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TNO Early Research Program 2015-2018
Annual report 2017

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1 Introduction

In this report we present the progress made during the third year of TNO's Early Research Program 2015-2018[1]. For the 2017 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
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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	Peter van Dijken peter.vandijken@tno.nl
10.	Submicron Composite Materials	Pascal Buskens pascal.buskens@tno.nl	Jaap Lombaers Jaap.Lombaers@tno.nl

In the next chapters the progress in the ten projects is described in a concise format agreed with the ministry of Economic Affairs and Climate, explaining the setting of the research in national and international context, highlights of results obtained, the cooperation in ecosystems pursued, the use cases, and program dynamics. The plans for 2018 and beyond are described elsewhere[2].
In addition to these 10 topics we continued a seed project on: *Interaction Robotics (i-Botics)*, and we explored the potential for building applied knowledge positions on *Applied Artificial Intelligence, Bio-nano devices*, *Chemical sensing / The Exposome,* and *Laser satellite communication*. Progress is reported in chapters 12 - 16.

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. For five programs we have established (the seed for)

[1] TNO Early Research Program 2015-2018; Annual plan 2015, September 2014; TNO Early Research Program 2015-2018; Annual plan 2016, September 2015; TNO Early Research Program 2015 – 2018; Annual plan 2017, September 2016
[2] TNO Early Research Program 2018 – 2021; Annual Plan 2018, September 2017

strategic, program based cooperation: Quantum computer / Quantum internet: QuTech (partner TU Delft), Personalized Lifestyle for Health: Centre for Metabolic Health and Lifestyle (partner LUMC), 3D Nanomanufacturing: Nano Optomechatronics Instruments (NOMI, partner TU/e High Tech Systems Centre), Submicron Composite Materials: Brightlands Materials Centre (BMC, partners Chemelot Campus, TU/e, UM), Interaction Robotics (i-Botics, partner UT).

In 2017 TNO launched Nearfield Instrument BV to bring atom-scale metrology solutions, developed in ERP 3D Nanomanufacturing (2015-2017), to the semiconductor industry. A major investment in Nearfield Instrument, by the leading Semiconductor Industry Samsung Electronics, is convincing proof for the relevance of our technology.

We shared our plans and results in 2017 with many potential partners and stakeholders in the form of patents (60), publications (140), conference presentations and posters (115), and ERP dissemination events (15). Selected events are shown in the Table below.

nr	ERP	Dissemination Event (selected items)	Main Event Partners
1.	Quantum Computer / Quantum Internet	21th Annual Conference on Quantum Information Processing, Delft, January, 2018	QuTech, TU Delft
2.	Complexity	NWA Circular Economy, Utrecht, March 2017 NPCS[3] Think Tank Meeting, Enhancing Immune Fitness, where to start?, May 2017	NWA, MinI&W, 'Het Groene Brein', MVO nl NPCS partners
3.	Personalised Lifestyle for Health	"Lifestyle as medicine – Care to cure", Leiden, December 2017	LUMC
4.	Energy Storage and Conversion	"Energie producerende gebouwen: Demo Warmtebatterij, Delft, Sept 2017 "Elektrificatie Chemische Industrie, Vlaardingen, November 2017	Dutch Green Building Council Voltachem, ECN
5.	3D Nanomanufacturing	3rd yearly dissemination event, Delft, November 2017	Key lectures from TNO, IBM, ARCNL, J. Hopkins
6.	Structural integrity	In preparation: Energy and Transport Infrastructure, 2018	TUD, BAM, RWS
7.	Human Enhancement	Final Dissemination event, Spant! Bussum, November 2017	Stakeholders from industry, governments
8.	Sense Making of Big Data	Small Big Data Congress, Amsterdam Innovation Arena, October 2017 Applied AI conference, Soesterberg, November 2017	Big Data Value Centre VP National Security, Defense RVO Program
9.	Organ Function on a Chip	2nd yearly dissemination event, Leiden, November 2017	hDMT
10.	Submicron Composite Materials	Nano Technology Crossing Borders, Maastricht, September 2017	BMC, H Zuyd, U Hasselt

For any further questions on our Early Research, please check the TNO website (ERP link), or approach one of the TNO colleagues mentioned above.

[3] Netherlands Platform Complex Systems, founded by NWO, TNO, UG, UU, UvA, WUR, TU/e, and EUR to promote societal and industrial use of complex systems knowledge.

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	Mariëlle Beers-Homans (EZK)
Progress 2017	

Abstract

Roadmap A: Topologically protected quantum computing

Main objective: braiding with Majorana's within 4 years in order to create qubits with the potential of very long coherence times.

To demonstrate Majorana braiding, nanowire crosses will need to be integrated in a superconducting circuit with a microwave resonator and several Josephson junctions. In 2017 new in-plane nano-wires growth has been achieved. Furthermore, detailed studies on materials and nano-fabrication workflows were performed.

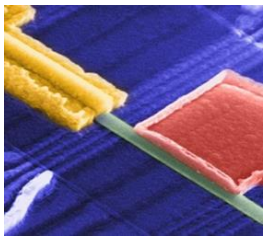


Figure 1 Majorana device

Roadmap B: Fault- tolerant quantum computing

Main objective: a 49 qubits device within 4 years, controlled with surface code driving. Two principle types of qubits are under investigation.

The transmon qubits are relatively speaking the most advanced type of qubits. In 2017 a full-stack Quantum Computer demonstrator has been established with a 2 qubit transmon processor (http://quantuminfinity.tnw.tudelft.nl/), where simple quantum algorithms can be executed. The development of a 7 and a 17-qubit design was established and mobility measurements were performed. This is the smallest set of qubits required to demonstrate surface code protection.

Spin qubits may intrinsically have longer coherence times, and also use surface code protection for scalable operation. Current research topics include scaling to circuits of 5 qubits, and 2D configurations.

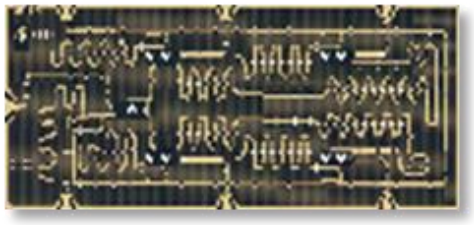


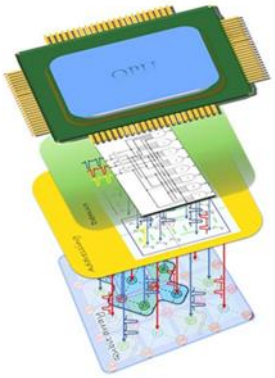
Figure 2 Transmon qubit

Roadmap C: Secure Quantum Internet

Main objective: a demonstrator network within 4 years.

The fourth type of qubit is based on the N-V color centers in diamond. In 2017 the efficiency of wavelength conversion was improved. Furthmore, a quantum internet simulator was created (NetSquid), which can be used to develop and test new internet protocols.

Figure 3 Quantum Internet proof-of-principle at TU Delft campus

	Roadmap D: Shared Development  This roadmap aims for development of partnerships and technologies with external parties. Besides the existing cooperation with Intel, in 2017 the cooperation with Microsoft was prolonged. Furthermore, a collaboration with SurfSara was set-up, to bring quantum technology to the Dutch academic society. A proposal for a European CSA (Coordination and Support Action) has been submitted. Other EU-projects may follow. Within this Roadmap the first steps towards system architectures of quantum computers are being made. Also a scalable surface code protection design was published in 2017. *Figure 4 Artist impression of the scalable architecture highlighted in Physical Review Applied.*
Short description	QuTech has the ambition to develop the first working prototype quantum computer, as well as a demonstrator for quantum internet. The envisioned developments cover many TRL's, multiple disciplines, and span about 15 years. This will result in a different approach during the subsequent phases of the development. The first phase (2014 – 2017; Proof of Principle) has been dominated by solving the current bottlenecks to accelerate the research, and by making the transition towards the mission-based way of working. The latter includes, amongst others, a better defined goal of the project, working out the project plan, system architecture considerations, and involving third parties. The next phase (2018 – 2022; Proof of Concept) will be used to demonstrate progress on key technologies (critical milestones), benchmarking, defining the requirements and system architecture, and updating the project plan including contributions by third parties and potential spin-off. Also a relevant mathematical challenge shall be selected for the demonstration. This challenge shall be mapped to the electronic hardware. During the final phase of the project (2023 – 2029; working demonstrator) all technologies shall be developed to the level of a working demonstrator. A convincing demonstration shall be executed. Positioning the Dutch industry (by knowledge transfer) is critical during this phase.
Topologically protected quantum computing roadmap	
Highlights	• MBE-ALD cluster and Materials development ○ Validation and further development of the unique MBE-ALD cluster tool, which serves to fabricate hybrid semiconductor / superconductor nanowire devices for Majorana application; integration of Hydrogen-cracker will enable H-assisted MBE growth; designing and procurement of novel sample holders, which minimize cross contaminations between different growth chambers ([4]) ○ Development of gold assisted InAs nanowire arrays, which is an important step towards developing in-situ nanowire networks ○ First demonstration of in-plane InAs nanowires by Selective Area Growth (SAG); this approach paves the route for a scalable fabrication process of semiconductor nanowires for Majorana based device ([3]) ○ Low temperature MBE manipulator will enable the integration (on semiconductor nanowire) of superconductor materials that requires extreme deposition conditions (i.e. deposition temperature lower than 0C for Aluminum); TNO provided requirement definitions and

[4] activity started as QuTech/TOPO and then continued as TNO/MS project

	developed concept designing for two manipulators ([3])
	• Sputtering tool ([3])
	  ○ Installation of a new deposition tool dedicated to superconductor materials; validation shifted to 2018
	• Nanofabrication
	  ○ Development of 3D substrate fabrication that results in manufacturing of complex nanowire networks (nanowire growth was performed at TU/e); published in Nature
	  ○ Introduction of mesa structure to align nanowire and connect nanowire via a superconductor bridge
	  ○ Application of previously developed hydrogen radical cleaning expertise (TNO/ASML project) to acquire the crucial electrical contact between nanowires and superconductors in Majorana devices ([3])
	  ○ Development of a “Angle evaporation” technique that enables to make a superconducting connection between a superconductor on a nanowire and superconducting leads on the substrate surface ([3])
	  ○ Achievement of a much higher device quality compared to the first results of 2012, which are now systematically reproducible thanks to superconductor materials optimization, nanowire characterization and developments in device design. Such developments lead to publications in Nature Communications and Nanoletters ([3])
	• Agreed way forward with Leiden Cryogenics for the development of low temperature fridges
	• Requirements specification, inspection and laboratory upgrade for novel clean room equipment (e.g., TEM, FIB, SEM, E-Beam, etcher, evaporation, etc.) ([3])
	• MS background IP of 1.7M€, in recognition of the IP, technology and process development performed in the QuTech/TOPO work for the 2015-2017 period; Shared Development roadmap will be the beneficiary of this acquisition in 2018
	• In this roadmap TNO contributed to three scientific papers, one in Nature, one in Nature Communications and one in NanoLetters.

Program dynamics	• The roadmap leader for this workpackage has changed: now Michael Wimmer is managing this roadmap, resulting in a different way of working. • Some activities previously developed by TNO within TOPO (MBE-ALD related projects, SAG device fabrication) will be part of a separate project TNO-MS; some of the materials fabricated will be further characterized by TOPO students.
Fault- tolerant quantum computing roadmap:	
Highlights	• All stations in QCLab2 are running QCoDes, ensuring robust and reliable software development. • On the qubyte device we have created a 5-dot system for the first time • Tools developed for measuring and using virtual gates matrices • Completed work on automatic tuning of tunnel barriers (paper to be submitted in January 2018) • In the Intel cooperation a full stack demonstrator was shown, serving two different qubit technologies. One with a two-qubit superconducting qubit and one with a semi-conducting qubit. • In this roadmap TNO contributed to two scientific papers, one in Nature and one in Physical Review Applied
Program dynamics	• The collaboration with prof. Leo DiCarlo has been very difficult the past few years. It has been decided that the way of working on transmon qubits will be organized differently in 2018. • Collaboration with Intel in this roadmap goes smoothly.
Quantum Internet and Networked Computing	

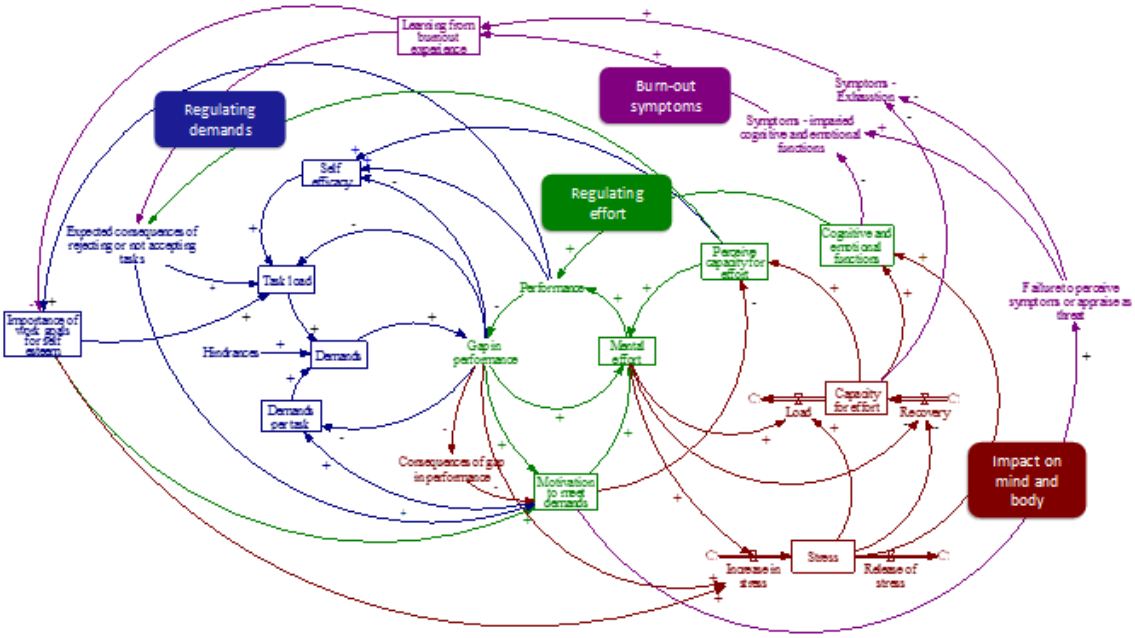
Highlights	• Successfully integrated microwave lines in qubit cavities, which enables qubit control. • We managed to implant nitrogen vacancy centres on predefined locations in a diamond, which opens new roads towards isolated quantum memories. • Development of NetSQUID, a quantum network simulator for researching quantum internet protocols.
Program dynamics	• The roadmap leader for this workpackage has changed: now Stephanie Wehner is managing this roadmap, resulting in a different way of working.
Shared development roadmap	
Highlights	• A full functional and architectural breakdown for a full-stack prototype quantum computer has been defined. • In this roadmap TNO contributed to 3 scientific papers, one in Nature and two of them with TNO scientists as primary author, one of which was selected as editor's suggestion of the month in Physical Review Applied and highlighted in several news items as a breakthrough in the scaling of control systems towards large numbers of qubits.
Program dynamics	• Within this roadmap we will develop a generic control platform that will serve different types of qubit back-ends and a simulation back-end. The simulation back-end, which has been developed by TU Delft, will be installed on the HPC facilities at SurfSara thereby offering a powerful tool for qubit simulations for academic users and business partners.

3 Complexity

General data	
Title	Complexity
'Topsectors'/Societal Themes	TKI Logistics, TKI Chemistry, TKI Agri&Food, TKI Water
Contact person TNO	Ardi Dortmans; Paul van den Avoort; Esther Zondervan
Contact person government	Mariëlle Beers-Homans (EZK)
Progress 2017	
Abstract	ERP Complexity builds new knowledge and networks on the topic of complexity science, with fs on models for technical systems with human decision making. The 3 pillars in ERP Complexity are logistics, health care and circular economy.
Short description	The Dutch society is going through a sequence of transformations that involve both technical and non-technical aspects. *E.g.* the energy transition will have a profound impact on the way we organise our society; the same applies for transportation and logistics, use of materials, health care and safety etc. It is therefore that complexity science is becoming increasingly important as it aims to provide a systemic view on these transitions with emergence, transitions and resilience as the dominating research topics. ERP Complexity has started in close cooperation with NWO program Complexity by defining joint projects in NWO calls. This is still an important mechanism to set-up new collaborations, and in 2017 it was extended through other (NWO) programs and by setting-up the StartImpuls 2 Circular Economy as a clear example of multidisciplinary cooperation for the materials transition (circular economy).
Highlights	**Logistics** Through the collaboration with NWO Complexity and other NWO instruments such as the Big Data ICT for logistics program, a set of 4 joint project with universities and industrial partners have been defined in 2016 and elaborated in 2017: • Trans-SONIC - Transport Self Organization through Network Integration and Collaboration (TUD, EUR, WUR); • ToGrip: Grip on freight trips (TUD); • Comet-PS: Complexity Methods for Predictive Synchromodality (VU); • Swarmport: Self-organization among autonomous agents in nautical processes in modern seaports (TUD, MU). In all of these projects private partners participate and the projects are aligned with the topsector Logistics roadmap. These projects are now in full mode of execution with academic and private partners. Because of limited space interested readers should visit the websites of these projects. In 2017 additional projects were submitted in the framework of the NWO call Sustainable Business Models as well as NWO call Complexity Programmable Self-organisation. The outcome is expected in 2018. **Health** The main objective is to set-up a knowledge base, embedded in a multi-year collaboration between academic/public/private partners and TNO, on simulation models to get grip on the complexity of chronic lifestyle-related health problems for which there is a commercial and/or public need. The purpose of the models includes understanding, complete new insights, identification of early warnings and key(f)actors, indicating high leverage interventions points for

initiating and maintaining behavioural change of life-style (stress, sleep, behaviour, nutrition, optimal drug use, exposome, social / cultural interactions, work-environment). The integrated approach will improve health(care) towards a person-based “promotion of health” instead of “treatment of symptoms”. In the future, the resulting models will be used (1) to gain new insights and offer decision support via *e.g.* web-based simulations used to inform persons and care givers and (2) to create virtual “wake-ups”. For sustainable “Promotion of Vitality” at work, a person-focused systems approach is needed taking into account the cross-interactions with nested complex systems in his/her context, such as behaviour, culture, diversity and infrastructure (leaderships) within teams and organisations. Models simulating retrospective and/or prospective scenarios in relation to objective facts, subjective perception, and behavioural choices are crucial to improve our understanding and identification of early warnings and key(f)actors, indicating high leverage interventions points for initiating and maintaining behavioural as well as cultural changes at work.

A first simulation model of tuning behaviour on development of chronic stress and burnout was successfully developed:



The optimal model methodology was chosen to be a semi-quantitative biopsychosocial health modelling in Ventana Systems (VENSIM) for mutual understanding and capturing insights of the processes involved, followed by quantitative simulations in Stock and Flow models. Apart from an insightful anecdotal systems dynamics model by Homer, no system dynamics models exist which can provide behavioural insight in the development and recovery of chronic stress and burn-out. A literature search of processes involved was performed by experts. Extensive literature and expert knowledge was collected focusing on the processes involved in chronic stress at an individual level. The same was true for processes involved in organisational issues and performance at team level. Very limited information is available on the crucial cross-interactions between the individual and colleagues, and remains to be investigated. Further development of this model was undertaken by cooperation with Institute for Advanced Study (IAS, prof . Sloot), Radboud University (RU, prof. Rouwette) and Utrecht University (UU, prof. Frank).
A system dynamics chronic stress and burn-out simulation model has thus been successfully developed. The model simulates the effect of behavioural changes of the individual and his/her context on chronic stress development and burn-out at work. It captures the dynamic interactions between individual characteristics, perceptions, and behavioural change, in relation to job demands, effort, resource appropriateness, need for recovery, and engagement, towards the

amount of stress and emotional exhaustion over time. The model simulates the development of burn-out, which is a clear tipping point from a desired healthy state towards an undesired unhealthy state.
We succeeded to gain the support of one private partner to start a PPS Research Program Grip on Vitality (health & wellbeing), co-funded with TKI from Topsector Life Science and Health, and are in contact with other partners to joint this PSS. The partners acknowledge the vision of TNO that an innovative integrative research approach -supported by innovative tooling - is needed for support and improvement of effective behavioural and cultural change towards “Promotion of Vitality” at work. This activity will be part of the VP Health in TNO and be the basis for further development of this model in the near future. As such it is a good example of the required system dynamics in this ERP where developments are initiated and transferred to VP in a later stage of development.

Circular economy
In 2017 we submitted a joint project proposal with WUR and NIOO-KNAW in the NWO call Closed Cycles. TNO’s contribution would be on research into the socio-economic aspects of the agriculture-food (manure) transition in the Province of North Brabant (topsector AgroFood). Unfortunately this project was not granted despite the significant amount of industrial and semi-government interest. The interest of North Brabant in this topic is still on the agenda and led to a joint workshop during the ManuResource conference in November 2017. A research proposal to come to an international perspective on a circular agricultural sector in North Brabant has been formulated as a result. In these activities we combine and extend knowledge on circular business models and human behaviour.

In 2017 we submitted a proposal for the Startimpuls 2 Circular Economy to MinIenW. Budget was made available by MinIenW together with MinOCW and MinBZK for a joint project between TNO, Hogescholen, universities and RKI (e.g. RIVM), together with industrial partners. This Startimpuls 2 has been approved by the NWO board and is being elaborated into a call for proposals early 2018. The focus is expected to be on the Transition Agendas Plastics and Constructions.

For TNO an important topic of research will be design for circularity of plastics and building materials, which requires both technical (materials recycling, life cycle analyses) and non-technical research (business models, human behaviour). Exploratory research into chemical recycling has been carried out in 2017, where we find the use of supercritical fluids an interesting topic, also for European projects to be submitted early 2018.

In 2017 TNO, together with prof. Jan Jonker of RU Nijmegen, prof. D. Loorbach of Erasmus, M. Schuurman of MVO Nederland and A. Heideveld of Groene Brein, initiated BOOST CE as the formulation of a large scale implementation plan for the NWA Circular Economy in close collaboration with the 5 Transition Agendas of NL Circulair. This plan has been discussed with a wide variety of stakeholders from government and industry and is expected to be part of the execution plan of the Transition Agendas in 2018.

Collaboration with universities
The connection with excellent groups of universities is intensified and growing. TNO has Ph.D. students at TU Twente and TUD and a number of master students from TUD for logistics research. Intensive contacts exist with Radboud University on circular economy (prof. Jonker), with UU, UvA on Health etc. The multiplier on knowledge influx by cooperation with academic partners is amply met through the joint projects in the NWO programs.

Collaboration with topsectors
In order to reinforce the collaboration with topsector Chemistry on circular economy, Ardi Dortmans has been appointed program manager Chemistry of Advanced Materials in TKI Chemistry per December 1, 2017. This will open additional ways for collaboration with academia and industry, *e.g.* through an expected NWO cross-over initiative on Circular Economy together

	with IAS, RIVM, composite producers and users, UT, TUD, RUG. The health model has been discussed intensively with topsector LSH and a TKI proposal is in preparation. The logistics activities have been defined in close cooperation with topsector Logistics and are supported with additional TKI funding. **Excellence of researchers** In 2017, there was high appreciation for TNO's excellent researchers. In particular we refer to: • Hans van den Berg has been granted the 2017 Arne Jensen Lifetime Achievement Award for his outstanding contribution to the field of performance, control and reliability of communication networks. This award is assigned by the International Teletraffic Congress (ITC), the first and most prestigious conference in this area. The award has been handed over at ITC-29 in Genoa, Italy, on September 7. The award was previously assigned to top researchers from Bell Labs (USA), Orange Labs (France) and TU Eindhoven. **Dissemination (selected items):** • Workshop Closing Nutrient Cycles, ManuResource, Eindhoven, November 2017. Organised together with Province North Brabant (approx. 25 participants from various European countries); • Workshop NWA Circular Economy, March 2017, Utrecht. Organised together with MinIenW, het Groene Brein, MVO Nederland, NWA (approx.. 125 participant from research, industry and government); • Workshop NWA Circular Economy, NWA Conference, October 2017 (approx. 30 participants from research, industry and government); • NPCS[5] Meeting March 2017: poster presentations on health; • NPCS Think Tank Meeting, IAS, "Enhancing Immune Fitness: where to start ?" 17-18 May, 2017.
Program dynamics	The contents of the plans for 2018 will further focus our activities in (self-organised) logistics and sustainability. The first will be expanded through additional projects with academic partners *e.g.* NWO programs or the expected NWA. The second will embed research on energy transactions models (Topsector Energy) as a new topic and circular economy (Topsector Chemistry, NWA). Research on Complexity in Health will be transferred to VP Health, at least for 2018.

[5] Netherlands Platform Complex Systems.

4 Personalized Lifestyle for Health

General data	
Title	Personalized Lifestyle for Health (PLH)
'Topsectors'/Societal Themes	LSH, Agri&Food
Contact person TNO	Ben van Ommen, Peter van Dijken, Nynke van Berkum
Contact person government	Mariëlle Beers-Homans (EZK)
Progress 2017	
Abstract	The ERP Personalized (Lifestyle for) Health (PH) 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 health 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 2017, the ERP Personalized Health was able to achieve its key deliverables, e.g. the Lifestyle as Medicine onboarding system, consisting of a health risk assessment tool, a consultation protocol and (referral) advice. Another example is the digital advice tool on "Opvoedwijzer". The use cases Healthy Aging and Early Life have given this program the focus to develop knowledge and technology to reverse T2D (Type two Diabetes) and unhealthy metabolic state in early life. The deliverables will both be transferred to the VPs and valorized in PPS and B2B. A dissemination highlight of this strategic period was the first annual dissemination event "Lifestyle as medicine – Care to cure" on December 7th. The symposium was also the official start of the joint knowledge and innovation center on metabolic health and lifestyle of TNO and LUMC. This Innovation Center will be the heart of the ecosystem of this ERP, in which the strategic alliance with the LUMC will continue to grow. In the next strategic period 2018-2021, the ERP Personalized Health will shift its focus in, and will build the biological basis for prevention, reversal and cure for diseases with a chronic inflammatory component with the focus on lifestyle modulation. The Use Cases will be fully joint as the goal of this ERP is to cover all stages of life. Therefore, the program will focus on 3 main trajectories for fundamental technology development: biology– towards inflammatory robustness, health by design and changing life, saving lives. These three components connect to the ambition of TNO to become number one in mechanism based n=1 sustainable personalized health advice systems. TNO will continue to closely collaborate with Leiden University (LUMC) in building a portfolio of fundamental and applied research in the area of lifestyle medicine. This ERP Personalized Health also continues to connect multiple strategic routes of the NWA, the topsectors and all 3 roadmaps of the Unit Healthy Living. This illustrates that ERP Personalized Health fits very well to a series of defined goals both inside and outside TNO, and as such many opportunities to establish cross-sectoral research consortia as PPP's are expected to emerge from this ERP.
Short	Lifestyle related diseases such as type 2 diabetes, cardiovascular diseases, cancer, obesity,

description	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 know that an unhealthy diet and lifestyle are the major causes of most of these diseases. The ERP Personalized 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, focusing first on the two use cases Healthy Aging and Early Life. The different fields of expertise are all present within TNO and integrating these individual technologies will result in impact in society, healthcare and economy. Healthy Aging Type 2 diabetes (T2D) is one of the major lifestyle related diseases. Current healthcare practice focuses on care and not cure. Cure is possible from a biological view, as most processes are reversible. Yet, due to inertia of the healthcare system, mixed stakeholder interests and absence of systems approaches in cure-focused programs, hardly any serious attempt to develop and implement T2D cure programs were made in The Netherlands, despite obvious enormous societal and economic benefits. This needs to fundamentally change as the T2D burden already has reached 1 million Dutch citizens and is still growing. The Healthy Ageing (HA) project coordinates all scientific developments of and contributes to the fundamental aspects of the TNO-component of the Lifestyle as Medicine program. Since this program is rapidly evolving into a multidisciplinary and multi-partner program, the actual work program of Healthy Ageing was continuously adapted to achieve its main objective: Implement a science based lifestyle as medicine program focusing on cure of type 2 diabetes patients in the Dutch Healthcare system. This involved two project lines: 1. Building fundamental components of a cure program (diagnostics, interventions, advice systems, coaching) 2. combining and proving these in real life settings (primary healthcare and work). Early Life In 2016 the early life program started in its present form. The emphasis is on expanding the available knowledge position of TNO in the area of Early Life and metabolic health in new innovative ways and at the same time on applying this knowledge base into new and improved forms of human studies that can actually contribute to improving health early in life. The pillars that are used for this are the following: 1. Systems Biology 4 Kids: understanding metabolic development, register currently available non-invasive diagnostics. 2. Advice Systems Filling the gaps in the Early Life knowledge base and translation of knowledge to health advice 3. Create new biology driven models for healthy development which support the biological understanding of healthy early life development.
Highlights	**Healthy Aging** The Healthy Ageing project has served as a basis for the formation of a Joint Innovation Center “Lifestyle as Medicine”, where TNO collaborates with Leiden University Medical Center (LUMC) and other partners (e.g., the Dutch Diabetes Fonds has decided to join and co-fund). In other words, TNO has decided to valorize the ERP Personalized Health deliverables in the setting of a partnership with high societal and economic impact. This partnership was officially initiated during a dissemination highlight of this strategic period: the first annual dissemination event “Lifestyle as medicine – Care to cure” on December 7th. A team of national and international

experts discussed how lifestyle changes can be expected to play such a vital role in curing a disease.

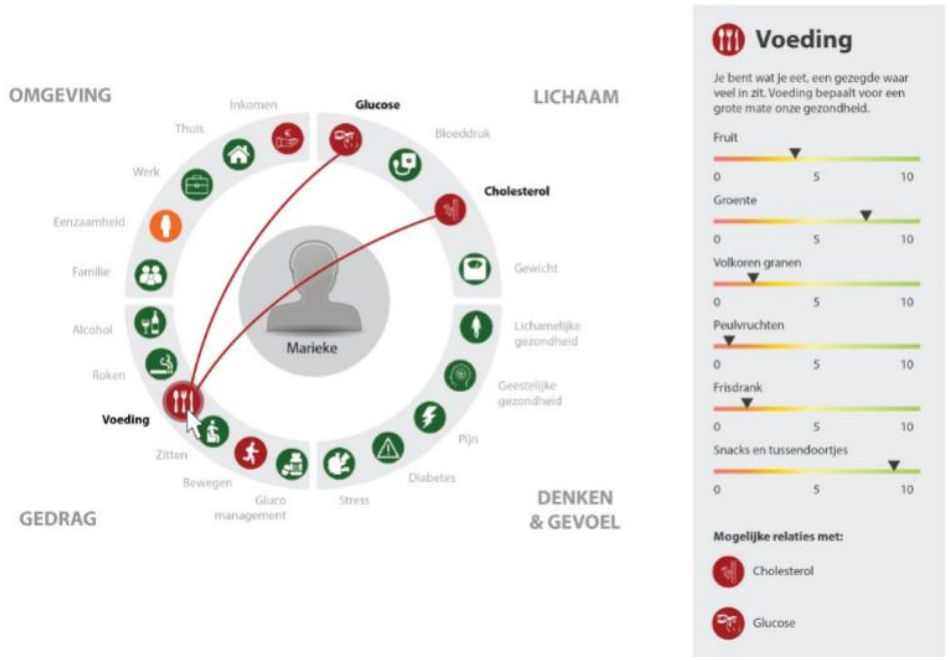
The Healthy Aging deliverables from the entire strategy period 2015-2017 has led to a toolbox of technologies from DIY (Do It Yourself) diagnostics to personalized lifestyle advice for T2D patients. One of the highlights within this toolbox is the Lifestyle as Medicine onboarding system, which consists of 3 parts:

1. A health risk assessment tool, which is based on a 360-degree diagnosis. There are 4 quadrants (body, thinking & feeling, behaviour, and social environment) and each quadrant contains several measurements. “Body” contains the medical biomarkers, like glucose and blood pressure. The measurements of the other three quadrants are based on questionnaires. For each measurement protocols for scoring and norming were developed. The norms are usually represented in 3 categories reflecting a traffic light: green, orange and red.
   The results of the 360° diagnosis are visualised in a so-called profile-wheel (see figure below). One can see the wheel and can click on the dot to see the underlying measures. For example, the systolic and diastolic blood pressure when you click on blood pressure. Also, the personal scores of the patient who filled the 360° diagnosis is represented. The content of the 360° diagnosis and the visualisation is designed in cooperation with the nurse practitioner of the primary care centre Lijn 2 in Rotterdam.

Visualisation of the 360° diagnosis in the Profile Wheel.

   This 360° diagnosis is part of TNO’s Diamonds infrastructure and is accessed through the Lijn 2 portal in TNO’s Sapphire. User acceptance tests have been conducted with 8 patients with T2D from Lijn 2. The patients thought it was easy to fill out the questionnaires and were pleasantly surprised about the visualisation of their own 360° diagnosis. The acceptance tests resulted in a list of improvements for this 1.0 version of the 360° diagnosis for next year.
2. Based on the profile-wheel the nurse practitioner and the patient discuss how the patient can improve the management of his T2D. For this we developed a consultation protocol. Part of the protocol uses additional functionalities for the profile-wheel, which were developed in the past year. The figure below shows one of these functionalities, namely visualising in the wheel that a bad diet relates to negative scores for glucose and cholesterol. Another designed functionality is that the profile wheel also offers advice (like another diet) to be discussed during the consultation. In successive steps goals and action plans are offered. Another part of the consultation protocol is based on motivational interviewing and shared decision making. The protocol is represented on a

set of paper cards that can be easily checked during the consult. The protocol was co-created with the nurse practitioner of Lijn 2.



Screenshot of additional functionalities of the profile wheel, which are used in the consultation protocol

3. The last part of the onboarding system is to provide (referral) advice based on the 360° diagnosis. Therefore, we designed a system how to collect lifestyle interventions (diet, exercise, smoking, alcohol, relaxation) available at the level of the specific health practice, the municipality and nationally, that are coded in order to tailor interventions to the specific 360° diagnosis. For instance, if someone has a low income (quadrant social environment), and he has to change his diet to improve his glucose levels, then low-budget food tips are provided. We have filled this system with examples fitting the Lijn 2 health practice. One of the interventions is to use the HowAmI app, also developed in this project in 2017, in order to monitor goal progress and receive e-coaching at home.

We are cooperating with the primary care health centre ‘Lijn 2’ (Rotterdam Zuid). As mentioned above, the nurse practitioner and patients already used the LaM onboarding system version 1.0. The onboarding system is setup as a flexible system, implying that questionnaires, biomarkers, the profile-wheel, consultation protocol and lifestyle interventions overview can be changed to fit the specific chronic disease (e.g. COPD, CVD) or health care practice. The onboarding system is now being discussed with other primary care centres in Leiden and The Hague. Currently, we have built a version 1.0 and collected and developed a long list of user requirements for version 2.0, to be developed in the future in close collaboration with these primary care centres.

Early Life

The Early Life part of the ERP focuses on the relationship between a healthy development and ways to stimulate this healthy development through, amongst others, lifestyle and nutritional interventions. The big difference between early life and adult life is the large number of changes which take place early in life and their importance for a stable health in later life. Knowledge of the healthy stable situation in adulthood cannot be simply translated into the developmental processes occurring in early life, even not for topics such as metabolic health where much

expertise is available within TNO around the adult situation. The Early Life project therefore focuses in particular on better understanding the biological processes involved in early development, the ability to measure parameters involved in these biological processes early in life and on ways to support and stimulate both parents and infants to take the measures which influence this development in a positive manner.

One of the major achievements of the Early Life project is the development of a science based framework incorporating all known nutritional factors influencing healthy development of infants with a specific focus on metabolic development, cognitive development and infection control. The results of this framework have been incorporated in a review paper. In 2016, 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. In 2017, this online advice tool for parents of toddlers ("OpVoedWijzer") was further developed and tested. One of the major achievements was the automated collection of knowledge via ERIS (Emerging Risk Identification Support) search or external sources and storage in NuSyBox. In addition, the relevant knowledge already present at TNO Child Health was added to NuSyBox as well. The knowledge was subsequently used for a systems decision support model.
Another accomplishment of the Early Life project is finalizing the advice systems for sustained weight management to guide parents of toddlers 4-6 with overweight/obesity. First decision points were defined for parental guidance and nutritional advice, based on identification of measurements for the key behavioral and biological factors and cut-off points. Next, decision rules were modelled based on combined risk factors and intervention options in order to provide personalized advice on nutrition for toddlers as well as parental guidance. This resulted in a proof-of-concept "Opvoedwijzer" (see figure below).

Screenshots of the "Opvoedwijzer", developed in 2017.

Program dynamics	Lifestyle related diseases to a large part are preventable, reversible and curable. The past strategic period this ERP therefore focused on reversing T2D using personalized advice on lifestyle and nutrition. Virtually all lifestyle related diseases have an inflammatory component. This inflammation can both be causal and result from its pathology. Although inflammation is a generic process, it manifests in many health issues and thus has a strong personalized etiology and subject-specific causes. This can be due to genetic variation, early life programming, immunological conditions, metabolic abnormalities and life-long environmental exposure. So far,

the inflammatory component and its relation to immune health has not been assessed. In the next strategic period 2018-2021, the ERP Personalized Health will shift its focus in and will build the biological basis for prevention, reversal and cure for diseases with a chronic inflammatory component with the focus on lifestyle modulation.

The Use Cases will be fully joint as the goal of this ERP is to cover all stages of life. Therefore, the program will focus on 3 main trajectories for fundamental technology development:

1. Biology – towards inflammatory robustness
   An enormous gain can be achieved in understanding the basic mechanisms of optimizing inflammatory control and robustness. New scientific insights emerge suggesting that flexibility, robustness and training of the defense (= adaptive homeostatic) mechanisms involved are key to health and a universal principle, from early life to healthy ageing and from subcellular to whole-organism. Three Initial (2018) concrete examples will be elaborated: in intestinal health (mycobiome, intestinal robustness and inflammatory health and disease), the pancreatic beta-cell (old age deterioration of insulin secretory capacity vs mitochondrial regeneration in dynamic ketosis), and liver health (personalized lifestyle – medicine treatments based on the above described mechanisms). Subsequent target may be developed in inflammatory-metabolic, inflammatory-immune and/or inflammatory neuronal disorders. This ERP will approach this topic from conceptual, molecular, biological, mathematical and behavioral angles.

2. Health by Design
   Next to the understanding of the biological mechanisms, a method needs to be designed to optimally intervene (= prevent, reverse and cure) in inflammation related processes and (pre-)diseases. Given the dynamic nature of the processes as described above, this cannot be done statically, i.e. a single prescription of medication, as this involves a (re-)gaining of inflammatory robustness and systems flexibility. The optimal personal treatment timeline requires regular diagnosis. Methods thus need to be developed which combine (continuous) health monitoring with model advice systems. Furthermore, self-learning algorithms need to be included which also exploit health timelines of other subjects, either from multiple timepoint intervention studies or real-world healthcare data (Health Data Cooperative). This method is strengthened if knowledge is combined with data. Thus, the NuSyBox-infrastructure will be included. The same infrastructure can be used to predict comorbidities, which can be included both in the advice system and towards product development.

3. Changing life, Saving lives
   Chronic inflammatory diseases are the result of predisposition and exposure, i.e. lifestyle. Biological interventions (1) and personalized advice (2) will thus only be effective within a sustainable lifestyle change, and it is useless to develop these if the means to implement are absent. Currently, our society allows and even stimulates its citizens to live an unhealthy life, and has a healthcare system ready to “take care” of the resulting diseases. Numerous attempts to change this have failed as neither a systems approach nor a disruptive approach was used. This now needs to change and TNO will provide both approaches in a connected manner, first in a regional setting, followed by national and as “export” model. The two connected solutions are personal health data valorization (as disruptor) and systems based behavioral change. Both aspects will be developed in an ecosystem of academic collaboration, where TNO develops the components which lead to valorization and economic development.

These three components connect in the ambition of TNO to become number one in mechanism

	based n=1 sustainable personalized health advice systems. TNO will continue to closely collaborate with Leiden University (LUMC) in building a portfolio of fundamental and applied research in the area of lifestyle medicine. It is without question that the ERP Personalized Health also continues to connect very well with at least two routes of the NWA: “Gezondheidszorgonderzoek, preventie en behandeling” and “Personalised medicine: uitgaan van het individu”. This furthermore aligns nicely with the KIA of the various Topsectors. For the most important one, TopSector Life Sciences and Health, these opportunities reflect in the Roadmaps 3 Homecare and Self-management, 5 Pharmacotherapy, 6 One Health, 7 Specialized Nutrition, Health and Disease, 8 Health Technology Assessment, Individual Functioning and Quality of Life and 9 Enabling Technologies & Infrastructure. Also within TNO, ERP Personalized Health will play a fundamental role in providing key technologies to all 3 roadmaps of the Unit Healthy Living: Biomedical Innovations, Digital Health and Sustainable Work. This all illustrates that ERP PH fits very well to a series of defined goals both inside and outside TNO, and as such many opportunities to establish cross-sectoral research consortia as PPP’s are expected to emerge from this ERP.

5 Energy Storage and Conversion

General data	
Title	ERP Energy Conversion and Storage
'Topsectors'/Societal Themes	TKI Chemie; TKI Urban Energy
Contact persons TNO	Ardi Dortmans (2017) / Pascal Buskens / Esther Zondervan
Contact person government	Mariëlle Beers-Homans (EZK)

Progress 2017	
Abstract	Energy Conversion and Storage becomes more and more important to achieve an increased use of durable energy. In 2015-2017 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 keep 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 chemicals and fuels. • Studying the feasibility of a process that directly uses sunlight for the production of 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"). Highlights have been described below per project.
Highlights	**Electrons to Chemicals** Related to energy storage, the possibility to use electrical energy for chemical transformations creates high attention. It is evident that electrocatalysis will improve the efficiency of electrochemical driven conversion. However, it is currently unclear how to translate fundamental insights on molecular level related to electrocatalysis towards large scale implementation. The E2C project aims at resolving this knowledge gap. The TNO strategy is aimed on **establishing tools and knowledge infrastructure enabling the combination of first class electrocatalysis with overall system development** (*e.g.* integration with separation technology). In 2017, TNO further expanded the infrastructure and knowledge to develop and asses electrochemical transformation towards organic molecules and towards CO2 neutral feedstocks and fuels. Main highlights of this project are described below. *Hydrogen peroxide (H_2O_2) demonstrator* For the H_2O_2 demonstrator, a new three compartment reactor was designed and constructed in conjunction with Hydron Energy. Preliminary experiments have shown electrochemical production of hydrogen peroxide. Experiments were performed to assess the influence of current density, electrolytes, anion exchange membranes on the current efficiency, cell voltage and

energy usage of the process. For instance, increasing space-time yield is considered of high importance as it would utilize installed capital to a higher extent. In our experiments it was shown that while increasing current density from 0.5 kA/m2 to 4.0 kA/m2, the current efficiency (CE) remained stable.

Paired electrosysnthesis
In 2016, an integrated continuous bench scale setup was designed and built for electrochemical conversion of HMF to FDCA (building block for plastics). This work is finalized in 2017. Furthermore, new show cases for the electrochemical conversion of biobased starting materials have been developed (propanediol to lactic acid), showing high efficiency and selectivity. Based on the results obtained, one patent has been filed and two patent proposals are in the process of filing. A state of the art infrastructure has been established. The work related to electrochemical conversion of biobased materials will be continued in 2018 within the VP Sustainable Chemistry.

Reactor and system development CO_2
The goal is to demonstrate and scale up technology to electrochemically reduce CO2 back into feedstock and fuels. In the previous year, the CO_2 reduction to ethylene using Cu based electrodes has been tested. The low amounts of ethylene detected under the conditions tested lead to a reconsideration of the target product. The reduction of CO2 to carbon monoxide has attracted a lot of interest in both academia and the commercial companies. Therefore, in 2017, instead of ethylene the formation of carbon monoxide was chosen. The electrocatalytic reduction of CO_2 to CO using Au based electrodes is demonstrated experimentally. The Au nanoparticle catalysts were prepared at TNO and for the reference measurements, Au plate was used. The work was continued later in the year within the VP program of sustainable Chemistry and the VP program of Energy. It has been identified that it is crucial to integrate electrochemical conversion with CO2 capture, related from a CO2 cost perspective and related to a process efficiency perspective. Based on concepts developed within the ERP, three patents are in the process of filing.

Photons to Chemicals
In 2016, we showed the concept of photons to chemicals in the Suzuki reaction using gold-palladium nanoparticles. In 2017, the synthesis procedure of gold palladium was optimized for the gold nanorod aspect ratio and palladium depositions within TNO. Then the synthesis of the optimised particle was successfully scaled-up in a 2L batch reactor.

In the project Interreg EnOp cofinanced by this ERP, the aim is to develop a new generation of photoactive materials to produce solar fuels from CO2. In 2017, the reactor was designed, tested and validated. New catalysts based on ruthenium were synthesized and tested. As a significant result the methane production increased 1,5 times for the ruthenium catalyst compared to commercial Ni-Al2O3/SiO2 material.

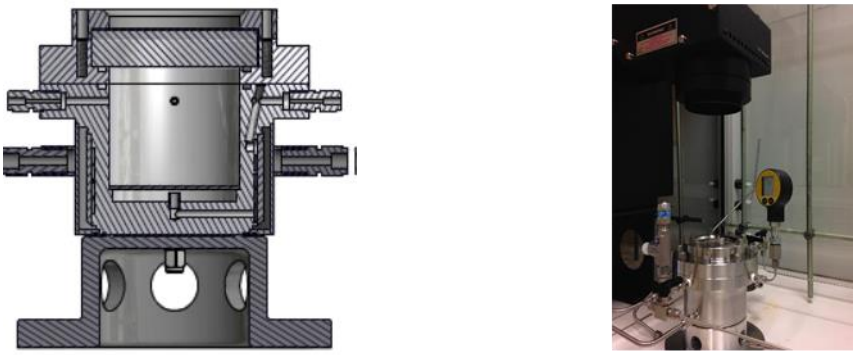


Figure 1: Left. Photoreactor drawings. Right. Photograph of the system used showing the photoreactor and the solar simulator on top.

Furthermore a business case was set up for the conversion of CO_2 to methane and methanol. For both conversions competing scenarios compared to current production technology are available. The outcome of this study is that we need to focus on reduction of the hydrogen price which can be done by photon catalysis or electron catalysis, and on optimizing the reaction for higher conversion and shorter residence time.

Thermochemical storage
R&D activities aiming to create a breakthrough in compact thermal storage, addressing different scale levels of the envisaged challenge and different routes of bringing technology to the market. 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 and 2017.
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).

For use case 1, stabilized $K_2CO_3 \cdot 1.5H_2O$ is the most suitable salt. Microencapsulation with ethylcellulose gave most successful stabilization concepts for this salt, because of manufacturability, effective Q/V of ~0.7 GJ/m^3, multicyclic performance and stability. The particles are optimized for the salt particle (core) itself and, second, the layer (shell) surrounding the thermochemical storage material core.

For use case 2, the selection process already started in 2016. In 2017, a structural analysis of the formerly identified systems from a lattice level has been performed which helps to select and to understand promising (partial) hydration reactions of the identified candidates, and to identify salt reactions with promising kinetics. Based on this study the system most suitable based on the defined criteria is the salt hydrate $CaCl_2 \cdot 2\text{-}4\ H_2O$, and alternatively, if choosing another sorbent, $CaCl_2 \cdot 8\text{-}4\ NH_3$.

In addition, TNO has available a full set of techniques to characterize the performance of the material, of the grains and of the packed bed. Furthermore, the particle model developed in 2016 is further developed to design criteria for salt-sorbate systems (including composites) on component and reactor level in thermal storage. The model helps to understand the basis of the dominant time and length scales on the level of the thermochemical material and material/flow/heat exchanger interaction.

Self-Organising Smart Energy Networks (SOSENS)
The goal of the SOSENS project is to develop and validate an algorithmic framework for the second generation transactive energy (TE) systems that form an essential step in achieving radically higher levels of sustainability and energy efficiency in Europe and beyond.

Highlight of this project is the development of the SOSENS demonstrator which is capable to run different scenarios (network topologies, different devices in/belonging to households (like storage, heat pump, micro-CHP, solar panel, and fixed demand and electric vehicle) and finds optimal cost solutions in the scheduling of the electricity demand. Most optimal scenario is the combination of SOSENS locational Power matcher, using locally adjusting prices to mitigate congestion whenever is necessary, combined with day ahead planning (algorithm also developed within SOSENS). In this optimal scenario network congestion is solved and at the same time households profit from their shiftable devices.

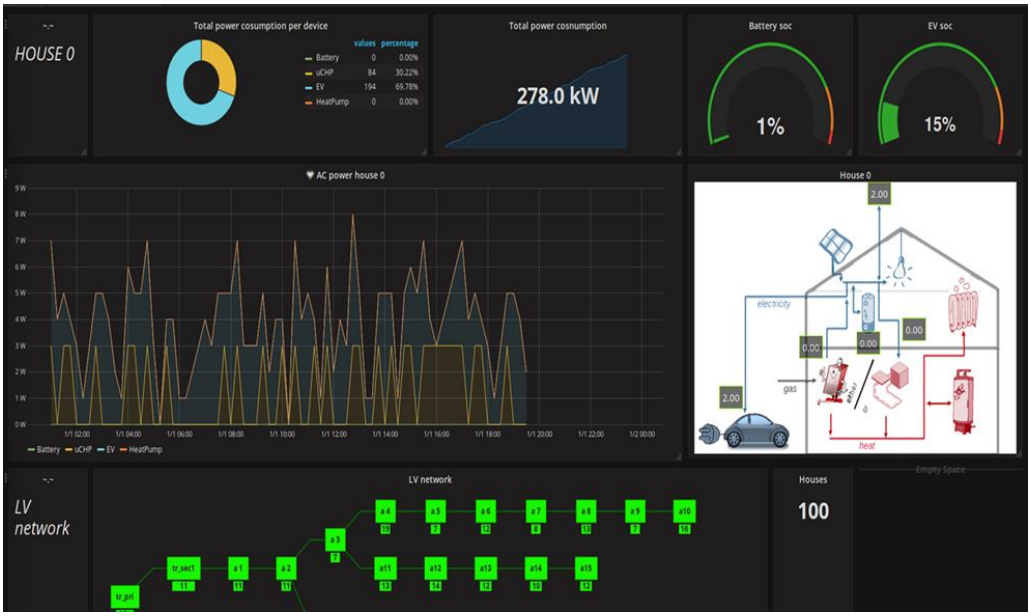


Figure 2 Test run of SOSENS demonstrator for 100 households.

Collaboration with universities

The connection with excellent groups of universities is intensified and growing. TNO has Ph.D. students at TU Twente, RUL, TUD, UU, TU/e and, KU Leuven and the University of Strathclyde (UK). The multiplier on knowledge influx by cooperation with academic partners is thus amply met. One of the Ph.D. students (Pim Donkers) of TU/e graduated in 2017 and started working at TNO.

Excellence of researchers

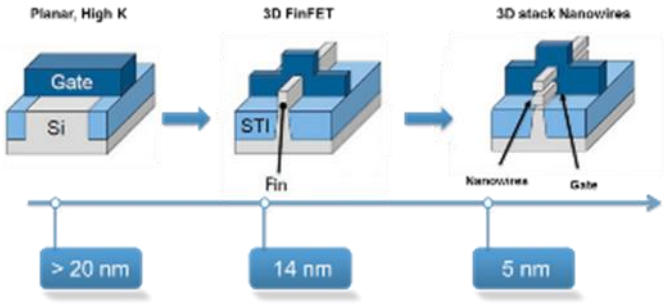
In 2017, there was high appreciation for TNO's excellent researchers. In particular we refer to:
he 'Habilitation' of TNO Principal Scientist Pascal Buskens was completed in 2016 and awarded with the Friedrich-Wilhelm award for the best 2016 Habilitation at RWTH Aachen in November 2017;
ascal Buskens started a guest-professorship at Hasselt University since October 1st 2017;
he cooperation with TU/e to create a part-time professor chair for Koen Kok related to Transactive Energy;
he cooperation with TU Delft to create a part-time professorship for Earl Goetheer related to large scale energy storage, and Earl Goetheer was member of 5 national and international review/advisory commissions incl. ECCM.
oen Kok was invited to organise as Guest Editor-in-Chief a special issue in the IEEE Transactions on Power Systems journal, on the subject of Transactive Energy;
laf Adan continued his professorship at TU/e for another 5 year period and was member of 9 review/advisory commissions.

Dissemination

The progress of ERP Energy Storage and Conversion was disseminated at various events to inform the Dutch stakeholders, i.e. Voltachem event at 9 Nov 2017 (180 participants), TCS Warmtebatterij at 28 Sep 2017 (70 particpants), Nanotechnology crossing borders event, at 28 Sep 2017 (100 participants), and Transactive Energy Research Directions Workshop at 6 Dec 2017 (20 participants). In addition there were several contacts with the media: Telegraaf (jan 2017), RTL news (May 2017) and Nieuwsuur, Journaal (Nov 2017). Finally, there are good connections with TKI Energy, TKI Chemistry, TKI HTSM, Ministry of EZC, NWA route energy transition, NWO and DIFFER.

	Finally, 10 patents are filed (2015-2017), 5 patents are in progress and 1 patent is under investigation. In 2017, 23 publications are published, 1 publication is submitted and 4 publications are in preparation. At least 7 oral presentations and 6 poster publications were given at international conferences.
Program dynamics	The contents of the plans for 2018 are changed compared to the original plan 2015-2017 to maximize impact and further focus the research within ERP Energy Storage and Conversion for 2018, as requested by the Board of Directors. This resulted in a strong focus on cost efficient conversion of CO2 to carbon based fuels by light or electrons for the program in 2018. The SOSENS topic will be continued within ERP Complexity as there is a strong link with focal topics addressed there: sustainable business models, logistics, self-organisation. Connections with ERP Complexity were already made in 2017. The topic TCS will have a reduced size in 2018 and focus on research with academic partners. The position of lead scientist is vacant, recruitment has started.

3D Nanomanufacturing Instruments

General data	
Title	3D Nanomanufacturing
'Topsectors'/Societal Themes	HTSM
Contact person TNO	Hamed Sadeghian, Rogier Verberk, Nicole Nulkes
Contact person government	Mariëlle Beers-Homans (EZK)
Progress 2017	
Abstract	By the end of 2017 there will be more than 8.4 billion connected devices (Gartner 2017). In 2020, the number of connected devices will increase to more than 20 billion. This means nearly every device we own or can imagine will be connected to the Internet. The range is from our mobile phones, wearables, home appliances to even our cities. This full integration of data can have an unprecedented impact in our society by better management of water, energy, transportation and safety, and reaching fully sustainable cities, cognitive computing, bio-medical for early diagnosis, cancer detection and Quantum computing. Growth in (Internet of Things) IoT requires more powerful and energy efficient nanodevices. To enable the power and efficiency demand, 1) the device dimensions shrink to atomic dimensions and 2) 3D nanoarchitectures are needed to enable new functionalities and to make optimum use of the available space. The technologies currently used for production and quality control approache physical boundaries and are no longer technologically or economically feasible. As a result of both challenges breakthroughs in manufacturing and metrology methods for (3D) nanoarchitectures are required.  To support the development of 3D nano-electronics the ERP 3D nanomanufacturing (2015-2017) has developed key technologies on instrumentations, processes and techniques for manufacturing and metrology of nanostructures: 1- High throughput scanning probe microscopy for nanometrology applications 10 nm resolution. 2- Mask-less nanopatterning technique for 10 nm structures 3- Subsurface nanoimaging for alignment, overlay and buried defect applications Our focus is to capitalize the knowledge generated in the ERP. Nearfield Instrument BV, a partner of the ERP ecosystem was launched in 2017 by TNO to bring atom-scale metrology solutions, developed in ERP (2015-2017) to the semiconductor industry. Major investment in Nearfield Instrument, by leading Semiconductor Industry Samsung Electronics, has shown the relevance of our technology. November 2017 TU Eindhoven's High Tech Systems Center (HTSC) joined forces with TNO in the NOMI (Nano Opto-Mechatronics Instruments) collaboration. To strengthen this collaboration, Dr. Hamed Sadeghian, principal scientist and scientific lead of ERP 3D Nanomanufacturing, became associate professor at TU/e November 1st, 2017.

	Over the last three years the program has 59 patents filed, 28 invited lectures delivered, 157 conference posters presented and 28 journal papers published.
Short description	**Main Objectives for 2018-2021** To bring potential solutions to the nanometrology and nanotomography challenges mentioned, strategic period (2018-2021) will focus on the following topics. 1. Nanometrology and nanotomography: a. 3D nanometrology focusses on 1 nm resolution, mainly for gate all around nanowires as next generation nanodevices and b. Subsurface nanoimaging and quantum sensing focusses on resolving the depth of features. 2. Nano-motion control and Dynamics a. This platform focusses on accuracy and throughput increase which is extremely important for adaption of the developed techniques by industry. 3. Establish with our academic and industrial partners an excellent innovation center to serve R&D for 3D nanomanufacturing and nanometrology. For development of our strategic collaborations the ERP 3D Nanomanufacturing has the following objectives to further enhance 1- An incubation program to generate more (joint)ventures and to 2- Further establish a long term joint development program with several industrial partners.
Highlights	**Main achievements of ERP 3D Nanomanufacturing (2015-2017)** To support the development of 3D nano-electronics, the ERP 3D nanomanufacturing (2015-2017) has developed key technologies on instrumentations, processes and techniques for manufacturing and metrology of nanostructures. Examples are: 1. High throughput scanning probe microscopy for nanometrology applications with 10 nm resolution. 2. Mask-less nanopatterning technique for 10 nm structures 3. Subsurface nanoimaging for alignment, overlay and buried defect applications Especially the concepts developed on through layer Nano imaging have gained attention from leading semiconductor companies. ASML is a partner in our program and invested heavily in 2017 into our research lines. Samsung invested in 2017 in Nearfield BV, the spin-off of TNO for the development of Parallel and High Throughput Atomic Force Microscopy. **External connections** *Top sectors, NWA and ERP 3D Nanomanufacturing* The topics of the Early Research program are addressed in Top-sector roadmap “Semiconductor Equipment” and the NWA “Route Quantum and Nano”. The challenges of 3D nanometrology and nanomanufacturing are mentioned in the roadmap as a result of “more Moore”. Metrology and characterization techniques are relevant to manufacturing industry, because miniaturization of features require new and innovative imaging techniques. The NWA route Quantum and Nano explicitly mentions the challenges of nanomanufacturing processes and the quantum sensing as a method to further enhance the resolution and sensitivity in characterization techniques. **Strategic collaborations** *Spin-off company Nearfield Instruments* Our focus is to capitalize the knowledge generated in the ERP. Nearfield BV, a partner of the ERP ecosystem, was launched in 2017 by TNO to bring atom-scale metrology solutions,

	developed in ERP (2015-2017) to the semiconductor industry. Major investment in Nearfield Instrument, by leading Semiconductor Industry Samsung Electronics, has shown the relevance of our technology. *Academia* November 2017 TU Eindhoven's High Tech Systems Center (HTSC) joined forces with TNO in the NOMI (Nano Opto-Mechatronics Instruments) collaboration. To strengthen this collaboration, Dr. Hamed Sadeghian, principal scientist and scientific lead of ERP 3D Nanomanufacturing became associate professor at TU/e November 1st, 2017. *NOMI JIC* (Nano Optical Mechatronic Instruments Joint Innnovation Collaboration) In 2017 we started with the development of NOMI JIC. We target to have NOMI JIC up and running (operational) in 2018. Aim is to include industrial partners in 2018. **Dissemination** High-level experts from leading semiconductor companies like SEMATECH, Intel and ASML contributed to and attended the dissemination event of the program in November 2017.  *Dissemination event 6th of November 2017* **Main challenges** The main challenge of the program was to engage more industrial development partners, equipment and senior experimental-theoretical physics researchers for further growth and development of proof of principles.
Program dynamics	Overall the ERP follows the ideas as described in the multiannual plan. In 2018 the program will focus on improving the depth sensitivity for our subsurface nanoimaging to enable imaging subsurface structures with higher contrast. New nanotomography techniques will be ranked on their feasibility. Optical metrology will be studied to identify the uniqueness for TNO. For STED (Stimulated Emission Depletion) manufacturing the feasibility to manufacture with high throughput will be investigated. In 2018 the program has the objective to start a joint development with partners for the development support of sensors and tips to improve nanotomography. We will also further enhance our collaboration with Samsung and others on topics related to nanometrology and nanotomography.

6 Structural Integrity

General data	
Title	Structural Integrity
'Topsectors'/Societal Themes	Energy, HTSM
Contact person TNO	Henk Miedema, Peter Paul van 't Veen, Peter Laloli
Contact person government	Mariëlle Beers-Homans (EZK)
Progress 2017	
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. The use cases are: 1. Concrete bridge (e.g. 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.
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.
Issue 1: *"Advanced sensing and inspection technology"*	
Highlights	*1) Monitor system that can classify number and size of cracks in a concrete slab* In 2017, a new ultrasonic technology was introduced, entitled Direct Velocity Mapping (DVM). This technology has been studied and experimentally verified to map the local velocity in concrete. Once the velocity is known this can be translated to a Young's modulus map (using some a-priori assumptions), which is a key parameter for the use case concrete bridge to model the current status of the structure. When successful, the nondestructive nature of this technology and the ease of application would provide large benefits over the current destructive material sampling (drill cores). A concrete sample was manufactured with a hollow tube half-way the thickness of the sample. The tube can be pressurized with oil to mimic rebar corrosion. Rayleigh waves are excited using a single piezo element and a contact probe is used to scan the surface, recording the full wave field at the surface. The recorded wave field is processed such that a local velocity map is obtained. From the processing, a wave amplitude and propagation direction map is obtained that can be linked to the Young's modulus of the concrete. In 2018 the validity of DVM as an indicator of Young's modulus will be further evaluated and it's potential to map the cracks & re-bar corrosion will be further investigated. *2) Multi parameter fiber optic sensor system to monitor load, vibration & chemicals*  BAM BLEIB set-up  Shaker & moving weight(s)  BAM test campaign 2017 The reference site of partner BAM (Bundesanstalt für Materialforschung und –prüfung, a materials research institute with 1600 employees, based in Berlin) was used to test various fiber optic measurement techniques. For BAM this is part of the BLEIB (Bewertung, Lebensdauerprognose, Instandsetzung von Brücken) project. These techniques aim at (distributed) measuring of strain and vibrations (for damage identification through eigenfrequency analysis and for crack detection through sound analysis)
Program dynamics	In 2017 it was aimed for to use the Full Wave Field Model (FWFM) as new modeling engine to improve the performance of existing logging tools to detect the presence of cement behind multiple casings for the use case well integrity. The first tests of using full-wavefield modeling for this purpose showed better images of defects (size & depth) than the corresponding images obtained with ray-tracing as modeling engine. It turned out that the FWFM becomes instable when imaging defects with large contrasts. This makes it unsuitable for borehole applications, where the contrasts are large, as is the number of iterations required.
Issue 2: *"(Multi-scale, multi-physics, probabilistic) models"*	
Highlights	Highlights for modelling are formulated for each of the four use cases.

Concrete bridge
The modelling activities resulted in a ready-to-use advanced baseline assessment method which can take damage into account and which can incorporate inspection and monitoring data thereby reducing uncertainties. Also a first concept of the service life prediction method on a structural scale was made, with focus on use of corrosion data. Full- probabilistic simulation tools (SFEM, DARS) have been enabled in Python environment for commercial FEM software (DIANA v10) and other non-commercial FEM models to cope with baseline assessment of existing concrete bridge, making use of stochastic input generation for FEM incl. random corrosion fields. A methodology for damage identification in existing structures has been developed. The preparation of one full-scale case study for baseline assessment has been successfully concluded.

Offshore Wind
TNO created a robust tool to perform state estimation and tested it up to noise levels much higher than expected in the field and found it to be accurate and stable. The tool is flexible for the adjustments needed for field applications, amongst which: integration with measurement databases, data driven automatic processing of measurement data, streamlining and handling specific data and coupling with other tools such as Multi Asset Correlation (MAC).
Tests on welded crack growth specimens have further validated our corrosion fatigue propagation model. The deterministic model has been extended into a probabilistic model. Preparations have been made to incorporate the influence of cathodic protection.
TNO now has a design methodology with which to apply 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 into a toolbox, which include FEA subroutines, FEA postprocessing software, and Python routines that are able to translate from one condition to another. Especially in 2017, the cost of applying this technique was reduced enough to now be more relevant for industry.

Well Integrity
A methodology for probabilistic numerical simulations of leakage was developed and this has been incorporated in a quantitative risk assessment procedure. Steps have been taken to use numerical simulation tools for uncertainty assessment by stochastic modelling. This is an important step in risk assessment quantification. The computer codes and methodology developed can be applied for optimizing abandonment as well as evaluating the possibility of reuse of a well (CO2 storage, geothermal use). Insight has been obtained in the key parameters and processes that might lead to leakage of a wellbore. Current monitoring equipment does not fulfil the needs to measure these parameters and processes. Hence, the results identified crucial knowledge and technology gaps and could therefore steer future development in experimental studies and technology development.

Composite Vehicle
The overall objective is to enable quantitative assessment of the residual structural performance and protection level of composite panels subjected to out-of-plane dynamic loading. In 2015-2017 this resulted in a thorough knowledge base, a scaled experimental setup and test procedure, and knowledge on the FEM modelling of composite materials loaded by high-amplitude, geometrically concentrated impulsive loadings. Some composite material concepts have been devised, which show high potential and are interesting concepts for further development and integration testing. The composite material concept that was developed in 2017 is so strong that it exceeds all expectations and is currently outperforming the traditional blast solutions.

Program dynamics	- Offshore wind: The results of the model development have been discussed with the offshore wind industry. Based on brainstorm sessions, the key parameters have been defined to bring the model development further and applicable to the design of offshore wind substructures. This has led to the writing of project proposal Corrosion-Fatigue Life Optimisation (C-FLO), which has been written in the framework of GROW, with several industrial and academic partners from the Netherlands and Korea. - Composite Vehicle: The demanding FEM modelling of composite material during blasts has proven difficult due to limitations in the commercial software used. However, the link between modelling (predictive) capability and experimental capability is important – a validated FEM modelling toolbox can accurately estimate the effectiveness of a material concept without the need for rather expensive experimental tests. This was and will be managed by keeping in close contact with the FEM modelling software developers to search for the best solutions when modelling difficulties arise. Another aspect that reduces the risk is the refocus on the structural response and not only on the final failure.
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 important peers are involved such as TU Delft; ECN; Bundesanstalt für Materialforschung und –prüfung (BAM); Kyoto University. *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 the city of Amsterdam, we have selected a bridge for demonstration. We will invite industrial as well as knowledge partners to participate in the demonstration. In addition to such a field lab in the Netherlands. we are exploring the possibilities in Germany with BAM/BASt and in Japan with Kyoto University. 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. With the advanced models we have developed we have been asked to evaluate the validity of current state of the art models. *Offshore Wind* TNO is regarded as the specialist on (corrosion) fatigue and fracture related challenges. We further improved this position and extended it 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. *Well Integrity* The geomechanical model will be applied in the ERA-ACT ALIGN project to evaluate mechanical degradation upon cold and batch wise injection of CO2. The risk assessment tool, including the numerical models, is one of the key methodologies for further development for the purpose of CO2 storage in the SECURE project. Discussions are ongoing with the National Re-Use & Decommissioning Industry Platform of EBN/Nogepa (WWW.NEXSTEP.NL) to use the tool to

	assess the Dutch sector for re-use and abandonment planning. The first externally sponsored projects foreseen are demonstration projects at operators' assets to show the added value. Anticipated next step is to develop indutry sponsored projects to improve and tailor the features of the tool to specific client's interests and transfer the technology with supporting consultancy work of TNO. Finally a sponsored project is anticipated in a call by State supervision of the mines (Sodm) on well integrity risk assessment. *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. TNO collaborates with a composite manufacturer and a vehicle manufacturer. Also the Ministry of Defence is involved closely.
Program dynamics	In 2017 partners for creating demonstrations/living labs in 2018 have been chosen, and preparations are currently being made. The basis for a long term program Macro Structures Research (MASTRE) has been put in place, by further strengthening the relations with two international key players. Due to the fact that some of these partners are reporting to departments of their national government, formalizing the relation is intertwined with the formation of a new government, which was not yet in place in 2017. Meanwhile the actual cooperation is growing.

7 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	Mariëlle Beers-Homans (EZK)
Progress 2017	
Abstract	In 2017, in the Early Research Program Human Enhancement, TNO has strengthened its knowledge position on a number of strategic topics nationally and internationally: situation awareness, division of work and resilience. Distinctive is the multidisciplinary system approach, in which human factors knowledge for improving human-technology performance is developed, integrated into formal models and tested in field experiments. The integral analysis of people, work and technology provided a unique basis for strengthening people in complex technology-rich environments and developing the required personalization. The ERP research into situation awareness has yielded new knowledge and methods on the reliability of data-driven inferences of technological support. In the ERP, structural partnerships with universities have been intensified (University of Twente, University of Groningen, Delft University of Technology). By organizing an international symposium on Human Factors in Automation (October 12-13, 2016), a national final event for stakeholders (November 16, 2017), (invited) conference presentations, magazine publications and participation in European projects, the ERP has shown its international knowledge position on these topics. More specifically, 2017 has been the year in which algorithms and support systems were finalized and tested with end users such as car drivers, experienced Dynamic Positioning operators, and police employees.
Short description	The demands made by our work are changing in many sectors. Technological developments are happening faster than ever. Just think about digitalisation, robotisation, the Internet of Things, big data. As a result, jobs are disappearing and new ones appearing, and most of all, the actual work itself is changing. The new demands being made by technology have to be aligned with the human being to optimise how humans perform with the technology. TNO develops new methods, models and tools to realise the best human-work-technology alignment, geared specifically to adaptive support in highly demanding, complex and dynamic operating environments. **Situational awareness**, or having an overview of the situation and being able to respond effectively, is key here. In traffic, whether on the road or on the water, the transfer of tasks plays an important role. Self-driving cars are on the rise as is autonomous, unmanned, sailing. But it will still take some time before this is fully operational. Until then the driver or operator will have to directly intervene to take over the tasks of the technical system. This brings together expertise on technology and behaviour, a unique combination offered by TNO. We develop state-of-the-art methods and tools to assess the mental and physical state of the human driver in real-time to ensure the seamless transfer of control between the human and the automation so that driving and sailing becomes safer, more productive and more comfortable.

	Resilience of employees is a second key element. In the safety and security domain it is vital to strengthen resilience so that soldiers, the police or fire-fighters can handle stressful situations effectively. The risk of excessive stress and a potential burn-out are always just around the corner. We develop methods and tools that make use of wearable technology to monitor people both physiologically and psychologically over an extended period. We also develop predictive models specific to individuals to provide recommendations on stress management at both an individual and organisational level. **Security** is the third key aspect. In the cyber domain we are seeing a huge increase in the number of attacks on computer systems. Computer Security Incident Response Teams have to be able to respond effectively, and the human factor is an essential component for these teams: situational awareness, information management, training and support are crucial to the efficient and effective operation of these teams. TNO develops tools for this.
Highlights	*Automotive use case* TNO has developed two important algorithms that will improve safety and usefulness of (partially) automated vehicles and create a value proposition for automotive OEMs and increase acceptance and actual use of automated driving. These are (1) Personalized ACC (Adaptive Cruise Control) that automatically adjusts settings to personal driving style, and (2) Driver Readiness Model for truck platooning. 1. Personalized ACC Current automated functions in cars and trucks are generally implemented as a one-size-fits-all solution, at most with a limited number of adjustable settings. This may lead to suboptimal system behaviour and reduced user acceptance for a large number of drivers or driving situations. This may lead to under trust of the system, and people not using it because it does not fit their expectations and needs. TNO has developed an approach in which driver support functions automatically adapt to the driver, the driver state and driving and traffic conditions. This approach has been implemented in an ACC algorithm; the P-ACC (Personalized ACC). The P-ACC algorithm uses critical elements from manual driving to tune specific elements in the P-ACC to fit to the user preferences and profile without any manual settings. It has been tested in on-road studies showing increased acceptance and comfort compared to driving with ordinary ACC. This personalized approach can also be applied to numerous other driver support functions, which will increase brand loyalty and brand image, increase actual use and comfort and even lead to safer and more comfortable driving. 2. Driver Readiness Model In truck platooning and highly automated driving, the car or truck temporarily takes over driving tasks from the driver. Depending on the level of automation, it may drive automatically through traffic in a platoon of vehicles. However, in case of unforeseen situations or limitations in the functional envelope of the systems, the driver will be requested to take over control from the automation and switch back to manual driving. This requires a complicated interaction between automation and driver. The automation allows the driver to be temporarily out of the loop and do other things but needs the driver to resume control in due time in order to ensure safety. This means that the system not only needs to monitor technical status and driving conditions, but that there needs to be some information about the time the driver needs to take back control under various conditions. TNO has developed a unique Driver Readiness Model that detects the real time status of the driver and predicts real-time the required time that the driver needs to safely take over control from the automation at any moment. This driver readiness algorithm uses driver indicators like vigilance, eye movements, secondary task, feet position, hands on steering wheel, body posture and many more as an input. These driver readiness times are combined with information about the status of technology and the driving conditions, altogether feeding into a prediction what is the most appropriate level of automation. With this prediction of the time that the

driver needs to take over control (for normal take-overs and critical take-overs), automation systems will be able to anticipate on a safe handover from machine to the driver. This will improve the combined driver / automation behaviour and performance.

Floating Production, Storage, and Offloading use case
In collaboration with Bluewater, RH-marine and the STC-group, the research line Adaptive Maritime Automation developed in 2017 an Intelligent Operator Support System (IOSS). The system is able to take over the monitoring duties from the DP (Dynamic Positioning) operator, allowing the operator to leave the bridge and perform other duties. While roaming, the DP operator carries a smart watch and tablet. The starting point in the development of the IOSS is that the DP operator will be supported but that he himself is responsible and continues to do the real thinking.
IOSS includes the following functionalities:
1. Human aware artificial intelligence, to follow the operator in what he does and does not do and to adjust the support accordingly;
2. Explainable artificial intelligence, to think along with the operator and explain;
3. Data analytics, to monitor the environment and to supervise the system;
4. Procedural support, to make working arrangements and support procedures.

The combined A.I. and interaction technologies were evaluated with five experienced DP Operators during different simulated Floating Production, Storage, and Offloading scenario's where the officers were able to experience the supported roaming way of working compared to the standard practice.
Results reveal that all DP operators acknowledge that a system like the IOSS could bring them a great advantage during their work. While they were generally sceptical regarding the possibility of leaving the bridge and to transfer decision authority to the IOSS, they were enthusiastic about the more advanced type of notifications providing additional information to the operator. Especially the integrated A.I.-based predictive weather models were received well as the advance weather warnings provide the operator ample time to anticipate by for instance manoeuvring the ship. They also saw an added advantage in the capability of the IOSS to suggest courses of action. While the operators still wanted to be in control of which decision was ultimately made, they felt supported by the IOSS. An interesting find was that some operators mentioned they were not particularly interested in the IOSS delivering an estimate of the certainty of its decisions. The operators felt that the system should simply work, and demonstrated immediate trust in the system, which was further reinforced as the IOSS suggested courses of action the operator also agreed with. The operators did mention that it would be important to them to know why the IOSS failed if that was to happen. In hindsight they acknowledged that a level of certainty of the suggested decision would be beneficial to their level of trust in the system, even if it would suggest a wrong course of action. Here a link was made between the performance of humans in uncertain task environments, the operators felt they would be more understanding of the IOSS making a 'mistake' as long as it demonstrated its insecurity, like humans would in judging a novel complex situation.

Police use case
In 2017, the research line Human Resilience closely collaborated with the Dutch Police (National team Veilig en Gezond Werken and unit Oost-Brabant) in field trials delivering data for the TNO research project and insights for the Police concerning possibilities to support and enhance the employability of their personnel. The research line finalized the first data trial with the Dutch police and conducted a second data trial with an improved prototype of the Wearable Resilience System, developed in this ERP. In these trials, 35 Police employees used the Wearable Resilience System for four or five weeks, both during working hours and outside of working hours.

The application
- measured relevant resilience factors, both psychologically and physiologically;
- calculated a daily resilience score for the user which was communicated to the user by means of the mobile resilience app (part of the Wearable Resilience System);
- provided the user with insight in the relations between relevant factors (e.g. sleep, motivation, stress, exhaustion) by means of a dashboard containing graphs of the daily collected data;
- gave the user information on how to improve resilience related factors (e.g., sleep);
- provided the user with personalized advice regarding the use of resources to deal with stress.

Data and insights collected in these trials were used to further develop the models of resilience and the technology of the Wearable Resilience System. In addition, qualitative research was conducted to determine in what way resilience-related data, daily collected at the individual level, can best be communicated to the organizational level. Insights stemming from this research were integrated in a demonstration dashboard for managers and HR and safety professionals.

Figure 1. *Visualisation of the Wearable Resilience System, consisting of: 1) a smartwatch, measuring the user's physiology; 2) daily questions about subjective experiences via a smartphone application; 3) personalized feedback via the resilience app; 4) an organizational dashboard with anonymized resilience data at the team level.*

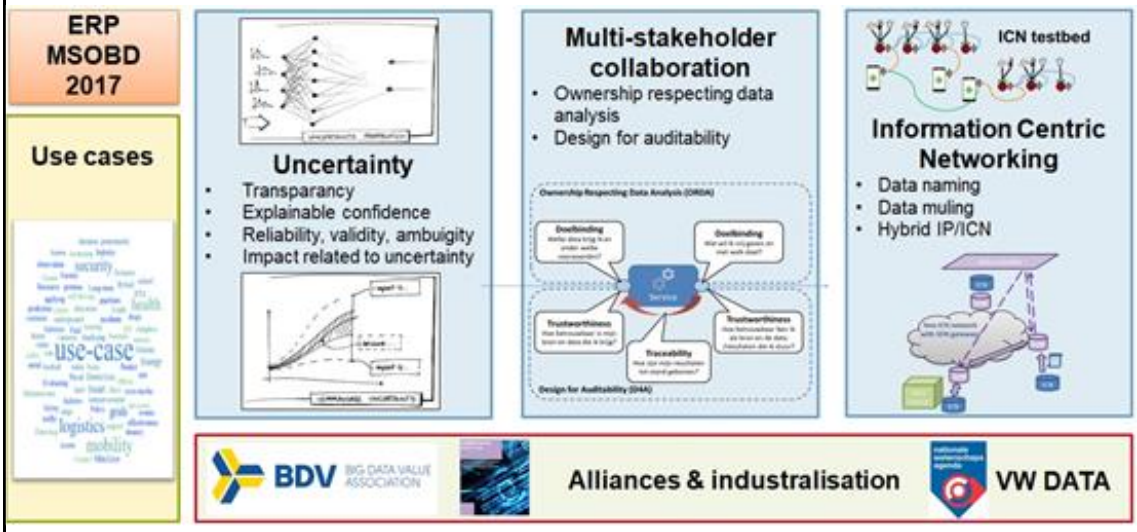
A short movie about the project (*How to handle stress? Improving Resilience Using Wearable Technology)* can be found here: https://www.youtube.com/watch?v=zvdw_YQJakA&feature=youtu.be

Cyber use case

Response to cyber incidents is a special case of crisis management in which the digital environment is responsible for unique challenges. Cyber incidents are time-critical, complex, have many unknowns, involve multiple parties, have large financial consequences and require very specific knowledge in order to be managed and resolved. Though much that is already known about crisis management can be applied to cyber incident response, the unique context requires a special approach. It is exactly this area, in which the unique aspects of cyber incidents come together, that there is room for new knowledge about how they are interrelated, and can be

	influenced in order to bring about a more effective response. Though state-of-the-art technological tools are paramount for effective cyber incident response, they are not enough. Cooperation and teamwork must also be supported for Cyber Security Incident Response Teams (CSIRTSs) to perform optimally. The focus of this project is on how to improve these social processes in order to improve overall cyber incident response. In this project we identified the most pressing problems that CSIRTs encounter, using a Backward & Forward needs assessment analysis. The resulting needs fell into one of four categories: Organisation, Team performance, Individual and Instrumental. The challenge was to develop a support concept based on the identified needs. For this, we turned to the application of collaborative sense-making, the focus of which is to cooperatively give meaning to information and context such that tasks are effectively distributed and carried out. This makes use of for example hypothesis testing, perception sharing and data visualisation techniques. Collaborative sense-making was operationalised in the form of The Reporter, an automated team member tasked with assisting in developing a shared awareness of the incident (incident size, urgency, etc.), of the work processes and status (who is doing what, are multiple people working on the same task, who may need help, etc.), and of the state of the team members (tired, stressed, overloaded etc.). The Reporter prototype was developed in order to visualise what such a concept might look like in real life. Alternative operationalisations may include apps for tables and smartphones or feedback on team members' physiological states via wearables.
Program dynamics	The Early Research Program Human Enhancement will not be continued after 2017. In order to strengthen the uptake of the knowledge developed within this ERP, a transition document has been written in which transitioning of knowledge of the four use cases to more applied programs of research is described.

8 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	Mariëlle Beers-Homans (EZK)
Progress 2017	
Abstract	The term 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 top capabilities (tools, models, methods) that enable a stakeholder to design and implement a data-driven-innovation in a multi-stakeholder setting. The research in the first two years provided TNO with a technology position over the total, wide scope of big data innovations. In the last two years the program is focussed on niche topics with high potential value; in 2017 on Uncertainty, Multi-stakeholder collaboration (MSC) and Information Centric Networking (ICN). For Uncertainty an overall vision and framework was developed, which is recognized in both science and business. A scan of 20+ big data use cases revealed 5 typical challenges, of which two challenges (propagation of uncertainty and communication of uncertainty sources) were investigated in depth. Within MSC the topics privacy respecting data analytics and traceability are researched, both connecting business and technology. Finally, the activity on ICN focused on data muling and data naming. Next to generic technology development tests have been carried out on a selection of use cases. In 2018, the topics ICN and Ownership Respecting Data Analysis (part of MSC) will be transferred to the VP ICT. The topic of Uncertainty will be continued, with a focus on finishing the work on propagation, integrating the research on traceability (previously in MSC) and starting a new project on model bias in machine learning. In 2018 a new seed ERP Applied Artificial Intelligence will be started with a program strongly related to ERP MSOBD, i.e. explainability. We expect that the ERP MSOBD will feed into a new ERP Applied AI. 

	In 2017, the MSoBD program was reviewed by an external advisory board consisting of internationally renowned big data scientists[6], who confirmed that the results delivered in MSoBD were relevant to society and of high quality and that the recommendations given in 2016 had been implemented in an effective way. Within the ERP MSoBD strong collaboration with various partners outside TNO is key. On an international level, TNO is representing Dutch academic partners in the European Big Data Value Association, where TNO is board member. A Big Data PPP/BDVA project: BigMedilytics (Big Data for Medical Analytics) was granted in 2017. 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. As an example TNO will participate in four WPs in the NWA project Responsible Data and a number of Commit2Data projects are granted. MSoBD has also a focused collaboration with CWI, University of Amsterdam and Leiden University. Collaboration with Amsterdam Data Science (UvA, CWI, VU) is foreseen on the topics AI and Responsible Data Science, working title "Responsible control of autonomous systems". The multiplier of the ERP is mainly through TKI proposals such as the TKI Disac (on potatoes) and the TKI Jongvee (agro) and health related H2020 projects such as BigMedilytics and Recap.
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. In 2017 the ERP MSoBD was focused on three main technology lines: Uncertainty, Multi-stakeholder collaboration (MSC) and Information Centric Networking (ICN). Uncertainty was started as a new technology line, with the ambition to investigate the end-to-end approach to identify, quantify and visualize uncertainty in big data inference systems for real operational use cases in contrast to laboratory settings. In the final year, the program is continuing the Uncertainty research line and has spawned the 'seed ERP' applied AI.
Technology line: *"Uncertainty"*	
Highlights	The **Technology Line *Uncertainty*** has as focus to tackle real-world challenges in big data where multiple, unstructured, relatively "ambiguous" (belonging to different domains or contexts) datasets are analyzed in combination. This means identifying and quantifying sources of uncertainty and dealing with uncertain results by e.g. an interactive visualization. The ambition of this work package is to become really good at applying the academic state-of-the-art knowledge –that is generally developed on constrained, controlled and clean datasets,- to real world contexts where uncontrolled, heterogeneous, ambiguous, unstructured datasets are often the only available resource. The work package aims to address the whole socio-technological system "from data to decision": data creation, preprocessing, combining, transforming, analyzing (in various steps), visualizing/communicating, and finally the decision that the end user takes. The goal is to provide tools to the user to understand the sources of uncertainty in her data, tools to provide her with insights on how these uncertainties impact the (socio-technological) system

[6] Prof. Max Welling (UvA, CIFAR), Prof. Peter Apers (UT), Barteld Braaksma (CBS), Prof. Stefan Manegold (UL, CWI)

	decisions, and tools or advices on how to optimize the system behavior given such impact. The first phase of the project was an exploration phase. A scan of 20+ big data use cases revealed 5 groups of challenges, loosely categorized as •when is a result "good enough"? •when is data representative and how to cope with representability? •when is the modelling choice adequate? •how to propagate uncertainty correctly? •how to best communicate uncertainty to the user? The overall vision and framework developed for this new topic is recognized in both science and business and is published in a whitepaper[7]. After the exploration phase the work focused on two of these challenges: Propagation of uncertainty through the system and communication of the uncertainty to the end user. The propagation analysis activity was done on two use cases. The approach was different for each use case; the use case "aerial observation" followed a 'probes and quality modelling' approach, and the Estimated Time of Arrival (ETA) case, being based on deep learning, followed an approach where different sources of uncertainty could be distinguished in the overall end uncertainty. Communication to the end user was based on the analysis framework created in the Exploration phase. The various sources of uncertainty were modelled in an ontology, based on existing ontologies. A system was designed aimed at creating a structured way of communicating uncertainties to various groups of users. The added value of communicating the uncertainty in the network was hard to determine. More can be expected from adding reasoning about the uncertainties for decision support. Another strand of research on the 'communication to the end user' topic was done by supporting the startup of a PhD research (W. Venrooij), resulting in a number of fundamental insights into how visualization relates to uncertainty, both technical uncertainty and uncertainty in the quality of the decision/interpretation of the end user. The first aspect, technical uncertainty and how to present this to the end user, has received most attention in 2017. There has been cooperation with: CBS and City of Rotterdam; Various universities (attracting students); Use case owners: the company that processes ETA data (Hermess)
Technology line: *"Multi-stakeholder collaboration"*	
Highlights	The aim of the **Technology Line *"Multi-stakeholder collaboration"*** is to develop a methodology for implementing *Ownership Respecting Data Analysis (ORDA)* techniques and to develop a methodology and tools for Auditability (D4A). Many organizations make a transition to become more digital or at least to benefit from creating value with data. In many cases, organizations offer services that are based on processing and analysis of data that they generate or collect. In this technology line, we address the challenges of processing data in a multi-stakeholder context. One of the most significant challenges is to serve the interest of the data subjects, which we took as a starting point for our research in data processing. The ORDA technology development is based on market pull from different sectors. Based on interviews with different stakeholders we developed a generic, multidisciplinary approach to use data from other parties with respecting each other's privacy. With this methodology the results cannot be traced to individuals and

[7] Whitepaper: "Total Uncertainty in Big Data Analyses", Maaike de Boer, Serena Oggero, Michael van Bekkum, Freek Bomhof, Fieke Hilleström, Rob Knegjens, Maarten Kruithof, Niels Neumann, Judith Dijk; TNO Den Haag, June 2017

	the different parties gain no knowledge about the source data of the others. The results are reported in a cookbook[8]. The main technology addressed is Multi-Party Computation (MPC). With the cookbook it can be concluded whether (one of the) MPC (techniques) fits the needs of the organization. This cookbook then supports in advising organizations how to make a plan of action for implementing MPC-techniques. Furthermore, the cookbook sketches the position of TNO for MPC and the roadmap for further development. Design for Auditability (D4A) is a way to support organizations to setup their data-storage and –processing, according to principles of lawfulness, reliability and trustworthiness. TNO developed a maturity model for data storage and –processing, focused on legal and business obligations and technical capabilities. Part of D4A is traceability, i.e. backtracking how a specific result has been produced by the (pipeline of) data driven services, which is even harder in big data systems. TNO developed a methodology of full system traceability which covers both traceability in the design phase as in the operational phase. In this technology line we adopted the GRC concept (Governance, Risk management and Compliance), which helps stakeholders to minimize the amount of work they need to do in order to realize the 'GRC-objectives'. This way of thinking is strongly related to the Networked Risk Management (NRM) method. Part of this technology line was dedicated to the PhD research of Frank Berkers on the topic "Assessing business model designs in Data-Driven Innovations for collective action". On this topic a literature review and a research proposal were written. In this research a method will be developed which supports decision making over multiple collaborative digital Business Models.
Technology line: "*Information Centric Networking"*	
Highlights	The TNO ambition is to become the European research center on ICN. Our vision regarding ICN research within TNO is to develop an "ICN for massive IoT" proposition. Because of ICN's fundamental advantage in dealing with heterogeneous network boundaries, the clear benefits when connecting low-power intermittently connected devices, and the ability to efficiently 'mule' data on behalf of other nodes, we believe that ICN is uniquely positioned to enable massive IoT infrastructures, where billions of sensors make data available in a completely decentralized fashion. Working on this topic also offers us the possibility to collaborate with the UCLA on their proposal for the US NSF as external partner. As a first step towards this vision, we focused on accessing and exchanging data from moving sensors (e.g. people or cars), static sensors (e.g. on buildings or traffic lights), in order to seamlessly support the requirements of multiple heterogeneous applications which may not be known a priori. We developed a proof-of-concept (PoC) of the "ICN for smart cities" vision, within the TNO premises. The PoC enhances the current ICN testbed, in order to include heterogeneous sensors, and allowed research on the two topics mentioned below: new forms of data naming and data muling. Data Naming and Data Muling in IoT has enabled hands-on research in the field of ICN as well as comparison with the current Internet Protocol (IP) to assess the technological impact of ICN deployment in smart cities scenarios characterized by many sensors and intermittent connectivity Next to this, knowledge was developed on the "SDN-for-ICN" concept, which is also worked out in a Proof of Concept. In this PoC two or more separate "ICN islands" are automatically

[8] Oosterheert , L, c.s. Cookbook for data processing in a multi-stakeholder context, TNO rapport TNO 2017 R11474, 2017

	connected on demand. This aspect is of great importance to realize the “phasing out” of IP from the Internet and its progressive replacement with the ICN paradigm A last research topic was the impact of ICN on Internet business chains and ecosystems. We explored how the shift from the current IP-based Internet paradigm to an ICN paradigm affects the business relations and dependencies between operators, content providers, technology vendors and cloud vendors. During this project we worked together with the international ICN community, NDN Consortium, IETF Standardization, ACM ICN TPC. For KPN we are investigating the applicability of ICN in the upcoming 5G networks, as well as contribute to the standardization of ICN. Additionally, the project has enabled TNO to acquire the necessary knowledge and international visibility to start field labs and SRP’s with industrial parties like Cisco, Bosch, ETRI as well as the European operators. As a final highlight: One of our recent conference publications[9] is selected for best paper award of ICOIN 2018.
Topic: *“Use cases”*	
Highlights	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. These use cases are e.g. - Estimated time of arrival of sea ships - Estimation and prediction of traffic jam duration - Youth health case for municipality - Youth health case for premature born children - Video based intelligence - Aggression detection in video 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 and part of the NWO call on Complexity. There is a good connection to the High Tech Top Sector HTSM and for Personalized Health to the top sector LSH.
Topic: “Alliances”	
Highlights	Within the ERP Making Sense of Big Data strong collaboration with various partners outside TNO is key. 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. A Big Data PPP/BDVA project: BigMedilytics (Big Data for Medical Analytics) was granted in 2017. 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. As an example TNO will participate in four WPs in the NWA project Responsible Data and a number of COMMIT2DATA projects are granted. MSoBD has also a focused collaboration with CWI, University of Amsterdam and Leiden University. Collaboration with Amsterdam Data Science (UvA, CWI, VU) is foreseen on the topics AI and

[9] Rietberg, L. D’Acunto, R. Kooij, H. van den Berg, “Analyzing Information Availability in ICN under Link Failures”, IEEE ICOIN, January 20-12 2018, Chiang Mai, Thailand

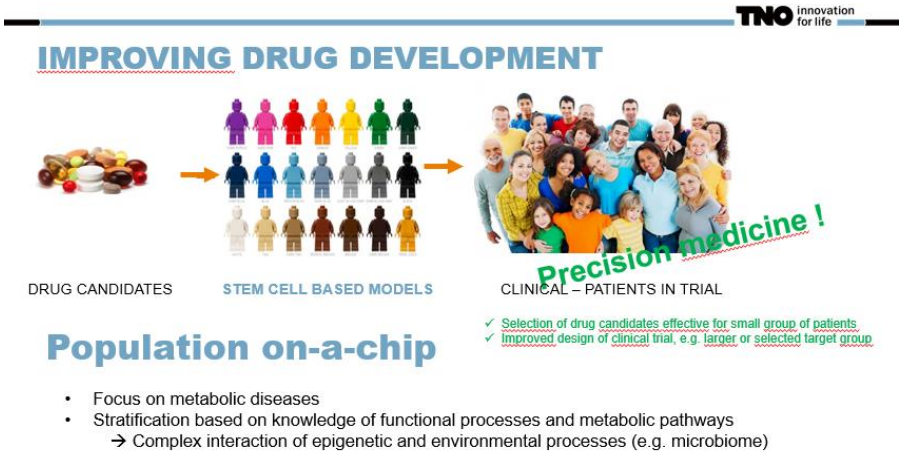
	Responsible Data Science, working title "*Responsible control of autonomous systems*" . Two TNO scientists are affiliated to CWI (Veugen, van den Berg), one is affiliated to Leiden University (Kraaij), participating in local data science programs and preparing new NWO and STW proposals. The multiplier of the ERP is mainly through TKI proposals such as the TKI Dinalog (logistics), the TKI Jongvee (agro) and the TKI ICN (ICT) and health related H2020 projects such as BigMedilytics and Recap.
"Advisory board and seed ideas"	
	In 2017, the MSoBD program was for the second time reviewed by an external advisory board consisting of internationally renowned big data scientists. This board confirmed that the results delivered in MSoBD were relevant to society and of high quality. The board concluded also that the recommendations given in 2016 had been implemented in an effective way. Similar as in 2017, one call for seed ideas to spark new knowledge initiatives have been conducted with great success. From this call, three seed ideas have been granted. **Seed idea sonar** The idea of the seed idea for sonar was to generate the perfect sonar pulse by generating a lot of sonar pulses and use these to train a neural network on the inverse relation between the signal and the sonar pulses. Based on this inverse relation, the signal for the perfect sonar pulse could be generated. Unfortunately, this effect could not be reached within the budget available. Possible reasons for this are e.g. that the parameters space was too big, or that there were missing constraints. **Seed idea bias** The question for this seed idea was "Can we detect discriminatory bias in big data systems / results, based on machine learning?" The rationale for this is that there should be trust in Big Data / AI system, but all traditional evils of social discrimination (and possibly new ones) exhibit themselves in the big data ecosystem. There are two different steps that can be identified: determination of a possible bias and correction for this bias. In this project we did a literature scan. In this scan we did not find a bias tester for industry. After that we implemented a FairTest Library in a web based environment. In this tool we can add explanations and visualizations for different datasets. The topic of bias will be incorporated in the uncertainty project in 2018. **Seed idea quantum** Quantum computers make use of quantum-mechanical phenomena, such as superposition and entanglement, to perform operations on data. Where classical computers require the data to be encoded into binary digits (bits), each of which is always in one of two definite states (0 or 1), quantum computation uses quantum bits, which can be in superpositions of states. Quantum computers would theoretically be able to solve certain problems much more quickly than any classical computer that uses even the best currently known algorithms, like integer factorization using Shor's algorithm or the simulation of quantum many-body systems. A practically usable quantum computer is expected to be developed in 2020. The question in this seed idea is what are the first important application areas of the quantum computer, both worldwide and for TNO (and its clients) in particular. For this we have looked at the possible scope of problems that will be solved (or strongly accelerated), and (even important) which problems are not. In the future, Quantum computers can play an important role in solving a specific set of computational hard problems. We think that in the near future hybrid approaches will be of interest, using the Quantum computer for a specific task within the chain of computations. The majority of computational hard problems within TNO, mostly with an application in the Defense domain, coop with pattern

	recognition. An proposed first step, within the expected capacity of the first Quantum computers, is the Quantum-assisted Helmholtz machine, which is a tool for unsupervised learning. Part of this research was funded through the RVO Defence program.
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 focused on three areas in which we can achieve an unique position: 1) Uncertainty: quantifying and visualizing uncertainty of big data inference systems, 2) Multi-stakeholder collaboration and 3) Information Centric Networking. For the transition to 2018, some topics are mature enough to be transferred to the VP ICT. The topic of uncertainty will be continued, with a focus on finishing the work on propagation, integrating the research on traceability and starting a new project on model bias in machine learning. At the same time a new seed ERP Applied Artificial Intelligence will be started with a program strongly related to ERP MSOBD, i.e. explainability. We foresee that the ERP MSOBD will feed into ERP applied AI.

9 Organ Function on Chip

General data	
Title	Organ Function-on-Chip
'Topsectors'/Societal Themes	LSH, A&F, HTSM / Work & Health, Defence
Contact person TNO	Peter van Dijken; Evita van de Steeg, Ivana Bobeldijk-Pastorova
Contact person government	Mariëlle Beers-Homans (EZ)
Progress 2017	
Summary	Over the last 3 years, the ERP Organ function on-a-chip made the right steps and evolved from a seed ERP (2015) into a full ERP (in 2017). For both subprograms important technical developments as well as ecosystems development were achieved in 2017. In 2017 the program team participated in a Business Innovation Bootcamp and focused the two use cases: gut- and liver -function on a chip, further into development of population on a chip application. In 2017, TNO was an active strategic member of hDMT (human organ and Disease Model Technologies), a national pre-competitive institute focusing on state-of-the-art technologies around organ on-a-chip. The hDMT is composed of several institutes, academic groups and companies. Membership in this network group emphasizes TNO's right to play in this area. The collaborations with companies and academia which were established in 2015 led to three grant applications (still in review) for DTL (Dutch Techcentre for Life Sciences). In addition to academic collaborations setup in 2015-16, new collaborations with academia were setup, such as University of Maastricht for imaging, University of Utrecht for technology development and University of Leiden and Academic Medical Centre for biology. Consortia with small industrial partners such as Takara and Invitrocue have led to very active and successful collaboration in the development of advanced in-vitro liver models. Further industrial collaborations and joint application for grants are currently being explored together with business developers, TNO strategy and external consultancy Catalyze. The internal collaborations between Metabolic health research, Microbiology and systems biology, Environmental modeling, sensing and analysis were further strengthened by joint development of microfluidic systems and readout methods. 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 detection of biological processes, such as fibrosis, using Atomic Force Microscopy were setup with Optomechatronics. The results achieved were disseminated in presentations at scientific events as well as during two business trips to pharma and nutrition companies. Two scientific manuscripts are in preparation. A dissemination event 'Organ on a chip: from dream to implementation' for both internal and external stakeholders was organized in November 2017. The attendance of this event by colleagues, collaborators from academia and industry was even better than in 2016, indicating a growth of interest in TNO as established partner in this area, demonstrating the position of TNO in this fast evolving area of research and development. The program succeeded in achieving the goals set for 2017: bringing the development of advanced in-vitro models a major step further including new successful internal and external collaborations. For 2018, we expect further development of the technology, coupling of organs for new applications, submission of at least two manuscripts and most importantly the establishment of broader collaborations with industry in order to accelerate applications in the market.

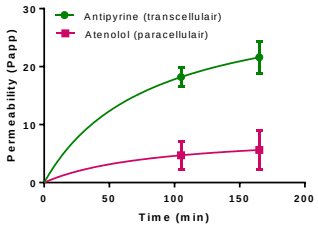
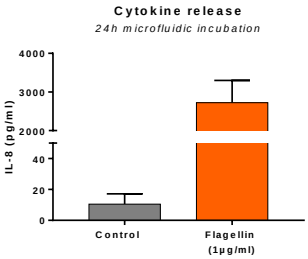
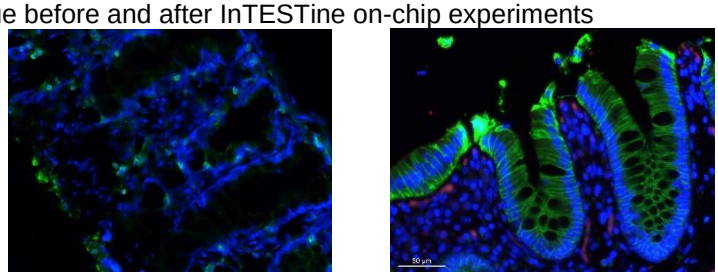
Short description	The objective of the ERP organ on chip program is to improve the development of better predictive, more physiological (personalized) human *in vitro* models. We focus on tissues and disease areas in which TNO has extensive knowledge, experience, and market position ("right to play"), and will develop validated applications relevant for pharmaceutical and nutrition industry.

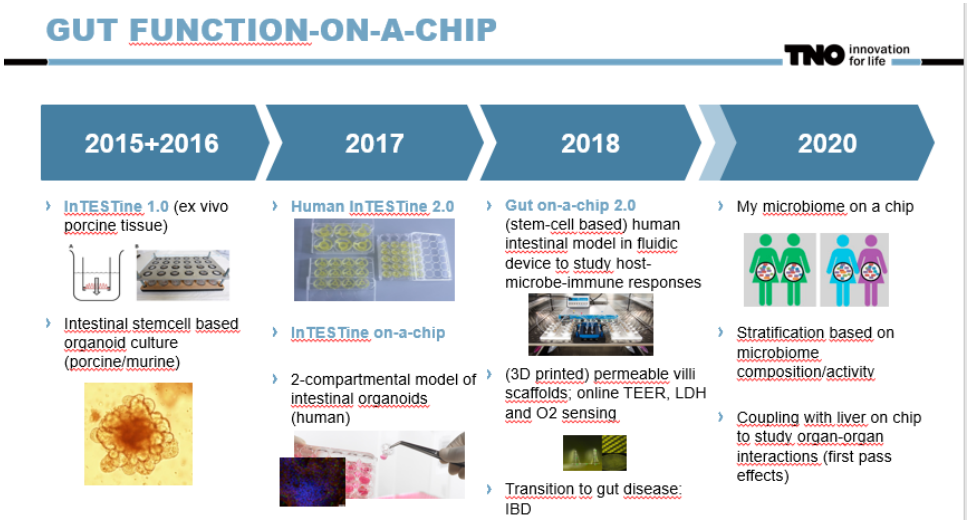


In 2017 we focused on applications with two organs and evaluation of different readout and fluidic technologies.

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 (stratified) 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.
3. Development and evaluation of different readout technologies such as gas detection, AFM imaging of biological systems, ring resonators for detection of cell viability.

Technology line 1: *"Gut function-on-a-chip"*

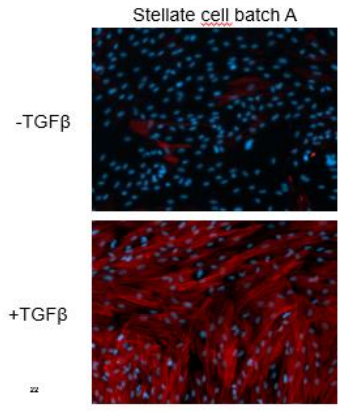
Highlight	In 2017 we have achieved stable 3D culturing of human stem cell derived intestinal organoids. In order to develop a 2-compartmental in vitro human intestinal model that can be used to study absorption and impact of drugs, nutrition and environment on gut health, we successfully developed a confluent monolayer of intestinal organoids on permeable membrane inserts, with proper distinction of paracellular and transcellular transport.  *Other results achieved in 2017:* • Extended viability of human intestinal tissue in InTESTine by applying luminal and basolateral microfluidic flow, using newly designed 3D printed chip inserts, resulting in detectable immune functions of the intestinal tissue. • Generation of permeable villi scaffolds for cell culturing • Scaling up microfluidic chip capacity from n=4 to n=20 for application of intestinal tissue or stem cell derived intestinal organoid culture  • Immunohistochemical detection of tight junctions and CD3 positive T-cells in human intestinal tissue before and after InTESTine on-chip experiments 
Program dynamics	The dynamics of the developments within the program for Gut function-on-a-chip are shown in the figure below. For 2015 -2017 the achievements thus far are schematically summarized. In addition to plans for 2018, also an outlook towards 2020 and beyond is shown. In 2018, 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 2020 we will have validated the model combined with microbiota derived from healthy 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 in order to generate a “GI-tract-on-chip”, or adapted to different 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, first steps will be undertaken in 2018.

Technology line 2: *“Liver function-on-a-chip”*

Highlight

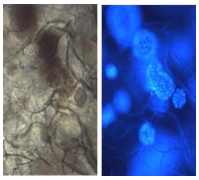


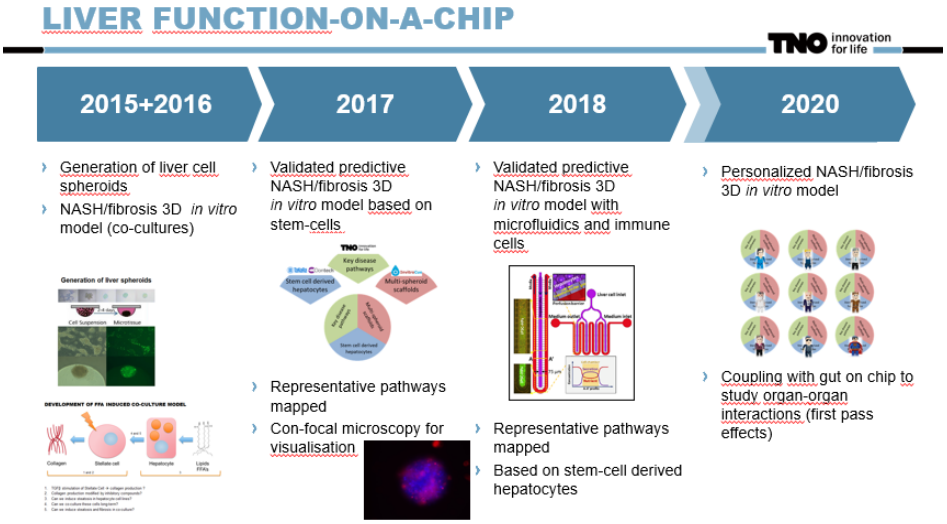
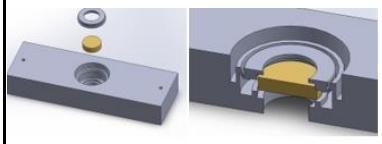
In 2017 we have achieved 3D co-culture of human stem cell derived hepatocytes and stellate cells, in which a fibrotic signature could be induced using a ‘diet-induced’ approach. In collaboration with InVitrocue, provider of 3D culturing scaffolds, we were able to co-culture 3D spheroids in the scaffold composed of human stem cell derived hepatocytes and stellate cells. We were able to induce steatosis in the hepatocytes by loading them with a mix of fatty acids. The developed steatosis, in addition with low concentrations of inflammatory mediators, stimulated fibrosis in the co-cultured stellate cells, as measured by a fibrosis specific gene expression. Next steps will be to monitor this at protein level.

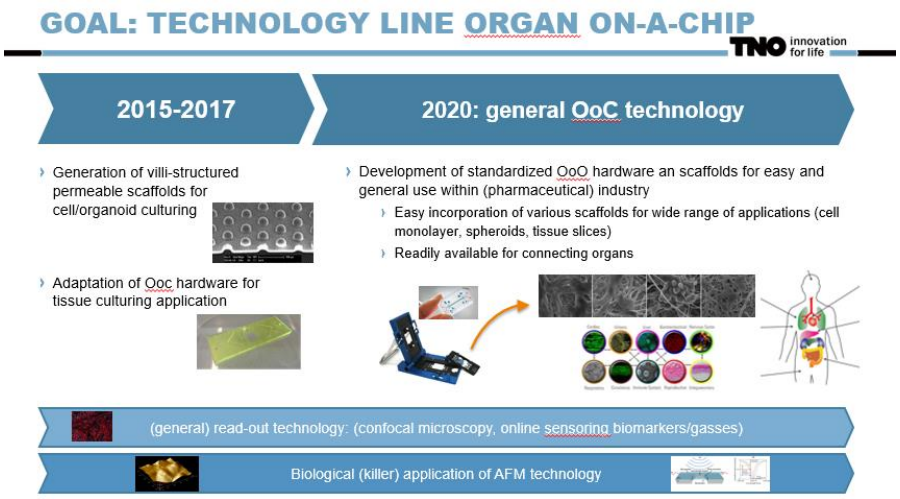
In 2018 we plan to extend this model further by adding Kupffer cells for a more pronounced inflammatory process onset and move to the use of stem-cells. This 3D co-culture model will mimic diet-induced onset of liver fibrosis.

Other results achieved in 2017:

- 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
- Initiated collaboration with LUMC on electron microscopy based collagen detection in spheroids
- Initiated collaboration with Maastricht University on Second Harmonic Generation/multiphoton imaging for analysis of collagen structure and mitochondrial dysfunction in scaffold-



	cultured 3D 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 -2017 the achievements thus far are schematically summarized. In addition to plans for 2018, also an outlook towards 2020 and beyond is shown. In 2018 we plan to further develop the personalized 3D in vitro model and take first steps towards the 'personalized' version and couple the model to the models of other organs, such as gut.  In 2018 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) at protein level • 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: "*Organ-on-a-chip technologies*"	
Highlight	For the organon a chip project several organ on a chip inserts that can be used in the combination with the chips by Micronit were designed and 3D printed by the EfAM department of TNO. One chip insert is for the use with a membrane (Gut on a chip) and the other one is specifically designed for use with the 3D scaffolds necessary for liver on a chip models. Parts were designed in Soldiworks CAD software, and then printed in a S60 mini stereolithography system by Rapidshape, which was co-developed by TNO EfAM. Parts were printed using a photopolymer acrylate resin (developed by TNO EfAM and MAS). Functional testing of the developed chip parts will continue in 2018.  *Other results achieved in 2017:* • Setup of ring resonator for detection of LDH (cell viability) in organ on chips models • With AFM we showed that we can perform nano-mechanical measurements on cell cultures (in this case CACO-2 cells) with the goal to measure the stiffness of specific organelles of the cells (membrane, tight junction and cytoskeleton) • Setup oxygen and CO2 detection in the Gut on a Chip system • Plan for development of functional microbiome readouts in lung models in collaboration with LUMC
Program dynamics	The dynamics of the developments within the program for the new technologies are shown in the figure below



In 2018 we will:

- Further develop the biological application with AFM
- Adapt our functional microbiology analysis for application in lung-on-a-chip models, in collaboration with LUMC and Emulate
- Make first steps towards coupling of the different organs, by developing technology in collaboration with UMCU
- Further evaluate suitable readouts for gasses (sensors) or proteins (ring resonators)

10 Submicron Composites

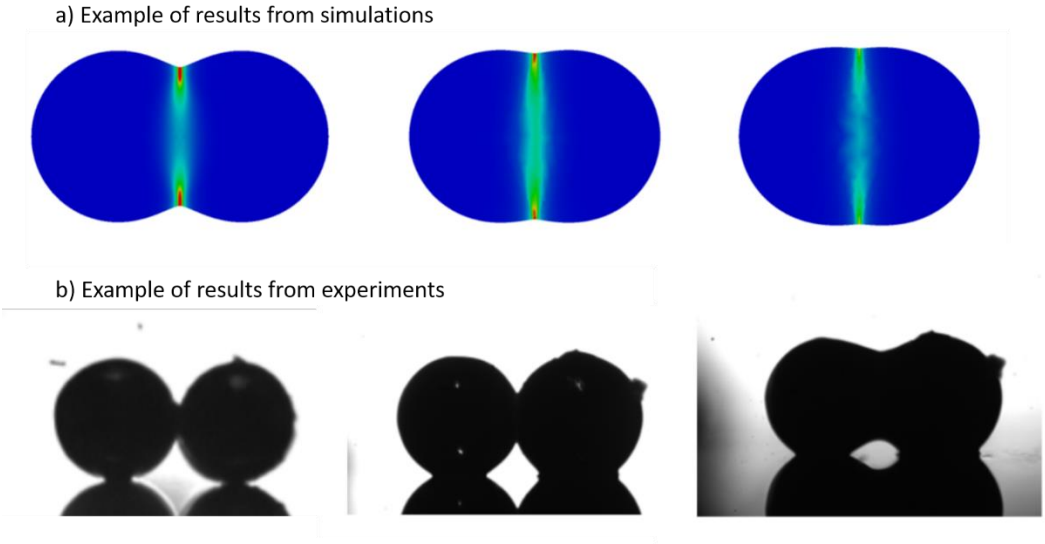
General data	
Title	ERP Submicron composites
'Topsectors'/Societal Themes	HTSM en Chemie
Contact persons TNO	Pascal Buskens / Jaap Lombaers / Aike Wypkema
Contact person government	Mariëlle Beers-Homans (EZK)

Program report 2017

Abstract

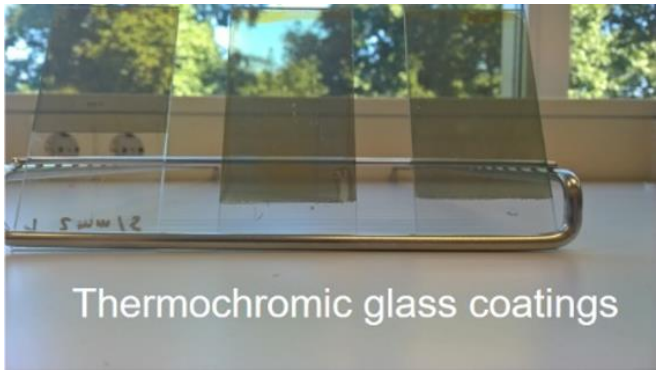
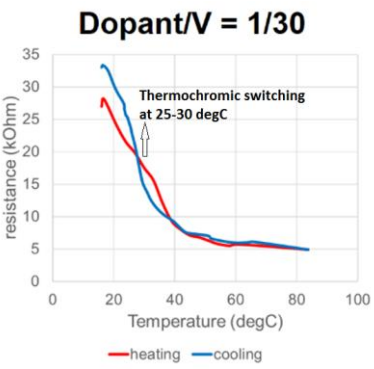
Within the scope of this ERP we develop new materials with optimized composition and microstructure for advanced optical and mechanical performance and multiple functionalities. Within the framework of the Brightlands Materials Center, we collaborate with academic partners, and with industrial partners within the value chain to develop new products for innovative 3D printing (for example for dental, automotive or electronic applications) and for advanced light management for sustainable building envelopes.

Additive manufacturing (AM) provides excellent opportunities for the production of complex, customized products at low cost, such as for example implants and prosthetics or high-tech industrial spare parts. While new materials and processing techniques are being introduced in the market, AM technology is still immature: product quality is inferior to that obtained with conventional methods and the choice of available materials is limited. Quality of the materials in the obtained products in many cases is still limited to allow the full potential of the manufacturing technology. We focus on materials modelling and material development to assess and to optimize product quality of 3D printed products.



Coalescence of polymer particles; a quality determining step in AM

Within the innovative building envelopes program, we focus on thermochromic materials. The 'window of the future' allows for smart control of thermal as well as visible radiation to create energy-efficient buildings under different seasonal conditions.

	 
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 focused on three topics related to the quality of the material: a) Improving mechanical properties and long-term performance 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) Mechanical and geometrical properties of photocurable polymers; 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 focused on thermo-chromic materials (i.e. materials that adapt their optical properties as a function on temperature). These 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	The project consisted of 4 parallel activities focusing on different aspects: **1. (Additive manufacturing) 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 ('PhD project 1') • Computational modelling of viscoelastic non-isothermal sintering process ('PhD project 2') • Experimental characterization of the sintering process and microstructure ('PhD project 3') • 3-D manufacturing of plastic products by melt jetting ('PhD project 5') 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 (PhD project 1,2 and 3). 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.

PhD project 1 tackles the question of why the properties of sintered powder differ significantly when compared to the traditional molding process, in particular its long-term behavior. To start with, the deformation kinetics for PA12 has been successfully described using the Ree-Eyring approach which takes into account two possible deformation mechanisms for the plasticity controlled region before failure. In this way the long-term performance can be predicted by using experiments in a smaller time scale. The effects of water uptake (related to processing laser sintered powder) but also how post-condensation (aging state) affect crystallization kinetics are yet to be investigated.

PhD projects 2 and 3 are somewhat complementary. For the purpose of further understanding of the sintering process during SLS printing a model system was chosen, consisting of the sintering of two viscoelastic particles, for the common numerical study and experimental validation. The computational description (PhD project 2) includes so far the coalescence of two particles during sintering. The main driving force considered in this case is the surface tension which starts acting once the particles surface is melted. The results obtained so far include validation of the model with analytical solutions and study of the rheological properties on shape evolution, stresses and strain. The first steps in the experimental characterization (PhD project 3) consist in the creation of the measuring setup, particle manipulation in the sub-mm range and sample preparation of spherical non-crystalline thermoplastic powder. At present the setup is capable of real-time control over the laser energy used, temperature, imaging from two distinct planes and the possibility of coupling to in-situ x-ray measurements. Besides the setup itself, clear imaging has been achieved for the real-time tracking of two particles allowing comparison of geometries between experiment and simulations.

2. (Additive Manufacturing) Mechanical and geometrical properties of photocurable polymers

This workpackage includes 2 PhD projects at TU/e, focusing on mechanical properties of photocurable polymers:

- Reversible Multiple Networks for 3D printing materials (‘PhD project 6’)
- Intrinsic mechanical properties for photocurable polymers(‘PhD project 8’)

PhD project 6 focuses on new chemical concepts to decrease internal stresses in 3D printed products prepared from photocurable polymers. A synthetic route has been developed to produce photopolymer building blocks and thermal and mechanical characterization of the materials has been carried out. Details of the stress relaxation will be evaluated in the next phase.

PhD project 8 seeks understanding at the single layer level of the mechanical properties of photocurable polymers. To reach this a methodology for controlling the process parameters during printing is developed where not only the layer thickness is taken into account but oxygen inhibition, thermal/uv post-curing and solvent are considered. The resulting properties of the material after processing are characterized using micro -tensile and -compression tests. The first results obtained for varying chemical compositions show potential to tune materials with increased crosslinked densities and glass transition temperatures. Ongoing work aims at understanding the role of increased molecular weight in the prepolymer and comparison of the behavior between acrylate and methacrylate chemistries.

Furthermore, this work package aimed to build a multi-scale model of a layer wise photocuring process that predicts thermomechanical behavior and geometry of 3D products prepared by vat photopolymerization. The multi-scale model consists of a product model and

a material model. For ease of use and compatibility with 3D printers an STL format has been adopted for the input of the geometries. A more elaborated kinetic model has been also implemented to account for differences during the validation phase.

The model has also been validated. After parametrization using experimental data, samples are used to compute the warpage of single geometries, in this case beams with rectangular shape. Additional studies as a function of parameters such as dye concentration and partitioning schemes are under its way to revisit the range and applicability of the model.

This framework is currently being used to accelerate the design of resin formulations with specific properties, e.g. resulting in minimal warpage (maximum deflection of bottom compared to reference) in a given direction. It is also used to bring further insight into trends after modification of material or process parameters.

3. (Additive Manufacturing) New functionalities in photocurable polymers
This workpackage includes 1 PhD project at TU/e:

- Modelling the 3D-Printing of Electromagnetically Active Components ('PhD project 4')

Within the PhD project 4 a model has been set up for the prediction of alignment of electromagnetically active particles in a viscous resin. The model includes the interactions between particles in the presence of an external field with adjusted long-range interactions. Validation has been proven in comparison of results of the model with analytical solutions. The predictive capabilities of the model allow for knowing the morphology of the arrangement of the particles as a function of volume concentration, intensity of the field and viscosity of the medium. At present the numerical model seems quite robust and a more in depth exploration can be realized. This means understanding the formation of structures such as chains, spirals or percolating networks from the various types of applied field (e.g. time dependent electric field). Other uses of the model relate to investigation of the structure formation in polydisperse composites and during solidification of the photocurable resin.

4. (Sustainable Buildings) Thermochromic windows
In 2017, we have realized single-layer solution processed coatings comprising vanadium dioxide, which switch between high and low transmission of IR light based on the material's semiconductor-to-metal transition at about 68˚C. The chemical composition of these coatings was confirmed using X-ray photo-electron spectroscopy and Raman spectroscopy. We have developed two base coating systems for producing these VO_2 based coatings, starting from a V(V) and V(IV) precursor. Furthermore, we have established an infrastructure to reliably apply such coatings to glass and other rigid substrates in a climatized dip coating unit, and cure them in a tube furnace comprising a ceramic tube. Although we realized switchable coatings, the conditions in the furnace during curing (temperature, atmosphere) could not be sufficiently controlled and regulated, resulting in significant batch-to-batch variations. Therefore, in 2018, we need to validate different furnace set-ups to ensure reliable curing results.
Through suited doping of the VO_2 base coating with other metal oxides, we managed to lower the transition temperature, with the lowest achieved transition temperature of about 30˚C. Through optical simulations, we confirmed that nanocomposite VO_2-based coatings can have a balance between transmission in the visible and switching performance in the infrared part of the spectrum, which is acceptable for most applications: 70% transmission in the visible, and a switch from 85% to 35% transmission at a wavelength of 2 µm. The concept has been protected with a patent application. Together with Zuyd University of Applied Science and Hasselt University, we will investigate this concept in more details.
One of the ways to produce nanocomposite coatings is through use of vanadium dioxide nanoparticles. We started preparing VO_2 nanoparticles through hydrothermal conversion of

	aqueous solutions comprising V^{4+} complexes in autoclaves. We managed to prepare vanadium dioxide particles with a size significantly larger than 1 µm. Through ball milling, however, we managed to reduce the particle size to about 100 – 200 nm. The switching of the particles, which is a first order phase transition, was confirmed through differential scanning calorimetry. The chemical composition/crystal structure was confirmed using XRD.
Program dynamics	No major changes in the additive manufacturing program and the sustainable buildings program have taken place.

11 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 / Chris Jansen
Contact person government	Mariëlle Beers-Homans (EZK)

Program report 2016

Abstract

In succession of 2016, we further explored enhancements in interactive robotics, as well as, the potential of starting of a public private joint innovation center (JIC; together with University of Twente (Prof. S. Stramigioli)).
The first important step this year was to showcase the R&D results of the previous year 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). Knowledge has been increased on haptic control, by combing power touch feedback on the hands (see figure below). A test battery is available for testing the dexterity that can be achieved using this system.

VR exoskeleton hand that will be combined with tactile glove for advanced haptic feedback on the hands.

In addition, a mixed reality has been designed and setup in which virtual objects can be manipulated (using above device, as envisioned).

Impression of the virtualized world of the operator (best viewed in virtual reality), in which depth image information, 3D scans, and real-time footage are used to create a combined mixed world in which virtual objects can be added.

In a third research line, exoskeleton control has been improved by trying to predict initiated movements (using EMG), in order to minimize delays, and regulating co-contraction for better control. Wearable trunk support robotic devices have been improved.

12 Applied Artificial Intelligence (exploratory)

General data	
Title	ERP exploratory project Applied Artificial Intelligence
'Topsectors'/Societal Themes	HTSM, LSH, Logistics
Contact persons TNO	Wessel Kraaij, Albert Huizing, Mark Neerincx
Contact person government	Mariëlle Beers-Homans (EZK)

Program report 2017

Abstract

AI is increasingly being used to automate processes that previously could only be performed by humans such as face recognition and autonomous driving. However, one of the main obstacles for the introduction of AI in safety-critical applications is the lack of trust and transparency that is caused by the inability of a machine to explain its decisions and actions to human users and/or co-workers. With its strong links to AI research at universities, expertise in humans factors and systems engineering, and knowledge of application domains, TNO is uniquely positioned to develop the multi-disciplinary approach that is needed to harness the benefits and solve the shortfalls of current AI technology.

A multi-year research roadmap with concrete steps and goals for the three research topics ***Uncertainty, Explainability*** and ***Autonomy*** has been developed. In 2018, the Seed ERP Applied AI will focus on the development of explainable AI techniques, which enable more effective and efficient human-machine teaming. This includes Human Aware AI challenges such as building mutual trust and transparency.
In 2017 we established connections with:

- NWA Data: VW Ddata program on responsible data advocating FACT/FAIR.
- NWO Efficient Deep Learning
- ECSEL project PRYSTINE
- University of Utrecht (PhD program)
- Amsterdam Data Science (UvA, CWI, VU) on Responsible data science

One of the highlights of the ERP was a national symposium on Applied AI on November 2nd, 2017 organized together with the Early research program for defence and the Vraaggestuurd Program on national Security, with keynotes, break-out sessions and demonstrations e.g. on Personalized Health.

As a first test, we participated in an Intel/mobileODT 'Kaggle challenge' addressing image analysis for cervical cancer. Apart from expanding our knowledge on deep learning based image processing, our incentive was to implement a simple form of transparent AI, allowing medical professionals to explore the training and relevant test data of an image classifier when making a diagnosis of a new patient. In this short-running project, we obtained a reasonable score in the top 30%, with a Kaggle Rank of 236 out of 850!

13 Bio-nano devices (exploratory)

General data	
Title	ERP exploratory project Bio-nano devices
‘Topsectors’/Societal Themes	HTSM Nanotechnology, LSH
Contact persons TNO	Arnold Storm / Tom Constandse
Contact person government	Mariëlle Beers-Homans (EZK)
Program report 2017	
Abstract	This program aims to develop technology for the detection and characterization of biomolecules at the single-molecule level with high-throughput, which is not possible today. The first focus is on the biomolecules: DNA and proteins. In 2017 TNO has started the system architecture for a high-throughput protein fingerprinting set-up together with the TU Delft and designed the setup that will be built in the beginning of 2018 at TNO. To sequence single DNA molecules, solid state nanopores with a readout mechanism is the future generation method. In 2017 a first array of solid state nanopores in SiN is made and a review on several readout mechanism is performed. The main engineering activities for DNA sequencing in 2018 are optimizing the processing of the fabrication of nanopores in SiN, and start manufacturing readout mechanisms.

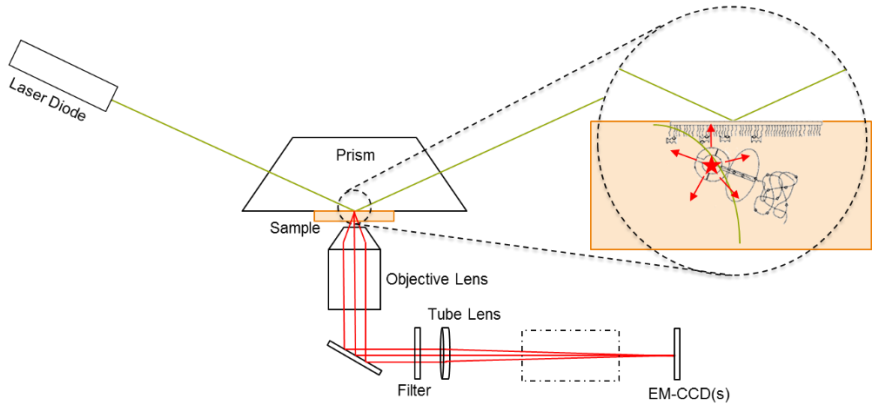


Figure 1: Schematic design of protein fingerprinting setup

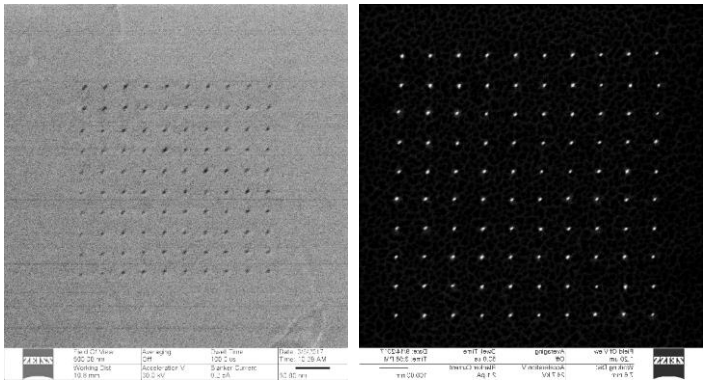
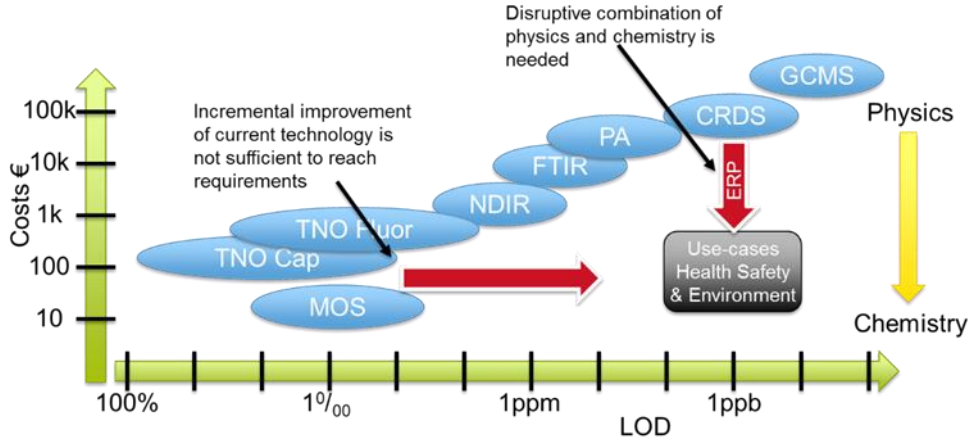
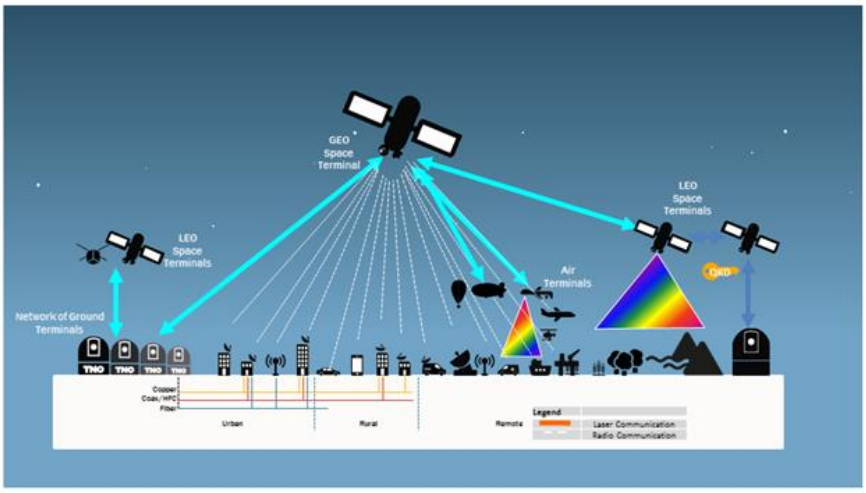


Figure 2: Nanopore array in a) graphene and b) a SiN membrane

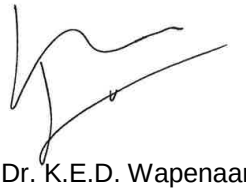
14 ExpoSense (exploratory)

General data	
Title	ERP exploratory project ExpoSense
'Topsectors'/Societal Themes	Chemical industry, LSH, Occupational / Environmental Health
Contact persons TNO	Stefan Bäumer / Anjoeka Pronk / Ingeborg Kooter
Contact person government	Mariëlle Beers-Homans (EZK)
Program report 2017	
Abstract	Several external developments have prompted us to explore a joined value proposition of 'Chemical Sensing' and 'Exposome' research resulting in the name "ExpoSense". TNO is an active member of the TI-COAST (Top Institute Comprehensive Analytical Sciences) network. The idea of a network around "Evidence Based Sensing", which is initiated by TI-COAST, is actively supported by DSM, Akzo, Philips, TNO and several academia. TNO is also partner of the NWA start impulse "Meten en Detecteren van Gezond Gedrag". In this NWA route cooperation with academia is setup, with the aim to bring analytical techniques from the laboratory setting into the outside world. All these initiatives confirm a growing need for disruptive sensing technology (see e.g. Fig. 1). An Exposome Center of Excellence @ Utrecht is being established, which is a collaboration between TNO, UU, and RIVM. This collaboration will consist of a coordinated strategy to align exposome knowledge development in the three centers (TNO: ExpoSense and VP activities, UU: interfaculty exposome hub, RIVM exposome line). The Exposome Center of Excellence already has an eco-system of co-developers, end users and other knowledge partners. In addition a collaboration was set up to integrate the exposome approach into a newly established TKI LSH consortium on promotion of lung health (P4O2).  Figure 1: State of the art (blue) and need (grey) for gas sensors First results of the Exposense exploratory project are: • A conceptual framework for the combination of sensor data and model data to obtain personal exposure estimates for external exposure levels; • For multi-component gas sensing to distinguish e.g. benzene versus toluene, a system architecture of a future gas sensor was designed, and fiber measurements with a concentrator coating were carried out showing the feasibility of the concept.

15 Optical Satellite Communication (exploratory)

General data	
Title	ERP exploratory project Optical Satellite Communication
'Topsectors'/Societal Themes	HTSM Space Instruments, ICT
Contact persons TNO	Niek Doelman / Kees Buijsrogge / Erik Fritz
Contact person government	Mariëlle Beers-Homans (EZK)
Program report 2017	
Abstract	Our Digital Society will require an omnipresent, ultra-high broadband communication infrastructure, which fully supports the information-oriented character based on concepts like Cloud Computing, the Internet of Things, the Internet of Everything and High-speed Connectivity. Satellites play a key role in the overall communication infrastructure. Satellite Communication faces the disruptive transition from radio-frequency waves to optical waves. Optical communication offers various strong advantages together with a number of technological challenges. The main challenges are: distortion due to atmospheric conditions and clouds, extreme high precision laser pointing, development of photonic devices (high power and space qualified), low mass and low volume satellite optics and extreme secure coding. This project will address the key fundamental and applied research questions in this field. Research has been started into optical communication technology, in particular a high-power multiplexer, quantum key secured optical links and Adaptive Optics for geo-satellite feeder links (which match the scope of the Eco-system's activity). The following partners are now involved: TU/e, TUD, Leiden University, National University of Singapore, Airbus DS Netherlands, DLR, ESA and NICT. Furthermore, where applicable it will connect to other National platforms and NWO programs and explore potential cross-overs of the knowledge/technology towards other applications.  For the upcoming years the research eco-system will be further matured with the underlying aim to create a strong technology and market position for Dutch industry.

Signatures
Delft, February 2018



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

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