namely 1) matrix-stabilization and 2) microencapsulation. The overall working principle w.r.t. salt stabilization is that the salt is confined in a second inherently stable material. Within those two fundamental stabilization strategies, several experimental procedures for the preparation of composite salts were established. The potentially most successful stabilization concepts using CaCl2 as the starting point are 1) matrix-stabilization with expanded graphite, 2) microencapsulation using fluidized bed coating and 3) microencapsulation applying the “Dry Water” concept. Some concepts are shown in the figure.



- WP3. Standard characterization & tool-box for multi-scale material performance

Various characterization methods have been developed (vacuum TGA), upgraded (pT-o-meter) and started-up (Quantachrome VSTAR) together forming the ‘standard characterization toolbox’ that is now fully functional. For these characterization methods, standard operating procedures and protocols have been developed and used. Results obtained in WP2 have been achieved with these methods.
In addition to the available tools, TGA/DSC equipment for use with relative humidity is in the process of installation, and microscopy with %RH is going to be installed soon.

• WP4. Salt-sorbate design criteria (Modelling)
In 2016 a model was devised using three key processes, transport of moisture, reaction and heat

	transport. Some first conclusions could already be drawn: - Heat transport within the crystal lattice is not a limiting factor. - Hydration kinetics is the key process to focus on, as it is the slowest process of the two processes (hydration and dehydration). • WP 5. Roadmap, multiplication and external interaction The Draft Roadmap that has been made in 2015 was updated to a full report and a summary in Powerpoint. Two meetings with our advisory board took place.
SOSENS - Self Organising Smart Energy Networks	
Highlights	**WP1: Benchmark Smart Grid Coordination Case** The benchmark is a fully defined model & data set of electricity consuming and producing devices, situated in a smart grid context, plus full scenario data (weather time series, usage patterns, etc.), plus clearly defined performance metrics. These can be used to compare smart grid coordination approaches unambiguously. A Renewables Integration Scenario has been defined, with a focus on energy balancing. This is a Northern-European scenario, based on future scenarios for Denmark and Germany, the latter combining wind energy with Photovoltaic (PV) solar energy and the former projecting a high electricity generation share from wind. Based on analyzed energy scenarios, an energy mix and device mix has been chosen. Large-area correlated wind data is acquired using Using data from DTU's CORWIND Model, which is based on a mesoscale weather model (the Weather Research and Forecasting (WRF) Model) with added stochastic variance following probabilistic wind energy variance models. **WP2: Market integration: utility based cooperative planning** We started a literature scan and based on that started developing algorithms that can anticipate on expected future energy demand and production. Special effort was taken to let these algorithms deal with uncertainty in the future energy demand and supply. We applied these algorithms for a bidding strategy for buffered storage. Together with WP3 much effort and time went into aligning the scenario, data, and other details and technicalities. The MATLAB code for the simulations is still in progress. Student Sven van der Kooij supervised by TNO professor Van den Berg finished his thesis. A new H2020 proposal TEMEDRI was initiated. **WP3: Market integration: (near) real time** We started to investigate the current barriers aggregators have for commercialization of their services in the Dutch energy system. Then research is done on how to determine the value of energy flexibility for aggregator services. Two reports were issued describing techniques to characterize aggregated energy flexibility as well as to characterize multiple aggregator applications. In the meanwhile a machine learning flexibility forecast model is created and verified in multiple simulations. This all led to four publications, two publications on the flexibility forecast model, one on the characterization of aggregated energy flexibility and one on using the flexibility model for trading flexibility on multiple energy markets. **WP4: DTU Fellowship** The fellowship started in August 2015 and will run for 2 years.
Program dynamics	The lead scientist and the program manager will change in 2017. The contents of the plans for 2017 are in line with the original planning at the start of the ERP.

6 3D Nanomanufacturing Instruments

General data	
Title	3D Nanomanufacturing
'Topsectors'/Societal Themes	HTSM
Contact person TNO	Hamed Sadeghian, Rogier Verberk, Nicole Nulkes
Contact person government	Michiel Ottolander (EZ)
Progress 2016	
Abstract	Towards enabling reliable manufacturing and metrology of 3d nanostructures, in 2016 several technical and partnership milestones have been achieved. Here we summarized these achievements. Within the ERP 3Dnano two methods for manufacturing nanostructures with very high resolutions have been experimentally demonstrated. One relies on the nanomechanical modification of materials, and the second method is based on the concept of thermal nanolithography, developed originally by IBM Zurich and turned into an instrument by the company Swiss Litho. In a collaboration with SwissLitho, the combination of the high-throughput parallelized AFM technology developed by ERP 3Dnano, with the SwissLitho NanoFrazor made a major breakthrough towards industrial application of the NanoFrazor lithography and the parallelized scanning probe technology for high-throughput manufacturing and metrology. Several subsurface nanoimaging methods have been also experimentally demonstrated in 2016, which is considered as breakthrough in metrology of a new generation of nano products such as memory and processors. This technology can also be used for imaging inside biological samples at cell level, which can reveal more information compared to morphological imaging. Within the technology platform of optical nanometrology, the concept of super oscillatory lenses for super resolution imaging have been experimentally demonstrated and the benefits and the drawbacks of the technology have been determined. Feasibility study and experiment on miniaturized positioning and metrology platform has been performed. This platform is required for several metrology applications, in order to meet the requirements, i.e. accuracy, speed and stability. These technology platforms, will contribute to the following applications; - Critical dimension metrology for beyond 10 nm nodes - Alignment and overlay measurement , with the use of imaging through layers - Manufacturing and overlay metrology of 10 nm contact holes - Low cost per device or surface area, very high speed of measurement. - The ability to flexibly manufacture and resolve 3D features below 10 nm with high aspect ratio. Moreover, serious efforts have been started on development of X-Ray metrology, in collaboration with TU/Eindhoven and TU/Delft. Several collaborations with industrial and academic partners were intensified and started. These resulted in 5 new PhD projects, 9 new industry related projects. In total the program has yielded 43 patents filed, 18 external conference papers, 10 invited lectures, 59 conference posters and 6 journal papers.
Short description	Reliable manufacturing and metrology/inspection of 3d nanostructures allows development of several important applications, among them Internet of Things, medical diagnosis devices (cancer, bacteria, virus) for ultra-early detections at cell and sub-cell level. Moreover, the market growth of semiconductor industry has a great impact on Dutch and European economy. Using strategic innovation, the Netherlands has been able to keep a competitive advantage in the

	development of equipment and instruments for nanometer-sized patterning, manufacturing and measurement. Examples include UV-light assisted patterning (ASML) and electron beam imaging (FEI). In order to sustain a competitive edge for the semiconductor industry, enhancing yields and reducing the cost and the time-to-market are essential. This has to be done while simultaneously maintaining reliable (nano-) manufacturing. The process geometries and device dimensions are shrinking to the level that conventional technologies currently used for production and quality control are approaching physical boundaries and will appear neither technologically nor economically feasible. Besides shrinking the critical dimensions even further, 3D scaling is anticipated to introduce new functionalities and to make optimum use of the available space. Primary Use case: The primary application focus of this ERP will be on equipment and instruments for 3D "nanomanufacturing" and "nanometrology" of future 3D nano-electronics devices. The major requirements are (from ITRS): - Very high resolution and sensitivity to be able to detect 3D structures down to ~10 nm and high aspect ratio (20). - Very high speed of measurement on large area such as 100 cm2 / hour. - The ability to flexibly manufacture and resolve 3D features below 10 nm with high aspect ratio. - Low cost per device or surface area. 4-year Target: Proof-of-concept of technologies for 3D nanomanufacturing and nano-metrology in experimental setups/hardware/built devices for the main applications mentioned above.
3D Optical Nano Metrology	
Highlights	Results of our research on Nano-antenna's, Flat lenses and SIL microscope. **Nano Antenna's**: The performance of Nano-antenna's for particle detection is simulated (in rough approximation) and looks promising. Due to the low TRL of the technology the follow-up research will be done by a master-student together with AMOLF. **Flat lenses**: A feasibility study on the application of Multi Lens Arrays for Mask less Lithography has been done. This can be a solution for an application with little volume for optical components.. **Sil Microscope**: For the SIL microscope, technology limitations are investigated such as objectives for 193nm and different SIL materials and manufacturing processes. **Our results on the feasibility of SOL lens**: Imaging of sub-diffraction limited structures is experimentally shown. The experimental images were taken from isolated features. There are doubts about the feasibility to image extended, random objects because of inherent stray light issues of SOL lenses. This has been shown in simulations and is confirmed by first tests. Final tests are still being executed. **Our results on X-ray metrology**: These measurement systems could characterize the 3D shape (and/or composition) of nanoscale-structures based on determining the phase of x-ray wavelength electromagnetic radiation that has interacted with these structures. A technology overview of different x-ray principles has been made. Promising techniques for semiconductor metrology are: CD-SAXS, X-ray microscopy, x-ray ptychography.
3D Nanotomography	
Highlights	We have developed two concepts for subsurface nanoimaging: **Sub Surface Probe Microscopy (SSPM):** Acoustic excitation from bottom by transducers or from top by AFM tip, detection by AFM tip.

Photo Thermo Acoustic Imaging (PTAI): Allows optically excite and detect, has a good depth and can potentially look deeper than SSPM.

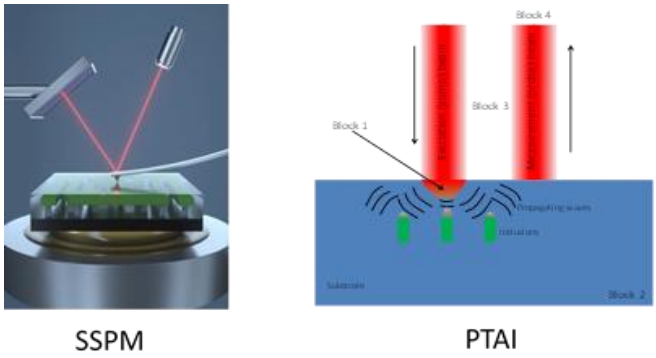


Figure 1: SSPM (Sub Surface Probe Microsopy) and PTAI (Photo Thermo Acoustic Imaging.

Sub Surface Probe Microscopy (SSPM)

Theoretical and experimental study of the different contrast mechanisms of subsurface for MHz and for GHz for several use cases have been done and documented. Theoretical and experimental study of new AFM modes and excitation modes for nanoimaging:

- A dedicated non resonant AFM mode was developed, implemented and verified to minimize tip sample interaction forces and contact time. The feasibility study showed that the developed mode has the desired potential for non-destructive sub surface nanoimaging.
- Pulsed acoustic excitation. The feasibility has been studied. The conclusion is, that the interference pattern is significantly reduced when applying a short pulse

First experimental results using GHz excitation have been achieved and proven feasible.

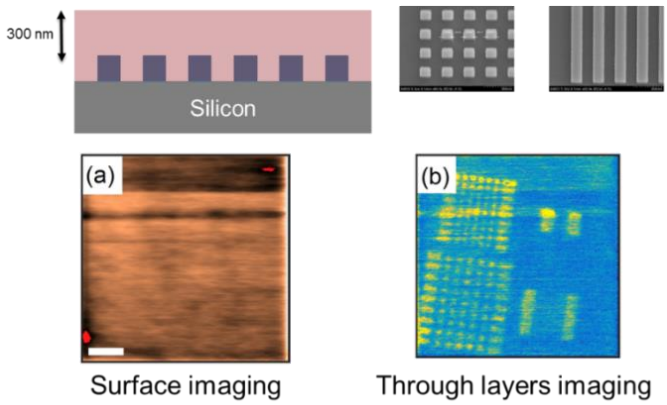


Figure 2: experimental proof of principles of subsurface nanoimaging in hard patterns under soft resist.

Photo Thermo Acoustic Imaging (PTAI)

Theoretical feasibility study of Photo Thermal Acoustic Imaging (PTAI) for sub surface nano-imaging. Conclusion from this analysis is that for some cases only detection of a nanostructure is possible, and in other cases, the size of the surface displacement might allow for resolving and imaging of the nanostructures.

Patents and papers to secure IP and create right to play.

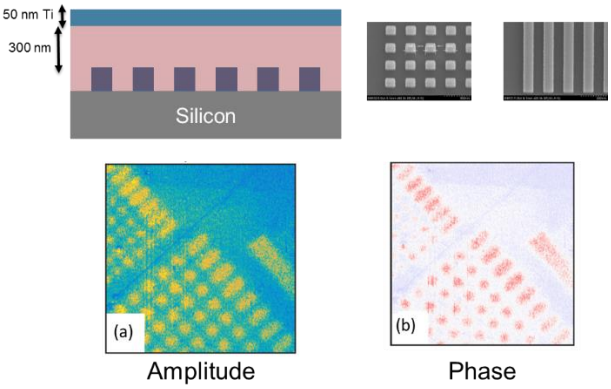


Figure 3: experimental proof of principles of subsurface nanoimaging in hard patterns under multiple layers.

Cooperation with other parties

Qtech, supplied samples with buried nanowires free-of-charge.
Smart Tip supplied electrostatic cantilevers.
For ASML we did a feasibility study for the use of TNO Sub Surface Nano-Imaging for metrology applications.
For Intel we performed the feasibility of aligning contact holes on top of the lines via subsurface nanoimaging.
Figure 4 shows one image proof of principle of subsurface nanoimaging of 50 nm periodic dense nanowires.

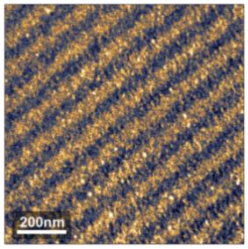


Figure 4: subsurface

3D Nanomanufacturing

Highlights

In 2016 a collaboration with IBM and SwissLitho (50%-50 %) started to show the proof of principle of scanning thermal nanolithography.

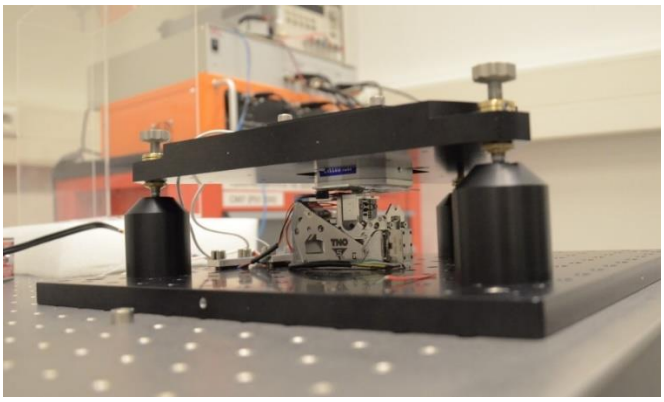


Figure 5: Experimental setup developed in collaboration with Swiss Litho for nanopatterning.

Figure 6: Swiss Litho and TNO logo patterned by the experimental setup shown above.

Following the collaboration with TU Delft (in 2 PhD projects), within the ERP 3D nano on interactions at nano-scale and the application in nanomanufacturing, Intel Corp. started a

collaboration on the feasibility of manufacturing 10 nm contact holes (for future memory applications).

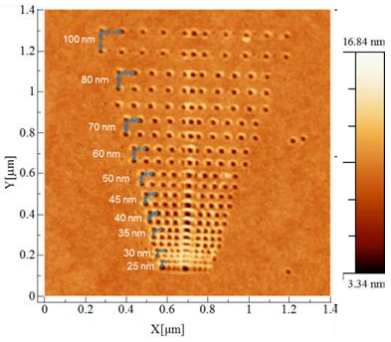


Figure 7: nanopatterned contact holes with the method developed within ERP 3Dnano and in collaboration with Intel. The sample was provided by Intel.

A collaboration was started with HTCS, TU/e (2 PhD projects, one financed via Impulse program TU/e) for developing technologies for nanomanufacturing and in-situ metrology with the use of self-assembled monolayers and Direct self-assembly.

Advanced Control and Mechatronics

Highlights

Positioning Platform is a flexible, wireless, multi-tool positioning platform which can position tools on a wafer or a mask independently. The architecture of the positioning platform has been setup in 2016, the first version is being realized to verify the feasibility and critical technologies. Main purpose is high throughput and parallel 3D nano imaging and manufacturing. The small footprint enables:

- multiple tools per wafer or mask
- flexible parallelization and high throughput by using multiple independently positioned carriers.

The carriers are based on magnetic levitation which enables combination of large stroke and fine resolution with little disturbances from the environment. A matching metrology system for measuring the multiple carriers' positions has already been identified as critical and is being investigated separately.

<u>Application area's</u>

- Positioning of AFM, optical and manufacturing tools
- Wafer and mask Inspection
- Lithographic processing and repair tools.
- Rapid manufacturing tools with increased speed (by parallelization).

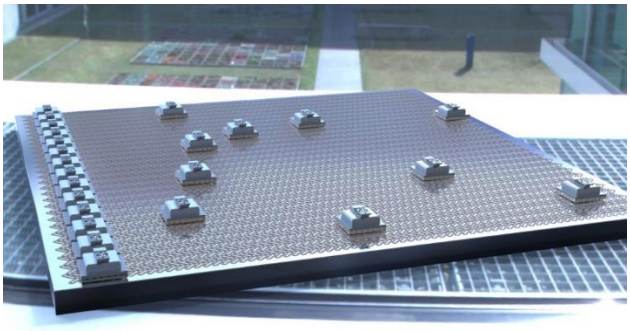


Figure 8: Positioning platform

Cross over projects

Highlights

<u>Bio nano medical Instruments</u>

In 2016 the in-line cell monitoring versus external stimulus was experimentally demonstrated. Hands on experiments have been done to gain experience of AFM measurements on biological samples. An initial long-term roadmap on the development of bio-nano instruments has been developed. This roadmap is currently used to tailor the research on bio-medical instrumentation within and outside this ERP. A collaboration with TNO Zeist and ERP organ on a chip was intensified.

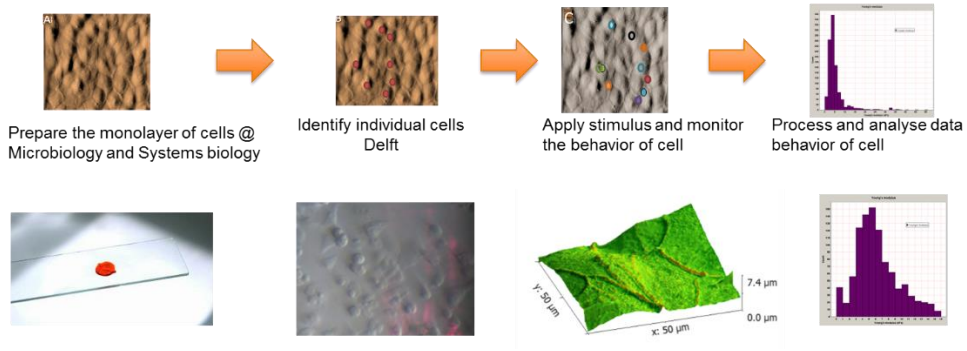


Figure 9: In-line cell monitoring versus external stimulus

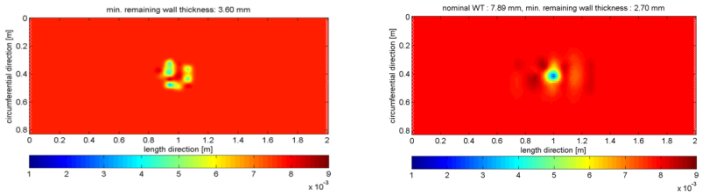
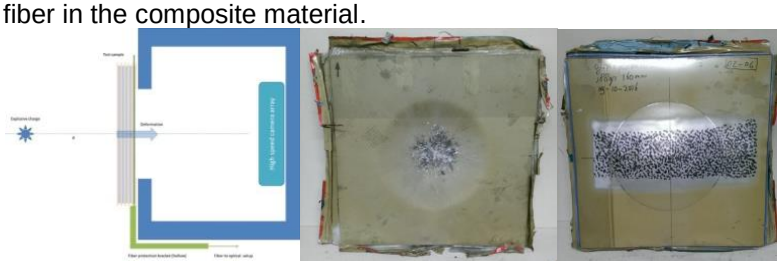
Granted spin off projects
- H2020 - FETPROACT proposal VIRUSCAN (2017 – 2021)

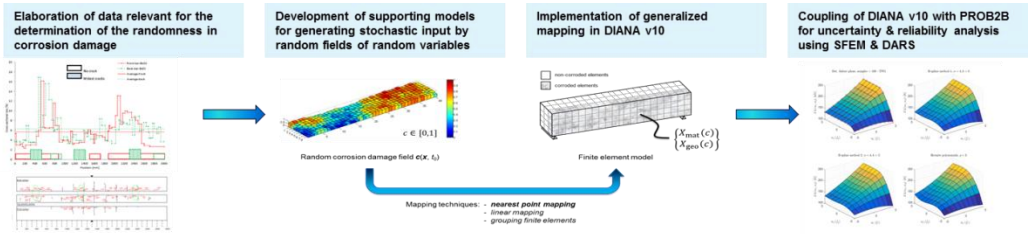
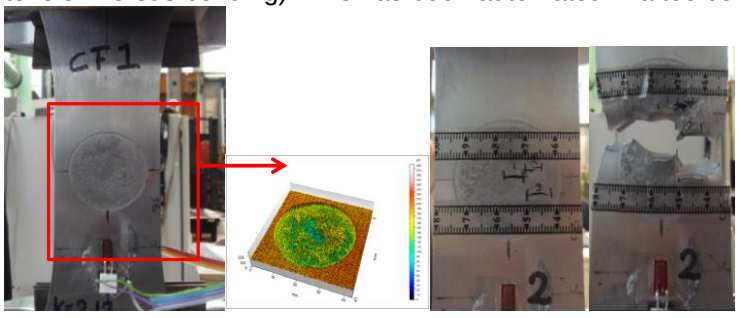
Collaborations
- VIRUSCAN consortium (e.g. RUG - Wouter Roos).
- Collaboration with CBRN protection
- Investigating MSc/PhD possibility for next years

Program dynamics	The research topic of Metamaterials will be to a large extent re-oriented. It has been concluded that the super oscillatory concept cannot surpass the resolution of 100 nm, which is not sufficient for Nano inspection. The concept of hyper lens will not actively been persuaded, and only via the ongoing PhD collaborations with TU Delft. More focus have been put on the nanomanufacturing (collaboration with SwissLitho). The Nanoantenna's imaging will be done via collaboration with AMOLF and not at TNO, since they are more experienced in this topic. Instead we will focus on development of X-ray nanometrology which has shown to be promising for sub-10 nm imaging. Several PhD collaborations with TU/e and TUD started for the development of X-ray nanoimaging.

7 Structural Integrity

General data	
Title	Structural Integrity
'Topsectors'/Societal Themes	Energy, HTSM
Contact person TNO	Henk Miedema
Contact person government	Michiel Ottolander (EZ)
Progress 2016	
Abstract	Early Research Program (ERP) Structural Integrity (SI) aims to safeguard structural integrity of macro structures (e.g. bridges, offshore windmills, wells etc.) while reducing maintenance costs and maximizing the availability of the structures. The main principle of the ERP is optimising the operation and maintenance of a structure by knowing the exact state of a structure and being able to predict its future state (Condition-Based Maintenance, CBM).  ERP SI works use case driven, and 4 use cases are addressed simultaneously: 1. Concrete bridge (corrosion of steel rebar) 2. Offshore wind (support structure) 3. Well Integrity (abandonment of wells) 4. Composite Vehicle (lightweight military vehicles) Knowing the exact state and predicting the future state of a structure requires advanced models and new sensing technologies. Both are being developed in ERP SI for each use case.
Short description	Condition-Based Maintenance (CBM) based on monitoring and forecasting the integrity of structures, is the most effective way to safeguard structural integrity while reducing maintenance costs and maximizing the up-time of the structures. It can also be used to allow utilisation of a structure in a different way than it was originally designed for. The multi-disciplinary and challenging nature of the problem, its current embryonic stage of development, and its tremendous potential for safety and economic benefits qualify CBM as a 'grand challenge'. ERP Structural Integrity aims at breakthroughs with respect to this grand challenge which enable: *"detection and monitoring of (precursors of) degradation inside steel/cement/concrete structures"* and use this information for *"diagnosis of their structural health and forecast the service life for various intervention options"* The program will have wide application for maintenance of macro-structures, in particular in the *transportation infrastructure* and the *energy production infrastructure*. In addition it will be the basis for improved design of macro-structures. It is important that the sensing and inspection technology as well as the models for structural integrity are developed in this single program. The output of sensing and inspection is input for modelling and vice versa modelling defines the parameters to be observed. Hence, the input data that models require and the information that sensing and inspection can provide must match. Advanced acoustic sensing, fibre optic sensing, (multi) sensor systems and sensor system design and corresponding modelling tools (incl. interpretation methods and handling procedures)

	will be developed for monitoring loads, resistance and time dependent degradation in all four use cases.
Issue 1: *"Advanced sensing and inspection technology"*	
Highlights	1. *Delphi full-waveform model (use case well integrity)* Good progress has been realized in adapting the Delphi full-waveform model from seismic applications covering large area using low frequency to Non Destructive Test (NDT) covering small areas with high resolution using ultrasound. The method is found to produce improved reflectivity images with less noise and a better resolution. It is concluded that it can be used to enhance the performance of the existing logging tools.  Coorossion spot detection: isotropic ray-tracing (left) and anisotropic Delphi Wave-field extrapolation (right) Another important outcome is that the full-wavefield modelling tool is also suitable for application as modelling engine in tomographic inversion, applied in the TNO ultrasonic corrosion monitor method. In this application there is no reflectivity, but the speed of sound varies laterally because of defects. This causes the wavefield to become rather complex after they have passed the defect. Ray tracing (the conventional forward modelling engine) does not give satisfactory results for all defect sizes and shapes. The first tests of using full-wavefield modelling for this purpose show better images of defects (size, depth) than the corresponding images obtained with ray-tracing as modelling engine. 2. *Active acoustic monitoring of number and size of cracks in a concrete slab (use case concrete bridge)* Tests have been carried out together with our strategic partner BAM. The feasibility of using ultrasonic bulk waves for inspection of the interior of concrete structures has been demonstrated. Based on the acquired insight from numerical and experimental evaluations, the presented characterization framework enabled quantitative classification of concrete cracks in the measurement area in terms of total crack zone width (translatable to number of cracks if the width of one crack zone is known). The framework is likely to be extendable to crack width detection, and also to be implementable in a tomographic scheme for improved assessment. 3. *High speed strain sensing for blast testing of composite material (use case composite vehicle)* Tests demonstrated that it is possible to measure rapid strain deformation during a blast. Fiber optic deformation measurements during an explosion were successfully carried out after embedding the fiber in the composite material.  Schematic overview (top view) of test setup and test sample (d = 160 mm) front (left) and back (right)

Program dynamics	The work on Measuring small leak flows above the sealed area of an abandoned well ("smart plug") was stopped since the fiber optic technology could not meet the requirements and did not give the outlook to a solution useable in practice. In order to make faster progress in one area, after basic experiments the work on active acoustics for rebar corrosion was stopped and focus was put on the work on Active acoustic monitoring of the number and size of cracks in a concrete slab
Issue 2: *"(Multi-scale, multi-physics, probabilistic) models"*	
Highlights	Highlights for modelling are formulated for each of the four use cases. *Concrete bridge* Major steps have been made 1. to enable accurate and efficient full probabilistic numerical modelling of reliability and residual strength of existing concrete bridges , 2. to enable the use of in-situ data for model selection and model updating, 3. to account correctly and non-conservatively for the effect of corrosion damage in analysis of structural response of a bridge, 4. to enable monitoring of a corrosion process in existing concrete structures, 5. to simulate corrosion propagation in case of chloride-induced pitting corrosion. In particular: full- probabilistic simulation tools (SFEM, DARS) have been coupled with PROB2B environment (TNO proprietary tool) for commercial FEM software to cope with baseline assessment of an existing concrete bridge, making use of stochastic input generation for FEM including random corrosion fields.  *Offshore Wind* TNO now has a design methodology incorporating a more fundamental understanding of fracture mechanics. This methodology will eliminate many of the current weaknesses in fracture mechanics assessments, namely sensitivity to geometry, loading rate, loading history, and type of loading (e.g. tension versus bending). This has been automated in a toolbox.  In addition, newly acquired testing facilities enable validation of improved corrosion fatigue models. With the improved corrosion fatigue models, input can be provided for the update of design codes and maintenance guidelines of steel structures in corrosive environments which now tend to be conservative because special guidance for the fatigue strength in corrosive environments is lacking.

	Well Integrity Geomechanical and geochemical models have been developed at the required field scale and simulations were performed to identify the critical uncertainty parameters which significantly affect model outcome and leakage probabilities. The Baysian Believe Network (BBN) has been further developed using insights from the simulations to build the framework of causal relations between primary parameters and relevant degradation processes. For the numerical models computer codes were written to perform Monte Carlo simulations and the first sets of simulations were performed to assess the range in simulation outcomes on leakage probability using the key uncertainty parameters. This workflow was applied to a real and representative offshore well, critically evaluating all data available from the well and translating the data to model input. This exercise demonstrated the use of the BBN to evaluate leakage risks of wellbores and showed for which critical parameters should be measured or monitored in a well in order to decrease the uncertainty in leakage probability. *Composite Vehicle* Major steps have been made: 1. TNO now has a reliable load- prediction model taking into account the structural response during the blast load, 2. the extreme load conditions can be moderated by the target, 3. the material has been modelled for a flat & curved geometry, 4. the "bonding-debonding" effect has been evaluated for the flat configuration, confirming the original TNO idea, 5. the 2 test series and the extensive analyses revealed a "treasure" of information on the dynamic response and damage mechanisms of the material
Program dynamics	- Increased focus on demonstration cases for all applications - Development of framework for FEM model updating for use case Bridge moved from 2017 to 2016 in order to enable implementation of US (Acoustic tomography) measuring method for reliability assessment in 2017 - Data assimilation moved from 2016 to 2017 for use case Bridge and Well Integrity. This is due to preparation time needed for the experimental part of demonstration case. - Work on an idea for a Non-destructive fracture testing method was stopped. This experimental method was tested at the TU Delft Materials Sciences laboratory. While the experiment did not show the desired failure mode, the concept behind it opened up further concepts. Several new ideas have been identified based on the same theory that are much more promising, and they are currently being evaluated for possible joint industry projects.
Issue 3: "*Building the ecosystem"*	
Highlights	Involving stakeholders and crucial peers from the start and by organizing field tests of the technology developed for each of the four use cases, will be useful in addressing the ERP's challenges. Related to the use cases, TNO initiated several applied and scientific projects with involvement of industrial partners across the supply chain and in collaboration with research institutes. An important aspect of creating the ecosystem is bringing together the value chain from industry with academia and RTOs. From the scientific network the most important peers are involved such asTU Delft; ECN; Bundesanstalt für Materialforschung und –prüfung (BAM). *Concrete bridge* For the use case Concrete Bridge we aim at a demonstrator setup similar to the earlier one for steel bridges (Van Brienenoord bridge). With two major cities (Rotterdam and Amsterdam), we

	are making plans for a demonstrator. In addition to such a field lab in the Netherlands. we are exploring the possibilities in Germany with BAM/BASt, in Japan with NEDO (New Energy and Industrial Technology Development Organization) and in South Korea with KICT (Korean Institute of Civil Engineering and Building Technology). The Technology position of TNO is enhanced in this field in such a way that we are becoming the most interesting knowledge partner for bilateral collaboration and H2020 projects. Our unique expertise is our integrated concepts and tools for evaluating existing bridges. *Offshore Wind* TNO is regarded as the specialist on fatigue and corrosion related challenges. We extended this position towards being an expert on structural health prediction. The knowledge obtained through the fracture portion has made TNO into a leader in an analysis method that can be applied for a number of different fracture applications and will bring us in many fracture projects. TNO is one of the founders of GROW: a consortium of around 20 leading players to reduce the costs of offshore wind to a competitive level in the near future. Several new national and international initiatives utilize developments in the ERP SI related to monitoring strategies (e.g. in TKI wind op Zee Monitor-2) and multi-physics models (e.g. in TKI HTSM Material Transition Program). *Well Integrity* Market consultation is ongoing (national and international regulatory agencies, industry operators, investors, and well integrity risk consultancies). There is also a permanent need for input for TNO's governmental advisory task on well integrity issues (ministry of economic affairs via SoDM, primarily through the Advisory Group of Economic Affairs (AGE)). TNO is main partner in a H2020 project consortium led by the British Geological Survey (with other members a.o. the Polish, Danish, and French geological surveys, and Shell). This project (to be submitted January 2017) develops Best Practices and performs field validation of quantitative risk assessment for leakage risks in CO2 storage and unconventional gas. TNO's work in the ERP has resulted in a leading role in the well-integrity risk component. A strong link with the national program "Mijnbouw effecten" ("Mining effects") will be elaborated in 2017. *Composite Vehicle* The use case Composite Vehicles links with the TNO-TU Delft collaboration on "impact dynamics of structures and materials" and the European Defense Agency (EDA) L-AMPV project. This project of EDA (Germany, Italy, Spain, Portugal, The Netherlands) expresses the need for low weight (i.e. composite) development for Force Protection applications and aims at a full scale demonstrator product. In 2016 TNO collaborated closely with a composite manufacturer and a vehicle manufacturer, in 2017 this will be continued and strengthened. Also the Ministry of Defence will be involved closely.
Program dynamics	In 2016 the ecosystem has taken shape. While initially there were many potential partners, we have put focus on strengthening relations with complementary knowledge partners and seriously interested market parties. Also 2016 is the year in which first steps towards a long term program Macro Structures Research (MASTRE) have been made, materializing this program will be a key issue for 2017.

8 Human Enhancement

General data	
Title	Human Enhancement
'Topsectors'/Societal Themes	High Tech Systems & Materials; Logistics; Energy; Water; Life Sciences & Health
Contact person TNO	Jan Maarten Schraagen
Contact person government	Michiel Ottolander (EZ)
Progress 2016	
Abstract	For the Personalised Adaptive Cruise Control (P-ACC) use case a first version of a driver style model has been develop for certain scenarios. To be able to implement the driver style model in a car, also a car following scenario recognition algorithm has been developed. For the Adaptive Virtual Tow Bar (A-VTB) use case, we have developed a first version of a driver readiness model, in which we predict how long it will take for a driver to get back in control. We found that we need to combine information on feet-pedal position, hand position, eye scanning behaviour, seating position and either having or not having a secondary task to predict driver readiness. This is very important in order to predict whether it is or is not safe to hand over control. The driver readiness model, based on literature findings, was implemented in a demo version on a computer and in the driving simulator. The mail goal for 2017 is to develop the first computational driver models for P-ACC and A-VTB in a (simulated) vehicle. This will be done based on the data gathered in the different experiments in 2015 and 2016. For the stationary Dynamic Positioning (DP) use case, we believe that alarm-based DP systems cannot be advanced further increasing automation. Therefore, we propose a human-centered approach to DP systems which combines multiple technologies in an intelligent software agent, called IOSS (intelligent operator support system). IOSS allows the operator to be roaming and do other tasks in quiet conditions. When conditions become more demanding, the IOSS calls the operator to return to his stationary position. In 2016, a proof of principle for the IOSS was developed (published through the TNO YouTube Channel: https://youtu.be/MH0Vj-rChrM). The main goal for 2017 is to add capabilities to the IOSS in order to support operator situational awareness in all the phases of the task execution. In 2016, knowledge development in the Research Line Human Resilience was driven by two use cases: professional sports and police. Close collaborations took place with NOC-NSF, specifically the KNKV (Koninklijk Nederlands Korfbal Verbond), and the Dutch Police (see https://time.tno.nl/nl/artikelen/hoe-we-beter-met-stress-kunnen-omgaan/). The data collected in the trials with the KNKV and the Dutch Police were used for furthering the knowledge development concerning resilience modelling, monitoring, measuring, and providing resilience feedback. In 2017, the research line Human Resilience will conduct a second data trial with the Dutch Police. Informed by the trials, the modelling approaches and the monitoring and feedback platforms will be further developed.
Short	We are currently facing an increasing level of automation of systems that process a large size and

description	diversity of data in e.g. the industrial (maritime and offshore) sector, but also in the mobility sector (automated driving) and the public sector in general (eCoach apps)[9]. Although fully automated systems may be a future vision, it is broadly accepted that at this point in time the behaviour and interaction of users with these systems is still the key to successful innovation, which requires an optimized human-system interaction and collaboration. We need further breakthroughs in our knowledge to be able to develop the next generation of adaptive systems for persistent, safe and efficient operation, which perform well both for nominal and off-nominal situations (e.g., adapting to patterns and anomalies in process data). The first ambition of this Early Research Program (ERP) Human Enhancement is to develop a *transparent* (human-in-the-loop) adaptive automation platform that substantially improves safety and efficiency for scheduling, supervision, control and modification tasks, based on a computational human model to assess current and predicted human task load, and a domain model to assess the goals, processes and resources. This will be the focus of the use case ***Adaptive automation.*** The *second* research ambition of the Early Research Program (ERP) Human Enhancement will be the development of a multidimensional prospective model for human resilience and related monitoring instruments and organizational interventions. At present, almost half of all work disability is related to psychosocial factors, which is a rise from 30% since 1998[10]. Front runner companies realize that an increase of human resilience and intrapreneurship are prerequisites for improvements in human health and organizational performance. However, adequate resilience tools and interventions are lacking, resulting in large personnel and organizational costs[11]. This means that measures to improve resilience are not only important for maintaining health and operational performance, but will also result in potential large financial savings. Although the importance of supporting employee's resilience is widely accepted, an integrated theory is still lacking, mainly due to the large number of factors determining human resilience. Therefore, the ambition of the research line ***Human Resilience*** in the Early Research Program Human Enhancement is the development of a model based resilience monitoring suite for personalized resilience advice and organisational interventions.
Highlights	*Automotive use case* The philosophy that one system fits all is changing in the automotive world. However, most systems are still sold as a system with specific characteristics, for which some settings are adjustable, but not adaptive. Although the automotive industry is asking for these features, there is not much research being done in how to tackle this area of expertise. For TNO, discovering the world of adaptive automation is extremely important, since it cannot only lead to more driver comfort and acceptance, but it may therefore also lead to safer situations. This is twofold. On the one hand, if there is less automation surprise, people will overrule the automation less often, and on the other hand when automation can predict whether a driver is able to perform the driving task well or take over control in time, this will also be beneficial for traffic safety. This means that we will develop two approaches that are unique: - Online (momentary) driver style and adaptation of automation to the driver style - Driver readiness models, predicting how long it will take a driver to get back in the loop and how much support needs to be provided after this transition.

[9] Kenniskamer Intelligente Robots: Feiten, fabels en ficties. Publicatienr: j-9163. Pagina 45-49. Den Haag: Ministerie van Veiligheid en Justitie.
Kool L., J. Timmer and R. van Est (ed.), Sincere support. The rise of the e-coach. The Hague, Rathenau Instituut 2015.
[10] Minister Sociale Zaken en Werkgelegenheid. Kamerbrief hoofdlijnen aanpak psychosociale arbeidsbelasting. 2014.
[11] RTO-MP-SAS-095. Cost–Benefit Analysis of Resilience Training. How to reduce post-deployment psychosocial strain, psychopathology, and associated costs. V.L. Kallen & J.E. Korteling

In 2016, for the P-ACC use case a first version of a driver style model has been developed for certain scenarios. The concept is that it mimics the driver style, although we are not sure if this is what all drivers prefer. The selected scenario is ‘car following’. To be able to implement the driver style model in a car, also a car following scenario recognition algorithm has been developed.

For the A-VTB use case, we have developed a first version of a driver readiness model, in which we predict how long it will take for a driver to get back in control. For this we have found an important time difference between driver monitoring the system and surroundings and a driver being out of loop. Also we found that we need to combine information on feet-pedal position, hand position, eye scanning behaviour, seating position and either having or not having a secondary task to predict driver readiness. This is very important in order to predict whether it is or is not safe to hand over control. The driver readiness model, based on literature findings, was implemented in a demo version on a computer and in the driving simulator. For demonstration in the truck, driver monitoring was first considered out of scope for the EcoTwin III project. However, later RDW and SWOV emphasised the importance of driver monitoring to ensure timely response of the driver to take over during platooning.

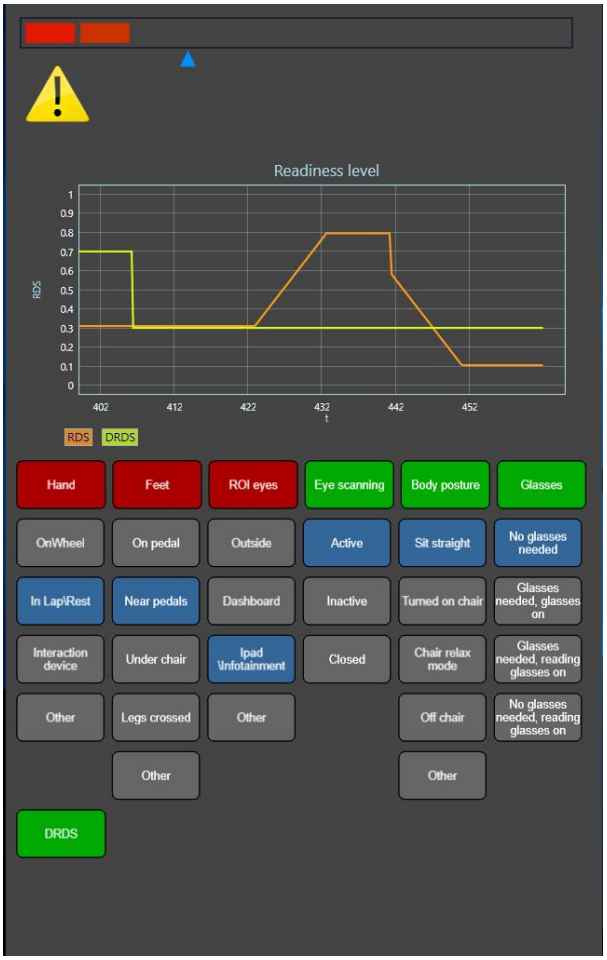


Figure 1. *Driver readiness model (demonstrator in truck simulator)*

Maritime use case

Dynamic positioning (DP) is a computer-controlled system which aims to maintain a vessel's position and heading using dedicated propellers and thrusters. DP operations form the basis of Floating Production, Storage and Offloading (FPSO) platforms and are a typical example of a highly automated control task that still requires human supervision: four operators are working in shifts 24/7 to monitor the system and resolve malfunctions in case this cannot be done automatically. Alarms are typically used to detect whether measured values are beyond threshold values, and serve as the primary means to trigger operators to solve malfunctions and abnormalities. Monitoring alarms is a tedious task for which human operators are not well-equipped and which may result in out-of-the-loop performance problems. Introducing a more self-sufficient control system, that is, automation that can deal with an increased range of conditions, will cause the DP operator to be less occupied during his work shift, but still requires the operator to be present. Therefore, such a system does not lead to reduced personnel costs, and, even worse, safety problems might be introduced caused by drowsiness of the operator whose job has become very dull and who is out of the loop in case sudden interventions are required.

We believe that alarm-based DP systems cannot be advanced further to solve this impasse (which is sometimes referred to as the automation paradox). Therefore, we propose a human-centered approach to DP systems which combines multiple technologies in an intelligent software agent, called IOSS (intelligent operator support system). IOSS allows the operator to be roaming and do other tasks in quiet conditions. When conditions become more demanding, the IOSS calls the operator to return to his stationary position.

We take a systematic approach of alternating technological and human factors (HF) perspectives which we have followed to develop the first prototype of IOSS. In 2016, we incorporated predictive analytics technology in IOSS, a technique which we believe is crucial in enabling a roaming operator, and which generally is expected to play a major role in future maritime systems. Predictive analytics can be used to predict future situations based on data from the past using machine learning algorithms. For example, to predict whether conditions are expected to stay stable, allowing the operator te leave, or to predict when alarms are likely to come up, requiring the operator to return to stationary position. We have closely cooperated with Rotterdam Mainport University, Bluewater and RH Marine in conducting task analyses of the DP operator and acquiring realistic data sets.

Figure 2. *IOSS in stationary condition*

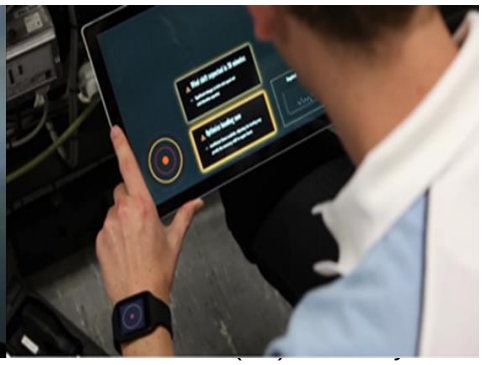


Figure 3. *Using IOSS in mobile condition*

We ha

will then be provided once it has been detected on the basis of eye movements that the operator's SA has decreased.

Sports and police use cases

In 2016, the knowledge development in the Research Line Human Resilience was driven by two use cases: professional sports and police. Close collaborations were continued with NOC-NSF,

specifically the KNKV (Koninklijk Nederlands Korfbal Verbond), and the Dutch Police. Two data collection trials were conducted at the KNKV. A total of 35 athletes (consisting of the national korfbalteam and the junior national korfbalteam) used the mobile resilience application developed in the ERP for 2 periods of 4 weeks, collecting physiological and psychological data. The athletes received feedback about their resilience, and possibilities to enhance their resilience. After processing the data collected in the KNKV trials, and further developing the mobile resilience application, another data trial was conducted at the Dutch Police, in collaboration with the department of Veilig en Gezond Werken and the operational unit of Maas en Leijgraaf. Thirty-five police officers used the mobile resilience application for a period of 5 weeks, collecting relevant resilience data. All work packages contributed to the data trials, and used the data from these trials to further develop models, frameworks, and technology.

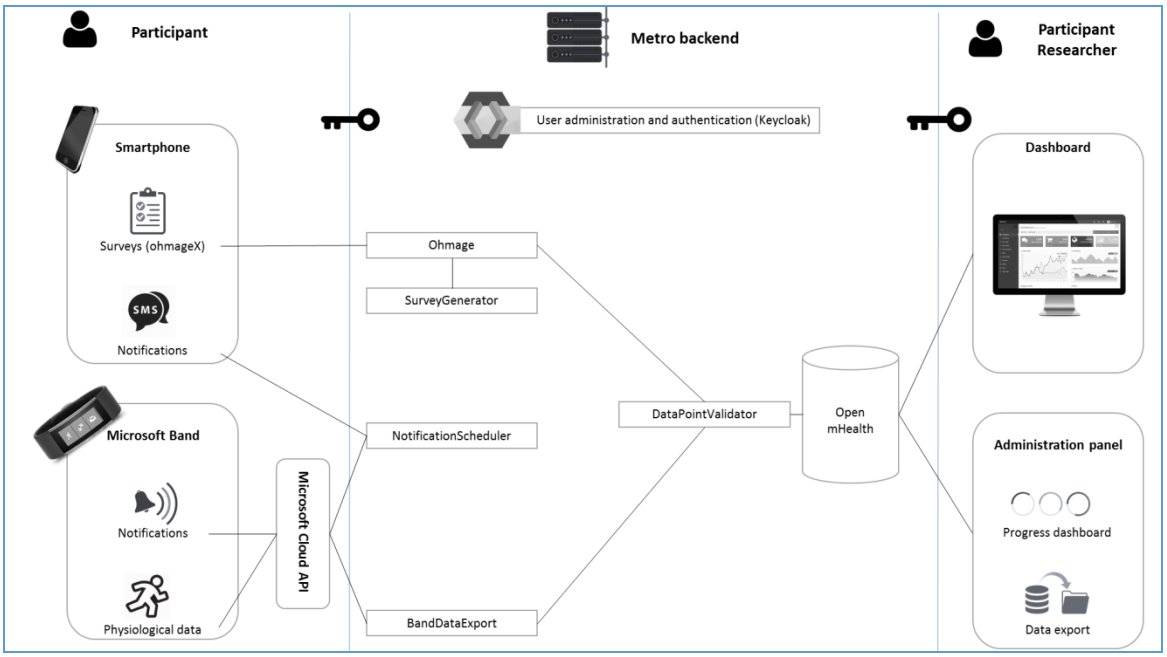
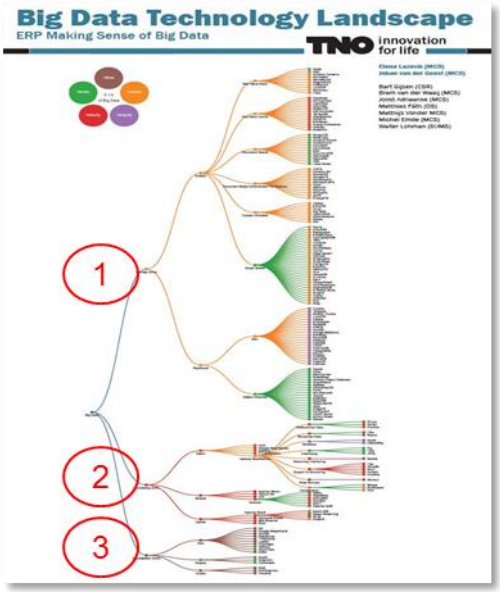


Figure 4. *Graphic representation of modular architecture used for prototype of wearable resilience application.*

Program dynamics	With regard to the original plan, the research line Adaptive Automation will be extended with a third use case in the area of Cyber Security. This implies reductions for the automotive and maritime use cases, as the total budget has not increased. Fortunately, all use cases will also receive additional funding from the respective VP's, so their ambitions can remain more or less intact. With regard to the original plan, the ambitions of the research line Human Resilience have been matched with the adjusted end date of the Early Research Program (2017 instead of 2018), as well as with a budget reduction in 2017. Consequences are that no additional use cases will be included in the research line, and that the modelling approaches, platforms, and prototypes will have just one additional cycle of development, instead of the originally planned two or three additional cycles. Consequently, the readiness level of the knowledge and technology developed in this project will be lower than originally planned.

9 Making Sense of Big Data

General data	
Title	Making Sense of Big Data (MSoBD)
'Topsectors'/Societal Themes	HTSM, LSH, Agro, Logistics
Contact person TNO	Wessel Kraaij, Henk-Jan Vink, Judith Dijk
Contact person government	Michiel Ottolander (EZ)
Progress 2016	
Abstract	In 2016 the ERP MSoBD had five main technology lines: creating value, extracting meaning and distributed data infrastructures, human machine interfaces and Big Data architectures. Next to generic technology development the technology in these technology lines have been tested on relevant use cases, e.g. Deep Learning technology for incident duration prediction in a mobility use case, multi-view learning technology for early health risk warning in longitudinal population health data provided by the municipality of Rotterdam and evaluation of the Damian 2.0 tool on Safety Issues for the city of Tilburg. Other results include the development of a cookbook for different big data architectures and the development of a model for the influence of uncertainty of big data solutions on the visualization for different users.  The research in these two years provided TNO with a technology position over the total, wide, scope of big data innovations, the remainder of the program will focus on niche topics with high potential value. In 2016, the MSoBD program was reviewed by an external advisory board. This board confirmed that the results delivered in MSoBD were relevant to society and of high quality. We were challenged to further focus the research on topics were TNO could acquire an unique position. We also concluded that several research topics had been developed to the point that justified the (partial) transfer to VP's, showing the progress made in the knowledge position. Based on both observations the program will focus on three areas in 2017: Quantifying and Visualizing Uncertainty, Multi-stakeholder collaboration, and Information Centric Networking (ICN). These topics are aligned with the embryonic and growth knowledge areas identified within the TNO (technology) roadmaps. Within the ERP Making Sense of Big Data strong collaboration with various partners outside TNO is key. One of the goals of the ERP is to strengthen these collaboration and to build a national and international ecosystem. Good progress has been realized as is explained in the report.
Short description	Big Data is used for collections of data so large and complex that it becomes too difficult to process using on-hand data management tools or traditional data processing applications.

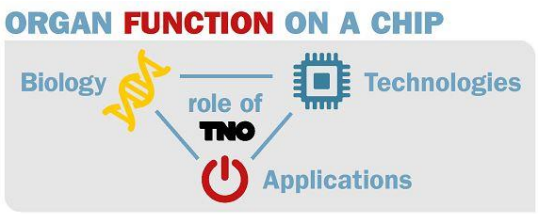
	The goal of the ERP is to create a capability (tools, models, methods) that enables a stakeholder to design and implement a Data Driven Innovation (DDI) in a multi-stakeholder setting. Big Data applications hold an enormous potential in various fields, ranging from health, food security, climate and resource efficiency to energy, intelligent transport systems and smart cities. In the ERP we will test, validate and experiment the developed knowledge in use cases in the domains of Logistics & Mobility, Personalized Health and Security.
Technology line: *"Creating Value"*	
Highlights	The aim of the **Technology Line *Creating Value*** is to develop knowledge on how value can be created within data-driven innovation and to apply this knowledge to create (validated) tools that can be used, together with stakeholders, to increase their value creation with (big) data. Therefore, we developed a quantitative modelling extension to the successful qualitative DAMIAN ecosystem method already available. This extension can be used to assess the strengths of the actors involved, by identifying the crucial assets and predicting which actors can steer (or block) the data-driven innovation. The extended DAMIAN method has been applied and validated in a use case provided and co-funded by the municipality of Tilburg, where the challenge addressed was how the use of big data can improve the safety and reduce crime in business parks. The analysis proved useful for the municipality and the stakeholders involved as it provided two specific results: (1) better status quo information: understanding the existing situation related to safety at business parks and (2) dynamic information: incident reporting. The extended DAMIAN method is also applied to the logistics use case. Here the challenge is to develop a data-driven innovation that provides better Estimated Arrival Times for sea ships heading for a terminal (in this case the Harbor of Rotterdam) by assessing: the client profile, the data sources, adoption of the service and the added value and roles of the different stakeholders to this data driven innovation. This lead to the refinement and adjustment of the initial idea and to an entirely new concept for the 'ETA Maritime' service covering larger geographical area. A second challenge in this technology line is responsible data innovation, which is key for adoption by end users. For this aim we developed a framework that can be used to systematically analyze how data driven innovations might affect people's freedom/autonomy, how it promotes or stifles fairness/equality, how it enables transparency/accountability and helps in understanding where a data driven innovation can expect challenges in adoption.
Technology line: *"Extracting meaning"*	
Highlights	Data analysis is the core of many big data challenges. The aim of the **Technology Line *"Extracting Meaning"*** is to improve data-driven applications for real-world (not controlled) applications. In 2016, the focus was on predictive modeling, which was studied for two use cases using two different machine learning approaches. The first machine learning approach was Deep Learning (DL). Deep Learning is in most cases applied to imaging data with a classification task. In this work, we applied standard Deep Learning technology also on other data sources. For streaming video it was found that the results improve when a memory component is introduced in the model. Deep Learning technology was also applied on the mobility use case, where a temporal and spatial neural network is trained on "fingerprints" of the traffic data. Based on this data the duration of an incident can be predicted (just after the incident has occurred). State-of-the-art travel time models can be improved using this incident duration as input parameter. The second machine learning approach we focused on was Multi-View Learning (MVL), a

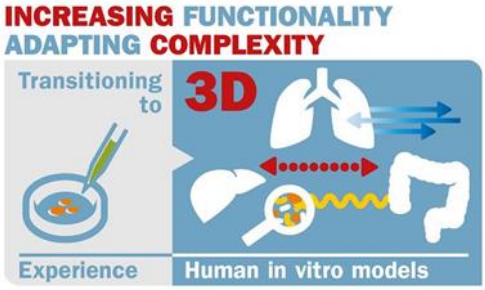
	machine learning framework that is expected to be very well suited for creating predictive models. The developed multi-view learning technology was applied on data related to youth obtained from the municipality of Rotterdam. Here the effects of interventions can be predicted learning from different input variables over time, enabling evidence based policies for interventions. For two relevant topics whitepapers were written: the first one is for uncertainty and the second one for the concept of prescriptive analytics. The first paper deals with different concepts clustered under the name of *uncertainty* within a big data context. A conceptual framework to describe a data-driven decision making process is proposed. This framework allows to further identify types and sources of uncertainty at various levels in the process, and to make sure different data professionals can find a common ground to discuss this topic. The importance of thoroughly dealing with uncertainties in big data, on the one side, and the specific needs identified in multidisciplinary real world applications, on the other side, pose an opportunity for TNO. The second white paper is on the topic of prescriptive analytics, one of the big data buzzwords from recent years. In this paper the difference between prescriptive analytics and descriptive & predictive analytics is described and challenges and requirements for prescriptive analytics is given. For many application domains situations in which prescriptive analytics are useful are described.
Technology line: "*Distributed data infrastructures"*	
Highlights	The aim of **the Technology line *Distributed data infrastructures*** is to implement, validate and demonstrate solutions for distributed data infrastructures (1) Data management & semantic interoperability , (2) Privacy & anonymization and (3) Data Transport, Storage & Processing. For the topic '***Data management and semantic interoperability***' a reusable, adaptive data transformation component and a metadata component were created. These tools enable unambiguous exchange and integration of data in heterogeneous environments. This interoperability tool was tested on a use case for research on pharma. For the topic ***Privacy & anonymization*** first implementations of a demonstration of multi-key fully-homomorphic encryption were tested and computational complexity was evaluated for performing single multiplication and addition operations. Moreover the first security analysis of these schemes was done. A focus point in this research is the conditions for which homomorphic encryption is secure and successful, as these conditions determine the parameters that can be chosen and therefore the efficiency of the algorithms. Theoretical boundaries for these parameters are determined and validated trough simulations. Next to that, the processing speed of the algorithms is optimized. Here, a relation with the error tolerance is found, the higher the error tolerance the lower the processing time. For the topic ***Data Transport, Storage & Processing*** a number of technologies were investigated. Software Defined Networking (SDN) has the potential to facilitate and speed up the deployment of architectures and services difficult to realize before. A prominent example of an architecture which could benefit from support of SDN is Information Centric Networking (ICN). We have created a framework which allows for installing highly flexible and parameterizable matching and forwarding rules on SDN switches. These rules allow for the traffic of the previously unsupported type to flow through the SDN network. The proposed framework can be used for virtually any existing and future protocol. For ICN, such a mechanism could facilitate its deployment and uptake. The Cloud Broker technology has as goal to out-scale Distributed Data Analytics in the Cloud. Here a tool was developed which can be used to design distributed analytics tools instead of single machine applications. This technology is tested in many practical cased such as the gas domain, maritime domain,

Technology line: "*Human machine interfaces"*	
Highlights	The first goal of the **Technology line: "*Human machine interfaces"*** is to optimize the interactive visualization of the predicted effects of (multiple) interventions and the uncertainty in these predictions to improve the decision support for multiple stakeholder. Here we prepared a set of theory-based interactive visualizations of uncertainty in predicted effects of (combinations of) interventions over time, based on previous results and studied the generic effects of different ways to visualize uncertainty on the user's interpretation of data. Our results show that the availability of an uncertainty visualization reduces overall observer bias in ensemble predictions, while the actual interpretation of a visualization depends both on its visual characteristics and on the type of estimate required (i.e., whether the estimate is relative to a range or its average value). Our current findings suggests that graphical uncertainty representations may be optimized by adapting them to the user and the task at hand. The second goal of this technology line is to individualize and personalize the visualizations and determine how to evaluate these factors regarding generality, so that it best fits to the role and purpose of the end user. For this we made an inventory of factors that are relevant for the personalization of visualization and formulated hypotheses regarding the impact of personalization of visualization of uncertainty. We chose a first relevant (set of) factors and developed an adaptive, user-centric demonstrator for these factors as an example.
Technology line: *"Big data architectures"*	
Highlights	The objective of the **Technology line: *"Big data architectures"*** is to ascertain integration and cooperation between big data building blocks to make applicability in real-life more achievable, in a multi organizational and/or multi domain environment and typical IT environments found at customers. Therefore a Big Data Analyses Architecture cookbook was written with guidelines for data analytics infrastructure(s) composed of building blocks that can be distributed over many heterogeneous analytics platforms and use data from many heterogeneous data storage systems and or locations. This provides an approach how to develop a collaborative IT-architecture for a joint big data service offered by multi parties. The approach focusses on two topics: a joint business purpose and the development of an architecture using different design perspectives in a cyclic way. Using this approach, an IT architect can develop an IT-architecture for a specific joint big data service, in an easier, faster and more complete way. Next to the cookbook, the big data IT technology landscape was visualised based on the *5 V's of Big Data.* This visualization is separated into three main categories of typical technological stack: 1) storage, (2) processing and (3) visualization. The end point technologies are prioritized on a combination of several criteria (using an expert opinion) : maturity, usage popularity, community size and activeness, and commercial support.
Topic: *"Use cases"*	
	The knowledge and tools developed within the ERP are tested, validated and applied to use cases in the domains of Logistics & Mobility, Personalized Health and Security. The role of the use cases is to steer the research questions in the ERP to real world challenges. Next to that, the applicability of big data applications is shown. The use cases are well connected with the ecosystem on big data. All topics are mentioned in the COMMIT2DATA roadmap. There is a good connection to the High Tech Top Sector HTSM and for Personalized Health to the top sector LSH.
Topic: "Alliances"	

	The alliances with knowledge partners develop well. On an international level, TNO is representing Dutch academic partners in the European Big Data Value Association, where TNO is board member. On a national level, representatives of MSoBD do closely work with academic partners to shape national programs related to big data and sense making, such as COMMIT2DATA and the NWA roadmap Big Data. The COMMIT2DATA program has started with 3 NWO calls in cooperation with TNO. The primary role of TNO within this program is to disseminate and valorize the data. For this an approach of regional Big Data hubs was developed, and in 2016 the first Big Data hub was opened in the Amsterdam ArenA to create an Innovation Centre as a smart city accelerator. In 2016 also the Center for Big Data Statistics (CBDS) under the lead of the CBS was launched, with TNO as one of the partners. MSoBD has also a focused collaboration with CWI, University of Amsterdam and Leiden University. Two TNO scientists are now affiliated to CWI (Veugen, van den Berg), one is affiliated to Leiden University (Kraaij), participating in local data science programs and preparing new NWO and STW proposals. As a recognition of the role of TNO in the computing science/ data science field, TNO has been invited to join the Informatica Platform Nederland (IPN) representing academic computer science research institutes in the Netherlands. TNO has intensified cooperation with municipality of Almere, resulting in a 'FoodCube' facility to be developed by TNO in cooperation with the Big Data Value Centre. TNO has organized a Small Big Data Congress to make our big data innovations visible to our colleages and the outside world. The multiplier of the ERP is mainly through TKI proposals such as the TKI Dinalog (logistics), the TKI Jongvee (agro), the TKI Smart Data Factory Innovations (logistics) and the TKI ICN (ICT). Next to that, also other projects such as with the Bill and Melinda Gates foundation and the H2020 PM1 project Recap are based on the results of MSoBD.
"Advisory board and seed ideas"	
	In 2016, the MSoBD program was reviewed by an external advisory board. This board confirmed that the results delivered in MSoBD were relevant to society and of high quality. We were challenged to further focus the research on topics were TNO could acquire an unique position. We also concluded that several research topics had been developed to the point that justified the (partial) transfer to VP's, showing the progress made in the knowledge position. These observations were used for focusing the program in 2017. Also in 2016, two calls for seed ideas to spark new knowledge initiatives have been conducted with great success.
Program dynamics	The research output of ERP MSOBD reflects the gradual steps towards a unique knowledge position in this very competitive and fast moving domain. In 2015 the ERP was started with three main technology lines: *creating value*, *extracting meaning* and *distributed data infrastructures.* In 2016 we focused these three activities by selective continuation and added two technology lines: *human machine interfaces* (to emphasize the human element in sense making) and *Big Data architectures* (to position TNO innovations in overall big data processing architectures available on the market). The research in these two years provided TNO with a technology position over the total, wide, scope of big data innovations. In 2017 we focus on three areas in which we can achieve an unique position: *quantifying and visualizing uncertainty of big data inference systems*, *multi-stakeholder collaboration* and *Information Centric Networking*. These areas have been selected in consultation with a panel of external big data experts.

10 Organ Function on Chip

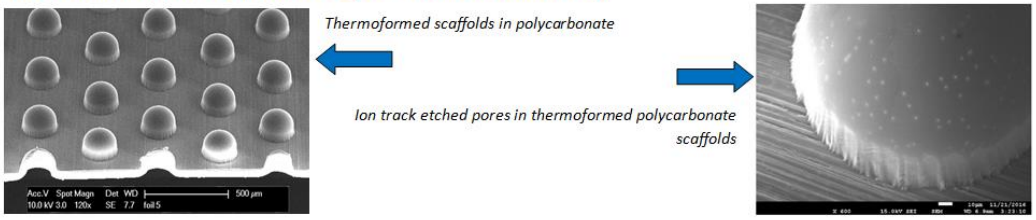
General data	
Title	Organ Function-on-Chip
'Topsectors'/Societal Themes	LSH, A&F, HTSM / Work & Health, Defence
Contact person TNO	Cyrille Krul; Evita van de Steeg, Ivana Bobeldijk-Pastorova
Contact person government	Michiel Ottolander (EZ)
Progress 2016	
Summary	Over the last 2 years, the ERP Organ function on-a-chip evolved from a seed ERP (2015) into a full ERP (in 2016) and is still further growing towards 2017. The program has three use cases: gut-, liver- and lung-function on a chip. In addition, nanopore technology capable of detecting individual bio-molecules (for example proteins) was explored. In 2016, TNO became a member of hDMT, *the* national collaboration of institutes, academic groups and companies focusing on state-of-the-art technologies around organ on-a-chip. In collaboration with companies and academia a number of grant applications (still in review) for TKI/ Dutch digestive foundation and ZonMW MKMD were put forward. New collaborations with academia were setup, such as University of Amsterdam and Erasmus Medical Centre on intestinal organoids, and LACDR on readout technologies. Consortia with small industrial partners such as Takara and Invitrocue have led to very active collaboration in the development of advanced in-vitro liver models. Negotiations with large industrial partners are also in place. Internal collaborations are diverse and fruitful, i.e. Metabolic health research, Microbiology and systems biology, Environmental modeling, sensing and analysis. Equipment for additive manufacturing (EfAM) and the department of Nano Instrumentation contributed to the program with development of (3D printed) scaffolds for cell culture, and first plans have been setup with Optomechatronics in the area of Atomic Force Microscopy and with the Optics group.   Close cooperation is in place with several roadmaps, Food and Nutrition, Predictive Health Technologies, Environment and sustainability and Defence, safety and security in order to develop sound business cases for the most important markets. Based on the business cases, the technical work in 2016-2018 is focused on the expected most successful product-market combinations. Various potential collaborators, customers and stakeholders were visited in 2016, providing them with an update about the ERP program. In addition the Organ-function on-a-chip team published a white paper, 'Biology, technology and application: the 3Dimensions of organ on a chip' describing our strategy and views in this area. Coupled to the publication of the paper, a dissemination event for both internal and external stakeholders was organized on 31st

	of October. The attendance of this event by colleagues, collaborators from academia and industry extended our expectations and showed recognition of TNO as a partner in Organ on a Chip technology, biology knowledge and applications.
Short description	The objective of the ERP organ on chip program is to improve the development of better predictive, more physiological (personalized) human *in vitro* models. We focus on tissues and disease areas in which TNO has extensive knowledge, experience, market position ("right to play"), and will develop validated applications relevant for pharmaceutical and nutrition industry.  and In 2016 we focused on applications with three organs and evaluation of one bionanoscience technology. : 1. Gut function-on-a-chip , with the aim to develop a personalized and translational *in vitro* model of the human gut, representing all the different epithelial cells in co-culture with human microbiota and immune cells. The model will be applied in food and pharma industry to study (drug) absorption and impact of drugs, nutrition and environment on gut health. 2. Liver function-on-a-chip will be a predictive *in vitro* disease mimicking (i.e. non-alcoholic steatohepatitis; NASH) model using co-culture of human pluripotent stem cell-derived hepatocytes and stellate cells (or other liver cells) on an *in vitro* 3D cell culture platform that will have its application in testing the effect of compounds on the disease development, prevention and or treatment. Besides for the pharmaceutical industry, this will also be relevant for applications in the nutrition industry. 3. Lung function-on-a-chip with the long term goal to establish a biosensor, which is able to monitor the biological effects of exposures in our surroundings (complementary to chemical sensors). This is both in a working-environment in the chemical industry (including the military) as well in a daily-living environment (urban city etc). 4. Development of a new technology for the detection and analysis of individual biomolecules (proteins or DNA) together with a world leading group in bionanoscience, namely the group of prof. Cees Dekker at the TU Delft.
Technology line 1: *"Gut function-on-a-chip"*	
Highlight	To approach the human intestine epithelium architecture as close as possible, we adapted a fabrication process that makes porous 3D villi scaffolds[12]. In a 50 µm thick polycarbonate film, latent tracks are made with high energy ions that are shot through the film and leave tracks of defects in the polymer. These films are then thermally formed in a hole patterned mold with a hot embosser. The polycarbonate is heated above its glass transition temperature and mechanically pushed into the mold. This gives an array of hollow scaffolds, which have currently a diameter of 200 µm and are 200 µm tall (photo 1). The perforations in the polycarbonate film are then made by wet chemical etching of the latent ion tracks that were irradiated in the first step. Here, they have a diameter of about 500 nm and a density of 10^4 pores per mm^2 (photo 2). The scaffolds are inert, biocompatible and will be used to grow intestinal stem-cells on, and to determine the effect of the villi structured scaffold on functionality of the intestinal cells and epithelium. The porosity of the scaffolds enables analysis of transport

[12] Truckenmüller *et al.* Flexible fluidic microchips based on thermoformed and locally modified thin polymer films. Lab Chip, 2008 (8)1570-1579

of drugs, nutrients and metabolites across the intestinal epithelium. Currently we are focusing on improving the aspect ratio of the villi in order to more closely mimic the human gut epithelium.

Fabrication of a 3D porous gut villi scaffold array



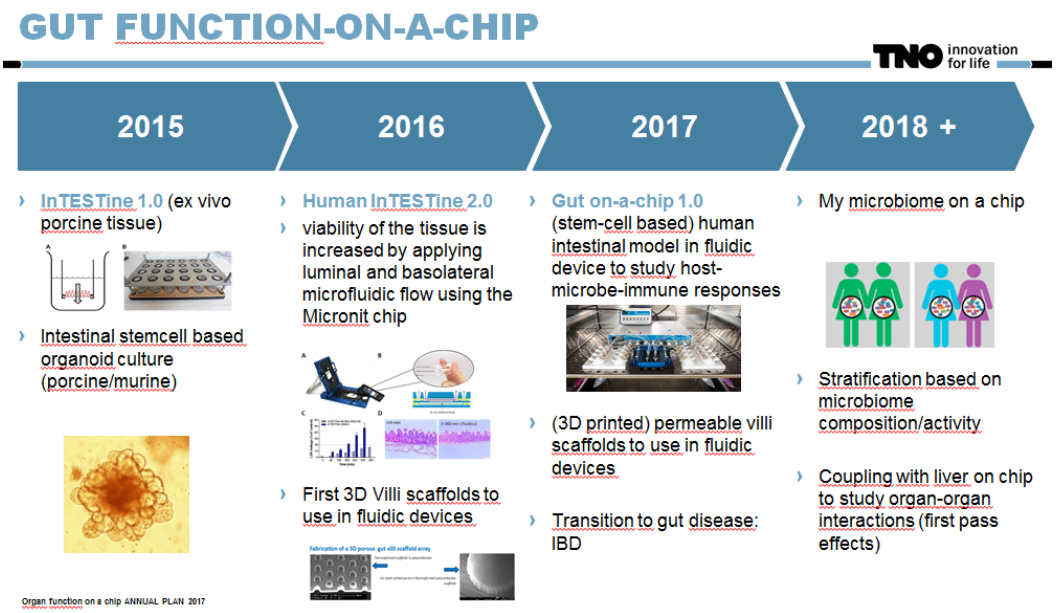
Other results achieved in 2016:

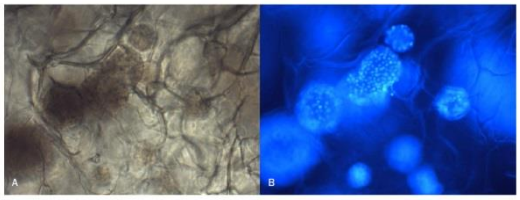
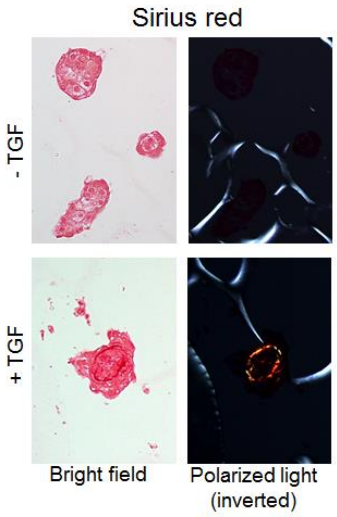
- Extended viability of human intestinal tissue in InTESTine by applying luminal and basolateral microfluidic flow.
- Culturing of human stem cell derived intestinal organoids using modified medium (together with partners from AMC and HU).
- Formation of human intestinal monolayer representing all the different intestinal cell types derived from intestinal organoids

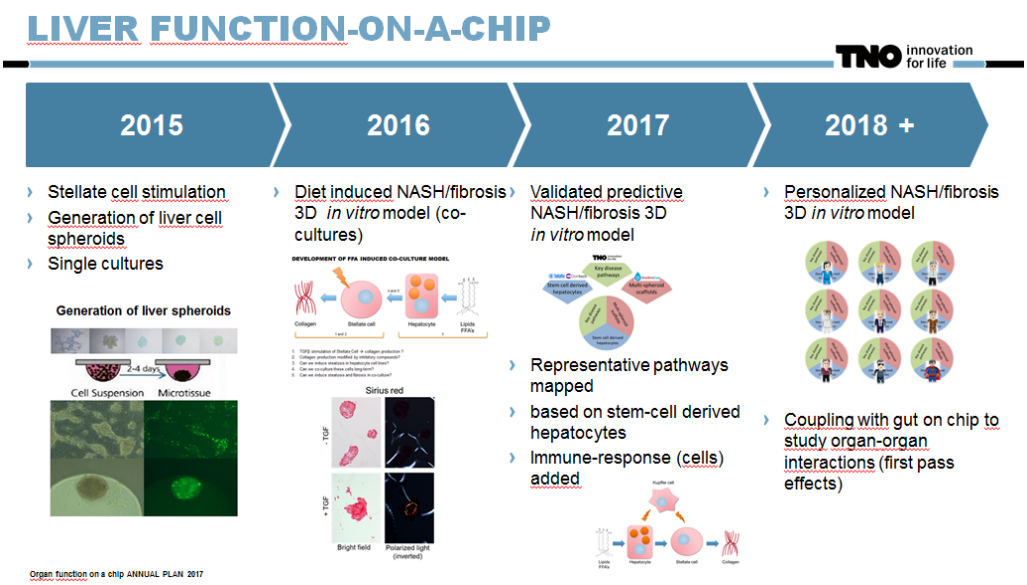
Program dynamics

The dynamics of the developments within the program for Gut function-on-a-chip are shown in the figure below. For 2015 and 2016 the achievements thus far are schematically summarized. In addition to plans for 2017, also an outlook towards 2018 and beyond is shown.
In 2017, we will:

- Develop a validated 2-compartmental intestinal barrier model based on tissue derived stem cells from small intestine and colon
- Develop or implement a set-up to study anaerobic gut-microbe interactions in vitro
- Initiate transition to disease modelling (IBD)
- Set-up early immune response and co-culture with immune cells in the developed devices
- Make first steps towards coupling of gut-function on a chip and liver-function on a chip in one device



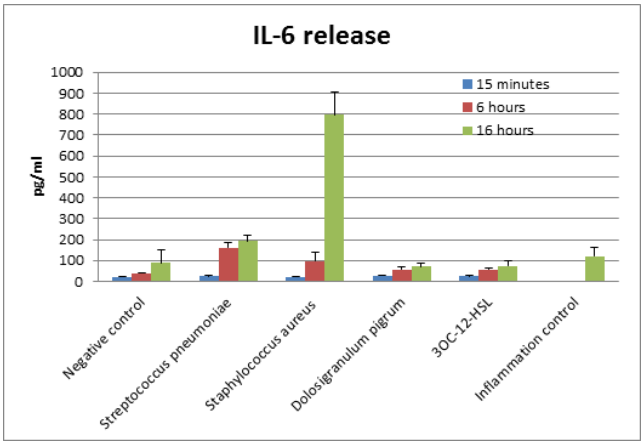
	In 2018 the developed model will be combined with microbiota derived from health or diseased (e.g. IBD, obese, diabetic) people in order to study the role of microbiota in (gut) health and disease. Moreover, luminal conditions (e.g. pH, microflora) and intestinal physiology may be adapted to different intestinal regions (duodenum, jejunum, ileum, colon) in order to generate a "GI-tract-on-chip", or adapted to differences phases of life (babies, children, adults, and elderly). In the future, the gut-on-a-chip can be combined with liver-on-a-chip models in order to more accurately predict human oral bioavailability of compounds.
Technology line 2: *"Liver function-on-a-chip"*	
Highlight	In 2016, first steps in co-culture of 3D models with human hepatocytes and stellate cells were made. In collaboration with InVitrocue, provider of 3D culturing scaffolds, we were able to co-culture 3D spheroids composed of human hepatocytes and stellate cells.  Fibrosis was induced in the stellate cells and the production of collagen was visualized with polarized light. In 2017 we plan to extend this model further into a 3D co-culture model that can mimic diet-induced onset of liver fibrosis  *Other results achieved in 2016:* • 2D in-vitro model for fibrosis based on culturing of stellate cells, including modulation by therapeutic compounds • 3D culture (single spheroids) of human stem cell derived hepatocytes • Culture medium selection / optimization for co-culturing hepatocytes with stellate cells • Started a collaboration with Italian company focusing on fatty acid delivery and membrane optimization of in vitro cells to human in vivo situation, • Initiated collaboration with LUMC on electron microscopy based collagen detection in spheroids
Program dynamics	The dynamics of the developments within the program for Liver function-on-a-chip are shown in the figure below. For 2015 and 2016 the achievements thus far are schematically summarized. In addition to plans for 2017, also an outlook towards 2018 and beyond is shown. In addition to achievements 2016 and plans for 2017, in 2018 we plan to further develop the personalized 3D in vitro model and couple the model to the models of other organs, such as gut. In 2017 we will: • Further develop and validate the 3D model for diet-induced liver fibrosis 1.0 • Test the effect of inflammatory cells and fluidics on hepatocyte maturity • Work on the proof of principle; 3D model for diet-induced liver fibrosis 2.0 (stem cell based) • Test stem cells form various donors; test effect of origin on disease mimicking / pathways • Analyze pathways in model 1.0 and 2.0: what part of patient is represented?



Project 3: "*Lung function-on-a-chip*"

Highlight

We set up an in-vitro model using lung epithelium tissue (host) combined with bacteria to be able to investigate the effect of different bacterial populations on the host by measuring various parameters (LDH, cytokine release, CBF).
A culturing method was setup for the lung cells without using antibiotics (as these would kill the bacteria). Subsequently, a method was devised to co-culture the lung cells with bacteria. In 3 experiments, the relevant bacterial populations (as they occur in lungs) were co-cultured with the lung cells. Also, negative and positive controls were included that were expected to have respectively no effect or a major effect on the host.

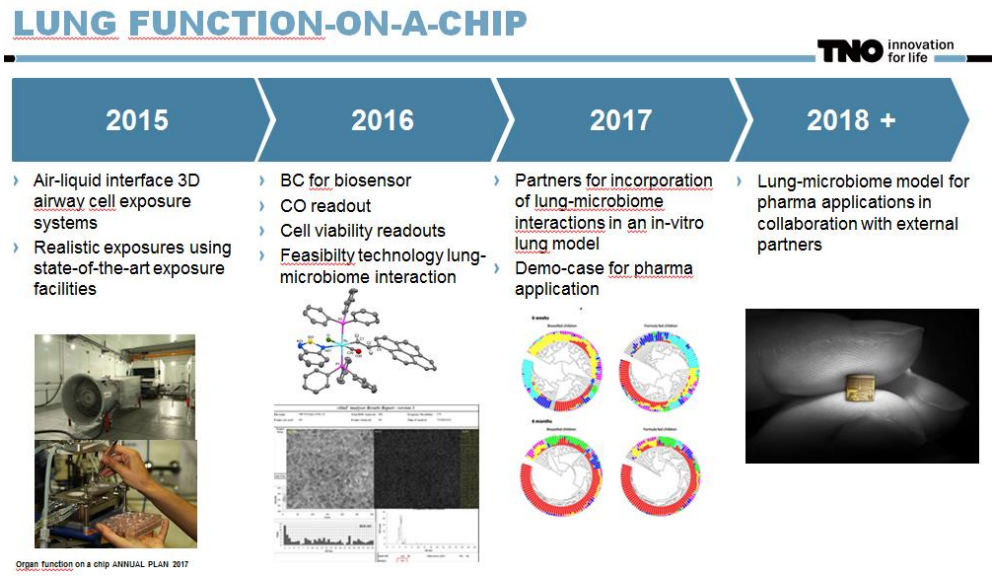


The experiments showed that it was possible to successfully culture the cells without antibiotics. It was also shown to be possible to culture lung epithelium together with bacteria, with both lung cells and bacteria remaining viable for sufficient time. Difference in viability of bacteria at different times was demonstrated, making certain bacteria suitable as e.g. positive control for the in vitro model. Effects of various bacteria on cytokine release (inflammation) were demonstrated (IL-6 and IL-8).

The results indicate that the technical setup of the in in-vitro model including microbiome was successful. Different microbiota induced different inflammatory responses in the lung cells.
In 2017 we will setup a collaboration with a provider on in-vitro lung models on a chip, in order to further develop a demo case for application of this system in pharma industry.

Other results achieved in 2016:

- Business case for development of a biosensor (the recommendation is negative)

	• Setting up of a detection method for the measurement of oxidative stress in cells • First feasibility experiment of co-culture of lung epithelial cells and lung microbiome • Feasibility testing of cilia beat frequency measurements for the measurement of the viability of lung cells in culturing experiments.
Program dynamics	The dynamics of the developments within the program for Lung function-on-a-chip are shown in the figure below.  In 2017 we will: • Discontinue the developments towards a biosensor as there is insufficient market need • Evaluate the market need for the lung-microbiome interactions • Seek a partner for further technical developments of the lung-microbiome system • Setup collaborations with pharma industry to develop a demo case
Project 3: Bionano technology	
Highlight	This project evaluated the possibility of a collaboration with the bionanoscience department at TU Delft (prof. Cees Dekker c.s.). Main result is that recent findings at TU Delft show significant potential for valorisation, in particular single-biomolecule analysis using nanotechnology. TNO has relevant expertise in the fields of nanotechnology, optics, spectrometry, biochemistry and bio-informatics, which is largely complementary to TU Delft. The use and business case for this emerging technology appear very promising. Protein fingerprinting is based on fluorescent labelling of amino acids, and detection using single-molecule fluorescence. This technology is a potential game-changer for proteomics, and already attracted attention from commercial businesses. Additionally, solid-state nanopores appear promising for DNA sequencing at the single molecule scale. Key technology here is the use of optical nano-antennas to characterise the molecules with spectroscopy.
Program dynamics	Discussions with TU Delft will continue in 2017 to define the follow-up of this evaluation.

11 Submicron Composites

General data	
Title	ERP Submicron composites
'Topsectors'/Societal Themes	HTSM en Chemie
Contact persons TNO	Pascal Buskens / Jaap Lombaers / Aike Wypkema
Contact person government	Michiel Ottolander (EZ)

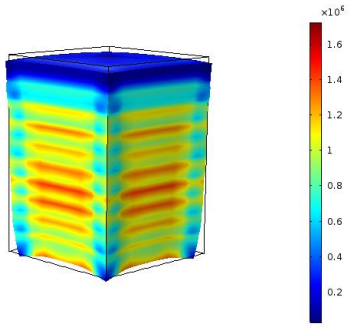
Program report 2016

Abstract

Within the scope of this ERP we develop new materials with optimized composition and microstructure for advanced optical and mechanical performance and multiple functionalities. Within the framework of the Brightlands Materials Center, we collaborate with academic partners, including Eindhoven University of Technology and Maastricht University, and with industrial partners within the value chain to develop new materials and products for:

- additive manufacturing (3D printing),
- light management for optics and electronics,
- lightweight materials for automotive.

Within the **Additive Manufacturing** topic, fundamental knowledge regarding the relation between laser sintering process conditions & mechanical properties of polyamides has been built up in 3 PhD projects at the Eindhoven University of Technology. This has led to the development of a finite element (FE) model for the sintering of two viscoelastic polymer particles and a detailed crystallization kinetics for PA-12.
Good project progress has been achieved for two other PhD projects which has led to the synthesis of new monomers for 3D printing materials and a photopolymerization set-up that allows detailed characterization of intrinsic mechanical properties has been developed.
TNO's task aimed to build a multi-scale model of a layer wise photocuring process that predicts thermomechanical behaviour and geometry of 3D products prepared by vat photopolymerization. One of the applications of this model is to predict and then prevent warpage of a 3D-printed product. The modelling results will be compared with experimental data in 2017.



Within the **Optics and Electronics** program the original goal of this project was to establish relationships between surface texture, surface chemistry and surface energy of coatings and their interactions with powders. In particular, we wanted to focus on the ability of coating layers to adhere or repel dust particles. After Q1 2016, the goals of the BMC program were revised, which led to the definition of a new focus area 'windows of the future' based on thermochromic materials. Thermochromic Materials (i.e, materials that adapt their optical properties as a depending on temperature) are regarded as most promising basis for the glass window of the future: a window that can help to reject heat on a hot summer's day and, on a winter's day, reflect radiator heat back into the house whilst at the same time taking optimal profit from any available solar heat. An experimental plan was made and first work started at the BMC lab in Geleen.

For the **lightweight automotive** case, an inventory of fundamental mechanisms has been made that determine the mechanical performance of thermoplastic composites, with special emphasis on the case study around anti-ballistic properties.

Short description	The overall goal of this ERP is to achieve a level of control over structure and chemical composition of materials that enables the development of materials with programmable functionality. We will demonstrate the knowledge gained within the framework of this ERP in selected use cases chosen in collaboration with the Brightlands Materials Center and its partners. Within the **additive manufacturing** program, we will focus on three topics related to the quality of the material: a) Improving mechanical properties of AM materials, including the intrinsic properties of AM processable materials and the effect of processing conditions on mechanical properties in the obtained 3D product; b) Minimization of internal stresses by AM processing, which can cause both geometrical defects in carefully designed 3D products as well as adverse effects on long-term performance (for example, very small warpage effects can cause a strong misfit in dental prostheses); c) Introduction of novel functionalities in AM materials, such as improved optical properties and multicolor esthetics for dental crowns and bridges, electrical and magnetic properties for 3D printed electronics. Within the **innovative building envelopes** program, we will focus on materials that adapt their optical behavior in order to optimize energy performance of various parts of buildings, including windows. This can be achieved by active heat control, ie coatings that can switch from heat-reflective to heat transmitting whilst being transparent in the visible part of the light spectrum. The work on building envelope materials within this ERP will focus on Thermochromic Materials (ie, materials that adapt their optical properties as a depending on temperature) are regarded as promising basis for the glass window of the future: a window that can help to reject heat on a hot summer's day and, on a winter's day, reflect radiator heat back into the house whilst at the same time taking optimal profit from any available solar heat.
Highlights	**Program: Additive Manufacturing** ***Workpackage 1: Mechanical properties of AM processed thermoplastic polymers*** This workpackage includes 4 PhD projects at TU/e, focusing on understanding the relation between AM processing conditions and material properties: • Structure-property relations and long-term performance of sintered polyamide • Computational modelling of viscoelastic non-isothermal sintering process • Experimental characterization of the sintering process and generated microstructure • 3-D manufacturing of plastic products by melt jetting Fundamental knowledge regarding the relation between laser sintering process conditions & mechanical properties of polyamides has been built up in 3 PhD projects at the Eindhoven University of Technology. This has led to the development of a finite element (FE) model for the sintering of two viscoelastic polymer particles and a detailed crystallization kinetics for PA-12. Validation of the FE model will be performed in 2017. ***Workpackage 2: Mechanical and geometrical properties of photocurable polymers*** This workpackage includes 3 PhD projects at TU/e, focusing on mechanical properties of photocurable polymers: • Reversible Multiple Networks for 3D printing materials • Controlled Polymerizations in Stereolithography • Intrinsic mechanical properties for photocurable polymers Good project progress has been achieved in collaboration with TNO. This has led to the synthesis of new monomers for 3D printing materials and a photopolymerization set-up that

allows detailed characterization of intrinsic mechanical properties has been developed.

One of the goals of the TNO part of workpackage 2 was to create a multiscale model containing the physics and chemistry describing the photopolymerization process during SLA printing which would lead to a better understanding of the interplay between material and process parameters. In this respect we have initially implemented a single layer model that contains the physics related to reaction kinetics (e.g. as a function of the incident light), thermal effects (e.g. due to exothermic heating) and mechanical changes (e.g. volume shrinkage). It was learnt from this single-layer model that the we are able to produce critically important effects such as warpage, due mainly to the inhomogeneous distribution of stresses during printing. Moreover we have confirmed that such warpage varies (non-linearly) with different parameters such as the reaction kinetic constant or the light intensity. This opens the possibility to tune the process parameters to control/reduce such undesired effects.
In addition the single-layer model has been extended to the printing of equally-shaped layers. We have been able to successfully implement a realistic 3D printing process that can calculate the accumulation of stress due to the curing of subsequent layers. As it is now the model allows for the exploration of different process, surrounding and material conditions such as light exposure, presence of fixed glass substrate and presence of photo-inhibitor in the resin.
Currently we are in the validation stage. For that it is necessary to plan experiments accordingly taking into account additional measurements on the material properties. In order to calibrate the model for a given formulation we have designed initial experiments that aim to characterize relevant properties during curing (such as viscoelasticity or degree of curing). This work will be continued in 2017.

Workpackage 3: New functionalities in photocurable polymers

This workpackage includes 1 PhD project at TU/e:
- Modelling the 3D-Printing of Electromagnetically Active Components

First, a desk study was performed to identify state-of-the-art and requirements for electromagnetically active AM materials. A first generation model for the manipulation of nano- or micro-particles in a photopolymer matrix was set up.

In addition, this workpackage included the development of (a) biocompatible nanocomposite photopolymers with low absorption and high scattering, (b) transparent biocompatible nanocomposite photopolymers with good abrasion resistance, and (c) colored biocompatible photopolymers suitable for processing by inkjet printing. The experimental work performed by TNO for (a) and (b) will be continued in 2017.
Regarding goal (c) some preliminary experiments regarding the inkjet printing of biocompatible photopolymers was performed and it was concluded that a more detailed study regarding the inkjet printing process was needed. A EFRO project proposal on the topic of multimaterial 3D printing was submitted and granted, in which this topic will be studied in more detail, together with project partners Océ and NextDent.

Program: Innovative building envelopes
The original plan of work was to perform a literature study on the formation of well-defined nanostructures and textures in and on coatings using nanoparticles aiming at anti-dust functionalities. After Q1 2016, the plan of work was revised to:
(a) Find out which optical functionalities of building envelopes would contribute most to the improvement of the energy-efficiency of buildings?
(b) Find out if these functionalities should be static or adaptive?
(c) Find out which submicron particles and structures are most promising in providing the functionalities that are searched for
(d) Find out what technological steps have to be taken to develop these particles and structures and integrate them into a functional coating for building skins?

	After Q1 2016, we worked according to the revised plan of work and came to the following conclusions:
	• The energy-efficiency of building can be improved significantly with an adaptive window of the future: a window that is functionalised to optimally interact with visible and infrared light thus leading to a lower indoor energy need for keeping comfortable indoor climate.
	• Thermochromic Materials (i.e, materials that adapt their optical properties as a depending on temperature) are regarded as most promising basis for the glass window of the future: a window that can help to reject heat on a hot summer's day and, on a winter's day, reflect radiator heat back into the house whilst at the same time taking optimal profit from any available solar heat.
	• Thermochromic glass windows based on multistack ALD layers have recently appeared in the market. These layers are costly and difficult to process and will expectedly appear only in niche applications. We will focus on two alternative, promising routes for thermochromic windows that, if successfully developed further, have the potential for wide-spread application, including the retrofitting to improve the energy performance of existing buildings:
	  • Wet-chemical coating formulations that can be used to directly functionalize glass and other transparent substrates. This route provide more design freedom and compositional flexibility needed for high performance thermochromic windows.
	  • Development of versatile thermochromically adaptive 'pigments' that can in turn be used as the functional sub-micron ingredient to turn coatings and composites (foils) into advanced thermochromic systems.
	• Thermochromic coatings and foils are expected to have wider application areas than functionalized glass windows, due to their ability to be applied in existing buildings and during renovations.
	
	A detailed experimental plan was made and started recently. Results will be reported in 2017.

Program dynamics	No major changes in the **additive manufacturing** program have occurred. In the course of 2016, the materials modelling activities have suffered from limited availability of scientists with relevant expertise. Recently the materials modelling team has been strengthened and activities in this field have been speeded up since. In 2016, the program focus of 'Materials for Optoelectronics' has been defined as 'Materials for sustainable building skins' and as such the focus of the ERP has been amended accordingly.

12 Interaction Robotics (seed project)

General data	
Title	ERP seed Interaction Robotics
'Topsectors'/Societal Themes	HTSM Smart Industry, Water Maritime & Offshore, Energy Oil & Gas Maintenance, Chemical industry Maintenance, I&M Rijkswaterstaat
Contact persons TNO	Jan van Erp / Arjen de Jong
Contact person government	Michiel Ottolander (EZ)

Program report 2016

Abstract

Together with the University of Twente (Prof. S. Stramigioli) we equally invested in, and explored the potential of starting a public private joint innovation center (JIC) in all forms of robotics where there is a direct interaction with humans. Several work packages were conducted together to combine fore-front know-how of both organizations with the best robot hardware presently available (see figure below). In parallel a technology roadmap has been developed together with industry. On October 6th 2016 a workshop with several industrial partners took place at TNO New Babylon discussing the roadmap and involving partners at an early stage in the definition of the following research lines.
The results were concretized into demonstrators that have been showcased by TNO and UT at the newly set-up I-Botics facilities (inside the MEC Lab, Delft) on January 24th 2017 for a mixed audience of e.g.: Offshore, Oil & Gas, Chemical, Transport, Inspection, Construction and Robotics industry, representatives of the ministries of EZ (smart industry) and I&M (Rijkswaterstaat), and Robovalley, A plan for further strengthening the knowledge base is presented to both UT and TNO management, and will be decided on in due course.

Hardware to be used in the i-Botics program, from left to right: KUKA robotic arm, Force Dimension haptic feedback Devise and a 4 fingers dexterous hand from Shadow Robot Company.

13 Signatures

Delft, 27 February 2017

Prof.dr.ir. J.T.F. Keurentjes
Chief Science Officer TNO

Dr. K.E.D. Wapenaar
ERP program manager