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Chemistry Roadmap

for Research Infrastructures 2025–2028
by the Swiss Chemistry Community

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1 Executive Summary

Chemical innovation affects almost every aspect of our daily life: it affects, for instance, what we eat and wear, the structures we live in, how we communicate, how we go to work and travel around the world, how we produce and store energy and how we diagnose and cure disease. Consequently, chemical innovation is key to improving our health and protecting the environment. It will contribute to the reduction of our carbon footprint and to the discovery of virtuous resource and energy cycles, paving the way towards a truly sustainable economy and society. Chemical innovation is only possible with detailed insights into chemical structures and processes. This is what then opens the possibility to design novel compounds and materials and to access sustainable production processes.

Regarding chemical research, Switzerland is among the leading nations of the world. This remarkable success results from the interplay and mutually beneficial relationship between top ranking universities and a strong chemical and pharmaceutical industry. The Swiss chemical and pharmaceutical industry generated more than 50% of total Swiss exports in the first half of 2020, and is the second most competitive worldwide. This economic sector directly employs more than 74,000 people in Switzerland with another 203,000 jobs in associated branches.

This industry is attracted to Switzerland and is retained here because of the world class academic research and education environments arising from the Swiss universities of applied sciences, the renowned Swiss universities and federal institutes of technology (ETH domain).

Academic research in the chemical sciences is undergoing a profound transition. Characterised by studies carried out at the single laboratory level in the past, research is increasingly oriented towards multi-laboratory collaborative endeavours in decentralised networks; it also requires access to more advanced tools at highly specialised facilities and across disciplinary expertise. This transition is propelled by the increasing scope and complexity of chemical problems which today require exchanges across classical disciplinary boundaries together with the need for research infrastructures that provide state-of-the-art instrumentation and expertise at the edge and beyond the classical boundaries of chemistry.

For decades, the essential infrastructures for chemistry research could be provided at single university, institute or even laboratory level. However, frontier instrumentation is no longer affordable to single institutions. Not only does cost become prohibitive, but the expertise required to develop and operate the instrumentation is rare. Furthermore, the complexity of the data generated, from acquisition to interpretation, also requires novel approaches, which is being propelled by the ongoing digital revolution where chemistry applications emerge among the most demanding today. Consequently, a set of national hubs/centres are needed to provide state-of-the-art infrastructure to all Swiss researchers across the chemical sciences and, thereby, maintain Switzerland at the forefront of chemical research and innovation.

Following established models, these infrastructure-hubs can either be organised as central national facilities, for instance around the synchrotron radiation sources today offered at PSI, or as distributed networks linking multiple sites that host complementary instrumentation and expertise. All the hubs will be made accessible to researchers across Switzerland and developed as international centres. Since frontier instrumentation requires specific skills for operation as well as specialised expertise for data analysis, these hubs will provide both frontier tools and expert staff to the broad user community.

Moreover, the proposed infrastructures should foster multinational scientific exchange and collaboration. Presently, Switzerland is a member of several international research organisations, including CERN, the European Synchrotron Radiation Facility (ESRF) comprising the Swiss-Norwegian Beamline (SNBL), the European X-Ray Free Electron Laser (European XFEL), the European Spallation Source (ESS) and the European Life Science Infrastructure for Biological Information (ELIXIR). This international connectedness is crucial for the high quality of chemistry research in Switzerland. The national infrastructures proposed in this roadmap will continue to pursue an international vision, that will also help to attract further international talent, foster exchange at the international level and develop the international competitivity of the Swiss research environment.

This roadmap recommends to set-up or consolidate seven national infrastructures grouped into two pillars of discovery- and challenge-oriented infrastructures.

A first group of discovery-driven infrastructures will provide essential capabilities for characterisation at different temporal and spatial resolutions and to study fundamental structure-function relationships under relevant conditions, which is at the basis for rational development and innovation. This first group comprises:

1. A magnetic resonance and magnetism hub,
2. A centre for *operando* synchrotron studies,
3. An electron microscopy and diffraction hub.

The second group of infrastructures builds on the insights from fundamental structure-function relationship studies to tackle major social challenges. These challenge-driven infrastructures are oriented to screen, discover, generate and develop lead chemicals and materials for specific applications related to energy, health and sustainability. This second group comprises:

1. A facility to produce Terbium radionuclides for diagnostics and treatment of disease,
2. A mass spectrometry-based screening platform for (bio)catalysts and environmental samples,
3. A centre providing state-of-the-art instrumentation for translational chemistry and managing a national library of compounds synthesised in academic laboratories across Switzerland,
4. A catalysis hub *(CAT⁺)* to discover and develop catalysts and catalytic processes.

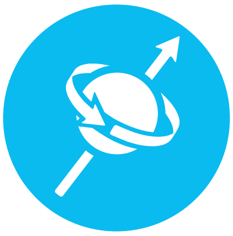
The proposed infrastructures were identified in the course of an 18-month process starting in summer 2019. All public institutions conducting chemistry research were represented throughout the process. Moreover, the input from chemists across Switzerland was collected in a survey conducted by the SCNAT Platform Chemistry and organised in close collaboration with the Swiss Chemical Society. The elaboration of this roadmap constitutes an important first step towards long-term strategic consultation and planning within the Swiss chemistry community.

2 Findings and Recommendations

General Findings

Finding: Frontier instrumentation can often no longer be accommodated at a single university or institution, both due to cost and because of requirements for highly specialised advanced skills for operation and data analysis. While the user groups have expertise in their specific fields of application, they often lack access to the most advanced instrumentation and are short on the comprehensive skills required to run such instruments and fully process and analyse the data obtained. Consequently, research groups in chemistry now require state-of-the-art research infrastructures with well-trained staff.

Recommendation: It is recommended to develop national infrastructures accessible to all researchers in Switzerland, as well as in other nations, to provide access to advanced instrumentation and expertise. Trained permanent staff should support and advise users regarding data acquisition and data analysis.



Magnetic Resonance and Magnetism

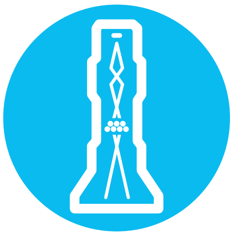
Finding: Switzerland is a global leader in magnetic resonance. Infrastructure in EPR, magnetic measurements, and high-field NMR is essential for the community across the whole of chemistry, from chemical biology to materials chemistry. Our capacity in this area will no longer meet the international standards in 5 years from now. Single institutions or local consortia can no longer meet this need.

Recommendation: There is the need for the creation of a new distributed infrastructure serving the whole Swiss community. The infrastructure will maintain international leadership in magnetic resonance and support academic and industrial research across the chemical sciences.

Centre for *operando* Synchrotron Studies

Finding: The Swiss chemistry and material science communities have an increasing need for multiple-technique beamlines for *operando* synchrotron-based studies. However, the present shortage of multiple-technique beamlines will not be alleviated by the planned upgrades of existing beamlines in Switzerland and Europe (SLS 2.0 and ESRF-EBS), which aim to further specialise single-technique beamlines. Moreover, synchrotron experiments produce increasing amounts of complex data generating a need for expertise and support for data analysis.

Recommendation: A centre for *operando* synchrotron studies localised at two complementary synchrotrons and centred around multi-technique beamlines should be launched to alleviate these bottlenecks. The new centre will exploit synergies between multi-technique beamlines at ESRF and SLS and provide a gateway between home laboratories and the upgraded synchrotron facilities. Moreover, the centre should provide expertise tools for data management and analysis and provide standardised setups for *operando* experimentation to facilitate efficient use of beamtime.



Electron Microscopy and Diffraction

Finding: Electron microscopy (EM) is a powerful analytical method that can simultaneously provide structural, compositional and chemical information for complex structured materials at atomic resolution. Recently implemented *in situ* and *operando* capabilities allow the observation of materials under application-relevant conditions. Furthermore, the development of both, highly sensitive and very fast detectors as well as pulsed electron sources, open the door to mechanistic studies of dynamic chemical processes and structure determination of beam-sensitive substances at the atomic scale.

Recommendation: To establish a distributed electron microscopy facility, each of the participating units will provide a station offering support, expertise and innovative EM infrastructure specifically configured for structure determination of beam sensitive substances or the study of fundamental chemical reactions and processes with frontier space and time resolution into material, physical and (bio)chemical systems. This unique, decentralised EM facility, building a consortium with highest expertise in particular fields of applications, will provide fundamental and applied knowledge in various areas of chemistry and material research.

Radiochemistry: Targeted Alpha Therapy using Terbium and Other Oncological Solutions (TATTOOS)

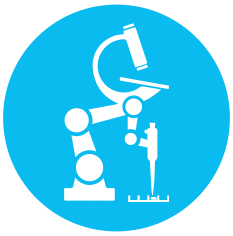
Finding: Nuclear medicine uses radionuclides for the diagnosis and/or treatment of disease. Today, radionuclides of highest purity are made available at PSI for preclinical and first in-human clinical studies. However, some of the desired radionuclides (such as ^{149}Tb and ^{152}Tb) are difficult to produce by currently available means, but can be produced via ISOL techniques proven at CERN.

Recommendation: A facility at PSI should be extended to produce additional radionuclides, in particular the extremely promising radionuclides ^{149}Tb and ^{152}Tb. The extended facility will allow for performing the entire process onsite, comprising spallation, collection and chemical separation of these radionuclides, followed by the production of radiopharmaceuticals. Through this facility novel radiopharmaceuticals will be made available and enable world-first clinical studies throughout the country.

High-throughput Screening Hub for Chemical Biology

Finding: The competitiveness of Swiss academia and the Swiss pharmaceutical and chemical industry builds on the discovery and development of powerful catalytic entities and their effective and resource-saving implementation in challenging syntheses and manufacturing processes. To develop sustainable (bio)catalysts, fast analysis of samples at miniaturised scale is central. Such capacities would be provided by a high-throughput screening hub dedicated to apply and further develop mass spectrometry-based rapid analysis of chemical entities, which is currently lacking in Switzerland.

Recommendation: We recommend to create an open access high-throughput screening hub to accelerate the development of new (bio)catalytic entities and bioactive compounds. Embedded at a central location such as the Zurich University of Applied Sciences, the hub will build on cutting-edge high-throughput screening technology. In particular, microfluidics and acoustic mist ionisation coupled to mass spectrometry will be implemented.



National Centre for Translational Chemistry

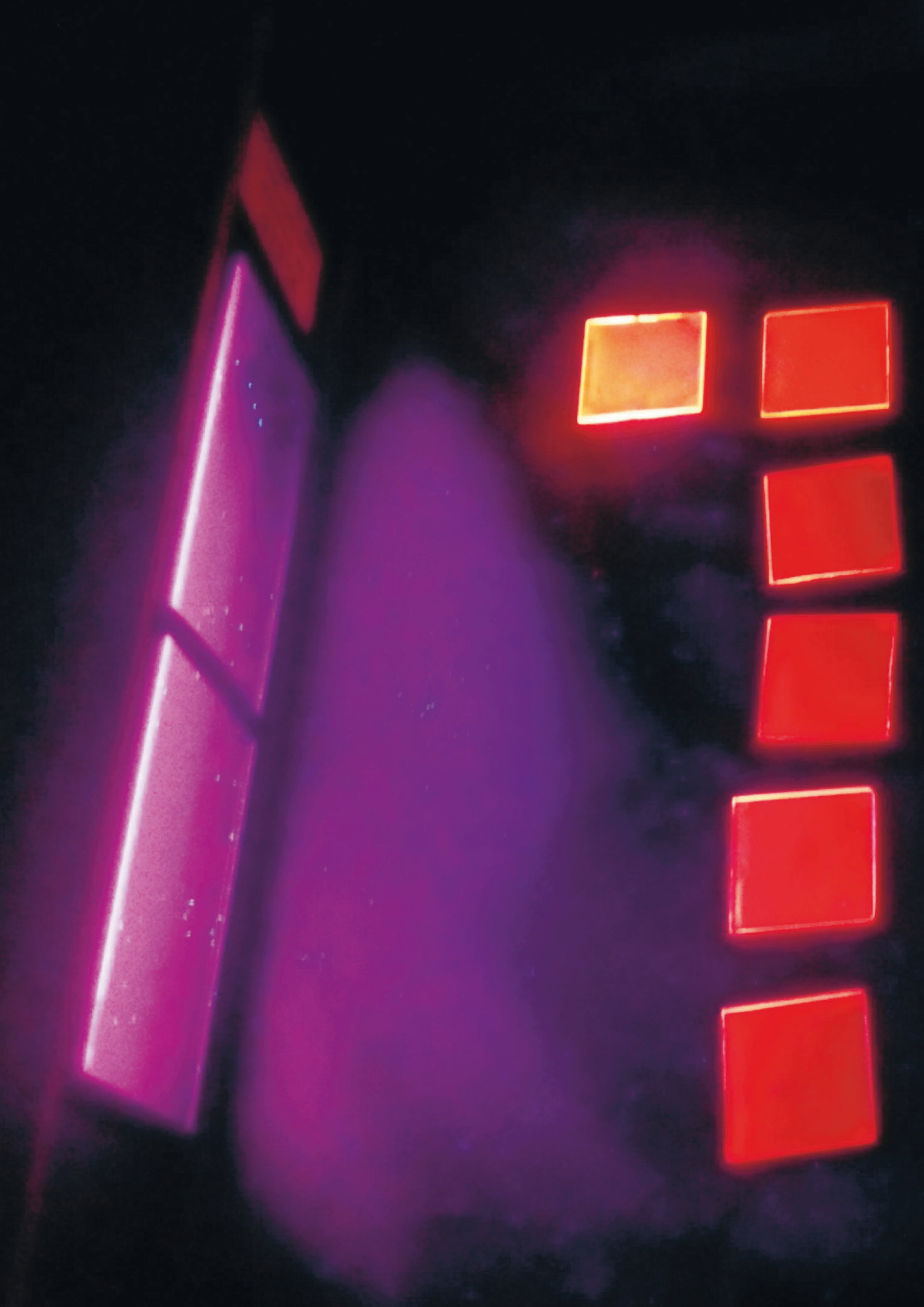
Finding: The ACCESS platform of the NCCR Chemical Biology has emerged as an important tool to harness chemistry research in (Swiss) academia to respond to societal challenges, particularly public health (for instance, the rapid identification of anti-SARS-CoV-2 drug candidates). The number of requested screens has steadily increased over the years, especially for translational studies. However, the NCCR Chemical Biology will expire in 2022, and the costs to continue ACCESS are too high for a single institution.

Recommendation: It is recommended to transform the NCCR-based ACCESS platform into a National Centre for Translational Chemistry. Investments are required to significantly upgrade the platform, broaden its scope and to assure that the top standards applied serve the whole Swiss community. Through the envisaged National Centre for Translational Chemistry, Switzerland may also assume leadership on the European level.

Catalysis Hub

Finding: Sustainable development, such as producing goods without impact on our environment, is one of the greatest challenges facing humankind in the 21st century. It will require the acceleration of the development and discovery of efficient and sustainable chemical processes using alternative feedstocks. In addition, the arrival of robotics and the possibilities offered by advanced spectroscopy/microscopy, computational chemistry and data science, as well as the new NCCR Catalysis, offer new opportunities to discover and develop catalytic sustainable processes to maintain Swiss competitivity in chemical research.

Recommendation: The Catalysis Hub *(Cat^{+})* launched in 2021 should be consolidated to provide the access to state-of-the-art instrumentation and expertise in high-throughput experimentation and data analysis that is needed for the Swiss catalysis research community, in both academia and industry. This research infrastructure would put Swiss Research on the forefront for the development of sustainable chemical processes and digital catalysis discovery.



3 Introduction

The present roadmap for future large research infrastructures represents the view of the Swiss scientific community in the field of chemical sciences. It is a formal element of the process to elaborate the 'Swiss Roadmap for Research Infrastructures 2023' according to Swiss law (art. 41 Federal Act on the promotion of research and innovation; art. 55 of the corresponding ordinance). The roadmap describes the community needs in terms of national or international research infrastructures for the funding period 2025–2028. It shall serve as an additional basis for the decision-making on new or major upgrades of national infrastructures and/or major participations in international network infrastructures and user facilities.

The responsibility for the elaboration of the 'Swiss Roadmap for Research Infrastructures 2023' rests with the State Secretariat for Education, Research and Innovation (SERI). It has thus launched a process that includes (phase 1) the selection of infrastructures by the ETH Board and swissuniversities, (phase 2) the evaluation by the Swiss National Science Foundation, and (phase 3) the assessment of the feasibility again by the ETH Board and swissuniversities. The result will be submitted to the Federal Council for consideration and decision in the context of the Dispatch on Education, Research and Innovation 2025–2028. This whole process is complemented by a preparatory phase to establish the needs of the various scientific communities. The SERI has formally mandated the Swiss Academy of Sciences (SCNAT) with the elaboration of these discipline-specific community roadmaps to which the present one belongs.

SCNAT has initiated the work to elaborate such discipline-specific community roadmaps in the fields of biology, geosciences, chemistry, and in sub-fields of physics in the last quarter of 2018. Its Board defined a process that provided for an overall strategic project lead and for community-specific sub-projects, all headed by acknowledged researchers. The whole process was modelled in analogy to the long-standing experience of SCNAT in the fields of astronomy and physics, where roadmaps for research infrastructures had been elaborated in earlier years by the various communities, which were assembled for that purpose around a so-called 'Round Table'. Accordingly, starting in 2019, such Round Tables were also established in biology, chemistry and geosciences. In the past two years, hundreds of researchers were invited to take part in this process and dozens of them actively participated in each of the various Round Tables. Whereas this effort was run under the overall responsibility and guidance of SCNAT, including the provision of considerable scientific, editorial and administrative manpower by its office, the final result must be considered a genuine bottom-up contribution by the various scientific communities.

The roadmap at hand presents the vision for the future development of chemical sciences in Switzerland. During the elaboration of the document, all public institutes for chemistry research were represented at the Round Table, namely the Swiss universities and universities of applied sciences as well as the institutions of the ETH domain. Starting from key existing infrastructures as well as fields of research with potential infrastructural needs, working groups were created on eleven distinct topics. In a second step, the needs identified by the working groups were consolidated to seven proposals for new or major updates of existing infrastructures. The consolidation efforts were also extended to the other community roadmaps, namely the Photon Science and the Neutron Science Roadmaps. A video presentation of the proposed infrastructures was published online in conjunction with a survey to collect the feedback from numerous researchers in chemical sciences across Switzerland.

4 Purpose and scope of this roadmap

Our century is facing many challenges, from immediate health concerns to global environmental threats and energy issues. Our response to these challenges will require the identification and development of novel (bio)molecules, materials, and sustainable processes. To this end, Swiss researchers in academia and in the world-leading chemical and pharmaceutical industry will need to contribute ground-breaking innovations. The recommendations expressed in this roadmap aspire to provide critical elements of the infrastructure required to maintain Switzerland at the forefront of chemical research.

Ground breaking chemical research requires state-of-the-art equipment and infrastructures with sufficient support from expert staff. Recently, pivotal discoveries were made by means of massive screening and high-throughput experimentation combined with modern data analysis. High-throughput screening is used to profile biomolecular pathways for large cohorts or to identify chemicals with desired properties, for instance potential drug candidates, from among innumerable possible compounds. Moreover, key developments have also been based on our advancing ability to understand the relation between structure and function through so-called structure-property relationships. These studies benefit from recent developments in analytical tools such as spectrometers and microscopes, which have enabled us to observe detailed structures at different length and timescales. These insights are critical to our ability for rational design and the development of novel molecules and materials. In this chemical revolution Switzerland has certainly been a key player, highlighted by its many Nobel laureates and other prominent scientists recognised worldwide, as well as its renowned chemical industry.

The last century has seen constant expansion of research in the chemical sciences. These endeavours could be confined by and large within small laboratory units at the level of professorships and group leaders, where each chemist could conceive, test and analyse molecules and materials largely independently. However, chemical research is rapidly transforming and today requires access to research infrastructure offered by universities (e.g., electron microscopy, NMR and X-ray facilities, mass spectrometry centres and screening facilities) and in some cases national facilities (especially lasers and synchrotron radiation sources). While technical advances have led to the miniaturisation of many instruments, which can be hosted in research laboratories, the frontier instruments have now become too costly to be run by a single research group or even at university/research institute levels. The latter type of infrastructure includes robotised screening devices, (bio)molecule databanks and high-end analytic devices, such as microscopes and magnetic resonance spectrometers. Furthermore, the operation of frontier instrumentation and comprehensive analysis of the obtained data require specific expertise outside of the scientific fields of its various users (e.g., applied mathematics and physics, data analysis, electronics and informatics).
In order to remain competitive, this ongoing transition of chemical research must be supported by the creation of open national hubs for frontier experimentation on molecules and materials. Establishing such hubs and centres will be critical to maintain Switzerland at the forefront of science and technology in the areas of health, energy and sustainable development. These efforts should be directed at providing access to high-end instrumentation and expertise not available at a single university: robotised synthesis and experimentation, high-throughput screening, tools for efficient data banking and data analysis, and high-end analytical instruments across a broad range of length and time scales. The envisaged changes to the chemistry research landscape enabled by these new national infrastructures are expected to enable discovery and rational development to speed up technology transfer. Moreover, they aim at speeding up data standardisation and, thereby, will contribute to the larger Swiss effort for open data.

To address the bottlenecks identified, the chemistry community proposes to establish national research infrastructures divided in two main pillars: the so-called *discovery-* and *challenge-driven* infrastructures.

5 Societal, economic and scientific impact of chemistry research

Chemistry is a fundamental and enabling science that synthesises and studies molecules and materials and how they interact. Chemical innovation affects all our daily lives whether we realise it or not: it affects, for instance, what we eat and wear, the structures we live in, how we go to work and travel around the world, how we produce and store energy and how we diagnose and cure disease. Without the accumulated knowledge generated by decades of research in chemical sciences, many of the everyday products and services we use today would remain unknown or be less effective. Looking forward, research is continuously extending our understanding of chemical principles leading to new discoveries. In this way, research in chemical sciences will help us solve many of the future challenges including sustainable energy and food production as well as maintaining human and environmental health.

In March 1942, Anne Miller was close to death. In their quest to save her, doctors administered an experimental drug, penicillin, which had been discovered by Alexander Fleming 14 years earlier. Within hours Miller recovered, becoming the first person in the world to be saved by an antibiotic. In the decades that followed, medicinal chemistry led to the development of a plethora of additional antibiotics and potent medicines for a wide range of diseases which have saved millions of lives worldwide. In Switzerland, the availability of new medicines contributed to increasing the average life expectancy from 47 years in 1900 to 83 years in 2018.

Advancements in biotechnology, genetic engineering and the introduction of the Darwinian principles of evolution to the laboratory have taught chemists how to access larger molecules and to construct biological entities such as antibodies and enzymes with new or improved properties. Whereas antibodies have been engineered to treat a multitude of cancers and autoimmune diseases such as rheumatoid arthritis, improved enzymes represent an efficient and environmentally friendly addition to traditional chemistry in the production of bulk and fine chemicals, biofuels, detergents, consumer products, materials, and intermediates for the pharmaceutical industry.

Chemistry did not only help cure devastating diseases, it also contributed to more productive food-growing processes necessitated by the increase in the world's population (1900: ~1.6 billion; 2020: ~7.8 billion). The development of an efficient, scalable production process of ammonia, which is the world's primary fertiliser, unlocked the increase in agricultural output after 1950. More recent efforts strive to produce large quantities of agricultural goods in more sustainable ways, applying novel fertilisers and application techniques.

Similar efforts are currently deployed to develop more sustainable materials and procedures for various sectors. These efforts are summarised as 'Green Chemistry' (also 'Green and Sustainable Chemistry'). Central goals of Green Chemistry research are to produce chemicals that are non-depleting, non-toxic and non-persistent while minimising the environmental footprint of chemical manufacturing processes. Complementary approaches seek to replace petrochemicals as the feedstock for chemical synthesis by renewable materials. Such innovations build on insights from various fields of chemistry research, including the discovery of new synthetic methods, catalytic agents and alternative reagents. They harbour the potential to transform the industrial production of chemical commodities, fine chemicals, agrochemicals and pharmaceuticals across the entire value chain from feedstock to application.

The ability to harness and store electrical energy is another of the ground-breaking inventions of chemistry that have significantly benefitted society. Lithium-ion batteries have revolutionised energy storage and paved the way for wireless electronics such as mobile phones, laptops, cameras and many other modern applications which are inextricably linked to our daily lives. Moreover, major steps have been made to improve fuel cells, to establish hydrogen as an energy carrier, and to provide a CO_2 neutral energy supply for example by solar conversion. The rapid progress in these fields has made electric vehicles commercially viable, enabling the current transition to fossil fuel-free transportation. As the climate crisis becomes ever more critical, batteries, fuel cells and the production of non-fossil fuel, are among the key technologies required for the development of cleaner and more efficient energy storage, contributing to reduced emissions of greenhouse gases and, therefore, to a more sustainable development and economy.

As a direct result of this implication in all aspects of society, the economic impact of chemistry research is tremendous. The chemical industry has been a vital sector of the modern industrialised economy, and a significant contributor to the prosperity of the world economy by supporting employment and trade. In 2018, the total revenue of the global chemical industry amounted to 4.61 trillion euros with the global pharmaceutical industry accounting for 1.26 trillion euros. The chemical industry directly supported 15 million jobs in 2017, while additional jobs were created through the purchases made by the chemical industry and by subsequent expenditure-induced activities. It is estimated that for every person directly employed in the chemical industry, seven jobs are supported in other sectors of the global economy.

The Swiss chemical and pharmaceutical industries are among the most competitive worldwide. This outstanding competitivity results from consistently high R&D activities as well as the growth and high performance of the Swiss chemical and pharmaceutical industries in recent years. In terms of value creation, the Swiss pharmaceutical and chemical industries rank 4th and 27th worldwide, respectively. The combined sales of the Swiss chemical and pharmaceutical market amounted to approximately 116 billion euros in 2019. In total, the pharmaceutical and chemical sectors employ around 74,200 people in Switzerland (full time equivalent, FTE) and create another 203,000 jobs (FTE) in related branches.

The export earnings of the chemical and pharmaceutical industry amounted to approximately CHF 115 billion in 2019. Contributing more than 40% of total Swiss exports annually since 2013, and as much as 53.3% between January and September 2020, this sector is one of the major contributors to the Swiss economy. Pharmaceuticals (medications, diagnostic products, active pharmaceutical ingredients) constitute the lion's share of these exports (more than 80%). Other exported chemicals include organic products, dyes, agents for crop protection, fragrances, flavours and other food additives.

In 2018, the total investment in pharmaceutical R&D in Switzerland was more than CHF 6.9 billion and the industry generated around CHF 36 billion in direct added value. In addition, Swiss companies in other sectors benefit indirectly from production and research in the pharmaceutical industry. Every Swiss franc of value added generated an additional CHF 0.73 in other Swiss industries. As reported in 2018, the total employment effect of the pharmaceutical industry amounts to around 254,000 people, which correspond to about one in twenty employees in Switzerland.

Research and development are essential to the outstanding performance of the Swiss pharmaceutical sector. In addition to financial investments in R&D, Switzerland has created and maintained its place as a leader in the chemical sector due to its highly qualified workforce, educated at its top-ranking universities, as well as the high level of technological and scientific know-how that fosters an innovative environment.

The consequences of chemical research are thus far-reaching, and society has benefited hugely from advances in the field. The chemical industry is an important driving force for economic growth, which creates opportunities for millions of people in Switzerland and around the world. Continued investments in chemistry research will ensure progress in the development of scientific and technological solutions that will help tackle many of the challenges we face as a society today.

6 Landscape analysis

Research infrastructures in the chemical sciences in Switzerland have enabled the leading position of Switzerland on a global level for the past decades. From an institutional point of view, these infrastructures are diversely located at the research group level, the department level, the university level, and finally on a national and international level, thereby facilitating flexible access to core technology to user groups. As a consequence, the research infrastructures used by the Swiss chemistry community are located throughout Switzerland, both in the cantons with and without universities. In addition, some key infrastructures are located abroad.

Different organisational frameworks have been developed to facilitate operations, ranging from knowledge-based resources that can be hosted on servers, to multi-user distributed networks and national centres. Examples of knowledge-based resources include UniProt, a proteomics database co-hosted by the Swiss Institute of Bioinformatics and international partners, and enviPath, a database on microbial biotransformation of organic environmental contaminants closely tied to Eawag. Distributed networks often form around the SNF National Centres of Competence in Research (NCCR), for example MARVEL (EPFL), Chemical Biology (University of Geneva/EPFL), Molecular Systems Engineering (University of Basel/ETH Zurich), Bio-Inspired-Materials (University of Fribourg), and Catalysis (ETH Zurich/EPFL). Networks are well-suited to share computational tools and expertise for data analysis (e.g., the bioinformatics resource portal Expasy). By contrast, instruments and analytical devices must be installed and maintained in a defined location. At present, many research institutions offer high-end analytical services primarily to local users. In addition, national centres provide unique state-of-the-art equipment open to all researchers in Switzerland, such as the Swiss Spallation Neutron Source (SINQ), the Swiss X-ray Free-Electron Laser (SwissFEL) and the Swiss Light Source (SLS) at PSI, as well as the 30 % share in two Swiss-Norwegian Beamlines (SNBL) at the European Synchrotron Radiation Facility in France (ESRF). The 2019 Swiss Roadmap for Research Infrastructures lists further national infrastructures that will be accessible to all Swiss researchers, namely the Neuchâtel Platform of Analytical Chemistry, a facility dedicated to high-field NMR, and the Catalysis Hub. The installation of the NMR facility and the Catalysis Hub starts in 2020/2021.

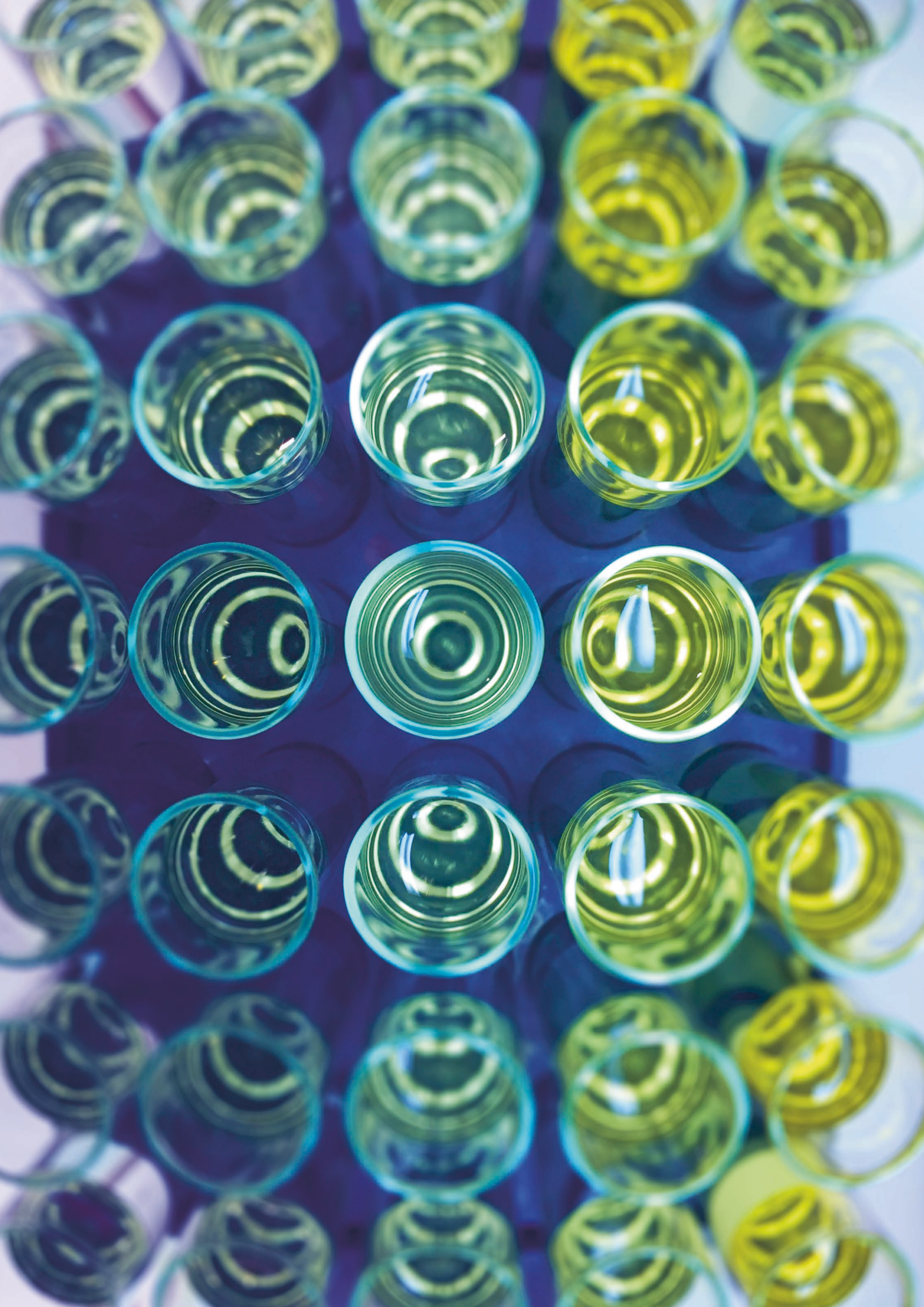
Many of these infrastructures require highly skilled staff for operation and can serve as beacons in research and training. At Swiss institutes of higher education, more than 7,000 technicians are employed in research and development (3,791 FTE). The number of chemistry students in Switzerland steadily increased by approx. 23% over the last decade. In 2019, 482 students were enrolled in MSc chemistry study programmes and 1,147 students were enrolled as PhD students in chemistry. The next generation of scientists is trained on cutting-edge instruments, and will, therefore, obtain key skills for the decades to come. In addition, these infrastructures often also attract top talent worldwide, and serve the educational aspects of international mobility for universities and research centres alike. PSI, for example, hosts approx. 5,000 visiting scientists from various fields every year, mostly from Switzerland and other European countries, who perform experiments on PSI's large research infrastructures.

International connectedness is a decisive ingredient to the successful and visible research activities in Switzerland. The high exchange of Swiss researchers with their peers abroad is reflected by the scientific publications by Swiss authors, 85% of which are published together with international co-authors. Moreover, Switzerland is currently member of several international research organisations, including CERN, the ESRF including SNBL, the European X-Ray Free Electron Laser (European XFEL), the European Spallation Source (ESS) and the European Life Science Infrastructure for Biological Information (ELIXIR). It should also be pointed out that these research infrastructures are facilitating research on several levels, from single-user access to large, multinational and interdisciplinary collaborations (synchrotrons, XFELs, CERN, etc). In particular the role of national user laboratories to facilitate international collaboration cannot be overestimated, and they will be key drivers for innovation in the future.

Virtually all research infrastructures in Switzerland also benefit the private sector and enable collaborations with companies, thereby improving the competitiveness of the Swiss-based economy. These collaborations have direct as well as indirect benefits ranging from the outcome of measured data to the education and training of future employees that are well-qualified to succeed on the skills-based job market of the future. The economic impact of research is very strong: The return of public investment in research and innovation is estimated at around 20%.

Bird's eye view of the Paul Scherrer Institute with the SLS in front (photo PSI)

Research infrastructures, especially on the international level, require long-term commitments in funding, which can often interfere with short-term funding cycles. Thus, in order to maintain and to expand the key position of Switzerland in terms of infrastructure, the long-term planning in the context of Swiss roadmaps is welcomed as essential.



7 Vision for the future

Today, Switzerland is a globally recognised centre for chemical research in academia and in industry. To keep this leading role, Switzerland must develop the available research infrastructure in a strategic and coordinated manner. This development of research infrastructures should support and accelerate the ongoing transition from research in single laboratories to cooperative research endeavours. The Swiss chemistry community has understood the necessity to join forces to provide access to frontier instrumentation on a national or international level. This necessity arises because the full spectrum of state-of-the-art instruments can no longer be hosted by each single institution. Herein, the Swiss chemistry community proposes seven research infrastructures that will help to keep Switzerland at the forefront of chemical research and innovation.

Chemical research and innovation is key to translate knowledge into solutions to current global challenges. In particular, scientific discoveries are anticipated that will allow us to tap renewable energy sources, improve energy storage, protect the environment, improve human health and implement sustainable, effective manufacturing procedures.

Chemical research contributes to these new solutions in two ways: The first pillar of discovery in chemical sciences is the study of fundamental structure-function relationships. The second pillar is the identification of compounds and materials for well-defined purposes. It combines fundamental insights on structure and function with the screening of compounds and materials for specific applications. Both pillars of chemical research require complementary, dedicated infrastructures.

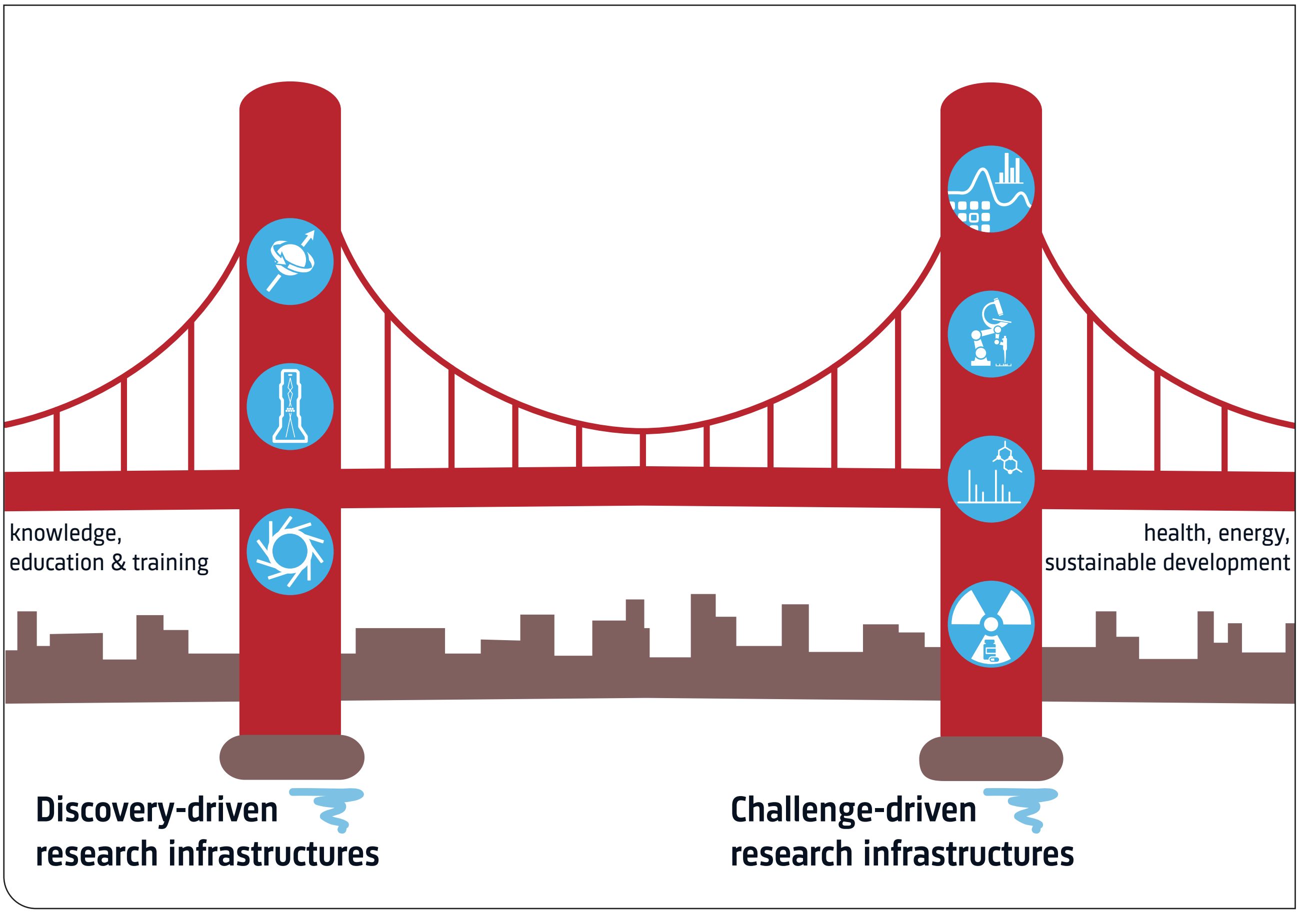
The **'discovery-driven research infrastructures'** supporting the first pillar will provide essential capabilities to characterise molecules and materials at different spatial and temporal resolutions, and to determine the fundamental structure-function relationships that provide the basis of rational development and innovation. The Swiss chemistry community has identified the need to create or consolidate three infrastructures of this kind:

1. A magnetic resonance and magnetism hub,
2. A centre for *operando* synchrotron studies,
3. An electron microscopy and diffraction hub.

The **'challenge-driven research infrastructures'** supporting the second pillar are oriented to screen, discover, generate and develop lead chemicals and materials for specific applications related to energy, health and sustainability. The Swiss chemistry community has identified the need to create or consolidate four infrastructures of this kind:

1. A facility to produce Terbium radionuclides for diagnostics and treatment of disease,
2. A mass spectrometry-based screening platform for (bio) catalysts and environmental samples,
3. A centre that provides state-of-the-art instrumentation for translational chemistry and manages a national library of compounds synthesised in academic laboratories across Switzerland,
4. A catalysis hub *(CAT$^+$)* to discover and develop catalysts and catalytic processes towards a sustainable society.

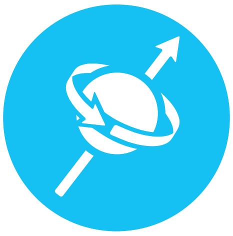
All of these research infrastructures should be organised as central national facilities or as distributed networks joining multiple sites that host and develop complementary instrumentation and offer expertise in specific areas as well as data science. All of the infrastructures will be established and managed by at least two closely collaborating universities or research institutions except for the radiochemistry facility and the high-throughput screening hub, which foresee a single research institution in charge. Irrespective of their organisation, all hubs will be made accessible to researchers across Switzerland and beyond, from academia and the private sector. One of the missions of the hubs will also be support the user community with expert staff for data acquisition and analysis. The infrastructures will also provide educational opportunities, in particular to PhD students, who will be able to perform advanced research experiments in collaboration with experts from various universities across Switzerland.



The Swiss chemistry community proposes three discovery-driven research infrastructures and four challenge-driven research infrastructures to provide instrumentation and expertise to various user communities (Yvonne Hari)

7.1 Capability- and discovery-driven research infrastructures

Infrastructure of this kind provides the enabling tools that allow us to design, model, synthesise, characterise and test molecules and materials at different length and time scales (from atomic scale through to meso-scale components). These tools enable the determination of detailed and precise structure-property relationships, and thereby propel discovery and rational development. This type of infrastructure includes large-scale, campus-based, open facilities as well as distributed and often internationally-based state-of-the-art infrastructures and major university-based clusters of capability, e.g., SLS at PSI.

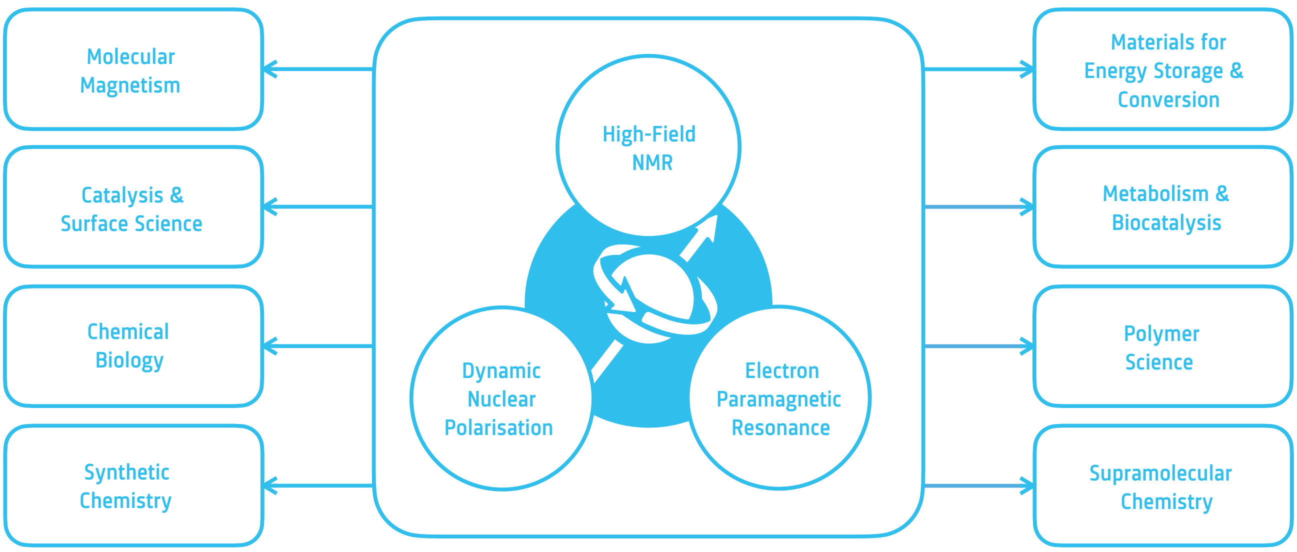


7.1.1 Magnetic Resonance and Magnetism

Context (national and international), scientific rationale and challenges
Magnetic resonance techniques, such as nuclear magnetic resonance (NMR) and electron paramagnetic resonance (EPR) spectroscopies, are indispensable for structural characterisation of biological systems and materials on length scales between a fraction of the length of a chemical bond and about 10 nanometres, and for their characterisation of dynamics on time scales from picoseconds to hours. For condensed, non-crystalline matter, NMR and EPR provide unparalleled probes. For magnetic molecules and materials, they are complemented by measurements of magnetism, for instance, with superconducting quantum interference devices (SQUID).

The complexity of biochemical systems and materials under investigation at the forefront of science continuously increases. This development can only be supported in the longer run if techniques for the characterisation of structure and dynamics keep pace. In NMR this has notably been the driving force for the push to higher and higher magnetic fields. We see today that especially for solids and for chemistry in cells, NMR and EPR still have a great potential for further methodological developments and applications. In NMR, this development continues to focus internationally to a large extent on overcoming the main Achilles' heel of the technique, which is low sensitivity. Significant progress has been made in the past decade with dynamic nuclear polarisation (DNP) approaches, which would benefit from combined NMR and EPR infrastructure, as they rely on paramagnetic species as a polarisation source for nuclear spin transitions. For EPR spectroscopy, novel fast electronics and microwave technology, currently under development for communication systems, enables largely digital spectrometers and consequently development of much more complex measurement schemes than are currently available.

Switzerland is a leading country in magnetic resonance, with two Nobel laureates in the field and with the leading instrument manufacturer being based in Switzerland. Foundational textbooks have originated in Switzerland, and groups especially at ETH Zurich, EPFL, and the Biozentrum in Basel, are internationally highly respected in



Schematic representation of the core techniques in the magnetic resonance infrastructure, and the connection to some of the key users communities that will directly benefit from the facility (Lyndon Emsley, EPFL) the field and currently very well equipped. Major investment in high-field NMR spectrometers and DNP instruments is being made internationally, in particular in China, but also in Germany, the USA, France, the UK and Italy. In the USA and in the UK in particular, NMR groups are complementing their portfolio with advanced EPR spectroscopy to measuring distance distributions in the nanometre range. Until now, Switzerland has been able to invest in frontier NMR and EPR at the institutional level. However, with the next generation of NMR magnets costing around 15–20 MCHF, this will no longer be possible. Indeed, the acquisition of the 1.2 GHz NMR system for structural biology, included in the 2019 Roadmap for Research Infrastructures, required co-funding by ETH Zurich, University of Zurich, University of Basel and the SNSF. This system, dedicated to research in structural biology, has now been installed in 2020 and is in the test phase. There is no equivalent national capacity for chemistry focused high-field NMR, and there is now a clear danger for Switzerland to be left behind, if the country does not continue to develop and invest in shared national infrastructures for NMR and EPR.

Advanced instrumentation for magnetic resonance, here featuring the world-wide unique 900 MHz gyrotron DNP NMR spectrometer at EPFL, has always enabled new discoveries in applications across the chemical sciences, and will continue to do so in the future (photo Lyndon Emsley, EPFL)

Aims of the Proposed Infrastructure

While state-of-the-art NMR infrastructure is today accessible to some extent at all leading Swiss universities, advanced EPR infrastructure with the capability to support projects in life sciences, materials sciences, and catalysis currently exists only at ETH Zurich. The latter infrastructure was created for research on EPR method development. It is neither sufficient nor well adapted for catering to the needs of researchers in application fields for all of Switzerland. As discussed above, next generation high-field NMR instrumentation for chemistry will be beyond the reach of single institutions. Instrumentation for magnetisation measurements is only locally available to individual research groups or small clusters of research groups.

We propose to establish two Swiss shared application facilities for magnetic resonance and magnetism, one at ETH Zurich and one at EPF Lausanne to cater for the needs of Swiss universities. The establishment of two centres capitalises on the specific expertise of the strong local research groups that will lead the infrastructures, and allows for specialisation.

7.1.2 Centre for *operando* Synchrotron Studies

Context (national and international), scientific rationale and challenges

Understanding the geometric and electronic relations between structure, property and performance is crucial for the rational design of new molecules and materials and thus for the discovery and optimisation of chemical and physical processes of fundamental or practical interest. The chemical sciences not only require experimental tools probing structure at different length scales, from atomic to nanometre to mesoscopic, but also, very importantly, under relevant conditions where the investigated molecule, material or process is functioning/working (so-called *in situ* and *operando*) conditions. X-ray based methods are among the most powerful methods for studying structure under such *'working'* conditions. As synchrotron light sources provide orders of magnitude higher brilliance in comparison to conventional X-ray sources, they are the facilities of choice for real time X-ray based structural studies.

Various complementary synchrotron-based X-ray techniques (see textbox) are used by the chemistry and material science communities to study compounds and materials, material synthesis or reaction mechanisms under operating conditions in devices or cells utilising the high penetration depth of hard X-rays. These communities profit from the local proximity of competitive state-of-the-art single technique beamlines at the Swiss Light Source (PSI, Villigen) as well as the European Synchrotron Radiation Facility (Grenoble, France), where the Swiss-Norwegian beamline has been tuned to the need of chemists. The techniques most extensively used by the community are XAS, total scattering and XRD. The Swiss chemistry and materials science community that needs access to synchrotron facilities is rapidly growing, and addresses questions of increasing complexity. This has revealed four principal challenges during the last five years: First, novel materials exhibit unprecedented complexity, which necessitates appropriate combinations of synchrotron techniques to elucidate their properties. This requires a multi-technique approach under true working conditions (an approach that has been pioneered at the Swiss-Norwegian Beamlines at ESRF). Second, at synchrotron facilities worldwide, there exists a significant delay between proposal writing and assigned beamtime, typically of at least 4–5 months. Furthermore, only around 30% of proposals are accepted and allocated beamtime, strongly supporting the need for an increase in capacity. Third, the major bottleneck is increasingly the large amount of data produced on experimental stations, which can easily amount to several TB of data per day. Data processing, storage and analysis nowadays requires expert support. The fourth challenge concerns the reproducibility and transferability of experiments between the home laboratories and synchrotron beamlines, and also between different beamlines.

Storage ring of the Swiss Light Source (SLS) at PSI (photo PSI)

Techniques for real time X-ray based structural studies at synchrotron light sources include:
- High resolution X-ray diffraction (XRD) providing precise information on the complete atomic-level structure in crystalline materials.
- X-ray total scattering provides information on local structures up to a few nanometres, for materials with or without long-range order.
- Diffuse scattering for single crystals provides structural information at the nano-scale, as do high resolution X-ray diffraction and X-ray total scattering.
- X-ray absorption spectroscopy (XAS) provides information on the local atomic-level structure up to 6 Å around the element of choice, and on the oxidation state of the element.
- X-ray emission spectroscopy (XES) provides electronic information on the filled density of states including valence electrons and spin state.
- Resonant X-ray emission spectroscopy (RXES or RIXS) combines XES and XAS in one experiment and provides full information on electronic structure(s).
- Near ambient X-ray photoelectron spectroscopy (XPS) provides surface sensitive information on the chemical and electronic state of elements.
- Small angle X-ray scattering (SAXS) provides information on nano and mesoscopic scales such as the size and shape of nanoparticles, density fluctuations and order therein.

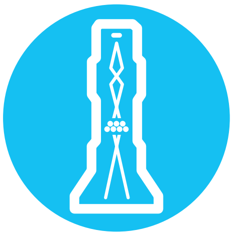
New developments in laser-based X-ray spectroscopy could potentially lead to laboratory-based setups that cover some of these techniques, albeit at lower time-resolution compared to synchrotron-based X-ray spectroscopy. Free electron X-ray lasers, such as the new SwissFEL at PSI, provide access to many of these techniques on the femto- to picosecond time scales, and might therefore become a relevant tool for fundamental chemistry research and beyond in the decades to come.

Experimental set-up for X-ray absorption and emission spectroscopy with enhanced chemical sensitivity and time resolution (SuperXAS) (photo Maarten Nachtegaal, PSI)

Aims of the Proposed Infrastructure

Aiming to alleviate all of the aforementioned bottlenecks and challenges, a centre for *operando* studies comprising two complementary hubs is proposed. The centre should capitalise on existing facilities and committed future investments. The West Hub will consist of the two SNBL beamlines (30% Swiss share at ESRF). The East Hub will consist of the projected Debye beamline, as well as shares of other single technique SLS beamlines and complimentary *operando* IR/Raman/UV setups available at PSI. As both synchrotrons have been or will be upgraded to a diffraction limited light source, these facilities will remain at the forefront of X-ray science. The upgraded light sources will remain complementary in terms of the provided energy range, brilliance and beam type (focused vs. unfocused). The need for combined technique beamlines (with emphasis on XAS and XRD) has grown rapidly, as has the need for direct and rapid access for high impact science and industry to these resources. To fulfil this need, SNBL at ESRF has recently been upgraded and offers access to very high X-ray energies used for complex combined experiments. Furthermore, an additional new beamline, the Debye beamline, has recently been funded by the ETH domain and is to be constructed at SLS by 2023 for high throughput combined experiments.

The backbone of the proposed centre is comprised of five elements:
1. (synchrotron) instruments dedicated to *operando* X-ray diffraction and spectroscopy,
2. X-ray techniques and their combinations focused on obtaining crystal, molecular, atomic and electronic structures,
3. setups for *in situ* and *operando* experimentation compatible with synchrotron instrumentation,
4. data management and data analysis tools facilitating effective use of synchrotron beamtime,
5. direct beamtime allocation, rapid access, mail in service and remote access models.



7.1.3 Electron Microscopy and Diffraction

Context (national and international), scientific rationale and challenges

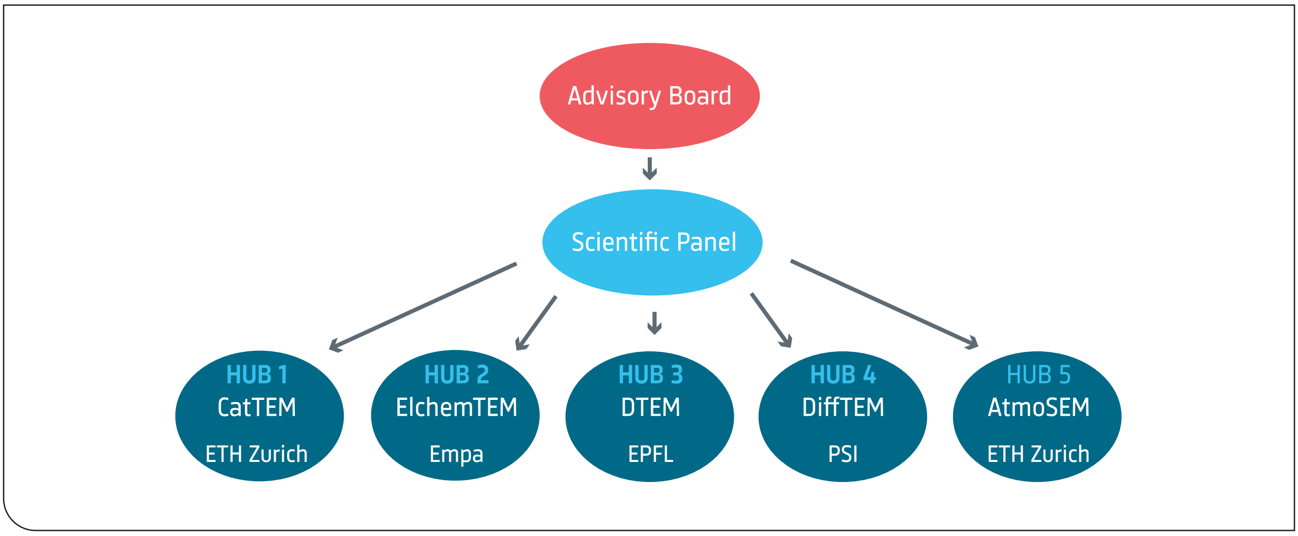
Transmission electron microscopy (TEM) has become an indispensable tool in life and physical sciences. It is capable of providing simultaneous structural, compositional and chemical information about complex structured materials at atomic resolution. While direct atomic-scale imaging has immediate impact on scientific progress in nano- and materials sciences, it is not universally applicable. Especially with respect to chemistry and life science, the requirement of a high vacuum in the microscope has, for a long time, limited the ability to study materials in their natural or application-relevant environments. Furthermore, the use of strongly interacting electrons for the imaging process limits the possibility to study electron beam-sensitive materials. The Nobel prize in Chemistry in 2017, which was awarded for the development of cryo-TEM, highlights the importance of minimising radiation effects and of preserving the native state of the structure under investigation.

Recent hardware developments have unlocked three research fields for the application of electron microscopy which are highly relevant in chemistry: 1) *in situ* and *operando* capabilities, 2) time resolution and 3) structure determination for sub-micrometre sized crystals.

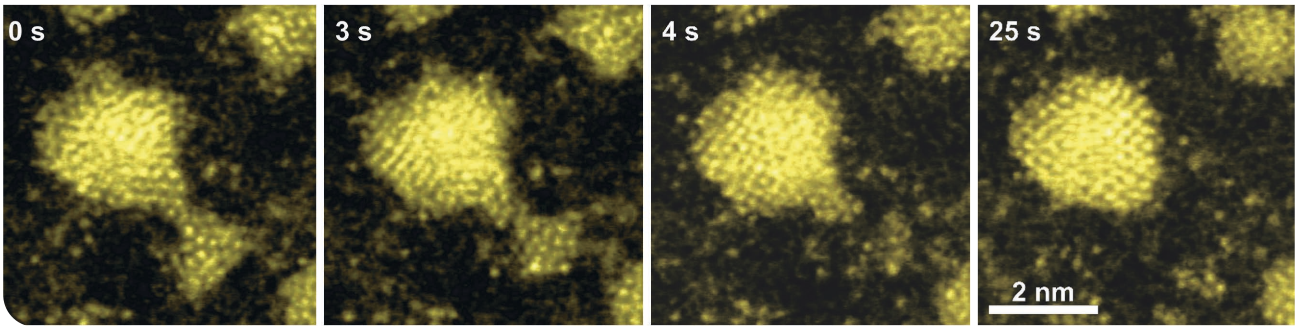
1. With the development of commercial instruments and tools for *in situ* scanning electron microscopy (SEM) and TEM, it has become possible to investigate samples under well-defined *in situ* and *operando* conditions. With regards to chemistry, the ability to follow dynamic processes caused by the interactions between a sample and its gaseous or liquid environment at near atomic resolution is a breakthrough. It can potentially revolutionise our understanding of (electro-)catalysis, chemical energy storage and conversion, interfaces, material synthesis and evolution.

2. In addition to the determination of the local geometric and electronic structure of samples (the latter through electron energy loss spectroscopy) in their relevant environments, time resolution is crucial for studying dynamic processes. New detection strategies based on 'noise-free' ultra-fast direct electron detectors have boosted the sensitivity and dynamic range of detectors and increased their speed from several frames per second (fps) to several thousand fps. Owing to the faster and more efficient signal detection, beam exposure can be reduced and swift changes can be captured. Furthermore, this development opens the door to electron ptychography and 4D scanning TEM methods. For many dynamic processes, acquisition speeds in the low micro-second range are still far too slow. With the application of a pulsed-electron beam, which allows for imaging with individual, well-defined electrons or electron bundles (ultra-fast electron microscopy), the temporal resolution in nanoscale observations can be extended to the sub-nanosecond regime.

3. Another important aspect in chemistry concerns structure determination, particularly in pharmaceutical chemistry. While X-ray diffraction is the method of choice for micrometre-sized crystals, structure determination of smaller crystals has been a challenge. The combination of real-space imaging to find sub-micrometre sized crystals and electron diffraction for their structural analysis is a strong asset of TEM. Electron



Organisational chart of the proposed microscopy network (Rolf Erni, Empa)



Formation of nanoparticles by liquid-phase scanning transmission electron microscopy (photo Debora Keller, Empa)

nano-crystallography has, therefore, been recognised as one of the ten most relevant scientific breakthroughs of 2018 by the journal Science. The technique enables full structure determination, including hydrogen atom positions, of sub-microscopic crystals at minimal electron doses. It is thus ideally suited for structural investigations of pharmaceutical compounds and, for example, the identification of polymorphs of drugs. Moreover, novel applications for studying non-crystalline samples by single molecule diffraction are under development.

For Switzerland's research in chemistry and in light of the local (pharmaceutical) companies and the future energy agenda, it is important to remain at the forefront of the developments in electron microscopy. It is also important to work in close collaboration with Swiss companies that provide leading technologies in this area, such as high-speed, 'noise-free' direct electron detectors.

Aims of the Proposed Infrastructure

The aim of the proposed decentralised infrastructure is to implement advanced electron microscopy modalities in order to a) realise *in situ* and *operando* observations of (dynamic) chemical reactions and b) establish platforms for structure determination, particularly with a focus on pharmaceutical chemistry. These goals can be achieved by implementing a set of complementary, dedicated high-end electron microscopes, each embedded within an existing facility with corresponding expertise. The dedicated electron microscopes will be located across Switzerland in a five-hub network based on existing facilities. Each hub will have specific capabilities and a primary research focus, namely catalysis, electrochemistry, ultra-fast imaging, structure determination and *in situ* scanning electron microscopy, where the different research modalities uniquely benefit from the locally established expertise.

The Swiss microscopy network will consist of the following five hubs:

Hub 1: Catalysis. An advanced analytical (scanning) transmission electron microscope with gas-cell and environmental capabilities dedicated to *in situ* research on catalysts, including direct electron detectors, spectrometers, gas analysis and possibly protection of critical microscope parts to probe reactive environments in the microscope. Proposed location: ETH Zurich.

Hub 2: Electrochemistry. An advanced analytical (scanning) transmission electron microscope with liquid-cell and electrochemistry setups dedicated to *in situ* research activities in the areas of batteries and corrosion. Proposed location: Empa.

Hub 3: Ultra-fast imaging. An advanced (scanning) transmission electron microscope with a laser-pulsed or single-electron-controlled electron source for studying chemical reactions at the nano-scale with nano-second resolution, combined with advanced detection technologies, spectrometer and energy filter. Proposed location: EPFL.

Hub 4: Structure determination. An advanced cryo-(scanning) transmission electron microscope equipped with a) advanced direct electron detectors for electron diffraction, backed-up by b) advanced computational resources for ptychographic reconstructions and c) dedicated to structure determination of crystals that are too small to allow for X-ray diffraction analysis. Proposed location: PSI.

Hub 5: Dedicated *in situ* SEM providing an improved base pressure in high-vacuum mode and the ability to work up to pressures of 0.5 bar in the *in situ* mode, including a gas-feeding station, mass-spectrometer, heating stage and a variety of complementary electron and X-ray detectors, particularly complementing Hub 1. Proposed location: EHT Zurich.

7.2 Application- and challenge-driven research infrastructures

These infrastructures have an identifiable direct relevance to industrial sectors or end-user groups within the economy such as the pharmaceutical, chemical, crop protection, and materials industry in Switzerland and beyond. The complexity of the user problems will often require these infrastructures to be used in concert with other infrastructures. These infrastructures tend to be part of wider initiatives targeted towards addressing major scientific, technical, innovation, societal or policy challenges for which additional government funding has been committed, for example the Swiss Competence Centre for Energy Research (SCCER). They often build on outstanding, existing capability which has been built up over many years through capability-driven investments.

7.2.1 Radiochemistry: Targeted Alpha Therapy using Terbium and Other Oncological Solutions

Context (national and international), scientific rationale and challenges

Nuclear medicine uses radioactive elements, or radionuclides, for the diagnosis and/or treatment of disease. The decay of each radionuclide is unique, and the type of radioactive decay it undergoes dictates what medical purpose the radionuclide can be used for. The chemical nature of the radioactive element determines how it binds to a specific biological molecular target which, in turn, determines how it is taken up in the tumour. Furthermore, elements containing multiple radionuclides that undergo different types of radioactive decay, called 'sister' nuclides, are of particular interest for radiopharmaceutical applications. The use of sister nuclides ensures that tissues can be both identified diagnostically and treated with the appropriate radioisotope (known as theragnostics).

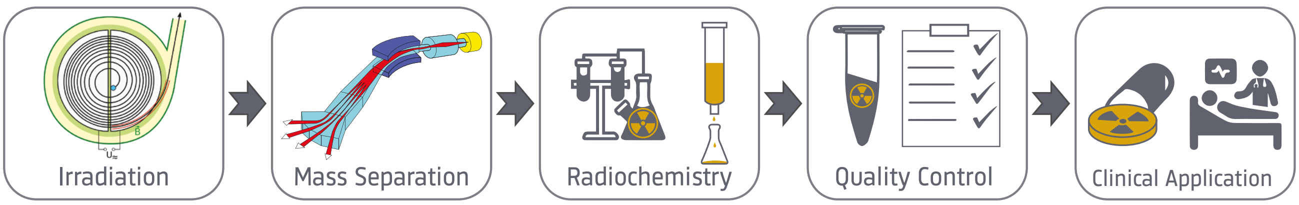
Terbium is unique in that it exhibits four interesting sister radionuclides applicable to all the modalities used in diagnostic and therapeutic nuclear medicine: ^{155}Tb gamma-ray emission makes it suitable for Single Photon Emission Computed Tomography (SPECT) imaging. ^{152}Tb emits positrons, which is useful for Positron Emission Tomography (PET) imaging. ^{161}Tb and ^{149}Tb emit radiation which is effective for cancer therapy. These four radioisotopes allow to prepare chemically identical radiopharmaceuticals with identical pharmacokinetic profiles. This is a unique situation that could serve the concept of personalised medicine.

The aim of this venture is to make all four Tb sister nuclides available throughout Switzerland, as well as abroad, for the preparation of radiopharmaceuticals in view of clinical translation.

The Tb radioisotopes are seen as the 'lighthouse' project towards this goal. Other novel radionuclides for theragnostics can be produced using the envisaged ISOL procedure. The production capabilities can be extended in the future using UCx/ThCx targets to produce α–emitting nuclides, e.g., ^{211}At, ^{223}Ra and ^{225}Ac. Moreover, ^{67}Cu and ^{47}Sc are also envisaged as potential therapeutic radionuclides towards matched-pair theragnostics.

Generally, the availability of an irradiation station with high-energy protons at PSI, at the heart of this infrastructure, will considerably enlarge the radionuclide production portfolio. The spallation process induced by high-energy protons utilising various target material grants access to a plethora of exotic radionuclides not otherwise accessible. Separated at unprecedented amounts, these exotic radionuclides have great scientific potential for nuclear physics, astrophysics and fundamental radiochemistry.

The infrastructure will also serve users from other areas, such as physicists performing basic research at ISOLDE (CERN) who may have the opportunity to obtain radionuclides at activities not achieved previously, due to the increased beam intensity available at the PSI site. Astrophysicists can benefit in a similar manner.



Essential steps for the production of radiopharmaceuticals from the generation of radionuclides to the synthesis of therapeutic agents for clinical applications (Nicholas van der Meulen, PSI)

Facility for Isotope Separation On-Line (ISOL) at CERN (photo Noemí Carabán, CERN)

This proposed infrastructure will form part of a larger project for nuclear physics research at PSI's High Intensity Proton Accelerator (HIPA) complex, which also involves an upgrade of a muon target station situated in close vicinity of the proposed infrastructure.

Aims of the Proposed Infrastructure

In order to reach the goal of making all four Tb sister nuclides available for clinical applications, researchers with expertise in different disciplines (physics, radiochemistry, radiopharmacy, radiobiology, nuclear medicine) need to work closely together. The production facilities for ^{155}Tb and ^{161}Tb, including chemical separation methods, modules and laboratories for the GMP synthesis of radiopharmaceuticals, are being implemented at PSI. PSI has the capability of producing therapeutic ^{161}Tb, utilising its SINQ neutron source (with collaborators in Europe and Africa), while ^{155}Tb will be produced at HIPA in the near future. However, production facilities for the remaining two Tb sister nuclides (^{149}Tb and ^{152}Tb) have yet to be established. ^{149}Tb and ^{152}Tb can be produced via Isotope Separation On-Line (ISOL) techniques as proven at CERN. The facilities at PSI should be expanded by an ISOL facility. It is envisaged to perform the entire spallation, collection and chemical separation process (developed at PSI) for these two radionuclides, followed by the production of radiopharmaceuticals onsite (currently expressed as Targeted Alpha Therapy using Terbium and Other Oncological Solutions – TATTOOS).

The products from the new ISOL facility can be transferred to the GMP facility on the same site (at the Centre of Radiopharmaceutical Sciences – CRS), which are then used for the labelling of biomolecules. From there, the resultant radiopharmaceuticals will be transported to imaging and therapy centres for patient applications. There is a unique opportunity at PSI to produce and process radionuclides at the same site, which will be particularly important for the relatively short-lived ^{149}Tb ($T_{1/2}$= 4 h).

PSI will become the only facility worldwide that combines all essential steps for the production of radiopharmaceuticals: the generation of radionuclides by means of proton activation, neutron activation, and spallation reactions, mass separation of the generated radionuclides, their incorporation into desired compounds by radiochemical means, and finally the production of radiopharmaceuticals therefrom. The facility will assist basic research and application studies as part of a 'bench-to-bedside' principle.

The respective radiopharmaceuticals will be made available especially to therapy centres, enabling first clinical studies throughout Switzerland. Swiss medical centres can benefit in particular, as the short half-life of ^{149}Tb limits its logistic capability for therapeutic use: The distance between the site of production of the radionuclide and the medical centres, where the patients are treated, should be as short as possible for an optimal therapeutic effect.

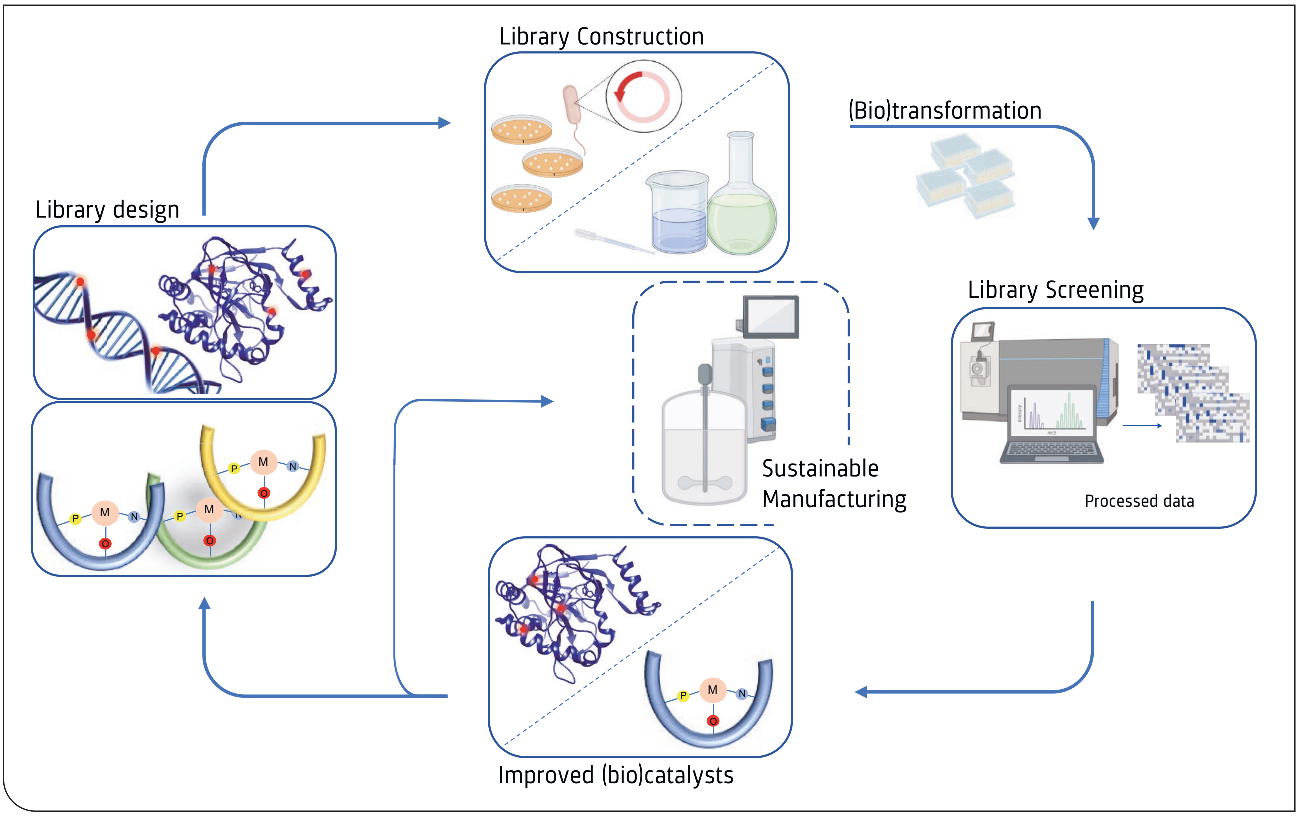
7.2.2 High-Throughput Screening Hub for Chemical Biology

Context (national and international), scientific rationale and challenges

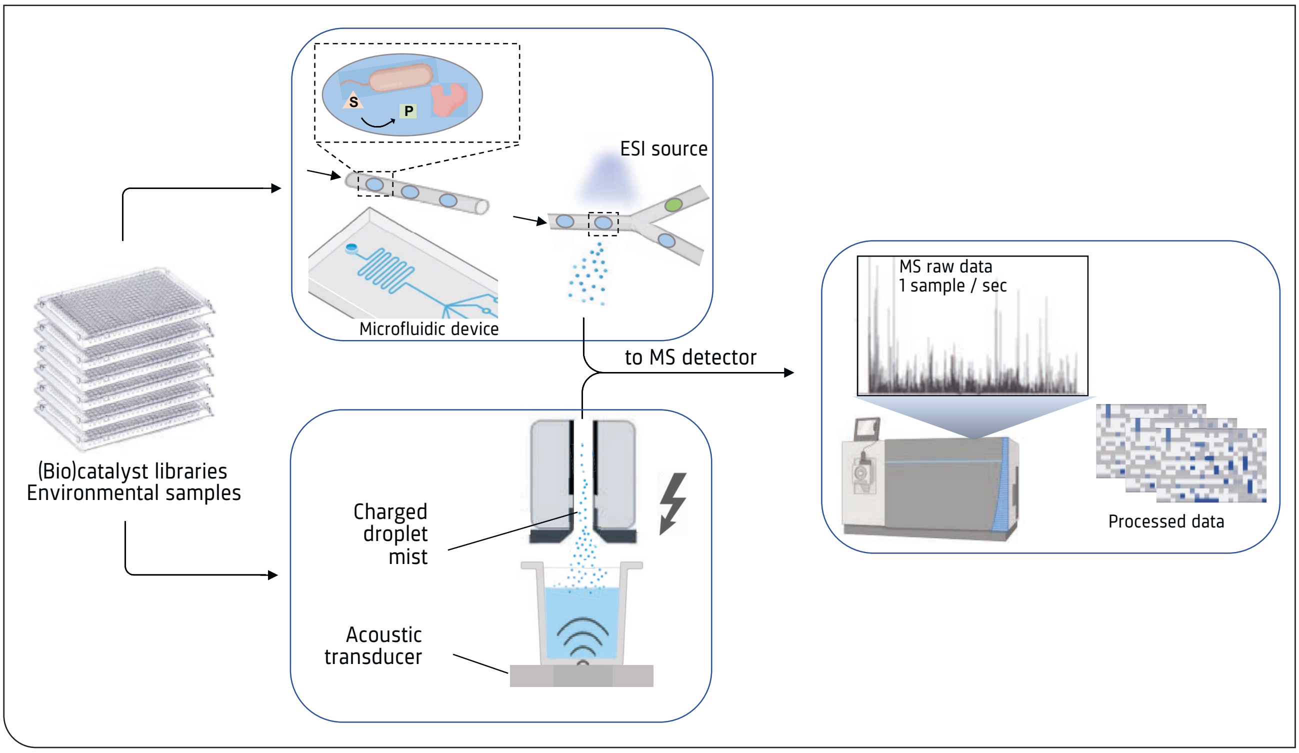
Many, if not all, chemical and biochemical experiments require that a meaningful, reliable read-out (analysis) of the generated data can be performed. In many chemical and biological disciplines, an additional imperative is that high numbers of samples need to be analysed rapidly, preferably using low sample volume (nL), to save time and resources. For example, drug discovery efforts rely on the ability to analyse compound libraries consisting of millions of molecules in a fast and reliable way. Consequently, high-throughput screening (HTS) is of utmost importance when looking into the timely discovery and development of new drug candidates for existing and emerging disease.

In addition, HTS has high relevance in chemical biology. When considering enzyme engineering, in which a biological catalyst is tailored toward catalysing an industry-relevant reaction, it is desirable to screen more than a million reaction samples in a matter of days to identify improved biocatalysts for sustainable chemical manufacture. Furthermore, monitoring environmental quality, as well as industrial chemical processes, ideally provides spatially and temporally resolved chemical data *in situ* to allow real-time control of detrimental factors.

Today, bottlenecks in compound screening and (bio)catalyst development often lie in sample preparation and data analysis. An additional issue is cost per sample, as conventional analysis techniques require non-negligible amounts of supplementary chemicals in each experiment. To address this challenge, current development efforts of consortia consisting of pharmaceutical (e.g., Merck, AstraZeneca and others) and technical companies (e.g., Labcyte, Waters and others) have yielded the technology of acoustic mass spectrometry, a combination of acoustic mist ionisation (AMI) and mass spectrometry (MS) that has the potential to reduce both cost and cycle time due to low sample volumes (nL) and rapid measurement cycles (sec). This technology can be complemented by systems which couple solid phase extraction with mass spectrometry giving access to fast (sec) and robust assay development capabilities and allowing to measure an even wider molecular diversity. Further automation can be offered by microfluidic devices which can create, assay and sort microscale samples by the generation of nanoscale reactors in droplets which can house, for example, single cells.



High-throughput (bio)catalyst library design, construction and screening leads to improved catalytic entities for potent and sustainable chemical processes (Rebecca Buller, ZHAW)



The mass spectrometry-based high-throughput instrumentation at the core of the 'Screening Hub for Chemical Biology' will allow to overcome current bottlenecks in (bio)catalyst development and environmental sample analysis (Rebecca Buller, ZHAW)

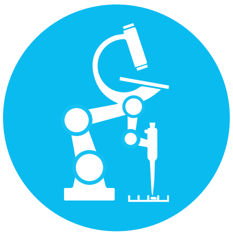
Today, microfluidic devices typically rely on fluorescent properties of the analyte to sort the droplets. Consequently, the instruments are unsuitable for many real-world applications dealing with non-fluorogenic compounds. However, first prototypic examples highlight the possibility to couple microfluidic devices to high resolution MS-based analyses, thus extending the current application scope of microfluidics considerably.

Looking forward, an extension of these fast analysis technologies to encompass also chiral information is desirable, for current chiral analysis is much slower (in the range of minutes). In addition, further improvements in overall instruments robustness, resolution and the establishment of reliable and sensitive quantification protocols at low volume are targeted.

Aims of the Proposed Infrastructure

The introduction of a 'Screening Hub for Chemical Biology' infrastructure aims to reduce existing bottlenecks in the development of new (bio)catalysts and bioactive compounds, both in terms of cost and throughput. The infrastructure will be key in the development of novel catalysts for sustainable production processes and novel products in the Swiss chemical industry. Conceptually, it is placed upstream of the 'National Centre for Translational Chemistry' (NCTC) also proposed in this roadmap, and complements NCTC's efforts in the determination of biological activity of small molecules. In addition, the Screening Hub for Chemical Biology will support environmental quality monitoring, such as water quality control, for which high-throughput analysis is important. To further improve the technological readiness of high-throughput devices, available prototypes will be developed in constant dialogue with academic and industrial partners. Research efforts will target more robust instruments and new protocols that help to solve current challenges such as the rapid chiral analysis and reliable quantification at nanolitre scale.

The 'Screening Hub for Chemical Biology' can be embedded into the Competence Centre of Biocatalysis (CCBIO) at the Zurich University of Applied Science. Moreover, it would tie in seamlessly with the automated (bio)catalyst development infrastructures already in place (Catalyst Hub at ETH Zurich and CCBIO at ZHAW). In addition to academic users, Swiss industrial partners and start-ups will be able to access the instruments to leverage the state-of-the-art infrastructure and technical know-how further fuelling Switzerland's vibrant biotechnology and pharmaceutical sector.



7.2.3 National Centre for Translational Chemistry

Context (national and international), scientific rationale and challenges

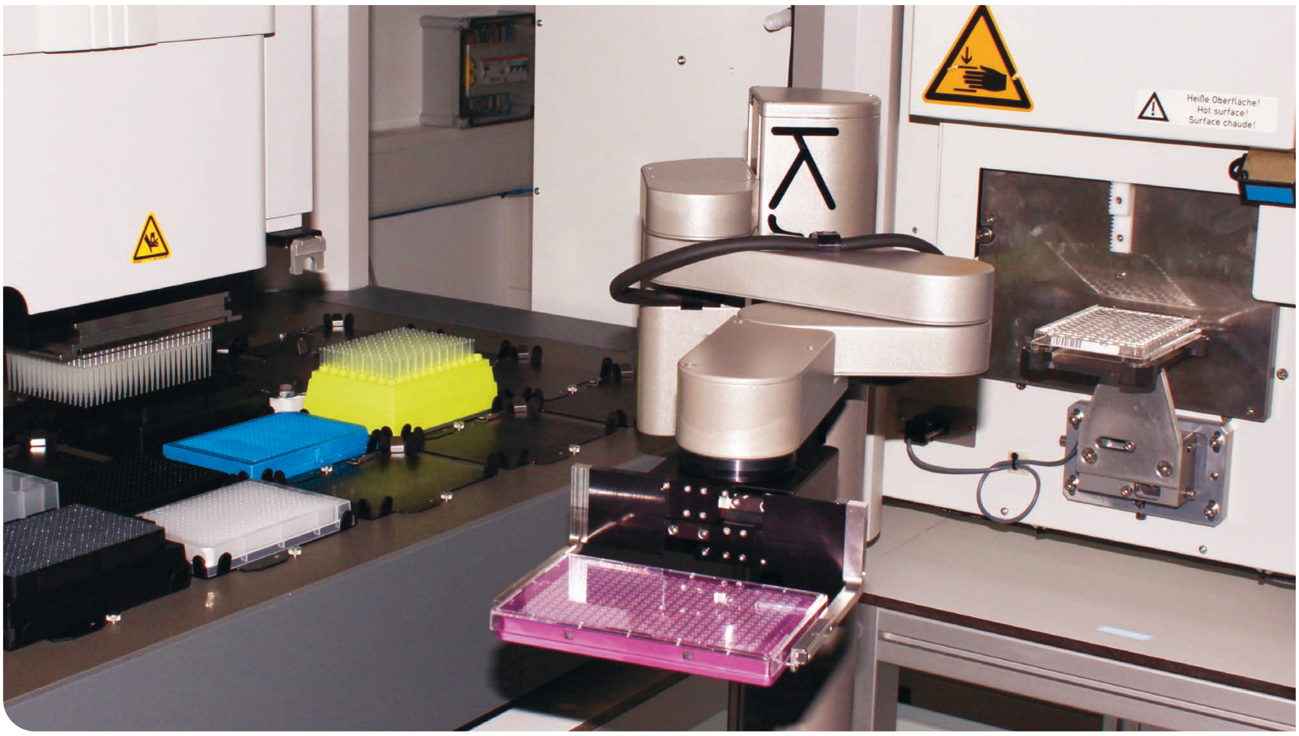
We propose to build a national multidisciplinary centre to provide the scientific community in Switzerland with: Chemical diversity, screening platforms at the EPFL and the University of Geneva, know-how in chemical genetics and expertise in medicinal chemistry for drug discovery, chemical biology and systems biology-related projects. The scope includes screening large chemical libraries for other application areas such as sustainable chemistry-related projects. The National Centre for Translational Chemistry (NCTC) will give access to a national repository of chemical collections, composed of a unique collection of molecules synthesised in Swiss academic labs in addition to more than 100,000 commercially available compounds.

This public screening centre with unique knowledge and expertise will perform screening projects for translational research countrywide for a broad range of assays. The screening centre masters state-of-the art technologies and innovative methods implemented or developed for designing a variety of tests in the search for active molecules. The tests offered cover the classic pharmaceutical target-based *in vitro* biochemical assays and innovative phenotypic image-based cellular assays using relevant cell types and physiologically relevant cellular models (i.e., models derived from stem-cells and organoids).

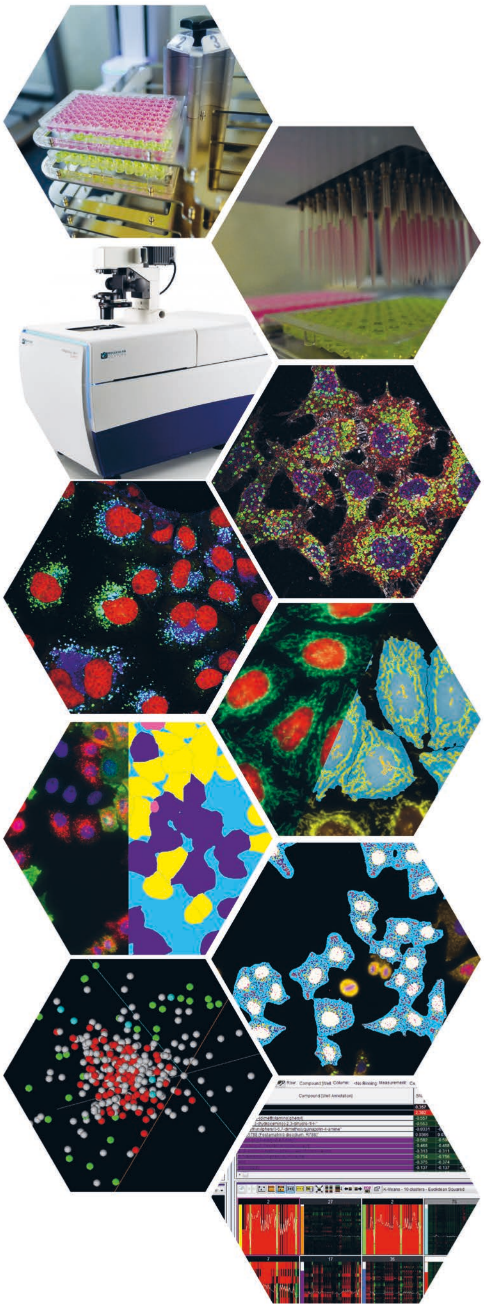
The vision of NCTC will focus on translational research though the development of existing infrastructures towards a complete academic drug discovery setting. The new centre will address public health challenges in various therapeutic areas not necessarily addressed by the pharmaceutical industry, and perform chemical screening and medicinal chemistry campaigns. The capabilities offered will be beneficial for chemical biology and life science research in general as well as investigations in other fields, including studies on environmental sustainability.

This major infrastructure could capitalise on pioneering efforts in Switzerland, namely the project ACCESS (an ACademic ChEmical Screening platform for Switzerland) created by the NCCR Chemical Biology[1], which is equipped with significant instrumental infrastructure and know-how in place and which has achieved relevant successes over the years (expires end 2022). The ACCESS platform of the NCCR Chemical Biology is receiving an increasing number of screens, no longer originating exclu-

1 https://nccr-chembio.ch/projects/project5



High-throughput screening facility at EPFL (photo BFS-ACCESS EPFL)



Academic Screening Platform for Switzerland (ACCESS)
(photo ACCESS Geneva)

sively from the host institutions of the platform, EPFL and the University of Geneva. 30% of the requests for screens come from other Swiss universities.

To build on these rewarding investments and ensure long-term, sustainable excellence in chemistry, chemical biology and academic drug discovery, it appears crucial to federate efforts and resources through a national entity allowing rational, centralised investments for further expansion within Switzerland. Nationwide effort and coordination are key, as a single university would not have the capacity or financial means to serve all the needs for academic screening in Switzerland.

An important part of the new centre will be a 'Swiss Compound Library', which collects, archives and makes available compound synthesised in Swiss academic laboratories. A Swiss Chemical Collection[2] (SCC) has been compiled in the NCCR. To this end, procedures were put in place for the collection of compounds (approx. 700) from seven organic chemistry groups, not commercially available and atypical compared to the structural space covered by commercial libraries. The compounds were assayed in NCCR screens and profiled in cellular assays such as cell toxicity assays. The US National Institutes of Health (NIH) have similar, very successful facilities (NCATS). These facilities received well-deserved attention because they perfectly illustrate the added value of collections and because prominent researchers with otherwise unrelated interests were involved. Through the NIH facilities, unexpected drug candidates for the treatment of cancer and neurodegenerative disease were identified. While the essential contribution of high-throughput screening to such discoveries is not always highlighted, high-throughput screening is an imperative infrastructure for translational research.

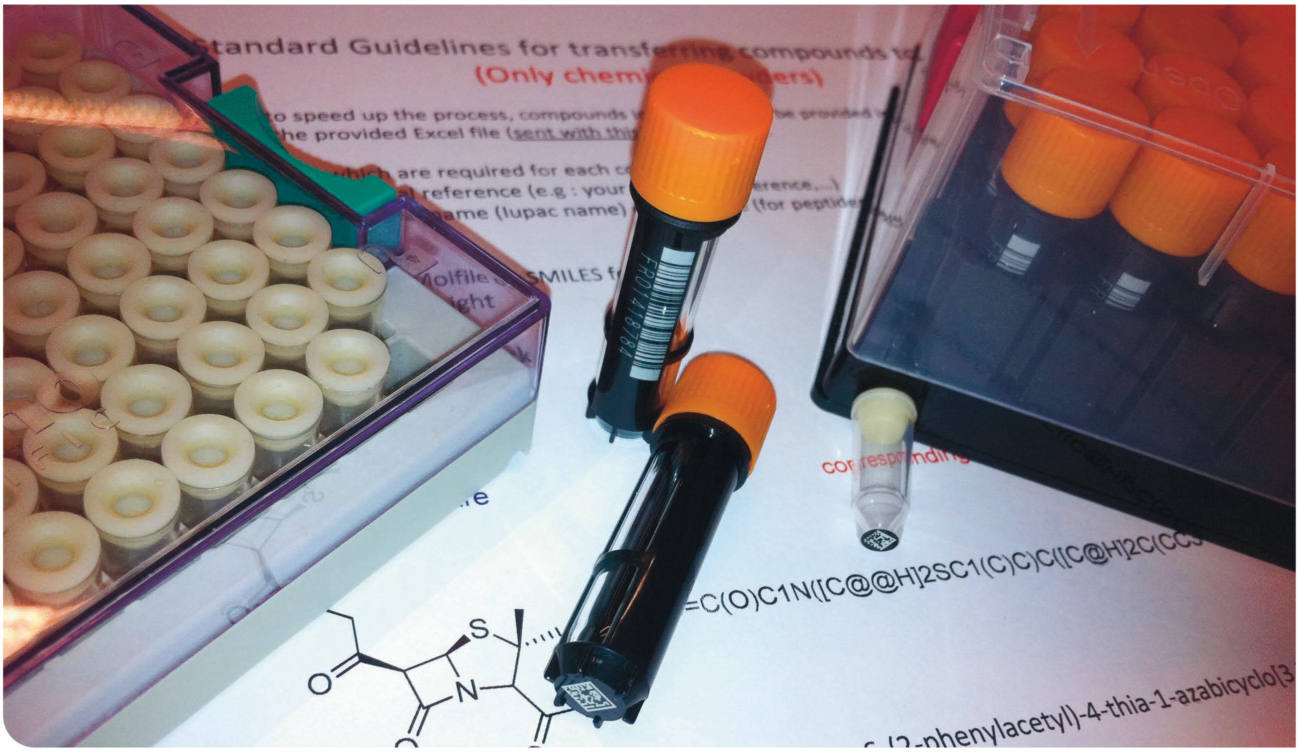
The Swiss Compound Library will serve three main purposes: First, it will archive 'all' molecules and their properties made in Swiss academia. Second, it will maximise added value for Swiss chemistry research by promoting the discovery of unexpected desirable activities by screening a unique chemical space. Third, the Swiss Compound Library will provide a unique tool to respond quickly to public health demands.

Aims of the Proposed Infrastructure

This project proposes the creation of a centre that will provide access to state-of-the-art instrumentation and expertise for translational chemistry research to the Swiss community.

We propose the NCTC is built on the solid foundations of the existing screening facilities: the Biomelcular Screening Facility (BSF) created at EPFL in 2006 and further developed by the NCCR Chemical Biology (BSF-ACCESS) and the screening facility at the University of Geneva, ACCESS-Geneva created in 2015 by the same national consortium. These two platforms have already started to work with partners in Switzerland beyond the local environ-

2 https://nccr-chembio.ch/technologies/facilities/the-swiss-chemical-collection



Chemical compounds collected from Swiss academic labs for high-throughput screening (photo BFS-ACCESS EPFL)

ment of the Leman area. Planned investments are allocated to imaging screening facilities, automation and readout equipment, biosafety class 2 and 3 pathogen screening units, a chemogenomic and personalised medicine unit, management infrastructure for compound collections, and a medicinal chemistry laboratory.

It is a major aim of the project to further extend existing activities in the field of screening to develop a centralised and structured entity for sustainable drug discovery and research endeavours. The new entity will include the SCC, conceived to access a unique chemical space, to provide added value and to archive Swiss chemistry research. This infrastructure, focussing mostly on imaging-based translational screening, is located downstream from the complementary mass spectrometry-oriented Screening Hub for Chemical Biology also proposed in this roadmap. An important developing area of application concerns drug discovery for rare diseases or other diseases where treatments are not financially viable for the pharmaceutical industry. In the national interest we also aim at building specialised platforms to screen for pathogens and to address current public health issues and major challenges related to infectious diseases, such as pandemics from new viruses or the spread of pathogens resistant to antibiotics.

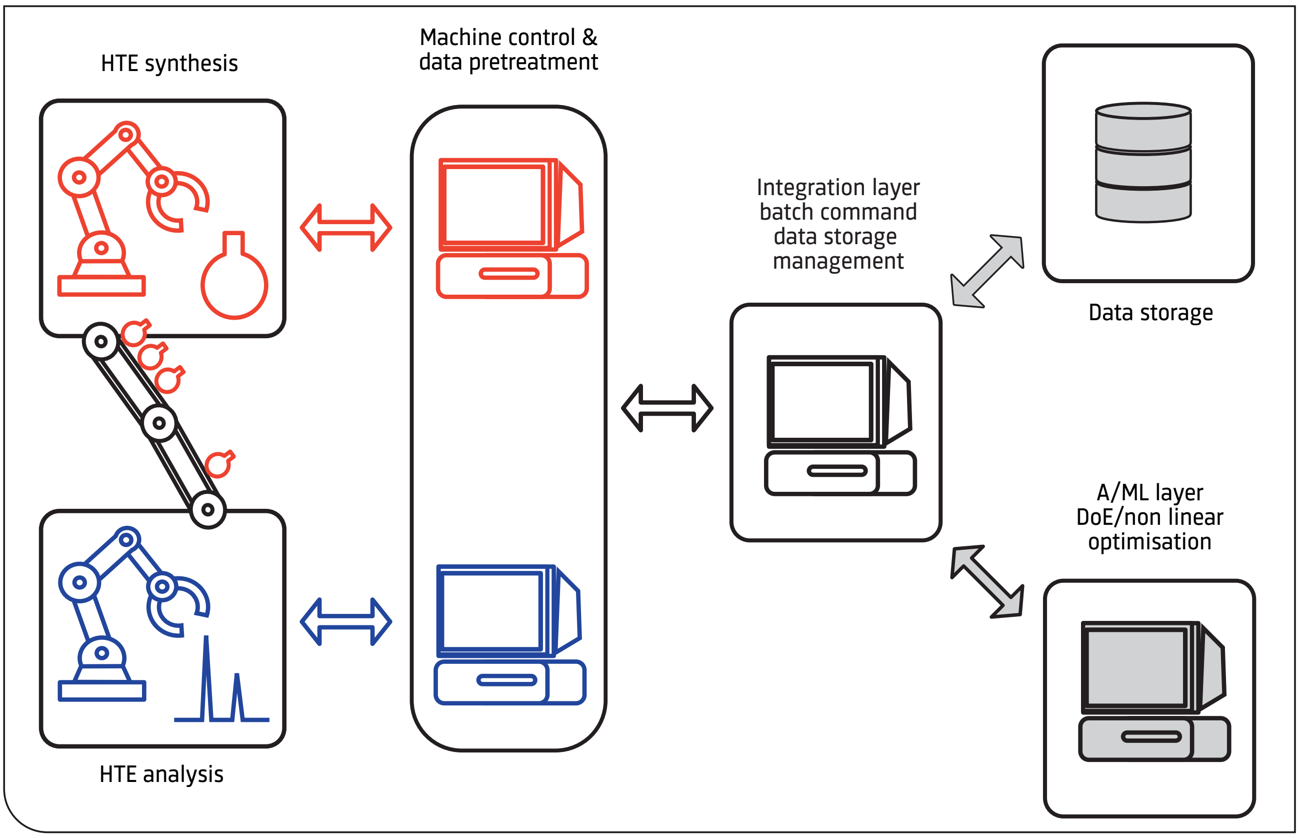
7.2.4 Catalysis Hub

Context (national and international), scientific rationale and challenges

Swiss chemical, agrochemical and pharmaceutical companies are world leaders in the transformation of petrochemical-based building blocks into complex molecules with high value. Irrespective of their target function, these compounds mostly originate from crude oil, a limited natural resource not available in Switzerland. Moreover, their production leads to increased levels of atmospheric carbon dioxide (CO_2) and global warming. The use of natural resources available in Switzerland could allow Switzerland to decrease fossil-based petrochemical feedstocks with the ultimate goal to become carbon neutral. These natural resources include plentiful carbon in unused (inedible) waste biomass, hydrogen in water, and abundant renewable electricity, as well as alternative lower footprint carbon sources such as methane. The development of greener and novel catalytic processes and the usage of renewable energy sources such as hydro, solar or wind power to drive chemical reactions are key technologies to move from an oil-based economy to a sustainable economy for the production of fuels, feedstocks, fine chemicals and pharmaceuticals.

In a global context, several high-level catalysis centres have been established over the last years to embrace this challenge (Merck Catalysis Centre at Princeton, UPenn/Merck High Throughput Experimentation Laboratory, the Gordon and Betty Moore funded Centre for Catalysis and Chemical Synthesis at Caltech, UK Catalysis Hub, joint Catalysis Research Laboratory of the University of Heidelberg that is supported by BASF (CaRLA) or the Netherlands Institute for Catalysis Research). Therefore, immediate action is required to maintain the internationally-recognised quality of catalysis research in Switzerland at the highest competitive level.

To achieve this goal, the ETH domain has just established a Catalysis Process Discovery Hub *(Catalysis Hub – Cat^+)* co-based at ETH Zurich and EPFL that builds on the assets of the ETH domain and is open to the entire Swiss community. During the first phase of the Catalysis Hub (2021–2024), catalysis research facilities with state-of-the-art high-throughput experimentation (HTE) equipment will be built at EPFL and ETH Zurich/Empa to provide access to advanced synthesis, characterisation, testing and opti-



Organisational scheme of the catalysis hub (Christope Copéret, ETH) misation of catalysts, in both homogeneous and heterogeneous phases. High-throughput experimentation (HTE) has indeed emerged as an essential tool for catalyst discovery and development enabling a rapid evaluation of multiple parameters, from catalyst composition to reaction feeds and conditions. In parallel, machine learning and artificial intelligence have just emerged as powerful tools to investigate large parameter spaces. This research infrastructure thus has the goal to integrate high-throughput experimentation and computational chemistry together with machine learning and Quantitative Structure Activity Relationships (QSAR) to discover catalysts and catalytic reactions with unprecedented efficiency, to accelerate process development, and to revolutionise the way chemistry is performed.

To invent rather than follow, we seek to build an unprecedented integrated infrastructure pairing the massive synthesis and screening power of HTE and the most advanced characterisation tools with the advances of digital technology and future machine learning artificial intelligence in a Catalysis Hub designed to reinvent chemistry.

Set-up for high-throughput catalysist screening (photo Christope Copéret, ETH)

Aims of the Proposed Infrastructure

Most fine chemicals for the chemical and pharmaceutical industry are produced from oil using catalytic processes. The goal of this ETH domain hub is to build on the ETH domain combined excellence in chemistry and chemical engineering to make possible the use of renewable energy, CO_2/H_2O and waste biomass to produce synthetic fuels and feedstock chemicals. The necessary key ingredient is the reinvention of chemistry, based in particular on catalysis, to move away from simple petrochemical feedstocks and to access more value-added fine chemicals. To accelerate the discovery process and the transfer of technology, we propose integrated cross-cutting research approaches: computer guided automated synthesis, characterisation and continuous-flow evaluation of massive catalyst libraries, and computational approaches through a Catalysis Process Discovery Hub that pools capacities across the entire ETH domain. This goes well beyond research undertaken within the existing competence centres of the ETH domain, such as SFA Energy Research or SCCER programmes. Combining computational and high-throughput catalyst discovery with machine learning will lead to breakthroughs in catalytic and sustainable processes. The key ultimate goals include:

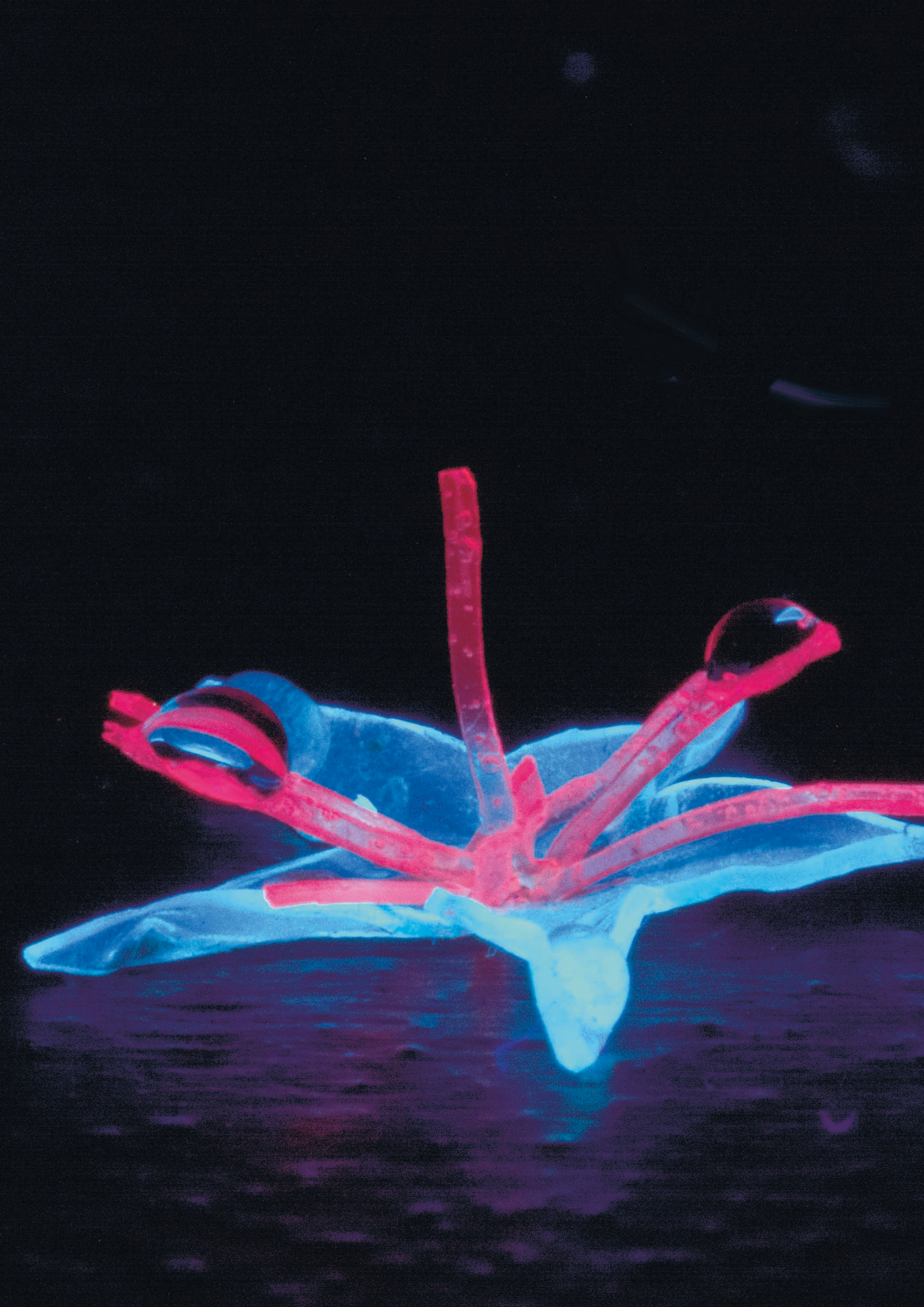
– The development of artificial intelligence-based discovery approaches in catalysis based on high-throughput experimentation combined with a machine-learning artificial intelligence approach in order to accelerate discovery and guide to unexpected solutions

– The development of *in situ* and *operando* spectroscopic tools and methods with unprecedented resolution, together with computational methods, to drive the rational design of novel and improved catalysts and to understand how to overcome limitations such as catalyst stability/deactivation.

– The development of highly efficient, novel catalysts, processes and catalysis concepts for conversion of abundant feedstocks into high-value compounds.

– The discovery of novel catalytic processes that will allow the rapid synthesis of highly complex molecules and smart materials in a highly efficient and sustainable way.

Catalysis Hub – Cat⁺ is located on two campuses in the East and the West of Switzerland to best exploit world-class expertise in both locations. Each of them will concentrate on specific and complementary topics: solid (heterogeneous) catalysts in the East and molecular (homogeneous) catalysts in the West, based on the respective existing critical expertise. This platform will be open to the entire Swiss community, both from academia and industry, and will guarantee a rapid access to the state-of-the-art research infrastructure in catalysis.



8 Conclusions

This Chemistry Roadmap proposes the discovery-driven and challenge-driven research infrastructures (RI) that are required to keep the Swiss chemistry community in academia and in industry at the forefront of international research in the chemical sciences. The proposed infrastructures will enable scientists to translate knowledge into solutions for the current global challenges in energy, environment, health and sustainability.

The Swiss chemistry community has realised the necessity to join forces and to collectively install frontier instrumentation at a higher level than is possible by individual university units. The community underlines the need for national infrastructures in order to enable access to state-of-the-art large instrumentation and expertise that can no longer be hosted by single institutions. Moreover, these facilities should provide inter- and transdisciplinary support and expertise to users to improve data acquisition and analysis, one of the key challenges in chemical research and a necessary step toward improving scientific quality and in moving towards quality open data.

Seven key enabling infrastructures have been identified, three discovery-driven research infrastructures and four challenge-driven research infrastructures.

Discovery-driven research infrastructures:

→ Discovery RI-1) A magnetic resonance and magnetism hub

→ Discovery RI-2) A centre for *operando* synchrotron studies

→ Discovery RI-3) An electron microscopy and diffraction hub

Challenge-driven research infrastructures:

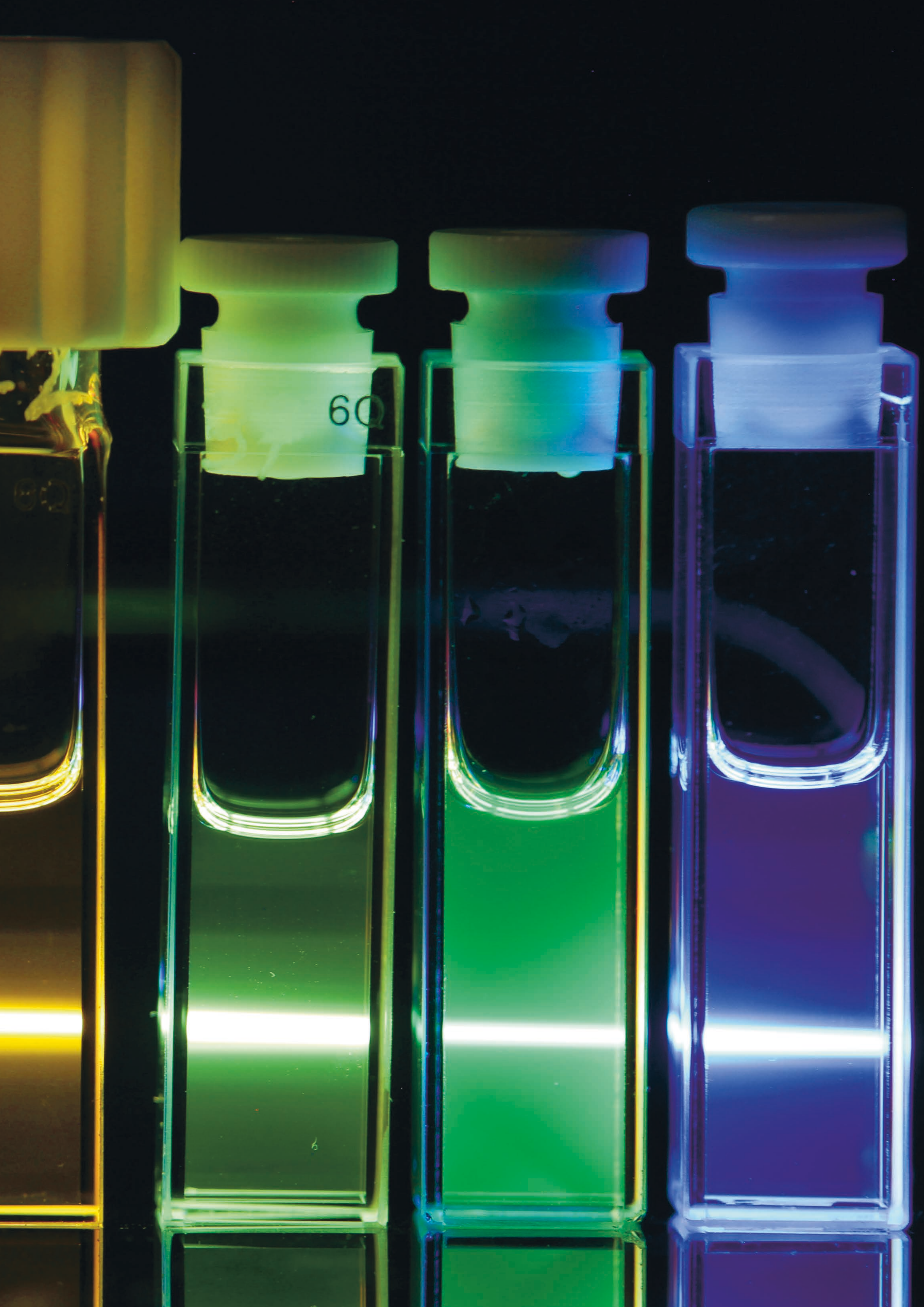
→ Challenge RI-1) A facility to produce Terbium radionuclides for diagnostics and treatment of disease

→ Challenge RI -2) A mass spectrometry-based screening platform for (bio)catalysts and environmental samples

→ Challenge RI -3) A centre that provides state-of-the-art instrumentation for translational chemistry and manages a national library of compounds synthesised in academic laboratories across Switzerland

→ Challenge RI -4) A catalysis hub *(CAT^{+})* to discover and develop catalysts and catalytic processes towards a sustainable society

The infrastructures proposed in this Chemistry Roadmap for Research Infrastructures will build on existing Swiss expertise and aim to be tightly linked to other community roadmaps, namely the Photon Science Roadmap, the Neutron Science Roadmap and the Biology Roadmap. The ultimate goal is to provide unique world class facilities to the Swiss and international science community. As a result, Switzerland will remain attractive and innovative in chemical sciences, one of the key assets of Switzerland at the international level, and an essential component for a sustainable development of Switzerland.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SCNAT – network of knowledge for the benefit of society

The **Swiss Academy of Sciences (SCNAT)** and its network of 35,000 experts works at regional, national and international level for the future of science and society. It strengthens the awareness for the sciences as a central pillar of cultural and economic development. The breadth of its support makes it a representative partner for politics. The SCNAT links the sciences, provides expertise, promotes the dialogue between science and society, identifies and evaluates scientific developments and lays the foundation for the next generation of natural scientists. It is part of the association of the Swiss Academies of Arts and Sciences..