Roadmap
Chemical Sensing & Enabling Technologies

Note to reader: This is a dynamic document. In Q1 2021 we expect some last finetuning of the roadmaps, and potentially some additions of topics. If in doubt whether your proposed research fits in to one (or more) of our roadmaps, always contact the office of ChemistryNL via tkichemie@tkichemie.nl.

To guide you through the landscape of roadmaps and KIA's we will shortly also publish a quick guide to the connection between the mains tasks of each roadmap with the national mission and key technology KIAs.

ChemistryNL

Roadmap
Chemical Sensing & Enabling Technologies

Enabling & sensing technologies
for chemistry, health, energy, food and agriculture.

Summary

Well recognized as an important pillar in chemical technologies, CSET (Chemical Sensing & Enabling Technologies) is regarded as a science domain within all key enabling clusters. Equally important is the innovation potential high-tech systems industry in The Netherlands; with a significant number of SMEs and large industries focused on the design, development and application of chemical technologies, strengthening this domain will positively impact the earning capability of the Dutch economy. Therefore, CSET forms an important and key asset in the mission-driven innovation program, addressing the sustainability challenges and the national focus areas as defined in the KIA 2020 - 2023.
In the CSET roadmap 2020 - 2050, the technological challenges related to these "sleutel technologieën" are discussed within the framework of the four other innovation themes, yet with a certain degree of specificity and restricted to the overall innovation challenges increasing focus and allowing breakthroughs within the forthcoming decade. This roadmap will allow multi-disciplinary research consortia between industry, (technical) universities, HBOs and TO2 to be formed within the context of the following focus areas:

Energy Transition & Sustainability,

- Design and development of robust and universal multi-model sensing technologies for both chemical (molecular) and physical (fluidics) information.
- Improved statistical and data sciences of sensor readouts (digitalization).
- Flow chemistry, design and development of novel flow reactors for µL to multiple L flowrates, with increased understanding of, e.g., mass and heat transport facilitating electrification.
- New materials for (re)design of sensor and enabling technologies.

Agriculture, Water & Food,

- Sensitive and selective detection of food quality during processing for improved health and wellbeing and decreasing food waste.
- Sensors for real-time monitoring of critical molecular parameters for sustainable food processing and more efficient food production.
- Membrane and purification technologies with on-line sensing in water security; detection of large variety of compounds ranging from heavy metals to chemical impurities.

Health & Care

- Advances in "Organ-on-Chip" like high throughput screening technologies combined with approaches in on-line detection.
- Improved accuracy and specificity in (hand-held) diagnostics technologies increasing homecare. Including but not restricted to all classical clinical biomarkers, medication.
- 3D printing technologies for the preparation of personalized medication at pharmacy or home.

Key Enabling Technologies;

- Development of new micro/nano-fabrication technologies to create functional materials and the chemical modification of materials surfaces.
- Design of new robust (e.g., anti-fouling) materials in novel chemical technologies.
- Multi-modal sensing, advanced reactor design and novel modelling tools, supporting process intensification and allowing reduction of carbon footprint.
- New fundamentals in advanced detection technologies in continuous manufacturing.

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Vision / Goals

It is our mission and ambition to create and national roadmap with high degree of focus on a restricted number or urgently required technological innovations within the context of the national innovation themes. The objectives within this mid (2030) and long-term (2050) vision document describe new technological solutions on the short term, and fundamental breakthroughs on the longer term. The choices made will allow short-term solutions by e.g. implementation of validated sensor technologies in new application domains. On the longer term, fundamental breakthroughs in the CSET-relevant technologies should create advanced materials for all type of advanced (chemically) functionalized surfaces, fluidic, sensor and reactor technologies. Digitalization, defined as the combination of validated multi-model sensor and data processing tools, is considered essential in order to provide fundamental knowledge of causality in e.g. chemical processes and within all other sciences domains, omics sciences in health care, and customized continuous manufacturing in the chemical industry.

Introduction

CSET (Chemical sensing and enabling technologies) is organized within the domain of the chemical sciences, and by their nature are applied among many science areas being essential in clinical diagnostics, food safety, the production of industrial chemicals and throughout the complete R&D value chain in drug discovery. They encompass the technological sciences related to, e.g., fluidics systems (micro flow-reactors, lab-on-the-chip), the fabrication of e.g. chemical functionalized surfaces or materials (3D printing technologies, energy storage) and a wide range of sensor technologies (micro-spectroscopy, diagnostic binding assays). Its importance for the Dutch National Science (NWA) agenda is well described in the routes "Measuring & Detecting" and "Advanced Materials" and referred to in routes such as "Precision Medicine" and "Smart Industry". The roadmap chemical and enabling technologies strongly relates to the KIA Key technologies. The contribution of CSET to the KIA Key technologies is partly embedded in the multi-year plans (MJPs) MJP 71 *Measuring and detecting technologies* and MJP 72 *Evidence based sensing*. The KIA has clusters key technologies into key technology clusters.

Likewise, sensing and enabling technologies are on a National and European level regarded as an important asset within the "Key Enabling Technologies". The "Nationale Sleuteltechnologieën", are one of the five major pillars of the mission-driven strategy for research in the Netherlands, encompassing nine major technology platforms, all covering a wide range of enabling technologies. The Suschem Strategic Innovation and Research Agenda (SIRA), compiled by the Federation of European Chemical Industry (CEFIC), has been accepted as integral part of the European JTI SPIRE, whereby chemical sensing and enabling technologies (digitalization) will form one of the three pillars for the calls dealing with the "chemical industry transition" within the Horizon Europe framework. Overall, the design and development of advanced fabrication, sensing and enabling technologies are regarded pivotal to create sustainable "continuous customized manufacturing" in the chemical industry, to improve clinical diagnostics and treatment, to secure food and water safety, to develop efficient energy storage and conversion, and will form an integral part of high-tech systems for aerospace, homeland security and intensification of the agricultural sector.
Well recognized as an important pillar in chemical technologies, the chemical sensing & enabling technologies (CSET) is regarded as a science domain within all key enabling clusters. Therefore, the CSET roadmap forms an important and key asset in the mission-driven innovation program, addressing the sustainability challenges and the national focus areas as defined in the KIA 2020 - 2023. The CSET roadmap 2025, the technological challenges related to these "sleutel technologieën" are discussed within the framework of the four other innovation themes, yet with a certain degree of specificity and restricted to the overall innovation challenges increasing focus and allowing breakthroughs within the forthcoming decade. This roadmap will allow multi-disciplinary research consortia between industry, (technical) universities, HBOs and TO2 to be formed within the context of the following focus areas:

Energy Transition & Sustainability,
With the long-term vision on energy and sustainable "customized continuous manufacturing", the chemical and high-tech materials industry will have to undergo and fundamental transition from a highly intensified and efficient, to a flexible and tailored portfolio of different products and processes. The quality of feedstock, originating from fossil or biobased materials or even recycled materials, the security in having access to water and energy (electrification) will required advanced materials in membranes, robust chemical inert surfaces of sensors and a multi-modal solution for the detection an extremely wide range of chemical entities. Connected with these needs, digital sciences are and logical aspects to be accounted for.
In this mission, focus will be on;

- Design and development of robust multi-model (spectroscopy) sensing technologies for both chemical and physical readout, based on advanced surfaces and materials.
- Digitalization of sensing technologies combined with novel chemometric and modelling tools.
- Novel fraction technologies, e.g., 3D printing, chemical modification of surfaces, design and development of novel flow reactors for □L to multiple L flowrates, with increased understanding of, e.g., mass and heat transport allowing electrification.

Agriculture, Water & Food,
As the timely harvesting of e.g. corn will reduce the overall waste of food feedstocks, infrared cameras in drones have shown their added value. Likewise, sensors applied for the early detection of food decomposition will lead to a significant reduction of discarded "expired" food. Although some promising and effective applications have been implemented, advanced and more sensitive and selective sensing technologies are required to reduce waste to a minimum. In this mission, focus will be on;

- Sensitive and selective detection of food quality during processing, decreasing food waste.

- Membrane and purification technologies with on-line sensing in water security; monitoring of large variety of compounds ranging from heavy metals to chemical impurities.

Health & Care

Together with the development of multi-modal sensing technologies, higher sensitivity and increased selectivity is a prerequisite in bringing clinical diagnostic tools to the home environment, allowing diabetes and cancer patients to control their personalized medication and well-being without being hospitalized. The same holds for the water companies and the larger chemical industrial sites, facing ever-increasing demands regarding water quality, and the reduction of small molecular pollutants like catalysts or drug degradation products. General societal challenges related to the enormous amount of micro-plastics and other health-impacting microparticles in the environment can only be addressed successfully by the development of new sensing approaches. In this mission, focus will be on;

- Advances in "Organ-on-Chip" like high throughput screening technologies combined with approaches in on-line detection.
- Improved accuracy and specificity in (hand-held) diagnostics technologies increasing homecare. Including but not restricted to all classical clinical biomarkers, medication.
- 3D printing technologies for the preparation of personalized medication at pharmacy or home.

Key Enabling Technologies;

Micro/nano-fabrication processes play an ever-increasing role in the design and manufacture of new materials, sensing and processing devices, and other technological developments. Development of such fabrication techniques will continue to integrate and bridge the molecular scale with/to the macroscopic one. At the same time, these technologies bestow materials with increasingly advanced functionalities, such as dynamic and life-like properties, anti-fouling and self-healing properties, and the ability to perform complex operations. Micro/nano-fabrication technologies pervade all areas of the KIA, and are an essential pillar of the Key Enabling Technologies.

Well-engineered Chemical Sensing and Enabling Technologies and novel instrumentation performing at ultimate length or timescales, are likely to generate advanced know-how of chemical and biochemical (biological) reaction pathways on a (supra)molecular scale, and they will generate crucial knowledge of meso-macroscopic properties of novel (bio)materials that can give us (nano) tools in mimicking for diagnostic sensing of (bio)chemical processes at different timescales. The importance of innovations in chemical sensing and enabling technologies can be regarded a pre-requisite for nearly all other domains of sciences and societal as a whole. New sensing techniques allowing multi-modal (both physical and based on chemical principles sensing) real-time monitoring of chemical and biotechnological continuous production processes are needed. The combination with efficient chemometric and big data (AI and ML) methodologies will enable the efficient extraction of pivotal information from the sensing data. In the design of flow- & micro-reactors, lab-on-a-chip devices or (bio)sensors have generated fundamental insight in e.g. single cell processes, while classical analytical technologies such as NMR spectroscopy (Ernst, Nobel prize 1996), and very recently super-resolution fluorescence microscopy (Betzig, Hell & Moerner, Nobel prize 2014) have shown their pivotal importance in the molecular profiling and imaging (structure, heterogeneity) of ever more complex (polymeric, fine- & bio-) chemicals, materials and (bio)processes [2]. The integration of these type of technologies, e.g. mass spectrometry and electron microscopy, are examples of technologies able to simultaneously address the morphology and the chemical composition of complex materials. In biology, label-free sensing technologies are highly required.

- Development of new micro/nano-fabrication technologies to create functional materials and the chemical modification of materials surfaces.
- Design of new robust (e.g., anti-fouling) materials in novel chemical technologies.
- Multi-modal sensing, advanced reactor design and novel modelling tools, supporting process intensification and allowing reduction of carbon footprint.
- New fundamentals in advanced detection technologies in continuous manufacturing.

It is this council's ambition to address all these technological challenges and create on the short (2030) and long term (2050) a path forward in the design, development and implementation of "The technologies of the Future". Our roadmap encompasses the scientific and industrial communities engaged in nanomaterials development, (flow) micro reactors with sensors to monitor (bio)chemical and biological cell systems, (bio)sensors measuring at different time scales and classical state-of-the-art analytical technologies with ultimate chemical or spatial resolution. It anticipates on societal and industrial trends like biomimicking materials, "bringing the lab to the sample", value-added process control (reliability) by multiplexed sensing, and personalized medicine. Meanwhile, it seeks for a clear link with the other "Topsector Chemistry" roadmaps, being well addressed in the National Research Agenda and the European Horizon Europe Program, further improving cross-science synergy, regarded as a key differentiator for the position of the Dutch economy and the sustainability of basic and applied research. Hence, an intensive interaction between academic research in nano-chemical and analytical technologies, industrial R&D organizations and the large number of SMEs marketing novel instruments truly valorizes the "excellences in Dutch research communities" into innovative and novel products. This approach will to a large extent solve the identified "TRL" problem, well-known as the "valley of death", being one of the top priorities in the European Horizon 2020 program. Additionally, in this way options for valorization are created in "non-chemistry" domains such as security and law enforcement, e.g. handheld devices to screen for drugs at crime sites. In relation to nanotechnologies, "nano-safety" will be a generic topic throughout the research and development foreseen in the different tasks and related to the RIVM research and relevant programs addressed within the roadmaps and R&D focus of the ISPT, MinacNed and NanoNextNL organizations.

Key technologies

The Key (enabling) Technologies defined as the fifth mission, are regarded an integral and an essential toolbox, facilitating solutions for the globally defined societal challenges and enabling the objectives of the National Mission Driven Innovation platforms to be met. Organized in nine "sub-classes", they cover a wide variety of sciences including chemical, life sciences and logically the recently introduced digital and quantum technologies. While an important pillar in chemical technologies, the Chemical Sensing & Enabling Technologies (CSET) can be considered as an overarching science domain being, to a larger and lesser extent, interlinked with the majority of these eight pillars. This is visualized in Table 1, depicting the interlink, and the impact (number of links with the different sleutel technologieën) of classical chemical technologies.

Knowledge on microfluidics, either in micro flow-reactors or as basis for sensors, is of added value in the design of organ-on-the-chip (life sciences) devices and sensitive and specific sensors for food safety require the development of novel (chemically) functionalized surfaces (molecular imprinted polymers). Likewise, cantilevers being an essential part of atomic force microscopy, are of comparable importance for sampling in single cell analysis (nano technologies). Sensors based on comparable principles, yet applied in the chemical industry require more "inert" materials able to withstand hazardous (oxidation, corrosion) conditions, while the high quality manufacturing of enabling technologies, heavily relay on new engineering and fabrication (3D printing) technologies. The widely applied nearby infrared (NIR) sensors form an important class of instrumentation in the photonics and light technologies.

		Technology							
Key technology cluster	**Connection to the CSET roadmap**	**Microfluidics**	**Spectroscopy**	**Separation techniques**	**Sensors**	**Process modelling**	**Data science**	**Imaging & morphophy techniques**	**Chemical element analysis**
Chemical technologies	Very strong	x	x	x	x	x	x	x	x
Life Science Technologies	Very strong	x	x	x	x	x	x	x	x
Advanced Materials	Strong		x		x	x	x	x	x
Nanotechnologies	Strong	x	x	x	x			x	x
Engineering and Fabrication techr	Strong	x		x	x	x		x	x
Photonics and light technologies	Medium		x		x			x	
Digital technologies	Medium				x		x		
Quantum technologies	Weak				x				

Table 1: Key technology clusters and their connection to the CSET roadmap

Although different in application, the challenges for all technologies can be summarized in a set of general nominators. The robustness, accuracy/ precision, standardization, sensitivity, selectivity, dynamic range, speed are some of them and form a set of "application requirements" in the (re)design of future sensing, micro-fluidics and micro/nano fabrication processes.
Micro/nano-fabrication processes play an ever-increasing role in the design and manufacture of new materials, sensing and processing devices, and other technological developments. Development of such fabrication techniques will continue to integrate and bridge the molecular scale with/to the macroscopic one. At the same time, these technologies bestow materials with increasingly advanced functionalities, such as dynamic and life-like properties, anti-fouling and self-healing properties, and the ability to perform complex operations. Micro/nano-fabrication technologies pervade all areas of the KIA, and are an essential pillar of the Key Enabling Technologies.
Well-engineered Chemical Sensing and Enabling Technologies and novel instrumentation performing at ultimate length or timescales, are likely to generate advanced know-how of chemical and biochemical (biological) reaction pathways on a (supra)molecular scale, and they will generate crucial knowledge of meso-macroscopic properties of novel (bio)materials that can give us (nano) tools in mimicking for diagnostic sensing of (bio)chemical processes at different timescales. The importance of innovations in chemical sensing and enabling technologies can be regarded a pre-requisite for nearly all other domains of sciences and societal as a whole.

New sensing techniques allowing multi-modal (both physical and based on chemical principles sensing) real-time monitoring of chemical and biotechnological continuous production processes are pivotal for the envisioned age of "customized continuous manufacturing" of base chemical, circular materials and personalized combination drug treatment (delivery of personalized drug formulation during chemocures).

While classical technologies such as NMR spectroscopy (Ernst, Nobel prize 1996), and very recently super-resolution fluorescence microscopy (Betzig, Hell & Moerner, Nobel prize 2014) have shown their importance in the molecular profiling and imaging (structure, heterogeneity) of ever more complex samples [2], the obtained information can be regarded still limited. The integration of these type of technologies and the fusion of their data is a highly needed perquisite in order to simultaneously address the morphology and the chemical composition of complex materials. Multi-modal and integrated sensing and enabling technologies are defined as critical in the CSEY roadmap!

Technological challenges

As mentioned above all challenges of particular importance for specifically the sensing and enabling technologies are related new approaches in the fundamentals of sensing technologies, new measurement principles, e.g., creating high selective detectors. Improved robustness can be can be reached by the design and application of new materials, while pricing and miniaturization (standardization) are relaying on improved fabrication processes. In short, the technological challenges are in general both fundamental by nature, still in the lower TRL level stages 2-6, envisioned to serve the long term planned innovations. Not aiming to be comprehensive, the CSET roadmap focusses on the following technological challenges;

- Development of new micro/nano-fabrication technologies to create functional materials and the chemical modification of materials surfaces.
- Design of new robust (e.g., anti-fouling) materials in novel chemical technologies.
- Multi-modal sensing, Integration of classical high-resolution technologies, e.g. AFM-Raman, EM-MS,
- Advanced reactor design and novel modelling tools, supporting process intensification and allowing reduction of carbon footprint.
- New fundamentals in advanced detection technologies in continuous manufacturing.

Cases

Multi-modality Sensing (for in-situ analysis of chemical conversion processes).
Task
The fundamental principles of chemical conversions, and the mechanisms underlaying the well described heterogeneous- or bio-catalytic processes are still considered incomplete, newer approaches such as photo and electrochemical-catalysis will need novel multi-modal approaches to correlate reaction mechanisms, kinetics and physical parameters (quantum yields in photo (liquid) in catalysis. Here multi-modal technologies could combine information of materials morphology and molecular identification, or combined micro- or milli second reaction kinetics analysis combined with stereoselective detection. Central in this task, is the technological integration of technologies, simultaneously with the fusion of data increasing high density information, compared to the currently “single data point” analysis of dynamic processes.

Goals

Goal	**Year**	**TRL**
New chemometric tools, combined with fusion and analysis approaches for data originating for different sensing technologies, with improved information density	2030	4-8
Integration of measurement of classical detection and sensing technologies	2040	5-9
Integration of data from physical and molecular sensing technologies allowing the causality analysis of dynamic processes	2050	2-6
Cross validate new multi-modal detection technologies to other science domains, mechanistic research of dynamic processes in cellular systems.	2050	5-9

Challenges and Route

The most ideal approach to tackle these problems, by creating multi-disciplinary research consortia, e.g., having a solid background in chemistry, catalysis, analytical chemistry and instrument engineering. Likewise, to support personalized drug treatment linking the speed and concentration dependent administration of multi drugs with the continuous monitoring of evident biomarkers, or the concentration of the drugs in-vivo, requires, pharmacists, medics and analytical chemist together. From an technological perspective, the engineering of the new integrated “multi-modal” technologies requires knowledge on instrument engineering, not per definition a strongly develop competence at universities. Collaboration between instrument manufactures and academia, TO2 and Universities of Applied Sciences is a pre-requisite!

Possible Research

a. Integration of physical and chemical sensing technologies; dynamic light scasttering, viscosity and UV/VIS in polymer analysis.
b. Multi-modal spectroscopic imaging (fluorescence and IR)
c. Combining morphology (EM) and spectroscopic or spectrometric technologies.
d. Data fusion and chemometric tools in the digitalization and data fusion, e.g., NMR and MS imaging technologies.

Development of new micro/nano-fabrication technologies to create functional materials and the chemical modification of materials surfaces.

Task

State-of-the-art sensor technologies based on molecule-molecule interaction frequently suffer form a-specificity, e.g., as is the case in antibody – small interactions in ELISA type principles. Measurements of "heat of interaction", or change of angel of light incidence (SPR) still often allow very sensitive measurements. Central in this task is the (re)design of sensors based on novel principles, e.g., molecular kinetics not leading to loss of sensitivity. Integration of various sensors in one array would facilitate multi-modal detection. Despite "molecular imprinted polymers" have shown their value, still improved fabrication methodologies are needed. Central, in this task is the development of new functional surfaces supporting new measurement principles.

Goals

Goal	Year	TRL
Redesign and improvement of selectivity of existing sensor technologies	2030	6-9
Proof-of-Concept in new measurement principles based on advanced functionalized (sensor) surfaces. Application of new materials with improved physical properties (conductivity, stability)	2040	3-6
New improved (low costs) fabrication processes for functionalized materials and surface for new sensor technologies, fluidics-based production processes.	2050	2-6

Challenges and route

The challenges related to this task are to a large extend related to the availability of new functionalized materials and/or material surfaces. In addition, standardization and validation of new (nano) fabrication technologies is regarded essential. As for all other research within this roadmap, multi-disciplinary teams address the challenges are the most effective approach.

Possible research

e. 3D-printing technologies for the fabrication of inert materials.
f. New chemical processes for the functionalization of surfaces.
g. Fabrication processes for array detection, incorporating different sensor technologies
h. Combining morphology (EM) and spectroscopic or spectrometric technologies.

Design of new robust (e.g., anti-fouling) materials in novel chemical technologies.

Task

In-line with new measurement principles (previous task) and the introduction of new functionalized surfaces and the fabrication thereof, robustness of sensor technologies remains an essential property, especially when applied in industrial production processes. The future sensing technologies are expected not to be prone to signal instability due to fouling, signal drifting due to corrosion of the sensor material or even limited live time linked to frequent recalibration. The robustness as such is there for highly linked to fabrication (high quality standards), and the availability of new materials. Yet, is tends to go beyond these as aspects and therefor deserves and special attention.

Goals

Goal	Year	TRL
Continue design and optimization of currently developed new materials, validation of these current approaches in industrial setting	2030	4-9
Development of multi-array sensor technologies to compensate for "natural drift" of sensing technologies.	2040	4-6

Continued research new materials (diamond based) able to handle "hazardous conditions	2050	2-6

Challenges and Route
Many challenges are related to the availability of anti-corrosive materials which due allow efficient light transmission, sensitive detection. Also, it should have properties such that high-throughput production is possible.

Possible Research

a. Translation of anti-fouling properties of biomedical application or anti-corrosive coatings applied in off-shore application to sensor technologies.
b. Novel chemometric and statistically approaches in compensating sensor fluctuations.
c. Cross validation of e.g. quartz sensor probes from chemical industrial application to biomedical methodologies.

2 Energy transition and sustainability

2.1 Climate and energy

Climate and Energy refers to a reduction of greenhouse gases by 49% in 2030 compared to 1990 and to almost zero in 2050. Important aspects are the multitude of sustainable energy sources (wind, solar, biomass, etc.), the need to convert energy from these sources into a form that people can use in their lives (electricity, liquid, gas, etc.), storage of energy when supply is bigger than demand, and release in case of the reverse scenario. Given the cost of sustainable energy, efficiency is vital for its introduction. In general the generation of renewable energy requires improved materials and systems. Due to the scale that is needed for this transition, the challenge will be to scale-up existing technologies to very large scale in the next 10 years and come up with new, improved technologies for the long term. Electrification, re-use of waste streams and Carbon Capture and Usage (CCU) have a need for new materials and processes.

In this roadmap, we discuss the creation of materials, processes, devices and systems in order to:

- Store 'sustainable electrons' in cheap, stationary batteries with a high conversion efficiency. Affordable and available raw materials are needed when scaling-up to the GW range.
- Convert 'sustainable electrons' into chemical bonds to obtain a gaseous (e.g. hydrogen) or liquid (e.g. methanol or ammonia) fuel that can be stored more easily.
- Improve the conversion efficiency of photovoltaics and thermoelectric conversion devices.
- Develop heat pumps for cooling and/or heating in the urban environment.
- Develop heat storage materials (phase change/hydration) in which the nanostructure (essential for fast kinetics) remains intact. Nano-structured thermal insulation materials for houses.

Technological innovations are needed in the fields of:

- Novel characterization technologies; e.g. for studying (electro-)catalytic processes in operando.
- Novel tools and methodologies for R&D, for example to understand charge transfer processes in complex, multicomponent systems.
- Investigate nanoscale electrochemistry and nanofluidics.
- Novel materials & processes; e.g. for the electrochemical conversion of CO_2 and H_2O into hydrogen and hydrocarbons, for third generation solar cells, and the electrochemical conversion of N_2 to NH_3.
- Novel fabrication technologies, for nanostructured dimensions; e.g. for the controlled fabrication of large scale (>>m^2) nanostructured surfaces with high-performance photovoltaic or catalytic functionalities (and combinations thereof), e.g. for the development of hybrid organic/inorganic membranes.

Cases

Electrochemical reduction of CO_2 with minimum over-potential

Task

In the coming decades we will see a transition from CO_2 as a pollutant to CO_2 as a resource. CO_2 capture will become common practice and its conversion to fuel a necessity. Fuels have the advantage that they can be stored for long times to bridge seasonal inbalance. Hydrocarbons are easily integrated in the present fuel infrastructure and can be directly used as a resource in the chemical industry.

In order to deal with the enormous seasonal mismatch in energy use and production, it is vital that we connect the fuel infrastructure to the electricity grid. Thus, electrochemical conversion processes will become key in a sustainable society. These processes, however, suffer from low conversion efficiencies, poor selectivity, a high demand for precious metals and a poor resilience against fluctuating process conditions. To solve this a revolutionary breakthrough in the field of electrochemistry is required.

Goals

Goal	Year	TRL
Computational methods to reliably determine the nature of the intermediate state during the reduction of CO_2 on complex nanostructured surfaces, taking the electrolyte into account.	2030	4
New *operando* methods covering all aspects of electrochemistry.	2040	6
Devices combining short term storage and electrolysis at local scale.	2030	8
Solar fuels, including water splitting.	2040	6

Challenges and Route

To address this task successfully collaboration is required of the electro-catalysis community with scientists specialized in nanotechnology and classical catalysis, and the *operando* surface characterization communities. The electro-catalysis community has so far focused its research on elemental electrodes and phenomenological studies on the processes involved in electro-catalysis. Computational studies have shown that elemental electrodes will not be able to catalyse oxidation/reduction reactions at sufficiently low over-potential. Stepped, non-elemental surfaces are needed to provide intermediate states at low enough energy. This opens a new area of application for the nano-community to develop tools to design and develop manufacturing methods to produce large area nano-structured surfaces for electro-catalytic applications. Besides nano-structuring for tuning of electrode selectivity and stability, this can also aid in optimization of transport phenomena and manipulation of gas bubble dynamics on electrode surfaces. The nature of such surfaces cannot be established from computational methods alone. Therefore, in electro-catalysis there is a great need to develop methods to investigate the charge transfer processes on an atomic scale in *operando* conditions.

Possible research

- Computational methods to reliably determine the nature of the intermediate state during the reduction of CO_2 on complex nanostructured surfaces, taking the electrolyte into account.
- New operando methods covering all aspects of electrochemistry.
- Efficient (bio)chemical sequestration of CO_2 .
- Devices combining electrochemical storage and electrolysis at local scale.
- Nanostructured alternatives for lithium-based storage systems.
- Solar fuels, including water splitting.
- Energy production and storage at point of use.

Towards a third generation solar cell

Task

Solar energy is the largest renewable energy source on the earth. The sun delivers around 2000 times more energy than the current global primary energy consumption (550 EJ). Direct conversion of solar radiation into electrical energy using solar cells has proved to be a viable option for electricity generation. The challenges for an accelerated large-scale implementation of solar cells are both cost reduction and efficiency enhancement of solar cell technologies. Reduction of costs can be realized by replacing expensive bulk semiconductors (e.g. silicon) by photovoltaic materials that can be deposited by cheap (wet-chemical) techniques. The efficiency of a conventional solar cell is limited mainly by the fact that 1) infrared photons with energy below the band gap of the photovoltaic material are not absorbed, and 2) the energy of absorbed photons in excess of the band gap is lost as heat. The third generation solar cells to be developed should be based on cheap materials and the above-mentioned limitations to the efficiency must be overcome (e.g. tandem solar cells)

Goals

Goal	**Year**	**TRL**
Development of cheap photovoltaic materials with optimum optical and electronic properties.	2030	6
Efficient up- and down conversion technology implemented.	2030	6
Improved architectures of nano-materials with optimized device performance.	2040	8

Challenges and Route

Cheap photovoltaic materials need to be further developed. Examples of materials include organic (molecular) materials, colloidal semiconductor nanocrystals (quantum dots, nanorods and nanosheets), and perovskites. For large-scale application, it is essential that these materials do not rely on critical elements. Moreover, a rational design approach will be needed to develop processes that combine large-scale production with the nanoscale precision and long lifetime required.

The optical and electronic properties of these materials can be tuned by variation of both chemical composition and nanostructure.

It is important to develop materials in which infrared photons can be upconverted to shorter wavelength photons; e.g. by fusion of low energy triplet excitons into higher energy singlet excitons that emit light at shorter wavelength. Spectral down conversion of photons with energy exceeding twice the material band gap is another option to enhance the solar cell efficiency. To this end materials for quantum-cutting need to be developed.

A very promising novel approach to boost the current delivered by a solar cell involves excitation of two or more electrons by the absorption of a single energetic photon. To realize the above, architectures of (composite) nanostructured materials need to be developed and their performance in real devices optimized.

New heat pump technology

Task

Nowadays a large percentage of the total energy consumption is coming from heating and cooling technology. The state of the art technology are based on compressors using refrigerants that have a large Global Warming Potential and have a negative impact on the ozone layer. In the Kigali amendment to the Montreal protocol the phase out of these gasses is planned. Alternative gases are flammable hydrocarbons or carbon dioxide. The latter one can only be applied at very high pressure which drives down the efficiency and increases the costs. Therefore new technology needs to be developed.

Goals

Goal	Year	TRL
New solid state magneto-caloric materials with improved performance	2030	6
Improved thermo-acoustic technology	2030	8
Heat-pump technology with zero GWP and no ozone depleting gasses	2040	8

Challenges and Route

One route to complete this task is the development of a thermo-acoustic device or use of solid state materials. The latter one uses the magneto-caloric effect of soft magnetic materials. Present materials are made of earth abundant and affordable raw materials, such as Mn, Fe, P and Silicon. The performance is approaching commercial viability, but further improvement in material properties are crucial for replacement of the existing compressor technology. In the heat pump the magneto-caloric energy is transported by a heat transfer fluid. In that case the use of gases phased out faster.

Heat pumps can also be used for heating of residential areas building heat-nets. As cold source for the heat-pump the constant temperature of a drinking water company can be used.

In the industry low temperature waste heat can upgraded to a temperature where it can be used for heating or distillation.

Grid storage and hydrogen production

Task

Currently, large wind-parks in the North-Sea and large solar farms on land are realized. This means that the inbalance in the production of electricity will increase dramatically. Therefore large scale battery systems are required for short term buffering of this inbalance. In the summer period large excess of renewable energy is produced at times when the consumption is low. This large excess can be converted by electrolysis of water into hydrogen. The hydrogen can be stored in salt caverns and be stored for times when it is needed.

Goals

Goal	Year	TRL
To develop efficient technology for hydrogen production and storage.	2030	8
To develop large scale battery systems with improved materials for short term storage of excess renewable energy.	2030	8
Installation of infra-structure for energy storage and transport of renewable energy.	2040	8

Challenges and Route

For this task improved battery materials are required. Improved or next generation Li-ion batteries, Sodium-sulphur batteries, Redox flow technology or Ni-Fe battery materials. The latter has a high potential because this battery becomes an electrolyser when overcharged. That means that from a system perspective less power electronics are needed and this could lead to lower capital than a combination of a battery and an electrolyser. The Ni-Fe technology is also able to switch instantaneously from charging to discharging when power is needed to stabilize the net frequency. For an electrolyser this can only be done by a solid state electrolyser or a PEM electrolyser. The solid state electrolyser requires improved materials and electrolytes, whereas for the PEM electrolyser (Pt and Iridium-oxide) new materials are needed to make large scale use possible.

2.3 Circular economy

In an attempt to reduce waste and handle the criticality in raw materials, the circular economy is seen as a valuable alternative in manufacturing. Despite the fact that in some areas (agriculture, constructing, materials industry) good results were obtained e.g. for polyester materials, the developments in chemical industry (with a clear link to food, pharma and materials) have been lacking behind. Thus, a "cradle to grave" approach is more advised for chemical products themselves which provides environmental health & safety (EH&S) compliance and tracking inventory across the whole supply chain from manufacture to disposal. Companies like BASF see such approach as holistic when involving the entire value chain and point here at "traceability" of all impacts (BASF's Sustainability, Eco-Efficiency and Traceability (SET) Initiative in Schoener et al., Int. J. Food System Dynamics, 2012, 119-131). Green Chemistry is often said to be a 'cradle to grave' approach (Ed Marshall, Imperial College, www.ch.ic.ac.uk/marshall/4l10).
In line with the search for alternatives, the EU is committed to development of a state-of-the-art industrial infrastructure focused on innovative and specialty (consumer and industrial) products, together with addressing the so-called TLR 4-6 gap, referred to as the "Death Valley". Translated to "the chemical environment", the EU Horizon 2020 program embraces a number of "Key Enabling Technologies", KETs, like nanotechnologies (*Research in this area will lead to new products and services developed by the industry, capable of enhancing human health while conserving resources and protecting the environment*), and advanced manufacturing and processing (*The aim is to increase the competitiveness and energy efficiency of the construction sector, to increase sustainability of production processes and make the process industry more resource- and energy efficient*). An application area, asking for major technology breakthrough, is the so-called Bio-based chemistry. A considerable part of the Horizon 2020 is directed to this theme, being also embedded in the TopSector roadmap "making the molecules of the future".
A promising technological trend that has been developing, and which is of added value for the bio-based industry, is (micro) flow (bio) chemistry. Over the last decade significant academic research has been performed, some small-scale systems are commercially available, and the potential to further improve resource (raw materials) efficiency, process reliability have been demonstrated. Moreover, increased attention in microreactor (gas, liquid or solid phase chemistry) sciences are carried out on lab scale, either with the hope of generating enough material that scale up will not be needed, or with the hope that the information gathered from the lab experiments can be better translated to continuous large-scale processes. For the translation of small to large scale flow chemistry, process monitoring and control technologies (sensing) and general analytical technologies to characterize the feed-stock, the product and the catalyst *in operando* at ultimate length and time scales, is crucial. Overall, it is anticipated that this trend will continue, and we see several immediate and long-term ambitions. We have a chemical industry that is able to develop clean processes with minimal waste under a competitive time pressure, on a small lab scale, such that these clean processes are easily scaled up to reliable robust plants. The reliability is especially relevant for varying feed stocks, which is destined to become more prominent as biomass and other sustainable sources of chemicals come to the forefront.

This task discusses the required innovations in order to

- Improve resource (raw materials) efficiency, e.g. high selective processing and recycling of non-reacted material or development of devices allowing novel chemistry (e.g. photochemistry).
- promptly design and development of "one time right" (having fundamental understanding of processes on molecular level) innovative (larger scale) chemical production processes at larger scale, e.g. feasibility studies on feedstock variability for novel (bio) chemical processes like catalysed depolymerisation at micro-scale leading to "process mapping".
- Realize highly reliable (bio) industrial processes leading to ultimate quality and reduced "out of specification", e.g. tailored process monitoring of diary(colloidal systems) production.

Technological innovations are needed in the fields of:

- Novel micro- and large scale "flow" (gas, liquid and solid) reactors; e.g. for the production of nano-particle drug delivery systems, dairy products, mimicking biochemical processes and (catalyzed) cracking (e.g. pyrolysis) of emerging bio- feed stocks.
- State-of-the-art analytical technologies with ultimate chemical, spatial and temporal resolution for the (macro) molecular characterization (structure) of (bio)catalysts, emulsions or novel drug delivery technologies for complex (bio)pharmaceuticals.
- Novel tools and methodologies to create fundamental insight the body response to compounds, materials and devices; e.g. by characterizing the bio-functionality of surfaces and interfaces, and by realizing human disease and organ model systems on a chip.
- Novel on-, in- and at-line detection technologies (sensor systems) for real time detection of catalyst and other chemicals, at ultimate length scale.

- Advanced chemometric, statistical and process modelling technologies for the ultimate control of industrial processes
- Novel analytical technologies for detailed feed stock characterization, addressing envisioned need in handling larger varieties. (sensors and other on-, at- or in-line detection); base chemicals, raw milk, biomass, water, catalysts.

Cases

Recycling of (raw) materials

Task

An emerging approach to reduce the "inefficient use" of raw materials, limit the waste stream or even use waste (CO_2 in gas phase chemistry after pyrolysis) as energy source or material resource, "flow chemistry" and more generally process intensification have already proven as alternative of today's conventional processing.

Goals

Goal	Year	TRL
High efficient and sustainable (bio) catalyst embedded in flow-reactors.	2020	
Proof of concept for low energy, resource efficient and waste less chemical flow process, including up-stream and downstream processing, towards final product.	2030	
Operational "Factory of the Future" on the basis of efficient use of energy and resources, without waste streams lacking economic value.	2040	

Challenges and Route

The design and use of chemical flow reactors with an ultimate efficiency in resource efficiency, without any waste at an industrial scale is the main challenge.
To complete this task progress is required both scientifically, industrially and societally. Scientifically, new and intensified chemical routes and catalysts are to be developed to be open for the coming diversity of resources and propose end-to-end process designs with fully closed cycles. Enable to make new products and introduce new platform chemicals. Explore new processing, small-scale continuous (micro/milli-flow with nano-functionalities and -sensing), tailored solvents and alternative activation (photo-VIS, electrochemical, plasma, MW, US). In industry existing resources can be used more efficiently and prepared step by step to integrate new resources (biomass, CO2) in the existing Verbund production; close material and energy cycles within the integrated chemical production; switch partly from batch to continuous. For these innovations to be successful the societal image of chemistry has to be changed from one-way resource use/waste generation to sustainable, green enabler with well-balanced resource mix comprising renewables and most efficiently used fossil sources. Change from problem generator to problem solver. Keep and strengthen jobs within Europe. Prepare education for technology convergence.

Possible Topics

- High selective processing and recycling of non-reacted material.
- New and increasingly diverse resource streams: biomass economy, CO_2 as building block, alternative N-fixation, H_2 from photovoltaic water splitting, and artificial photosynthesis.
- New reaction pathways: direct ('dream') reactions using largely available, cheap starting materials and making former intermediate steps superfluous.
- Shrunk reaction pathways: all-continuous multi-step and telescoped syntheses (cascades), eliminating intermediate separation.
- Integrated process pathways: further improving the value added chains within a chempark and designing new processes with that vision.
- More efficient use of catalyst and recycling hereof and assorted components (e.g. ligands).
- Reduction of organic solvent load (carbon footprint), finally down to zero (solvent-less).
- Reliable (quality) nano-micro flow processes for the production of "nano-devices" serving as drug delivery systems.

3 Agriculture, water and food

In order to provide the future world population with sufficient, and healthy food products, and safe water, the way that agriculture and water production are currently carried out need to be rethought in such a way that the impact on our planet is reduced and ideally minimized, therewith adding to resilience. For example, the food industry is responsible for 10% of the greenhouse gases produced in The Netherlands, and this can be reduced considerably using advanced sensing techniques based on nanotechnology. Besides, there is an imminent climate effect in the choices made for ingredients (e.g. animal based proteins have ~ 10 times higher impact on our climate compared to their plant-based counterparts). Furthermore, water quality is becoming more and more of a worry due to increased prevalence of e.g. components related to medicine usage. In order to mitigate this, advanced nanofiltration techniques need to be developed.
Within this roadmap, we target (food)materials, processes, devices and systems that make food and water production intrinsically more sustainable, reliable, and safe. Points of attention are:

- Advanced sensing technology to allow precision nutrient dosing to agricultural crops either in the field, green houses, vertical farms etc.
- Sensors for the real-time monitoring of critical molecular parameters. The sensors will enable closed-loop control for sustainable food production and processing in different food chains.
- Smart controlled delivery devices that minimise e.g. herbicide usage
- Temperature sensors that allow food production systems to enhance food quality, and reduce food waste
- High-tech separation devices that facilitate production of effective raw materials (e.g. to facilitate the protein transition)
- Same, but for warranting water quality (and effective removal of e.g. pharmaceutical residues)
- Devices that allow high through-put screening of ingredient functionality to speed up food product design.
- Comparable devices as organs on chips but now specifically to test the effect of nutrients on organs. Ultimately these two last points will be the stepping stone toward personalised nutrition directed at creating health effects.

In all attention points, the use of nano/microtechnology is essential because the determining factors act on nano- and micrometer scale, which can uniquely be assessed by these technologies.
A special point related to the time that we live in is zoonotic diseases that are very much linked to food, and for which currently various techniques are under development.

Cases

Water purification and safety

Task

In order to make the Dutch water systems robust (management of scarcity and abundance), and safe (free of contaminants), advanced monitoring and separation methods are needed. Specifically the prevalence of pharmaceutical residues is become more and more of an issue, since these components can be hormonal in nature (birth control), and thus affect wild life in our rivers, and also humans if present in our drinking water. Furthermore, the presence of antibiotics will impact water purification plants as we know them, since the micro-organisms that are applied are affected by it, and also some species may become resistant to antibiotics leading to potential health threats.

Goals

Goal	Year	TRL
Advanced (membrane) separation, and hybrid technologies that allow specific removal of medical components.	2020	3
Separation devices with uniform pores in the (sub-)nanometer range, and anti-fouling properties that allow them to operate in tandem with microbial water treatment methods.	2030	
Innovative separation concepts directed toward removal / destruction of antibiotics/antimicrobial components to thus reduce resistance issues.	2030	
Integrated water treatment systems directed to affordable and inherently safe potable water for all.	2040	

Challenges and Route
It is of the greatest importance to develop advanced separation technologies that target these health threatening components. In the field of membranes, various options are available, but unfortunately the pore sizes that they have are not well enough defined, and that is what would need to be done if classic filtration is applied. Besides these membranes can be functionalized to make them more specific for a target components, and possibly, they can be used in combination with other driving forces as currently used (e.g. an electric field instead of the classic option pressure). In this way the separation technology can be made specific, and efficient; and for that structure formation at the nanometer scale would need to be carried out.

Microfluidic devices and sensors for food production and monitoring
Task
Chemical and biochemical research increasingly exploit the use of microfluidic devices and sensors for the detection and synthesis of compounds and for tailoring formulations to maximize the effectivity of the compounds. For example, in food production the quality of soil and water is continuously monitored to optimize production on the land, allowing for precise harvesting transport and storage strategies, that in turn lead to optimal food security and safety. In post-harvest processing, sensors with molecular precision will enable the real-time monitoring of critical molecular parameters. The real-time biochemical data will allow for closed-loop control in order to enable sustainable food processing in different food chains. The developed technologies will be a cost-effective means to increase product quality levels, reduce waste, reduce energy, and increase safety control of existing and new production methods. Micro-technologies allow for the synthesis of small amounts of high-value specialty products and allow controlled structure formation, relevant for food. Such technologies will enable the seamless upscaling from research to production ('scalable flow chemistry'), which will be very helpful for innovations in nutrition. Besides, microfluidic technology and sensing is of great relevance for testing technical component functionality. For example, to make the protein transition possible and allowing animal-based proteins to be replaced by their plant-based counterparts (one of the primary sustainability targets of the Dutch government), it is essential that functionality of these components can be tested on small scale, to allow for fast product formulation and development. Another illustrative example relevant to both food and medicine is the use of sensors on individual products to monitor the quality of the content; this would take us into a new realm in which the good to be used until date will be replaced by an indicator that directly indicates whether a product is safe to use, and thus greatly prevents waste.
Furthermore, there is a clear link with the previously addressed organ on a chip applications, that may be considered as a next step to link the properties of a food or medicine to effects created in the body. As such these devices will allow us to either eat, or keep ourselves healthy at a level that is currently unheard of. Application examples are miniaturized (multiphase) flow systems for enzymatic cascade reactions, and the development of encapsulates for targeted compound delivery with sustained activity ('formulation').

Goals

Goal	Year	TRL
Food testing is done in centralized laboratories.	2020	9
Highly efficient and sustainable food production lines make use of advanced sensing using micro- and nanotechnology, thus creating safe and healthy food, while minimizing food waste, waste water, and energy consumption. Sensors will first be used at-line (taking individual samples) and thereafter on-line (continuous sampling and measurement).	2025	at-line: 9 on-line: 6
Food products designed based on proven ingredient functionality, making flexible use of starting materials possible in a way that complies with circular economy principles.	2030	
Personalized food products and additives directed toward improving individuals' health based on organ on a chip analysis. [personalized eat yourself healthy strategies]	2040	
Integrated food concepts that can be prepared on demand, thus adding healthy years to a peoples' lives, and reducing dependency on health care.	2040	

Challenges and Route
The development of the previously mentioned microfluidic devices requires a crossover between partners in micro/nano-technology, chemical and food synthesis, and biomedical sciences, with a key role for innovative high-tech SMEs. In The Netherlands many micro/nano and biotech SMEs have emerged, backed by world-

renowned research groups at universities/institutes. Scientifically, microfluidic technologies are to be developed for the synthesis of new formulation concepts (e.g. encapsulates). Industrially, the added value of food should be improved and the food products are preferably personalized. A positive image of food in society can be achieved by focussing on sustainable and environmentally friendly food products, such as plant-based proteins, fermentation-based production, meat alternatives, and allergen-free products. Therefore the development of sustainable food production processes with intrinsic health benefits for consumers is key.

Sensors for agriculture

Photonic sensors, such as optical spectrometers, that convert chemical and physical quantities into readable signals, are becoming more widespread for metrology and security applications. Increasing health awareness of citizens in Europe has led to an expanding demand for sensorial information: people want to know what they eat and what they drink, what air they breathe, if their water is clean and their housing is not detrimental to their health, whether their heating operates efficiently and their car does not produce too much pollution, whether the public places they enter are safe, etc. There is an increasing role for sensing methods with important social themes. The instant availability of the compositions of materials and substances is a key factor for corrective and improvement actions.

In industrial society the contamination of our environment is becoming an increasing concern. An example is waste, another is food safety. Human and animal health worldwide is increasingly threatened by potential epidemics caused by existing, new and emerging infectious diseases (including from antimicrobial resistant pathogens), placing a burden on health and veterinary systems, reducing consumer confidence in food, and negatively affecting trade, food chain sustainability and food security. The increasing incidence and more rapid spread of such diseases are facilitated by modern demographic, environmental, technological and societal conditions. Many of the infections are zoonoses, necessitating an integrated, cross-border, “one health” approach to research and public health measures in the human and veterinary field, including the food chain. The European *RASFF* (The Rapid Alert System for Food and Feed) program[1] is an example of a program that addressed these hazards for which the spectroscopic techniques are highly relevant. Figure 1 shows the number of hazard notifications in 2019.

[1] See http://ec.europa.eu/food/safety/rasff/index_en.htm, see also the Appendix to this Project Plan.

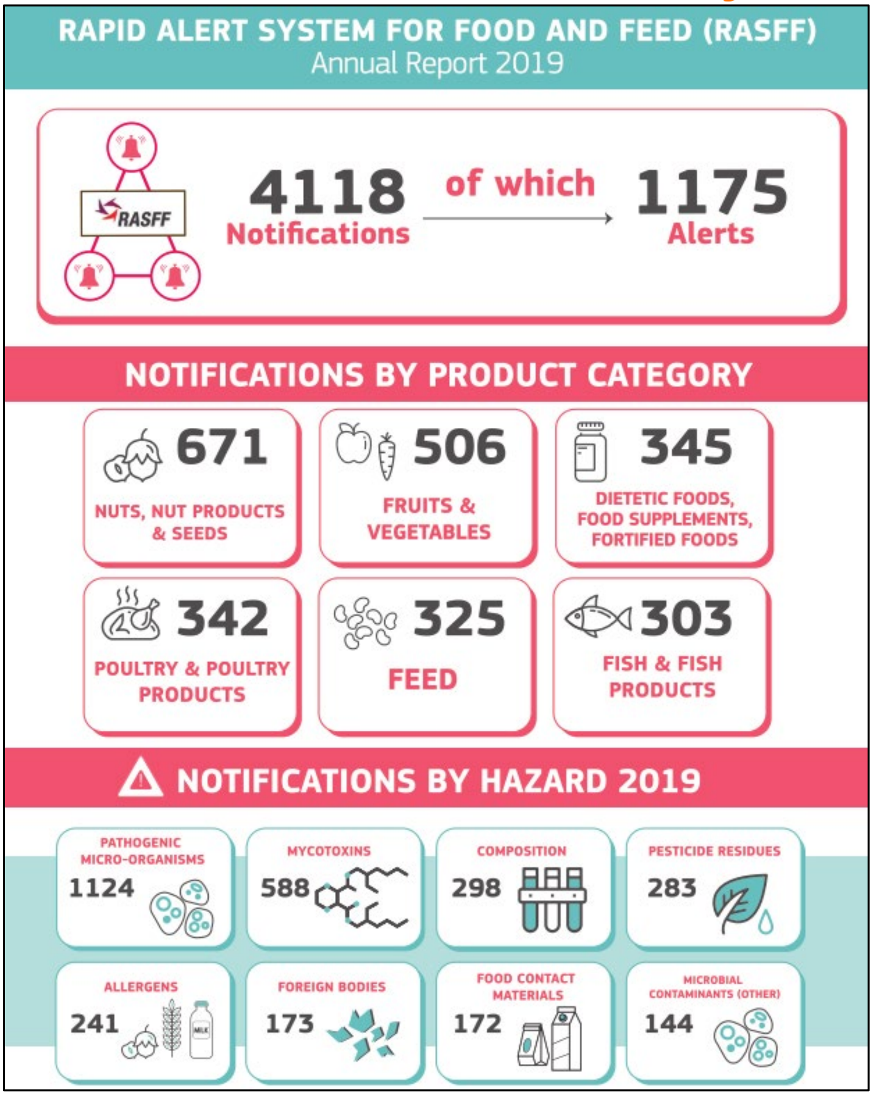

Figure 1: The number of hazard notifications in 2019 of the EU RASFF (The Rapid Alert System for Food and Feed) program.

Many corrective programs use spectrometry as a method to diagnose and monitor the critical elements in the (bio) chemical compositions of water, air, soil, biological tissues, packaging and waste. Target areas are animal health monitoring, food, feed & beverage safety (microbial contamination management, pesticide, agrochemical, veterinary drugs; air, water and soil contaminants. Other application are meat processing, milk analysis, crop management (chlorophyll, water, nutrition).

Microbial contamination management is a crucial task in the food industry. Undesirable microbial spoilage in a modern food processing plant poses a risk to consumers' health, causing severe economic losses to the manufacturers and retailers, contributing to wastage of food and a concern to the world's food supply, see Figure 2. The main goal of the food quality management is to reduce the time interval between the filling and the detection of a microorganism before release, from several days, to minutes or, at most, hours[1]. Spectroscopy is an ideal candidate technology for this application because sample preparation is minimal and results are available rapidly (seconds to minutes).

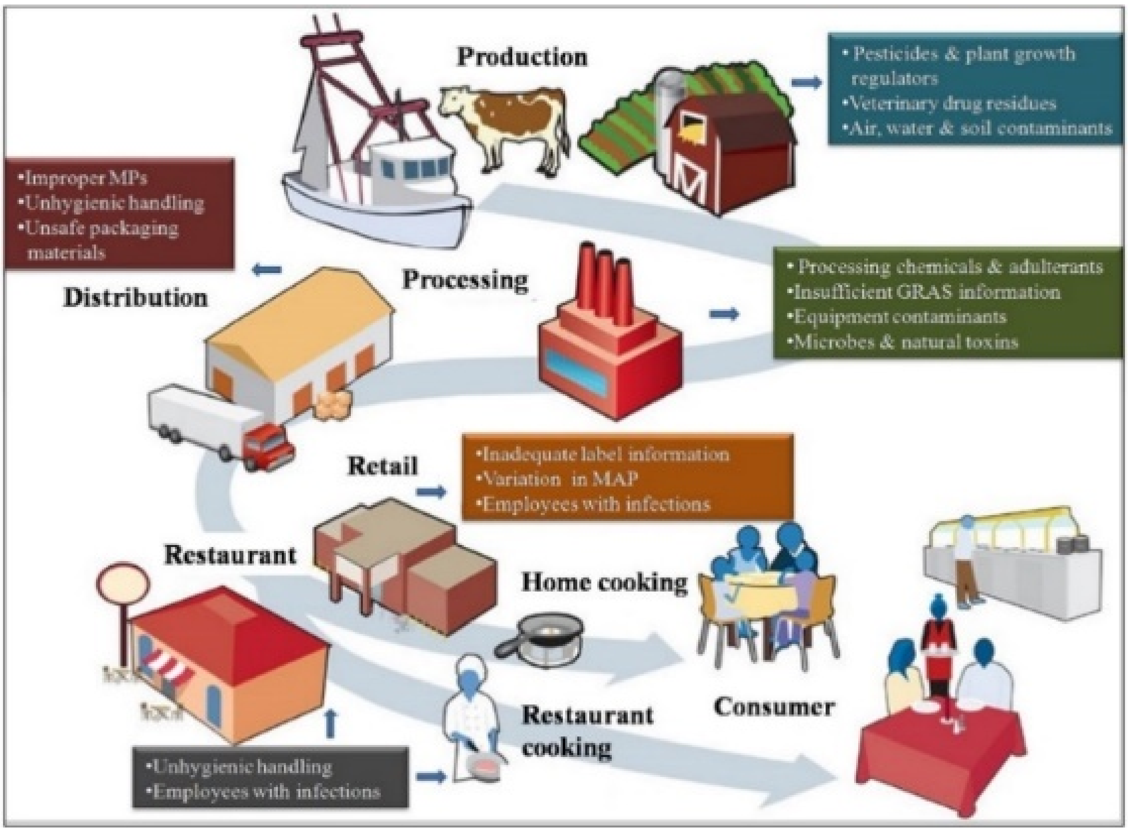

Figure 2: Potential sources of contamination in the consumable food. MPs: Manufacturing practices, GRAS: Generally Recognized As Safe, MAP: Modified Atmosphere Packaging. (Image: CKMNT; adapted from Centres for Disease Control and Prevention (CDC), USA).

The food diagnostic market for the detection of pathogens is expected to grow towards a total market size of $10 bn by 2020. The market is fragmented and players include 3M Company, Thermo Fisher Scientific, Neogen Corporation and bioMerieux. These companies are rapidly adapting their products to sustain their competitive advantage[2]. Competing technologies used for pathogen detection include other biosensors, such as electrochemical biosensors, piezoelectric biosensors and thermal biosensors.

Task

Spectral analysis is a versatile and powerful method to diagnose and monitor food, feed, water, air, soil, biological tissues, packaging and waste. To date there is no good solution for the new challenges in spectroscopy requiring compact and robust devices which can be produced at high volume and low cost.
In industrial society the contamination of our environment is becoming an increasing concern. But also food and feed security and safety, the sustainability of food production, processing and consumption in face of a growing world food demand have become major challenges. Current technology does not provide a solution.

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[1] Adley C.C., "Past, Present and Future of Sensors in Food production", 2014.
[2] Markets and Markets, "Food Diagnostics Systems Market", 2014.

Goals

Goal	Year	TRL
Low-cost, micro-spectrometers in the VIS-NIR and SWIR spectral ranges (price reduction: factor 10, production volume increase: factor 100).	2025	9
"Intelligent spectrometry" with embedded analysis for rapid alert.	2030	9
Low-cost, micro spectral-imaging in the VIS-NIR and SWIR spectral ranges (price reduction: factor 100, high-volume production: > Mio units/years).	2030	9

Challenges and Route

Miniaturization and affordability of the measurements.

Some optical spectrometers are versatile and compact, but better mobility and robustness, and further miniaturization will allow more applications in the field. The effects of miniaturization are threefold. Firstly, small spectrometers enable local measurements in confined environments and these can be configured as an array of sensors in a network. Secondly, small spectrometers are portable and can therefore be used on the spot anywhere where needed. Finally, small devices open the door for drastic cost reductions and volume production. These three effects reinforce and will create new volume applications and markets.

Need to measure in real-time and in-line.

Industry is changing from offline quality measurements towards real-time measurements at the production line. Tissue and waste materials are by nature heterogeneous and cannot be fully differentiated with (multi-spectral) imaging techniques. Most current spectrometry methods are performed through off-line measurements, requiring sample preparation and analysis in a lab environment. These methods are time-consuming, expensive and require users skilled in analytical spectrometry to perform the analysis. Therefore companies are looking for compact and robust spectral sensors and efficient data collection methods.

4 Health

The missions in the KIA "Gezondheid en Zorg" are:

- Mission I - Leefstijl en leefomgeving
- Mission II - Zorg in de leefomgeving
- Mission III - Mensen met chronische ziekten
- Mission IV – Dementie

For the Chemical Sensing and Enabling Technologies section of the Topsector Chemistry, many of the contributions are generic and do not apply to one mission only. There is quite some overlap from the technology side. Therefore, where applicable, the missions for which proposed activities are valid will be mentioned on the spot.

Quality of life (QoL) refers to the general well-being of individuals and societies. Important aims are to keep people healthy as long as possible, and to enable people in need of care to live a high-quality life in their own environment. Personalized (nano)technologies play an important role in achieving these aims, by monitoring personal biochemical health status and by enabling targeted and personalized drugs and food.
This chapter discusses the required innovations in chemical nanotechnology and devices in order to:

- Diagnose, monitor and stratify people; e.g. by measuring samples, such as liquid biopsies from people, or by measuring directly on people, e.g. on the skin or via a catheter (***Missions I, II, III, IV***).
- Treat patients; e.g. by drug delivery, regenerative engineering, neurostimulation (***Missions II, III, IV***).
- Increase efficiency in drug development and nutrition development; e.g. reduce/replace/refine use of animal models (3R), faster into human; human disease and organ models on a chip ("Organ on Chip") (***Missions II, III***).
- Synthesize and characterize novel "biological" drugs and specialty nutrition; as sole active ingredients and/or novel targeted or sustained release formulations (***Missions II, III***).

Technological innovations are needed (***Missions I, II, III, IV***) in the fields of:

- Novel materials & devices; e.g. for biochemical sensing technologies (in-vitro, in-vivo, minimally invasive), micro/nano-technological synthesis devices and for miniaturized Point-of-Care devices, in which assay complexity is solved by the device rather than a bulky instrument. This latter aspect requires precise control over surface properties allowing accurate flow and timing control.
- Novel fabrication & inspection technologies; e.g. for the development of functional materials, coatings and devices, with control on the nanometer length-scale
- Novel tools and methodologies for R&D, (i) to characterize complex molecular systems and interactions, novel drug and food delivery systems and biofunctional surfaces and interfaces; (ii) to model and understand the body response to compounds, materials and devices, e.g. by realizing Organs on Chip
- Novel methodologies to upscale microfluidic devices for production of medication and food ingredients, e.g. emulsions for targeted delivery purposes.

Cases

Bio-active sensing and actuation devices

Task

In the coming 10 years groundbreaking developments are expected to occur at the interface where nano-micro devices and complex molecular systems interact with biological systems. This will lead to highly sophisticated devices that are able to function with and within live biological systems. Novel bio-sensory and bio-actuation functionalities are expected, resulting from developments in bionanotechnology, biophysics, supramolecular chemistry, nanophotonic sensors, and regenerative medicine. Potential embodiments include smart patches, smart fibers, smart probes, smart catheters, smart implants, etc. The most advanced systems will combine and integrate molecular-based sensing and actuation principles of physical and (bio)chemical nature. Examples are: real-time sensing on the body or in the body; accurate drug administration using real-time data as an input; neuronal stimulation

Example of a small sensor that continuously monitors the biochemical status of a person based on objective signals from the body and/or the environment; point of care diagnostics and monitoring (e.g. in Personalized/Precision Medicine); critical care monitoring; etc.

A rapidly developing field in healthcare is the field of immunology, with new treatments and diagnostics being introduced based on the immune system. Presently, the inflammation status of patients is monitored by recording symptoms such as fever and blood pressure, and by measuring inflammatory markers using laboratory-based tools. However, the symptoms are not specific enough and laboratory-based testing procedures are slow, with data becoming available only after a day, which is unsuited for monitoring the markers of rapid inflammatory response. The present-day procedures are inappropriate for patients who can rapidly develop life-threatening conditions, such as cytokine release syndrome, a condition that occurs in patients with Covid-19 and patients receiving immunotherapies. Another important application is to measure and regulate drug levels, e.g. in case of antimicrobial therapies, for more effective life-saving treatments and lower risks to cause antimicrobial resistance. Also, devices for immunomonitoring would allow patients to be released from the hospital earlier, e.g. after having received an immunocompromising or a surgical treatment. Thus there is a clear and urgent demand for sensing tools to continuously monitor the condition of patients.

Goal	Year	TRL
Biomarkers (proteins, drugs) are measured in the laboratory	2020	9
Biomarkers are measured near the patient (POCT = point of care testing, individual samples are taken and measured)	2025	6
Biomarkers are measured continuously, samples are automatically taken via a medical device, e.g. via a catheter (continuous monitoring)	2030	6
Biosensors are worn on or in the patient (wearable, insidable)	2040	6

Challenges and Route
To accomplish this task collaboration of experts in the fields of device technology and chemical biology can be valuable. Device technology deals with the realization of novel device functionalities and related miniaturization and integration; partners can for example be found within the Top Sector HTSM, more specifically the roadmaps Nanotechnology, Photonics (linked to PhotonDelta, a national initiative financially supported by the (local) government with a European ambition - https://www.photondelta.eu/) and Advanced Instrumentation. In the field of chemical biology, chemical approaches are developed for biological systems. In The Netherlands we have excellent chemical biology groups (see e.g. Zwaartekracht Functional Molecular Systems www.fmsresearch.nl, and the NL Research School of Chemical Biology www.nrscb.nl). Furthermore, the Netherlands Institute of Regenerative Medicine (www.nirmresearch.nl) studies how human cells and tissue interact with materials and devices, and methodologies developed to understand such processes on different time- and length scales. Research collaborations of these different parties would be a great opportunity to focus on the interface between biochemical/biophysical devices and biological systems, which would also be of interest to large companies and SMEs operating in the field of materials, biotechnologies or medical technologies.

Scientifically, technologies could be developed to sense and control living systems in-situ and in real time. For example, small biochemical sensors integrated into medical devices and disposables, which are in contact with the human body and continuously monitor the biochemical status of patients. Materials and devices for drug delivery and for bio-mimetic stimulation. Systems for comprehensive biochemical profiling. Systems for closed-loop monitoring and treatment. In industry, novel products for biochemical patient (therapy) monitoring, drug delivery, neuro-stimulation and critical care monitoring could be developed. This can improve the added value of medication, therapy effectiveness and compliance, which would reduce the overall healthcare costs through disease management and early detection of exacerbation. Enable novel care models based on patient monitoring and decentralization.

Society could profit from these innovations by the introduction of personalized medicine, the possibility of early diagnoses and self-monitoring and improved therapy adherence. This in combination with the reduction of side-effects of medicine could reduce result in more people growing old healthy.

*Possible topics*Bio-interfaces, passive and active anti-fouling interfaces, biomimetic interfaces, biodegradable polymers and interfaces, degradation-resistant interfaces (e.g. for GI tract), interfaces and nanoparticles for release of bio-actives, interfaces for control of body reaction.

- Synthetic-biological concepts for sensing and actuation, bio-inspired devices, nanosensors.
- Minimally-invasive bio-functional healthcare devices.

- Novel scientific analysis tools, for studies with high spatial and temporal resolution (e.g. studies with single-molecule resolution) and for high-throughput screening studies (e.g. to screen novel materials with many degrees of freedom).
- Fabrication methods, on the one hand top-down (cf. device technology community), on the other hand bottom-up (cf. chemical biology community).
- Characterization of thermodynamics, kinetics, and transport processes in complex interaction systems.
- Analysis of samples of physiological origin, e.g. blood testing, skin sensing, mucosal fluid testing, interstitial-fluid testing, tear sensing.
- Integrated devices featuring combinations of bio-inspired techniques with other techniques, e.g. combining synthetic biological sensing with sample transport via capillary flow.
- Sampling devices; chemical & biochemical lab-on-chip technologies; increase information quality and quantity from small complex samples, such as liquid biopsies.

Human disease and organ model systems on a chip

Task

The development of novel pharmaceutical and nutritional compounds is complicated due to the inherent complexity of the human body and the variability between people. Furthermore, for ethical reasons the testing of new pharmaceutical compounds on animals and humans should be minimized as much as possible, while cosmetic compound testing on animals recently has been completely forbidden. This calls for the development of sub-cellular, multi-cellular and multi-organ human model systems on a chip. Such human model systems can support scientific research on how the human body works, and can help to improve and accelerate the testing and development of novel pharmaceutical and nutritional compounds. In the future, even personalized model systems may become available, e.g. built from induced pluripotent stem cells (iPS technology), which allow creating functional organs tissues on chip possessing the genetic (disease) profile of the patient and thus allow the realization of *precision* medicine.

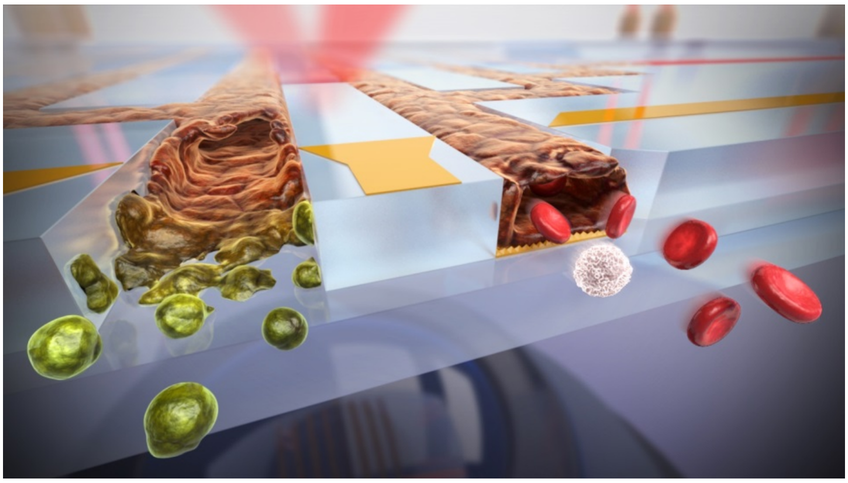
Goals

Goal	Year	TRL
Biomembrane / organelle / cell / multicellular system on chip		
Organ functionality on a chip / combination of organs / interacting organs mimic complex body function		
Transport processes in living systems, e.g. across membranes (artificial, biomimetic, biological), between cells, between cells and extracellular matrix, between cells and solid surfaces		
Minimal-system studies, i.e. what minimal system is needed to achieve a desired multi-cellular functionality		

Challenges and Route

The Netherlands has a leading position in Europe and plays an important role in the development of Organ-on-Chip technology and the applications of healthcare professionals (e.g. medical doctors, pharmacists). Chemical chip technologies (e.g. surface modification, biomembrane on chip technology, sensing on chip) and cell biological technologies will play an imminent role, while many technology solutions can be derived from earlier lab-on-chip developments. Novel methodologies and tools should be developed, for example, to understand how compounds interact with membranes, cells, and organs. A variety of tools should be developed ranging from high-throughput screening compatible methodologies for research to application dedicated equipment for personalized therapies.
The topic would partly fit within the Topsector LSH and HTSM, and Agrofood fields. Furthermore, the topic links to the MinacNed association, for micro/nanotech organizations (with a dedicated microfluidics/lab-on-a-chip cluster) as well as HollandBio for med/biotech organizations, including many drug development SMEs. The topic is the focus of the virtual hDMT (human Disease Model Technology) institute (www.hdmt.technology), which has been founded in 2015 and in which a crossover between device engineers, biologists, pharmaceutical and medical scientists, and nutritionists has been established.

Scientifically, multicellular human disease models and high-throughput organ-on-a-chip models should be developed. Interactions between organs and drug functionalities could be explored. Economically, the costs and time-to-market of novel drugs is currently very high and should be decreased drastically. Using precision medicine the effectiveness of patient treatment could be improved. Society will benefit from these innovations as personalized medicine will be available, side effects from drugs will partly be prevented and the need animal testing will be reduced. (***Missions I, II, III, IV***).



Artist's impression of microengineered iPSC-derived blood vessel structure with integrated microelectrodes for studying drug transport across endothelial blood vessel wall.

Microfluidic devices for synthesis of medicine

Task

Chemical and biochemical research increasingly exploit the use of fluidic microdevices for the synthesis of new compounds and for tailoring formulations to maximize the effectivity of the compounds. Microtechnologies and microfluidics allow for the synthesis of small amounts of high-value specialty products and allow controlled structure formation. Such technologies will enable the seamless upscaling from research to production ('scalable flow chemistry'), which will be very helpful for the emerging paradigm of Precision Medicine and for innovations in nutrition. Application examples are miniaturized (multiphase) flow systems for enzymatic cascade reactions, and the development of encapsulates for targeted compound delivery with sustained activity ('formulation'). This approach is valid for medication as well as for other sectors such as food, personal care, etc.

Goals

Goal	Year	TRL
Synthesis and formulation of pharmaceutical drugs, small molecules and biopharmaceuticals (active pharmaceutical ingredients, APIs), and food		
Specifically encapsulate components on chip, encapsulation of food ingredients		
High-throughput screening of functionality of components used in formulation in combination with the active compounds		
Development of production technologies for nanotech-based targeted drugs and formulations		
Surface modification, multiscale modelling and rational design of formulations, interfacial design, functional nanoparticles, nanosomes, microdroplet chemistry		
Lab-on-a-chip/microfluidics based flow chemistry systems including (integrated) analysis/monitoring and process control		

Challenges and Route

The development of microfluidic synthesis and formulation devices requires a crossover between partners in micro/nanotechnology, chemical and biochemical synthesis, and biomedical sciences, with a key role for innovative high-tech SMEs. In the Netherlands many micro/nano and biotech SMEs have emerged, backed by world-renowned research groups at universities/institutes. The topic also relates to the Future Medicine Initiative (formerly Chemistry for Future Medicine) and the Netherlands Center for Multiscale Catalytic Energy Conversion (cf. Zwaartekracht MCEC). Furthermore, the topic links to the MinacNed association, for micro/nanotech organizations (with a dedicated microfluidics/lab-on-a-chip cluster) as well as HollandBio for med/biotech organizations, including many drug development SMEs.

Scientifically, microfluidic technologies for the synthesis of new active pharmaceutical ingredients (e.g. biologics by cascade reactions) and new formulation concepts (e.g. encapsulates) should be developed. To achieve custom-made nano-medicines an integrated and flexible production of formulated drugs must be pursued. Industry benefits from innovations to improve the added value of medication and food and a reduction of the time-to-market for drugs. Personalized medicine and the possibility of targeted drug delivery will have a large impact on the overall health and disease treatment of society.

5 Industrial Safety and Process Development

CSET-relevant key technologies (Table 1) such as advanced analytics and sensoring, data science, and modelling will play a crucial role in developing new processes and improving the monitoring and control in the (petro)chemical, agro/food, and pharmaceutical industries. Applications of improved and extended sensing in the processing industries will benefit the design of new processes (e.g. by improving chemical understanding) and the efficiency and sustainability of processes at plant-scale, but also their safety aspects.
To implement "Factory of the Future" and "Industry 4.0" concepts in practice, developments in key CSET technologies are therefore needed and proposed in this roadmap. Case studies describing the role of such technologies for industrial safety and process design are described below.

Cases

Industrial safety
Task
Industrial manufacturing operations must be organized, managed and executed in such a way that employees and assets are protected by minimizing hazards, risks, and accidents. Whereas employee behavior, company culture, and HSE regulations are major drivers for a safe industrial environment, there are technological opportunities and challenges related to CSET that will contribute to the enhanced safety of both the occupational and process/production aspects of future manufacturing. The term "Safety by Design" is at present an integral part of the European "Joint Technology Initiative" SPIRE, recognizing the importance to consider safety as an integral part of industrial design. To this end, chemical sensors and advanced enabling technologies with high specificity and sensitivity must be developed for fixed deployment both in and around a production process as well as for flexible use by operators in a plant environment.

Goals

Goal	Year	TRL
Wearable, portable, or fixed sensors for continuous air monitoring of specific chemicals of concern in a production environment, including ATEX (Atmosphere Explosible in French) zones.	2030	8
Standoff portable sensors for rapid identification of leaked chemicals (e.g. liquids, solids) in a plant or in the environment.	2030	7
Drone-based miniaturized sensors for environmental surveillance of chemicals, e.g. in case of inadvertent release or leakage.	2030	7
Handheld rapid identity testing of raw materials to prevent chemical misoperations.	2030	7
In-/on-line process analytical technology that completely avoids manual sampling from a process pipeline or reactor.	2040	7
In-/on-line sensing techniques, including soft sensors, that provide early warning signals for potentially hazardous process deviations or upsets.	2040	7

Challenges and Route
The main challenges related to sensing for industrial safety are *i)* the development of new and/or improved sensing mechanisms for chemically specific detection and *ii)* turning such sensing mechanisms into low-cost, rapid, robust, small and sensitive physical sensors. This will require tight collaboration between research groups and instrument developers and vendors (e.g. high-tech SME or larger vendors). A particular additional challenge is the development of sensors that work robustly in chemically demanding (e.g. corrosive) environments.
With the growing importance of artificial intelligence (AI)-based process control mechanisms also comes an increased reliance on data quality, which means that sensors and their data must be(come) highly reliable and robust.

Industrial process development

Task

Processing industries such as (petro)chemical, agro/food, and pharmaceutical are under continuous pressure to maintain or increase their competitiveness in terms of economic efficiency, sustainability, flexibility, and safety. To address this challenge, it will be crucial to rapidly and effectively design and scale up new and improved processes (Factory of the Future). In turn, this will fuel the need for a more fundamental understanding of raw material characteristics (which, increasingly, are complex bio-based materials), (bio)chemical pathways and their corresponding thermodynamics. Flow chemistry will have important added value in this regard by its ability to translate processes at nano- or micro-scale to those at e.g. pilot plant scale.

Goals

Goal	Year	TRL
Novel multi-model analytical technologies with ultimate chemical, spatial, and temporal resolution. For example, availability of miniaturized in-/on-line detection technologies for *in situ* measurement of reactants, intermediates, and products and catalyst behavior at different time and length scales.	2030	5
Availability of innovative micro-flow reactor technologies for gas-, liquid- and solid-phase chemistries. Advances in molecular, process modelling and chemometrics (incl. soft sensors) for improved process understanding and control.	2030	7
Implementation of the “Factory of the Future” on the basis of flow chemistry in a variety of chemical production processes.	2040	6

Challenges and Route

Key in achieving the vision for the “Factory of the Future” using flow chemistry are smart analytical (nano)technologies which can create a more detailed understanding of chemical pathways and which are anticipated to be also applicable for larger scale flow chemistry. In general, the availability of in-/on-line analytical technologies will enable the characterization of chemical reactions and their catalysts at the spot, without time delay and without sampling demand or any other interference to the spot of information. Such developments in Process Analytical Technology (PAT) will become key enablers for realizing smart process control systems as envisioned by the Industry 4.0 platform. PAT sensors can be integrated into bigger modern process control systems such as Evonik’s EcoTrainer, which is a standardized process control platform for use not only in pilot and production, but also for the very first chemical laboratory measurements. Thus, the sensors and derived new process control concepts can lead to a unification of the formerly different and separate stages and thereby lead to massive shortening of process development time. This is to go hand in hand with bringing in advanced molecular and process modelling approaches (*in silico* experimentation) for improving our understanding of chemical processes and the way that such processes can be controlled. Also the increased interest in gas- and solid-phase flow chemistry is of importance and opens a new window in micro-reactor engineering, process modelling, phase separation (down-stream processing) technologies, and dedicated analytical technologies.

Apart from the search and implementation of new complex chemical processes, the increasing expectations from customers on “product quality” and the need for ultimate “reliability” of the complete production processes are regarded as decisive challenges. As an example, manufacturing of polymer-based biomaterials and chemically modified bio pharmaceuticals will face ever-increasing quality demands from regulatory bodies, also putting great emphasis on process reliability (PAT initiatives).