

**TNO report**

**TNO Early Research Program 2015-2018  
Annual plan 2017**

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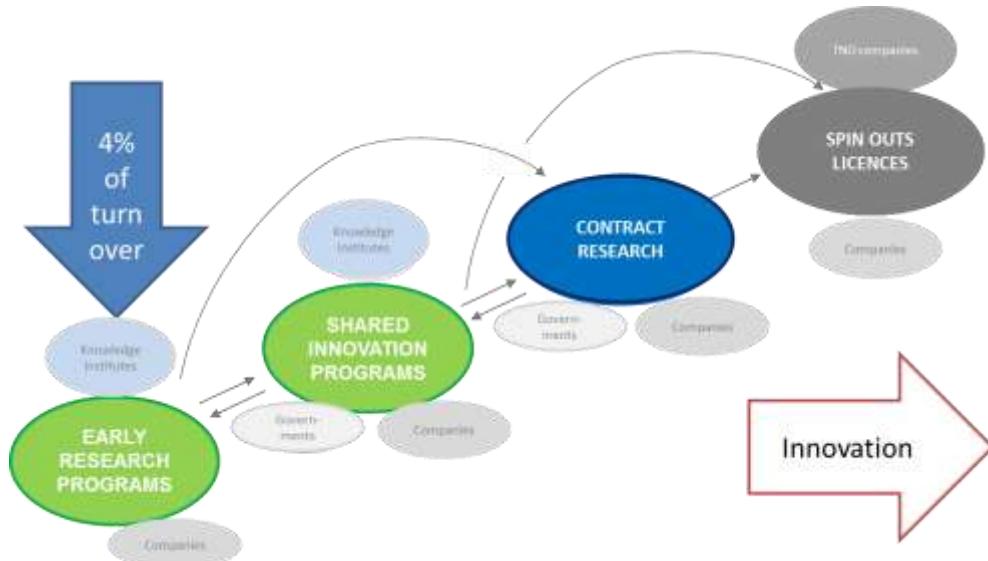
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## 1 Introduction

The Early Research Program presented here reflects TNO's vision where to put our innovative research efforts in the coming years, so to be able to maintain and grow strong technology positions and to contribute, together with knowledge partners and stakeholders, to several grand challenges. The major part of TNO's research, about 96%, is steered by TNO's stakeholders (clients, consultation by topsectors and Ministries, task financing by MOD, EZ, SZW). The 4% innovative research is meant to build, renew and maintain TNO's knowledge assets (Kennis als Vermogen).



The main characteristics of each program are:

- Use case inspired research. The portfolio of research projects is focussed on generating cutting edge knowledge and technology as an asset providing the basis for Shared Innovation Programs and Contract Research. However, from the start there must be concrete ideas about leading applications where this knowledge is needed, and concerted action (in our theme organization) to develop these applications;
- A potential to enlarge the research effort by collaboration with knowledge partners and stakeholders. Leveraging can be reached by aligning TNO programs with, e.g. TKI, NWO and EU schemes (established examples are: quantum computing, 3D nano-manufacturing, energy storage and conversion, submicron composites, making sense of big data, and complexity), and by attracting contributions from stakeholders and sponsors. Projects should become the nucleus of research ecosystems with the ambition to grow to a meaningful size like the TNO-Imec Holst Centre in the 2015-2018 TNO strategy period;
- A flexible portfolio of projects. In 2015 we started with eight projects, and room for seed projects and supportive actions. Two of the seed projects: 'Organ-Function on Chip' and 'Submicron Composites' (a collaboration established with the Brightlands Materials Center) have been added to the portfolio; a third seed project: 'Orchestrating Innovation' has been stopped. In 2016 a new seed project has been started: i-botics, in cooperation with university Twente. Technology needs and opportunities are scouted in the areas of artificial intelligence, chemical and bio-nano sensors. Progress is evaluated at least twice a year (May and September) on scientific output, and on the realization of use cases. We expect changes in the portfolio on a yearly basis, after an incubation period of about two years, because ERP projects will evolve into Shared Innovation programs or will fail to live up to expectations. The need for flexibility will restrain sponsoring of PhD research. There will be a shift towards in kind cooperation with universities.

In line with the request of EZ we inform Top-sectors and Ministries of this approach of building our knowledge base, aiming at early involvement of companies and other stakeholders in public private cooperation. March 31 TNO's CTO Jos Keurentjes informed the 'Topsector' Captains of Science about the ERP program. May 19 the ERP program manager Koen Wapenaar informed the 'Topsector' TKI directors on ERP program lines and progress. Information on our ERP research is also available online, and can be found [here](#).

## Projects 2017

External and internal progress meetings have confirmed that the 10 ERP research lines executed in 2016 fit very well to upcoming needs and to the future knowledge portfolio of TNO. In all cases there is a growing interest and participation of knowledge partners and stakeholders, although at different paces. For one of the programs (now called Personalized Lifestyle for Health) the focus has changed to such an extent that we have decided to change its name to better connect to the current focus. Lifestyle has become the prevailing health determining factor, and although food is one of the variables it is not the only and not the major one. The new seed project (on robotics) is gaining momentum. In December it will be decided whether this subject will be continued in the ERP portfolio 2017. A short overview of our 10 ERP projects 2017 is given below:

- Quantum Computer / Quantum Internet (QuTech), an early example of a newly emerging research ecosystem centered around TU Delft and TNO, announced September 2013 by Minister Kamp and started in 2014, with the support of NWO, EZ, the Topsector HTSM and industry. The technical ambitions are to develop a quantum bit that will replace the transistor allowing the paradigm shift from a binary computer to a quantum computer, and to develop secure quantum internet, thus providing the ultimate encryption.
- Complexity, "The study of the phenomena which emerge from a collection of interacting objects". Following on a 4 year NWO program, where the fundamentals and potential of this type of research were explored, NWO, TNO and stakeholders (Topsectors Logistics and Agrifood, and companies from these sectors, are the first participants) will embark on a new connecting 4 year program "Grip on Complexity" where explorative and applied research will be combined.
- Personalized Lifestyle for Health. The most important factor defining health is the ability to adapt to many different stresses and changes, in other words, being a flexible and resilient system. Multidisciplinary approaches are necessary to translate scientific knowledge to real-life implementation and improvement of a person's health status. Together with partners, we integrate nutrition, physical activity, biology, human behaviour, e-health, data management and education to develop an aligned approach. All fields are represented within TNO, and only by integrating will make an impact in society, healthcare and economy.
- Energy Storage & Conversion, to provide new solutions for large scale, central and small scale, decentral (local) energy supplies, and to increase the necessary flexibility of the energy system. The primary focus is on three different technology concepts for energy conversion and storage (electricity to chemicals and fuels, photons to chemicals, and chemical heat storage), and on a management control system for balancing energy supply and demand.
- 3D Nanomanufacturing, The market growth of the semiconductor industry has a great impact on Dutch and European economy. Using strategic innovation, the Netherlands has been able to keep a competitive advantage in the development of equipment and instruments for nanometer-sized patterning, manufacturing and measurement. Examples include UV-light assisted patterning (ASML) and electron beam imaging (FEI). The primary application focus of this ERP is on equipment and instruments for 3D "nanomanufacturing" and "nanometrology" of future 3D nano-electronics devices. The technology opens up many opportunities in other domains, e.g. Instruments for bio-medical and health-care.

- **Structural Integrity.** 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, maximizing the “up-time” of the structures and allowing utilisation in a different way than a structure was originally designed for. Our research aims at breakthroughs with respect to: *“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”*
- **Human Enhancement.** We are currently facing an increasing level of automation of systems in e.g. the industrial (maritime and offshore) sector but also in the mobility sector (automated driving). The challenge is to establish effective and resilient, joint human-automation behaviour patterns. The first goal of our research is to develop a transparent (human-in-the-loop) adaptive automation platform that substantially improves safety for manoeuvring and control tasks. The second goal is the development of a multidimensional prospective model for human resilience and related monitoring instruments and organizational interventions.
- **Sense Making from Big Data.** 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 our research is to create a capability (tools, models, methods) that enables stakeholders to design and implement a Data Driven Innovation (DDI) in a multi-stakeholder setting. The focus is on three Big Data challenges: Uncertainty, Multi-stakeholder collaboration, and Information Centric Networking
- **Organ-Function on Chip** models provide a promising approach to solve translational issues that are evident in not only the pharmaceutical industry, but also the nutritional, chemical, environmental and cosmetic industries. 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. The applications focus on three organs: Gut function on a chip, Liver function on a chip, and Lung function on a chip.
- **Submicron Composites**, The overall goal is to achieve a level of control over structure and chemical composition of materials that enables the development of materials with programmable functionality. Our additive manufacturing research is focused on better mechanical properties, lower internal stresses, and novel functionalities. The innovative building envelopes research is focused on materials that adapt their optical behaviour in order to optimize energy performance of various parts of buildings, including windows.

The Tables below present the relations between the topics and Social Themes / Top-sectors.

Social Themes

ERP	Social Themes				
	Environment and sustainability	Safety and security	Defense	Occupational health	Geological survey
Quantum Computer / Internet					
Complexity					
Personalized Food					
Energy Storage & Conversion					
3D Nanomanufacturing					
Structural Integrity					
Human Enhancement					
Sense Making from Big Data					
Organ function on Chip					
BMC-Submicron composites					

## Top-sectors

ERP	Topsector								
	Horticulture and source materials	Water	Agri & Food	Life Sciences & Health	Chemistry	Energy	High Tech Systems and Materials	Logistics & Mobility	Creative Industry
Quantum Computer, I-net							•		
Complexity	•	•	•	•	o	•	o	•	•
Personalized Lifestyle, Health			•						
Energy Storage & Conversion					•	•	•		
3D Nano-manufacturing							•		
Structural Integrity		•				•	o		
Human Enhancement							•		
Sense Making from Big Data			•	o		o	•	o	
Organ function on Chip				•					
BMC-Submicron composites					o				

• Active relationship; o Relationship under development

In addition to these ten topics we will explore one or two seed projects. Finally, efforts related to the benchmarking of TNO's knowledge position (Knowledge Position Audit) are part of the ERP programme.

In the next chapters the program adjustments of the ten projects are described in a concise format agreed with the ministry of Economic Affairs, explaining the dynamics, the use cases, the setting of the research in national and international context, the cooperation in ecosystems pursued, and the goals for 2017 and beyond.

## 2 Quantum computing and Quantum internet

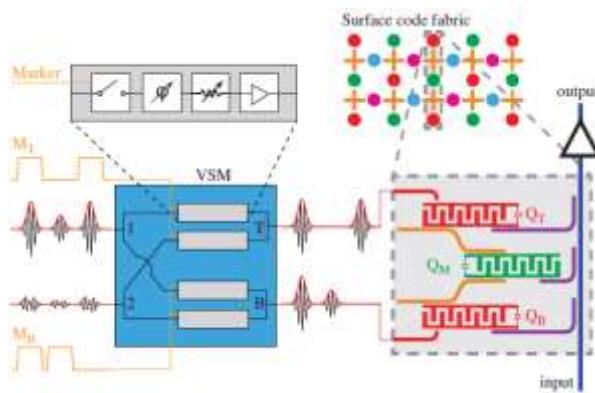
<b>General data</b>	
Title	ERP Quantum Computer / Quantum Internet
'Topsector'	HTSM Nanotechnology
Contact person TNO	Rogier Verberk
Contact person government	Michiel Ottolander
<b>Program adjustment 2017</b>	
Summary	<p>An increasing number of companies and institutes share the motivation to develop quantum computing and quantum internet. Driving are (1) future applications of the unprecedented computing power for sciences and Grand Challenges (including, e.g., development of high-temperature superconductivity for the energy challenges, and in the long run faster developments of drugs for the aging society), (2) computing power for industrial applications (big data search, logistical tasks), (3) being among the front-runners in the development of quantum communication (for national security as well as commercial applications), and (4) to develop a new industry based on Europe's leading scientific position in this field.</p> <p>QuTech, the quantum technologies research center by TNO and TU Delft, has made significant progress in 2016. Besides the cooperation with Microsoft and Intel, in 2016 IARPA granted a large project to a consortium led by QuTech. QuTech hosted together with the European Commission and the Dutch department of Economic Affairs a large conference in Amsterdam in 2016 for scientists, policy makers, and representative from industry. At this conference European Commissioner Oettinger announced the initiative for a European Flagship on quantum technologies.</p> <p>For further information on the ambition and people of QuTech, an introduction to quantum computing, and breaking news, please visit <a href="http://www.gutech.nl">www.gutech.nl</a>.</p>
Short description	<p>The TUD hosts a team of world class scientists in solid state quantum technology. Four out of the ten most-sited scientists of the Netherlands (all fields of expertise) work in Delft in this field (source: Volkskrant, October 2012). This team also had 10 papers in the Nature magazines in 2013. This is the scientific foundation of QuTech.</p> <p>On the other hand the Netherlands has a large ecosystem of high-tech / high-precision equipment manufacturing companies including an extended supply chain. This sector has developed and successfully commercialized tube technology for radio and television, transistor and chip technology, lighting and medical equipment, and wafersteppers. Each wave of innovation has led to a new wave of employment. And like ASML and FEI started as spin-off companies from Philips, it is now time to create the new seed for high-tech business. This infrastructure of high-tech industry will accelerate the development of the quantum computer now. In the future the quantum technology shall be a new unique selling point of this Dutch ecosystem.</p> <p>TNO is experienced in multiple technologies which are critical for the development of the quantum computer, and complementary to the knowledge of the TUD. Secondly, TNO brings to QuTech its experience in prototyping, mission oriented project execution, and contacts to the industry.</p>



By building prototypes and demonstrators, TNO/QuTech shall be positioned as a pioneer in quantum technology. Moreover, TNO/QuTech will invite industrial partners to participate in the development of the demonstrators to strengthen the relationships and have some of this work funded by industry and European projects.

On the other hand TNO has to develop some of its existing technologies further to meet the requirements of the quantum computer (e.g. RF-technology, nanofabrication, multiscale physics simulations). This will improve the competitive position of TNO in the existing (non-quantum technology) markets like nano-technology/semicon and RF-technology/Radar. These markets are already very important to TNO.

Finally, the further development of existing and new technologies generate possibilities for unforeseen spin-off.



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

Goals	<p>The envisioned developments cover many TRL's, multiple disciplines, and thereby 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) will be 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 architectural considerations, and involving third parties.</p> <p>The second 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 and mathematical challenge shall be selected for the demonstration. This challenge shall be mapped to the electronic hardware.</p> <p>During the third 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.</p> <p>QuTech works according to four Roadmaps, one for each type of qubit. The most critical enabling technologies that will be developed during the coming years are incorporated in the most relevant Roadmap.</p> <p>2017 Will be the first full year of the IARPA project. QuTech will have to show a more detailed plan as well as some first results towards a logical qubit.</p>
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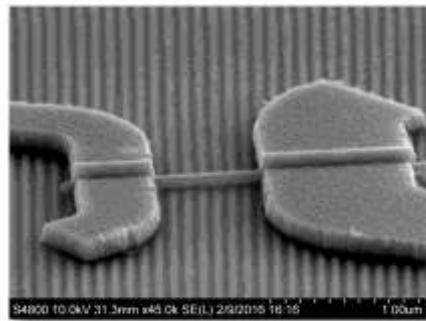
*Caption: TNO has developed and built, based on the expertise of the Radar Technology Department, dedicated electronics to control circuits of multiple (transmon) qubits.*

The European Commission has announced an European Flagship on quantum technologies as well as the High Level Group, the group of people that will manage the initialization phase of this Flagship.

QuTech will have to position itself in view of these European developments.

QuTech is in contact with multiple players in the communications and aeronautic industries. TNO/QuTech is currently developing plans to come to demonstrations of quantum technologies in these domains. In 2017 TNO/QuTech hopes to set up a first consortium with participants from academia, institutes, and industry.

An important scientific milestone for 2017 is the growth of semiconductor nanowires in the new MBE cluster tool. QuTech has made enormous investments in setting up a dedicated lab for this purpose in 2015/2016. In 2017 the first nanowires shall be grown, and mounted and connected for the electronic measurements. In the long run these nanowires may become the basis for a quantum computer based on Majorana bound states.



*Caption: Inspired by industrial processing technologies TNO developed an ultra-flat substrate including buried electrodes for scientific experiments on Majorana bound states in semiconductor nanowires.*

Dynamics	<p>The timing of the start of an European Flagship was difficult to estimate. The announcements by the European Commissioner in 2016 have made the timeline a lot more concrete. 2017 Will be a year of preparations, making it an important year to decide on QuTech's ambitions within this Flagship and to make these ambitions heard by the stakeholders.</p> <p>Under project name 'QuSpace', QuTech is investigating the possibilities to bring quantum technologies to satellites. After initial discussions with important industrial (KPN, ATOS, OHB, Airbus) as well as academic players (prof.dr. D. Bouwmeester, Leiden University), some ideas for consortia for scientific and demonstrator-like experiments are developing. In 2017 QuTech hopes to align with ESA and initiate new activities in this domain.</p>
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### 3 Complexity

General data	
Title	Complexity
'Topsectors'/Societal Themes	Water, Logistics, Life Sciences & Health, Horticulture and Starting Materials, Chemical Industry, Creative Industries, Agriculture and Food
Contact person TNO	Ardi Dortmans; Esther Zondervan
Contact person government	Michiel Ottolander (EZ)
Program adjustment 2017	
Abstract	<p>In the Early Research Program (ERP) Complexity, TNO combines beta and gamma sciences to be able to develop technical and social innovations for modelling and decision making. Modelling approaches in which a variety of qualitative and quantitative models are used and combined are most valuable to achieve this. Examples of relevant models are (heterogeneous) agent based models, multiscale physical models, Bayesian belief models, business models etc.</p> <p>Complexity is commonly briefly described as the science that deals with “the study of the phenomena which emerge from a collection of interacting objects”. The primary aspects investigated are fundamental dynamics of complex systems:</p> <ul style="list-style-type: none"> <li>– The emergence of collective behaviour;</li> <li>– The transition from one system state or phase to another;</li> <li>– Resilience to external shocks or disruptions.</li> </ul> <p>TNO works on the growth of the eco-system along three parallel lines:</p> <ul style="list-style-type: none"> <li>– Expansion of the cooperation with NWO and industrial partners, preferably also with TO2 partners;</li> <li>– Initiation of new activities through the Netherlands Complexity Platform Science (NCPS) platform;</li> <li>– Setting-up PPS activities for valorisation of the more fundamental research with NWO.</li> </ul>
Short description	<p>Complexity is commonly briefly described as the science that deals with “the study of the phenomena which emerge from a collection of interacting objects”. The primary aspects investigated are fundamental dynamics of complex systems. The NWO position paper “Grip on Complexity”<sup>1</sup> has identified 3 important areas where knowledge gaps exist and research is required:</p> <ul style="list-style-type: none"> <li>– the emergence of collective behaviour: how to create new properties transcending those of the constituent components with the key research challenge to foster or suppress the emergence of collective behaviour;</li> <li>– the transition from one system state or phase to another: how to predict and influence the dynamics of change with the key research challenge to detect, anticipate and influence critical transitions;</li> <li>– resilience to external shocks or disruptions: how to influence resilience to exert control with the key challenge to make systems more resilient or more fragile.</li> </ul>

<sup>1</sup> <http://www.nwo.nl/en/about-nwo/media/publications/ew/paper-grip-on-complexity.html>, September 2014

	<p>A small list of examples where complexity plays a role: traffic jams, epidemics, internet overload, criminal and terrorist organisations, quantum entanglement, animals or robots swarms, industrial value chains, stock markets, cell biology, oncology, cardiology, internal medicine, psychiatry etc.</p> <p>Similar research questions appear in topics addressed in TNO research and thus provide a good general starting point for defining research projects in the period 2015-2018 that will contribute to solutions for research questions mentioned above.</p>
<b>Research line 1: “<i>Grip on Health</i>”</b>	
Goals	<p>Application of complexity science offers a unique opportunity for a transition in food or health care to shift scientific thinking from reductionist thinking to complex thinking. Attention will then shift from quantity to quality, from looking at objects/molecules to looking at the relationships between the objects and a shift from looking at structure towards looking at processes. Those shifts in thinking require the application and development of different modelling techniques to support decision making processes for optimised (personal) health strategies. For 2017 we aim to realise:</p> <ul style="list-style-type: none"> <li>– D1 (Semi)-quantitative health model consisting of physiological, mental and social interacting domains;</li> <li>– D2 Application of the health model in two use cases e.g. Alzheimer and Diabetes.</li> </ul> <p>These activities will be part of the NWO call Complexity – Nutrition &amp; Health in 2016.</p>
<b>Research line 2: “<i>Grip on Logistics</i>”</b>	
Goals	<p>Ongoing globalization and the growth of network and information technologies, have brought cities more and more under the influence of a multiplicity of processes relating to various localities, regions, nation-states, environments and cultures. Within urbanization practices, this increased societal complexity has led to an enormous growth of resource interdependency, also in logistics and transportation. This has already proven to be a very fertile area for complexity research: efficient public transport systems, and the development towards smart self-organisation of passenger transport in the triangle of physical transport, ICT and human behaviour. For 2017 we expect to realise:</p> <ul style="list-style-type: none"> <li>– D1 An autonomous and portable descriptive model of the port sea side processes;</li> <li>– D2 Development of mathematical theories and models that describe the relation between the individual road trips, the road network performance and different situational variables.</li> </ul> <p>These activities will be part of the NWO call Complexity – Logistics in 2016.</p>
<b>Research line 3: “<i>Grip on Circularity</i>”</b>	
Goals	<p>A circular economy offers opportunities for both economic growth and for tackling major societal problems, such as reducing emissions of greenhouse gases, the availability of fossil raw materials, clean water and agricultural products, and maintaining soil fertility. Without exception, new developments must be sustainable. The cycles to be developed should be closed as much as possible, e.g. biomass waste flows must be used to maintain the capacity of the soil and the water to ensure a stable crop growth. Disclosing and introducing or reintroducing knowledge of the natural system and the biodiversity is necessary if we want to realise self-regulating and self-supporting systems without any undesirable, disadvantageous environmental other effects. This system innovation will benefit from complexity research on self-organisation, transitions and stability. For 2017 we expect to realise:</p> <ul style="list-style-type: none"> <li>– D1 Development of Sustainable business models;</li> </ul>

	<ul style="list-style-type: none"> <li>– D2 Model to predict the environmental and economic impact of a circular economy taking into account the uncertainty of fast changing economy and technology. These activities will be part of the NWO call Closed Cycles in 2016 and the expected NWO call Sustainable business models in 2016/2017.</li> </ul> <p>Apart from these, the further development of the Netherlands Platform Complex Systems (NPCS) will be on our agenda.</p>
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### Building the Ecosystem

Goals	<p>This ERP was set-up as to shape a close cooperation with NWO. The NWO EW program Complexity is an important instrument to define joint calls and project proposals with academia and industry. In 2016 this has led to the NWO call Complexity – Logistics<sup>2</sup> in close cooperation with top sector Logistics and NWO MAGW, and the NWO call Complexity in Health and Nutrition<sup>3</sup> in close cooperation with top sector Agriculture and Food. For 2017 a call is being prepared with NWO-EW on Complexity –Self-organisation, where at least TS Chemical Industry will be partner (HTSM and Energy are being consulted).</p> <p>Building on the experiences of 2015 and 2016 other NWO initiatives are being developed. The NWO ALW call Closed Cycles<sup>4</sup> is about the system transition Circular Economy where the 3 areas of research above play an important role, as outlined in the NWA route “Circulaire economie en grondstoffenefficiëntie”<sup>5</sup>. This call has been formulated in close cooperation with TO2 (in particular DLO, Deltares, ECN) and Hogescholen as well as the topsectors Agriculture and Food, Logistics, Horticulture and Propagation Materials and Water. Top sector Creative Industries is also interested to join project initiatives for this call.</p> <p>With NWO-MAGW initial discussions are being held to shape a call on Sustainable business models, which e.g. addresses some system dynamics research questions for Circular Economy. Also DLO is interested in this initiative, together with Het Groene Brein.</p> <p>The initiatives above shape an ecosystem in PPS format together with academia, hogescholen and industry through joint proposals. The ultimate quality check on content for these proposals will be the formal NWO quality evaluation. The industrial relevance for TNO comes from a significant industrial interest in these proposals that steers the knowledge development in ERP Complexity as work ahead of or as part of these projects. Evidently the formulation of these projects is aligned with activities in various TNO VP to assure proper alignment with other, demand driven, research.</p>
Program dynamics	Overall this the ERP Complexity moves along the lines outlined in the multiannual plan 2015-2018. The intense collaboration with NWO and industrial partners is shaping well, but is being extended to TO2 and hogescholen to build stronger PPS. Also it is becoming a collaboration with other NWO areas as ALW and MAGW to address relevant research issues with other stakeholders.

<sup>2</sup> <http://www.nwo.nl/en/funding/our-funding-instruments/magw/complexity-in-transport-and-logistics/complexity-in-transport-and-logistics.html>

<sup>3</sup> <http://www.nwo.nl/financiering/onze-financieringsinstrumenten/ew/complexity-in-health--nutrition/complexity-in-health--nutrition.html>

<sup>4</sup> <http://www.nwo.nl/en/funding/our-funding-instruments/alw/closed-cycles---transition-to-a-circular-economy/closed-cycles---transition-to-a-circular-economy.html>

<sup>5</sup> <http://www.wetenschapsagenda.nl/circulaire-economie-en-grondstoffenefficiëntie/>



## 4 Personalized Lifestyle for Health

General data	
Title	Personalized Lifestyle for Health (PLH)
'Topsectors'/Societal Themes	LSH Agri&Food
Contact person TNO	Peter van Dijken
Contact person government	Michiel Ottolander (EZ)
Program adjustment 2017	
Abstract	<p>The third year of the program is characterized by integration, expansion and implementation. The program builds on the assumption that improvement, maintenance regaining of lifestyle related health starts with self-empowerment of the citizen/patient. This requires integration of many disciplines (diagnosis, diet, behavioral change, information, e-health, etc.), and spans from early life to healthy ageing. The program is only successful if fundamental developments connect to economical and societal implementation.</p> <p>Therefore, the 2017 Personal Lifestyle and Health program will target on:</p> <ul style="list-style-type: none"> <li>- <b>Optimal resilience.</b> Identification and development of lifestyle interventions which promote health by restoring disease triggering biological imbalances.</li> <li>- <b>Healthy start for lifelong health.</b> Identification and development of healthy lifestyle interventions in early life.</li> <li>- <b>From care to cure for type 2 diabetics.</b> Design and implement a lifestyle based healthcare that changes current disease management into real and sustainable cure for type 2 diabetics.</li> </ul>
Short description	<p>Multidisciplinary approaches are necessary to translate scientific knowledge to real-life implementation and improvement of health status. We integrate nutrition, physical activity, biology, human behaviour, e-health, data management and education to develop an aligned approach. All fields are represented within TNO, and only by integrating will make an impact in society, healthcare and economy.</p> <p>From TNO's point of view the most important factor defining health is the ability to adapt to many different stresses and changes, in other words, being a flexible and resilient system. This system can be both the human body and its internal processes but also the human being under influence of its external environment. The concept of resilience has been extensively applied by TNO in investigating health in adults and elderly: stabilization of an existing healthy and flexible system or preventing a system from losing its flexibility (or even reverting to a more flexible system) plays a key role. The element of resilience, either in shaping or restoring, comes back in all three subprojects within this ERP.</p>
Project 1: " <i>Early Life</i> "	
Goals	The concept of resilience can also be applied to the early life situation where the major focus will be on the development rather than maintenance of a flexible and healthy system: in the important time period from conception to the age of two (also known as

the first 1000 days) nearly all systems in the human body are developed including the regulatory circuits which determine the responses to internal and external stimuli. This development is characterized by an inherent and essential temporal instability which enables the training of the system and which finally results in a stable and resilient situation. It also includes critical windows or sensitive periods in which the system is more open to external influences (which can be both positive and negative). Once this resilient system has been developed the foundation for a life long healthy situation has been created. This has been clear for hereditary diseases for a long time, but it is now becoming increasingly clear that this also applies to many other diseases.

TNO approaches the healthy system from different angles using different expertises. A first approach focuses on the human body itself and tries to understand the system from a biological point of view. This systems biology approach focuses on understanding developmental processes but also interdependencies between different parts of the system (such as the gut-brain axis). This includes the microbial populations (microbiota) inhabiting different parts of the human body. We have shown e.g. that the microbiota composition in the nose of young infants (4-6 weeks of age) determines the respiratory health of these infants up to the age of two, distinguishing between infants with a healthy and an unhealthy situation. This insight enables both the development of novel diagnostics and novel interventions.

A second approach focuses on the influence of the environment on the healthy system. Many different aspects of the environment are taken into account: this ranges from the effect of nutrition (which is closely related to the systems biology approach) to the influence of parents, stresses, child care etcetera on healthy development. Before pregnancy the health status of (future) parents already can be a determining factor. During pregnancy the in utero environment plays an important role and after birth the whole environment is influencing healthy development, including nutrition, lifestyle, the physical environment (soil, air, etc.) but also social and cultural aspects.

To stimulate and train flexibility a continuous interaction with the environment is essential. Understanding how the environment influences the system is essential and views on this may change. Creating a clean, hygienic environment for a long time has been considered essential to prevent infectious diseases but new insights increasingly show that this has also led to insufficient exposure to beneficial micro-organisms (the so-called old friends), leading to a disturbed training of our immune system. This then is related to the strong increase in immune related diseases such as allergic diseases (eczema, asthma), type 1 diabetes and even neurological disorders such as autism and MS. This leads to research questions like how to prevent this? How do specific foods influence this development? Is taking your child to a farm beneficial or not?

By replacing single issue thinking with an integrated approach to child health, we can develop and implement sustainable solutions utilizing the entire knowledge cycle from fundamental research to implementation research, within the life course continuum from prenatal through to the second year of life to achieve long lasting effects and improvements. In 2017 first demonstrators of this integrated approach will be started together with industrial and academic partners.

Current academic partners in this area include UMCU, EUR, LUMC, UvA, RUG, Spaarne Gasthuis, ZGV and RIVM with which different collaborations on better understanding Early Life development are underway.

#### Project 2: *"Lifestyle as Medicine"*

Goals	Lifestyle is both an enormously powerful and a strongly underestimated medication. Many diseases have a bad lifestyle as origin, and likewise can and be reversed and cured.
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This is based in the same biological flexibility that is exploited in all program parts. In practice, this means a personalized lifestyle based therapy (mainly optimal diet and physical exercise) and cures a type 2 diabetic within weeks or months, depending on intensity. Connected to behavioral change technologies are available that motivate the ex-patient to sustain a healthy lifestyle.

This TNO program, in a strategic collaboration with Leiden University Medical Center and together with other Medical Delta partners (UL, EUR), will develop and implement a compressive toolkit for first line healthcare. It includes personalized diagnosis, tailored nutritional and physical activity programs, a “data democracy” infrastructure that helps citizens to fully self-empower themselves based on their own health data, an e-health component and an extensive behavioral change program. It connects to a training and education program within the partnership.

Importantly, we chose to implement in a specific region (Leiden-Den Haag-Rotterdam) to concentrate multiple aspects that together strongly increase compliance. These include the involvement of the regional healthcare partners, local health insurance, employer health programs, local innovative lifestyle service providers, knowledge and technology partners and funding mechanisms. The aim is to generate a completely new, economically viable and sustainable healthcare system for type 2 diabetes that can later be exported both to other regions and other diseases. In this process the academic partners and TNO collaborate in both fundamental research and implementation into healthcare practice, with TNO bringing in its systems view on human health and is leading the translational part from a science driven to market oriented approach.

### **Project 3: “Lifestyle interventions and its impact on health”**

Goals	<p>Homeostasis is described above as a balanced system defining a healthy situation. Disturbance of this system has been observed in numerous human diseases and appears to be a central element in the transition from a healthy to a diseased situation. This situation, which is also called dysbiosis, plays a central role in the experimental part of this Program, focusing on the impact of lifestyle interventions on health and with a focus on prevention of disease. Three different aspects are taken into account:</p> <ul style="list-style-type: none"><li>• Intestinal microbiota, changes in the composition of which is related to nearly all human diseases</li><li>• Intestinal tissue, which is the entry of all food derived nutritional building blocks but also the gatekeeper prohibiting pathogens and toxins to enter the system</li><li>• <i>In vivo</i> mouse model, where all individual aspects come together</li></ul> <p>Achievements to date include the effects of antibiotic exposures on microbiota composition, the effects of pathogenic micro-organisms and metabolites produced by intestinal microbiota on intestinal organoids and the development of an early life developmental index (the so-called d-score, routinely used for infants) in the early life mouse model. Furthermore a mouse model with a lifestyle induced disturbed intestinal barrier function has been developed. For 2017 we aim at integrating the different technologies in an integrated demonstrator showing the added value of combining these technologies. Since dysbiosis is related to many different diseases and is influenced or caused by an unhealthy lifestyle (including unhealthy diets) our dysbiosis model may have broad applications in many different health related areas. The dysbiosis model will be further validated in 2017 and first applications with industrial partners are foreseen. Current academic collaborations in this area include Donders Institute (RU), ACTA (VU/UvA), EMC, AMC, UMCU.</p>
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## Program dynamics

Some major evolutions are occurring in the program:

- During the program the focus has changed to such an extent that we have decided to change its name to better connect to the current focus within the program. The major change is that lifestyle as health determining factor is prevailing and although food is one of the variables it is not the only and not the major one.
- The focus of this program has been discussed both with the Top sector Agri&food (by Peter van Dijken, director of innovation Food & Nutrition) and Top sector LSH (By Cyrille Krul, director of innovation Predictive Health Technologies).
- From single applications to a joint concept: the systems flexibility approach is applied from early life to ageing related disorders
- From single technologies to integration: the tools that were developed in the first two years, in the various TNO departments, are now intrinsically connected in their application. As example, in "Lifestyle as Medicine, 5 departments contribute to one solution including data and knowledge management, behavioral change, employer program, local multi-stakeholder integration, diagnosis, food intervention and physical activity. Previous attempts to implement lifestyle based healthcare failed because one or more of these parts were excluded
- From design to implementation. After two years of "building the parts", they are now brought to actual implementation in the Leiden-Den Haag-Rotterdam region.

## 5 Energy Storage and Conversion

General data	
Title	ERP Energy Storage & Conversion
'Topsectors'/Societal Themes	TKI Chemie TKI Urban Energy
Contact person TNO	Sjoukje Wiegersma / Pascal Buskens
Contact person government	Michiel Ottolander (EZ)
Program adjustment 2017	
Abstract	<p>Energy Conversion and Storage becomes more and more important to achieve an increased use of durable energy. In 2015 and 2016 we made good progress in our search for new conversion and storage processes as well as software tools for improved balancing between supply and demand of energy on the electricity grid. In 2017 we aim to:</p> <ul style="list-style-type: none"> <li>- Make a decision on the best salt composite tested so far for the ThermoChemical Storage concept. Salts appear to perform better when they are stabilised with polymeric material. Quantification of the effect will take place in 2017, which will be the starting point to the design of a small scale reactor.</li> </ul>  <p><b>Figure 1. A single family house with a solar collector which delivers thermal power to a compact seasonal storage unit (in the basement). The stored thermal energy is use for space heating.</b></p> <ul style="list-style-type: none"> <li>- The conversion of light to chemicals will progress with the development of a process that converts CO<sub>2</sub> into fuels, which might give great opportunities for small scale, local, productions of fuel from renewable starting products.</li> <li>- Regarding electrification (use of electricity for chemical production), goals for the next year are to continue the research work into the laboratory demonstration phase and to expand the VoltaChem program with new collaboration partners and new industry funded projects.</li> <li>- The software tool will be further developed towards a simulation environment for</li> </ul>

	<p>policy / decision support and will incorporate uncertainty of electricity consumption in forecasting and planning.</p>
Short description	<p>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.</p> <p>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:</p> <ul style="list-style-type: none"> <li>• Development of an electro-catalytic process that uses (green) electricity to produce fine chemicals and fuels.</li> <li>• Study the feasibility of a process that directly uses sunlight for the production of fine chemicals.</li> <li>• Study and develop new material combinations for efficient and safe storage of heat, generated with sun collectors.</li> <li>• Develop additional functionality of a software tool aiming at optimal matching of energy supply and demand by using market mechanisms. ("Powermatcher")</li> </ul> <p>Further details with regard to goals and program dynamics have been described below per project.</p>
<b>Project 1: Electrons to Chemicals</b>	
Goals	<p>The program addresses both the indirect and direct use of electricity within the chemical industry, and works from a systemic point of view. Significant steps have been made in 2016, related to developing showcases related to hydrogen peroxide, FDCA from HMF and CO<sub>2</sub> conversion. The main activities within the ERP in 2017 will focus on:</p> <ol style="list-style-type: none"> <li>1. <u>CO<sub>2</sub> (centralised bulk chemicals)</u> Together with UU, RUL and UT, improved catalytic systems will be developed to convert CO<sub>2</sub> to ethylene. This will be supported by NWO and Shell with 3 PhD students (~900 keuro program). TNO will focus on reactor and system development. UU and RUL will work predominantly on new electrode materials. Therefore, the focus of TNO shifted slightly from materials to process technology.</li> <li>2. <u>Electrochemical engineering scale up research focussed on biomass electrochemical oxidation/reduction (specialty chemicals/decentralised bulk)</u> Continuation of the oxidation showcase (butanol/HMF oxidation) <ul style="list-style-type: none"> <li>• Reactor and system development related to the conversion to "biowaste" materials (such as lignin, glycerol) to value added chemicals, focussed on paired electrolysis. IE reactions at the cathode and anode, leading to a significant reduction of associated capital cost per kg of product.</li> <li>• Developing generic toolboxes which have a quick scan possibility to identify technical and economic opportunities for the conversion of biobased materials based on holistic conversion/ downstream process system</li> </ul> </li> <li>3. <u>Oxygenate production (specialty chemicals/decentralised bulk)</u></li> </ol>

	<p>Based on HMF-FDCA showcase, it has been shown that cost effective renewable hydrogen (reduction) is coproduced. Systems will be developed to utilise this hydrogen for the production of oxygenates from CO<sub>2</sub> (methanol, DME, OME etc) in combination with oxidation of biobased chemicals such as HMF to FDCA. Oxygenates from CO<sub>2</sub> are ideal platform chemicals, storage media and transport fuels. The challenge is to develop reactor and integrated systems which can benefit from this oxidation-reduction system. This can lead to significant COST EFFECTIVE energy storage in to value added chemicals.</p> <p>4. <u>Scouting: Identification of routes for electrochemical produced small scale ammonia (energy storage and conversion)</u></p> <p>For the long term it has been envisaged that ammonia will be used as a high density energy storage media. Ammonia is currently being used as a fertilizer, produced via the very energy intensive haber bosch process. Within the fourth activitiy within the ERP, scouting research will be done to explore the technical and economic potential for the electrochemical production of ammonia. Amongst other, conceptual; process designs of lithium activated systems will be evaluated, specifically for small scale. Collaboration is foreseen with UU. This line is new within the ERP.</p>
Program dynamics	<p>In 2015 the Voltachem program has been set up succesfully to initiate and facilitate collaborative development of technology and business models with relevant stakeholders to help move innovation in the field of electrification and decarbonization faster towards commercial implementation. The program addresses both the indirect and direct use of electricity within the chemical industry, and works from a systemic point of view. The ERP project will be conducted in close relation to the Voltachem programm.</p>
<b>Project 2: Photons to Chemicals</b>	
Goals	<p>We aim at studying two different plasmon-assisted chemical conversions: (a) the Suzuki coupling of bromobenzene and <i>p</i>-tolylboronic acid, and (b) the reduction of carbon dioxide to methane. We work on case (a) together with the partners in the NWO project "Unravelling the mystery of solar steam nanobubbles", and on case (b) together with the partners in the Interreg project "EnOp". The key objectives for 2017 connected to these conversions are:</p> <p><i>Suzuki coupling:</i></p> <ul style="list-style-type: none"> <li>i. Quantify the contribution of the local heat generation and hot carrier generation to the chemical conversion, and apply this to estimate the energy conversion efficiency of plasmon assisted reactions.</li> <li>ii. Determine the local temperature under reaction conditions using RAMAN spectroscopy.</li> </ul> <p><i>Reduction of carbon dioxide:</i></p> <ul style="list-style-type: none"> <li>i. Design and build a reaction set-up.</li> <li>ii. Reproduce the work of Sastre <i>et al.</i> on the photocatalytic reduction of carbon dioxide to methane using Ni supported on silica-alumina, and quantify the energy conversion efficiency.</li> <li>iii. Design and validate new catalysts, including nanostructured metallic/semiconductor particles and surfaces (with DWI RWTH Aachen).</li> </ul>

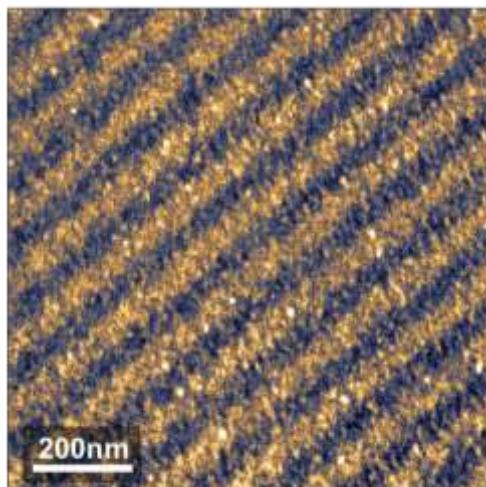
	<p>iv. Identify business opportunities, and perform technical and commercial evaluation for selected case (together with Holst Center). Where possible, further expand and strengthen the IP portfolio, and publish results in peer reviewed journals/scientific conferences.</p> <p>Involvement of other parties</p> <ul style="list-style-type: none"> <li>Partners in NWO project: Prof. Weckhuysen (Utrecht), Profs. Lohse/Zandvliet (Twente) and 3 Ph.D. students.</li> <li>Partners in Interreg project: amongst others Prof. Van De Sanden (FOM DIFFER), Dr. Buskens/Prof. Klankermayer (DWI RWTH Aachen).</li> <li>Holst Center for business development and nanotextured catalytic surfaces.</li> <li>Supervisory Board "Catalysis": amongst others BASF, Albemarle.</li> </ul>
Program dynamics	<p>Developments with respect to original plan:</p> <ul style="list-style-type: none"> <li>Study on Suzuki reaction progressed slower than expected, due to difficulties in producing the catalyst, stabilizing the catalyst in dispersion and accurately performing the kinetic studies required to quantify the contribution of the local heat generation and hot carrier generation to the chemical conversion. The issues related to the catalyst were solved in 2016, we are currently working on improving the procedure for the kinetic studies.</li> <li>Interreg EnOp facilitates combination of CO<sub>2</sub> chemistry and plasmon assisted conversions.</li> <li>Business development started 2016 in collaboration with Holst Center → subject in 3F roadmap as "seed". Currently, a list of potential business opportunities is studied in more detail (technical and commercial feasibility).</li> </ul> <p>Consequences of developments</p> <ul style="list-style-type: none"> <li>Expect to finish studying the Suzuki reaction in the course of 2017 → contribution of the local heat generation and hot carrier generation to the chemical conversion quantified, results applied to estimate the energy conversion efficiency of plasmon assisted reactions.</li> <li>Expect to demonstrate reduction of carbon dioxide to methane in TNO labs in 2017, incl. quantified energy conversion efficiency.</li> <li>Business opportunities expected to be ranked, most promising ones worked out in more detail end 2016/beginning 2017. First commercial players approach to participate in shared research program beginning 2017.</li> </ul>
<b>Project 3: ThermoChemical Storage</b>	
Goals	<p>The main use case we are aiming for, is the long term, compact, storage of heat, in which heat stored in summer can be used in winter.</p> <p>Several types of salt are potentially useful for this; they can store heat without loss in time. However all have a different combination of advantages and disadvantages, which have been inventoried in the previous years. One of the disadvantages is the stability of the salt crystals. Encapsulation techniques are being studied for the improvement of this stability, making it possible to use the salt for a longer period of time.</p> <p>Very accurate methods are required for characterisation, operating in vacuum, being able to add and distract small amounts of moisture, for a large number of cycles. Characterisation methods have been and are still in development.</p> <p>Our goals for 2017 are:</p> <ul style="list-style-type: none"> <li>Optimisation of the salt composites: <ul style="list-style-type: none"> <li>Synthesis of salt composites with optimum structure and form (based on</li> </ul> </li> </ul>

	<ul style="list-style-type: none"> <li>modelling) for optimal reaction kinetics</li> <li>o Minimizing the amount of stabilisation material</li> </ul> <ul style="list-style-type: none"> <li>• Develop and make a “mini-reactor” for measuring the realistic material performance, for example heat capacity, kinetics, of larger amount of composite in contact with heat exchangers (e.g. 100 gram).</li> <li>• Improve the model for prediction of the behaviour of salt composite in storage and release cycles.</li> <li>• Optional: Exploration of new salt-sorbent combinations</li> </ul> <p>Within this project we cooperate with TU/e and other partners from the EC project CREATE. An advisory board of representatives of the TU/e, University of Hamburg and EDF has been established for yearly feedback on our technical progress.</p>
Program dynamics	<p>As described in the original plan for this ERP program 2015-2018 “our ERP technology line primarily focuses on salt composites and aims to deliver an understanding on how the energy density and operational conditions of salt hydrates are influenced by confinement, i.e. due to composite structures through encapsulation, hybrid salts and impurities.” This is still our aim.</p> <p>The need to store (‘green’) energy is recognized widely in society, now even more than a few years ago. This is valid for electricity as well as for heat. Without storage capacity, green energy cannot be optimally utilized. This means that the development of storage techniques has become even more relevant since the initiation of this program.</p> <p>This field is still relatively new and requires a lot of research in order to fully understand the materials and the system, and the consequences of certain choices. Additional investments in equipment and personnel are essential to accelerate the required development.</p>
<b>Project 4: Self Organising Smart Energy Networks (SOSENS)</b>	
Goals	<p>The main use case we are aiming for is the use of flexibility from energy consumption and storage to cope with (1) changing renewable generation and (2) congestion in the electricity network. We advance the concept of Transactive Energy to create better energy management control systems to stabilize energy system dynamics by matching supply, demand and storage on a short timescale and on the micro (home, building, factory), meso (city, region) and macro (national/cross-border) levels.</p> <p>To realise this, we develop cooperative planning methods working on device, household and aggregate level that are able to participate in real-time markets in a cost-effective way. Further, we enable connection to the market for flexibility aggregator services based on the PowerMatcher technology and we acquire knowledge of aggregated flexibility characteristics.</p> <p>Evaluation methods to objectively compare the performance of smart grid coordination technologies are not well developed. Therefore, aims the project to define a number of benchmark simulation scenarios that can be used to compare smart grid coordination approaches unambiguously</p> <p>For 2017, we will further focus on the aggregation role which is currently emerging in</p>

	<p>the power sector. An aggregator bundles the flexibility capabilities of distributed generation, demand response and storage devices located in the distribution grid and operates the aggregate on the existing markets for electricity trade (futures, day-ahead, balancing). Additionally we investigate market models in which multiple aggregators operate and also interact with the active network operation by the distribution network operator (DSO).</p> <p>Within this project we cooperate with the DTU in Denmark and PNNL in the USA. An internal advisory board of a representative of TNO's Energy Theme and a principal scientist in the ICT field has been established for yearly feedback on our technical progress.</p>
Program dynamics	<p>The above is in line with the original planning at the start of the ERP. The need to perform energy management in the future smart grid is recognized widely in society. Our transactive energy approach is clearly gaining interest in the power sector, especially in North America. So, the further development of transactive energy methods and technologies has become even more relevant since the initiation of this program.</p> <p>With the Energy Theme organisation we are seeking to broaden the cooperation with PNNL, and start a cooperation with the National Renewable Energy Laboratory (NREL) in the USA. Further we aim to acquire an H2020 project with DTU, VITO and the University of Strathclyde.</p>

## 3D Nanomanufacturing Instruments

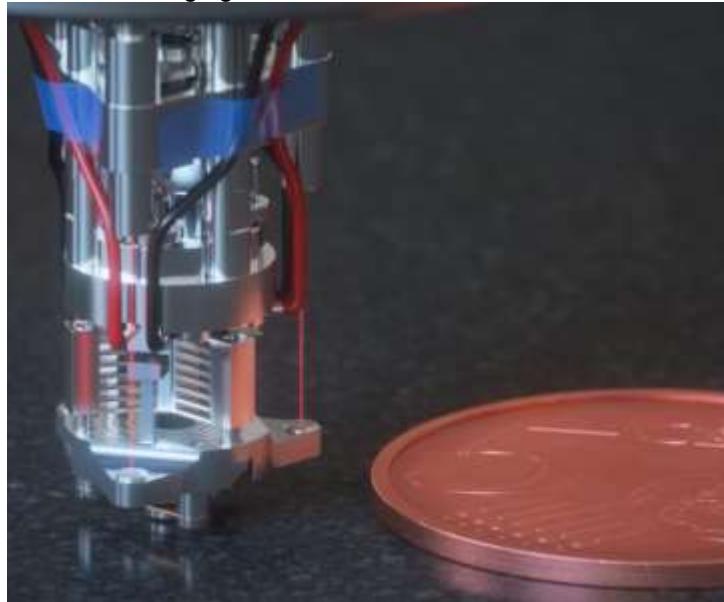
<b>General data</b>	
Title	3D Nanomanufacturing
'Topsectors'/Societal Themes	HTSM
Contact person TNO	Hamed Sadeghian, Nicole Nulkes
Contact person government	Michiel Ottolander (EZ)
<b>Program adjustment 2017</b>	
Abstract	<p>The program in 2017 to a large extent is the continuation of the goals according to the roadmap of the 3D nanomanufacturing program.</p> <p>In 2016 several key technologies have been developed, several collaborations with industrial and academic partners were established, within the context of the ERP Ecosystem. In 2017 the developed key technologies will be further enhanced towards proof of principles of the used-cases. The pillars of the program are Technology Platforms (TC), in which each of them consists of several research lines, all coherently contribute to required key technologies for 3D Nanomanufacturing.</p> <p><b>3D Nanomanufacturing</b></p> <p>In the first TC, so called 3D nanomanufacturing, with the target to make nanostructures, the developments are as follows:</p> <ul style="list-style-type: none"> <li>- In 2016 a collaboration (50%-50 % with industry) started to show the proof of principle of scanning thermal nanolithography. In 2017 the proof of principles of this technology will be demonstrated.</li> <li>- Following the collaboration with TU Delft ( in 2 PhD projects), within the ERP 3D nano on interactions at nano-scale and the application in nanomanufacturing, we started a collaboration with industry on the feasibility of manufacturing 10 nm contact holes (for future memory applications).</li> <li>- A collaboration is started with HTCS, TU/e (2 PhD projects, one financed via Impulse program TU/e) for developing technologies for nanomanufacturing and in-situ metrology with the use of self-assembled monolayers and Direct self-assembly.</li> </ul> <p><b>3D Nanotomography</b></p> <p>Within the second TC; 3D Nanotomography the targets are as follows:</p> <ul style="list-style-type: none"> <li>- Show the proof of principle of GigaHertz subsurface nanoimaging</li> <li>- Continue the collaboration with industry on the use of subsurface nanoimaging for metrology applications.</li> <li>- Showing the proof of principle of photo thermos-acoustic imaging for measuring buried structures, which are now common for below 10 nm node.</li> </ul> <p>Below shows one image proof of principle of subsurface nanoimaging of 50 nm periodic dense nanowires.</p>



**Figure 1: subsurface imaging of 50 nm periodic nanowires buried on a matrix.**

### **3D Optical Nano Metrology**

- A Collaboration with industry is expected on the topic high resolution optical nearfield imaging



**Figure 2: High resolution optical imaging concept with metainstrument.**

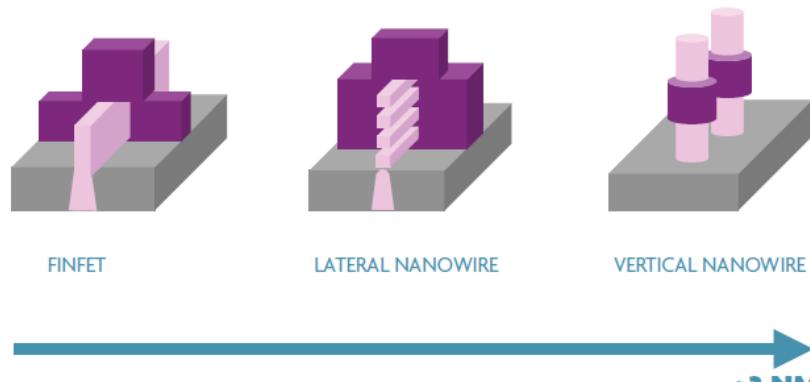
### **Advance Control and Mechatronics**

Within the TC Advance control and Mechatronics, the following targets are set:

- Feasibility study and experiment on miniaturized positioning and metrology platform, required for several metrology applications, in order to increase the specifications, i.e. accuracy, speed and stability.

These technology platforms, will contribute to the following applications;

- Critical dimension metrology for beyond 10 nm nodes
- Extracting LER (Line Edge Roughness) and LWR (Line Width Roughness) of nanowires FET transistors
- Alignment and overlay measurement , with the use of imaging through layers
- Manufacturing and overlay metrology of 10 nm contact holes

	<ul style="list-style-type: none"> <li>- Low cost per device or surface area, very high speed of measurement.</li> <li>- (The ability to flexibly manufacture and resolve 3D features below 10 nm with high aspect ratio.)</li> </ul>
Short description	<p>The market growth of semiconductor industry has a great impact on Dutch and European economy, but also on TNO as it includes the largest non-public account of TNO. Using strategic innovation, the Netherlands has been able to keep a competitive advantage in the development of equipment and instruments for nanometer-sized patterning, manufacturing and measurement. Examples include UV-light assisted patterning (ASML) and electron beam imaging (FEI).</p> <p>In order to sustain a competitive edge for the semiconductor industry, enhancing yields and reducing the cost and the time-to-market are essential. This has to be done while simultaneously maintaining reliable (nano-) manufacturing. The process geometries and device dimensions are shrinking to the level that conventional technologies currently used for production and quality control are approaching physical boundaries and will appear neither technologically nor economically feasible. Besides shrinking the critical dimensions even further, 3D scaling is anticipated to introduce new functionalities and to make optimum use of the available space, as shown by ASML in figure 1.</p>  <p>Figure 1 illustrates the transition of semiconductor devices from 2D towards 3D architectures with nanowires. The figure shows three stages of device evolution: FINFET, LATERAL NANOWIRE, and VERTICAL NANOWIRE. Each stage is represented by a 3D block diagram on a grey base. FINFET shows a 2D structure with a central pink vertical nanowire. LATERAL NANOWIRE shows a 3D structure with a central pink nanowire extending vertically. VERTICAL NANOWIRE shows a 3D structure with multiple pink nanowires extending vertically. A large blue arrow points to the right, labeled &lt; 3 NM, indicating the scale of the nanowires.</p> <p>Moreover, introduction of 3D architectures, such as nanowires requires a breakthrough in the manufacturing process potentially based on a hybrid 3D nano-manufacturing. Only using optical/electron subtractive technologies is not sufficient to manufacture the 3D nano architectures at the required scale. Classical optical equipment does not provide a resolution at the required feature size (less than half a wavelength), while electron microscopy (e-beam Litho and inspection) faces challenges of beam size, depth of field, feature resolution, throughput and true 3D information (both for manufacturing and inspection).</p> <p><u>Primary Use case:</u></p> <p>The primary application focus of this ERP will be on equipment and instruments for 3D “nanomanufacturing” and “nanometrology” of future 3D nano-electronics devices. The major requirements are (from ITRS):</p> <ul style="list-style-type: none"> <li>• Very high resolution and sensitivity to be able to detect 3D structures down to ~10 nm and high aspect ratio (20).</li> </ul>

- Very high speed of measurement on large area such as 100 cm<sup>2</sup> / hour.
- The ability to flexibly manufacture and resolve 3D features below 10 nm with high aspect ratio.
- Low cost per device or surface area.

Cross-over use cases:

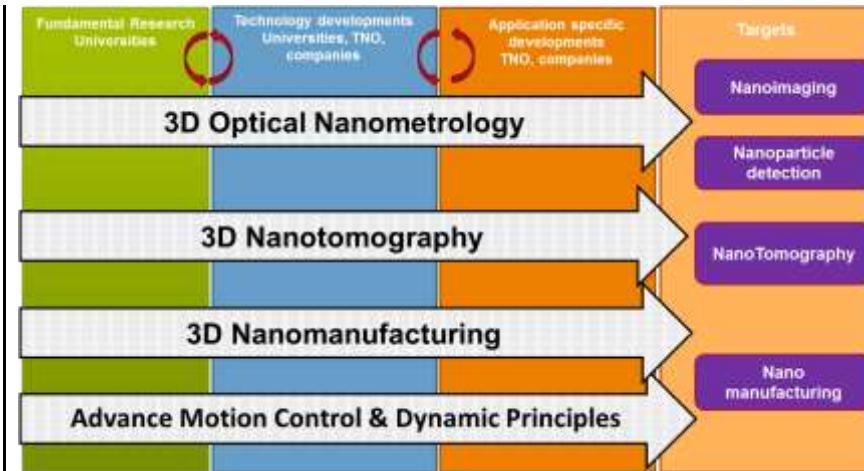
To achieve focus, a single primary use case has been selected that will guide the decisions during the research. However, the technologies developed for this primary application (3D nanomanufacturing for future 3D nanoelectronics architectures) are also very relevant for the application domains below:

- 1- Instrument for bio-medical and health-care: The developed knowledge in optics and photonics, nano-opto-mechatronics, control and microwave frequency can be to a large extend used in the domain of biological applications. For example ultra-high resolution microscopy and characterizations, either optical or AFM have been extensively used in bio applications. However, due to low technical readiness level, there are very little industrial applications and so far this field is limited to academic and research environment. TNO has shown the capability to bring these technologies closer to industrial applications. On the other hand, TNO has also a long track record in the field of medical, pharma and bio-chemical related applications. The combinations of the two cross-over expertises will pave the way towards developing next generation of instruments for the aforementioned bio applications. The target of this cross-over use case is to develop new instruments, where the core is based on nano-opto-mechanics for medical and biological applications. For simpler and more accurate detection, new tools for biological research at the single molecule and cellular level are needed. This gives insight into how a biological matter interact with their physical surrounding.
- 2- 3D nano-manufacturing and nano-metrology of printed large-area electronics and of photonics and photovoltaics devices. This is an important cross-over use case, as nanostructures are expected to strongly enhance light incoupling in solar cells and light outcoupling in lighting devices such as OLEDs. Manufacturing of novel batteries with enhanced performance thanks to 3D structuring at nanoscale.
- 3- Miniaturized electromagnetic/quantum mechanics systems for Defense and Space applications to improve the performances of complex measurement systems. The fabrication and the performance of metamaterials, as an enabling technology for radar applications, is also to a large extent related to the technologies which will be developed in this ERP. Free-form 3D manufacturing of metamaterials and inspecting the shape and performance in 3D is the key challenge for this cross-over application.

4-year Target:

Proof-of-concept of technologies for 3D nanomanufacturing and nano-metrology in experimental setups/hardware/built devices for the main applications mentioned above.

Goals	The goals of the program for 2017 is two folded: technical development goals and goals regarding enhancing the current business and knowledge ecosystem. Both technology and ecosystems are geared to each other as shown below.
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As it can be seen for lower technical readiness levels, collaborations with academic and other research institute will be enhanced, and for higher TRL developments, involvement of industrial consortia is further increased.

### 3D Optical Nanometrology

For technology platform 3D Optical Nanometrology, the following goals are targeted:

- Proof of principles of high resolution optical nearfield imaging using Solid Immersion Lens. For this a collaboration with industry will be expected to start in 2017. A PhD collaboration with HTSC in TU/e on the topic of X-ray metrology (financed by Impulse program of TU/e) will be started.
- A European collaboration between university of Jena, EPFL and TNO will be started, in the framework of PhD research's (spend considerable time at TNO). The name of the project is NOLOSS and the topic is nanostructures holographic imaging.
- A feasibility study on the technology of Through Focus Microscope will be executed.

### 3D Nanotomography

#### Sub Surface Nano Imaging

For the technology platform 3D Nanotomography we will continue our work on sub surface nano imaging in the direction we are already heading. The following goals are targeted:

- First, we will continue to work on our understanding of the contrast mechanisms (both viscoelasticity and scattering), and the dependency of those contrast mechanisms on excitation frequency. This will be realized by extensive modeling, simulation and experimentation using the calibrated test samples developed as part of the program. This understanding will in the end lead to the ability to systematic characterization and quantitative measurement of sub surface features.
- We will continue our work on the non-resonant sub surface nano-imaging by proving the feasibility and added value of this method in an experimental setting.

#### New Sub surface imaging techniques

We explore new sub surface nano imaging techniques which can face the challenges we encountered.

	<ul style="list-style-type: none"> <li>- <u>Photo Thermal Actuation (PTA)</u>, excites the cantilever by a modulating laser beam. We do a feasibility study. If this is successful we show the principle by means of a simple experimental setup.</li> <li>- <u>Photo-Thermo-Acoustic Imaging (PTAI)</u>, We show the proof of principle by means of experiments on a an experimental setup.</li> </ul> <p><b>Advanced Control and Dynamics</b> On the topic of advance control and mechatronics, the proof of principle of one miniature positioning platform and metrology will be shown.</p> <p>Collaborations and Ecosystem for 3D Nanotomography we will collaborate with industry and TU/e For the technology platform 3D Nanomanufacturing, collaboration with industry will be continued. The research project with industry on manufacturing contact holes will go to the next level and a PhD collaboration with TU/e HTSC on the topic of nano-scale manufacturing will be conducted. Further feasibility study of STED (Stimulated Emission Depletion) nanomanufacturing and 2 photon lithography will be done.</p>
Program dynamics	<p>The research topic of Metamaterials will be to a large extent re-oriented. It has been concluded that the super oscillatory concept cannot surpass the resolution of 100 nm, which is not sufficient for Nano inspection. The concept of hyper lens will not actively been pursued, and only via the ongoing PhD collaborations with TU Delft (financed by TUD).</p> <p>The Nanoantennas imaging will be done via collaboration with AMOLF and not at TNO, since they are more experienced in this topic. Instead we will focus on development of Xray nanometrology which has shown to be promising for sub-10 nm imaging.</p>

## 6 Structural Integrity

General data	
Title	Structural Integrity
'Topsectors'/Societal Themes	Energy, HTSM
Contact person TNO	Henk Miedema
Contact person government	Michiel Ottolander (EZ)
Program adjustment 2017	
Abstract	<p>Early Research Program (ERP) Structural Integrity 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 that the use and maintenance of a structure can be optimized by knowing the exact state of a structure and being able to predict its state (Condition-Based Maintenance, CBM).</p> <p>ERP SI has chosen to work use case driven, and 4 use cases are tackled simultaneously:</p>  <ol style="list-style-type: none"> <li>1. Concrete bridges (corrosion of steel rebar)</li> <li>2. Offshore wind</li> <li>3. Well Integrity for Abandonment of oil and gas wells</li> <li>4. Composite Vehicles (lightweight vehicles for Defence)</li> </ol> <p>Knowing the exact state and predicting the future state of a structure requires advanced models and state of the art sensing technologies. Both are being developed in ERP SI for each use case. In addition to further development of sensing (fiber optics, ultrasonic technologies, sensor data fusion) and models (loads, local degradation, structural safety), an important goal for 2017 is to develop field labs, so that demonstrations of the technology can be given and the potential of the developments in this ERP for CBM and can be made visible to a larger audience. This makes 2017 a very exiting year, with the first demonstrations while still developing technology.</p>
Short description	<p>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, maximizing the “up-time” of the structures and allowing utilisation in a different way than a structure was originally designed for.</p> <p>The multi-disciplinary and challenging nature of the problem, its current embryonic state 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:</p> <p><i>“detection and monitoring of (precursors of) degradation inside steel/cement/concrete structures”</i></p> <p>and use this information for</p> <p><i>“diagnosis of their structural health and forecast the service life for various intervention options”</i></p> <p>The program will have wide application for maintenance of macro-structures, in</p>

particular in the *transportation infrastructure* and the *energy production infrastructure*. In addition it will be the basis for improved design of macro-structures.

The technology developed in the program is directed at the following four use cases

1. Concrete (rail)road supporting structure (reinforced concrete bridge) integrity
2. Offshore wind structure integrity
3. Well integrity for sustainable energy supply
4. Vehicle protection and integrity

It is important that the sensing and inspection technology as well as the models for structural integrity are developed in this single program. The output of sensing and inspection is input for modelling and vice versa modelling defines the parameters to be observed. Hence, the input data that models require and the information that sensing and inspection can provide must match.

Advanced acoustic sensing, fibre optic sensing, (multi) sensor systems and sensor system design and corresponding modelling tools (incl. interpretation methods and handling procedures) will be developed for monitoring loads, resistance and time dependent degradation in four use cases.

#### Issue 1: "Advanced sensing and inspection technology"

Goals	<p>The sensing development concentrates on acoustics &amp; ultrasound, fiber optics and multi sensor fusion. The plans are depicted in the figures below.</p> <p><b>Sensors 1 Acoustic/ultrasound</b></p> <ul style="list-style-type: none"> <li><b>Delphi processing</b> Imaging layered structures (using all multiple reflections)</li> <li><b>Tomography</b> Monitor concepts for cracks and stiffness properties</li> <li><b>Topography</b> Modeling cracks, fractures &amp; pits</li> <li><b>Active acoustics</b> Stiffness properties &amp; Number &amp; size of cracks</li> <li><b>Passive acoustics</b> large area Crack detection</li> </ul> <p>2015: 2D Modelling Of layered structures</p> <p>2016: 2D Inversion For imaging</p> <p>2017: 3D Modelling &amp; Inversion Imaging layered structures</p>
	<p><b>Sensors 2 Fiber optics</b></p> <ul style="list-style-type: none"> <li><b>Special FBG sensor</b> <ul style="list-style-type: none"> <li>Chemical Sensing</li> <li>Strain sensing fiber</li> <li>Embedded FBG in composite</li> </ul> </li> <li><b>High speed &amp; performance</b> <ul style="list-style-type: none"> <li>Large number of sensors</li> <li>DAS / E-DAS</li> <li>Special multiplexing scheme for strain sensor array (FBG / fiber laser)</li> </ul> </li> <li><b>Fiber Interferometer</b> <ul style="list-style-type: none"> <li>High speed Strain sensing for blast Test composite (1D) (fiber in contact)</li> <li>High speed Proof of Concept (3D) (non contact)</li> </ul> </li> </ul> <p>2015: Chemical Sensing</p> <p>2016: % level DCS1.0, PPM level DCS2.0, Heating FBG leak flow, Embedded FBG in composite, Full fiber Strain in composite</p> <p>2017: Full fiber Chemical sensing, DAS / E-DAS, Special multiplexing scheme for strain sensor array (FBG / fiber laser)</p>

	<p>For the topics within Acoustic / Ultrasound sensing the end goals are:</p> <ul style="list-style-type: none"> <li>- Delphi Modeling; Improved logging performance of acoustic/ultrasound tools using the Full Wavefield Model (FWMod) for a multi-layer well. It is aimed for to size multiple defects in 3D in the order of 1 cm within a radius of 1 meter of a multi-layer well;</li> <li>- Tomography to derive stiffness properties and number and size of cracks in a concrete slab or bar (coverage area is a few meter)</li> </ul> <p>For the three research topics within Fiber Optics the end goals are:</p> <ul style="list-style-type: none"> <li>- Special FBG sensor; Ability to detect small leakage rates in a well by either detecting the actual flow rate or the change in environmental condition due to the leakage;</li> <li>- Special FBG sensor; Strain sensing in composite material.</li> </ul> <p><i>Note: It is aimed for to demonstrate the two objectives above using the full fiber, so without the need for having FBG's in a fiber (fully distributed versus multi-drop).</i></p> <ul style="list-style-type: none"> <li>- High speed and performance; Provide strain monitoring within a composite plate during impact to validate the advanced models used;</li> <li>- Fiber interferometer; Non-contact ultrasound measurements for inspection purposes to localize &amp; characterize damage.</li> </ul> <p>For the two research topics within MSDF the end goals are:</p> <ul style="list-style-type: none"> <li>- Multi-sensor node for rebar corrosion; ability to detect corrosion rate- and condition properties on existing structures with post-installed sensor node;</li> <li>- Monitoring system for corrosion probability &amp; rate; Provide multi-sensor data-fusion algorithm to measure probability and speed of corrosion of steel bars in concrete.</li> </ul>
Program dynamics	<p>The work on topography using Finite Difference method was stopped. It was aimed for to model small pits and cracks at the surface using 3D Finite Difference code. A so called topography grid was implemented but it turned out that it was too time consuming to implement. The code currently is used for 2D.</p>
<b>Issue 2: “(Multi-scale, multi-physics, probabilistic) models”</b>	
Goals	<p>Goals for modelling are formulated for each of the four use cases.</p> <p><b>Concrete bridge</b></p>

- Proof-of-concept of the baseline assessment approach
  - o Implementation and application of the random field model for corrosion, constitutive models for damaged concrete and bond of corroded reinforcement to full-scale case studies
  - o Verification and validation of FEM stochastic input generation tool concept in full-scale case studies
  - o Implementation and application of SFEM and DARS simulation tools in full-scale case studies
  - o Further development of FEM model updating and reliability assessment method aided by in-situ load testing
  - o Frameworks of uncertainty reduction in stochastic input for FEM based on in-situ US testing (incl. methods for assimilation of acoustic tomography data)
- Proof-of-concept of service life prediction
  - o Extension and validation of propagation model for pitting corrosion and concept of model assimilation in service life prediction tools

#### Offshore wind structure:

- Base modules for the Optimal State Estimator.
- Development of the core of the probabilistic model for the Multi Asset Correlation Tool (MACT) for multiple assets based on assumed parameters
- Framework for the prediction of the growth of corrosion fatigue cracks.
- Multimode fracture framework for the determination of the critical crack length.

#### Well Integrity:

- risk assessment model for leakage probability
- Integration of the risk assessment in a Bayesian Belief Network (BBN) which takes advantage of quantitative as well as qualitative data for optimal prediction
- Demonstration case. A demonstration case that illustrates the workflow with coupled geochemical/geomechanical modelling, Monte Carlo simulations, data assimilation and risk assessment for an existing well. A CO<sub>2</sub>-injection well has been selected for this purpose.
- Extension of risk assessment model from wellbore to field/basin scale; performing Monte Carlo scenario simulations to evaluate varying geochemical/geomechanical conditions, as applicable to the Dutch subsurface.

#### Composite vehicle:

- In close collaboration with the industry, the further development of innovative TNO composite plate solution. Optimization based on possible production techniques and reduction of costs suited for a demonstrator in 2018.
- The experimental capability for instrumented dynamic testing at component and material level supported by advanced computational models dedicated to these set-ups and composite materials and additional fiber optic recording options

Given the common overall objective of developing methods and tools of ERP Structural Integrity, which is to obtain the maximum value of information for the problem at hand, generic goals for modeling are formulated as well:

- Measurement uncertainty and uncertainty propagation analysis: An uncertainty quantification is of interest to understand how the uncertainties on the measured parameters affect the assessment of structural performance. For that a generic model/framework needs to be developed that fits multiple Use Cases. Each Use Case can subsequently adapt the model to its specific needs.
- Several standalone models are under development in the Use Case Offshore Wind and Concrete Bridge. The current level of development allows developing a plan on how the models can be linked and what data has to be stored and exported. In order

	<p>to bring a product or service to the market the ERP will provide evidence to stakeholders that these models can be coupled, integrated in their operation and provide answers to their questions.</p>
Program dynamics	<ul style="list-style-type: none"> <li>- Increased focus on demonstration cases for all applications</li> <li>- Development of framework for FEM model updating for use case Bridge moved from 2017 to 2016 in order to enable implementation of US (Acoustic tomography) measuring method for reliability assessment in 2017</li> <li>- Data assimilation moved from 2016 to 2017 for use case Bridge and Well Integrity. This is due to preparation time needed for the experimental part of demonstration case.</li> <li>- Stopped work on the original idea for a Non-destructive fracture testing method. This experimental method was tested at the TU Delft Materials Sciences laboratory. While the experiment did not show the desired failure mode, the concept behind it opened up further concepts. Several new ideas have been identified based on the same theory that are much more promising, and they are currently being evaluated for possible joint industry projects.</li> </ul>
<b>Issue 3: “Building the ecosystem”</b>	
Goals	<p>An important aspect of creating the ecosystem is bringing together the value chain from industry with academia and RTOs. From the scientific network partners the most important peers are involved: TU Delft; ECN; Bundesanstalt für Materialforschung und –prüfung (BAM); University of Kyoto, <i>fib</i> (International Federation for Structural Concrete); DIANA , University Gent.</p> <p>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. TNO initiated several applied and scientific projects with involvement of industrial partners across the supply chain and in collaboration with research institutes</p> <p>For the use case Concrete Bridge we aim at a demonstrator setup similar to the earlier one for steel bridges (Van Brienenoord bridge). Currently we are in contact with two major cities (Rotterdam and Amsterdam), to discuss the options. In addition to such a field lab in the Netherlands., we are exploring the possibilities in Germany with BAM/BASt and in South Korea with KICT.</p> <p>For the use case Offshore Wind we aim to have as a minimum of one windfarm as demonstrator for tools developed in the ERP. Several new national and international initiatives leverage on developments in the ERP SI related to monitoring strategies (DemoWind, Monitor-2) and multi-physics models (Material Transition Program). Discussions with Offshore wind service providers are ongoing on how to incorporate the developed components into their services.</p> <p>For the use case Well Integrity we are in contact with ITF and several individual companies in the oil and gas industry. Attendance of SPE workshops is foreseen in order to discuss our state of the art risk assessment with relevant industry. A strong link with the national program “Mijnbouw effecten” (“Mining effects”) is present and to be elaborated in 2017.</p> <p>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</p>

	applications and aims at a full scale demonstrator product.
Program dynamics	In 2017 several changes will be taking place in the program. Some of these are related to new insights, others are due to the acceleration of the program. The first demonstrations have been moved to 2017 in order to make the potential of CBM and the developments in ERP SI visible to a larger audience. This makes 2017 a very exiting year, since we are creating demonstrations while still developing technology. In 2017 further steps towards a long term program Macro Structures Research (MASTRE) will be made.

## 7 Human Enhancement

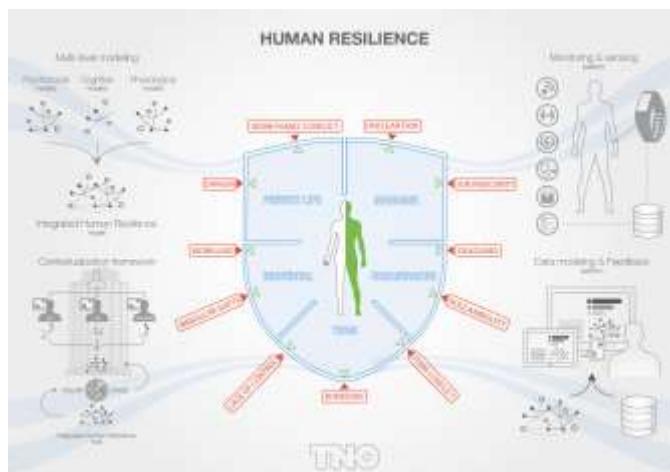
General data	
Title	Human Enhancement
'Topsectors'/Societal Themes	LSH, HTSM
Contact person TNO	Michael Holewijn, Mark Neerincx
Contact person government	Michiel Ottolander (EZ)
Program adjustment 2017	
Abstract	<p><b>Research Line Adaptive Automation</b></p> <p>In the mobility sector, driver support and automation of driver tasks (up to highly automated driving) is a major trend. It was first introduced by active safety functions like Automatic Braking Systems (ABS) or Electronic Stability Program (ESP), but it will for sure lead to fully automated driving. The role of the driver in this transition is clearly changing from being in full control towards having a supervisory role over automated processes. The consequences for the driver in his changing task are substantial: the boundaries of his operational tasks are becoming unclear, his attentiveness towards his operational responsibility might reduce as the vehicle takes over, while he still has the responsibility and is the safeguard of the system. This may result in the driver being out of the loop and confronted with automation surprises.</p> <p>The Maritime &amp; Offshore sector is challenged to operate in increasingly harsh conditions, such as deeper water, colder weather, and higher waves. Many, surface and deeper sea-based, operations require precise and complex maneuvering and ROV (remote operated vehicle) based tasks. Optimized human-machine interaction is crucial for safe and efficient operations. The next generation of adaptive automation is a huge opportunity for cost-effective and safe operations and also for the competitive position of our industry. Support for minimizing risks in complex operations with potentially catastrophic effects on the environment (fragile areas like Deep Sea and Arctic) are also of societal importance.</p> <p>The challenges in both domains as described above, require a next step in the knowledge and system development for <i>adaptive automation</i> of scheduling, supervision, control and modification of complex tasks. Our ambition is to develop smarter automation, by shifting tasks between humans and machines dynamically, depending on environmental factors, operator state, and system performance. The goal of this automation should be to help humans in their work, by adjusting the automation of maneuvering and control tasks (e.g. car driving and ship maneuvering) in an adaptive manner.</p>  <p>The conceptual diagram illustrates the 'Observability' of three interconnected components: Operator, System, and Environment. The Operator is aware of the system state, which includes fatigue, loss of attention, work overload, and task demands. The System is aware of the operator state, such as performance, fuel resources, and pressure. The Environment is aware of the system state, listing seabed, waves, currents, and weather conditions. A central circle labeled 'Observability' represents the dynamic interaction and information exchange between these entities.</p>

## Research Line Human Resilience

The research line Human Resilience focuses on the development of knowledge concerning how employee resilience can be supported using (wearable) technology. Knowledge developments relate to:

- predictive modelling, integrating psychological, physiological, and social factors to provide users with relevant feedback to improve well-being, performance, and motivation;
- measurement of relevant resilience factors with wearable technology in a user-friendly and valid manner;
- individual and organisational use of resilience data (personalization of feedback and aggregation for use by different organisational aspect systems)

In 2017, the project will collaborate with the Dutch Police in a field lab in which police employees will use during regular work hours, the prototype of a wearable resilience application developed to measure and provide feedback about relevant resilience factors. The data and insights gained from the field lab with the Dutch Police will result in an integrative predictive modelling approach for resilience in organisations, a monitoring and feedback platform for personalized resilience support, and organizational dashboards for monitoring and interventions.



Short description	<p>We are currently facing an increasing level of automation of systems in e.g. the industrial (maritime and offshore) sector but also in the mobility sector (automated driving). It is broadly accepted that the behaviour and interaction of users with these systems is the key to successful innovation and that the system behaviours should be well-adapted to these users. The challenge is to establish, effective and resilient, joint human-automation behaviour patterns. That is, we need further breakthroughs in our knowledge to be able to develop the next generation of adaptive systems for safe and efficient operation. New validated and transparent (human-in-the-loop) automation modules are required.</p> <p>The first research ambition of this Early Research Program (ERP) Human Enhancement is to develop a transparent (human-in-the-loop) adaptive automation platform that substantially improves safety for manoeuvring and control tasks, based on a computational human model to assess current and predicted human state (i.e., situation awareness and task load). This will be the focus of the use case Adaptive Automation for the automotive and maritime domain. The following main research questions will be addressed:</p> <ul style="list-style-type: none"> <li>• How can a human state estimator be extended with real-time human state prediction</li> </ul>
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	<p>(for near and future predictions in time) and how can its concepts be formalized in a reusable and extendable ontology?</p> <ul style="list-style-type: none"> <li>• Which layered set of algorithms can (1) map unobtrusive measurements and human input into a model of the problem space, and (2) support the required resultant model-based decision-making processes with high level of accuracy?</li> <li>• What are the specifications for a modular, layered and extendable architecture that uses multiple data sources to estimate and predict the required level of automation and transition of the supervisory control task, and that automatically handles multiple situations in order to be able to function on multiple use cases and scenarios?</li> </ul> <p>The second research ambition of the Early Research Program (ERP) Human Enhancement will be the development of a multidimensional prospective model for human resilience and related monitoring instruments and organizational interventions. At present, almost half of all work disability is related to psychosocial factors, which is a rise from 30% since 1998. Front runner companies realize that an increase of human resilience and intrapreneurship are prerequisites for improvements in human health and organizational performance. However, adequate resilience tools and interventions are lacking, resulting in large personnel and organizational costs. This means that measures to improve resilience are not only important for maintaining health and operational performance, but will also result in potential large financial savings. Although the importance of supporting employee's resilience is widely accepted, an integrated theory is still lacking, mainly due to the large amount of factors determining human resilience. In order to develop an integrated model of human resilience the research will be structured around the three activities:</p> <ul style="list-style-type: none"> <li>• For the modelling platform, a multi-factor and multi-level human resilience risk profile be developed, integrating psychosocial and physiological factors that drive resilience development and a tool to calibrate and validate the model for specific (team, and organisational) contexts or use cases will be developed.</li> <li>• For the sensing and monitoring platform, the identified factors in the model and the key environmental moderators will be operationalized so that it can be used to conduct semi-continuous automated data-collection that is minimally intrusive for the individual.</li> <li>• For the data modelling and feedback (=coaching) platform, a research infrastructure will be developed consisting of a data management and modelling environment that can produce contextualized and personalized output about the status of resilience development. In addition, the data management and modelling platform will include a user-friendly context sensitive feedback system that can provide individuals with personalized feedback.</li> </ul>
Goals	<p><b>Adaptive automation</b></p> <p>In 2017, we will determine what signals are most effective to get the driver ready to take over in a situation that the truck cannot control. These new tests will be preceded by a literature study for selecting the most promising signals (visual, auditory, etc.), and results from the experiments of the Marie-Curie project Human Factors in Automated Driving will be used to update the concept. Also a first idea for testing in 2017 in the real truck platooning concept (with professional drivers who know the system) to get some hands-on experience in real driving.</p> <p>Within the use case Personalized Adaptive Cruise Control (P-ACC), we will perform larger and longer tests under various traffic conditions under more naturalistic driving conditions (more people and more different traffic conditions) or even interpersonal</p>

variations (e.g. fatigue after long drive). Once the capability of the P-ACC is shown, other effects like weather conditions (e.g. level of rain, fog, slippery roads) can be added in projects for customers. Another long-term goal would be to link this to possibilities for adaptive automated driving (including lateral control and including driver state). In this, adaptive settings for different traffic situations also need to be taken into account. We need to make the automation adaptive to the traffic conditions as well, avoiding that the driver will continuously need to change the settings.

Involvement differs for the different application domains. In private mobility: involvement of industrial stakeholders (OEMs and suppliers) for adaptive ADAS. Approach is to develop an open source demonstrator (specific application) in 2016 and invite OEMs and suppliers to join for next step in development (OEM specific solution) in the years after.

For commercial transport: approach of virtual tow bar is a multi-OEM solution, starting with a single OEM (DAF in 2014). OEMs are interested in driver vs automated driving behaviour, transition of control is a key topic that is addressed in the project. I&M wants to use the project for developing a legal framework for admission of automated (test) vehicles on public roads. The role, capabilities, responsibilities (behaviour) of the driver will play an important role.

In the maritime domain, for 2017 the intention is to build up a new use case based on DP tracking. The build-up of the use case will contain a domain description and an analysis in terms of use case scenarios, type of accidents and operational failures and risk description, level and frequency of operator involvement, business case effects (efficiency, manning, safety, down time, production loss, technical failures, human failure etc.). Furthermore it will entail to seek collaboration with market stakeholders, hence ship-operators in this domain. The end product of this work package will be: a domain description, contracted involvement of one or more operational stakeholders, a description of the kind of operator support to work on in 2017.

To accelerate adaptive automation solutions, collaboration is needed. TNO will stimulate and participate strongly the co-operation with public and industrial stakeholders. The OIL majors and energy companies with development of sustainable energy solutions are also looking into reliable and (risk based) predictable operations by the contractors. We will maintain and extend our contacts with Bluewater, RH Marine and STC. Additional effort will be done in relation to the MKC and Maritime Council to support this initiative by joining hands together. Marin has a strong position on several JIP's and simulations in this domain. The Dutch industry plays a quite unique role in these offshore operations. Also Dutch universities develop knowledge on this domain.

### **Human resilience**

In 2017 the research line Human Resilience will finalize the first data trial and conduct a second data trial with the Dutch Police. In these trials, 35 Police employees will use a prototype of a wearable resilience application for a number of weeks, both during working hours and outside of working hours. The application measures relevant resilience factors, both psychologically and physiologically, which is used in feedback to the user. Informed by these trials, the modelling approaches and the monitoring and feedback platforms will be further developed. This will result in:

- A modelling approach capable of integrating trait and state level psychological and physiological measures for resilience predictions at population level
- Algorithms for personalized and predictive feedback, based on individual level modelling

	<ul style="list-style-type: none"><li>– A feedback platform for individual level personalized feedback, and organizational level tailored feedback for different aspect systems including an organizational intervention framework</li><li>– An enhanced prototype of the mobile employee resilience monitoring suite</li><li>– A validated resilience knowledge management tool for analysis and visualization</li></ul> <p>The research line will closely collaborate with the Dutch Police (National team Veilig en Gezond Werken and unit Oost-Brabant) in field trials delivering data for the TNO research and insights for the Police concerning possibilities to support and enhance the employability of their personnel. Continuation of the collaboration with NOC-NSF is expected, based on the field labs that took place in 2016 with the national Korfbal team.</p> <p>Furthermore, the research line will collaborate with Hanze University of Applied Sciences and the University Medical Center Groningen (UMCG) in a joint PhD project concerning predictive modelling for mobile resilience applications. Collaboration with the Vrije Universiteit (Amsterdam), department of Social Psychology, surrounding the topic of emergence of resilience in teams, is also expected to be continued through student internships and bachelor/ master theses.</p>
Program dynamics	With regard to the original plan, our ambitions will be downsized to some extent, due to the acceleration of the program from four to three years, as well as the inclusion of a third use case in 2017, namely Adaptive Cyber Threat Analysis Automation. This additional use case will result in less budget for the Maritime and Automotive use cases that therefore will have to focus more. In 2016, we will carry out an exploration on the most promising research topics in the Cyber use case. The implications for the program in 2017 are not known yet, but promising venues for research include: smart visualizations to support cyber teams; supporting distributed situation awareness in cyber teams; enhancing team resilience to dynamic threats.



## 8 Making Sense of Big Data

General data	
Title	Making Sense of Big Data
'Topsectors'/Societal Themes	HTSM, LST, Agro, Logistics
Contact person TNO	Wessel Kraaij, Judith Dijk
Contact person government	Michiel Ottolander (EZ)
Program adjustment 2017	
Abstract	<p>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.</p> <p>In the first two years(2015-2016), this ERP explored the complete big data value chain, including data governance, analysis and distribution. A natural next step in the ERP roadmap is to intensify research on a small list of topics that are crucial to safely unlock the wealth hidden in big data and show the potential to lead to a distinctive technology position for an ecosystem of TNO, knowledge partners and stakeholders. In consultation with the external advisory board, three specific topics have been selected. The program focus will also be enhanced by putting more emphasis on talent development and allocating a smaller number of high potential researchers with a large time contribution. The three topics are: Uncertainty, Multi-stakeholder collaboration and Information Centric Networking.</p> <p>The technology line <b>Uncertainty</b> has as focus to tackle <b>real-world challenges</b> in big data where multiple, unstructured, relatively "ambiguous" (belonging to different domains or contexts) datasets are used. This means identifying and quantifying sources of uncertainty and dealing with uncertain results, for example by an interactive visualization. The ambition of this technology line is to achieve excellence at applying academic state-of-the-art tools and methods for descriptive annotation and predictive modeling of large scale heterogeneous real world (noisy, incomplete, ambiguous) data, –tools that are generally developed on constrained, controlled and clean datasets.</p> <p>The technology line <b>Multi-stakeholder collaboration</b> has as focus on multi-stakeholder aspects in big data innovations. Lack of technical safeguards, fear of disclosing sensitive data and increasingly tight EU regulation regarding handling personal data are a barrier to big data innovations that depend on the combination of data collections from different stakeholders. The ambition of this technology line is to develop governance principles and technology supporting a multi-stakeholder big data innovation, with an architecture for data combination that enforces data protection compliant handling of personal data and providing safeguards to prevent misuse of the data.</p> <p><b>Information Centric Networking</b> is an alternative networking paradigm for the internet. The goal of ICN is to transform the current IP-based internet from a network based on addressing devices to a network based on addressing data itself, independent of the location of this data. With ICN the fundamental nature of the internet will change</p>

radically. The center of gravity of the ICN research is currently the US and Asia. Our ambition is to position TNO as the ICN research center in Europe, and to collaborate with international partners on the future of the internet.

Within the ERP Making Sense of Big Data strong collaboration with various partners outside TNO is key. One of the goals of the ERP is to strengthen these collaboration and to build a national and international ecosystem.

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 perform experiments with the developed knowledge in use cases in the domains of Logistics & Mobility, Personalized Health and Security.

Short description	<p>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. In 2017 we will focus on three Big Data challenges:</p> <ul style="list-style-type: none"> <li>- Uncertainty</li> <li>- Multi-stakeholder collaboration</li> <li>- Information Centric Networking</li> </ul> <p>The relation between the topics of the ERP in 2016 and 2017 is shown in the figure below. The 2016 topics are given in the orange blocks, the 2017 topics in the blue blocks.</p> <p>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 &amp; Mobility, Personalized Health and Security.</p>
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#### Issue 1: “**Uncertainty**”

Goals	<p>Information extracted from imperfect and incomplete heterogeneous big data can lead to actionable insights only if the reliability of the information is also determined in the right operational context and communicated in an operational-friendly way.</p> <p>The technology line <b>Uncertainty</b> has as focus to tackle <i>real-world challenges</i> in big</p>
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	<p>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. Typical research question are:</p> <ul style="list-style-type: none"> <li>- How can models be transparent for all the uncertainties introduced?</li> <li>- How can we make absolutely clear where our confidence for a particular result stems (or not) from?</li> <li>- How can we deal with reliability, validity and ambiguity questions, with the integration of datasets from different contexts?</li> <li>- How can “predictions with uncertainty” be translated into impact for the user’s situation</li> </ul> <p>The ambition of this technology line 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.</p>
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#### Issue 2: “*Multi-stakeholder collaboration*”

Goals	<p>The technology line <b><i>Multi-stakeholder Collaboration</i></b> focusses at aspects in big data innovations where multiple parties, probably from different domains, want to collaborate. In these situations, data, processing and storage are usually distributed, while they may be shared under certain conditions. Issues will arise on topics like data availability, data quality, interoperability, security, and auditability. Adequate data governance processes need to be defined and implemented to tackle these, and new IT knowledge and tooling is needed for this.</p> <p>In this work package, two issues are addressed:</p> <p><b><i>Ownership respecting data analysis:</i></b> enabling the analyses of datasets owned by different stakeholders especially when there are restrictions on the usage of the data. Sub topics are:</p> <ul style="list-style-type: none"> <li>– Technical solutions for purpose limitation: restricting data usage to specific conditions</li> <li>– Architectural solutions for analysis of multiple datasets that are not allowed to be processed outside specific locations.</li> </ul> <p><b><i>Design for auditability:</i></b> enabling the analysis of the data collection, storage and processing in order to assure that the data is / was handled according to legal and business restrictions. Sub topics are:</p> <ul style="list-style-type: none"> <li>– Design patterns for data (collecting, processing) ecosystems that enable trace back of analysis steps and data sources</li> <li>– Trustworthiness: methods to assess how adequate input data is (including its provenance) to ensure usefulness for the end user.</li> </ul> <p>The ambition of this technology line is to develop the methods and tools for ICT applications on this domain. The developed methods and tools need to be further developed in subsequent projects, e.g. TKI, Horizon 2020 or B2B projects.</p>
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#### Issue 3: “*Information Centric Networking*”

Goals	<p>Information Centric Networking is an alternative networking paradigm for the internet. The goal of ICN is to transform the current IP-based internet from a network based on addressing devices to a network based on addressing data itself, independent of the location of this data. With ICN the fundamental nature of the internet will change radically. This paradigm shift will not only provide large efficiency and scalability gains for the data transport, but also fundamental advantages for security and privacy challenges.</p>
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In the technology line **ICN** we study three topics:

- Data naming: basis of ICN is naming of the data, both its semantics and its syntax. Developing a flexible framework for different domains is a key element of ICN.
- Data muling: transport and storage of data on behalf of other entities without the local notion of the type, origin or purpose of the data. One of the benefits of ICN is that it can be used across heterogeneous network boundaries, whether IP-based or not. This makes it particularly suitable for the Internet of Things.
- Combination of software defined networks (SDN) and ICN. SDN can be used for implementation of ICN and for transforming the current IP based internet into a hybrid IP/ICN based network.

Results of these topics can be successfully applied in future applications even without the global implementation of ICN. This balances the long term and short term possibilities of the research.

The center of gravity of the ICN research is currently the US and Asia. Our ambition is to position TNO as the ICN research center in Europe, and to collaborate with international partners on the future of internet.

#### Issue 4: “**Collaboration, use cases and Ecosystem**”

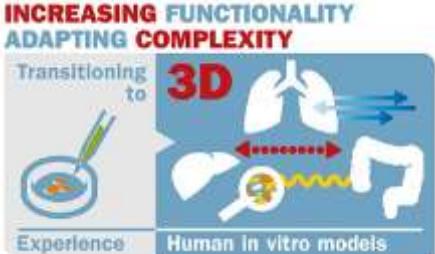
Goals	<p>The knowledge and tools developed within the ERP are tested, validated and applied to use cases in the domains of Logistics &amp; Mobility, Personalized Health and Security.</p> <p>The goal of the <b>Logistics and Mobility use case</b> is to optimize transport of both goods and persons. For logistics we focus on improving the Estimated Arrival Times (ETA's) for sea ships heading for a terminal, from last port of departure. This insight will also enable a better division over different modalities for this transport, in other words using more inland ships and trains and less trucks. The Mobility part focusses on the transport on the public roads, where large traffic jams are predicted, and prevented.</p> <p>The goal of the <b>Personalized Health</b> use case is to develop new methods for health-related decision support that are personalized (precision medicine) using <i>predictive</i> modeling relying on big personal health data, improving treatment effectiveness by a large margin. More importantly, cost will decrease due to an increased focus on prevention. In the ERP we focus on two specific areas: healthy development of children and youth and monitoring of the effects of the environment on health.</p> <p>The goal of the <b>Security</b> use case is to develop methods for situational awareness and intelligence gathering based on a large amounts of data. Goal of security is to prevent potential threats from happening as well as to detect and prosecute illegal activities in a background of normal activities. The first goal needs early detection of developing threats, allowing timely intervention by security personnel to prevent the actual threat to occur. For the second goal legal and privacy restrictions do not allow to act before the actual illegal activity has taken place; actual detection is key to successful prosecution, and will depend on very selective analytics.</p> <p>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. Target for the use cases in 2017 is to launch a PPP project on making sense of big data within its domain. The use cases are well connected with the ecosystem on big data. All topics are mentioned in the COMMIT2DATA roadmap. There is a good connection to the High Tech Top Sector HTSM and for Personalized Health to the top sector LSH. Collaboration with academia is covered through TNO part-time professors, PhD</p>
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	<p>students connected to the program and the COMMIT2DATA TNO-NWO program on Big Data. There is a close link to the Nationale Wetenschapsagenda, especially for route 9. Collaboration with non-academic partners is mainly channelled through the Big Data Value Center, COMMIT2DATA (NWO TNO collaboration) and the European Big Data cPPP. The ERP is connected to different topsectors: HTSM, LSH and Agro.</p>
Program dynamics	<p>In 2015 the ERP was started with three main technology lines: <i>creating value</i>, <i>extracting meaning</i> and <i>distributed data infrastructures</i>, based on the three main roles for Big Data ecosystems identified by the European Big Data Value Association. In 2016 we added two technology lines: <i>human machine interfaces</i> and <i>Big Data architectures</i>. The research in these two years provided TNO with a technology position over the total, wide, scope of big data innovations. In 2017 we focus on the three points mentioned before, this means that a significant part of the ERP portfolio will be changed, by focusing on three areas in which we can achieve an unique position. In addition the seed idea sub-program, introduced in 2016, will continue. Our focus on less topics also means that we will execute the work with less people and departments, to ensure that we develop a dedicated group of people with in depth expertise for domain specific challenges.</p>

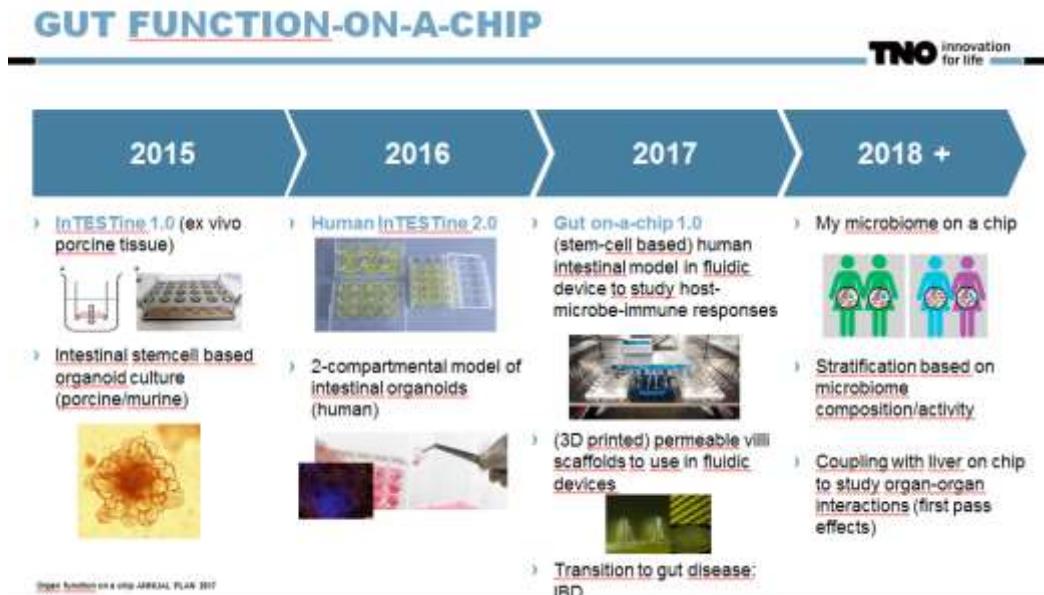


## 9 Organ Function on Chip

General data	
Title	Organ Function-on-Chip
'Topsectors'/Societal Themes	LSH, A&F, HTSM / Work & Health, Defence
Contact person TNO	Cyrille Krul; Ivana Bobeldijk-Pastorova
Contact person government	Michiel Ottolander (EZ)
Program adjustment 2017	
Abstract	<p>Over the past few years, the development of alternative, more physiologically relevant human cell based <i>in vitro</i> models has evolved. These so called organ function-on-a-chip models are designed to better mimic tissue function and architecture than conventional cell based models. With these models, it will be possible to study biological mechanisms and predict pharmacological effects in humans. Organ function-on-a-chip models provide a promising approach to solve translational issues that are evident in not only the pharmaceutical industry, but also the nutritional, chemical, environmental and cosmetic industries. The ultimate goal of organ-on-a-chip models is mimicking human (patho)physiology within an <i>in vitro</i> system which has simple readouts. Science and in particular drug development can greatly benefit from human functional organs-on-a-chip technologies, both in terms of reliability of results and in costs.</p> <p>Although the latest developments in the organ-on-a-chip models are very promising for the future, one should handle the promises with some caution. The challenge is to bring the models to a next level: organ-on-a-chip for human diseases, long term exposure, patient-derived stem cells, providing an unique opportunity to discover personalized human drug targets, related to the underlying genetic background of the patient and to test and select the specifically designed medicines.</p> <p>One can try to mimic an entire organ on sophisticated chips, but for what purpose (if it is even achievable)? We believe that a more relevant approach is to (partly) mimic organ functionality or mechanisms with only as much complexity as is required. One or several specific processes relevant for the required application of the model need to be identified and then mimicked in the organ on a chip system, combining technologies and biology. In our view this bottom-up approach not only provides focus, but also ensures the development of models with a clear and sound application.</p>
Short	The objective of the ERP organ on chip program is to improve the development of better

description	<p>predictive, more physiological (personalized) human <i>in vitro</i> 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.</p>  <p>The applications focus on three organs:</p> <ol style="list-style-type: none"> <li>1. Gut function-on-a-chip</li> <li>2. Liver function-on-a-chip</li> <li>3. Lung function-on-a-chip</li> </ol>
<p><b>Technology line 1: "Gut function-on-a-chip"</b></p>	
Goals	<p>There are currently no <i>in vitro</i> models available to study the complex interactions at the gut wall. TNO, in collaboration with other research institutes and industry, therefore aims to develop a translational <i>in vitro</i> model of the human gut, representing all the different epithelial cells in co-culture with human microbiota and immune cells. This gut-on-chip model will therefore have its application in the pharmaceutical and nutritional industry by providing a predictive human <i>in vitro</i> model to study intestinal absorption, digestion, and metabolism of their compounds, and to study the effect on microbiota/microflora composition, mucus interaction and immune response/allergy.</p> <p>In 2016 we have developed a physiological human gut-on-chip model, consisting of <i>ex vivo</i> human intestinal tissue mounted in InTESTine model. This model is now applicable for market applications. One limitation is the relatively short viability of the tissue segments. Therefore, we additionally focused on the culture of human intestinal stem-cell based organoids. These 3D intestinal organoids portray a self-renewing capacity and express different important intestinal epithelial cell types, resembling the intestinal epithelium.</p> <p>In 2017 we aim to further develop this translational stem-cell based <i>in vitro</i> model of the human gut. We will focus on the application of fluidics to simulate anaerobic luminal conditions and serological (blood) flow.</p> <p><i>Main collaborators in 2017:</i>        RAAK-2 real guts consortium (HU, Danone, Micronit), AMC (Prof. de Jonge), Erasmus MC (Prof. Peppelenbosch).        Industry: Two big pharma companies, a biopharmaceutical company and a microfluidic company.        (joint TKI project proposals were submitted in 2016 and collaborative grant applications are in preparation)</p> <p><i>Main deliverables in 2017:</i></p> <ul style="list-style-type: none"> <li>- Human stem-cell based (organoid) intestinal model in fluidic device with relevant read-outs for host-microbe immune response</li> <li>- (3D printed) permeable villi scaffolds to use in fluidic devices</li> <li>- Transition to an <i>in vitro</i> IBD efficacy model</li> </ul>
Program dynamics	<p>The dynamics of the developments within the program for Gut function-on-a-chip are shown in the figure below. For 2015 and 2016 the achievements thus far are schematically summarized. In addition to plans for 2017, also an outlook towards 2018</p>

and beyond is shown.

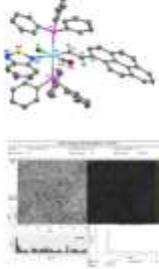
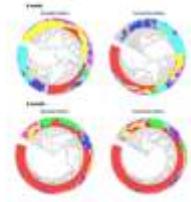


In 2018 the developed model can be easily combined with microbiota derived from health or diseased (e.g. IBD, obese, diabetic) people in order to study the role of microbiota in (gut) health and disease. Moreover, luminal conditions (e.g. pH, microflora) and intestinal physiology may be adapted to different intestinal regions (duodenum, jejunum, ileum, colon) in order to generate a “GI-tract-on-chip”, or adapted to 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.

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

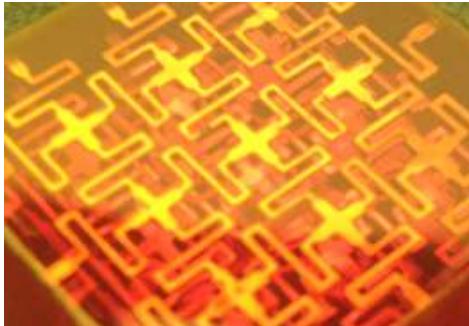
Goals	<p>The “liver-disease-on-a-chip” will be a predictive <i>in vitro</i> disease mimicking (i.e. non-alcoholic steatohepatitis; NASH) model using co-culture of human pluripotent stem cell-derived hepatocytes and stellate cells (or other liver cells) on an <i>in vitro</i> 3D cell culture platform that will have its application in testing the effect of compounds on the disease development, prevention and or treatment. Besides for the pharmaceutical industry, this will also be relevant for applications in the nutrition industry. The combination of disease, materials, stem cells system biology and read-outs is challenging and will give opportunities for broader applications towards a personalized health approach and stratification (“population on a chip”).</p> <p>In 2016 a 2D liver fibrosis model is developed. In addition, first steps in co-culture models with human hepatocytes and stellate cells are made.</p> <p>In 2017 we plan to extend this model further into a 3D co-culture model that can mimic diet-induced onset of liver fibrosis.</p> <p><i>Main collaborators in 2017:</i></p> <ul style="list-style-type: none"> <li>– SGF (MaagLeverDarm Stichting) TKI grant: TNO, Erasmus, a big pharma company, Takara Sweden, InvitroCue Singapore</li> <li>– Partners of the hDMT consortium</li> </ul>
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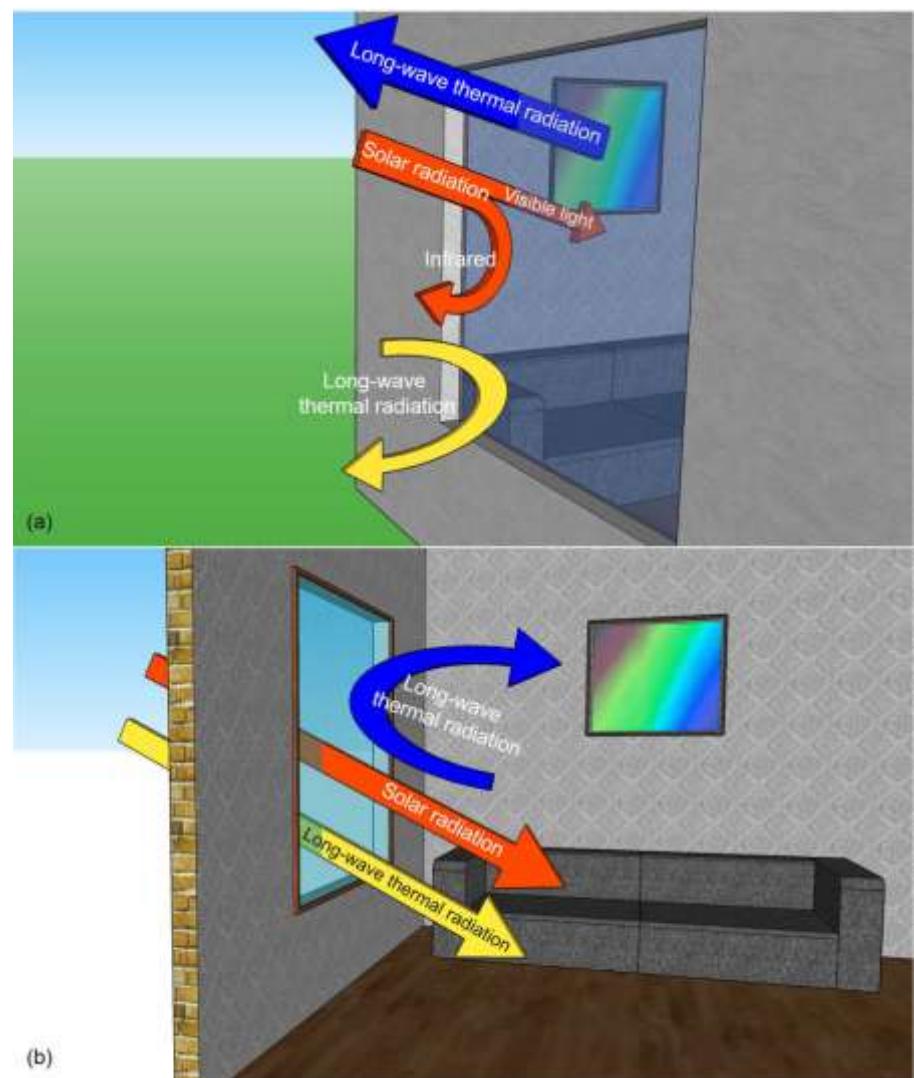
	<p><i>Main deliverables in 2017:</i></p> <ul style="list-style-type: none"> <li>- First version of 3D disease-mimicking model for liver function</li> <li>- Description of the pathways that are represented in the model</li> <li>- Validation report of the model with known stimulations and interventions.</li> <li>- Demo case for application in pharma industry.</li> <li>- Test report model with stem cells from various donors</li> </ul>
Program dynamics	<p>The dynamics of the developments within the program for Liver function-on-a-chip are shown in the figure below. For 2015 and 2016 the achievements thus far are schematically summarized. In addition to plans for 2017, also an outlook towards 2018 and beyond is shown.</p> <p>In addition to achievements 2016 and plans for 2017, in 2018 we plan to further develop the personalized 3D in vitro model and couple the model to the models of other organs, such as gut.</p> <p>The diagram illustrates the progression of Liver Function-on-a-Chip research from 2015 to 2018+.</p> <ul style="list-style-type: none"> <li><b>2015:</b> <ul style="list-style-type: none"> <li>Stellate cell stimulation</li> <li>Generation of liver cell spheroids</li> <li>Single cultures</li> <li>Generation of liver spheroids</li> <li>Cell Suspension</li> <li>Microtissue</li> </ul> </li> <li><b>2016:</b> <ul style="list-style-type: none"> <li>Diet induced NASH/fibrosis 3D in vitro model (co-cultures)</li> </ul> </li> <li><b>2017:</b> <ul style="list-style-type: none"> <li>Validated predictive NASH/fibrosis 3D in vitro model</li> <li>TNO-CT™</li> <li>Two disease platforms</li> <li>Two different treatments</li> <li>Multi-organ platform</li> <li>Representative pathways mapped based on stem-cell derived hepatocytes</li> </ul> </li> <li><b>2018 +:</b> <ul style="list-style-type: none"> <li>Personalized NASH/fibrosis 3D in vitro model</li> <li>Coupling with gut on chip to study organ-organ interactions (first pass effects)</li> </ul> </li> </ul>
<b>Project 3: "Lung function-on-a-chip"</b>	
Goals	<p>The long term goal is to establish a biosensor, which is able to monitor the biological effects of exposures in our surroundings (complementary to chemical sensors). This is both in a working-environment in the chemical industry (including the military) as well in a daily-living environment (urban city etc).</p> <p>Essential for this is system model development of the in vitro inhalation model on one hand and development of (oxidative stress) read-out parameters on the other hand.</p> <p>System development:</p> <ul style="list-style-type: none"> <li>○ Addition of relevant cells (immune cells (PBMC) and/or fibroblasts)</li> <li>○ Relating read-out parameters of model system to human exposure characteristics</li> <li>○ Development of host-microbe model using relevant bacteria</li> </ul> <p>Development oxidative stress read-out parameters</p> <ul style="list-style-type: none"> <li>○ In vitro testing CO probe</li> </ul>

	<p><i>Main collaborators in 2017:</i></p> <p>LUMC Prof. Hiemstra      Emulate via Marie Curie fellow ship Anne vd Does LUMC      TU Twente (Andre Poot, Severin Le Gac)      Triskelion      INERIS (France), LIST (Luxembourg)</p> <p><i>Main deliverables 2017:</i></p> <ul style="list-style-type: none"> <li>- Detailed plan for technology development depending on business case</li> <li>- Depending on the outcome of the results in 2016 (business case biosensor development for application in Chemistry) system requirements for biosensor</li> <li>- Collaboration partnerships for development of biosensor</li> <li>- First version of in vitro inhalation-microbiome model that is representative for human</li> </ul>
Program dynamics	<p>The dynamics of the developments within the program for Lung function-on-a-chip are shown in the figure below.</p> <p><b>LUNG FUNCTION-ON-A-CHIP</b></p> <p><b>2015</b></p> <ul style="list-style-type: none"> <li>› Air-liquid interface 3D airway cell exposure systems</li> <li>› Realistic exposures using state-of-the-art exposure facilities</li> </ul>  <p><small>From: Function-on-a-chip ANNUAL PLAN 2017</small></p> <p><b>2016</b></p> <ul style="list-style-type: none"> <li>› BC for biosensor</li> <li>› CO readout</li> <li>› Cell viability readouts</li> </ul>  <p><b>2017</b></p> <ul style="list-style-type: none"> <li>› Lung-microbiome interactions</li> <li>› Oxidative stress detection</li> <li>› Next generation 3D human respiratory cell system (co-cultures)</li> </ul>  <p><b>2018 +</b></p> <ul style="list-style-type: none"> <li>› Lab scale biosensor model of test system with integrated read-out</li> <li>› Lung-microbiome model for pharma applications</li> <li>› Partner network for biosensor development</li> </ul> 



## 10 Submicron Composites

General data	
Title	ERP Submicron composites
'Topsectors'/Societal Themes	HTSM, Chemie
Contact persons TNO	Tessa ten Cate / Maurice Mourad
Contact person government	Michiel Ottolander (EZ)
Program adjustment 2017	
Abstract	<p>Within the scope of this ERP we will 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 will collaborate with academic partners, including Eindhoven University of Technology and Maastricht University, 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.</p> <div style="display: flex; justify-content: space-around; align-items: flex-end;"> <div style="text-align: center;">  </div> <div style="text-align: center;">  </div> </div> <p>For example, 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, the choice of available materials is limited, yield is low by process-induced defects, and production speeds are typically low. Quality of the materials in the obtained products in many cases is still limited to allow the full potential of the manufacturing technology. Within the scope of this research program we will focus on materials modelling and material development to assess and to optimize product quality of 3D printed products. We aim to control the material microstructure to optimize long-term mechanical performance and to introduce additional functionalities, such as tunable optical and dielectric properties or microporosity.</p>



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	<p>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. Furthermore, we aim to progress from state of the art of monofunctional materials via materials with multiple passive functionalities to active and adaptive materials. 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.</p> <p>Within the additive manufacturing program, we will focus on three topics related to the quality of the material:</p> <ol style="list-style-type: none"> <li>Improving mechanical properties of AM materials, including the intrinsic properties of AM processable materials and the effect of processing conditions on mechanical properties in the obtained 3D product;</li> <li>Minimization of internal stresses by AM processing, which can cause</li> </ol>
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	<p>both geometrical defects in carefully designed 3D products as well as adverse effects on long-term performance (for example, very small warpage effects can cause a strong misfit in dental prostheses, and internal stresses can make a material more sensitive to fracture under high humidity conditions);</p> <p>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.</p> <p>Within the innovative building envelopes program, we will focus on materials that adapt their optical behavior in order to optimize energy performance of various parts of buildings, including windows. This can be achieved by active heat control, ie coatings that can switch from heat-reflective to heat transmitting whilst being transparent in the visible part of the light spectrum.</p> <p>The work on building envelope materials within this ERP will focus on Thermochromic Materials (ie, materials that adapt their optical properties as a depending on temperature) are regarded as promising basis for the glass window of the future: a window that can help to reject heat on a hot summer's day and, on a winter's day, reflect radiator heat back into the house whilst at the same time taking optimal profit from any available solar heat.</p>
Goals	<p>Within the scope of the Brightlands Materials Center we will cooperate with academic as well as industrial partners to develop new numerical as well as experimental methodologies, and to demonstrate those in relevant application areas.</p> <p>Regarding improving mechanical properties of AM materials, we will collaborate with the Eindhoven University of Technology to gain better understanding of the structure-properties relations of AM products. In 2017, we aim to develop a multiphase kinetic crystallization model to predict microstructure under relevant process conditions. Also, a dedicated set-up will be developed to study structure formation in thermoplastic powder fusion. We will also develop a method to study intrinsic mechanical properties and long-term performance of photopolymers.</p> <p>Regarding the minimization of internal stresses induced by AM processing, we will develop a multi-physics material model to predict thermomechanical behaviour and geometry of 3D products prepared by vat photopolymerization, and can be used to understanding the relation between material parameters and process settings and to optimize process parameters to improve thermomechanical as well as geometrical quality. In addition, we will cooperate with the TU/e to develop a prototype photopolymer system based on dynamic covalent chemistry that minimizes internal stresses caused by cure shrinkage.</p> <p>Regarding introduction of novel functionalities in AM materials, we will assess the feasibility of producing photocurable materials or products with tunable optical and dielectric properties, in close collaboration with the TU/e. Based on the results obtained in 2016, we will collaborate with industrial partners (e.g. NextDent B.V.) to develop 3D printed dental products with</p>

	<p>improved esthetic properties. In addition, we will develop multi-phase photocurable materials with controlled micro-porosity.</p> <p>Thermochromic glass windows based on multistack ALD layers have recently appeared in the market. These layers are costly and difficult to process and will expectedly appear only in niche applications. We will focus on two alternative, promising routes for thermochromic windows that, if successfully developed further, have the potential for wide-spread application, including the retrofitting to improve the energy performance of existing buildings:</p> <ul style="list-style-type: none"><li>a) Wet-chemical coating formulations that can be used to directly functionalize glass and other transparent substrates. This route provide more design freedom and compositional flexibility needed for high performance thermochromic windows.</li><li>b) Development of versatile thermochromically adaptive 'pigments' that can in turn be used as the functional sub-micron ingredient to turn coatings and composites (foils) into advanced thermochromic systems.</li></ul> <p>Thermochromic coatings and foils are expected to have wider application areas than functionalized glass windows, due to their ability to be applied in existing buildings and during renovations.</p>
Program dynamics	<p>No major changes in the additive manufacturing program are foreseen. We will include more focus on structuring of multi-phase composites, among others by strengthening the link between the PhD-project on "Modeling the 3D-Printing of Electromagnetically Active Components" at TU/e and the material development of micro- and nanocomposite photopolymer resins at TNO. In the course of 2016, the materials modelling activities have suffered from limited availability of scientists with relevant expertise (e.g. Sander Gielen leaving TNO). Currently, we are working to strengthen the materials modelling team to speed up activities in this field within a few months.</p> <p>In 2016, the program focus of 'Materials for Optoelectronics' has been defined as 'Materials for sustainable building skins' and as such the focus of the ERP has been amended accordingly.</p>

## 11 Signatures

Delft, 30 september 2016



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

Dr. K.E.D. Wapenaar  
Editor