Corporate Staff
Anna van Buerenplein 1
2595 DA Den Haag
P.O. Box 96800
2509 JE The Hague
The Netherlands

www.tno.nl

T +31 88 866 00 00

TNO report 2017 S 105

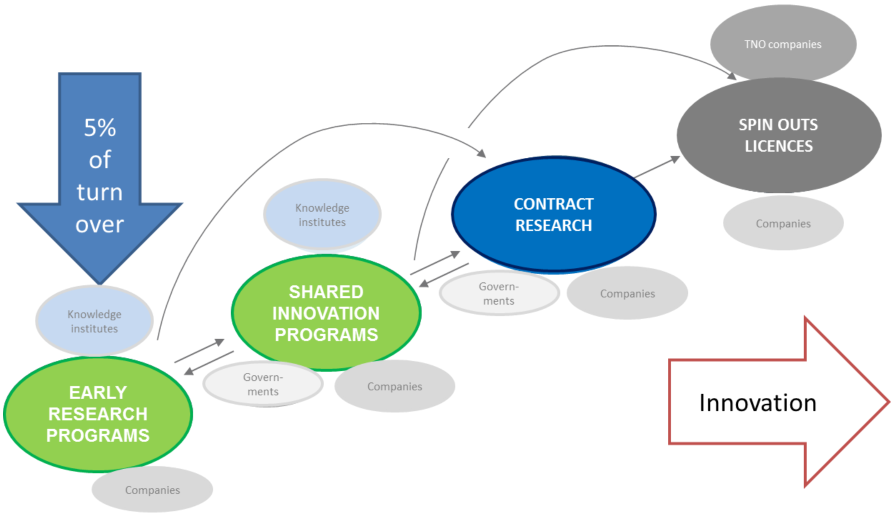
TNO Early Research Program 2018-2021
Annual plan 2018

Date	30 September 2017
Editor	Dr. K.E.D. Wapenaar
Copy no	
No. of copies	
Number of pages	73 (incl. appendices)
Number of appendices	
Sponsor	
Project name	
Project number	

Contents

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 95%, is steered by TNO's stakeholders (clients, consultation by 'Topsectors' and Ministries, task financing by MOD, EZ, SZW). The 5% innovative research is meant to build, renew and maintain TNO's knowledge assets (Kennis als Vermogen).



The main characteristics of the 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 were 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 2018-2021 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, that is pursued as ERP project in 2018. In 2017 the ERP Human Enhancement is finalized and the technology handed over to the participating roadmaps. Also in 2017 technology needs and opportunities are scouted in the areas of applied artificial intelligence, chemical and bio-nano sensors, and optical satellite communication.
  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. The aim is to intensify and broaden this cooperation by further alignment of research programs, e.g. in the context of the execution of the National Science Agenda (NWA).

TNO is an active member of the knowledge coalition that formulated the NWA in 2016. On the initiative of OCW a first start of the execution of the NWA could be made in 2017 by a 'Startimpuls' funding for eight of the 25 routes that were put on the agenda. TNO participates in six of these eight routes, with several strong ties with the ERP program.
Together with EZ we inform Topsectors and Ministries of our approach of building our knowledge base, aiming at early involvement of companies and other stakeholders in public private cooperation. In 2016 TNO's CTO Jos Keurentjes informed the 'Topsector' Captains of Science about the ERP program, and ERP program manager Koen Wapenaar informed the 'Topsector' TKI directors on ERP program lines and progress. Every program builds intimate relations with Topsectors and other stakeholders, as is elaborated in this multi-annual plan. Information on our ERP research is also available online, and can be found here.

Projects 2018
External and internal progress meetings have confirmed that 9 ERP research lines executed in 2017 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. One of the programs (Human Enhancement) is finalized, and the technology is being handed over to the participating roadmaps. The seed project on robotics has gained considerable momentum and will be continued in the ERP portfolio 2018. A short overview of our 10 ERP projects 2018 is given below:

- Quantum Computer / Quantum Internet (QuTech). Quantum technology is seen as the basis for the "second quantum revolution". The first quantum revolution – understanding and applying physical laws in the microscopic realm – resulted in ground-breaking technologies such as the transistor, solid-state lighting and lasers, and GPS. Today, our ability to use previously untapped quantum effects in customized systems and materials is paving the way for new systems and new concepts e.g.: quantum computing, networking, sensing, positioning.
- Complexity, "The study of the phenomena which emerge from a collection of interacting objects". The primary aspects investigated are fundamental dynamics of complex systems, i.e. the emergence of collective behaviour, the transition from one system state or phase to another, resilience to external shocks or disruptions. Our research focuses on 2 important areas: 1) Self-organisation in Logistics; 2) Value Creation by Sustainability. TNO works in an eco-system with various partners, e.g. NWO/academia, industry, TO2; examples are the joint project calls with NWO on Logistics, Self-organisation, Health, Closed Cycles, Sustainable Business models etc.
- Personalized Health. This Program will build the scientific and technological foundations for a healthcare economy and healthcare system focusing on preventing and curing lifestyle related diseases, applicable for a wide range of metabolic-inflammatory diseases (type II diabetes and related complications such as cardiovascular disease, fatty liver related diseases, intestinal diseases, neurological disorders, osteoporosis, etc.). The technologies will focus on the biological, physiological and biomedical aspects, and the behavioral and medical technology aspects, including e-health and health data infrastructures, and decision support systems for organizational change.
- Energy Storage & Conversion, becomes more and more important to achieve an increased use of durable energy. Our focus will be on Solar-to-Fuels processes that convert electricity from renewable sources (solar, wind) or sun light directly into energy that is stored in chemical bonds

(fuels): electron-to-fuels and photon-to-fuels. Typical goal for 2021 is an efficient production process for carbon based fuel at a cost of 800 Euro/ton.

- 3D Nanomanufacturing. Recent growth and future expected growth in the wearable electronics, and to a larger extent the growth of the internet of things scales up the demand for new innovative nanomanufacturing processes and instrumentation. All these developments require the continuation of Moore's law in scaling the dimensions and the further development of 3D architectures such as Gate All Around nanowires FETs (GAA) and 3DNANDs. The developments of these nanodevices highly depends on the 3D nanomanufacturing processes and nanometrology systems and methods to control yield of the devices. Our research will be focused on: metrology in the 1 nm resolution range, subsurface nano-imaging and quantum sensing, and nano-motion control and dynamics.
- Structural Integrity strives to make important macrostructures (e.g. in the transport and energy infrastructure, defence vehicles) safe, and perform optimally at the lowest possible cost to society. This is achieved by adding intelligence to these structures. In future the structures will assess their condition by themselves, forecast their future state and, based on that, will signal the need for action. They will propose action plans, including suggestions for specific inspections and maintenance. In addition and closely related, is the aim of using the knowledge acquired in developing intelligent macrostructures for improving the structural design and investigating the potential of applying new materials in macrostructures.
- I-Botics. Robotic Technology will affect many aspects of our professional and private lives: it will raise efficiency in industrial production, increase safety levels in amongst others transportation and it will provide enhanced levels of service at home. Robotic technology will become a significant element in solving societal challenges posed by an ageing population, the need to bring manufacturing back to Europe, the demands for more efficient, clean transportation and energy, and the want for a safe and secure society. Many research and technology endeavours on robotics focus on increased autonomy of robots. i-Botics however is focussing on interactive robotics, hence i-Botics.
- 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 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.
- 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. The ultimate goal of organ-on-a-chip models is mimicking human (patho)physiology within an in vitro system which has simple readouts. We focus on applications for two organs: Gut function on a chip, and Liver 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 Health					
Energy Storage & Conversion					
3D Nanomanufacturing					
Structural Integrity					
i-Botics					
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									
Personalized Health									
Energy Storage & Conversion									
3D Nano-manufacturing									
Structural Integrity									
i-Botics									
Sense Making from Big Data									
Organ function on Chip									
BMC-Submicron composites									

In addition to these ten topics we will explore four seed projects: Applied Artificial Intelligence, Chemical Sensing, Bio-nano-technology, and Optical Satellite Communication. The ambitions for these subjects are presented in the last four chapters. 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 plans for the ten projects are described in a concise format agreed with the ministry of Economic Affairs, explaining the program development, the external connections with knowledge partners and stakeholders, the use cases, and the goals and activities for 2018 and beyond.

2 Quantum computing and Quantum internet

General data	
Title	ERP Quantum Computer / Quantum Internet
'Topsector'	HTSM Nanotechnology
Contact person TNO	Richard Versluis, Garrelt Alberts, Rogier Verberk
Contact person government	Mariëlle Beers-Homan (EZ)

Program 2018 – 2021 and activity plan 2018	
Abstract	Quantum technology is seen as the basis for the "second quantum revolution". The first quantum revolution – understanding and applying physical laws in the microscopic realm – resulted in ground-breaking technologies such as the transistor, solid-state lighting and lasers, and GPS. Today, our ability to use previously untapped quantum effects in customized systems and materials is paving the way for a second revolution. TNO aim to exploit these effects in new systems and new concepts using our core quantum technology expertise: 1. Quantum control engineering (software and hardware) 2. Nanofabrication of quantum devices 3. Quantum encryption and protection In the following technology fields: • Fault Tolerant Quantum Computing • Topological Quantum Computing • Quantum internet & secure communication • Quantum sensing and positioning - The first mentioned three technology fields will mainly be addressed through the QuTech cooperation between TNO and the TU Delft. Where the first phase of QuTech (2014 – 2017; Proof of Principle) focused on accelerating research and making the transition towards a mission-based way of working, 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 by building or contributing to pre-prototype fault tolerant quantum computers based on three qubit technologies (superconducting qubits, electron spin qubits and spin qubits in NV centers) accessible online and a pre-prototype quantum internet (with a 2021 milestone of a four-node internet between Amsterdam, The Hague, Leiden and Delft, accessible through an online portal allowing quantum communication between nodes). - Investments will also be made in explorative research in the field of quantum sensing and positioning, with market potential in the aerospace and defense industry. Long term goals are to develop new sensing and positioning systems, based on quantum mechanical properties as super-position and entanglement, to increase the sensitivity of sensing beyond classical limits and to achieve improved positioning information which can for instance increase the security level of information transfer by location tagging. For further information on the ambition and people of QuTech, an introduction to quantum computing, and breaking news, please visit **www.qutech.nl**.

Description	*Fault Tolerant Quantum Computing* Surface codes use a 2D array of data plus ancillary qubits. Data qubits carry the quantum information, ancillas detect errors (via parity checks) induced on data qubits by decoherence and faulty gates, and classical feedback electronics analyze the detected error signals and issue all corrective actions. The smallest circuits for demonstration of surface coding require 13 and 17 qubits. We pursue their realization with three approaches: superconducting qubits, electron spin qubits in quantum dots, and spin qubits in diamond. Superconducting quantum processors with five qubits are already operational, with basic gate, readout and feedback operations demonstrated. Current emphasis is on maximizing the multiplexing of control technology to allow double-digit qubit numbers. The overall goal with quantum dot spin qubits is to demonstrate and exploit millisecond coherence and qubit control, initialization and readout at 99.9% fidelity in a surface-code compatible architecture. In the third system, using electron and nuclear spins of atomic impurities in diamond, all basic gate, readout and feedback operations are in place. Increasing the speed of multi-qubit logic gates (via photonic coupling) is a major objective. This roadmap interacts with multiple industrial sectors. We collaborate with cryogenic equipment manufacturers (for example 'Leiden Cryogenics') to develop bigger and more powerful dilution refrigerators housing quantum processors and the classical electronics. Multiple connections are being established with manufacturers of digital electronics to explore cryogenic solutions. For the control of quantum processors, we discuss the tailoring of test and measurement equipment with leading manufacturers. Finally, FEI and ASM support the materials development within this roadmap. *Topological Quantum Computing* Quantum states are fragile and tend to decohere quickly. This decoherence would be suppressed if the quantum state would somehow be stored in a topological variable. The roadmap "Topological Quantum Computing" aims at such topological protection. The five-year objective of the Topological Roadmap is the realization of a topological qubit encoding a quantum state that is protected for at least a second. As building blocks we use pairs of Majoranas that emerge in semiconductor nanowires in contact with a superconductor. A small circuit with Majoranas enables to demonstrate non-Abelian statistics. This involves exchanging, or braiding, Majoranas around each other. Braiding can change the quantum state in a controlled manner which constitutes a quantum gate operation. We will test the stability of this quantum gate and aim to demonstrate that conventional decoherence plays no role in topologically protected states. The Topological Roadmap is in close collaboration with Microsoft Research Station Q, located in Santa Barbara and headed by Dr. Michael Freedman. *Quantum internet & secure communication* Our goal is to build an optically-connected network of many (small) quantum computers. Such a network enables the exchange of quantum bits between any of the connected quantum processors in order to solve problems that are intractable classically. A quantum network in which the processors are located at different geographical locations is called a quantum Internet. Our goal is to develop the technology to enable quantum communication between any two places on earth. One application of such a quantum internet is to provide a fundamentally secure way of communication in which privacy is guaranteed by the laws of physics. Quantum processors can also be connected into a quantum network in order to

	assemble a large quantum computing cluster. This approach is called networked quantum computing and offers a natural path towards scalability. Combining a quantum internet and a networked quantum computer finally allows remote users/providers to perform secure quantum computing “in the cloud”. *Quantum sensing and positioning* The detailed program for quantum sensing and positioning will be developed in 2017 and 2018.
External Connections	• The goals of this program are well aligned with the goals of the HTSM ‘Topsector’ and the goals of the NWA route 18. Co-operation with various partners is taking place through ongoing co-operations, such as in IARPA sponsored projects. • The calls for the European Quantum Technology Flagship will be published in fall 2017. Investigating possible consortia has started well before publication date since the deadline for the calls will be short requiring pro-actively contacting European industry to prepare for these calls. Several partners have been identified and contacted. • Conversations are taking place with QuTech’s industrial partners to add-on industrial research projects in the field of topological quantum computation. • QuTech is highly involved in NWA18 (Quantum nano revolution), and TNO is partner in two projects: protocols for the quantum internet (collaboration between QuSoft and QuTech) and Quantum Chemistry on a quantum computer (collaboration between University of Leiden, TU Delft, TNO, Intel and Shell). • The activities related to nano-fabrication are well in-line with the NanoNextNL-program of the Strategic Research Agenda. The state-of-the-art facilities of NanoLabNL offer a unique platform to create better devises for quantum computations and quantum sensing.
Program development	• In 2017 Microsoft announced the start of StationQ Delft. This marks a transition phase for topological quantum computation. The cooperation between StationQ and QuTech requires a re-focus of the long term goals and the efforts needed to reach these goals, the details of which need to be worked out in due course. • A lot of effort will be put into understanding the operation principle of quantum internet and networked computing by analyzing the existing scientific setups, improving the critical building blocks and supporting science with engineering. Some highlights from 2017: evaluating designs and breadboards for frequency conversion (Optics department) to enable entanglement over larger distances, improvements of the Qubits with nano fabrication methods (Nano Instrumentation) and yielding more light from the Qubits (Optics), improvement in Qubit control (Radar Technology) improving efficient coupling of the RF signal to the Qubit and the development of simulation software to test the principles of Quantum Internet protocols (Distributed Sensor Systems) used for baselining the timing and infrastructure requirements.
Activity plan 2018	*QuTech cooperation* • In 2018 a mid-term evaluation based on initial targets of the cooperation will be executed according to the Standard Evaluation Protocol (SEP) of the VSNU. This activity will be coordinated by Anne Mollema of the Delft University. *Fault Tolerant Quantum Computing* • Currently the requirements and architecture for the pre-prototype quantum

	computers are being defined. In 2018 the detailed design of the systems will be defined and reviewed in order to initiate the procurement of equipment and integration of the systems. • Only limited partnerships can be pursued in this sub-area beyond the substantial participation of Intel and Microsoft. Only partners that fit the 'consortium' can be invited in close consultation with the existing partners. One of the most likely and valuable new partner would be ASML *Topological Quantum Computing* • The cooperation between StationQ and QuTech requires a re-focus of the long term goals and the efforts needed to reach these goals, the details of which will be worked out in due course. *Quantum internet & secure communication* • In 2018 the design for the engineering model nodes will be manufactured (design obtained from reverse engineering the scientific nodes in 2017). With this step a node is made available that is capable of operating over >1.3km, is robust and can be controlled remotely. This design is used for further detailing the requirements and design for the 2020 demonstrator nodes. • A laboratory breadboard and field test of quantum cryptography through free space will be made. • Partnerships will be started based on 'open innovation' and pre-competitive research. In principle, every party could participate. One of the key partners could be KPN. *Quantum sensing and positioning* • The ambition to extend the range of applications requires developing a technology roadmap for quantum sensing and quantum positioning and scouting for industrial partnerships to these fields.

3 Complexity

<table>
<tr><td colspan="3">General data</td></tr>
<tr><td colspan="2">Title</td><td>Complexity</td></tr>
<tr><td colspan="2">‘Topsectors’/Societal Themes</td><td>Logistics, AgriFood, Chemistry, Energy / Circular Economy</td></tr>
<tr><td colspan="2">Contact person TNO</td><td>Ardi Dortmans; Esther Zondervan</td></tr>
<tr><td colspan="2">Contact person government</td><td>Mariëlle Beers-Homan (EZ)</td></tr>
<tr><td colspan="3"></td></tr>
<tr><td colspan="3">Program 2018 – 2021 and activity plan 2018</td></tr>
<tr><td>Abstract</td><td colspan="2">The TNO ERP Complexity combines beta and gamma sciences to develop tools for modelling of complex transitions and decision making processes in order to better understand their characteristics and improve their behaviour. Modelling approaches are most valuable to achieve this, employing a combination of various possible qualitative and quantitative models. Examples of relevant models are (heterogeneous) agent based models, multiscale physical models, Bayesian belief models, value creation models etc.

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, i.e. the emergence of collective behaviour, the transition from one system state or phase to another, resilience to external shocks or disruptions[1].

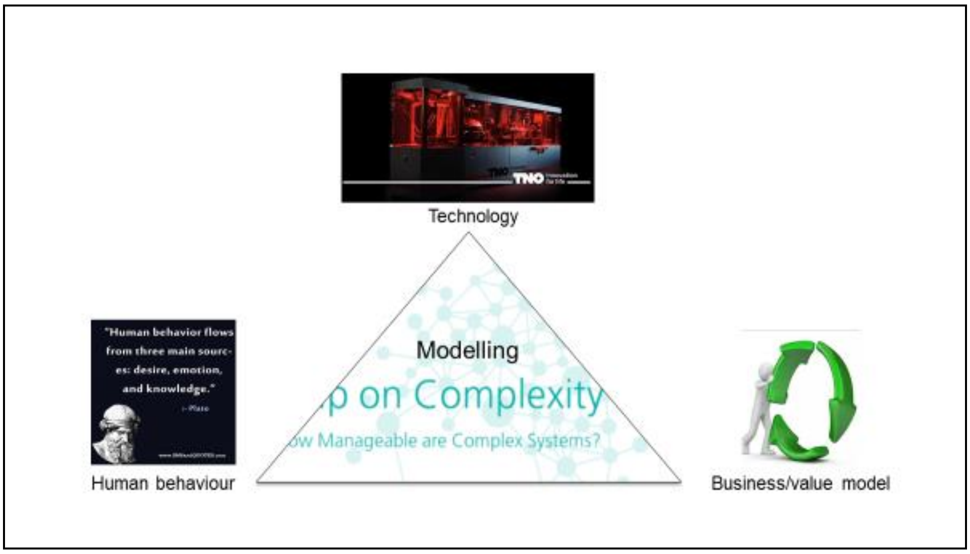
Our research focuses on 2 important areas:
1) Self-organisation in Logistics;
2) Value Creation by Sustainability.

Self-organisation in Logistics basically is about the possibilities offered by new (ICT) technologies to plan and execute transport of goods in networks with reduced environmental loads. Examples include the system of sea container logistics to, in and from seaports and the distribution of packages of items purchased by consumers online. These systems will eventually contain elements of self-organisation that in the future could enable the Physical Internet.

Value Creation by Sustainability focuses on the transition towards a more sustainable economy where combinations of new technologies, new value creation approaches and human behaviour are critical to realise the disruptions needed. In this area both the material transition and the energy transition are equally important.

TNO works in an eco-system with various partners along three parallel lines:
• Expansion of the cooperation with NWO/academia and industrial partners, preferably also with TO2 partners; existing examples of this are the joint project calls with NWO on Logistics, Self-organisation, Health, Closed Cycles, Sustainable Business models etc.</td></tr>
</table>

[1] https://www.nwo.nl/en/research-and-results/programmes/complexity

	• Initiation of new activities through the Netherlands Complexity Platform Science (NCPS) platform; • Setting-up PPS activities for valorisation of the more fundamental research with NWO. https://www.tno.nl/en/collaboration/expertise/early-research-programme/early-research-program-complexity-grip-on-complexity/
Description	**Context** The Netherlands is an important hub for transport of people and goods through the world. The number of passengers at Schiphol airport is continuously increasing, the same applies for the number of containers in Rotterdam harbour and the amount of agri-food products transported to the rest of Europe. This important worldwide position is, next to infrastructure and location, also due to our excellent know-how on transport- and logistical processes. In order to maintain or even reinforce our position we need to solve some serious challenges, one of the most important being to meet the climate arrangements of Paris. Transport emissions must be reduced by at least 80% in 2050 w.r.t. 1990, i.e. a factor of 6. This can partly be solved by significant hardware modifications (e.g. fuel), but much more must be done: smarter ways to organize transport and mobility, more fuel efficient transport by shared transport etc.[2] ICT and other new technologies are critical to initiate this transition on the one hand, but also result in possibilities to provide more individualized services and higher customer intimacy on the other hand. Thus we see the consequences of the need to reduce greenhouse gases emerging as system transition in transport and logistics. The climate agenda must and will lead to many more of these system transitions and disruptions. From a complexity perspective these are most interesting topics of research, because any system transition is likely to include elements of systems dynamics, notably also the energy and materials transition. From a somewhat higher point of view, these transitions contain very similar ingredients that must be matched: new technologies, new value creation models and adaptation/acceptation by individuals and organizations. Approaches to one transition are thus likely to be relevant to other transitions as well. 

[2] MU Transport and Logistics 2017, NWA route Logistics and transport in an energetic, innovative, and sustainable society

Essential building blocks for TNO ERP Complexity

Approach
In order to come up with concrete, demonstrable solutions and realize impact this ERP focuses on 2 important areas that are also connected:

- Self-organisation in Logistics
- Value Creation by Sustainability

Self-organisation in Logistics
Ongoing globalization and the rapid developments in ICT, 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 (a higher level of) smart self-organisation of transport of goods in the triangle of physical transport, ICT and human behaviour. In 2016 and 2017 we realised joint multiannual projects with academia, industry and top sector Logistics on[3,4]:

- Portable quantitative models to enhance the performance of the complex chains of port sea side processes (Swarmport);
- Complexity methods for predictive synchromodality (Comet-PS);
- Transport Self Organization through Network Integration and Collaboration (Trans-SONIC);
- Grip on freight trips (ToGrip).

These activities will be part of this ERP 2018-2021. In addition we will develop projects in the joint calls with NWO on Complexity-Self-organisation and with NWO on Sustainable Business Models, all in alignment with top sector Logistics. This set of projects provides the scientific backbone and basic industrial network for realizing an extensive, powerful self-organisation tool box in close alignment with and then transferred to VP Logistics.

Value Creation by Sustainability
Throughout the world sustainable development is a key issue for the next decades. This poses a formidable task as we must secure economic growth and tackle major societal problems such as large scale introduction of clean energy, the reduction of emissions of greenhouse gases (industry, cities), secure the availability of raw materials, clean water and agricultural products, and maintaining soil fertility. The energy and material transition are prime examples of areas where coordinated efforts must be made and where complexity approaches can provide useful insights. As an example: the final disruptive state of the material transition (a circular economy) will have material flow cycles that are (nearly) fully closed: 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. Thus

[3] https://www.nwo.nl/en/news-and-events/news/2016/magw/seven-consortia-complexity-in-transport--logistics-granted.html
[4] https://www.nwo.nl/onderzoek-en-resultaten/onderzoeksprojecten/i/14/29614.html

	this system transition will benefit from complexity research on self-organisation, transitions and stability. For 2018-2021 we will focus on further development of our relation with NWO and related networks and built know-how on: • Sustainable business models for the energy transition, in particular in relation with value creation in energy distribution networks; • Novel operational mechanisms to coordinate stochastic renewable energy generation, flexible energy use in industry and smart homes and dynamically operated, constrained energy distribution grids; • Models to predict the environmental and economic impact of a material transition[5] taking into account the uncertainty of fast changing economy and technology. If granted the project submitted with WUR in the NWO call Closed cycles will be part of this activity, as well as activities in the proposed StartImpuls 2 Circular Economy. We will contribute to the NWO calls Sustainable business models in the next years and aim to embed this topic in the expected cooperation between TNO and NWO TTW. *New initiatives* Part of this ERP will be devoted to exploring new initiatives for the next years, in close collaboration with NWO and other partners. Typically we will look for modelling of phenomena in transitions with high societal impact over the next years: E-health, smart cities, smart industry etc. **Academic network** The academic network for this ERP is shaped through the collaboration with NWO in various project calls and contains most universities in the Netherlands. Existing projects are with e.g. TUD, UT, CWI, WUR, UU, RU, EUR, UL, TU/e etc. In this network also contacts exist with Hogescholen through NWO-SIA and international collaboration through e.g. DTU Copenhagen, Nanyang Technological University Singapore, the Sante Fé Institute, the Pacific Northwest National Laboratory and partners in the joint research program on Smart Grids of the European Energy Research Alliance EERA. **Transfer to VP** This ERP has close connections to the demand-driven programs VP Logistics, Environment and Sustainability and Sustainable Energy and results in transfer of basic know-how and networks as well as the initiation of joint initiatives.
External connections	Societal Themes: Energy and CO2, Mobility and Transport, Circular Economy, AgriFood. NWA routes: Circular Economy and Resource Efficiency, Energy transition, Logistics and transport in an energetic, innovative, and sustainable society, Sustainable production of safe and healthy food.
Program development	This ERP was set-up as to shape a close cooperation with NWO. The NWO ENW program Complexity is an important instrument to define joint calls and project proposals with academia and industry. In 2016 this led to the NWO call Complexity – Logistics in close cooperation with top sector Logistics and NWO SGW, and the NWO call Complexity in Health and Nutrition in close cooperation with top sector Agriculture and Food, while in 2017 joint calls were prepared with NWO ENW on Complexity – Programmable Self-organisation (top sector Chemistry), with NWO-SGW on

[5] https://www.nwacege.nl/

	Sustainable Business Models (top sector Logistics) and with NWO-ENW on Closed Cycles (top sectors Agriculture and Food, Logistics, Horticulture and Propagation Materials and Water. Top sector Creative Industries. We aim at extending the way of working introduced to other areas of NWO, notably NWO TTW, in 2018 for which in 2017 the basis has been discussed between TNO and NWO TTW. Close connections are maintained with the Groene Brein and MVO Nederland on joint initiatives and valorisation of the research of the NWO programs. In 2016 and 2017 TNO has coordinated the NWA route Circular Economy and Resource Efficiency, also in close connections with Min. EZ and Min. I&M and the MU Circular Economy. We aim to realise the StartImpuls 2 for this route in 2017 and contribute significantly to the development of the KIA Circular Economy for the next years. Part of this could be a significant joint initiative with RU and EUR (prof. Jonker) to boost the formation of a circular economy research network in the Netherlands, together with Min. EZ, Min. I&M, provinces and companies.
Activity plan 2018	*Self-organisation in Logistics* • We will continue the work in the currently running multi-annual projects with academia, industry and the top sector Logistics, that were set-up in a joint call with NWO on Complexity in Logistics in 2016/2017 (Swarmport, Comet-PS, Trans-SONIC and ToGrip; see above). These projects can be seen as first steps towards the realization of efficient and robust logistic chains through incorporating increased flexibility in decision making at lower levels in the systems, leading to systems that have a higher level of self-organisation. For 2018 the project activities will be mainly on (i) further development of initial (sub)models, (ii) data gathering for setting up useful scenarios for testing and shaping the initial models together with the industrial partners, (iii) implementation of initial models in simulators and/or analytical tools, and (iv) performing first tests. • In addition, we aim at developing an additional project in the recently launched joint call with NWO on “Complexity - Programmable Self-Organisation” (preparations to be started in Q4 2017). The goal of this project is to investigate and establish more fundamental concepts for (a higher level of) self-organization in Logistic systems, building on the insights, knowledge and (practical) experience (to be) gained in the currently running projects and the experience in other application areas. • We will also deploy a special activity in the beginning of 2018 to bring together the work/intermediate-results of the currently running projects (e.g. in one or two joint workshops) in order to learn from each other, to identify and exploit opportunities for achieving synergy, jointly refine the project goals if appropriate, and identify important areas within the scope of the ERP/Logistics that are not covered by the current projects. For such emerging gaps in our portfolio we will then deploy actions to get these gaps filled up through e.g. initiating new joint efforts with NWO and/or the top sector Logistics to define appropriate research programmes. *Value Creation by Sustainability* • Energy transition decision making evolves in two different timescales. Firstly, there is the long timescale of investment decisions, development of new business models and human adaptation (e.g. through strategic coalition forming). Secondly, there is the much shorter time scale of the operation of physical energy distribution networks, coordinating the control actions of network operators, energy users and

producers, and market parties. These two timescales are a source for uncertainty and undesired disruptions and thus highly relevant for complexity research. Projects will be developed in close collaboration with academic partners in the NWO program Duurzame Business modellen e.g., but other ways will be explored such as the NWO TTW Open Technology program.

Regarding the long time scale the activities in 2018 are:
- Enhance TNO's Value Case Methodology with specific methods for value determination incorporating dependencies on behaviour of other actors and uncertainties in the value of: energy flexibility, CO_2 rights and future innovation options.
- Development of a decision simulation environment for complex investment decisions and value creation mechanisms in order to enhance traceability and insight for decisionmakers. This builds forth on existing simulation and modelling tools (e.g. Joint Decision Making Lab of RU, POWER-TAC of EUR, E3-value of VU). Simulation supports parties to implement/change sustainable business models and investment strategies.

These activities will be performed in interaction and consultation with societal stakeholders such as Havenbedrijf Rotterdam (combining CO_2 targets with maintaining/enhancing their competitive position), the participants of the energy treaty in Gelderland and other energy regions with a strong transition need (e.g. the province of Brabant).

Regarding the short time scale the activities in 2018 are:
- Develop a local energy flexibility market as an automated coordination mechanism in the complex interaction system between energy demand, supply and distribution network operations (TRL level 3). This market is based on existing transactive energy knowledge and tools present at TNO augmented with external knowledge on receding horizon markets. This activity will be performed in interaction and consultation with societal problem holders such as distribution network operators (e.g. Alliander, Stedin), aggregation companies (an upcoming new role in the electricity market, e.g. REstore) and knowledge partners.

- Material transition decision making evolves in two different timescales as well. Similar to the energy transition, there is a long timescale in investment decisions, development of new business models and human adaptation. Also there is the much shorter time scale of the operation of physical material distribution networks, by material producers, suppliers, users, recyclers etc. Projects will be developed in close collaboration with academic partners in the NWO program Duurzame Business modellen II, NWO TTW Open Technology program, the expected NWA StartImpuls 2 Circulaire Economie, NWO call Gesloten Kringlopen, initiatives with prof. Jonker, SRE Eindhoven etc. Research in this area will benefit from and will be aligned with the research in the energy transition as similar modelling approaches can and will be pursued and similar external networks are relevant.

4 Personalized Health

General data	
Title	Personalized Health
'Topsectors'/Societal Themes	LSH, AgriFood, Chemical Industry, HTSM, Creative Industry / Min. VWS
Contact person TNO	Ben van Ommen
Contact person government	Mariëlle Beers-Homan (EZ)
Program 2018 – 2021 and activity plan 2018	
Abstract	Lifestyle related diseases[6] to a large part are preventable, reversible and curable. For a variety of reasons, this is not properly implemented in our health care system and economy. Since lifestyle diseases comprise ~60% of total healthcare costs, and proper lifestyle adds 7 years to life, this needs to change. *Objectives 2018-2021:* The ERP Personalized Health will shape the scientific and technological foundations for a healthcare economy and healthcare system focusing on preventing and curing lifestyle related diseases. In order to successfully transform both economy and healthcare from "care to cure", a fundamental and integrated research portfolio will be implemented consisting of • a completely new form of integrated healthcare and health research, exploiting personalized health interventions in real-life healthcare in all relevant lifestyle related areas with "big-data embedded n=1 research". • an integration of metabolic-inflammation-endocrinal biology and medicine, prevention, safety, behaviour, e-health, health data, health systems and health economics. During previous strategy periods, most foundations were laid (systems biology, personal health, fundamental knowledge in disease processes, behavioral changes technologies, system dynamics modelling). It is now time to integrate all aspects, from biology to behavior and social interactions and from technology, modeling, and data to economics. This integrated research portfolio can then be applied to solutions in all life stages, lifestyle as medicine, work health and systems medicine. The concepts of systems flexibility and resilience, shaped and developed by TNO over the last 10 years, now come into practice in a wide range of connected application areas, thus becoming a "unifying concept" for all biological, social, psychological and economic areas. TNO Life has all above mentioned scientific disciplines available, has an extensive national and global academic supply chain and has the mission and mandate to implement a transition towards a sustainable healthcare system focusing on prevention and cure. This research program will act as core Early Research Program of the new TNO LIFE Unit, connecting all six research groups and delivering to all Roadmaps from this Unit, with the explicit aim to produce a major social, economic and scientific impact. With respect to the KIA of the various Topsectors, the ERP Personalized Health fits very

[6] excluding smoking which is primarily a political issue

<table>
<tr><td></td><td>well to a series of defined goals and as such many opportunities to establish cross-sectoral research consortia as PPP's will emerge from this ERP.

Milestones for 2018:
Within the first year of this new strategy period, the program aims to make the next steps in broadening the fundamental knowledge build up so far, in continuous technology development and in integrating current research technology portfolio. For the different technologies, this translates into the following:
Research methodology Innovation: set up the "Lifestyle & Research Community" and develop the methodology to combine research and personalized healthcare.
Microbiome: Develop an approach to quantify microbiome function (microbiome challenge test) in relation to human health
Behavior Change: develop interventions supporting maintenance of behavior change.
Models: develop models for predictive health, diagnosis-interventions, metabolic-inflammatory health and co-morbidity.
All of the above will be applied in Lifestyle as Medicine, and life stage (child, adult, work and ageing) related health.</td></tr>
<tr><td>Description</td><td>Objectives program 2018-2021
This Program will build the scientific and technological foundations for a healthcare economy and healthcare system focusing on preventing and curing lifestyle related diseases, applicable for a wide range of metabolic-inflammatory diseases (type II diabetes and related complications such as cardiovascular disease, fatty liver related diseases, intestinal diseases, neurological disorders, osteoporosis, etc.). The technologies will focus on the biological, physiological and biomedical aspects, and the behavioral and medical technology aspects, including e-health and health data infrastructures, and (together with other TNO programs) decision support systems for organizational change. Technologies will be developed together with end users for optimal implementation in real life, and on site monitoring of changes towards a sustainable transition, healthcare and healthcare economy

For this objective, the ERP will have a number of technology work packages and a number of use cases, which serve to connect to the TNO Roadmaps, specifically in the area of health and healthcare.

Technologies
1- Research Methodology Innovation
For a number of reasons, the classical "randomized clinical trial" research methodology is not optimal in the area of personalized health, as it excludes studying multiple (personalized) interventions in one study. Furthermore, current health research cannot be integrated with healthcare, as research needs to follow strict protocols which are not necessarily optimal for the individual situation of the subject / patient. A new research methodology needs to be developed which optimally combines research and personalized healthcare. Previous research by TNO and partners has shaped the basic ICT environment that allows individual subjects / patients to store, share and valorise their health data both for their own health (self-empowerment and shared decision) and for research purposes (big data embedded n=1 research). TNO, together with LUMC, will implement this in the area of lifestyle related disease and healthcare. Characteristics are:
the patient/citizen owns and valorises personal health data,
research and healthcare are fully integrated,
embedded intervention studies can be executed,</td></tr>
</table>

- all stakeholders (individuals/participants, healthcare professionals, economic parties, researchers, policy makers) are involved,
- prototypes of new advice models, e-health modules etc can be tested,
- emphasis will be put on “care2cure”,
- research communities will be shaped,
- innovations in Health technology Assessments can be made,
- Big-data embedded n=1 research will be facilitated.

In 2018, the first research&health (R&H) communities will be shaped around type 2 diabetes care2cure, i.e. the “Leefstijl als Medicijn” living cohort in the Zuid-Holland region (Den Haag, Leiden, Rotterdam), and child health. This will subsequently grow into a Nation-wide “lifestyle as medicine / health community in all relevant health areas (CVD, COPD, osteoporosis, gut health, work health, various areas of child health, etc), and revolutionize personal health research, commercial health service development and healthcare. This R&H community will become the new testing bed for all major healthcare improvements and assessments. All technologies described below will be tested in the R&H community.

2 - The Microbiome

It is becoming clear that microbes are an integral part of human physiology. Microbes can be used as sensors for human health and as useful collaborators to stimulate health or combat disease. Based on the impressive scientific developments in both microbiome and systems biology of the last decade the foundations of an integrated view on human health are emerging. We will combine knowledge of both the human and microbial systems and integrate these into a systems approach to the combined microbe human system. This will include development of both theoretical approaches (knowledge systems, modeling and visualization technologies), and analytical methods to quantify the physiological contribution of microbes.

Specific attention will be given to:

- Variation in microbiome composition from a functional perspective: how different is different?
- Microbiome related metabolic activities in relation to health effects of nutrients and drugs
- Bacteria fungal interactions
- Microbiome in relation to inflammation
- Role of microbiome in food appreciation, choice and reward pathways in relation to health status

In 2021 we aim to have a thorough understanding of the relationship between microbiome and human health which forms a foundation for directed interventions promoting health. In 2018 a first step in this direction will be taken by developing an approach to measure/quantitate microbiome related health effects (microbiome challenge test).

3 - Behavior change

Changing your lifestyle, although very rewarding for health, is not easy. Many “behavior change technologies” are becoming available but are not yet integrated and applied in a personal and practical manner. Therefore, we will build a package of behavioural change technologies based on the personal bio-socio-psychological profile, and apply the right combination of technologies at the right phase of learning new behaviour (initiation, continuation, maintenance and habit-shaping). This will include a number of activities:

- development and evaluation of effectiveness of interventions that support maintenance and habit formation of behavior change;
- extend this for people with low socio-economic position;

- focus on dietary interventions suited for people from non-Western cultures;
- communication and coaching by the practice nurse of patients with T2D;
- combine behavior change and dietary knowledge (biology and psychology of eating);
- use the social environment to change behavior, like a social network and a community approach.

4 - Models

In lifestyle related health, a large body of studies has been performed and data and knowledge is available. Yet, this information is fragmented and scattered, and originate from non-personalized intervention and observational studies, i.e. need to be transformed for personalized health purposes. For this purpose, models (theoretical tools that describe and predict aspects of human health) are useful as advice systems, predictors of therapies, simplifiers of complex biology and methods to exploit multidisciplinary knowledge. A number of modeling approaches will be developed, exploiting fundamental technologies in connection to personalized health, pharma and drug development, lifestyle as medicine, child health, and other application areas. These are described below. The outcome of these models will be applied in personal health advice systems and as such tested and validated in the R&H community (see 1).

- Data Driven Predictive systems modelling

A new generation of personal health advice models will be designed and built for clinically relevant outcome measures, as current models were not designed with predictive health in mind. The predictive models will initially focus on type 2 diabetes related biological (mostly metabolic and inflammatory). Lifestyle and behaviour related models will focus on behavioural change and maintenance as well as prediction of compliance and adherence. The " care2cure" research community (see below) will provide a living lab for testing and optimizing these models. Algorithms proven to be successful in the development phase will be added to a growing portfolio of data mining and advice tools that will help this community to improve their health. Visualization methods fine-tuned to the user groups will be developed and included.

- Metabolic-Inflammatory Networks

TNO has developed a large number of diagnosis-intervention combinations in the area of personalized health, and stored these in a knowledge system called NuSyBox. Also, TNO has a number of physiological models in the area of metabolic-inflammatory health and disease.
We will now combine these and create an innovative working model which systematically selects, proposes and visualizes personalized diagnosis-intervention combinations. The first target area is insulin resistance / type 2 diabetes, as prototype for other lifestyle-related metabolic-inflammatory health issues (complications of T2D, CVD, fatty liver, osteoporosis, intestinal disorders). This toolbox thus becomes a major TNO asset in the science and economy of "personal health services". The model will be extended to genetics, microbiome, socio-psychological and environmental aspects, and to application during various life stages (pregnancy and early life, child growth, healthy ageing).

- Health by Design modelling

Connected to the previous topic, fundamental bioinformatics models will be developed and implemented to gain mechanistic information regarding disease processes and associated co-morbidities, their age- and time-dependent progression, susceptibility markers (e.g. genetics) and intervention opportunities. This knowledge will allow exploitation to drug development, side effect prediction, "rare-lifestyle-disease" aspects, and diagnostics. Strategies will include disease-disease network modelling, text- and data-mining, omics-based data-mining technologies, in silico target and biomarker prediction, and connection to in vivo (mouse) models. The disease networks and predicted biomarkers will be valorised in "TargetTri", a drug target-oriented TNO knowledge base that is being developed together with pharmaceutical industry.

Use cases

Use cases are a minor but important part of the program, as they will help guide the development of the technologies by connecting them to concrete and societal and business opportunities. Use cases are always connected to TNO Roadmaps, and are positioned within the Joint Innovation Centre "Metabolic Health Innovations". The detailed programming will partly depend on the topics of the various PPS projects that are currently being shaped (i.e., gestational diabetes, on line glucose monitoring in newly diagnosed diabetics, etc.).

Three application areas are envisioned, under the umbrella of "lifestyle as medicine": in personalized healthcare, connected to various life stages and to various life environments.

- Healthy citizen - Lifestyle as Medicine

Integration of all technologies mentioned above into a personalized holistic approach and implementing this primarily in the Dutch healthcare system will allow the "care2cure" transition to occur, which is so desperately needed in the healthcare of lifestyle related diseases. Focus will be on the "Leefstijl als Medicijn" living cohort in Zuid-Holland.

- Growing up Healthy and Life stage related health

The ERP deliverables are deployed in a number of life stages: gestational diabetes, first foods (year 1 onwards), childhood obesity and metabolic syndrome, healthy ageing and elderly. Although each of these have unique needs, both the systems approach and the personal health data based advice systems are joint features.

- Healthy Worker

Work related health provides a practical use case as business-wise, these are among the first to adopt personalized health guidance with commercial benefit (productivity, sustainable employability, safety, prevention of calamities, prevention of burn out, etc).

The ERP will be embedded in the "TNO-LUMC Institute for Lifestyle Medicine", a strategic non-exclusive Joint Innovation Centre between TNO and LUMC, with the strategic objectives:

1. Unravel the personalized biology of all lifestyle related diseases (starting with type 2 diabetes)
2. Develop a (digital) ecosystem for lifestyle based health advice and sustained behavioural change
3. Implement Lifestyle Medicine in healthcare, economy and society, starting in The Netherlands

For each of the three objectives, we will create a series of Public Private Partnerships, of which a number are currently shaping:

- pre-terms: data-driven precision care
- Healthy toddler development (1-4 yr)
- "Co-creation towards Prevention"
- Lifestyle as Medicine (multinationals PPS)
- Regional integration in Lifestyle as Medicine (Focus on Zuid-Holland)

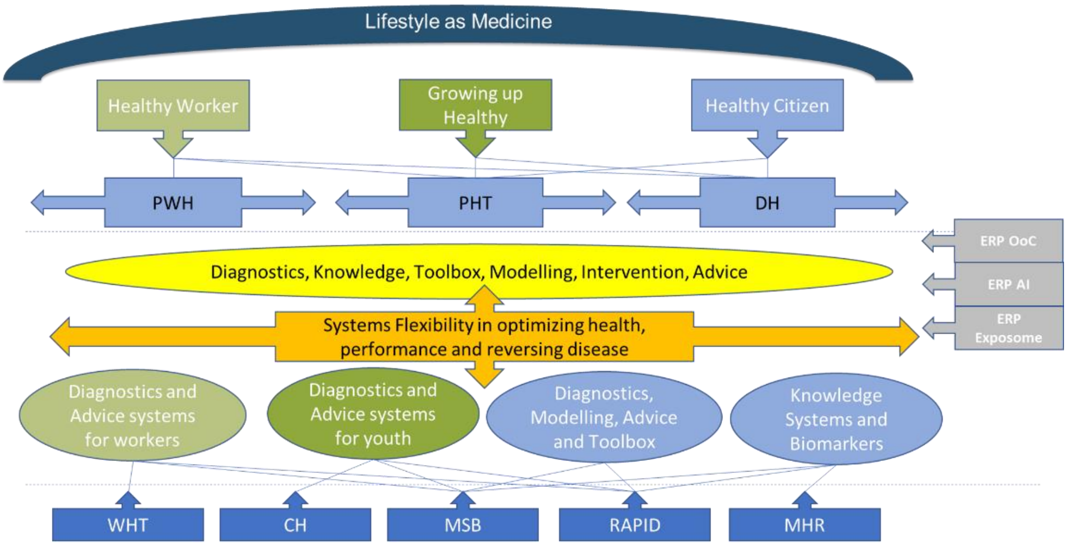


Figure 1 - schematic overview of the central positioning of this ERP in the new TNO LIFE Unit

Goals and deliverables 2021

Figure 2 presents all goals and deliverables of the ERP Personalized health. These can be categorized into for groups:

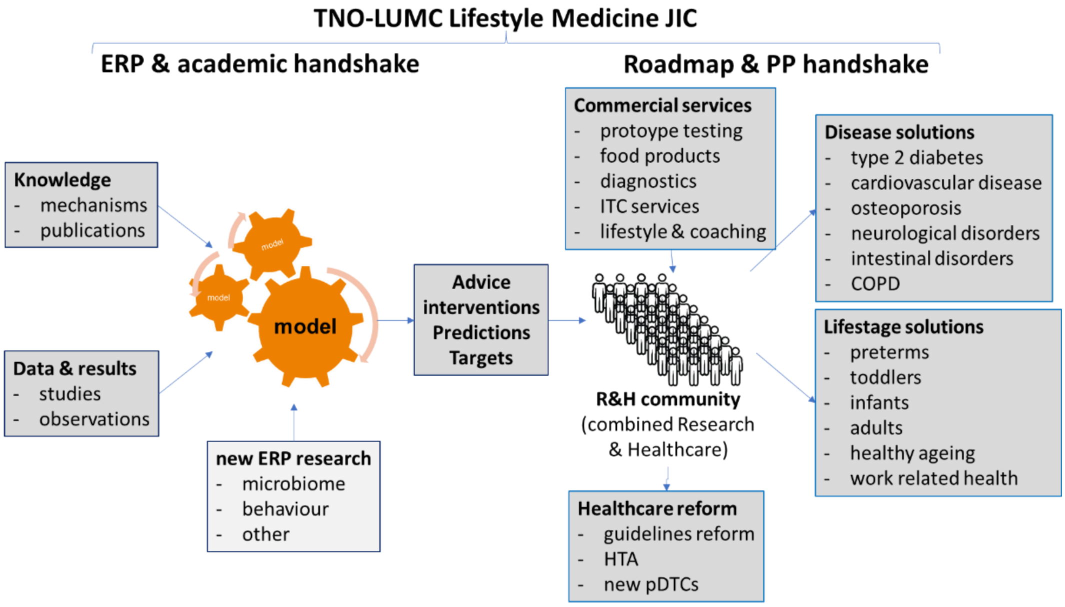


Figure 2 - Flow, dependencies and deliverables of the ERP Personalized Health 2018. Centrally positioned are the modeling and R&H community, which will exploit past and current research for exploitation in health economy and health care. Specifically, Lifestyle solutions will be provided for all major lifestyle related diseases and life stages

- **Commercial services to industry:** Prototype testing, personalized food products and services, personalized, non-invasive and continuous diagnostics, ITC services in the area of personalized health, and new services and companies in the area of lifestyle & coaching.
- **Healthcare reform":** The research will initiate new guidelines and accreditations in the area of personalized medicine, Health Technology Assessments (HTA) needed for the introduction of multiple practices and a new category of "personalize diagnosis-

	treatment combinations (pDTC). • **Disease solutions** in the areas of type 2 diabetes, Cardiovascular disease, Osteoporosis, Neurological disorders, intestinal disorders (IBD, Crohns), COPD and possibly others. • **Life stage solutions** for a range of specific age-groups (preterms, toddlers, infants, adults (connected to personalized nutrition), healthy ageing (connected to the disease solutions above), and work related health (shift work, burnout).
External connections	The ambitions in ERP Personalized Health fit very well to the need to better support citizens to be optimally resilient during the various stages of life, and in the wide range of health-threatening situations that occur therein. This requires further development and integration of personalized (or precision) diagnostics and intervention/advise/support technologies, making citizens increasingly self-sufficient while reducing health care costs. It is without question that the ERP Personalized Health connects very well with at least two routes of the NWA: “Gezondheidszorgonderzoek, preventive en behandeling” and “Personalized medicine: uitgaan van het individu”. This furthermore aligns nicely with the KIA of the various Topsectors. This ERP therefore appears to fit very well to a series of defined goals and as such many opportunities to establish cross-sectoral research consortia as PPP’s can emerge from this ERP : • For TopSector Life Sciences and Health these opportunities reflect in the Roadmaps 3 (Homecare and Self-management), 5 (Pharmacotherapy), 6 (One Health), 7 (Specialised Nutrition, Health and Disease), 8 (Health Technology Assessment, Individual Functioning and Quality of Life) and 9 (Enabling Technologies & Infrastructure). • In the care2cure ambitions of the ERP, efforts will be focused in shaping PPPs to collectively combat T2D, both by developing effective cure strategies and by strengthening systems prevention efforts. Companies will be contracted to build research and implementation coalitions that are fundamental for changing health economy from care into cure. This requires broad spectrum participation of companies (large and small, pharma and food, health insurance and health providers, diagnostics and ICT, physical activity and mental coaching, etc) as well as participants and stakeholders from the care chain (from GPs to academic hospitals), local governments and patient organizations. • With Topsector AgriFood, this ERP defines several cross-sectoral ambitions in the field of nutrition and personalized health, especially focusing on target consumer groups (infants, pregnant women, elderly people, diabetics and other life style related diseases). Insofar existing and new customers active in the food production chain aim to contribute the health agenda of the ERP, they will be invited to join in PPPs. • The Topsector Chemical Industry has identified various intersections between their KIA and the EU Research Theme 1 (Living Longer and Healthier), implying that many cross-sectoral research opportunities are apparent from this ERP with industries and knowledge institutes of this Topsector. • For the Topsector High-Tech Systems and Materials, the ERP has a number of links with their “Health, demographic change and wellbeing – Personalized health” agenda in which various industrial sectors are listed. • Finally, the Topsector Creative Industry stipulates that Healthy Behavior, Quality of Life and Well Being as well as Human Empowerment are important themes in their KIA. Their largely ICT-based industrial background can show to be an important contributor to the goals of the ERP.

Program development	This Early Research Program builds on • A number of TNO research activities in the area of personalized health, which together deliver a prototype "Life Companion" in self-empowerment and shared decision making in lifestyle related health. • A number of external innovations which can be incorporated into the TNO "personalized systems flexibility" portfolio (microbiome, specific behavioural change technologies, big data based algorithms) • Recent developments at TNO towards the creation of a single knowledge IT-system that increases the efficiency, synergy and valorization of knowledge gained from projects surrounding this ERP. • The shaping of the "Joint Innovation Center Metabolic health Innovation", which allows for a pipeline of fundamental research to applied research to implementation • The major societal and economic shifts towards personalization, self-empowerment, and an organisational system transition towards prevention, and the positioning of TNO in this shift as one of the game changers.
Activity plan 2018	The first year of this new strategy period, the ERP Personalized Health aims to build the foundations of the proposed innovation methodology (see Figure 2), by constructing a prototype framework connected to three use case (type 2 diabetes in healthcare, toddlers in life stage related health and shiftwork in work related health). For each of these, all four technologies need to be included. Here, a generic technology basis (bio-passport and personal health data environment, advice system based on modelling, knowledge exploitation by biological networks, microbiome-health component by inflammatory robustness and modulation) is present. The ICT component will be provided by the relevant Roadmaps. Use-case specific aspects will be developed in collaboration with academic and commercial partners. For the various technology work packages, this translates in the following: • Research methodology Innovation: set up the "Lifestyle & Research Community" cohort and develop the methodology to combine research and personalized healthcare. Develop first generation models which exploit subgroup similarities for personalized health advice. Establish working relationships with the relevant stakeholders (local healthcare partners, diagnostics, ICT, etc.) and implement practical protocols. • Microbiome: Develop an approach to quantify microbiome function (microbiome challenge test) in relation to human health. Broaden current knowledge base with microbiome data. Diagnose and visualize microbial health • Behaviour Change: develop interventions supporting maintenance of behavior change. Include behavioural coaching focusing on short term rewards, intense initial guidance, shared decision making. Produce health literacy tailored visualization and information. Include Ecological Monitoring and Assessment / Interventions. Establish a prototype "just in time adaptive intervention" protocol. • Models: Further develop current advice models with predictive health models. Combine models for diagnosis-intervention, metabolic-inflammatory health and disease and co-morbid diseases. develop models for predictive health, diagnosis-interventions, metabolic-inflammatory health and co-morbidity.

5 Energy Storage and Conversion

General data	
Title	ERP Energy Storage & Conversion
'Topsectors'/Societal Themes	Chemistry, Energy, HTSM / Circular Economy
Contact person TNO	Ardi Dortmans; Esther Zondervan
Contact person government	Mariëlle Beers-Homan (EZ)
Program 2018 – 2021 and activity plan 2018	
Abstract	Energy Conversion and Storage becomes more and more important to achieve an increased use of durable energy. In recent years we made good progress in our search for new conversion and storage processes and we wish to continue these developments in close cooperation with industry, knowledge partners and government. Our focus will be on Solar-to-Fuels processes that convert electricity from renewable sources (solar, wind) or sun light directly into energy that is stored in chemical bonds (fuels): electron-to-fuels and photon-to-fuels. Routes to come to cost efficient Solar to Fuels production processes will thus be pursued to come to demonstration of feasibility and upscaling. We will focus on processes that convert CO_2 into fuels and base chemicals. Typical goal for 2021 is an efficient production process for carbon based fuel at a cost of 800 Euro/ton, a cost estimate based on indirect conversion of CO2 to methanol via hydrogen (with a hydrogen cost price of 4 euro per kg and CO2 price of 40 euro per ton). https://www.tno.nl/nl/samenwerken/expertise/early-research-programma/ http://www.voltachem.com/ http://www.grensregio.eu/projecten/co2-voor-energie-opslag-enop
Description	**Context** A strong acceleration is needed to timely transform the Dutch energy landscape from the current fossil fuel based one to a CO_2 neutral renewable energy infrastructure based on the goals as set by COP21 and 22 (UNFCCC),[7] and accorded by the EU (RED)[8] and the Energieagenda[9]. In the next 20 - 30 years, the way how energy is generated, stored, supplied, priced and sold will be fundamentally different from the current approach. A key step in the transformation to a renewable energy infrastructure is the conversion of renewable energy sources such as solar and wind into usable energy forms such as electricity or fuels[10]. Due to the intermittent nature of these renewable energy sources, however, there is a strong need to store energy on a large

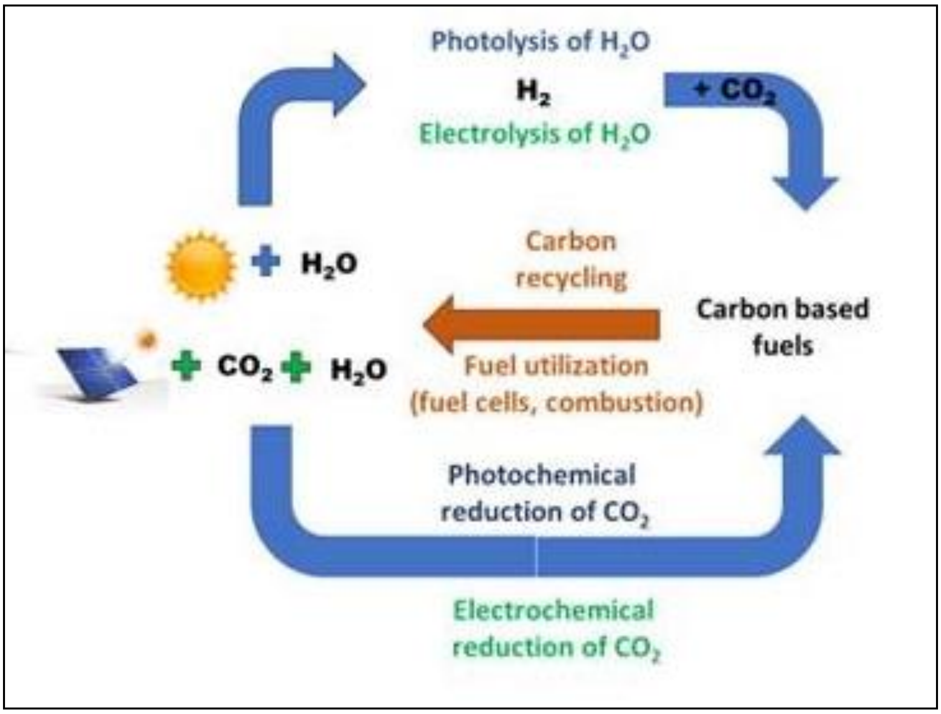
[7] Marrakech Action Proclamation for Climate and Sustainable Development (UNFCCC, 2016), https://unfccc.int/files/meetings/marrakech_nov_2016/application/pdf/marrakech_action_proclamation.pdf
[8] Directive 2009/28/EC of the European Parliament and the Council (European Union, 2009), https://ec.europa.eu/energy/en/consultations/preparation-new-renewable-energy-directive-period-after-2020
[9] Energieagenda (Dutch Ministry of Economic Affairs, 2017), https://www.rijksoverheid.nl/documenten/rapporten/2016/12/07/ea,
[10] Adviesrapport Electro Chemische Conversie en Materialen (ECCM), september 2017

scale in a cost efficient manner. Based on its high storage density, rather low cost, flexibility in use for various applications, and ability of use in the current infrastructure, conversion of renewable energy to fuels would be an ideal solution. It is to be expected that significant amounts of fuel are needed for e.g. the heavy transport sector and the chemical industry. *Therefore, an important aim of this ERP is to support and accelerate the development of techniques to convert CO_2 and water into carbon based fuels using electricity and/or sunlight (photons) as renewable energy source.*

In the next 30 years the energy sector and chemical sector will be closely integrated. The transition to this new way of producing fuels and platform chemicals from CO_2 is high on the political (e.g.. Min. EZ), regional (e.g. harbour of Rotterdam, Chemelot, Brainport), and industrial agendas (e.g. topsectors HTSM, energy and chemistry, and companies such as Shell, Avantium and Akzo). For instance, the Rotterdam Harbour is preparing itself for the impact of the availability of 90 GW of renewable energy coming from North Sea wind power, and at the same moment evaluates the effect of the “energieagenda” on the industrial symbiosis at the Harbour region.

Approach

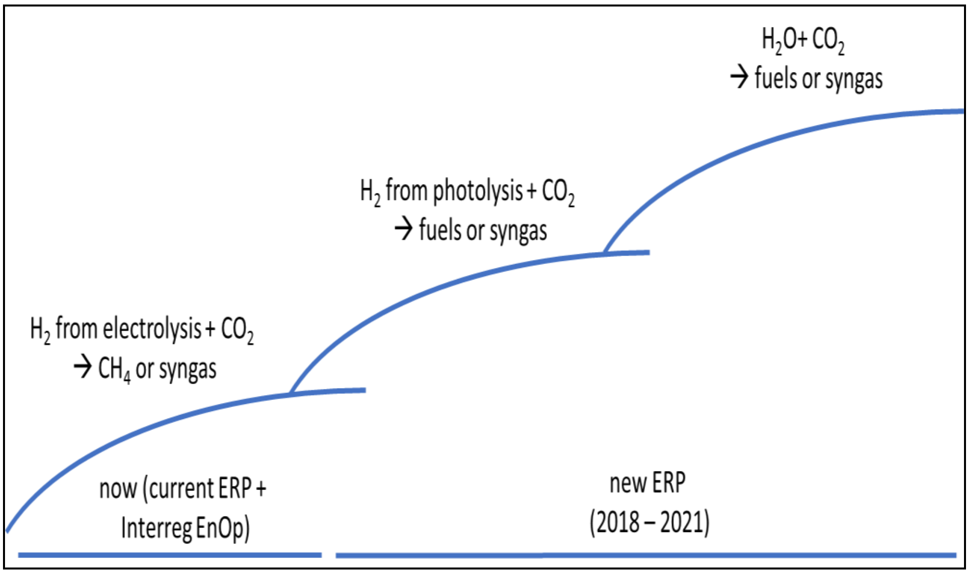
Based on the research within the ERP Energy Conversion and Storage in the period 2015-2017, we have identified two attractive routes towards hydrocarbon based fuels. These two routes are highly interconnected. In the figure below, these routes are depicted schematically. The first route (indirect) is based on generation of renewable hydrogen, and the subsequent reaction of this hydrogen with CO_2 towards hydrocarbons. The second route (direct) is based on the direct conversion of CO_2 and water towards hydrocarbons. The technology related to these routes is based on electrochemistry (direct: electrochemical reduction of CO_2, indirect: electrolysis of water) and on photochemistry (direct: photochemical reduction of CO_2, indirect: photolysis of water).



Scope for the Solar to Fuels research activities in the period 2018-2021.

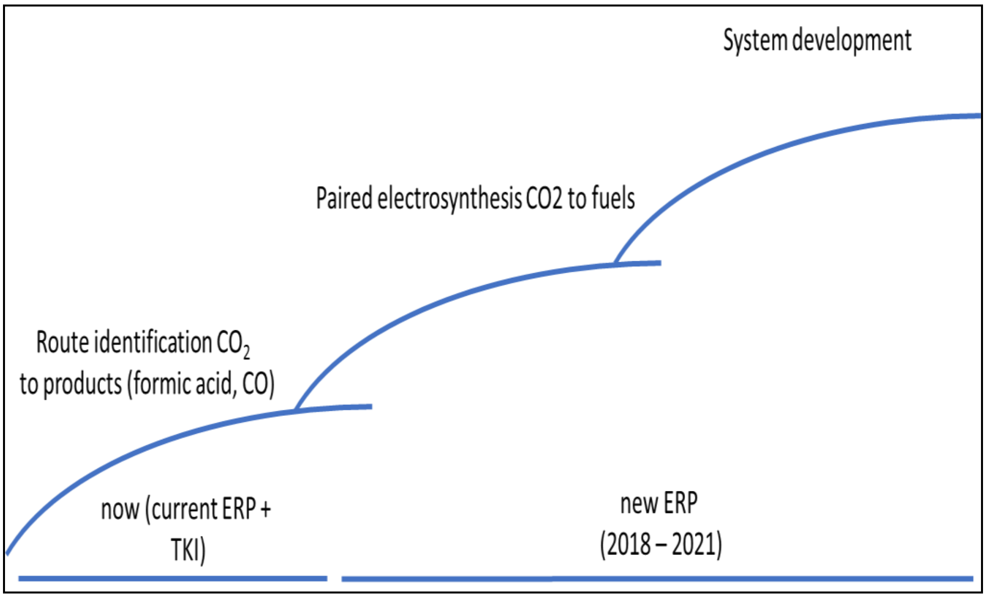
Photon to Fuels

Photolysis of water has a good perspective on the long term for cost effective production of hydrogen. The subsequent reaction of CO2 with this hydrogen can be done photochemically or with “conventional technologies”. Based on the knowledge obtained on photolysis the technology development needed for direct photochemical conversion of H2O with CO2 can be accelerated as a breakthrough development.



Electricity to fuels

TNO’s paired electro-synthesis concept based on CO2 can decrease cost of fuel production by more than 40%. System development is a key issue: reactor design integrated with separation is the breakthrough development.



The two technologies, photon and electron based, are strongly interrelated. Only the way of generating charge carriers for chemical conversions is different. After the charge carriers are generated, the following catalytic conversions are very similar. Similar types of catalysts are used, and process related questions are comparable.

	Conversions may even combine both photochemistry and electrochemistry in photo-electrochemical conversions. The integration approach with the current industrial sector is as well quite similar, and the industrial stakeholders/customers for both technologies are the same. This has already led to the establishment of one joint academic /advisory group guiding the research in the ERP EC&S 2015-2017. The whole field of energy storage and conversion is evidently larger than the proposed core of this ERP. Continuous attention for new promising developments is required to prepare for better or alternative solutions. This ERP will explore such new technologies, also to provide options for continuous renewal. Examples could include new storage and conversion technologies: heat storage, batteries, solar roads etc. **Academic network** A special academic/industrial commission ECCM on instigation of the topsectors HTSM, Energy and Chemistry has been established with the main task to advise the topsectors and the Ministry of Economic Affairs on a multiyear research program on solar fuels. There is currently already a strong network between the TNO groups active on solar fuels and the following universities: Utrecht, Leiden, Twente, TU/e / DIFFER, RWTH Aachen, Hasselt, TUD, 'Hogelschool' Zuyd, which was established in the framework of the ERP program 2015-2017 (exemplified by joint NWO, Interreg (VITO) and TKI projects). TNO is active member of this ECCM committee. ECCM is established as a Key Technology for the KIA/KIC 2018-2019, with strong links to various top sectors, NWA routes, societal challenges and other Key Technologies. The activities in this ERP will contribute to the formation of this network and related research programs such as Voltachem. **Transfer to VP** This ERP has close connections to the demand-driven programs VP Chemistry and Sustainable Energy as well as VP Buildings & Infrastructures. The Solar-to-Fuels activities have resulted and will result in transfer of IP, knowhow and networks to these VPs. The close collaboration in Voltachem, EnOp, ECCM etc. are good examples for this. For the next years the existing cooperation with ECN will be expanded in view of the integration of TNO and ECN.
External connections	Relevant external connections for this ERP are (see also above): • Societal Challenges: Energy and CO_2 • Key Technologies: Electrochemical conversion and materials, Advanced Materials NWA routes: Energy Transition, Circular Economy and Resource Efficiency
Program development	In the ERP period 2015-2017, we demonstrated the concept of plasmon-assisted photochemical conversions for the production of chemicals and fuels. Examples of realized plasmon-assisted conversions are Suzuki C-C cross-coupling reactions and hydrogenation of CO_2 to CH_4. For these conversions, we applied Pd decorated Au nanoantennae and metal oxide supported Ni catalysts, respectively. Preparation and characterization of such materials were an important part of the program, as well as the development of suited reactors for controlled photochemical conversions. In 2016 / 2017, we decided to fully focus on conversions of CO_2 to fuels using photochemical hydrogenations. When investigating the business cases of these conversions, however, we noted that they were heavily dominated by the price of green hydrogen coming from electrolysis. Reason for this is the direct coupling of the cost for hydrogen to the electricity price. For that reason, major focus of the ERP in 2018-2021 will be on

	photochemical splitting of water for the production of hydrogen (photolysis). This has the potential to produce hydrogen at lower costs, and decoupled from the electricity price, which we anticipate will make the business cases for photochemical hydrogenation of CO_2 more attractive. In the second stage of the ERP 2018-2021, we will aim at expanding our portfolio with direct photochemical conversions of CO_2 and H_2O to fuels. The established infrastructure and the acquired knowledge on synthesis and characterization of catalytic materials in the ERP 2015-2017 form an excellent starting position for the ERP 2018-2021. We will furthermore actively seek collaborations with academic and industrial partners, in analogy to the ERP 2015-2017. Related to electron to fuels, we have demonstrated the concept of using electrons for selective oxidation and reduction reactions for a wide range of added value chemicals and fuels. The main emphasis has been on process development of selective conversion of bio-based feed materials and CO2. The strategy for knowledge development was directed to a system approach, taking into account electro-catalysis, electrochemical engineering and separation technology. This combination of knowledge fields can be considered as quite unique for Europe. Breakthroughs have been achieved by cross fertilization of the above mentioned fields. Development of a so-called paired electrolysis concept (i.e. producing value added chemicals simultaneously at the anode and the cathode) has shown that it is in principal possible to reduce capital cost by 40% and increase electron efficiency to 150%. In the first part of the ERP 2015-2017, the focus was on creating and demonstrating the needed knowledge infrastructure using as showcases the production of value added polymer starting material (FDCA and lactic acid) based on the conversion of sugar and glycerol derived starting materials. To develop the paired electro-synthesis concepts, novel type of electrochemical reactors have been made for the production of hydrogen peroxide from water and oxygen. In the second part of the ERP, nanostructured electro-catalysts have been made based on copper and gold, showing that it is possible to produce carbon monoxide (one of the precursors needed to make carbon based fuels) selectively. To reduce overall cost, the first investigations have been made to integrate the capturing of CO2 with the electrochemical conversion. In the next phase, 2018-2021, the already obtained knowledge will be further expanded towards integrated CO2 capture and conversion processes based on the paired electrolysis concept.
Activity plan 2018	For 2018 our research activities will fully focus on: • Preparation and validation of new catalysts for the photochemical hydrogenation of CO_2 to CH_4 and CO (potentially also formic acid). • Inventory of existing catalysts for photochemical water splitting. • Testing of state of art catalysts for photochemical water splitting. • Development of electro-catalyst which can convert CO2 directly from a CO2 absorption liquid. • Anode development for electrochemical conversion: Selection of appropriate anodic reaction which can be used in the already developed paired electro-synthesis concept. • System approach: Proof of concept - demonstrating the paired electro-synthesis concept. • Dissemination of results in various networks, including a dissemination event for this ERP end September 2018.

6 3D Nanomanufacturing Instruments

General data	
Title	3D Nanomanufacturing
‘Topsectors’/Societal Themes	HTSM
Contact person TNO	Hamed Sadeghian, Nicole Nulkes
Contact person government	Mariëlle Beers-Homan (EZ)

Program 2018 – 2021 and activity plan 2018

Abstract

Introduction

For many years the main driver to develop and improve nanomanufacturing processes, instruments and materials where initiated by the demand for new smartphones, tablets, personal computers and servers. Recent growth and future expected growth in the wearable electronics and to a larger extent the growth of the internet of things scales up the demand for new innovative nanomanufacturing processes and instrumentation. Figure 1 shows the drivers for Moore’s law, the law of scaling of devices in nanomanufacturing processes.

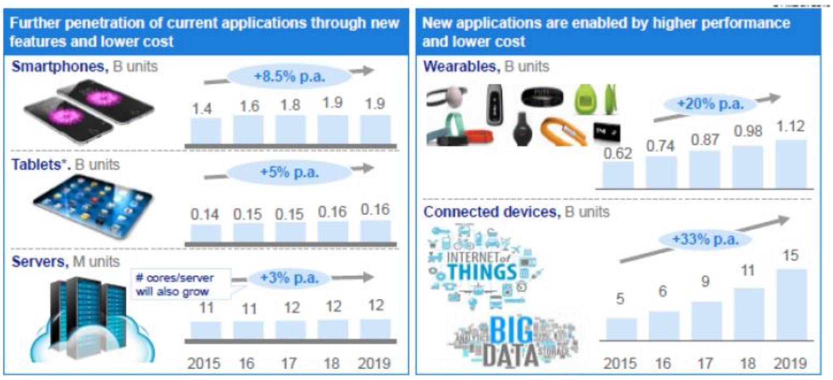


Figure 1:Market drivers for Moore’s law, source: Gartner 2016.

Currently in 2017 there are 8.4 billion connected devices and by 2020 this will scale up to 40 billion, as predicted by and shown in Figure 2.

Figure 2:8.4 billion connected device 2017, by 2020:40 billion.

Augmented and virtual reality devices (wearables and transmission of video data) boost the need to store and process information in the range of petabytes.
All these developments require the continuation of Moore’s law in scaling the dimensions and the further development of 3D architectures such as Gate All Around nanowires FETs (GAA) and 3DNANDs. The developments of these nanodevices highly depends on the 3D nanomanufacturing processes and nanometrology systems

and methods to control yield of the devices. *Figure 3* shows the evolution of iPhone and iPad by the Moore's law.

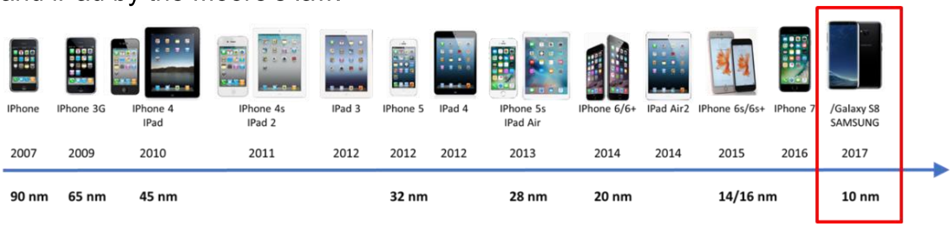


Figure 3:Scaling down and 3D architectures as innovation driver for Smartphones.

Besides the technology development, this program managed to initiate and establish an innovative ecosystem that consist of leading industrial partners, academia and research institutes.

Main Objectives for 2018-2021

To bring potential solutions to the nanometrology and nanotomography challenges mentioned, strategic period (2018-2021) will focus on the following topics.

1. Nanometrology and nanotomography:
   a. 3D nanometrology focusses on 1 nm resolution, mainly for gate all around nanowires as next generation nanodevices and
   b. Subsurface nanoimaging and quantum sensing focusses on resolving the depth of features.
2. Nano-motion control and Dynamics
   a. This platform focusses on accuracy and throughput increase which is extremely important for adaption of the developed techniques by industry.
3. Establish with our academic and industrial partners an excellent innovation center to serve R&D for 3D nanomanufacturing and nanometrology.

Description

Program 2018-2021

The industry is further increasing the complexity of 3D nanoarchitectures, besides just scaling down towards below 5 nm. As an example, recently IBM, its Research Alliance partners Global Foundries and Samsung, and equipment suppliers have developed a new transistor architecture based on stacked silicon nanosheets that they believe will make Fin FETs obsolete at the 5nm node. Compared to Fin FETs, the new architecture consumes far less power, according to the researchers. As it can be seen in figure 4 these structures are nanostructures of only 5 nm stacked on top of each other.

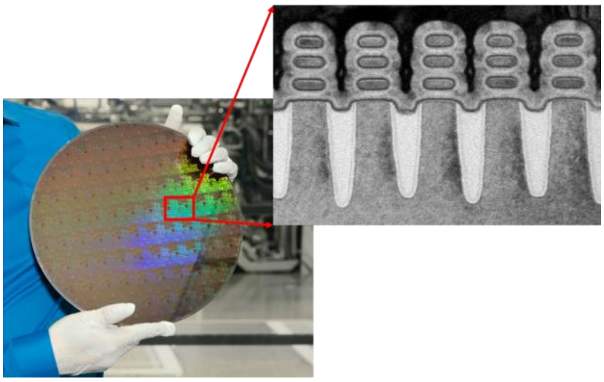


Figure 4: IBM developed a wafer of chips using 5 nm silicon nanosheet transistors. The figure is courtesy of IBM.

The roadmap for future of 3D nanodevices show drastic increase in the complexity, i.e. the number of layers are increasing from 64 to more than 256 layers, as shown in figure 5.

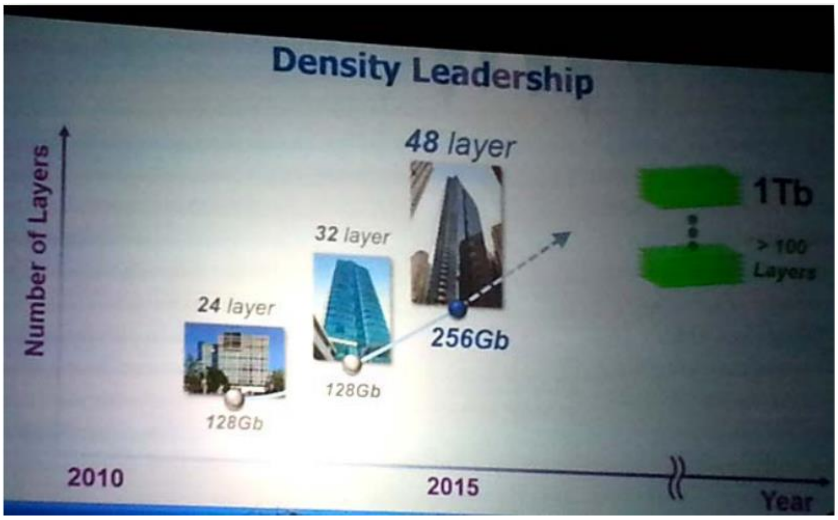


Figure 5:Vertical 3DNAND roadmap of Samsung, showing the number of layers will increase to more than 100 layers to reach 1 Tb capacity.

To be able to keep up with this roadmap and similar ones on other type of 3D nanoarchitectures, several technical challenges have to be resolved.
In terms of nanometrology, inspection and Nano characterization, figure 6 shows an overview of the applications.

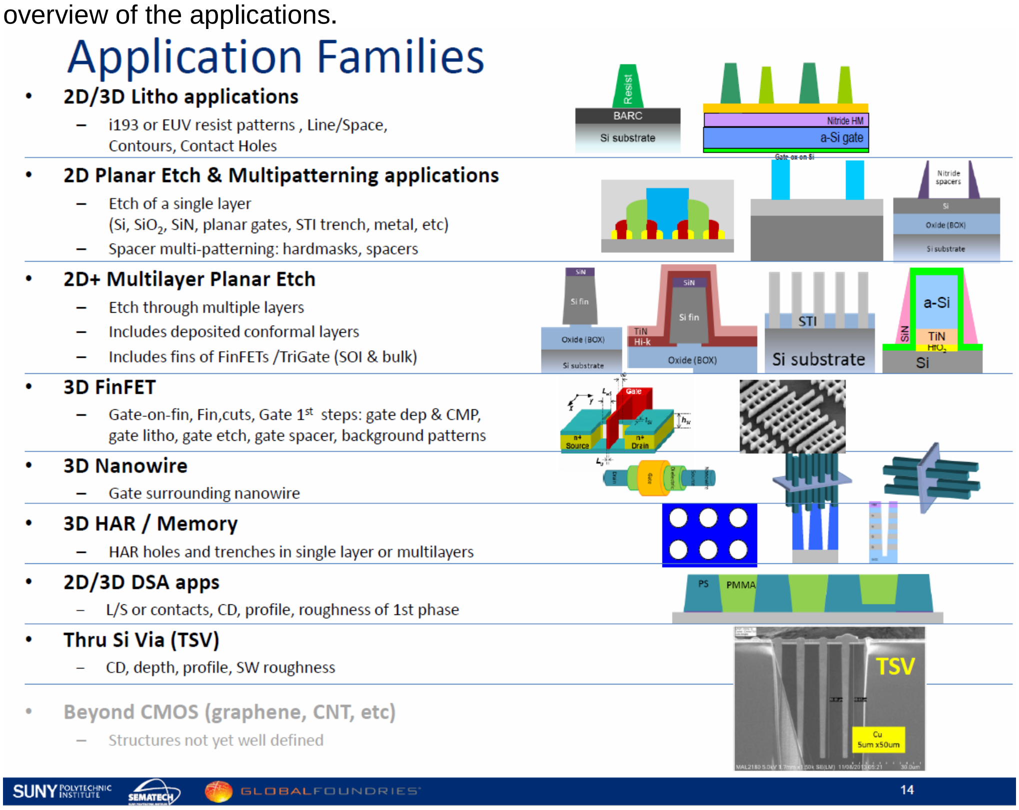


Figure 6: Application challenges for metrology and overlay.

There are still several technological gaps. Together with the partners in our ecosystem we plan to bring solutions for the future nanomanufacturing challenges of industry. Our Targets are:

1- **Nanometrology and Nanotomography**

a. Alignment through opaque layers,

b. Overlay measurement
c. Failure analysis
d. Depth analysis of 3D complex structures such as 3DNAND and Gate-All-Around Nanowires FETs
e. Quantum sensing, a new technique for atom-scale characterization of nanostructures. The quantum sensing allows to reduce the noise of the measurement below the thermos-mechanical noise of the system.

2- Nano-motion control and Dynamics
Accuracy and throughput increase which is extremely important for adaption of the developed techniques by industry.

Strategic collaborations
Spin-off company Nearfield Instruments
Our focus is to capitalize the knowledge generated in the ERP. Nearfield Instrument, a partner of the ERP ecosystem was launched by TNO to bring atom-scale metrology solutions, developed in ERP (2015-2017) to the semiconductor industry. Major investment in Nearfield Instrument, by leading Semiconductor Industry Samsung Electronics, has shown the relevance of our technology. The next step is to further enhance
1- An incubation program to generate more (joint)ventures and to
2- Further establish a long term joint development program with several industrial partners like Samsung Electronics.

For development of our strategic collaborations the ERP 3D Nanomanufacturing has the following objectives for 2021.
1- NOMI JIC, together with Technical University of Eindhoven,
2- Joint development with Adama Innovation, a manufacturing company for diamond probes, which are required for nanotomography.
3- Joint development with Smart Tip, From University of Twente, for integrated sensors and actuators which are required for nanotmography
4- A joint project(STW Perspectief) with ARCNL (Prof. Paul Planken and Prof Stefan Witte) on nanotomography for optically opaque media
5- Collaboration with Toshiba, on bringing the nanotomography development for memory applications
6- Collaboration with Intel on Solid Immersion Lens and Plasmonic nanoantenna, for single nanometer metrology
7- Further enhancing the collaboration with Samsung on various topics related to nanometrology and nanotomography.

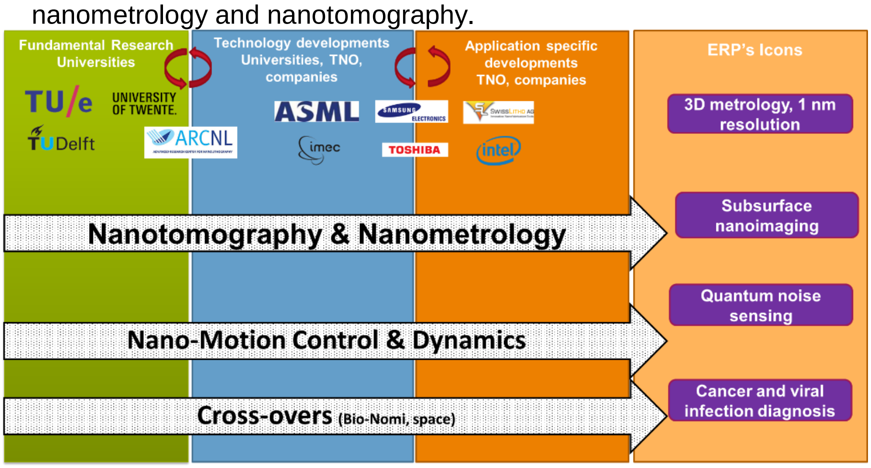


Figure 7:Technology platform and the current industry and academia involved.

<table>
<tr>
<td>External connections</td>
<td>The ERP 3D Nanomanufacturing Instruments and the Top Sectors and NWA
The topics of the Early Research program are addressed in Top-sector roadmap “Semiconductor Equipment” and the NWA “Route Quantum and Nano”. The challenges of 3D nanometrology and nanomanufacturing are mentioned in the roadmap as a result of “more Moore”. Metrology and characterization techniques are relevant to manufacturing industry, because miniaturization of features require new and innovative imaging techniques. The NWA route Quantum and Nano explicitly mentions the challenges of nanomanufacturing processes and the quantum sensing as a method to further enhance the resolution and sensitivity in characterization techniques.</td>
</tr>
<tr>
<td>Program development</td>
<td>Main achievements of ERP 3D Nanomanufacturing (2015-2017)
To support the development of 3D nano-electronics the ERP 3D nanomanufacturing (2015-2017) has developed key technologies on instrumentations, processes and techniques for manufacturing and metrology of nanostructures. Examples are:
1- High throughput scanning probe microscopy for nanometrology applications 10 nm resolution.
2- Mask-less nanopatterning technique for 10 nm structures
3- Subsurface nanoimaging for alignment, overlay and buried defect applications

Main Objectives for 2018-2021
To bring potential solutions to the nanometrology (and nanotomography) challenges mentioned, strategic period (2017-2021) will focus on the following topics.
1) Nanometrology and nanotomography:
a. <u>3D nanometrology focusses on 1 nm resolution</u>, mainly for gate all around nanowires as next generation nanodevices and
b. <u>Subsurface nanoimaging and quantum sensing</u> focusses on resolving the depth of features.
2) Nano-motion control and Dynamics
a. This platform focusses on accuracy and throughput increase which is extremely important for adaption of the developed techniques by industry.
3) Establish with our academic and industrial partners an excellent innovation center to serve R&D for 3D nanomanufacturing and nanometrology.

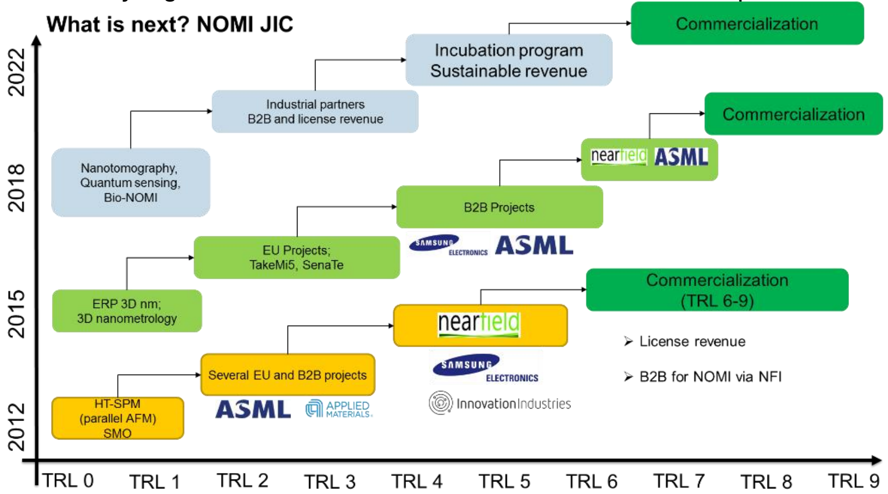
In summary, figure 8, below shows the current and the next steps:


Figure 8: Current and future steps.</td>
</tr>
</table>

Activity plan 2018	Objectives and deliverables 2018 • Subsurface SPM: research will be done on improving the depth sensitivity, the signal to noise ratio, to be able to image subsurface structures with higher contrast. That is required for several applications in nanoelectronics. Especial attention will be given to new actuation and detection methods such as integrated piezo and photo thermal actuation. Further enhancing the collaboration with industrial and academic partners will be done. Especially the target is together with ARCNL to have a collaboration on subsurface nanoimaging technique. • Photo-thermo-acoustic imaging: the experimental proof of principle setup will be ready in 2018. Experimental test will be performed to verify the functionality of the system. Again here this is a topic of the collaboration with ARCNL and TU/e. Several industrial partners are included (names are omitted due to confidentiality) • New nanotomography techniques and spectroscopy such as microwave nanoimaging, quantum sensing, Kelvin probe microscopy and photo-induced subsurface imaging will be studied. A feasibility and trade-off will be done to determine the applicability, pros and cons compared to existing subsurface techniques. We need to develop the concepts for quantum sensing for nanotomography. For this a collaboration with Qutech will be established. Moreover for microwave sensing a collaboration with the TNO Radar group will be required. • Optical metrology: further feasibility on nano-antennas and computational optics will be pursued, with a go-no go decisions every 3 months to find the uniqueness for TNO. • STED nanomanufacturing: further feasibility study (continuation of 2017) will be done to determine 1) do we have a feasible process for high throughput STED? 2) do we have a high throughput instrumentation concept? Industrial partners such as Samsung are being approached and this topic is being discussed to evaluate the interest from the industry. • NOMI JIC: We target to have NOMI JIC up and running (operational) in 2018. Aim is to include industrial partners in 2018. • Towards end of 2018 we will again organize the dissemination event together with industrial and academic partners.

7 Structural Integrity

General data	
Title	Structural Integrity
‘Topsectors’/Societal Themes	Energy, HTSM / Infrastructure & Environment, Defence
Contact person TNO	Henk Miedema
Contact person government	Mariëlle Beers-Homan (EZ)

Program 2018 – 2021 and activity plan 2018	
Abstract	 Early research program Structural Integrity (ERP SI) strives to make important macro-structures (e.g. in the transport and energy infrastructure, defence vehicles) safe and perform optimally at the lowest possible cost to society. ERP SI does this by adding intelligence to these structures. These structures will assess their condition by themselves, forecast their future state and, based on that, will signal the need for action. They will propose action plans, including suggestions for specific inspections and maintenance. In addition and closely related, is the aim of using the knowledge acquired in developing intelligent macrostructures for improving the structural design and investigating the potential of applying new materials in macrostructures. Reaching this advanced stage will require further developments with regard to (1) new sensing techniques, (2) advanced structural degradation modelling and reliability calculation methods, and (3) system integration. The approach is to develop the technology in the context of use cases which will make clear in which practical circumstances and requirements the technology must prove itself. Present four use cases are concrete bridges, offshore wind support structures, (abandonment or reuse of) gas wells, composite military multi-purpose vehicles) New use cases will be developed around the most important construction materials: concrete, steel and composites. In the 2018-2021 period ERP SI will create the first virtual twins of macrostructures that have the intelligence needed for self-assessment and forecasting their future state. These virtual twins then will be used in field sites demonstrating their capabilities and exploring further their potential.. In 2018 ERP SI will instrument field sites for validation and demonstration of elements of the technology ultimately needed with respect to the existing use cases, which will be used as an important basis for further research and development.
Description	**Context** The yearly expenses for the transportation and water infrastructure in the Netherlands are estimated to be 6 billion euro. Considering that most of transportation (infra)structure has been built in the 1960s & 1970 (water management structures on average 30 years earlier), and approach the end of their design life time, i.e. their integrity is becoming a serious concern for the asset owners and users. Without a paradigm shift in the asset

management of these macro-structures, the cost of our transportation and water infrastructure will rise sharply in the near future.
Wind energy is an important component of our future, sustainable energy system. Huge investments in the North Sea area are foreseen in order to meet the goals with respect the contribution of wind energy to the sustainable energy supply. The cost of offshore wind structure operation and maintenance, however, need to be brought down considerably in order to be able to compete in the coming decades with oil and gas.
Obsolete fossil energy infrastructure must be abandoned securely and safely, or given a second life as part of the sustainable energy system. This requires a thorough assessment and long-term forecast of their condition in order to be able to safely abandon wells or give them a future use for geothermal energy or storage of compressed air.
The development and use of new materials requires the ability to measure and predict the material behaviour over long periods of time, and, e.g. in the case of application in defence vehicles, under extreme conditions. Such developments are needed for military vehicles in order to meet the requirements of weight reduction while still providing the same level of protection against blasts and projectiles.
The need for condition based asset management can be illustrated with recent real life examples. Because of the unexpected closing of the Merwede bridge due to issues with its structural integrity, for over two months no trucks were allowed to cross the bridge. This restriction caused large traffic jams, as well as financial losses for transportation companies. With a rapid maintenance operation the bridge was repaired[11].

In the future intelligent macro-structures will self-assess their condition, forecast their future state and, based on that, will signal the need for preventative or corrective measures and, propose an action plan, including inspection and maintenance activities. This action plan then needs to be considered in the wider context of the management of the asset. Thus an asset needs to be equipped with capabilities for determining its current as well as for predicting its future state, for deciding what measures are optimal (with regard to cost, performance and risk) and for providing on the basis of these insights an action plan with regards to its use and maintenance.

Goals
The ERP SI aims at developing these capabilities with the purpose of safeguarding structural integrity of high value macro-structures (e.g. bridges, offshore wind, geo energy wells, military vehicles etc.) while reducing service life costs and maximizing the performance (e.g. availability) of the asset. In the next four years period the focus will be on degradation processes and their effect on reliability and service life, and on incorporation of the knowledge in instruments for Condition Based Asset Management. In addition and closely related, is the aim of using the knowledge for improving the structural

[11] https://www.rijkswaterstaat.nl/wegen/wegenoverzicht/a27/merwedebrug/index.aspx

design and investigating the potential of applying new materials in macro-structures. The ultimate goal for the technical development is to create Digital Twins of macro-structures enabling Condition Based Asset Management & Experience Based Design Optimization. This will require further developments with regard to (1) new sensing techniques, (2) advanced structural degradation modelling and reliability calculation methods, and (3) system integration. The ERP SI goals are:

- Field sites for validation and demonstration of *sensor-model system for representing an existing structure*. Main challenges will be selection of relevant data for condition identification, assimilation of data in the structural degradation modelling and reliability calculations, optimisation/reduction of computation time and effort incl. advanced simulation techniques, virtualization & high-performance computing.. The deliverable will be field sites demonstrating separate functionalities.
- First *3D demo of a virtual twin of a structure* assessing the present condition on the basis of a sensor-model system. A main challenge will be coupled probabilistic and nonlinear numerical modelling incl. model selection and model updating based on relevant data.. The deliverable will be a demo of an integrated 3D virtual twin of a structure having all the features needed to assess its condition.
- *Regular updating* of structural reliability assessment and forecast. Main challenges will be integration of all sources of data and assimilation of data by the sensor-model system. The deliverable will be an advanced condition prognosis module.
- *Sensor-model system for representing a collection of structures*. Based on detailed data for a limited number of structures and limited data for the others, this system will assess and predict the state of the structures. The main challenge is to find a limited set of parameters that can be assessed for a large number of structures, enabling a valid extrapolation from the few structures analysed in detail. The deliverable will be a maintenance planning module for a collection or network of structures.
- *'Near interactive' what if evaluation* for design optimization. A main challenge will be ultra-fast computation. The deliverable will be an advanced design module.

The deliverables mentioned will be handed over to the VPs.

Stakeholders

The main stakeholders are part of the chain that designs, creates, owns and operates high value assets. Because our current focus with respect to areas of application (use cases) is on concrete bridges, offshore wind structures, (abandonment and reuse of) oil and gas wells, and composite vehicles, the stakeholders involved in our development will be from the chains in these domains. New use cases will be developed around the most important construction materials (concrete, steel and composites) shifting the focus on stakeholders accordingly.

Partnerships

RWS and the cities of Rotterdam and Amsterdam are important asset owners that will be involved in the programme.

The German Bundesanstalt für Materialforschung und -prüfung (BAM) is a partner in the work on concrete (for sensors, models and testing facilities). Cooperation with the Bundesanstalt für Straßenwesen (BASt) is being discussed by comparing the research programs and identifying potential for cooperation. TU Delft is a partner in the work on concrete, steel and composites (for sensors, (multi-scale) models and testing). Norwegian research institute Sintef is a partner in the work on steel/cement (models and testing, mainly subsurface applications)

NMEMS is a Japanese Technology Research Organization, with participation of high ranking Japanese companies and institutions such as Toshiba, Mitsubishi, Fuji Electric,

	DNP, NTT-Data, NGK, MMC, NEXCO-East, NEXCO-Central, NEXCO-West, Hanshin-Exp, AIST, Univ. of Tokyo, Kyoto Univ. NMEMS is expected to become a partner in the work on concrete and steel (sensors). Grow is the consortium which aims to perform collaborative research in offshore wind (models and testing). Grow's founding partners are: Deltares, DOT, ECN, Eneco, Seaway, Shell, Sif, Tennet, IHC, Lagerwey, LM, Innogy, TNO, TU Delft, Van Oord and Boskalis. Lloyds Register Foundation (LRF) sponsors long term research and structural integrity is one of their topics. LRF and TNO are discussing how they can connect with respect to structural integrity subjects as addressed by ERP SI. In the context of the European Defence Agency, ERP SI collaborates with parties such as KMW and Airborne on composites (application, production techniques and testing). EBN and several operators are partners in research projects coordinated by TNO related to well integrity and abandonment. SodM as the responsible authority with respect to Oil & Gas infrastructure decommissioning is updated frequently about relevant developments.
External connections	Ensuring the availability of high quality infrastructure/assets at low risk and low cost is a societal challenge, since most of the costs and risks are directly affecting society. Thus, the ERP SI use cases are important for three Dutch Ministries: I&M, EZ and Defence. The current use cases link to various TKIs (the Well integrity use case to TKI Gas (upstream gas program on well re-use and decommissioning), the offshore wind use case to TKI Wind op Zee and to the Smart Energy agenda of EZ. The research in use case composite vehicle links to Defence programs (e.g. EDA) and to the first point on the KIA of the Ministry of Defence on enlarging and increasing flexibility of deployment: Vergroting en flexibilisering inzetbaarheid. The use case Concrete bridge is coupled to long term goals 4 and 5 of the Ministry of I&M: *4. Nederlandse economische kerngebieden zijn blijvend bereikbaar en kunnen wereldwijd met andere stedelijke regio's concurreren; 5. Personen en goederen kunnen duurzaam, veilig en binnen voorspelbare tijd worden verplaatst, ter land, te water en in de lucht*; All use cases link to national and international research agendas such as H2020, Infravation etc.
Program development	In 2018 the work of the previous period will be continued with (field) demonstrations for the four use cases, in order to validate the technology and to further involve the stakeholders. Simultaneously, partners will be given the opportunity to join the demonstrations with their technologies, thus creating living labs where new technology will be added and demonstrated continuously. The creation of the living labs is also a good way of handing over the developed technology (to the designated VPs within TNO or directly to market parties) in the next phase, and allows the ERP SI to focus on the next challenges. After 2018 ERP SI will shift most of its attention to new use cases with the focus still on the main materials for macrostructures: steel, concrete and composites. Further, from the ultimate goal for the technical development, the creation of Digital Twins of macro-structures enabling Condition Based Asset Management & Experience Based Design Optimization, additional new technological challenges are derived for ERP SI, as described in this document.
Activity plan 2018	The activities of the ERP SI are concentrated along the lines of increasing accuracy, increasing coverage and integration. Within these lines we distinguish research on the different materials (steel, concrete and composites).

Increasing accuracy
Main 2018 research topics are:

- Full probabilistic non-linear Finite Element Model (FEM), for the purpose of improving accuracy of reliability calculations and extending the modelling of damaged concrete structures, with rebar corrosion in particular, and for making time-dependent structural performance modelling possible and taking full advantage of sensor data. Deliverable: first version of a full-probabilistic non-linear FEM
- Ultra-high cycle fatigue (steel structures) models to reduce conservatism in failure models whereas many low stress cycles contribute significantly to the expected service life. Deliverable: Addition of Ultra High Cycle Fatigue to current chain of models applied on steel structures.
- Ductile fracture model for materials that operates at temperatures in the tough to brittle transition zone. Deliverable: set of parameters to be used for ductile fracture assessment for industrial application.
- Improving corrosion fatigue models by adding probabilistics. Further, the effects of (potential) environmentally friendly means of corrosion prevention on fatigue will be assessed. Deliverable: framework for probabilistic corrosion fatigue models established and feasibility assessed; quick scan on corrosion prevention means executed.
- FEM modelling capabilities for detailed analyses of dynamic failure mechanisms in composites enabling the precise prediction of material behaviour including damage development, in order to be able to theoretically test and evaluate a wide variety of material compositions at the decisive dynamic load and environmental conditions. Deliverable: In addition to the model capabilities, a composite material fulfilling the first level protection requirements
- The calculation load by our multiscale and probabilistic models is a serious restriction on further progress. We will therefore develop, in international cooperation new algorithmic and hardware solution for ultrafast computation. Deliverable: first step towards Computation Materials Science for macrostructures (combined multiple scale, probabilistic) modelling and drastic reduction of calculation time (by a factor of 10).
- Detecting cracks in concrete with acoustic tomography and making a 3D representation that can be fed into degradation and structural models. Deliverable: Acoustic tomography algorithms.
- The development of new sensing methods to characterize degradation defects in complex materials such as concrete & glass reinforced composites. Based on academic publications the state of the art will be transferred into practical concepts. Deliverable: Proof of Principle for at least one new sensing method for a complex material.
- Detecting and imaging defects related to absence of grout, fatigue cracking using bulk and guided ultrasonic waves. Deliverable: proof of principle of measurement / imaging technology.
- Mapping and 3D modelling stress in concrete, steel and composite material by deploying linear and nonlinear ultrasonic wave phenomena (polarisation direction, wave mode, wave mixing). Apart from being a design parameter (pre-stressed concrete construction), stress may also be an early indicator of degradation. Deliverable: proof of principle of mapping stress in laboratory set-up and 3D model for simulating the effect of stress on ultrasonic wave propagation.
- The development of high-sensitive fiber optic strain sensor array for large construction. The feasibility of a single sensor is demonstrated jointly with BAM on a concrete construction in 2017. For practical application, a system with multiple sensors (e.g. ~10) in an array configuration and a proper sensor packaging to enable field

	installation will be required. Deliverable: Concept of packaged sensor and proof of Principle of the multiple sensor configuration • The development of ultrasound measurement with fiber optic sensor will result in a permanently installed sensor network for crack and construction degradation measurement. Deliverable: Demonstration of the state-of-the-art high sensitive fiber ultrasound sensor and an evaluation of collaboration partner for the fiber optic ultrasound transducer technology. *Increasing coverage* • Developing service life prediction methodology for damaged concrete structures at structural scale. Deliverable: basic version of a model predicting service life, based on input from models on structural elements • Model which simulates the behaviour of wellbore materials and their interactions with downhole fluids during all the phases in the lifetime of a wellbore under a variety of subsurface and operational conditions. Deliverable: radial symmetric 3D geomechanical wellbore model • Validity, restrictions of scaling for blast loading (close-in explosion conditions) and the material and local structural response in metals and composites. This yields a validation of scaling rules for testing at impulsive loading conditions & development material solutions. Deliverable: Validated scaling rules. • Multi parameter sensing to cover a large area / entire assets, since there is no single parameter that can quantify all the different degradation mechanisms. Deliverable: Proof of Principle of multi parameter sensing for one use case. • A new type of light source (Mode Locked Laser) demonstrated to improve the sensitivity of various types of fiber optic sensors. Applying this light source to the TNO Distributed Acoustic Sensing (DAS) technology can potentially reduce the noise level and enables long length (>5 km) sensing fiber for a wide coverage. Deliverable: Evaluation of the noise level in TNO DAS system and Demonstration of the compatibility with the Mode Locked Laser light source. • Compressive sensing is a relatively new development that aims at collecting the required information with considerably less samples, in space (large surface area) and in in time, than conventionally would be required. Deliverable: demonstrator of compressive sensing using an ultrasonic 2D phased array for mapping spatially variant material properties and detecting degradation in concrete. *Integration* In 2018 the results of previous years will be integrated, linked to the (field) demonstrations. The transfer to VPs and projects directly for the stakeholders will be organized around these demonstrators: • Concrete bridge A bridge in a major Dutch city will be instrumented with various sensors and monitored permanently for research purposes. Models that have been developed can be validated in practice during the demonstration period. Also existing and new partners will be invited to join the demonstration by adding sensors or applying their models, if the asset owner approves. • Offshore wind An operational offshore wind turbine will be instrumented and monitored for research purposes. Several tools developed in ERP2017 and COTS technologies need to be combined to obtain an operable Operations & Maintenance (O&M) monitoring and decision tool for support structure on the wind farm level. Data reduction (filtering), assimilation, and presentation at the end users are key to success. Further,

	acceptance of the technologies by class organisations are key to introduce it into the market. Deliverable: frame work for O&M system defined and remaining key missing technologies identified. Assessment of what needs to be done to receive class organisation approval. • Well Integrity. In 2017 a demonstration workflow has been achieved for a single well type (i.e. an offshore CO_2 injection well), in 2018 other types (e.g. conventional gas well) will be added and demonstrated. • Composite vehicle Due to the destructive nature of the experiments and demonstrations in this particular use case, there will be only a limited number of life demonstrations of the performance of the newly developed composite material. In 2017 blast tests on samples at quarter scale were performed, in 2018 experiments will be done at full scale in collaboration with the Ministry of Defence. In the course of the demonstrations, the connections between sensor input and various models will be an important topic, including automating the flow of data.

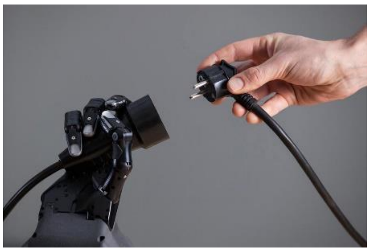
8 I-Botics

General data	
Title	i-Botics
'Topsectors'/Societal Themes	LSH, HTSM, Energy, Water (a.o. Maritime), Mobility and Logistics / Defence, Safety & Security, Sustainable productivity, Aging population, Participation Society
Contact person TNO	Jan van Erp
Contact person government	Mariëlle Beers-Homan (EZ)

Program 2018 – 2021 and activity plan 2018

Abstract

Robotic Technology will affect many aspects of our professional and private lives: it will raise efficiency in industrial production, increase safety levels in amongst others transportation and it will provide enhanced levels of service at home. Robotic technology will become a significant element in solving societal challenges posed by an ageing population, the need to bring manufacturing back to Europe, the demands for more efficient, clean transportation and energy, and the want for a safe and secure society. Indeed, in the National Science Agenda of the Netherlands (NWA) as well as in the European H2020 program, robotics is seen as an important and promising solution that will have a significant impact on society in the near future.



Many research and technology endeavours on robotics focus on increased autonomy of robots. i-Botics however is focussing on interactive robotics, hence i-Botics. Both R&D tracks, autonomy-based robotics and interactive robotics, are needed for achieving above mentioned societal goals.

One of the most important challenges in robotics both tracks are facing is: how to fully exploit and scale the combination of the cognitive- and motor intelligence of humans with the power, speed and accuracy of robotic systems. In this ERP we have two goals for 2020, having this challenge in mind:

(1) First to develop the knowledge and technology for a full telepresence robot for inspection and maintenance with 3D remote augmented vision and audition, and intuitive bimanual control with haptic feedback. The human-robot interface will be designed to evoke (the illusion of) 'body ownership' of the remote robot. This allows the operator to build superior situation awareness and to perform as being present at the remote location.

	(2) The second goal is to develop the knowledge and technology for a flexible robotic suit (exosuit) for two types of application: first, to provide mechanical support to workers that are involved in physically heavy, mobile, and 'difficult-to-automate' situations, and second, - to give mechanical support to people with impaired motor functioning (elderly, sick, disabled) at home or at work. The exosuit should act as a non-obtrusive, second skin, sense the human intention to move, add mechanical power and stability, use seamless integration with different levels of robot intelligence, and be highly adjustable to the individual preferences and industrial or 'assistive' context. 
Description	*Context* According to SPARC (the partnership for robotics in Europe), the interaction between robots and people will grow over time, and this is the core of this ERP project i-Botics. Industrial robots can function with a high degree of autonomy when the task variability is low and the task environment is well controlled. However, high degrees of autonomy are (technically) impossible to achieve in the near term and may even be undesirable in other situations. Examples include tele-inspection, tele-maintenance and tele-problem solving, and tasks where high variability requires human manual and decision making skills. i-Botics clearly links to the international concepts and trends by Industry 4.0 and Operator 4.0. Industry 4.0 has been classified as the fourth technological revolution, where cyber-physical systems monitor the physical processes of the factory and make decentralized decisions as a 'smart factory' (MacDougall, 2014). One of the philosophies of Industry 4.0 is technical assistance, whereby the system has the ability to assist humans with tasks that are too difficult or unsafe (MacDougall, 2014). There are many manual handling tasks that could be automated, but many others are difficult to do so as they require human precision, skills, decision-making, flexibility and movement capabilities. The associated evolution is Operator 4.0 which considers technology augmented workers. One such enhancement could be the use of exoskeletons which can help to reduce the trade-off between automation and manual tasks requiring human capabilities. A societal challenge relevant to i-Botics is that of sustainable employment. Despite automation and robotization, many workers in logistics, maintenance and manufacturing are still exposed to heavy, dangerous or dirty work. For instance, 30% of the EU working population is exposed to material handling, 63% to repetitive work, and 46% to awkward body postures. These figures contribute to the fact that yearly more than 40% of the workers suffer from low back or neck and shoulder pain (Eurofound, 2012). In difficult-to-automate situations tele-robotics as well as exoskeletons can reduce these exposures, prevent health and safety problems, and contribute to sustainable human employment. Here, i-Botics aligns to the Topsector Life Sciences and Health and its Knowledge and Innovation Agenda, in particular by addressing 'the vital functioning and quality of life of people and the potential contribution of technological innovation', which is increasingly important in our ageing (work) population. *Public Private Partnerships and use cases*

In the past years, various industries have explored and recognized the added value and importance of robotics. Joint research with a repute, independent coordinator is addressed as an important factor to formulate visionary goals and realise continuous success. Therefore the Joint Innovation Centre i-Botics was initiated by TNO and the University of Twente. This ERP project is part of the innovation centre which literally connects the full value chain in multiple domains in a Public Private Partnership (PPP). i-Botics already works closely together with knowledge organisations including TU Delft, VU University Amsterdam, Fraunhofer and NIOZ, major players such as Boskalis, Shell, Rijkswaterstaat, and ProRail, and many national and international industrial parties and RTO's and the number of partnerships will grow during the ERP project time.

Technological solutions for robotic challenges in various domains like (petro)chemical industry, defence, subsea/offshore industry, logistics, and search and rescue are jointly developed in the innovation centre. The ERP project provides the required fundamental IP and knowledge development. For a successful translation and valorisation of knowledge developed within the ERP, several use cases are defined. These use cases are closely linked to and in line with the objectives of the Topsectors Energy, HTSM, LSH and Water. Along these use cases, i-Botics initiates PPP agreements and Joint Industry Projects to assure industrial contribution (in-kind and in-cash). The following use cases are currently being developed or in progress, and will inspire and direct how this ERP achieves its goals:

- Subsea Blended Reality for Remote Operated Vehicles. This use case is in line with the Energy Transition Route and the Blue Route, as described in the NWA. An improved Human Machine Interface (HMI) can be realized by live fusion of the information of the different sensors in one virtual (3D) environment. This would create a blended reality vision system with Augmented Reality (AR) and Virtual Reality (VR), which will provide the operator with optimal situational awareness resulting in improved control, inspection and manipulation capabilities. With these developments, the costs are reduced which will contribute to more efficient offshore activities and asset integrity maintenance. These aspects are highly important for lowering Levelized Cost Of Energy for Renewable Energy and for other offshore installation, inspection and maintenance work. It thereby contributes to the Topsectors Water and Energy.
- Exoskeletons for Industrial implementation. Exoskeleton developments are important for the NWA Routes Gezondheidszorgonderzoek, preventie en behandeling, Logistics and Smart Industry. The goal of this use case is to bridge the gap from lab to application for exoskeletons. We realize this by bringing together leading exoskeleton-developers with end users in order to (1) evaluate the usability and performance, (2) evaluate the load on the human body and (3) define practical steps towards commercial implementation.
- Remote Operator robot with enhanced situational awareness for industrial application (onshore). This development fits well in the Smart Industry Route and Energy Transition route. This project develops a blended reality experience for the operator in which the operator can switch between various control modes and views for safe and efficient operation.
- Remote Operator robot with intuitive manipulator control for industrial application (onshore). Naturally, like the previous mentioned use case, this application fits well into the routes Smart Industry and Energy Transition. This project develops haptic controls of remotely controlled manipulators with an exoskeleton arm as input device.

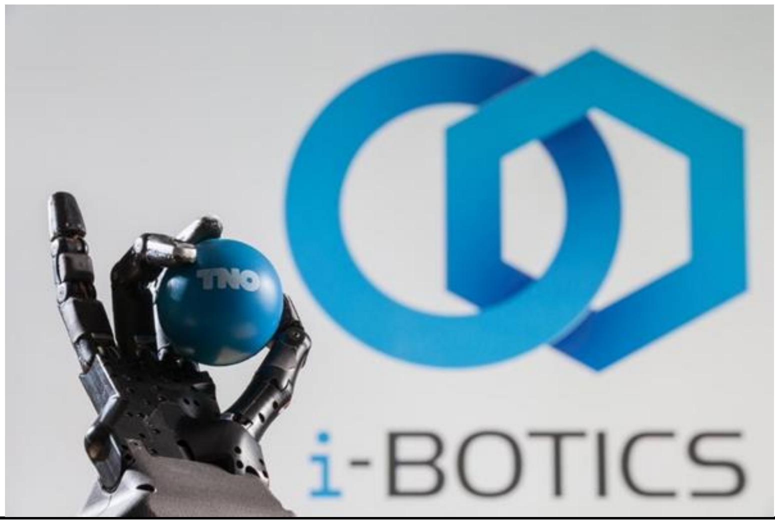
Ambition and goals
With respect to our first goal (telepresence robotics) we will integrate state-of-the-art Augmented Reality technologies in our tele-presence vision system, and add intuitive, bimanual and dexterous manipulation capabilities to our telepresence perception robot. With respect to our second goal (the exosuit), we will mainly focus on (1) our methodology to evaluate the biomechanical, kinematic and behavioural impacts of exoskeletons and (2) methodology to promote the acceptance of exoskeletons in industry settings.

Deliverables and knowledge transfer
In formulation of the anticipated developments in ERP i-Botics, various industrial parties have provided input and guidance, for instance in the roadmapping process. ERP i-Botics has an excellent fit to challenges in multiple domains and "Vraaggestuurde Programma's" (VPs) from a.o. Maritime & Offshore, Renewable Energy, Defence and Sustainable Employability, and i-Botics knowledge and (concept) products will be easily adopted by the various VPs. The subsea use cases follow the route of the TNO VP Maritime & Offshore. (inter)National cooperation with industrial and research partners are key to address the main elements of the Innovation Agenda of the Maritime Cluster: 'Winnen op zee', 'schone schepen', 'Slim en veilig varen' and 'effectieve infrastructuur'. The development of robotized and remote controlled systems makes offshore operations more efficient and effective. They thereby optimize the competitiveness of the Dutch Maritime and Offshore industry and reduce environmental impact. The exosuit goals have a close link to the VP Social Innovation, in which one of the two pillars is the physical and cognitive augmentation of human workers. Concerning Defence, the NL MoD states in its 'Strategic Knowledge and Innovation Agenda 2016-2020 (SKIA), that Man-Machine Teaming related to (un)manned systems is one of the seven top priorities for innovation. The SKIA recognized that technological developments on unmanned and more autonomous systems are not just replacing manned systems and humans, but require new concepts on human-machine/system/robot collaboration. The SKIA is an important official guideline for assigning NL MoD budget to R&D projects. ERP i-Botics is also closely linked to MoD research programs (doelfinanciering) V1719 on 'Behavorial Impact of Humans – Nonhuman-Intelligent-Collaborators Teaming, a V1717 project on telemanipulation for Countering IED and EOD applications, and NTP project exobuddy, and several projects on Telepresence control. These projects mutually benefit from transfer of knowledge and R&D equipment.

The excellent link to the various VP roadmaps enables easy knowledge transfer and co-financing of additional (national) PPP projects and participation in EU projects. This transfer of knowledge and technology from the current ERP to the various VPs is a continuous activity and is facilitated by (but not necessarily restricted to) the Joint Innovation Centre i-Botics and affiliated participants. Several examples illustrate the effectiveness of this construction, e.g. the EU H2020 projects HORSE (human robot collaborative systems) and TRADR (Urban Search & Rescue Robots), the TKI Dinalog proposal Man and Robot in the Warehouse about Man-Robot collaborations in warehouse operations, the STW perspectief proposal on exoskeletons, and the TKI LSH project on reducing physical impact and danger in specific operations in maintenance activities. Several Dutch industrial companies cooperate in this project to assess dangerous and heavy-duty tasks and defining cost-effective alternative

	solutions.
External connections	i-Botics as an open innovation centre, is initiated by request of industrial parties. Besides the founding knowledge partners TNO and University of Twente, major industrial parties are actively involved including Boskalis, Shell, and ProRail or expressed their interest in one of the use cases such as Bosch, Teledyne, Demcon, IHC, A-Hak, and KLM. i-Botics is not an initiative on its own. The growing relevance and activities around robotics, demand a strong collaboration nationally and internationally. i-Botics already has collaboration with other platforms in place: Holland Robotics, SPRINT Robotics, RoboValley, LEO Robotics and the new initiative for a physical hub; RoboHouse. For the international collaboration and coordination of activities, SPARC has been initiated several years ago. The i-Botics research program is directly linked to the agenda and challenges as defined as SPARC robotic abilities.
Program development	i-Botics starts in 2018 as a full ERP project. Before 2018, i-Botics was a KIEM project. The KIEM project formulated the i-Botics roadmap, developed an initial (concept) demonstrator and initiated the development of IP and knowledge development on three core topics in the roadmap: augmented reality for tele-perception, intuitive, dexterous interaction for tele-manipulation, and the use of an exoskeleton arm / hand as input device for tele-manipulation. The results of the KIEM project served as basis for the current project.
Activity plan 2018	*Telepresence robotics* With respect to telepresence robotics, we will integrate state-of-the-art Augmented Reality technologies in our telepresence vision system, and add intuitive, bimanual and dexterous manipulation capabilities to our telepresence perception robot. By the end of 2018 we will have intuitive control over a remote dexterous manipulator (four-fingered robotic hand), including a feedback scheme for critical haptic cues. These remote manipulation capabilities are combined with augmented, intuitive vision of the remote environment by mixing real-life footage with virtual information, amongst others rendered on the robotic hand. This setup allows unique opportunities to experiment with and optimize body ownership of the robotic hand leading to increased performance and decreased vulnerability for mismatches between the (form, size, capabilities of the) robot hand and the hand of the operator. In human-participant experiments we will quantify the body ownership of the robotic hand and the hypothesised effects on task performance. For the latter, we will implement a standard task battery covering the subtasks that are critical in tele-inspection and -maintenance. Relevant activities are: • Design, implement and test sensory substitution approaches. The current state of the art in haptic interfaces is (still) not able to reproduce all critical haptic cues for remote inspection and maintenance such as object slip. Sensory substitution aims to present this cues using a different sensory modality, for instance through visual cues (of slip in this example) displayed as an (AR) overlay over the visual images. By the end of 2018 we have a sensory substitution framework linking remote tasks, critical haptic cues and potential alternative sensory cues. We will run initial exploratory human-participant experiments using this framework. • Build a virtual 3D model of the remote environment using (pre-recorded or live) multi-sensor data. This virtual model allows fast and accurate (platform) navigation and robot control despite e.g. low visibility or a low bandwidth connection. Live camera images can be stitched onto the virtual model employing

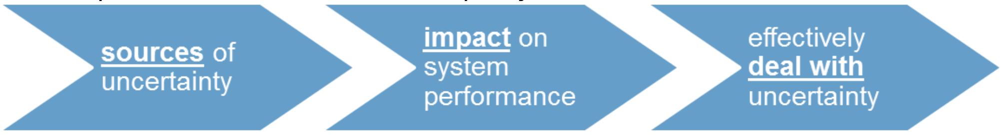
	a new approach to augmented reality (i.e. where virtual images are added to live camera images). These technologies will greatly improve the Situation Awareness (SA) of the operator. The effects hereof will be quantified in human-participants studies. • Extend the haptic interface. Haptic control of tele-robots requires an interface with the operator. Classic haptic interfaces (e.g. Haption Virtuose, Force Dimension Omega) are designed to control the end effector position of a robotic arm, and position and force information in up to seven degrees of freedom (translation + rotation + gripping action) is exchanged. These interface can be extended in several directions to improve tele-operation performance, e.g.: o *Interface with finger tracking devices/hand exoskeletons*. Many dexterous manipulation task require both the control of the a end effector position (robotic) arm and the end effector itself (robotic hand). Current interfaces require the operator to grasp a bar or handle that represent the object that is manipulated. In doing so the possibilities to control the end-effector are limited. Research objective: simultaneous interface with the human arm (for end-effector position) and human hand (for end effector manipulation [grasping]). o *Capture of body posture.* The degrees of freedom in the human arm are higher than the 6 that can be captured with a haptic device. If the number of degrees of freedom in a robotic application is also greater than six it can be beneficial to capture additional degrees from the human body and use these for robotic control. Research objective: capture 7+ DoFs in the human arms and use these for secondary control objectives (first objective is end-effector position control). o *Multi-point feedback.* Classic haptic interfaces generate forces and torque at a single point. In many cases this is sufficient, especially when the robot is using a tool with a single grip (screw driver, welding torch etc.) In some cases this is not sufficient e.g. when collisions at various points are possible. *Exoskeleton* With respect to exoskeletons, actuated devices that currently exist are still characterized by poor ergonomics and usability while the passive ones are limited in their applications and effectiveness. Main challenges relate to (1) the fit to the work: most developments are technology-driven, while an application-driven or user-centred approach is usually not applied. The specific requirements of user groups and the impact evaluations in terms of functionality, mechanical load reduction and energy expenditure need more prominent attention in WR design (2) the biomechanical fit: the challenge is to design WRs without limits in range of motion, unwanted interaction forces and pressure points; and (3) the anthropometrical fit: existing devices not aligning to the complex human body (in motion) of individual leads to discomfort and non-acceptance. Until now developing exoskeletons is an iterative process: Simulations with biomechanical models are performed, exoskeletons are built, and exoskeletons are evaluated. The loop is closed when experimental results are input for new biomechanical simulations. Closing the loop is essential since biomechanical models are not (yet) accurate enough for exoskeleton design. Simple models [e.g. (Kuo, Donelan, & Ruina, 2005)] have been validated but lack detail (e.g the models are 2-dimensional or lack knees). More advanced models [e.g. (Wang, Hamner, Delp, & Koltun, 2012)] have sufficient detail to model exoskeletons but have not been validated. To work towards a more structured design method for exoskeletons we

	propose an in-silico framework for rapid prototyping of exoskeletons. This requires the following activities. • Define work scenarios, risk factors, task characteristics. An important question is how we can model the relationships between work activity characteristics to design principles of wearable robots. • Simulate and validate the biomechanical / kinematical impact of design choices. Or more specifically: biomechanical modelling with OpenSim to evaluate the impact on the user of an exoskeleton in terms of user effort, joint loading, tissue stress, motion freedom and anthropometrical fit. • Capture of arm dynamics. Humans are able to modulate the dynamic properties of their extremities. The properties determine how humans interact with their environments (compliant or stiff). The dynamic are influenced by muscle activation, body posture and co contractions. Due to limitations in the communication (mostly time delays), these dynamics properties are not captured and transmitted by classic haptic devices. We will implement an innovative approach based on equipping the human arm with additional sensors (e.g. EMG) that estimate the dynamic properties and transmit these via a separate channel. 

9 Making Sense of Big Data

<table>
<tr><td colspan="2">General data</td></tr>
<tr><td>Title</td><td>Making Sense of Big Data (MSoBD)</td></tr>
<tr><td>‘Topsectors’/Societal Themes</td><td>HTSM, LSH, AgriFood, Logistics</td></tr>
<tr><td>Contact person TNO</td><td>Wessel Kraaij, Judith Dijk</td></tr>
<tr><td>Contact person government</td><td>Mariëlle Beers-Homan (EZ)</td></tr>
<tr><td colspan="2"></td></tr>
<tr><td colspan="2">Program 2018 – 2021 and activity plan 2018</td></tr>
<tr><td>Abstract</td><td>
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.

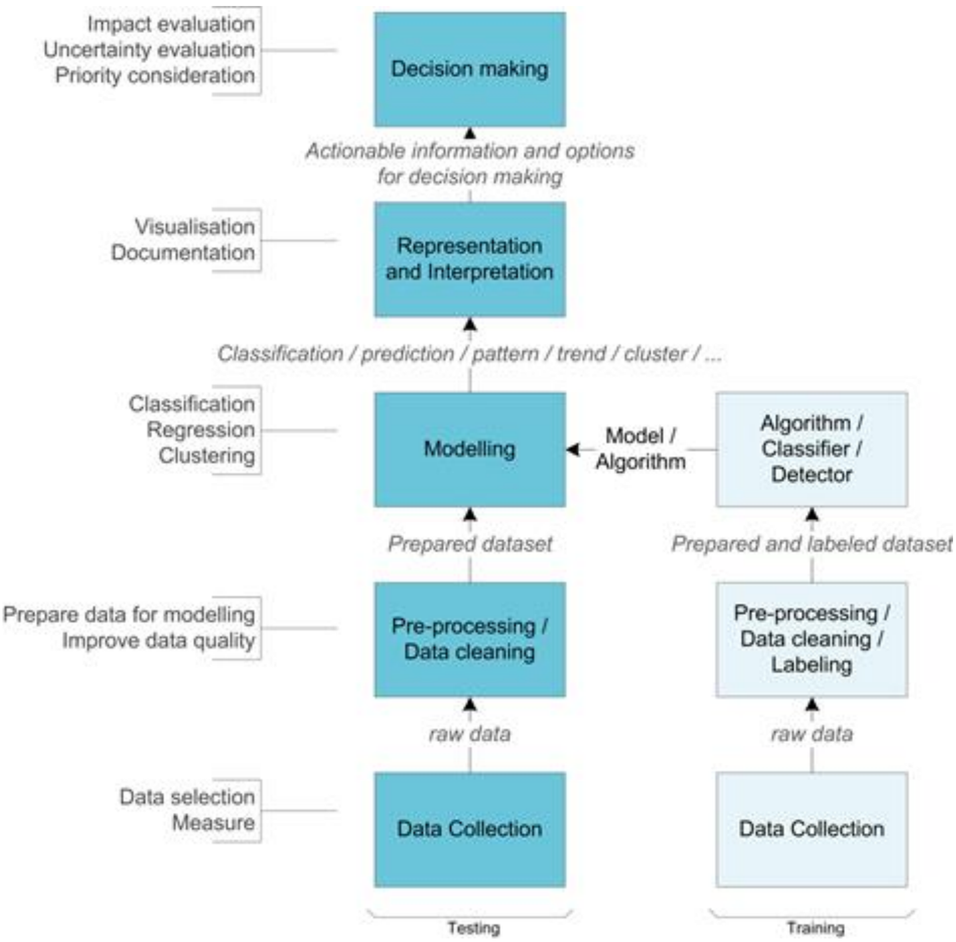
In the first two years (2015-2016), this ERP explored the complete big data value chain, including data governance, analysis and distribution. In 2017 the ERP focused on three topics that are crucial to safely unlock the wealth hidden in big data and show the potential to lead to a distinctive technology position for an ecosystem of TNO, knowledge partners and stakeholders. These topics are: Uncertainty, multi-stakeholder collaboration and Information Centric Networking.

The technology line Uncertainty will continue in 2018 focused to tackle real-world challenges 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 the overall assessment and improvement of the performance of data processing pipelines that process large scale heterogeneous real world (noisy, incomplete, ambiguous) data; and thus to lay the foundation for self-inspection of AI systems. This technology line will also include continued research on Data Traceability and Data Quality Assurance (previously part of the multi-stakeholder collaboration line). The combination of these topics contributes a better understanding of the impact of uncertainties and data quality in a data driven innovation.


Some of the ERP MSoBD 2017 results are mature enough to be brought to the market with support of the VP (vraaggestuurd programma) Networked Information. This is the case for the 2017 topics Information Centric Networking and Ownership Respecting Data Analysis. These technologies will be further developed in partnerships.

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
</td></tr>
</table>

	and to build a national and international ecosystem. This resulted in joint projects in the NWA route Responsible Value Creation, COMMIT2DATA and the European Big Data Value Association (BDVA).
Description	The goal of the ERP is to create top capabilities (tools, models, methods) that enable a stakeholder to design and implement a big-data-driven-innovation in a multi-stakeholder setting. For this purpose, new applied technologies are developed and their applicability is shown in various applications. The use cases of the program: Mobility and Logistics, Personalized Health and Security, 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 the KIA ICT. For the different domains there are connections to the specific Top Sectors, e.g. the top sector LSH and Agrifood Within the ERP Making Sense of Big Data strong collaboration with various partners outside TNO is key. On an international level, TNO is representing Dutch academic partners in the European Big Data Value Association (BDVA), where TNO is board member. On a national level, representatives of MSoBD do closely work with academic partners to shape national programs related to big data and sense making, such as COMMIT2DATA and the NWA roadmap Responsible Value Creation (VWADATA). As an example the COMMIT2DATA call 'evolving content…' has been written with input from TNO and will also be co-funded by TNO TKI in order to further strengthen cooperation between academic partners and TNO. Results for 2017 are: the BDVA linked H2020 Big Data Lighthouse project BigMediLytics, where TNO knowledge on multi-stakeholder collaboration and privacy respecting data analytics and several COMMIT2DATA projects (DACCOMPLI in the 'evolving content call' in collaboration with Leiden University and ECIDA with RUG and CWI, Data Logistics 4 Logistics Data in the logistics call). TNO is also part of the NWA Startimpuls project VWDATA related to FACT/FAIR data science: FACT: Fairness (e.g. non-discriminatory data mining), Accuracy, Confidentiality, Transparency, FAIR relates to the open science initiative that is coordinated from the Netherlands. In 2016 and 2017, the MSoBD program was reviewed by an external advisory board. This board confirmed that the results delivered in MSoBD were relevant to society and of high quality. Following their review, in 2017 the research was further focused 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. Of the 2017 topics, the technology line Information Centric Networking is handed over to the VP Networked Information. The technology line Multi-stakeholder collaboration results Ownership Respecting Data Analysis (ORDA) cookbook and the Design for Auditability (D4A) methodology are handed over to the VP Networked Information. The remaining subtopics Traceability and Data Quality Assurance have a close relation with the technology line Uncertainty and will be continued in that line. In 2018, the technology line Uncertainty will continue the 2017 focus to tackle real-world challenges 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 subtopics Traceability and Data Quality Assurance (initial results from the Multi-stakeholder collaboration work package in 2017) have a

<table>
<tr>
<td></td>
<td>strong relation to Uncertainty and have been integrated.
The ambition of this technology line is to achieve excellence at the overall assessment and improvement of the performance of data processing pipelines that process large scale heterogeneous real world (noisy, incomplete, ambiguous) data; and to lay the foundation for self-inspection of AI systems.


As the ERP program is scheduled to end in 2018, one of the main points of attention is transferring the resulting knowledge, ecosystems and other results to other programs and business lines within TNO. The main landing place for the uncertainty work will be the ERP Applied AI. Parts of this knowledge will also be applied in VP programs, such as Networked Information, Information Superiority and Personalized health.</td>
</tr>
<tr>
<td>External connections</td>
<td>Collaboration with academia is covered through TNO part-time professors, PhD 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. In this topic a joint StartImpulse project with the UvA, VU and University of Leiden has been granted and TNO will participate in WP0 (dissemination and coordination), WP4 (transparency) and WP5 (accessibility & interoperability).
Collaboration with non-academic partners is mainly implemented through COMMIT2DATA (NWO TNO collaboration) and the European Big Data cPPP (BDVA). Application of results is pursued in a collaboration with Rotterdam Municipality, CBS and the Ministry of BZK (Data Policy Lab). The ERP is connected to different top</td>
</tr>
</table>

	sectors: HTSM, LSH, Logistics and Agrifood.
Program developments	ERP Making Sense of Big Data started in 2015 and is scheduled to end in 2018. In 2015 the ERP was started with three main technology lines: *creating value*, *extracting meaning* and *distributed data infrastructures,* 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: *human machine interfaces* and *Big Data architectures*. The research in these two years provided TNO with a technology position over the total, wide scope of big data innovations. In 2017 we focused on the three points mentioned before, this means that a significant part of the ERP portfolio was changed, by focusing on three areas in which we can achieve an unique position. In 2018 the main focus will be transferring and consolidating the knowledge in VPs, ERPs or other projects of TNO. At the end of 2017, the technology line ***Information Centric Networking*** and the main part of the technology line ***Multi-Stakeholder Collaboration*** will be handed over to the VP Networked Information. The technology line ***Uncertainty*** will continue to develop knowledge for applying the academic state-of-the-art knowledge to real world contexts; some aspects of Multi-Stakeholder Collaboration have been merged with the Uncertainty technology line since the two approaches converged for a number of issues. 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.
Activity plan 2018	*Uncertainty* Organizations increasingly rely on data analytics for decision making and in their operational processes. 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 understandable and operationally relevant way. The goal is to improve quality and trustworthiness of data analysis pipelines. Quality and trust can be improved by: 1) incorporating quality-describing-data into the algorithms, 2) understanding their impact on the entire analyses pipeline, 3) being able to adapt to unforeseen changes in reality/context and when things went wrong and 4) to be able to backtrack how the results were produced. The first two steps are about improving the analysis, the last two steps about monitoring the results (and how they are constructed). This technology line has as focus to tackle *real-world challenges* in big data where multiple, unstructured, relatively “ambiguous” (belonging to different domains or contexts) datasets are analyzed in combination. This means identifying and quantifying sources of uncertainty and dealing with uncertain results by e.g. an interactive visualization. A number of **research questions** have been identified based on the 2017 results. The questions range from analysis-related questions (mainly addressing ‘static’, or ‘design-time’ aspects) to monitoring-related questions (mainly addressing ‘dynamic’, or ‘run-time’ aspects). The latter group of questions are based on the results from the ‘Multistakeholder Collaboration’ work package in 2017. 1. How can we **present** the total **uncertainty** assessment to an end-user in an actionable way? 2. How does the **choice of algorithms and models** influence the quality of the data

	analysis (robustness) and how to optimize this? 3. How can we determine the **minimum level** of **confidence** that is needed in a specific user scenario? 4. How can we assess & validate if the **quality** of the real world data streams are **applicable** for the big data pipeline, both in analysing and monitoring situations? 5. How can we **automatically backtrack** how **results** were **produced** through many systems and across multiple organizations? To achieve the ambition of this technology line, it is necessary 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. Additionally, it is necessary to be able to measure and model all uncertainties in a data processing pipeline, and to present an actionable analysis to stakeholders like system engineers, architects, and end users. The technology line activities will be tested on **use cases**. In 2017 these use cases were from the Safety&Security domain (detection of risk situations in aerial images), Mobility&Logistics domain (Estimated Time of Arrival of container ships in the Rotterdam harbor), and Health (evidence-based youth health policy). The main **deliverable** of this work package is a framework in which the total uncertainty of a big data pipeline can be modeled, analyzed, and presented. *Collaboration, use cases and Ecosystem* As mentioned in the description, the knowledge and tools developed within the ERP are tested, validated and applied to use cases in the domains of Logistics & Mobility, Personalized Health and Security. These use cases are well connected with the ecosystem on big data. In the previous years we invested in obtaining the datasets and challenges from these use cases. In this last year no development on the use cases per se is foreseen.. This program will align with the NWA Startimpuls project ‘VW Data’, more specifically WP4 (Transparency), in which uncertainty and the explanation of uncertainty is an important issue and to WP5 (Accessibility and interoperability) in which trustworthiness of different distributed datasets is an issue. There will be specific attention to position and develop TNO’s technology position on semantic interoperability and privacy respecting analysis in WP5. Building the ecosystem will focus on contributing to COMMIT2DATA and the NWA Responsible Value Creation roadmap in the Netherlands, and BDVA in Europe.

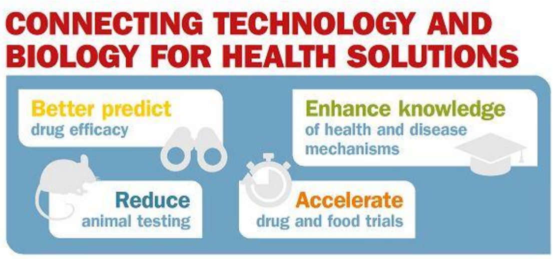
10 Organ Function on Chip

General data	
Title	Organ Function-on-Chip (OoC)
'Topsectors'/Societal Themes	LSH, A&F, HTSM / Work & Health, Defence
Contact person TNO	Evita van de Steeg; Ivana Bobeldijk-Pastorova
Contact person government	Mariëlle Beers-Homan (EZ)

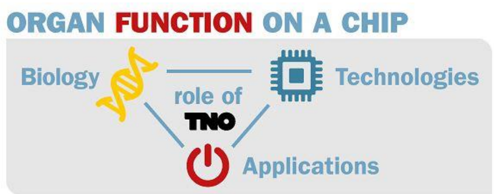
Program 2018 – 2021 and activity plan 2018

Abstract

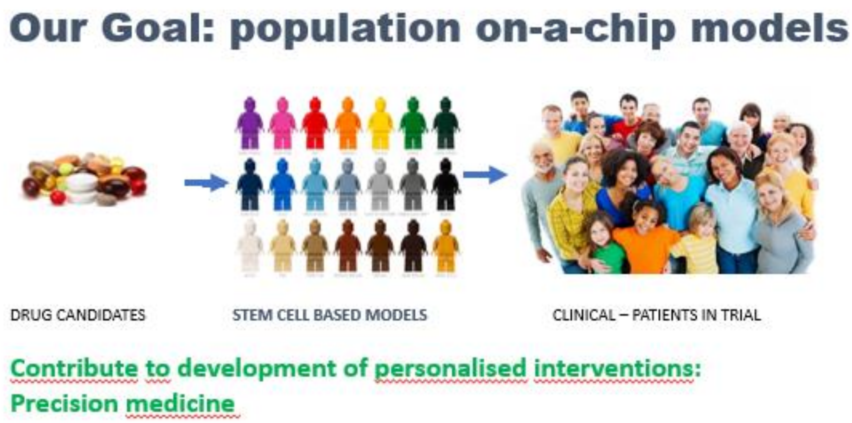
Over the past few years, the development of alternative, more physiologically relevant human cell based in vitro models has evolved. These so called organ function-on-a-chip models are designed to better mimic tissue function and architecture than conventional cell based models. With these models, it 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 in vitro 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.



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, with proven added value for science and industry: 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. We believe that the most relevant approach is to (partly) mimic organ functionality or mechanisms with only as much complexity as is required.



The main goal of this ERP is to contribute to the development of these stratified and/or personalized interventions by developing the concept of population on-a-chip. We will develop a stem-cell based in vitro pre-clinical toolbox, enabling the introduction of population variability earlier in compound development. This will empower development of precision medicine, support selection of drug candidates effective for specific group of patients and improve the design of clinical trial by pre-selecting patient groups already in a preclinical phase. Moreover, this will significantly reduce animal testing in preclinical development, and ideally fits with the national focus on "Nederland wereldleider proefdiervrije innovatie in 2025"

<table>
<tr><td></td><td></td></tr>
<tr><td>Description</td><td>
The objective of the ERP organ on chip program’ in 2018-2020 is to improve the development of technology for better predictive, more physiological (personalized) human stem-cell based in vitro models that will enable ‘population on-a-chip development. With these models we will help pharmaceutical industry to lower attrition rates in drug development, thus lowering the development costs and time to market as well as help both pharmaceutical and food industry to develop stratified and in the end personalised interventions for treatment of different metabolic and immune health dysfunctions.


We aim to achieve this by generating, optimizing and validating sophisticated generations of humanized in vitro “on-a-chip” models in a step-by-step approach, according to the market demand.
Since 2015 TNO Organ function on a chip focuses on tissues and disease areas in which TNO has extensive knowledge, experience, and market position (“right to play”), and develops validated applications relevant for pharmaceutical and nutrition industry. We focus on two different organs (liver and gut), with their own use cases, and we will focus on the development of technologies which can also be applied to other ‘organs’ on chip.
In both use cases we initially started the development of relatively simple, cell-based in vitro models with relevant readouts, which can as such already be used by industrial partners. In the coming years, we will gradually evolve these models into more complex “organ function on-a-chip” models which will mimic actual organ functionality and disease. In addition to these two use cases, a third line of the ERP will focus on the development of state-of-art organ on-a-chip hardware easily applicable for various imaging and readout technologies for applications within the focus use cases, but also applicable for other organs and disease areas.

Goals for 2020

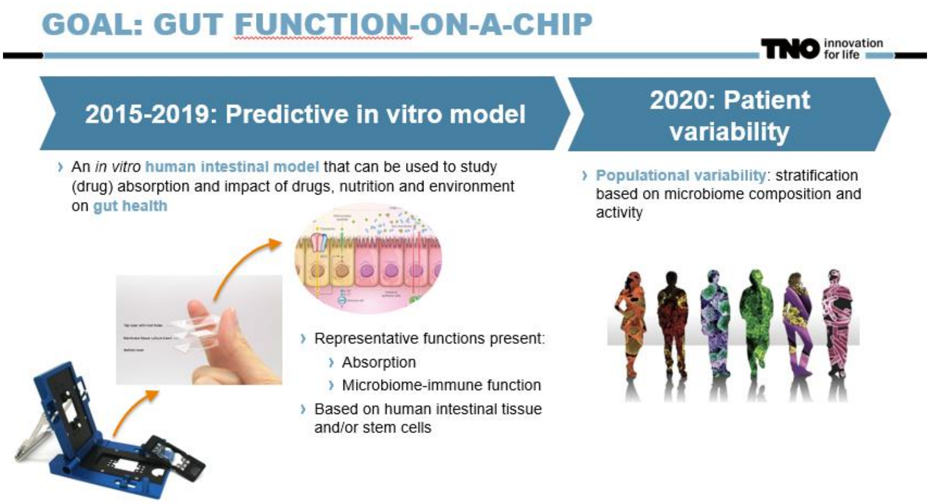
TNO will have proven (together with industrial partners) the added value of the concept of population on-a-chip technology for early screening of (populational variability in) drug efficacy and/or kinetics
TNO will help reduce testing of NASH treatments in animals by providing better predictive models
TNO will help to reduce attrition rates in drug development by better selection of drug candidates with better predictive models
TNO will help develop personalised/stratified (drug) interventions by application of TNO population on a chip models

</td></tr>
</table>

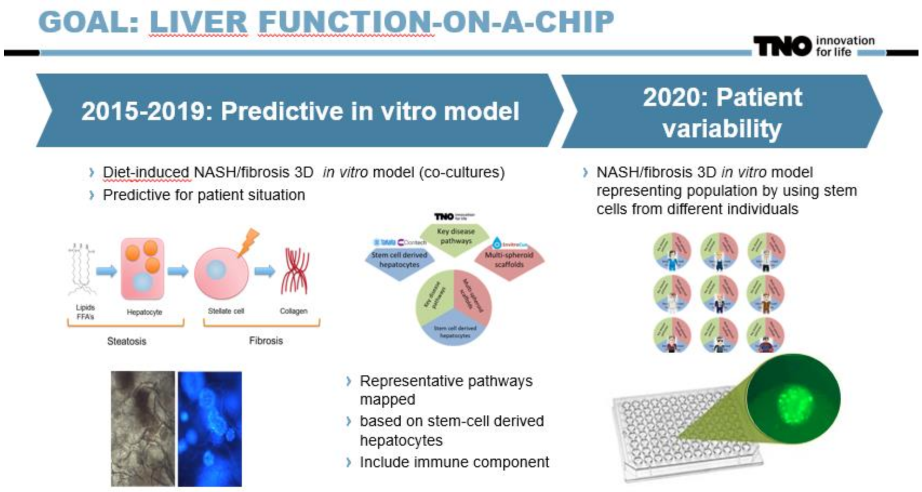
- TNO will be partner / initiator of several national or international consortia on developing and implementing of organ on a chip technologies

Program lines for 2018-2020
The focus of the program will be on two selected use cases, Gut and Liver. In addition we will focus on the development of advanced technology that can be applied in a broader Organ on a chip application and that will enable us to contribute to different academic and industrial organ on a chip collaborations.

1. Gut
Within the use case gut function on a chip we aim to develop and implement an advanced in vitro human intestinal model that can be used to study drug absorption and the impact of drugs, nutrition and environment on gut health. The ability to study (personalized) interactions between intestinal microbiota, gut epithelium and immune system is an important aspect of the model development, and will be of high relevance for both pharmaceutical and nutritional industry. By 2020 we will be able to stratify patients (and their clinical responses like drug absorption, metabolism and efficacy) based on microbiome composition and activity and the interaction with gut epithelium.



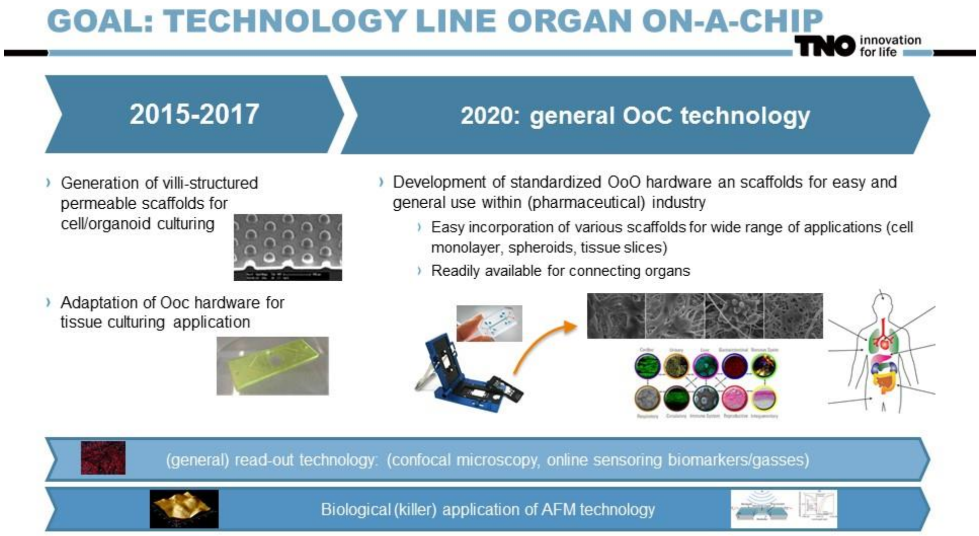
2. Liver
Within the use case liver function on a chip we will aim at and focus on addressing patient variability by development of stem cell based disease models for efficacy screening. By using stem cells from a large number of individuals, we will be able to mimic the population variability (which is often encountered during clinical trials) already in the preclinical drug development phase. By thorough characterization of the stem cells using the signatures and knowledge on disease mechanisms developed in Roadmap PHT and Biomedical health, we will be able to define patient subgroups. In this way, we will be able to study why some drugs only work in a limited number of patients and how the right drug can be selected for the right patient.



3. Technology

In addition to these two use cases, a third line of the ERP will focus on the development of state-of- art organ on-a-chip hardware which can easily be used in industrial applications (cell culture scaffolds, tissue slices), and which will enable the population on-a-chip application.

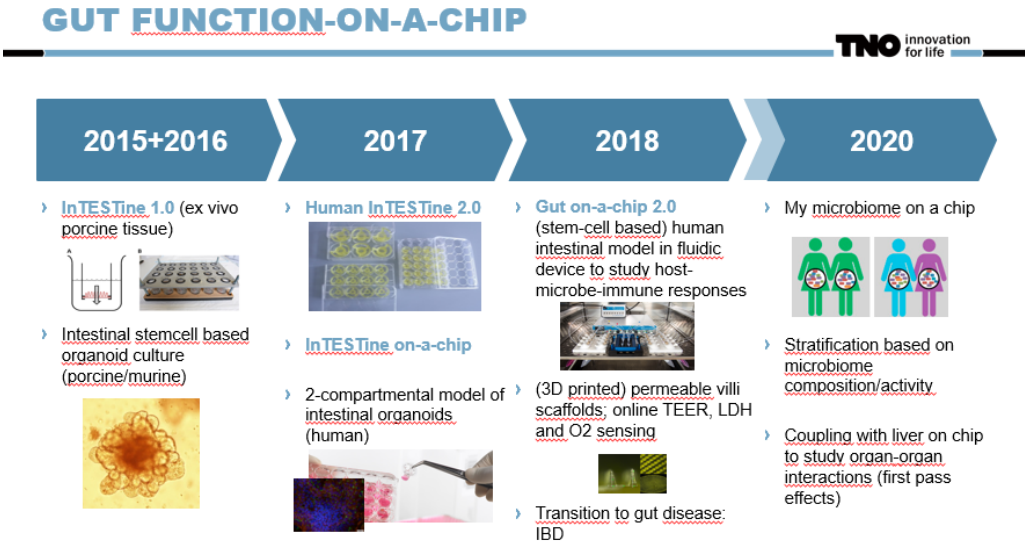
In the recent years, we mainly focused on read-out technology and online detection of biomarkers needed to support and further develop the selected use cases gut and liver, but the technology is also applicable in other (disease) areas as well as measurements of environmental exposure (link to exposome). From 2018 onwards we will start development of standardized organ on-a-chip hardware and scaffolds for easy, accepted and general use within industry, with focus on the population on-a-chip applications. We will do this together with, or based on our experience with, current chip providers and in close collaboration with end-users.



External connections	This program is linked to the knowledge agenda of the top sector LSH. It aligns well with two roadmaps and two gamechangers: **Roadmap 4 Regenerative medicine**: Developing curative therapies for diseases caused by tissue damage and ensuing organ dysfunction, through repair or renewed growth of the original tissue, or its replacement by a synthetic or natural substitute.

	Roadmap 5 Pharmacotherapy: Discovery, development and deployment of new, safe and cost-effective personalized medications in order to cure or prevent progression of a disorder or disease. **NWA route Personalized Medicine**: ..'Each individual should, if desired, be provided with reliable information on his or her own health status, in order to make informed choices of as effective and affordable interventions as possible….'. **NWA route Regenerative medicine: a game-changer moving to broad areas of application.** Regenerative medicine offers opportunities to repair damaged tissue and organs without resorting to transplantation, to test drugs without using laboratory animals, and to customize drugs to a specific patient. **Game-changer 'Exposome' Quality of the environment:.** To develop prevention measures for the health effects of pollution and environment, we need to know more about combined exposures and the revolutionary concept of the 'exposome' integrates all these environmental factors. **Economic Affairs goal "Nederland wereldleider in proefdiervrije innovatie in 2025"** Apart from being linked to the Knowledge Agendas of top sector LSH this program also links to hDMT (a strategic PPS, national initiative in the area of organ on chips technologies, TNO became partner in 2016), IVTIP (In vitro testing industrial platform), and has good connections with policy makers at ZonMW and Maag Lever Darm stichting. Moreover, the program is indirectly linked to VitalTissue, a new national initiative launched by TNO, which will provide vital tissue to researchers for development of novel advanced in vitro models.
Program development	Over the last 3 years, the ERP OoC evolved from a seed ERP (2015) into a full ERP (in 2016) and has further grown in 2017. The program started with three use cases: gut-, liver- and lung-function on a chip, and for all three subprograms important technical developments as well as ecosystems development were achieved in 2015-2017. In 2017, use case lung was discontinued, after a negative business case evaluation early 2017. The ERP is now focused on medical and food applications for gut and liver. In a Business case boot camp (sponsored by the TNO Board of Directors) further focus of the use cases (organs) was defined: development of population on a chip for better (stratified) candidate drug selection for gut on a chip and liver on a chip. For technology, in 2017 we started the development of several readout and imaging technologies that will be implemented in the two use cases, but their applicability is much broader and will further be explored in 2018. In 2018-2020 we will further develop knowledge and expertise on hiPSC and on host-microbiome interactions that are needed to develop population on a chip models and also develop microfluidic devices that will enable coupling of the liver and gut organs and thus create possibilities for new applications (use cases). **Gut function-on-a-chip** Within the "gut-function-on-a-chip" program we will combine biological and technical expertise and develop a predictive humanized *in vitro* model of the intestine to study the impact of drugs, nutrition and environment on gut health. This model should preferably mimic gut characteristics, such as structure, microbiota and absorptive and secretory functions. The model will be developed by applying intestinal stem cells (isolated from human intestinal crypts) and/or human ex vivo intestinal tissue segments (InTESTine) cultured on (3D printed) permeable villi scaffolds combined with (micro)fluidics to mimic luminal and blood flow.

The dynamics of the developments within the program for Gut function on a chip are shown in the figure below.

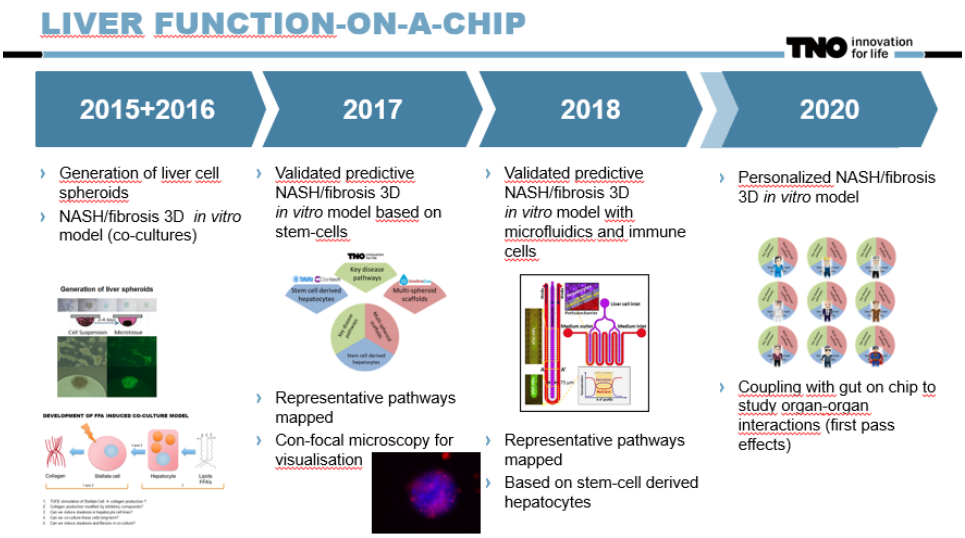


The developed model is applicable for combination with microbiota derived from healthy or diseased (e.g. IBD, obese, diabetic) people in order to study (personalized) interactions between intestinal microbiota, gut epithelium and immune system in health and disease. This gut on-a-chip model will therefore have its application in the pharmaceutical and nutritional industry by providing a high physiological predictive human *in vitro* model to study intestinal absorption, digestion, and metabolism of compounds. In the end we aim to be able to stratify patients (and their clinical responses like drug absorption, metabolism and efficacy) based on microbiome composition and activity and the interaction with gut epithelium and immune system. Moreover, gut on-a-chip will be combined with developed liver-on-a-chip models in order to study cross-talk between organs and more accurately predict human oral bioavailability of compounds.

Liver function-on-a-chip

The “liver-disease-on-a-chip” will be a predictive *in vitro* disease mimicking (i.e. non-alcoholic steatohepatitis; NASH) model using co-culture of human pluripotent stem cell-derived hepatocytes and stellate cells (or other liver cells) on an *in vitro* 3D cell culture platform that will have its application in testing the effect of compounds on the disease development, prevention and or treatment. Besides for the pharmaceutical industry, this is also relevant for applications in the nutrition industry. The combination of disease, materials, stem cells system biology and read-outs is challenging and will be a base for broader applications towards a personalized health approach and stratification (“population on a chip”), by implementation of a set of stem cells from various individuals into preclinical disease models.

The dynamics of the developments within the program for Liver function on a chip are shown in the figure below. In 2017 we will have achieved the growth of stem cell derived hepatocytes in multi-spheroid scaffolds and demonstrated diet-induced activation of stem cell derived hepatocytes in co-culture with stellate cells leading to a fibrotic signature.



Activity plan 2018

1. Gut function-on-a-chip

Main activities

- Stable culturing of human tissue derived intestinal organoids of healthy/IBD patients for application in gut on-a-chip
- Set-up microbiota biobank of healthy and diseased people to be applied in the gut function on-a-chip model
- Technical feasibility and application of co-culture of human intestinal cells/tissue with anaerobic microbiota in microfluidic device
- Development of a collaborative PhD student project together with academic partner as part of TTW perspective program
- Initiation PPS on human intestinal models: “patient stratification based om microbiome activity” with pharma companies, LSH, ZonMw

Deliverables:

- GCP certified microbiome biobank of healthy and diseased people
- Proof of concept for microbiota-induced variations in drug absorption and efficacy
- PPS on ‘patient stratification based om microbiome activity’
- Improved online read-outs for barrier integrity parameters (TEER, LDH) and gas monitoring (O2 and CO2)

Collaborations:

- Extend collaboration with University of Applied Sciences Utrecht and Nutricia Research within SIA funded RAAK 2-real gut program
- Extend collaboration with Amsterdam Medical Centre and Erasmus Medical Centre for banking and applying human intestinal organoids, and Wageningen University for applying microfluidic platform.
- Collaboration with MatTek on exploring opportunities to combine TNO’s expertise on microbiota and microfluidics with their human intestinal epithelial model
- Collaboration with BioMedical Metabolomics Facility Leiden on bile acid transport and metabolism in human intestinal model

2: Liver function-on-a-chip in 2018

Main activities:

- Stable culturing of human stem cell derived hepatocytes in co-culture with stellate cells based on stem cells from various individuals
- Validation of the 3D in vitro NASH model with clinical compounds

- Collaboration with imaging center University Maastricht for confocal imaging and specific fibrosis readout technologies.
- Collaborative PhD student together with academic partner as part of TTW perspective program
- Initiation PPS on 3D in vitro models / “targeting clinical trials models” with pharma companies, LSH, ZonMw

Main deliverables:
- Proof of concept that co-culture models using stem cells from different individuals show variation in response on disease induction
- Proof that 3D in vitro model responds to current clinically used compounds
- PPS initiated on “targeting clinical trials models”
- Improved read out for 3D in vitro model based on collaborative imaging studies

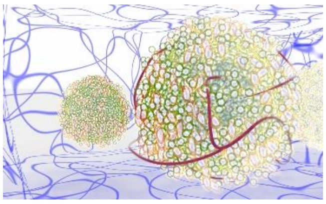
Collaborations:
- Collaboration with imaging center University Maastricht for confocal imaging and specific fibrosis
- Extension of new period of collaboration with Takara Bioscience, Sweden
- Extension of new period of collaboration with InvitroCue, Singapore
- Collaboration with BioMedical Metabolomics Facility Leiden on lipid metabolism in 3D NASH in vitro model

Line 3: Readouts, microfluidics main activities in 2018
Main activities:
- Development of scaffolds/ permeable membranes for growing cells
- Adaptation of current chip devices for use of tissues and cells, e.g. spheroid on a chip
- Application of iPSC technology for metabolism studies
- 3D printing of scaffolds for multi-spheroid growth
- Analysis of gasses as read-out for tissue function

Main deliverables:
- Proof of concept for scaffolds/ permeable membranes for growing cells and spheroids
- Proof of concept modified chip devices for easy use of tissues/spheroids in microfluidic device
- Initiate process to out license developed scaffolds and/or chip devices
- Gas analysis implemented in current gut-on-a-chip model
- First design for coupling liver and gut

Collaborations:
- AMC
- Collaboration with Micronit and/or Corning to explore opportunities to out-license developed scaffolds and/or chip devices for specific applications
- Set-up collaboration with University of Miami, who has extensive experience in adapting and developing chip devices that fit commercially available microfluidic chip providers

Line 4: Dissemination, communication and business models in 2018
Main activities:
- Contacts with LSH, ZonMW, Dutch Digestive foundation, define implementation role of TNO in the **Economic Affairs goal “Nederland wereldleider in proefdiervrije innovatie in 2025”**
- Further development of business case
- New business models development with TNO strategy and market directors of the

	new TNO Units • Evaluation of patent possibilities • Organization of an external dissemination event for academic and industrial partners • Writing of collaborative grant proposal for H2020 call • Updates of website • Writing of newsletters • Development of PR materials  *Main deliverables:* • Grant submission H2020 call • White paper on population on a chip • Updated business case with new business models • 2 newsletters • PR material: presentations, website update, animations, graphics (see example) *Main collaborations* • hDMT • ZonMW • Dutch Digestive Foundation (MLDS)

11 Submicron Composites

General data	
Title	ERP Submicron composites
'Topsectors'/Societal Themes	Chemistry, HTSM, Energy
Contact persons TNO	Pascal Buskens
Contact person government	Mariëlle Beers-Homan (EZ)

Program 2018 – 2021 and activity plan 2018

Abstract

The overall goal of this ERP is to develop and validate concepts for achieving a level of control over structure and chemical composition of materials that enables the development of materials with tailored functionality. Furthermore, in specific cases we aim to progress from static monofunctional materials 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 (BMC) and its partners. Within the framework of this ERP, we aim at facilitating a successful transfer from technologies delivered by academia at a TRL level of 2-3 to the applied research activities on a TRL level of 4.

In line with the BMC program Sustainable Buildings, we selected infrared regulating polymer foils, and coatings or materials that capture light on large surface areas and guide it to a position where it can be used e.g. in combination with photovoltaic modules. Both materials have the potential to contribute to improving the energy efficiency of buildings, which is highly relevant in view of European, national and regional ambitions regarding energy neutrality in the built environment. To achieve the required functionalities, we will design and synthesize functional nanomaterials, and disperse those in polymer matrix materials in a controlled fashion. The infrared regulating polymer foils are an illustrative example of a material with a dynamic functionality; they will be adaptive in response to temperature.

In line with the BMC program Additive Manufacturing, we will focus on developing concepts to realize automotive products with resistance against high thermal as well as high mechanical load based on structured AM processed polymers and composites. An example of an automotive part, that requires resistance against high thermal as well as high mechanical loads, which is the base of this use case, is an inlet manifold. This is an air/fuel duct operating under reduced pressure. It has a complex geometry that strongly benefits from the design freedom of AM, eliminating the need for assembly of multiple components. Traditionally, these manifolds are made from metals, but the use of polymer composites allows the production of light-weight alternatives.

Description	One of the three ambitious key targets the Topsector Chemistry has set itself is that “in 2050 The Netherlands are in the worldwide top-3 of producers of smart materials with high added value and smart solutions”. The route to proceed towards fulfilling this ambition is depicted in the roadmap of the program Chemistry of Advanced Materials. This ERP program mainly fits two of the three tasks depicted in the program roadmap: designing materials with the right functionality and thin films and coatings. As depicted in the roadmap, work in this area automatically overlaps with programs from topsectors HTSM and Energy. This is also the case for this ERP. Within the Brightlands Materials Center (BMC), a joint research centre established by TNO and the Province of Limburg, three research programs are currently active: additive manufacturing (3D printing), sustainable buildings and light-weight automotive. Within these programs, we perform dedicated research towards specific applications that were selected together with industrial partners, research and technology organisations and academic partners. Within the framework of this ERP, we aim at facilitating a successful transfer from technologies delivered by academia at a TRL level of 2-3 to the applied research activities on a TRL level of 4. We focus on activities that fit the scope of the BMC research programs sustainable buildings and additive manufacturing. In the coming ERP period (2018-2021), the developed concepts will be transferred to the BMC shared research programs (connected to specific TNO roadmaps). **Sustainable Buildings** In the period 2015-2017, we have successfully developed a new concept for advanced infrared regulating (IRR) nanocomposite coatings for use on windows in buildings. The functionality of these coatings – combining a high transparency in the visible wavelength range with an excellent thermal switching functionality in the IR – critically depends on the coating’s composition and nanostructure. These coatings autonomously switch from an IR transmissive to an IR reflective state above a specific switching temperature, and have a demonstrated transparency in the visible of >60%. This technology was picked up in 2015 at a TRL level of 2, is now at a TRL level of 4, patent applications are filed and the technology will be transferred in 2017 from the ERP to the VP Sustainable Chemical Industry (BMC Sustainable Buildings research program). In discussions with companies on this technology, they posed two additional requests which require low TRL (2-3) applied research: infrared regulating polymer foils comprising thermochromic nanoparticles as functional pigments, and coatings or materials that capture light on large surface areas and guide it to a position where it can be used e.g. in combination with photovoltaic modules. Within the ERP Submicron Composites, we want to focus on concept development for these two requests in the period 2018 – 2021. We will start with concept development for the polymer foils comprising thermochromic nanoparticles in 2018, and add the second concept development during the course of the ERP (start: 2019 or 2020). For the IR regulating polymer foils, we need to synthesize monoclinic VO_2 nanoparticles with a particle size preferably below 100 nm, and even more preferred below 50 nm to avoid substantial scattering in the visible. Development of this synthetic procedure, and characterization of the resulting nanoparticles to analyse e.g. their switching behavior (i.e. phase transition), forms the start of this concept development. After realizing this, the particles need to be dispersed in polyolefin foils resulting in a random particle distribution. For that purpose, a suited polymer processing technique needs to be developed and validated. For the light guiding materials, we need to develop composite polymer foils with a

refractive index of at least 1.8. For the development of this concept, we require high refractive index nanoparticles which do not cause degradation of the polymer matrix when embedded. These nanoparticles should be very small (below 30 nm) to avoid substantial light losses through scattering. The synthesis of such high refractive index nanoparticles, and their characterization forms the start of this concept. After realizing this, the particles need to be dispersed in foils resulting in a random particle distribution. For that purpose, a suited polymer processing technique needs to be developed and validated, which may be similar to the one needed to produce the IRR foils (vide supra).
We aim to transfer both developments at a TRL level of 4 to the VP Sustainable Chemical Industry (BMC Sustainable Buildings research program) in the period between 2018 and 2021.
For the successful development of both concepts, we will strategically collaborate with Zuyd University of Applied Sciences and the University of Hasselt. Zuyd University of Applied Sciences has excellent research groups active in the field of sustainable energy/energy saving in the built environment, i.e. the chairs Material Sciences (lector Gino van Strijdonck), Nanostructured Materials (lector Pascal Buskens) and Solar Energy in the Built Environment (lector Zeger Vroon). These chairs cover the chain from reactor development to materials and product development and validation. The latter two chairs have been established in strategic collaboration with TNO. We have started active collaboration with Zuyd in the field of IRR windows in 2016. The recently approved RAAK Pro project Window of the Future substantiates this collaboration. The University of Hasselt (Chemistry Department and IMO) houses excellent research groups in the fields of inorganic colloids and functional coatings (e.g. the group of Prof. Van Bael). Strategic collaboration has already been initiated in form of the Interreg project EnEf.

Additive manufacturing (3D printing)
In the period 2015-2017, the activities have been focussed on the development of structured composite materials for the additive manufacturing of patient-specific dental products. This technology concept, based on digital light processing of photopolymer materials, has already been partially transferred to the VP Flexible & Freeform Products (BMC Additive Manufacturing program), and will be fully transferred in 2017. Furthermore, we have made a start in 2016 with the development of technology concepts for the AM of automotive spare parts. AM of automotive parts requires higher performance polymers, and a different process for AM (powder bed fusion, PBF). In the period 2018-2021, we will focus on developing a strong knowledge base in understanding process-structure-properties relationships in AM processed polymers for automotive spare parts to improve product reproducibility and reliability, to predict lifetime of AM produced polymer parts, and to extend the range of polymers suitable for automotive products. We will focus on polyamide (PA) based materials.

Use case automotive spare parts: In July 2016, Daimler announced the production of the first spare parts by 3D printing, such as clamps and fixtures that are not subjected to high loads. For further implementation of AM products in the automotive market, however, products that withstand a high thermal and mechanical load are required. To date, such products produced by AM do not exist! In this ERP from 2018 to 2021, we will focus on developing concepts to realize such products based on structured AM processed polymers and composites. Current materials that can be processed by AM include polyamide-12 (PA-12) and PA-11, the AM products of which do currently not meet these high loads requirements. In addition, certification of the AM products to fit

	automotive safety regulations requires good reproducibility and lifetime prediction. For example, components currently produced by AM often show variability due to thermal stress or the presence of voids, leading to low repeatability, which is a challenge for high-volume industries such as automotive where quality and reliability are extremely important. An example of an automotive part, that requires resistance against high thermal as well as high mechanical loads, which is the base of this use case, is an inlet manifold. This is an air/fuel duct operating under reduced pressure. It has a complex geometry that strongly benefits from the design freedom of AM, eliminating the need for assembly of multiple components. Traditionally, these manifolds are made from metals, but the use of polymer composites allows the production of light-weight alternatives. We will target products prepared by AM from glass-filled polyamide-6, with mechanical properties and lifetime equal to injection moulded parts, pressure-resistant and leak tight. Currently, these materials are not processable by any AM technology. In our research, we will strongly cooperate with academic partners, in particular TU/e. The Polymer Technology group at TU/e has a strong expertise in the area of polymer processing and design, through the use of experimental and computational tools in the modelling of the full thermo-mechanical history of materials during their formation, processing and final design, to quantitatively predict properties of processed objects. We aim at fully transferring the developed concepts at a TRL 4 to the VP Flexible & Freeform Products (BMC Additive Manufacturing program) in 2021. Partial transfer is foreseen in earlier stages.
External connections	**Sustainable Buildings** The technologies contribute to reducing the energy consumption in the built environment, and to building integrated renewable energy generation. Furthermore, the developed thermochromic foils can be applied to other application areas that benefit from IR regulation, e.g. automotive glazing and greenhouses. The activities strongly link to the NWA routes “Energietransitie” and “Materialen – Made in Holland”. **Additive Manufacturing** The technologies contribute to efficient industrial production of high-performance automotive spare parts using AM. Furthermore, the development may provide ways for efficient AM product development in other high performance domains, such as medical implants. The activities strongly link to the NWA routes “Smart Industry” and “Materialen – Made in Holland”. Within the scope of the Brightlands Materials Center we 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.
Program development	**Sustainable Buildings** In the period 2015 – 2017, a concept for nanocomposite switchable IRR glass coatings was developed. In that framework, we studied in detail the formation of VO_2 from organometallic vanadium complexes using liquid chemistry and thermal curing. Furthermore, we studied the formation of nanocomposite VO_2 glass coatings. We set up the analytics to analyze the switching of the coatings, and its corresponding hysteresis. In the period 2018-2021, we will study the formation of small VO_2 nanoparticles from organometallic vanadium complexes using liquid chemistry. We will characterize them in detail, and study their switching behavior using e.g. differential scanning calorimetry. We will develop a polymer processing technology to disperse the

<table>
<tr><td></td><td>particles in polyolefin foils to ensure a random particle distribution. The resulting foils will be studied using the already developed infrastructure for studying the switching behavior of coatings. Furthermore, we will study the formation of small high refractive index nanoparticles using liquid phase chemistry. The developed process for integrating particles in polymer foils will be applied in this case to generate light guiding polymer composites.

Additive Manufacturing
In the period 2015-2017, we have started to develop modeling tools that enable the prediction of performance of 3D printed structured polyamide products under high mechanical and thermal loads. First experimental work using structured polyamides produced through powder bed fusion has been performed to validate the generated models. In the period 2018-2021, we will further refine and validate these models, and in detail study the relationship between AM process conditions, materials structure and product performance. Product performance will be studied directly after production, as well as over its entire lifetime.
Outcome of the ERP work 2018-2021:
Validated models to predict process reliability, product performance and product lifetime of polyamides process by PBF (2018 – 2019).
Concept to process high performance polymers and polymer micro- and nanocomposites by PBF to improve product properties, in particular stiffness and strength (2019 – 2020).
Investigate new chemical routes to develop materials that combine good mechanical properties with good AM processability, as well as tunable and responsive functional properties, such as optical and electrical properties (2020 – 2021).
In the year 2019 an evaluation is foreseen with the relevant stakeholders of BMC, in which the progress and future plans are evaluated. Based on this evaluation, the plans for this ERP Submicron Composites for the period after 2019 could be adjusted accordingly.</td></tr>
<tr><td>Activity plan 2018</td><td>Sustainable Buildings:
Liquid phase synthesis of monoclinic VO_2 particles with a size larger than 100 nm.
Milling of monoclinic VO_2 particles with a size larger than 100 nm to a particle size below 100 nm
Characterization of VO_2 particles, including the thermal switching behavior (together with University of Hasselt).
First polymer composites produced comprising VO_2 particles (together with Zuyd University of Applied Science).
Additive Manufacturing:
Model to predict product performance of polyamides process by PBF (together with TU/e).
Polyamide products produced by PBF AM process, and product performance tested (upon high mechanical and thermal load, together with TU/e).
First accelerated lifetimes tests performed on polyamide products produced by PBF AM process.
First glass-filled PA-6 AM parts produced and validated.</td></tr>
</table>

12 Seed Project Applied Artificial Intelligence

General data	
Title	ERP Seed Project Applied Artificial Intelligence (AAI)
'Topsectors'/Societal Themes	HTSM, LSH, to be determined
Contact persons TNO	Albert Huizing, Wessel Kraaij
Contact person government	Mariëlle Beers-Homan (EZ)

Description

The recent advances in Artificial Intelligence (AI) offer tremendous opportunities for businesses to develop new products and services that improve performance and cost-effectiveness in domains such as mobility and healthcare. However, the automation of processes with AI may also lead to potential dangers for human safety and negative side-effects for society. With its strong links to AI research at universities, expertise in humans factors and systems engineering, and knowledge of application domains, TNO is uniquely positioned to develop the multi-disciplinary approach that is needed to harness the benefits and solve the shortfalls of current AI technology.

Artificial Intelligence (AI) is increasingly being used to automate processes that previously could only be performed by humans such as face recognition and (autonomous) driving. However, one of the main obstacles for the introduction of AI in safety-critical applications is the lack of trust and transparency that is caused by the inability of a machine to explain its decisions and actions to human users and/or co-workers. In 2018, the ERP Applied AI will focus on the development of explainable AI techniques in order to build mutual trust and transparency, and enable more effective and efficient human-machine teaming.

The *kiem* ERP Applied AI is connected to the top sectors High Tech Systems and Materials (HTSM) and Life Sciences & Health with partners from universities (Leiden, Delft), industries, and TO2 in joint projects within the scope of national and European programs (e.g. H2020). Examples of large national programs with TNO contributions connected to this ERP are Commit2Data, the NWA Impulse program on Big Data and the NWO Complexity program. Internally the work is aligned with the Defense RVO program.

The need for trust and transparency is highlighted in the General Data Protection Regulation (GDPR) that gives citizens in the European Union from May 2018 a legal right for an explanation of an algorithmic decision that affects them. In the Netherlands, a large consortium of academic partners has proposed a program for Responsible Data Science, advocating FACT: Fairness (e.g. non-discriminatory data mining), Accuracy, Confidentiality, Transparency, which will be further developed in the NWA Impulse program VWData where TNO will participate in WP0 (dissemination and coordination), WP4 (transparency) and WP5 (accessibility & interoperability). The activities in this Kiem ERP will be linked to VWData activities in order to develop a unique market proposition.

The results for 2018 are 1) initial demonstrators of Explainable AI concepts 2) Use case analysis of explainable AI in the automotive domain and healthcare domain, 3) External profiling including organizing an International workshop on Explainable AI, Opinion setting whitepaper, PR campaign and collaboration with key experts on this field and 4) a detailed program of work for the envisaged ERP Applied AI starting in 2019.

13 Seed Project Chemical Sensing

General data	
Title	ERP Seed Project Chemical Sensing (CS)
'Topsectors'/Societal Themes	Chemistry, Water, LSH, HTSM, to be determined
Contact persons TNO	Stefan Bäumer, Ingeborg Kooter
Contact person government	Mariëlle Beers-Homan (EZ)

Description

In the coming years our society faces several large challenges in the areas of water quality and supply, food safety, clean environment and personal security. Examples range from the quality of the drinking water, optimizing production processes (including circular economy aspects), a clean environment for workers and citizens, safety in public spaces in relation to explosive and hazardous substances, as well as gaining information on the total human environmental exposures (exposome). In all of these and many more examples Chemical Sensing and monitoring is an essential step in taking the first step to improvement. Metrology will deliver the data and facts which then will interpreted and used to engage in actions. The requirements for the sensors will be to be accurate and measuring relevant concentrations and miniaturized and wearable to assure the direct monitoring at the place and time of the exposure.

Conventional measuring methods suffer from several drawbacks, e.g. either they are bulky, expensive and complicated to operate but measure in the relevant concentrations, or they show a lack of direct feedback because of the on-site sampling and off-site analysis. Sensor technology, as a research field, does not have these drawbacks. Bringing the two principles, namely that of spectroscopy based and surface interaction based technologies, together will pave the road towards integrated, respectively selective and more sensitive sensors.

There is a strong connection with the Key Enabling Technology 'Meet- en detectie technologie', as well as a connection to the topsector roadmaps of 'Chemie' (Evidence based sensing, Chemical nanotechnology and devices), 'HTSM' (Advanced Instrumentation), 'LSH' (Applied and Practice-Based Health and Functioning Science Research) is foreseen. In addition links with ministry I&M (recycling, air- and water quality, healthy and safe environment), ministry VWS (smart personal technology), Voedselagenda etc. are important. Collaboration exists with Universities (TU's, Radboud University etc.), Dutch Optics Centre, industrial partners, TI-COAST (COmprehensive Analytical Science and Technology) as the organization that is recognized as the analytical-science and –technology partner in the Netherlands. In addition there is an evident coupling between the ERP Chemical Sensors and the NWA route 'Meten en detecteren: altijd, alles en overal.' This route aims improvement of instrumentation for better resolution down to molecular levels in sensitivity and spatial resolution, as well miniaturized sensor for personalized use. And opportunities in upcoming H2020 calls are identified, e.g. NMBP-15-2019: Safe by design, from science to regulation: metrics and main sectors, DT-FoF-03-2018: Innovative manufacturing of opto-electrical parts.

The foreseen concrete results for 2018 are 1. the design of a the sensor platform to establish the requirements for all components (light source, detector, wafer); 2. Selection and testing of the concentrator coating; 3. Studying the interaction between coating and waveguide, resulting in set of design rules; 4. Development of knowledge eco-system with partners and stakeholders.

14 Seed Project Bio-NanoTechnology

General data	
Title	ERP Seed Project Bio-NanoTechnology (BNT)
'Topsectors'/Societal Themes	LSH, HTSM, to be determined
Contact persons TNO	Arnold Storm, Tom Constandse
Contact person government	Mariëlle Beers-Homan (EZ)

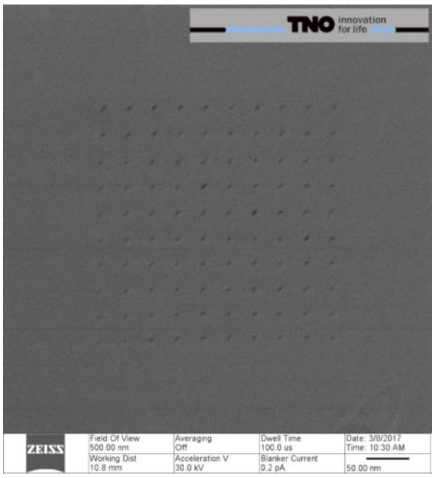
Description

As stated by the Topsector Life Sciences & Health, one of the biggest societal challenges is to increase the quality of life without increasing healthcare cost. Many diseases originate from a molecular defect or modification. One way to increase quality of life without increasing cost is to build a capability to fully characterize every individual biomolecule in a patient sample and be able to characterize all defects on molecular level. At that point, we will reach the ultimate sensitivity, ensuring all data from one patients' sample is retrieved and, as written in the NWA route 'meten en detecteren', these new single molecule measurement techniques will accelerate (biomedical) innovation in the future.

The state-of-the-art in bio-nanotechnology is that single molecule technologies are beginning to be implemented in commercial products for DNA sequencing. Yet two main challenges remain: single molecule DNA sequencing is still too expensive to perform routinely and accuracy needs to be improved. Analysis of protein molecules on single-molecule level is not feasible yet but would be extremely valuable for e.g. real time monitoring of patients. In this research program, we will look for new enabling technologies for both DNA sequencing and protein analysis.

The Netherlands excel in the area of bio-nanotechnology. The Topsectors Life Sciences and Health (LSH) and High Tech Systems and Materials (HTSM) expect a significant growth in this field.

Within this program, there is a strong collaboration with the bio-nanoscience department of the TUD, the Radboud Proteomics Center and the LUMC. Development of new nanoscale analysis technology is covered in the NWA route quantum/nano revolution. The technology will ultimately enable the ambitions of NWA routes 'meten en detecteren, Alles, Altijd en Overal' and personalized medicine.



Preliminary results of 2017 show that an optical instrument for single molecule protein analysis is indeed technically feasible. Solid-state nanopores are promising for single-molecule DNA analysis, and first nanopores have been manufactured in free standing graphene and metal. In 2018, a first setup for high throughput protein fingerprinting will be realized at TNO. This setup will be based on earlier work by our partners at TUD. Another goal for 2018 is to fabricate an array of nanopores with integrated readout system.

Figure 1: Array of sub 10nm nanopores in free standing graphene.

15 Seed Project Optical Satellite Communication

General data	
Title	ERP Seed Project Optical Satellite Communication (OSC)
'Topsectors'/Societal Themes	HTSM, to be determined
Contact persons TNO	Niek Doelman
Contact person government	Mariëlle Beers-Homan (EZ)
Description	
Our Digital Society will require an omnipresent, ultra-high broadband communication infrastructure, which fully supports the information-oriented nature, based on concepts like Cloud Computing, the Internet of Things, the Internet of Everything and High-speed Connectivity. In this communication infrastructure satellites and aerial vehicles play a key role. Satellite Communication faces the disruptive transition from radio-frequency waves to optical waves. Optical communication offers various strong advantages over radio-frequency waves but also brings several technological challenges. The main challenges are: distortion due to atmospheric conditions and clouds, extreme high precision laser pointing, development of photonic devices (high power and space qualified), low mass and low volume satellite optics and extreme secure coding. Optical Satellite Communication matches with three technology roadmaps of Topsector HTSM: Photonics, Space, and Security in ICT. Several industrial partners form these Sectors are partners in the TNO program. Knowledge partners in this program include: TU Eindhoven, TU Delft and University Leiden. Optical Satellite Communication fully matches with the EU's ambition for a Gigabit Society by 2025, which is reflected in several H2020 programs. The program also connects to several NWA routes, such as 'Quantum/nanorevolutie' and 'Materialen – made in Holland'. In 2018 the research and development activities focus on a quantum-key secure optical communication link, and essential optics and photonic devices for ultra-high speed (Tbit/s) communication links.	

16 Signatures

The Hague, 30 september 2017

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

Dr. K.E.D. Wapenaar
Editor