National Roadmap Large-Scale Scientific Infrastructure

December 2016

Foreword

Before you lies the 2016 National Roadmap for Large-Scale Scientific Infrastructure. Large-scale research infrastructure is playing an increasingly important role as an essential condition for internationally groundbreaking research in essentially all fields of science. This Roadmap provides an overview of the large-scale research infrastructure that has the highest priority for science in the Netherlands.



Widely accessible and state-of-the-art research facilities are clearly crucial to science. They make it possible to penetrate to the nucleus of an atom and to unravel complex genetic questions. They also make massive datasets available and accessible for researchers in the social sciences and the humanities. These facilities also contribute to technological and social innovations. The latter, in turn, create space for new hi-tech industries. A good ICT infrastructure is particularly important for large-scale research facilities. Developments in this are strengthening the Netherlands' already powerful position in this area.

The Dutch government invests in major facilities for scientific research through NWO. Large-Scale research facilities require investments that far exceed the financial capacity of knowledge centres. Establishing large-scale research facilities that are important for the Dutch research field therefore requires a concerted effort from all stakeholders. These investments also determine the priorities and direction of a research area over a longer period of time. This requires a strategic approach. That is why the cabinet has asked NWO to set up a Permanent Committee. This committee has been asked, among other things, to develop a strategic framework for large-scale scientific infrastructure.

An important initiative of the Permanent Committee was to bring together the research field with the request that they work together more, set clear priorities regarding investment needs and develop a national investment agenda. The result of this is clearly evident in this new Roadmap. It includes, in addition to already established clusters of facilities, 16 new clusters of research facilities. I whole-heartedly approve of this concerted effort and this outcome. The creation of these clusters is an important step towards achieving the most efficient possible expenditure of the available resources.

Stan Gielen
Chair NWO

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Introduction

Hans van Duijn, Chair Permanent Committee



1 | Permanent Committee for Large-Scale Scientific Infrastructure

The Permanent Committee for Large-Scale Scientific Infrastructure emerged from the Dutch Cabinet's '2025 Vision for Science: choices for the future' and was appointed by NWO on behalf of the Ministry of Education, Culture and Science. The committee's task is to develop a national strategy for investment in large-scale research infrastructures. In particular, the committee will determine the strategic framework for NWO's funding of large-scale scientific infrastructure, and it will draft the National Roadmap for Large-Scale Scientific Infrastructure.

The Permanent Committee has also been asked to make recommendations regarding the ICT infrastructure. To that end, it has set up a separate advisory committee. The ICT committee consists of several stakeholders, among which SURF as co-ordinator of the national ICT infrastructure. The Permanent Committee will offer its recommendations for ICT infrastructure in a separate document.

The Permanent Committee consists of members proposed by various stakeholders and reflects a broad area of expertise.

Last year, the Netherlands Royal Academy of Arts and Sciences (KNAW) developed an 'Agenda for Large-Scale Research Facilities'. It gives an initial impression of the research infrastructure that will be required in the distant future. This initiative helps to strengthen cooperation between researchers who often work in different disciplines but need the same research infrastructure. The initiatives on the KNAW Agenda are one of the sources for the future facilities of the National Roadmap for Large-Scale Scientific Infrastructure.

2 | Inventory and landscape analysis

The committee's first task was to determine all existing large-scale research facilities at universities, scientific institutes, applied knowledge institutions (TO2) and government institutions. The facilities concern both physical equipment – such as telescopes, particle accelerators and biobanks – and less tangible facilities such as databases and ICT facilities. The committee has also made an inventory of the new investments that will be needed in the coming five years for existing and new large-scale research facilities. The inventory was implemented across the entire research landscape, including the TO2 institutes. This inventory has played a key role in updating the National Roadmap for Large-Scale Scientific Infrastructure.

The committee used the following criteria to analyse the received facilities, which will also play an important role in the way resources are eventually distributed:

1. *Meets the definition of large-scale infrastructure and the type of infrastructure it involves*
   (national/international, single sited/distributed/virtual, hardware/e-infra/data/collection)
2. *The cohesion between the various facilities*
   (Uniqueness, overlap and cohesion, affiliation with ESFRI, cooperation and selectivity in the field)
3. *Affiliation with strategic developments*
   (Affiliation with the Dutch National Research Agenda (NWA); strategic goals and priorities of institutions, scientific fields, top sectors)
4. *Participation and use*
   (The facility's national and international target group and user group)
5. *Significance to science and society*
6. *Status/maturity of facility*
   (Phase of life, support, governance and organisational structure, substantiation of the investment plans, institutional commitment, funding also in the long term)

The committee received a total of 164 facilities from 54 different institutions. Of these, a total of 113 have been incorporated into the landscape of existing large-scale research facilities in the Netherlands (see www.onderzoeksfaciliteiten.nl). A number of facilities did not meet the financial lower limit (€10 million) for large-scale research facilities and have therefore not been incorporated into the landscape. For the first time, the landscape has provided an overview of existing large-scale research facilities, as well as the need for new facilities in the Netherlands.

Taken together, the 164 facilities have a combined investment need of more than €3,000 million for the coming five years. Of these, about a hundred facilities have indicated that they would like to be incorporated into the new National Roadmap for Large-Scale Scientific Infrastructure. These infrastructures have an investment need of more than €2,000 million. This amount is indicative and also includes the input of these facilities' own resources and third-party resources. Nonetheless, the committee believes that the investment need is not commensurate with the National Roadmap's available budget of a total of €200 million for the coming five years. Many infrastructures that are highly important to science in the Netherlands may therefore never see the light of day.

3 | Conclusions based on findings of the landscape analysis

The inventory provides a good picture of the large-scale infrastructures in the Netherlands, as well as the need for new facilities. The committee observes that there is an overlap between the various infrastructures. At the same time, various facilities are requesting similar equipment. The committee has also observed that new investments are being made or are in the pipeline, even though existing facilities still have available capacity.

The committee has come to the conclusion that the facilities need to harmonise and cooperate more effectively. On the one hand to prevent duplication, and on the other hand to use the available infrastructure in the most optimal way possible.

The imbalance between the investment needs and the available resources means that the research community has to make stricter choices and set clearer priorities. Indeed, the committee has noted that a number of research fields have already started this harmonisation and cooperation.

From landscape to Roadmap

The inventory is the basis for the National Roadmap for Large-Scale Scientific Infrastructure. The most important selection criterion for it is the importance of infrastructure for science. The committee has also explicitly focused on compliance with strategic priorities, particularly the NWA and the degree to which the plans are well-thought-out and designed.

Clusters of facilities

The conclusions of the landscape analysis prompted the committee to consult with representatives from facilities that are strongly affiliated or plan to develop or purchase similar equipment. The committee asked the research community to collaborate more and draft a joint investment plan. For this purpose the committee grouped related facilities into clusters in the Roadmap. The various research communities responded to this request positively and have underscored the importance of collaboration, in so far as they are not already working on it. The committee considers this collaboration to be of the utmost importance in order to set good priorities and agree on the desired investment, thereby taking an important step towards a national strategy for large-scale scientific infrastructure.

The committee will continue to encourage the creation of clusters of facilities and cooperation between research fields in the future as well and invites, where expedient, the research community to actively explore further cooperation. Indeed, the committee will also monitor the development of disciplines and adapt, when necessary, the arrangement of clusters.

Harmonisation with the field and the evaluation of the Permanent Committee has led to a new National Roadmap consisting of 33 facilities. These are in part individual facilities (16), as was the case with the previous National Roadmap. In addition, the National Roadmap consists of clusters of facilities (17) that are asked to draft a joint investment plan for the entire cluster. This National Roadmap is set to run for a period of 4 years. The next update of the National Roadmap will take place sometime in 2020. The Permanent Committee will evaluate the design of the current Roadmap following the upcoming round of funding. The committee will also provide the possibility of allowing limited additions to this National Roadmap in urgent situations prior to the formal update in 2020.

A number of facilities were not included in the National Roadmap by the Permanent Committee. It mainly concerns facilities that, despite being important to society, have too limited scientific value. Furthermore, a few facilities are not aligned with the strategic frameworks of a scientific field. A number of facilities are insufficiently developed to already be included in the National Roadmap.

4 | Strategic frameworks and conditions for the allocation of resources for the National Roadmap of Large-Scale Scientific Infrastructure

Introduction

The Permanent Committee has drafted a number of general strategic frameworks and conditions for the National Roadmap and for the facilities on the National Roadmap. The general frameworks are related to the balance between scientific areas, the formation of the clusters, the ICT infrastructure, harmonisation with the European Roadmap for Research Infrastructures (ESFRI Roadmap 2016) and other national and international strategic agendas, the importance of joint funding, the long-term sustainability of a facility, research data and access to the facility. The committee has offered the board of NWO a number of more detailed recommendations for the upcoming *call for proposals* in a separate document.

4.1 | Balance between scientific areas

The committee has concluded that there is a need in all scientific domains (humanities/social sciences, science/technology and the life sciences) for large-scale research facilities and that these are of substantial scientific importance. The committee deems it important that all scientific areas benefit from the limited resources for large-scale scientific infrastructure. To achieve this, the committee has developed financial frameworks for the allocation of the available resources across three scientific domains. This allocation ratio was developed on the basis of an analysis of the stated investment needs and historical figures from previous Roadmap rounds. A total amount of approximately €200 million will be available for the coming five years. Of this amount €20 million is available for the humanities/social sciences, €90 million for science/technology and €90 for the life sciences, or 10%, 45% and 45% of the available resources respectively. The committee recommends using this ratio for upcoming National Roadmap calls.

4.2 | National cooperation and funding

The available resources for large-scale scientific infrastructure are very limited in relation to the investment needs. This means that choices will have to be made. The most important strategic framework for this National Roadmap is to connect related facilities and the task given to the research community in question to develop one investment agenda that contains clear priorities.

The committee considers the facilities on the National Roadmap to be national facilities that require a joint effort from all involved parties. This means that institutions that want to develop a facility or participate in one will be asked to provide co-funding. The Permanent Commission is asking NWO to record and monitor any allocated co-funding.

4.3 | ICT infrastructure for research facilities

The committee has concluded that ICT plays an important role at a large number of facilities. That requires special attention as facilities draft their investment plans. The committee therefore recommends that applicants in the upcoming call for the 2017 Roadmap include a separate section regarding the use of ICT infrastructure. This section will also be taken on board in the evaluation of the request. In setting up the evaluation committee, the Permanent Committee recommends guaranteeing that there is sufficient expertise in the committee to be able to evaluate the ICT component.

4.4 | Alignment with ESFRI

The *European Strategy Forum on Research Infrastructures* (ESFRI) developed the European Roadmap for Large-Scale Research Facilities. The last update of this Roadmap was presented in the spring of 2016, and a new update of the ESFRI Roadmap is planned for some time in 2018. The Permanent Committee believes that it is important for the Netherlands to also harmonise, where possible, with ESFRI's European Roadmap. Dutch facilities that dovetail with an ESFRI infrastructure should therefore be part of the ESFRI infrastructure. The Permanent Committee has therefore decided not to include facilities in the National Roadmap that are aligned with an ESFRI facility but which are not part of it. In the current transition phase the committee will require facilities to which this applies to first become part of an ESFRI facility before submitting an application for Roadmap resources. In doing so, the committee will look at ESFRI landmarks, ESFRI projects and ESFRI emerging facilities. The committee generally believes that harmonisation with international priorities is important in order to prevent duplication.

4.5 | Long-term sustainability

Large-scale scientific infrastructure requires a substantial investment, not only in terms of its construction and accommodation, but also to in terms of its operation. The average operating cost amounts to approximately 10% of the annual investment. An outline of the costs over several years is required to successfully develop and operate a facility, one that describes all of the costs (investment, accommodation, upgrades, operation and any decommissioning costs) and how they will be covered. The committee has chosen a period of 10 years as a point

of departure. This will also give the commission insight into future expected costs for facilities, so it can anticipate these to the best of its ability. An estimate of the cost of the entire life span for facilities with a longer life span is expected as well.

4.6 | Research data

More and more, the increasing complexity of research questions requires combining data obtained through various techniques and from various sources. In addition, there is an increasing need to be able to reuse research data. This requires harmonisation between disciplines, and the development and availability of common technologies and standards. This is especially applicable to the large amounts of data generated by modern research facilities. To make it possible to combine data, the data needs to be made available according to the FAIR principles (Findable, Accessible, Interoperable and Reusable). The committee will as far as possible align with EU-policies.

There are expert centres in the Netherlands in the different scientific areas for the storage and availability of data, such as DANS, 4TU data centre, BBMRI and DTL/Elixir. The Permanent Committee is calling on the research community to make extensive use of these platforms and expert centres. It will make it possible to connect data from different domains of expertise, which will prevent efforts from fragmenting.

4.7 | Access to facilities

Good access to facilities is important to provide other researchers with the opportunity to also use the infrastructure. For that it is necessary for the infrastructures to provide good instructions on their website about how to gain access. The Permanent Committee has concluded that access to the facilities is not always equally clearly organised or described. The committee will devote extra attention to this, so that clear information can be obtained about accessibility and the related procedures for all facilities in the landscape of large-scale research facilities and on the National Roadmap via their websites. In doing so, the committee adheres to the European Charter for Access to Research Infrastructures. In addition to that, scientific infrastructures on the National Roadmap will in any case have to provide access based on scientific excellence or a broad access policy. Infrastructures on the National Roadmap are not allowed to only offer access on a pay-for-use basis.

Meril database of European research facilities (https://portal.meril.eu)
The Meril database (*Mapping of the European Research Infrastructure Landscape*) provides an overview of the European landscape of research infrastructures that have more than a merely national interest. A good overview of the available infrastructure is crucially important for the further analysis of the landscape, and it is the basis for cooperation and harmonisation between research infrastructures. This important for the Netherlands, but it is equally important for Europe as a whole.

The committee believes it is important for the Dutch research infrastructures that are accessible to foreign researchers to be part of the European landscape that is reflected in the Meril database.

4.8 | Life sciences facilities and clusters

In the life sciences the *Dutch Techcentre for Life Sciences* (DTL) is the national platform of expert groups with advanced facilities from a broad range of research techniques. DTL aims to create a cohesive research infrastructure in the broad field of life sciences, with special attention for the combining of techniques, for (FAIR) data stewardship and for education in this area.
The Permanent Committee supports this initiative and calls on the facilities in the life sciences to make use of this initiative. ELIXIR-NL is the coordination point for the development of the *linked (FAIR) data 'backbone'* for infrastructures in the life sciences. Research data must be made accessible and available for reuse according to international standards. The Permanent Committee asks the facilities in the entire domain Life Sciences to design their data policy in close cooperation with ELIXIR-NL.

Interview with State Secretary Sander Dekker (Education, Culture and Science)

‘The road to science with impact’



What is the significance of the National Roadmap?

‘The Roadmap is about large-scale facilities, so it's about tools that scientists need to perform their important work for society. This book lists the actual projects. They dovetail seamlessly with the Dutch National Research Agenda (NWA) (see also appendix 1: Alignment with NWA). Large-scale facilities are a condition for scientific progress. They bring together research from different fields, and that increases the chances of achieving scientific breakthroughs. They also hold great appeal for top-flight researchers, young talent and promising students. Not only science, but also the business world benefits from the work of the highly trained people at these facilities. Indeed, you always see interesting companies that use this knowledge emerging around these large-scale facilities. I think a nice example that we all benefit from is Wi-Fi, which is a spin-off of ASTRON's radio telescope.’

The proposals in this roadmap are largely clustered together. What do you think of this?

‘That's a great idea! It prevents overlap and means we can use the infrastructure that's already in place. I am glad that researchers, universities and knowledge centres made their own proposals. That will enable us to as many researchers from our country, but also abroad, access to these facilities. And the added benefit is that we are also

further enhancing cooperation between researchers. The best ideas often emerge from the cutting edge of disciplines.'

What's your appraisal of the future of large-scale scientific infrastructure?

'The Netherlands is never finished. Whether it's our health, our food supply or jobs for the future: we want to move forward. Scientific research is the key to progress. Excellent science requires a high-quality and accessible research infrastructure. Science has to have an impact. And that means working together, sharing knowledge and remaining curious. As the tools we need increase and become more expensive, we will also need to step up international cooperation. That's why I think our approach of developing joint agendas and roadmaps will be widely adopted internationally as well. The National Roadmap will point us down the right path.'


Domain
Humanities/
Social Sciences

Cluster: CLARIAH-PLUS

Digital revolution

The digitisation of analogue sources of text, image and sound improves researchers' access to large amounts of data. CLARIAH-PLUS develops smart, user-friendly techniques to structure collections and make them accessible.

Many institutions and institutes in the Netherlands have well-maintained collections of texts, images and/or artefacts. The National Library of the Netherlands, for example, has the largest collection of printed texts (books, newspapers and magazines), the National Archives of the Netherlands has the largest collection of manuscripts and the Netherlands Institute for Sound and Vision provides access to more than a million hours of television, radio, music, film and web video. In addition, there are specialised institutes such as the International Institute of Social History and the Museum of Literature, which have extensive collections of texts, images and sound, as well as libraries, museums and regional historical centres.

Until recently it took researchers in the humanities a great deal of time and effort to track down information relevant to their research in archives, libraries and museums. The large-scale digitisation of data from all these different sources has made that easier. Linguistic data from huge corpora; combining numerous events in which a politician was involved from newspapers and books; the development of sentiments about nations, social advances or ethnic groups; following ships in shipping reports and combining those with the names of crew and captains from other sources, it can all be done by 'pushing a button'. An additional effect is that other researchers can verify these data and test their interpretation. As a result, the empirical foundation of the humanities is expanding.



The digital revolution in the humanities is not an automatic process, however. For example, there is not a uniform approach on how to set up digital files or the tools to make them accessible and process them. In order to truly benefit from it, databases must be structured in such a way that search engines can make the desired selection. Moreover, the search engines have to be aligned with researchers' experiences and expectations.

Delpher is a national facility operated by the National Library that provides researchers with access to more than 60 million pages of digitised pages via full text search. The texts originate from more than 60 different institutions and institutes. Specialist users can also hook up their systems automatically via an API, or application programming interface, which allows computer programs to communicate with each other.


1645
SCHRIK NIET IK WREEK GEEN QUAAT MAAR DWING TOT GOET
STRAF IS MYN HAND MAAR LIEFLYK MYN GEMOET



The National Archives manage archives of the government and civil society organisations and individuals considered to have national significance. As a 'national memory bank' it records Dutch history and underpins citizens' right to information. It is also accessible to European institutions and organisations. Together with the regional historical centres in provincial capitals and other major cities, the National Archives of the Netherlands started digitising archives in 2015. The plan is have ten per cent of the national collection available in digital format by 2030 for citizens, researchers and other stakeholders.

Another example is The Language Archive, initiated by the Max Planck Institute for Psycholinguistics. It contains texts and images and sound fragments in more than 200 languages spoken around the world. An important part of it concerns endangered languages that were compiled in the framework of the DOBES programme (*Dokumentation bedrohte Sprache*). Part of the collection (102 languages) is recognised by UNESCO as belonging to the 'Memory of the World'.

Although there are already many initiatives and more still being taken to digitise texts, images and sound, an integrated digital database containing all data significant for the humanities is still years away. To prevent that every centre, institute or every collection approaches digitisation in its own way, there is an urgent need to improve data exchangeability and the tools used to do it. That is the only way to put researchers in the position to use various sources.

The Netherlands is playing a leading role in the digital revolution in the humanities in Europe, especially in the above-mentioned ESFRI infrastructure CLARIN and in DARIAH, which stands for Digital Research Infrastructure for the Arts and Humanities. To maintain this leading position, the involved



parties have joined forces in CLARIAH, the Common Lab Infrastructure for the Arts and Humanities. CLARIAH builds on previous projects that make digital databases accessible in such as a way that researchers are able to take data from different databases and create virtual collections tailored to their research issues.

CLARIAH-PLUS is an initiative of KNAW (IISG, Huygens ING, Meertens Institute), the National Library of the Netherlands, the National Archives of the Netherlands, the Max Planck Institute of Psycholinguistics, the Netherlands Institute for Sound and Vision, and Utrecht University, the University of Amsterdam, Radboud University Nijmegen, Tilburg University, Leiden University and the University of Groningen.

These facilities play an important role in the ESFRI facilities Common Language Resources and Technology Infrastructure (CLARIN) and Digital Research Infrastructure for the Arts and Humanities as a European Research Infrastructure Consortium (DARIAH).

Cluster: ODISSEI

Searching for patterns in society

***Open Data Infrastructure for Social Sciences and Economics Innovation* (ODISSEI) is an integrated, flexible infrastructure. It was established to gather, integrate, store and create access to data from the social sciences.**

The Netherlands has an impressive reputation when it comes to building and using data that were collected through registries, surveys or direct observation methods. Researchers are (also) using so-called Ecological Momentary Assessment (EMA) more and more often. These data originate from open sources such as Twitter and Facebook, and also from 'wearables', such as mobile phones, GPS trackers, wristband activity trackers, and medical sensors including blood pressure devices. It is difficult to predict what all these new kinds of data are going to bring, but clearly, the social sciences are on the brink of a big data revolution.

Anticipating this revolution, ODISSEI is bringing together existing big data collections in the social sciences. Although they are the foundation for much excellent research in the social sciences, researchers are still making too little use of the possibilities for synergy when gathering, storing and creating access to these data. Integrating collections of data avoids overlap and duplication. Moreover, it provides a unique opportunity to have a more targeted concentration of data. There is also the possibility of combining the wealth of existing data with new, yet-to-be collected data in the coming generation of databases and data analysis systems.



A recent example of integration, and therefore improved efficiency, is the implementation of the Dutch part of the International Social Survey Programme (ISSP). ISSP is a long-term international programme in which forty countries are participating. It consists of a relatively short questionnaire (60 questions) about a continuously alternating theme. Since 2016 the Dutch part has been operating via the LISS panel, which consists of 5,000 households that fill in questionnaires via the internet about a range of subjects. LISS stands for Long-term Internet Studies for the Social Sciences.

Other long-term, international projects also provide opportunities to improve efficiency through an integration of the data infrastructure. One example is sharing sampling frames. SHARE, an acronym for Survey Health, Ageing & Retirement Europe, is a multidisciplinary, transnational study among older adults (50+). For design reasons SHARE ends up throwing away a good proportion of their sampling frame (i.e. the young). Other European programmes, such as the





European Social Survey (ESS) and the Generations & Gender Programme (GGP) could collaborate in a central sampling process that is conducted once for all surveys rather than multiple times, which is very costly. Another possibility is to transfer the GGP respondents, who reach the age of 50, to SHARE. Synergy, in other words.

Irrespective of improved efficiency, large-scale cooperation based on a joint infrastructure often generates interesting new developments in a field, but more importantly also between fields. Examples of this include the partnership between biobanks (BBMRI, *page 67*) and the research infrastructure for the humanities (CLARIAH-PLUS, *page 14*). Cross-field partnerships will certainly be the case in the social sciences as well, now that all kinds of new sources of data are becoming digitally available. Clever algorithms, moreover, can correlate data from long-term surveys and from new sources to microdata, as maintained by Statistics Netherlands (CBS). As a result, a previously unimaginable wealth of information has been developed.

These kinds of integrated collections of data are interesting for researchers in the social sciences, but also for researchers in other disciplines, such as health research and ICT. Apart from that, learning to deal with large amounts of partially unstructured data is important for other disciplines as well. Ministries and other public authorities also have a vested interest in integrated collections of data for governance and policy. The development of 'smart cities', for example, is impossible without a good understanding of the degree to which citizens – young and old, poor and rich, male and female – can participate in them.

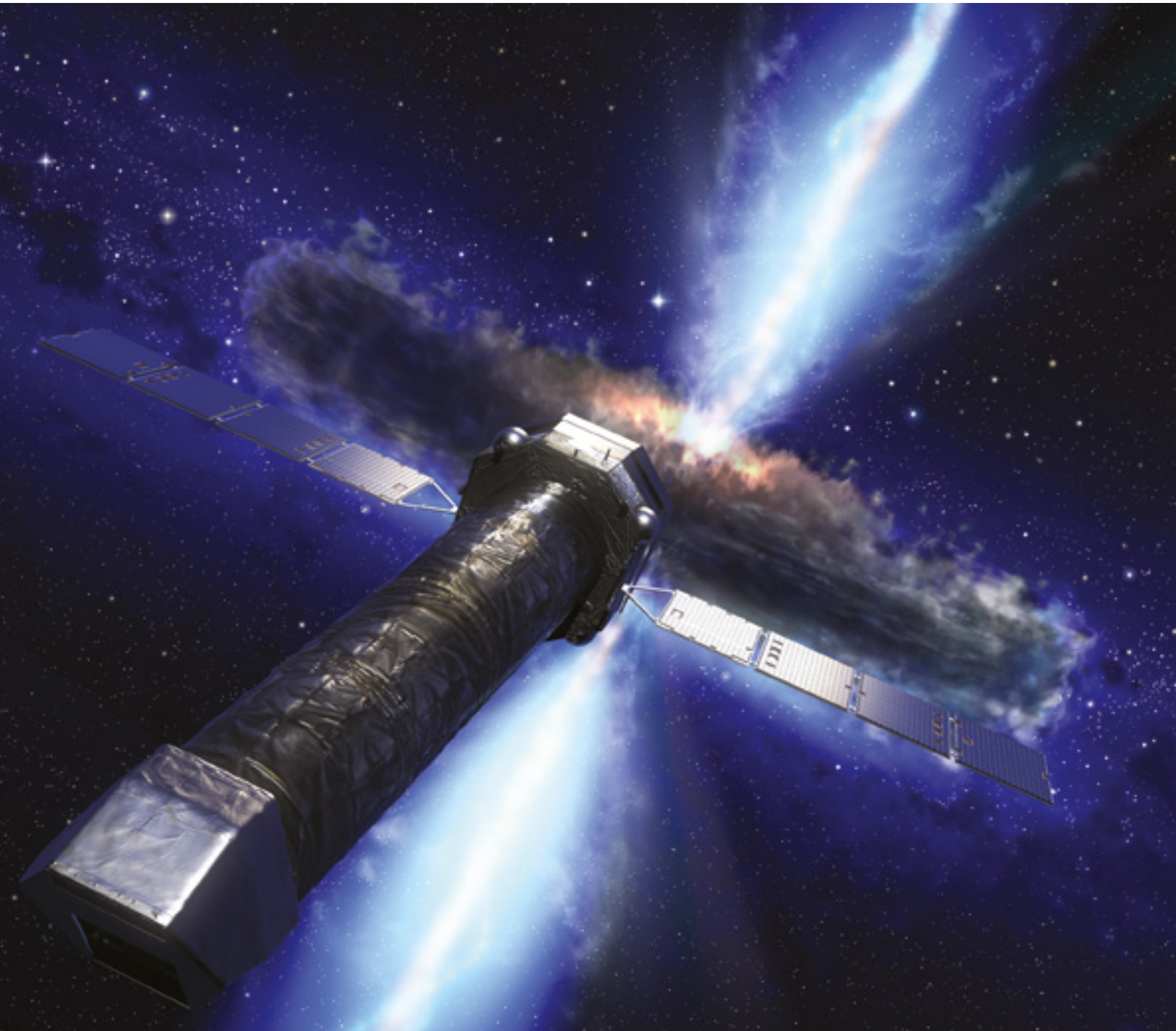


Exploring and exploiting these massive amounts of partially unorganised data not only requires innovative methods and models of analysis, but also a new flexible and integrated infrastructure for the storage and accessing of these data. ODISSEI is the key coordinating actor in the partnership: on the one hand, it serves as bridge between different scientific disciplines, and, on the other hand, it serves as bridge between researchers and (potential) users, such as administrators and policymakers, civil society organisations and industry.

ODISSEI is an initiative of universities, NWO and CBS, in which Erasmus University Rotterdam acts as lead applicant in the person of professor Pearl Dykstra. The foundation is the partnership between researchers who are involved in the major international, European and Dutch data collection projects.

This facility comprises the ESFRI facilities Survey of Health, Ageing and Retirement in Europe (SHARE), European Social Survey (ESS) and the forthcoming ESFRI facility 'Gender and Generations Programme'.


Domain
Science/Technology



ATHENA

A probing look at hot gases and black holes

Advanced Telescope for High Energy Astrophysics **(ATHENA) is a space telescope for the observation of X-rays in the 'hot and energetic universe'.**

Five percent of the universe consists of 'regular' matter. It is mostly trapped in enormous clouds of super-hot gases with temperatures of several million degrees Celsius ('the hot universe'). An X-ray telescope is essential for gaining a firm understanding of the origins and development of these gaseous structures. The same is true of the processes taking place on the edge of supermassive black holes, situated in the centre of galaxies ('the energetic universe').

Compared to the current X-ray telescopes (Chandra and XMM-Newton) ATHENA will be ten to a hundred times more sensitive. The field of view, and thus the part of space that is observed each time, will also be many times greater. That will make it possible for the first time to unravel the genesis of large-scale gaseous structures and chart the formation of supermassive black holes far back in time.

ATHENA is scheduled to be launched in 2028. In addition to an innovative telescope 12 meters long consisting of 100,000 mirror plates, ATHENA has two extremely sensitive X-ray cameras on board to record the observations. One of these cameras has to be cooled to 0.05 degrees above the absolute zero point (-273° C) in order to reach the desired sensitivity. ATHENA is the only planned major X-ray telescope in outer space in the second half of the twenties and is therefore a substantial addition to facilities such as SKA (*page 59*) and E-ELT (*page 31*), which are observing other parts of the electromagnetic spectrum.



Since the very first Dutch satellite (the ANS, launched in 1974) the Netherlands has built up extensive experience with X-ray telescopes. That has been acknowledged abroad as well. Indeed, Dutch researchers and companies are playing a key role in the design and construction of the telescope and one of the X-ray cameras. This knowledge is also relevant for other applications, for example in non-destructive research on materials.

ATHENA is a project of the European Space Agency (ESA), in which a leading role has been assigned to NWO institute SRON, with contributions of Leiden University, Radboud University Nijmegen, the University of Groningen, the University of Amsterdam, the technical universities and a number of Dutch companies.

CESAR

Shining new light on Dutch cloudscapes

Measuring and modelling Dutch cloudscapes generates more insight into the origins of clouds and rain and a better understanding of weather, climate and air quality.

The 213-metre-high mast for meteorological measurements is the most striking part of CESAR (Cabauw Experimental Site for Atmospheric Research). A broad range of advanced instruments measure wind, clouds, radiation, greenhouse gases and aerosols there. These and many other phenomena affect weather, climate and air quality. Models are developed, improved and validated based on the measurements. These models are used to analyse and predict extreme weather events and air pollution and to develop climate scenarios. The observations in Cabauw serve as a reference point for present and future satellite instruments for application in climate, weather and air quality.

Researchers already use the existing instruments to create a detailed one-dimensional, vertical profile of the atmosphere. For the next step in predicting future atmospheric conditions more accurately, there is a need for three dimensional observations and smaller scale modelling – to predict atmospheric conditions and the distribution of aerosols and gases that are present in the atmosphere in small quantities (trace gases).

More specifically, the new instruments are suitable for studying and modelling the chain of processes that lead to precipitate formation. How do trace gases create cloud condensation nuclei, moisture, turbulence, clouds and ultimately precipitation? Predictions made by these and other models can also be immediately compared with the actual observations. This improves the quality of the models and can – conversely – also test how representative the observations are.

The research results are important for policy and decision-making about water management, among other things. Data about ultra-fine and organic aerosols are important for public health. Predictions about wind speed and sunlight make it possible to more accurately anticipate supply of energy from sources of renewable energy.



CESAR is a partnership consisting of KNMI, TU-Delft, ECN, RIVM, TNO and Utrecht University and Wageningen University, as well as ESA-ESTEC. It is a hub in the European network infrastructure (ESFRI) for aerosols, clouds and trace gases (ACTRIS), and is part of the European (ESFRI) infrastructure for research on greenhouse gases (ICOS-ERIC).



DUBBLE

Radiation from particle accelerator films atoms in action

Highly intense beams of X-rays, produced by the particle accelerator (synchrotron) in Grenoble, are being used for both materials research and the physical and chemical research of matter. Researchers can also use the X-ray beams to monitor chemical and biological processes up to the atomic level.

At the European particle accelerator ESRF (European Synchrotron Radiation Facility), electrons are accelerated to almost the speed of light and injected into an electron storage ring. This rings acts as an especially intense X-ray source. Two of the 43 experimental stations (*beamlines*) where the light is used act as the *de facto* national facility for Dutch and Belgian researchers (Dutch Belgian Beamlines at ESRF, DUBBLE). They use these beamlines for a broad range of research.

The first beamline is suitable for X-ray scattering. Among other things, it is used to monitor the processing of synthetic materials, food and ceramic materials through time. This beamline is also suitable for analysing layers of paint in paintings, for example. Biomedical uses include analysing skin texture and changes that occur to it as a result of skin diseases such as eczema and characterising self-assembly processes such as cell wall formation. This generates leads for the development of tissue-engineered skin and new medicines, respectively.

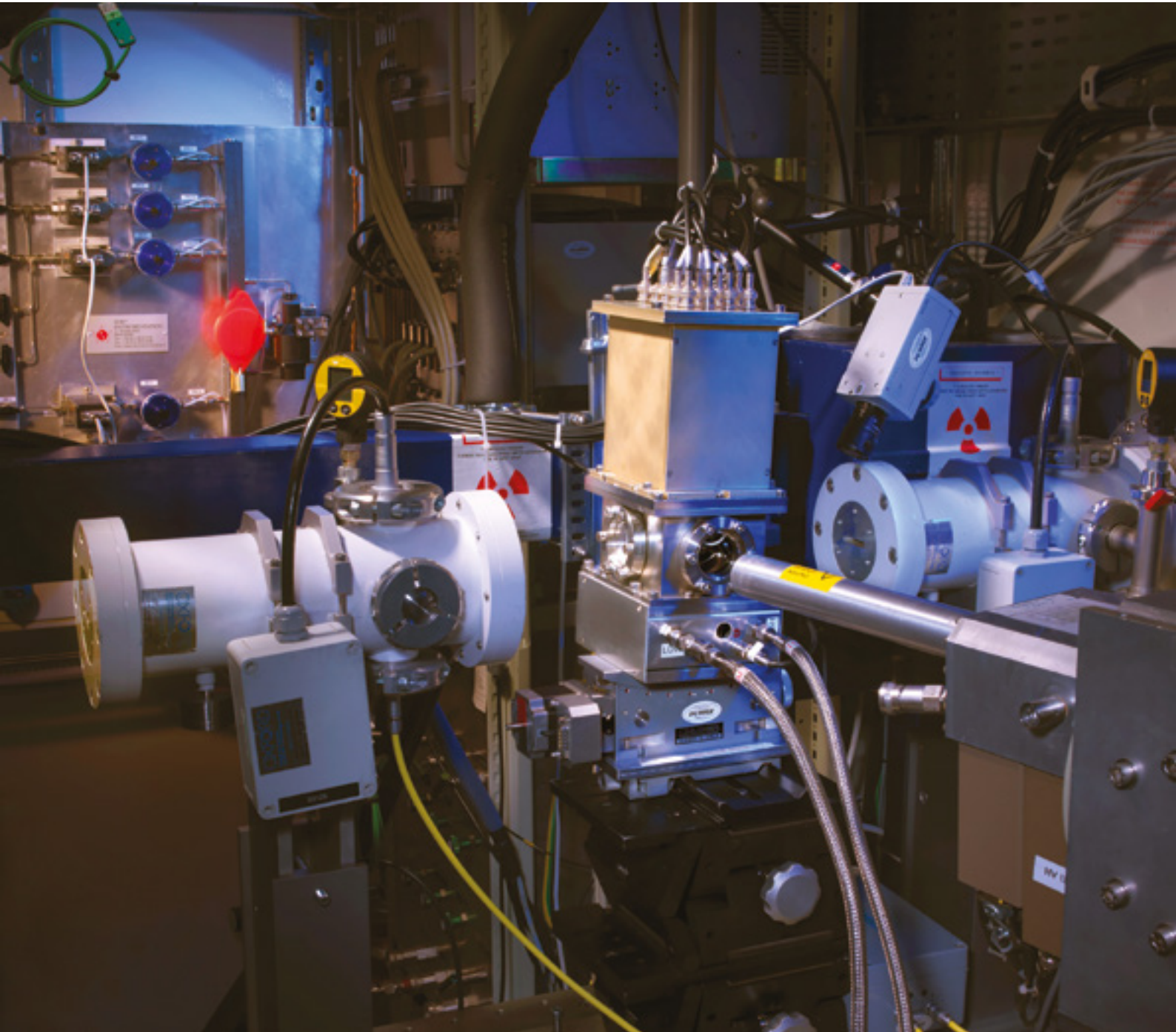


The second beamline is suitable for X-ray spectroscopy and is used to analyse catalytic processes, such as the conversion of lignocellulose (lignin) in chemical raw materials. Researchers can also use this beamline to replicate photosynthesis to convert CO_2 into fuel. Another possibility is analysing important biochemical cycles of carbon, nitrogen and phosphorus, for example.

The ESRF synchrotron will be upgraded during the period leading up to 2022. This will be an opportunity to further improve both beamlines. For example, the size of the X-ray beams can be reduced considerably. This will make it possible to conduct more biological experiments. Researchers can also monitor processes in a lithium-ion battery in greater detail and in a time-dependent setting. In addition, a third experimental facility can be opened for the creation of X-ray images to complement cryo-electron microscopy.

The examples mentioned above are only a few of the many kinds of experiments that can be carried out on the DUBBLE beamlines.

DUBBLE is part of ESRF and is financed by the Dutch and Flemish governments. Dutch and Flemish researchers use the facility 70% of the time. Currently the available time is oversubscribed by one and a half to two times. The available time for third parties (30%) is oversubscribed by four to six times.





E-ELT

Extreme astrophysics

The *European Extremely Large Telescope* (E-ELT) provides extreme sensitivity in the visible and infrared wavelength range due to its large diameter (39 metres). This optical telescope will broaden researchers' understanding of the formation and evolution of the universe as a whole, of galaxies and of individual stars and planets. E-ELT will also provide an impetus to the search for extraterrestrial life and the unravelling of the mystery of dark matter and dark energy.

E-ELT will generate new insights in many areas of astronomy: from our own solar system to the first stars and galaxies that were formed more than 13 billion years ago. Moreover, the telescope will enable astronomers to observe Earth-like exoplanets and measure the composition of their atmospheres in search of phenomena that suggest the presence of life.



The telescope will also be used to measure the accelerating expansion of the universe and the search for the potential variation of physical constants in time. If researchers can unambiguously demonstrate that these constants vary, this will have a huge impact on our understanding of the laws of nature.

The Netherlands Research School for Astronomy (NOVA) is leading a consortium of institutes from six countries that will build one of the first instruments for E-ELT: METIS (*Mid-infrared E-ELT Imager and Spectrometer*), a camera and spectrometer for mid-infrared wavelengths. The camera will be optimised for studying far-removed galaxies, the formation of stars and exoplanets, subjects in which astronomers in the Netherlands have built a proven track record.

Late 2014, ESO (*European Southern Observatory*) decided to build the E-ELT. Delivery is scheduled for 2024. The telescope will be situated in northern Chili. In collaboration with the industry, a new technology will also be developed in the Netherlands to use the telescope to extend frontiers.

ESO (www.ESO.org) is an organisation comprising 16 countries, that focuses on the construction and operation of groundbased telescopes. Dutch participants in the E-ELT and METIS are: NOVA, ASTRON, SRON, the Delft University of Technology, the University of Twente and the following companies: Airborne Composites, Janssen Precision Engineering and Airbus Defence and Space NL. TNO and VDL-ETG are conducting studies on the systems that carry and transform the segments of the main mirror to correct vibrations in the atmosphere.

This facility is part of the ESFRI facility European Extremely Large Telescope (E-ELT).

Cluster: EPOS-NL

Modelling the subsurface

EPOS-NL is the Dutch contribution to the *European Plate Observatory System* (EPOS), the European infrastructure for research in the solid Earth sciences. EPOS-NL provides facilities for research that serve the societal needs for the supply of natural resources and for protection against natural disasters. The EPOS-NL facilities will be used to study the safe use of the Dutch subsurface, addressing natural and human-induced earthquakes, sea level change, geothermal energy, subsurface storage of energy and waste products, as well as the future construction of subsurface infrastructure.

Traditionally, the deep subsurface has been used for the extraction of minerals and fuels, such as oil and gas. Industry is finding it increasingly difficult to locate extractable resources, whereas there is a rising global demand for raw materials and energy. At the same time, extraction is sometimes associated with unwanted changes in the subsurface, which can result in subsidence and earthquakes. The subsidence and induced earthquakes in Groningen as a result of the extraction of natural gas are a distressing example of such effects.

To improve extraction and prevent to the greatest possible extent any potential damage, also by natural causes, we need to obtain more knowledge about the processes taking place in the subsurface. In particular, we need to find out how georesources were formed, learn where they are located and determine how they can be safely extracted and used. This knowledge is needed not only for the extraction of raw materials and fuels, but also for the storage of energy and waste products, such as CO_2 and nuclear waste.

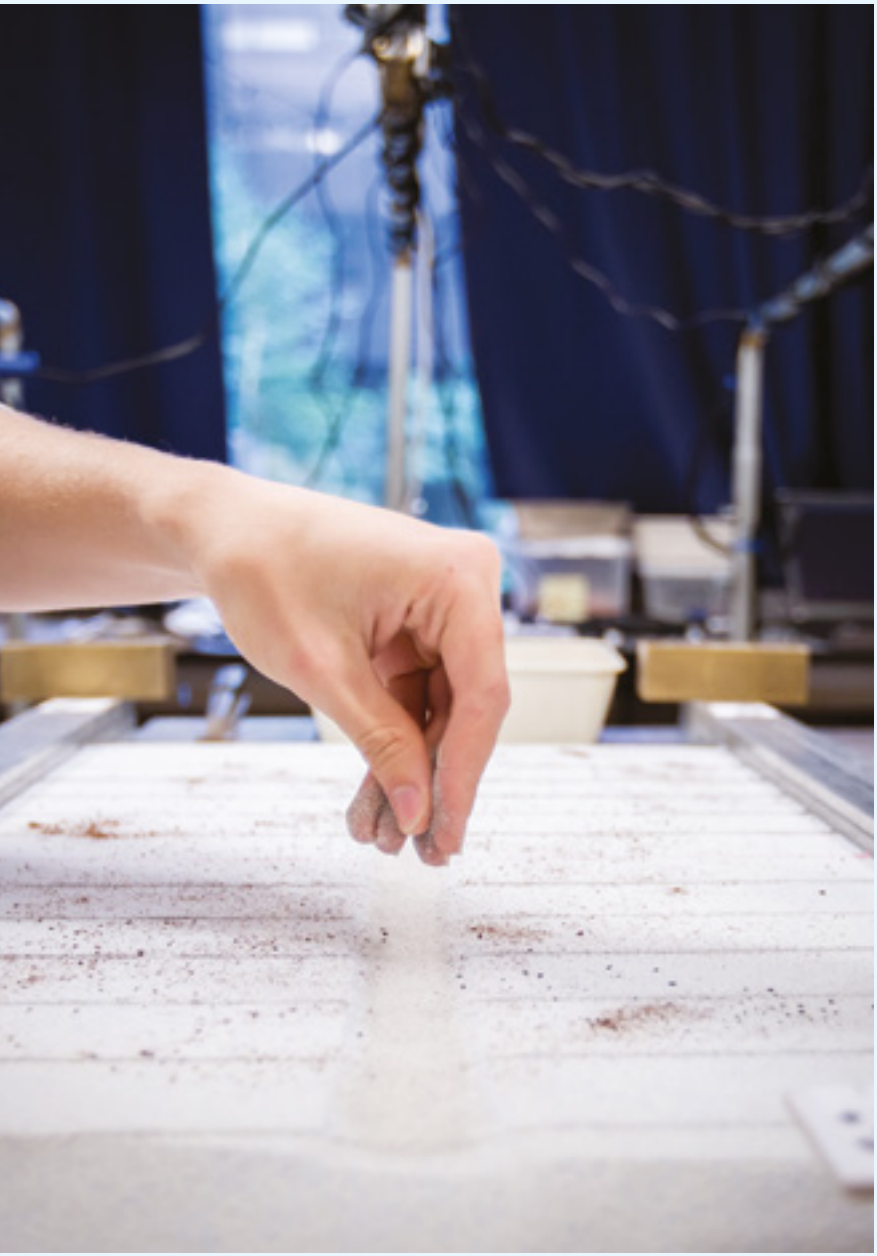


In addition to the 'traditional' fuels from the deep subsurface, there is also increasing interest in the use of geothermal energy. Modern drilling technology has made it possible to use the Earth's internal heat as energy in the Netherlands. This innovation is happening already: many greenhouses are heated by hot water originating from a depth of two kilometres and after the heat is produced the water is pumped back into the subsurface.

Geothermal energy has great potential. In addition to heating up greenhouses, it can also be used to heat houses and buildings. Together that represents more than half of the energy consumption in our regions. The development of this sustainable source of energy is stagnating, however, due to a lack of knowledge about the structure and properties of reservoir rock and the potential effects of pumping large amounts of water up from and back into the deep subsurface.

More knowledge and insight about the processes in the subsurface requires research facilities that use field observations and experimental results to develop models to simulate these processes. Researchers and companies can use these models to search in a more targeted way for





extractable reserves of ore, fuels and geothermal energy and identify the potential effects of extraction, both above and below ground. Modelling processes in the subsurface can also generate more insight into the origins of earthquakes caused either naturally or by human activity.

In order to make that research possible, a number of existing and new facilities are going to be integrated into EPOS-NL. The ORFEUS Data Centre, administered by KNMI, plays a key role in collecting and processing seismic data. It primarily concerns data from areas susceptible to earthquakes in Europe and the Mediterranean region, but also data on the induced earthquakes in Groningen.

Utrecht University's Earth Simulation Lab will have at its disposal a number of unique facilities for rock mechanics research, building reservoir models and analysing rock samples. The results of these observations and experiments can be processed in an advanced computing facility for modelling physical phenomena.

DAPWELL, finally, is a geothermal doublet, a complete installation for the actual extraction of geothermal energy in the Delft region. Hot water is brought to the surface through one pipe from a depth of 2,000 to 2,500 metres. After the heat has been produced, the water is pumped back down through another pipe. In addition to research the installation is being used to heat up part of TU Delft's buildings.

The integration of the research results will lead, as mentioned, to better models of the subsurface and thus also to more accurate predictions about the existence and productivity of reserves of minerals, fuels and geothermal energy and the potential risks associated with their extraction. They



also provide insight into the possibilities and limitations of underground construction and the underground storage of energy and waste products. The scientific challenge is to explain the structure and evolution of the complex systems in the subsurface and predict their behaviour.

The EPOS-NL facility is part of the ESFRI facility European Plate Observing System (EPOS). It is a partnership between Utrecht University, the Delft University of Technology (TU Delft) and the KNMI. The main facilities consist of the ORFEUS Data Centre for earthquakes, the Earth Simulation Lab at UU, as well as the DAPWELL installation for the extraction of geothermal energy at TU Delft.

ESS

Neutron radiation reveals the structure of living and non-living matter

***European Spallation Source* (ESS) produces neutron radiation that enables researchers to study structures and processes up to the nano-scale in biology, chemistry, materials science and art history.**

In addition to photons and electrons, neutrons can also shed more light on the structure and function of living and non-living matter. To achieve this, a source is needed that produces extremely intense neutron radiation at the desired pulse length–time duration. The strength of the neutron radiation produced by ESS will surpass all existing sources. As a result, researchers can study materials and systems at an even smaller scale and in real-world settings. That is not only important for science but also for the business sector and for finding answers to major social challenges.

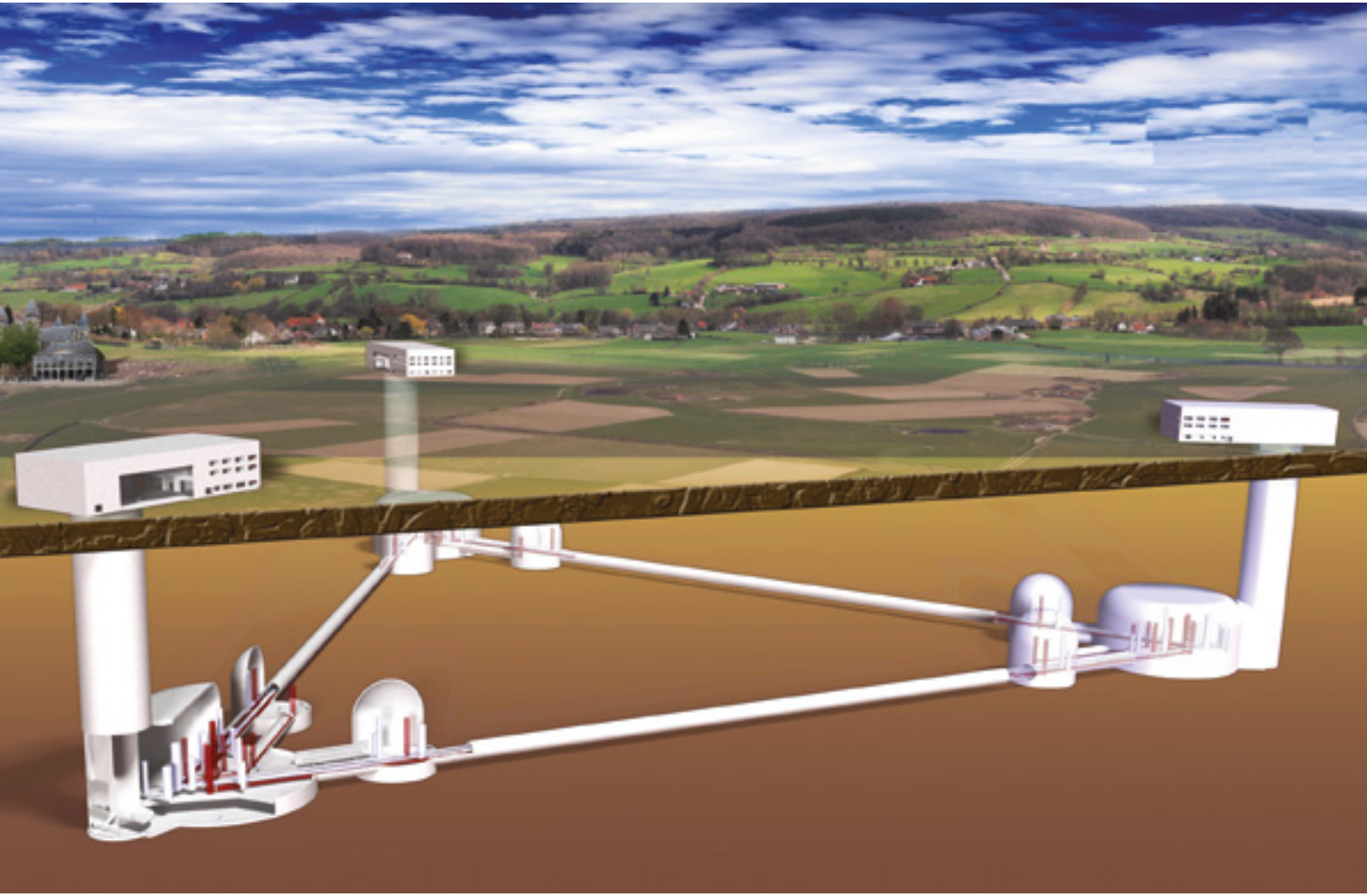
Neutron radiation, for example, plays an important role in research on proteins that are involved in the natural defences of plants against disease and plagues. Moreover, it sheds light on the molecular mechanisms that catalysts use to perform their work in the chemical industry. Neutron radiation is also important for the development of new nanostructured materials for data storage and – in an entirely different area – the storage of hydrogen or the development of new (flexible) plastic solar cells. Neutrons can make matter temporarily artificially radioactive. This enables researchers to examine the elemental composition of paint on old paintings, for example, or determine the origin of archaeological objects.

The ESS will be situated in Lund (Sweden) and will be fully operational in 2026. The affiliated centre for data management and software will be in Copenhagen. In addition to the source of neutron radiation there will be 22 instruments for using the radiation for research purposes that are as diverse as science itself. Until now, 16 of the 22 instruments have been selected in an open procedure, which are now being designed and built. The University of Groningen and the Delft University of Technology are actively involved in the development of two instruments and are establishing ESS's lines of research. At this point, the Netherlands still has the status of observer.



ESS is a European Research Infrastructure Consortium (ERIC) and part of the ESFRI facility European Spallation Source (ESS). TU Delft and NWO represents the Netherlands in the ESS Council. Other Dutch participants include the Eindhoven University of Technology, the University of Groningen and Wageningen University and Research.





ET

'Listening' to the universe

***Einstein Telescope* (ET) is the European initiative for a third-generation, underground gravitational wave observatory, designed to detect gravitational waves from space. South Limburg is a potential candidate for establishing this European facility.**

Gravitational waves are small ripples in spacetime. Albert Einstein already predicted their existence in 1916. A hundred years later they were actually detected by the LIGO detector in the US. This discovery gave rise to an entirely new field of research in which astrophysics, cosmology and fundamental physics converge.

For centuries, human beings have studied the universe by examining electromagnetic radiation such as light. But not every cosmic object emits radiation, and not all radiation reaches our detectors, because it could be blocked by cosmic dust, for example. Gravitational waves, however, fly through the universe unimpeded. The ET will therefore be able to detect signals from the farthest reaches of outer space.

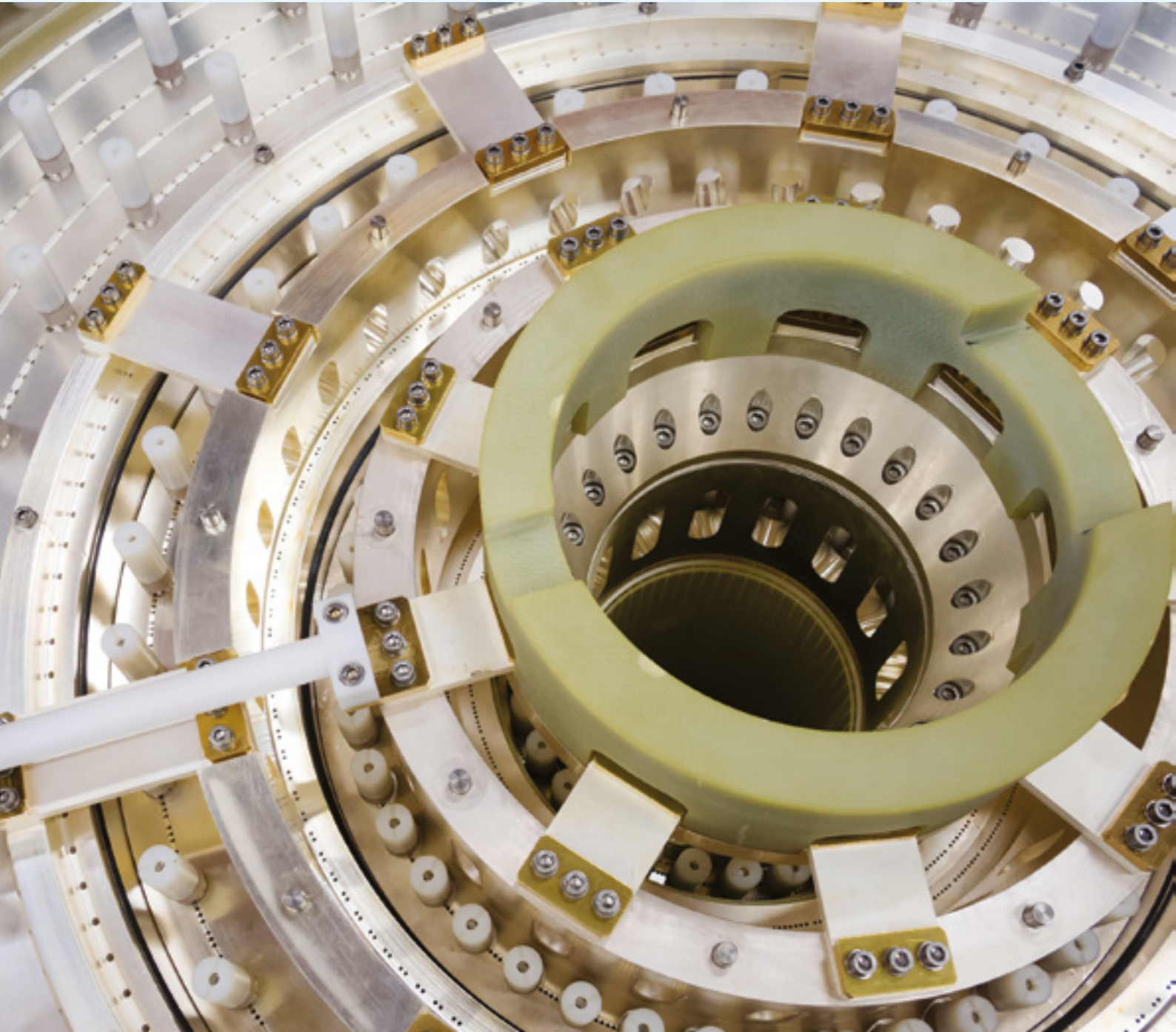
Gravitational waves betray their presence by the minute distortion of the two kilometre-long arms of a gravitational wave detector, which consequently take on different lengths. In order to measure these differences in length (10^{-19} m, smaller than the diameter of the nucleus of an atom), researchers use rebounding beams of laser light. The ET will have six of these interferometers, each 10 kilometres long. The ET will therefore be far more sensitive than the current generation of detectors, capable of increasing the number of observations by a factor of approximately 1,000. In order to prevent interference from disruptive external vibrations as much as possible, the telescope is going to be built about 200 metres underground.



The ET's great measuring accuracy and vibration frequency range will make it possible to study the most powerful phenomena in outer space. The ET will also provide observational data in the area of quantum gravity, which is where Einstein's general theory of relativity meets quantum physics. The ET will therefore steer us towards the correct theory of gravity.

The preliminary design of the ET has already been completed; the 'programme of requirements' is under preparation. In phase 1 research will be conducted on the optimal location (definitive choice is expected around 2020), the schedule and the funding, after which the telescope will be built in phase 2.

The ET is an initiative of ten European institutes, with Nikhef as the Netherlands' participating party. The research team currently consists of more than 220 researchers from 57 research institutes.



Cluster: HFML-FELIX

Research under extreme conditions

The combination of extremely intense infrared laser light and extremely high magnetic fields generates surprising discoveries. That explains the draw of the *High Field Magnet Laboratory* (HMFL) and the FELIX Laboratory cluster – both situated in Nijmegen – on researchers from around the world.

Frequently, researchers discover new phenomena by examining material properties under extreme conditions. An example of a phenomenon that would not even have been discovered were it not for a strong magnetic field is the quantum Hall effect. This effect is an important test of the mobility of electrons in a two-dimensional system and therefore of great importance in the development of semiconductors. High magnetic fields make it possible to influence superconducting material properties and unravel the underlying secrets of superconductivity.

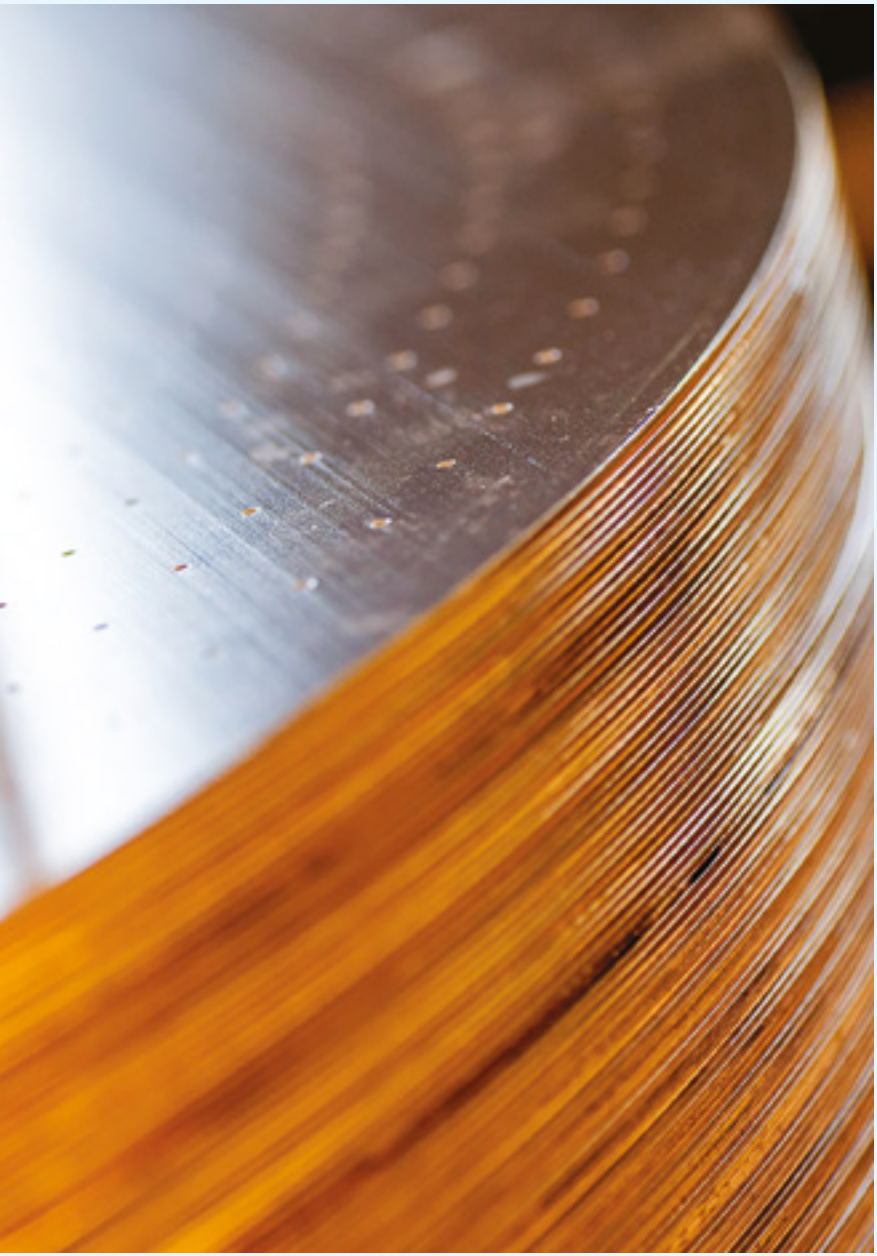
Under extremely intense infrared laser light, biological and non-biological materials reveal secrets about their electronic properties and the dynamics of their three-dimensional structure. An example of the latter is the constant folding and unfolding of protein in the human body. Sometimes it goes wrong and the protein misfolds. That can lead to brain diseases such as Parkinson's and Alzheimer's.



The HFML-FELIX cluster combines the extreme conditions of both facilities into an infrastructure for groundbreaking research in different areas of science. The use of the highest continuous magnetic fields and the largest tuning range in the infrared and THz regime makes it possible to study and manage various physical and chemical properties and processes. This appeal will only last, however, if there is continuous investment to improve the infrastructure.

HFML provides researchers with opportunities to experiment with extremely high magnetic fields up to 38 tesla. In addition, a hybrid magnet is being built that combines a copper coil with a superconducting coil housing. The hybrid magnet can generate a field strength of 45 tesla and is therefore one of the two strongest permanent magnets in the world. The magnet is expected to be available for researchers in 2018.

The FELIX Laboratory has four free-electron lasers that produce extremely intense radiation in the infrared and THz, which are tunable to a wavelength of between 3 and 1,500 micrometres. These wavelengths correspond to the frequencies with which atoms oscillate in a molecule. Studying these oscillations generates a great deal of



previously unknown data about the structure, properties and dynamics of the (bio)material in question.

Combining tunable intense infrared radiation with a very high continuous magnetic field is still a largely untapped area of research. The initial results are highly promising, however, and suggest that this combination of extreme conditions will yield many more discoveries.

One example is research on the structure and properties of graphene, for which Andre Geim and Konstantin Novoselov received the Nobel Prize in 2010. They developed a new area of research, namely that of the so-called 'two-dimensional materials'. Polycyclic aromatic hydrocarbons (PAHs), for example, turn out to have graphene-like properties. On the one hand, that makes them interesting for the development of organic semiconductors. And on the other hand, astrophysicists are also interested because they suspect that much of the interstellar carbon is stored in these molecules.

Another example are nanocapsules that can vary from a sphere or a rod to a disc or a bowl, depending on the composition of the solvent. Magnets help not only to determine their exact shape, but also to alter it, making such nanocapsules a potential way of accurately transporting medicines around the body.

The use of free-electron lasers and high magnetic fields with other analytical methods is also opening up prospects for the discovery of biomarkers, chemical or biological parameters that reveal the course of a disease or the effect of a treatment. There are also applications in the area of superconducting materials at high temperatures and in the field of 'spintronics', the use of



electron 'spins' for fast processes and memory applications that use much less energy.

The chance of (unexpected) discoveries sets HFML-FELIX apart in the global research landscape. At the same time, the need to continuously improve is an impetus for technological innovation. Together with industry, the scientific community is constantly seeking and extending the physical boundaries of conductive materials and high-power electronics.

HFML-FELIX is a partnership between Radboud University Nijmegen and FOM/NWO. Both laboratories are embedded in the European research landscape. HFML is a founding member of the ESFRI facility 'European Magnetic Field Laboratory' (EMFL), the European consortium of high magnetic field facilities. The EMFL was awarded Landmark Status by the European Strategy Forum for Research Infrastructures (ESFRI) in 2016. FELIX is a partner in FELs of Europe and LaserLab Europe, European consortia of synchrotron, free-electron laser and laser laboratories.



ICOS-NL

Data for the cash book for greenhouse gas housekeeping

With unprecedented precision, *Integrated Carbon Observation System* (ICOS-NL) is constantly monitoring the exchange of greenhouse gases between land, sea and the atmosphere.

It is common knowledge that greenhouse gases such as carbon dioxide, methane and nitrous oxide contribute to climate change. How great this contribution is and which sources are responsible for it is less well known, however. Greenhouse gases, both natural and anthropogenic in origin, are constantly emitted and then absorbed again by vegetation, coastal waters and oceans. Accurate data about these 'fluxes' are important because they provide researchers from all kinds of disciplines with more insight into the interactions between climate change, ecosystems and human activity.

Moreover, measurements at different levels of scale – city, region, country and continent – reduce the uncertainty about present and future concentrations of greenhouse gases. The measurements therefore make more accurate climate predications possible. Measurements at the local and regional levels are important to determine which activities – energy, traffic, agriculture, industry – contribute to greenhouse gas housekeeping and to what extent. The scientific significance aside, it is also important for decision-making on measures to reduce greenhouse gas emissions or improve their storage. Moreover, the measurements can be used to verify reported data on emissions.



ICOS-NL is a network of four longstanding measuring stations. In the meantime, it is part of the European network ICOS-RI, which has over ninety observatories in eleven participating countries. A carbon data portal ensures that observations are more accessible for researchers and policymakers. The industry is using the observatories as a beta test site for its new equipment.

The four stations in the Netherlands are class 2 stations, which means that they measure carbon dioxide and methane in a relatively clean environment. Dutch greenhouse gas housekeeping, however, is extremely complex because of a high population density and a great number of activities in a small surface area. In the near future the observatories will have to be upgraded to class 1, so that they can monitor more greenhouse gases in more detail. Moreover, the network will need to be expanded with a permanent offshore measuring station.

ICOS-NL is a consortium consisting of VU University Amsterdam, the University of Groningen, Utrecht University, Wageningen University and Research, as well as ECN, KNMI, SRON, TNO and NIOZ.

This facility is part of the ESFRI facility Integrated Carbon Observation System (ICOS).

KM3NeT

A neutrino telescope in the Mediterranean Sea

Studying neutrinos provides us with the opportunity to learn more about the nature of these 'ghost particles'. It also yields information about events taking place in the far corners of the universe.

Neutrinos are elementary particles. They are renowned for being difficult to detect. Yet the intrinsic properties of these particles appear to have played a decisive role in the creation of the first atomic nuclei in the early universe. It is even suspected that neutrinos are responsible for the huge volume of matter in the universe in proportion to the amount of antimatter. Neutrinos can also reveal to us what the origin is from cosmic rays (cosmic rays are atomic nuclei that continuously bombard the earth from space). They can therefore shed new light on the universe and its evolution, providing we can build the appropriate instrument.

To study neutrinos from outer space you need an enormous detector. A neutrino colliding in the detection medium would produce a small flash of Cherenkov light. This light then needs to be measured by a 3D network of sensors. The water of the Mediterranean Sea is the ideal detection medium.

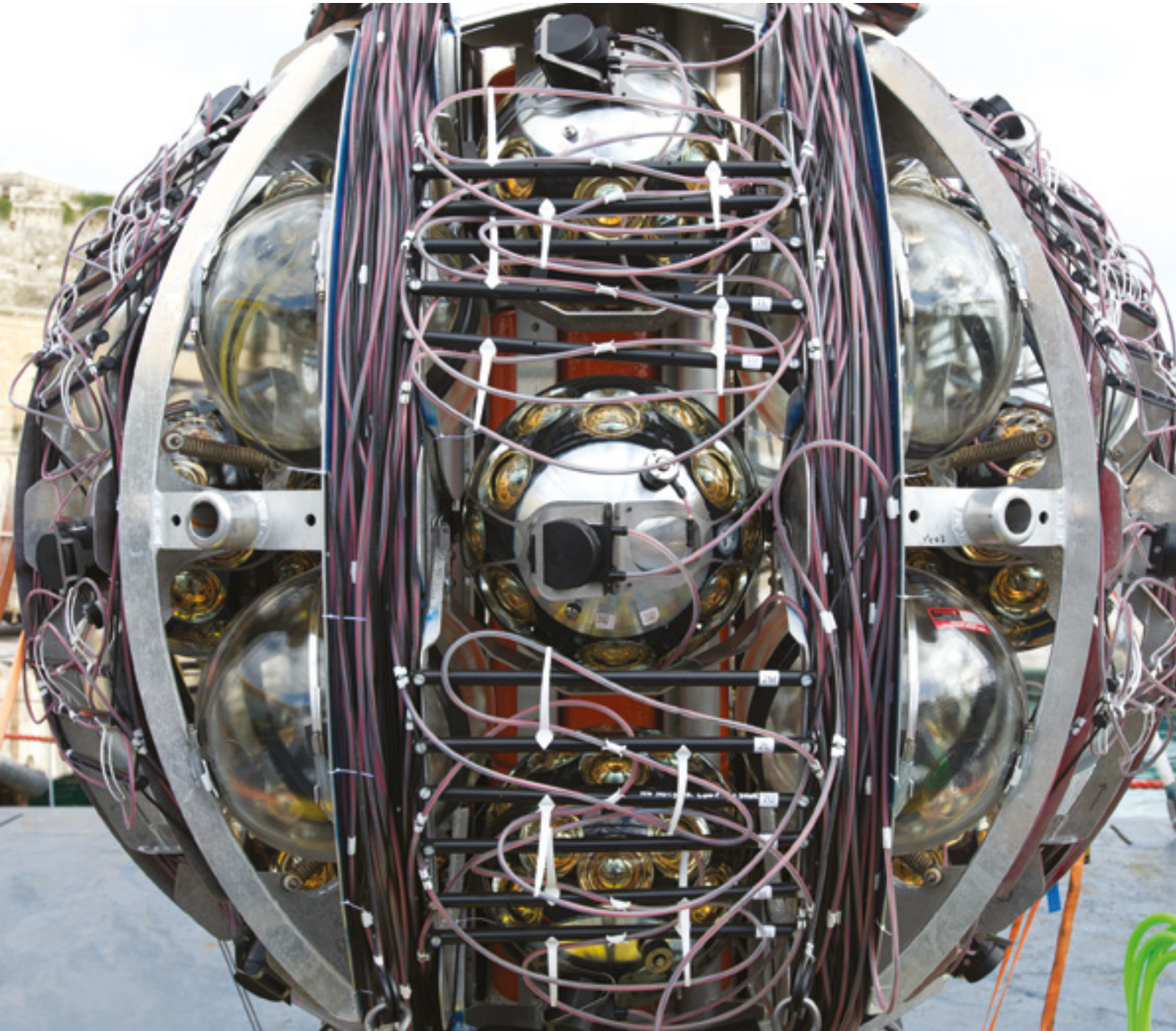


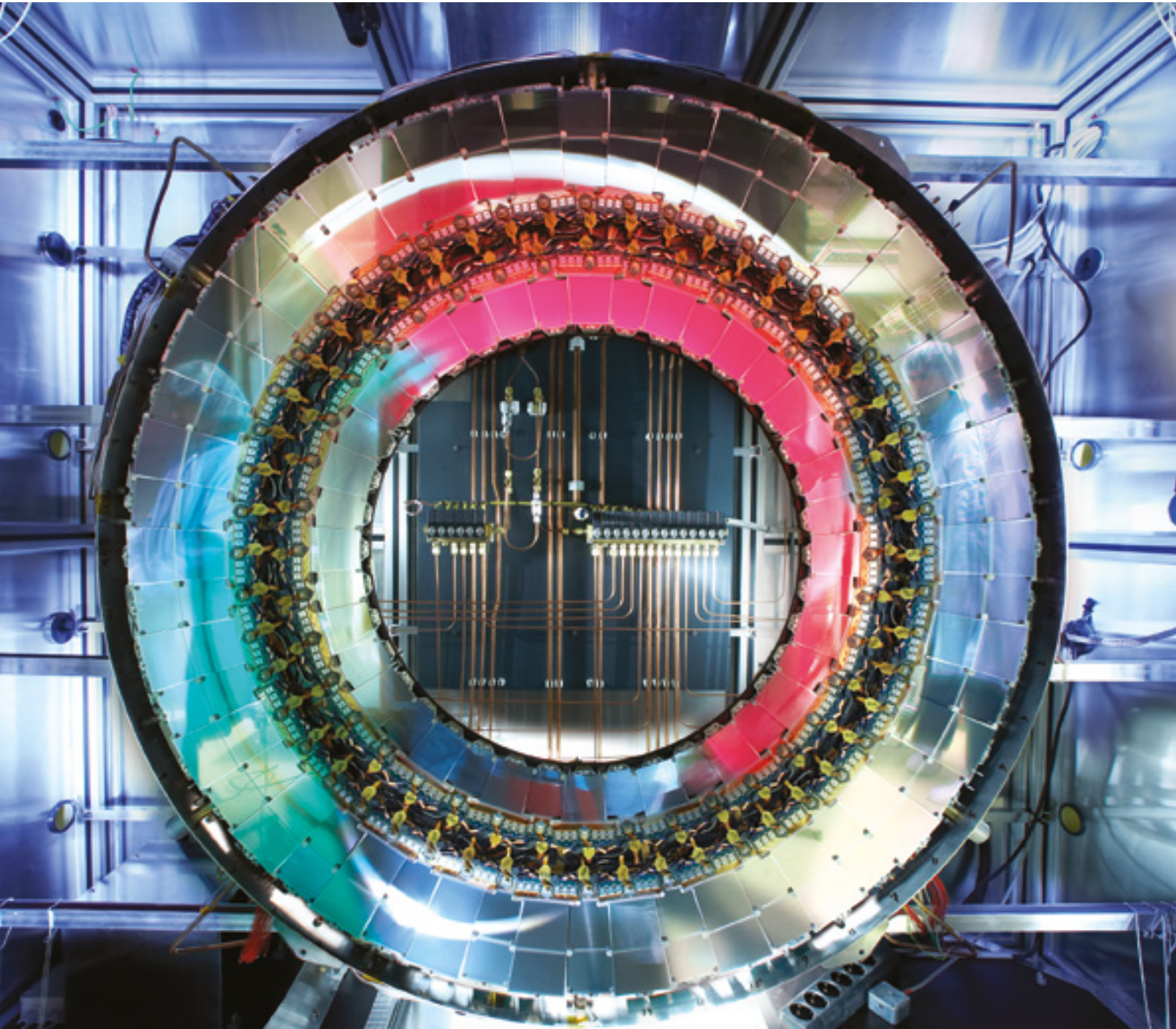
Part of KM3NeT will be placed 100 kilometres off the coast of Sicily (Italy), while another part will be 40 kilometres off the coast near Toulon (France). KM3NeT consists of detector lines with 18 modules. Each module consists of 31 light sensors. The lines are anchored to the sea floor. Thanks to the modules' ability to float, the light sensors stay in place, so that the weak Cherenkov light can be efficiently measured.

Energy and data networks were installed in the deep sea and the first optical modules were built and immersed in 2015. KM3NeT should be fully operational by about 2020. Researchers can use KM3NeT to discover where the particle accelerators are in the universe. They can discover how these particles accelerators produce cosmic rays. Ultimately, this will make it possible to access particles with energies that cannot be generated on earth. It will also enable us to penetrate the intrinsic properties of neutrinos.

KM3NeT is a European consortium, to which more than forty institutes from Europe and beyond are affiliated. The Dutch participants are: Nikhef, NIOZ, TNO and the University of Amsterdam, the University of Groningen and Leiden University. The headquarters will be in the Netherlands.

This facility is part of the ESFRI-facility KM3NeT.





LHC-detector upgrades

In search of the basic building blocks of matter and energy

Protons collide with each other at almost the speed of light in the *Large Hadron Collider* (LHC), CERN's underground particle accelerator. An analysis of the resulting 'fragments' provides insight into the basic building blocks of matter and energy.

The LHC is the most powerful particle accelerator in the world. It enabled physicists to discover the Higgs boson in 2012, after years of searching. This particle is the carrier of the Higgs field, which gives other particles their mass. This discovery confirms the accuracy of the so-called standard model of particle physics, but it also raises new fundamental questions about the building blocks of our universe.

After a planned shutdown, the LHC started taking measurements in July 2015 again to study the Higgs boson in more detail. A minute deviation of the predicted properties of the Higgs boson would imply a new physics that extends beyond the standard model. The scientists are also searching for new, as yet unknown particles that are being predicted by the theory of supersymmetry, for example. That theory was developed to answer fundamental questions about the standard model by capturing different kinds of particles and fields in a single theoretical framework. These 'superpartners' have not been detected yet, however.



The LCH could potentially also provide an explanation for the true nature of dark matter, one of the most exciting quests of our time.

LHC's current measurement period will run until 2018. After this period a number of parts in the two detectors (LHCb en ALICE) will be replaced or upgraded. The computer data infrastructure will be expanded as well. The following measurement period will run from 2020 to 2023 and will generate more than double the number of collisions. During the next shutdown the ATLAS detector will be expanded and upgraded as well so it can detect collisions with even greater beam luminosity. Indeed, researchers anticipate plans to upgrade the LHC, after which the luminosity will increase again by a factor of 10 (the High Luminosity LHC) compared to the original design.

Many hundreds of scientists are involved in the expansion and upgrading of ATLAS, ALICE and LHCb. The Dutch input takes place via the NWO institute Nikhef.

This facility is part of the ESFRI facility High Luminosity LHC (HL-LHC).



Cluster: NanoLab NL

Fabrication on the nano-scale

NanoLabNL provides researchers from universities and companies from the Netherlands and abroad access to equipment, technologies and expertise for the design and fabrication of materials, components, devices and systems on a scale of a millionth of a millimetre.

Major steps have been taken in recent years in the development and application of nanotechnology (technology on the nano-scale; 10^{-9} metres). Examples include nano-structured coatings that keep away the growth of algae and shellfish on ships, which allows them to sail more efficiently; organs on a chip that drastically reduce the need to use laboratory animals; lithographic techniques to manufacture more efficient, low-energy electronics; and a needle thinner than a hair with a tiny chip on its point, which can be used to stimulate the brains of people with Parkinson's Disease in a targeted way.

Dutch researchers realised early on what the potential of nanotechnology would be in various fields. They also managed to convince policymakers and industry of this technology's significance. This is one of the reasons why the Netherlands is a leading global player in this technology, both in terms of the number and quality of publications and the number of patents – which has resulted in a plethora of awards, distinctions and personal grants, including ERC grants and NWO Spinoza Prizes. The Dutch Nobel Prize for Andre Geim's discovery of graphene's extraordinary electronic properties can be partly attributed to nanotechnology. Thanks to excellent research, the Netherlands has also carved a prominent position for itself in two European flagship projects, namely Graphene and Quantum Technologies.



Nanotechnology is a key technology that is and will continue to play an important role in different fields. In health care the development of molecular motors is opening up prospects for the accurate administration of medicines. Another application is the miniaturisation of medical equipment, which enables it to be placed inside the human body. Think, for example, of insulin pumps and artificial kidneys.

Microreactors ('process-on-a-chip') can replace – sequentially – large-scale processes in the chemical and food industry ('factory-on-a-chip'), thereby drastically reducing the use of energy, water and raw materials. Tiny sensors and MEMS (micro-electro-mechanical systems) are already making a key contribution to the Internet of Things, in which machines are exchanging data and performing actions independently.

NanoLabNL has been playing a key role in the research, development and embedding of nanotechnology since 2004. Equipment and expertise are available at four locations (Delft, Eindhoven, Enschede

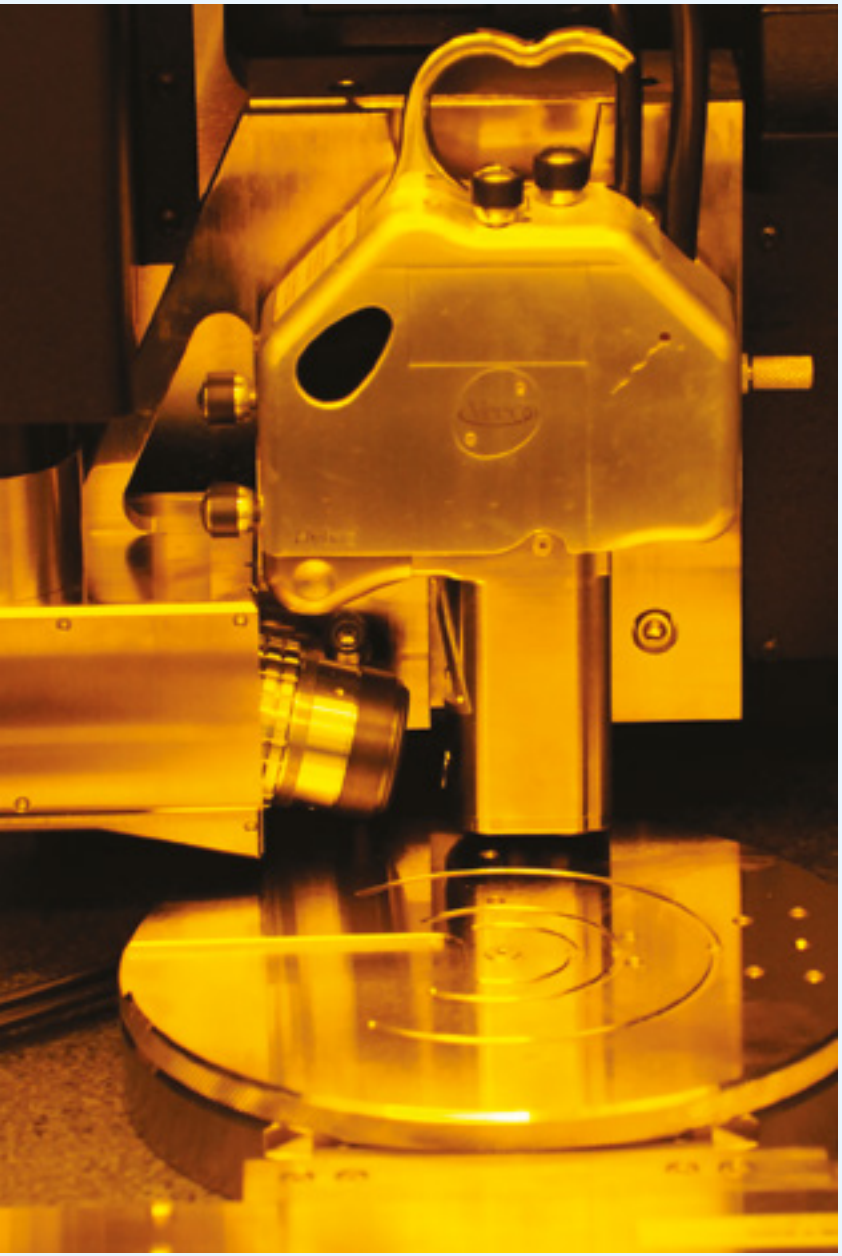


and Groningen) where microreactors, MEMS and electronic and optical components are fabricated on a nano-scale for a variety of applications. The four locations also have various facilities available for general fabrication at the nano-scale. Moreover, each facility offers unique equipment and expertise for the fabrication of quantum devices, for example, analysis of surfaces, lithography and microfluidics. This approach, in which facilities are geographically spread out and complementary, has turned out to be particularly effective.

In addition to fundamental research in the areas of photonics, electronics, new materials and quantum technology, the facilities are also being used to commercialise research by developing and testing prototypes and production of test series. Companies, including start-ups, not only have access to the equipment and expertise, but they are also part of the NanoLabNL community. Long-term cooperation has led to the emergence of an unique ecosystem for research, development and commercialisation, which is yielding a wealth of innovations.

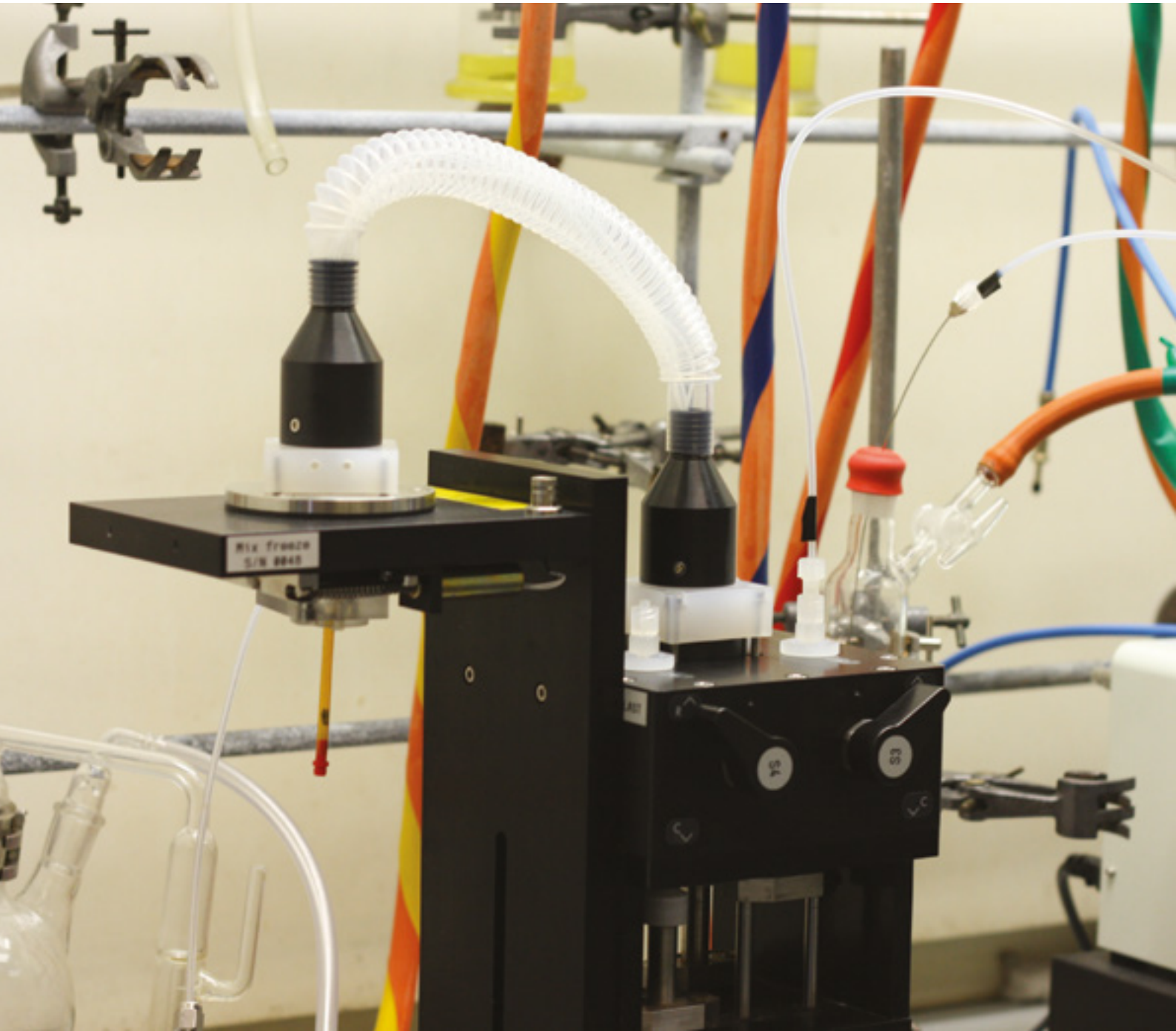
NanoLabNL also facilitates research that addresses knowledge issues that have been formulated in the Top Sectors and the Dutch National Research Agenda. Examples include nano-structured materials, regenerative medicine and the development of nanotechnology. In many cases this occurs together with civil society organisations.

NanoLabNL was also one of the partners to take the initiative to establish the EuroNanoLab consortium, which connects facilities for the research and development of key technologies in Europe with each other. Together, the parties in the consortium provide equipment and expertise based on an open access principle. Parties can also lend staff members to each other so they can exchange knowledge. The ultimate goal is an



infrastructure for nanotechnology throughout Europe, in which participants can further develop and make available their own expertise. This will enable them to expand the spectrum of possibilities and technologies for their users.

NanoLabNL is a partnership between six laboratories spread over four locations. In Delft it concerns the Kavli NanoLab and the Else Kooi Lab of the Delft University of Technology and the Van Leeuwenhoek Laboratory of TNO as an affiliated partner; in Eindhoven the NanoLab@TU/e of Eindhoven University of Technology and Philips Innovation Services as an affiliated partner; in Enschede the MESA+ NanoLab of the University of Twente; and in Groningen the Zernike NanoLab of the University of Groningen.



NC2SM

Characterising sustainable materials

Researchers at the *National Characterisation Center for Sustainable Materials* (NC2SM) are using advanced spectroscopic techniques to make detailed analyses of the structure and behaviour of materials for sustainable applications.

Chemistry plays a key role in the transition from a society based on fossil fuels to a sustainable society built on renewable raw materials and environmentally friendly materials and products. The use of sustainable sources of energy, such as sun, wind and water, also require new materials for the temporary storage of this energy. Finally, it is important to obtain insight into the ageing of materials in order to prolong the lifespan of objects – on the one hand with an eye to sustainability, and on the other hand with an eye to cultural heritage.

The transition to a more sustainable society requires new materials and new processes to convert sustainable raw materials into useful materials. Many 'fossil' industrial processes, for example, use catalysts – reaction accelerators – based on rare precious metals, such as platinum. Alternatives for that include a number of abundantly available transition metals and their compounds, such as iron, zinc and nickel. These elements are tricky to describe physically, and their chemical 'behaviour' is also difficult to predict.



The intended NC2SM national centre could make a series of techniques available for researchers. Researchers can use them to characterise materials and identify their chemical and physical properties. That will not only involve the catalysts and (in)organic materials mentioned above, but also pigments, ceramic materials and (bio)polymers, for example. The available techniques vary from the use of infrared and ultraviolet light to various forms of X-ray (new, unique lab technology). The national centre will also maintain a good relationship with Dutch Belgian Beamlines (DUBBLE, *page 28*) at the European Synchrotron Radiation Facility (ESRF) in Grenoble.

NC2SM is building on the equipment and expertise of the Van 't Hoff Institute for Molecular Science (HIMS) at the University of Amsterdam (UvA) and is supported by the University of Groningen, Utrecht University, the University of Twente, Leiden University, the Eindhoven University of Technology and the Delft University of Technology, as well as the Advanced Research Center for Nanolithography (ARCNL), the Hogeschool Zuyd and a large number of companies.

The Permanent Committee has introduced an additional condition for this facility: the facility must take on a national character, involving all possible partners. The facility has to expand its focus to include heterogeneous catalysis and materials research. Cooperation with DUBBLE at ESRF must be looked into because this facility is interrelated with the requested facility.


PELAGIA

RV Pelagia/National Marine research Facilities (NMF)

Seafaring platform for research in 'mare incognitum'

Compared to our knowledge of the land, seas and oceans are largely undiscovered areas. Dutch researchers and their (international) partners are changing that with the research vessel RV Pelagia.

Some 70% of the Earth's surface is covered with water. Physical, chemical and biological processes that take place in seas and oceans that are not only interesting in themselves, but are also extremely important for life on land. Examples include the effect of currents on the transport of sand along the coast, and the role the sea plays in the circulation of nutrients. In addition, seas and oceans have a major impact on the weather and climate by virtue of their enormous mass of water. Knowledge of these phenomena provides opportunities not only to explore the sea but also to sustainably exploit it, for example for energy, food, transport, mining and coastal protection ('Building with Nature').

The 25-year-old *Pelagia* is the Netherlands' only ocean worthy research vessel. It has a range of research facilities on board for biological sampling, chemical and physical analyses and seabed studies. Installations handle the placement and removal of anchored instruments on the seabed in depths of up to 8.5 kilometres. There is on-board space for nine containers, which can be used as laboratories, work stations or offices. In addition to on-board research opportunities of the vessel, *Pelagia* is also a passport for researchers to use the seagoing facilities of the European partners participating in the Ocean Facilities Exchange Group (OFEG).



In order to continue fulfilling its role as a platform for scientific research, the instrumentation and facilities on the *Pelagia* need to be modernised and expanded. Among other things, this involves autonomous instruments: equipment that can make measurements independently and send the recorded data to the ship. A new research vessel will be needed in the longer term (after 2020). A number of European partners, including the Netherlands, are currently developing a concept for a 'research vessel of the future'. This is a standardised design that can be used to build five to eight ships in a series.

The RV Pelagia is operated by the Royal NIOZ National Marine research Facilities (NMF). Dutch users include Utrecht University, both Amsterdam universities (UvA/VU) and the University of Groningen, the research institutes NIOZ, Nikhef, Wageningen Marine Research, TNO, and Deltares, and a series of international institutes for sea and ocean research.



SKA

Looking back at the dawn of the universe

The *Square Kilometre Array* (SKA) will be an extremely sensitive radio telescope that will enable astronomers to look back in time much further than is possible now. They thus hope to gain more insight into the fundamental laws of physics.

SKA will consist of an intercontinental network of thousands of radio telescopes and antennas. It is a kind of Swiss army knife for astronomers. To begin with, astronomers hope to use the telescope to make a 'film' of the transition from the cosmic Dark Ages (the period from 300,000 to 150 million years after the Big Bang, when the universe contained little radiation), to the period of reionisation. The universe as we know it today began to take shape during that period, about half a billion years after the Big Bang. But SKA will also be used to study gravitational waves by means of pulsars, as well as magnetic fields and their origins, dark matter, extraterrestrial intelligence (SETI) and many other phenomena.

The first phase of SKA is going to be five to eight times more sensitive than today's most sensitive radio telescope. Initially almost 200 15 meter diameter dish antennas will be placed in the South African semi-desert Karoo for mid and high frequencies. At the same time, 130,000 dipole antennas will be placed in the outback of Western Australia and will operate at low frequencies. Ultimately the radio telescope will have a total collecting area of more than one square kilometre and will be able to detect radio waves in the frequency range of 50 MHz to 30 GHz.



Once it is ready, the amount of data that SKA will generate in the space of 24 hours will be ten times greater than the amount of data transferred over the internet in the same time period today. This enormous amount of data will be processed in a number of Science Data Centres, which are connected to each other by means of a global network of fibre optic links. LOFAR, the low frequency telescope of NWO institute ASTRON in Drenthe is acting as an experimental facility for the global network of Science Data Centres.

Preparations for construction the SKA began in 2012. According to the schedule, the first construction stage will start in 2018. In South Africa 64 antennas of the MeerKAT precursor will be incorporated into SKA. The second construction stage will occur after 2025. Ultimately SKA will consist of more than 2,000 dish antennas and up to 1 million dipole antennas.

So far, SKA is a partnership between ten countries, including the Netherlands. At least another five countries have expressed an interest in joining the project. Dutch involvement includes NWO institute ASTRON and the University of Groningen, Leiden University, Radboud University Nijmegen and the University of Amsterdam.

This facility is part of the ESFRI facility Square Kilometre Array (SKA).

Cluster: Solar Cells

Getting more out of sunlight

In order to achieve the objectives of the 2015 Paris Climate Change Conference the cost of converting sunlight into electricity has to decrease fourfold in the next twenty years. Dutch knowledge institutions, largely united in *Netherlands Energy Research Alliance* (NERA), are examining different potential paths for achieving that objective.

The efficient conversion of sunlight into electricity (the photovoltaic effect) is the key to a power supply based on renewable energy. Whereas the very first solar cell by Charles Fritts in 1883 could only convert 1 per cent of the sunlight into electricity, the conversion efficiency of the current generation of solar cells is approximately 20 per cent. The biggest leap, from 10 to 20 per cent, was made in the past twenty years.

In the same period, the price of a complete system decreased by a factor of 50. As a result, the cost of generating electricity from sunlight in the Netherlands is now about 20 cents per kilowatt hour (kWh). As a result of taxes and transport costs that is less than what consumers pay for electricity. However, it is still three times more expensive than the cost price for electricity from coal.

If solar energy is really going to become competitive, then there has to be a three- to fourfold decrease in cost price per kWh. Only then will it be possible to increase the share of solar energy in our electricity supply. That share is currently approximately 1.5 per cent worldwide, which corresponds to a nameplate capacity of about 250 gigawatts. The nameplate capacity of solar energy in the Netherlands is about 1,500 megawatts. That is not even 1 per cent of the total nameplate capacity. To really make an impact, this capacity would have to increase at least several hundred times in the coming 25 years.



There are different ways of achieving that goal. At the moment, 90 per cent of the need for solar energy comes from the familiar silicon solar cells (wafer silicon). The other 10 per cent consists of thin film solar cells made of silicon, perovskite or synthetics. Both types will continue to dominate the market in the next ten to twenty years. The yield of energy will probably not increase by more than about 25 per cent during that period. That means that lowering the cost price has to come from other parts of the system, such as the electrical connections and the electronics and by reducing installation and maintenance costs.

Simultaneous to this path of gradual improvement in terms of both the energy and economic return, researchers are committed to developing new types of solar cells. One example is the hybrid solar cell, a combination of wafer silicon and thin film cells. These hybrid cells can convert a higher part of the spectrum of sunlight into electricity, thereby achieving a higher return than any one type can on its own.





Increasingly, researchers are also looking at other materials, such as gallium arsenide, or combinations of materials. The record is a conversion efficiency of almost 45 per cent by a solar cell made of alternating layers of gallium arsenide and indium phosphide. These materials are rare – and therefore expensive – and not particularly environmentally friendly either. An alternative is to use lithographic techniques, familiar in the chip industry, to install nanostructures on and in solar cells. This would enable researchers to control incoming photons, for example by sending them around a corner or concentrating them in one place – ('photon management').

Achieving these ambitions goes hand in hand with many scientific challenges. They all come down to achieving a conversion efficiency of 40 per cent with large surfaces, not only in direct sunlight but also when the light is more scattered due to cloud covers. A high conversion efficiency can probably only be achieved with new materials, which also have to be affordable and last more than 30 years. Moreover, we need more advanced technology to produce thin film solar cells, for example, and to develop new applications, such as transparent photovoltaic windows.

The Netherlands is, despite the modest share of solar energy, well positioned to make a substantial contribution to the growth of nameplate capacity. Our country has excellent public facilities to do research across the entire scope of fundamental to applied research and technological development. The results of the research are processed quickly and adequately by a large number of companies operating in the area of advanced materials, processes and equipment construction.



The Solar Cell cluster consists of the Netherlands Facility for Solar energy research, (an ECN facility) and Solliance (part of TNO). ECN is working on wafer silicon solar cells and other new concepts for solar cells together with AMOLF and the Delft University of Technology. TNO, ECN, the Holst Centre, the Delft University of Technology and the Eindhoven University of Technology are working at Solliance on thin film solar cells together with the Hasselt University (Belgium), Imec (Belgium) and Forschungszentrum Julich (Germany).


Domain
Medical/
Life Sciences



Cluster: BBMRI

Biobanking for better health

***Biobanking and Biomolecular resources Research Infrastructure* (BBMRI) makes biomaterials, images and data from (longitudinal) research retrievable, accessible and exchangeable for research on the prevention and treatment of diseases. The latter occurs on an individual basis to the greatest possible extent (personalised health & medicine).**

The Netherlands has more than 200 biobanks and cohorts that store the data of thousands of people. It concerns biomaterials, such as blood samples and tissues, images such as CT, MRI and PET scans, and data from hundreds of cohort studies. These are collected from population surveys, questionnaires, care institutions and apps and wearables (wearable sensors) that measure bodily functions such as heart beat and blood pressure. It partly concerns data from healthy people, as registered in Lifelines, a multi-year population survey among the inhabitants of the northern Netherlands. It party concerns clinical data, such as those available in laboratories for pathology, affiliated with the PALGA network, and hospitals affiliated with the Parelsnoer Institute.

The degree to which these data are accessible and exchangeable is extremely important if we are to gain insight into the factors that contribute to the cause and development of diseases and afflictions and the effect of interventions. New technological developments are making it possible to measure with unprecedented accuracy the functioning of our tissues and organs – often up to the molecular level. In addition, an increasing amount of data are available from apps and wearables, which provide insight into behaviour and lifestyle.



To be able say anything about the cause and development of diseases and afflictions, the researchers are attempting to correlate these data with each other. Why do some people with a genetic predisposition for autoimmune diseases, such as coeliac disease, diabetes and rheumatism, for example, become afflicted with these diseases while others with the same predisposition do not? Cohort studies, in which people are monitored for a longer period of time, in combination with biomaterials, images and clinical data, increase our insight into the complex interaction of genetics, nutrition, lifestyle and environmental factors. That interaction, which differs in each individual, ultimately determines whether someone becomes afflicted with disease early in life or maintains good health until old age.

The data, images and biomaterials that are registered in the more than 200 biobanks and cohorts are a good reflection of the considerable variation between (groups of) individuals in our society. Indeed, combining these sources generates an extensive and diverse wealth of data for research on personalised health & medicine. In other words, bringing together data from biobanks and cohorts makes it possible to generate new insights on biological modes of action and translate them

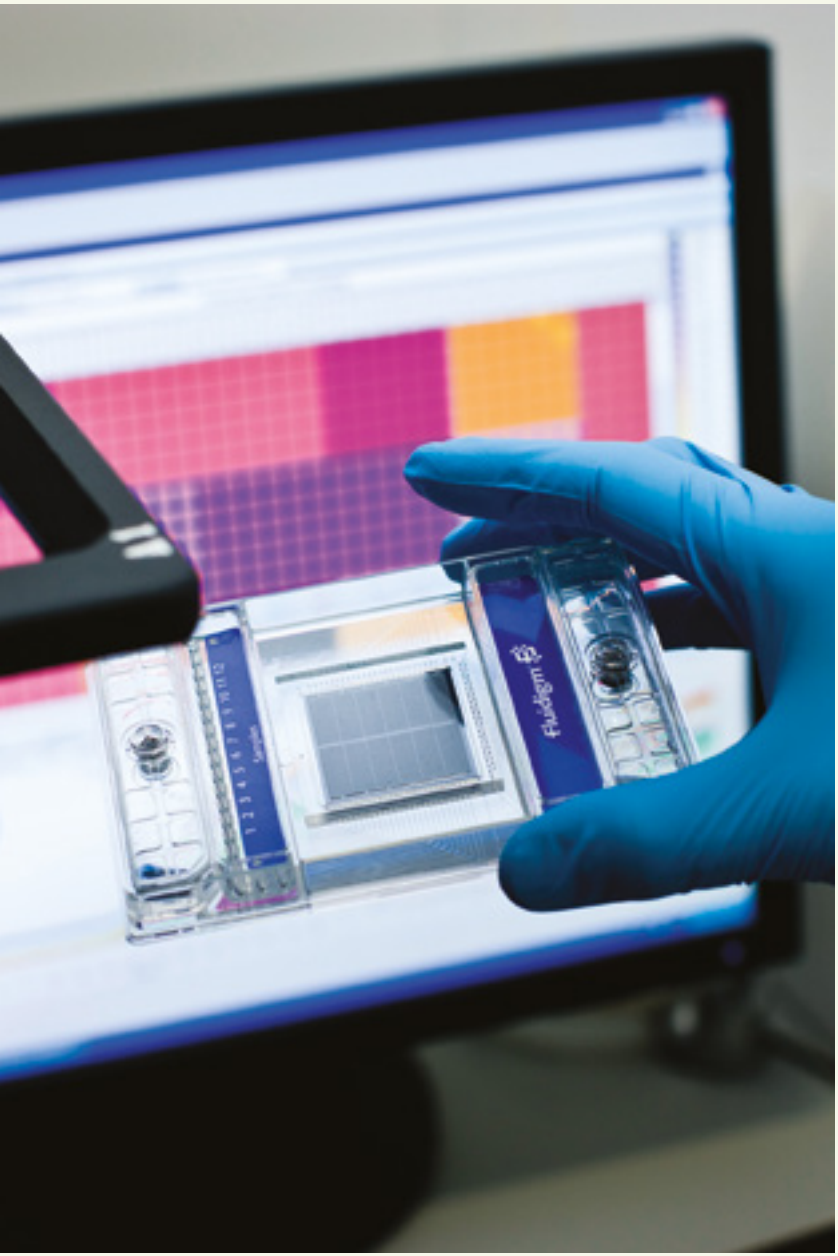


into better diagnoses and personalised interventions in order to prevent or treat diseases.

The truth is, however, that the infrastructure of biobanks is lagging behind what is technologically feasible today in the area of information and communication technology, (medical) imaging and genomics. As a result, the translation of new insights on biological modes of action into diagnosis and preventative and care interventions have been delayed. It may take ten years for this to be achieved, even though the images, biomaterials and clinical data are available. Better access and exchangeability of biomaterials, data and images would reinforce the scientific foundation of personalised health and medicine. Moreover, it would help to improve the health-care system in the coming decades and keep it affordable.

Ethical, social and legal dilemmas show that the use of body materials and associated data for research is no trivial matter. Indeed, funding agencies and scientific journals are demanding open access to databases for other researchers, while the European and Dutch authorities set strict requirements when it comes to protecting patients' privacy. For data on genetic properties there is the additional issue that while a patient may grant permission, the data may also pertain to his or her family members. These contradictory requirements mean that biobanks and cohort studies will have to make an extra effort in the coming years to make data accessible and exchangeable and simultaneously protect people's privacy.

An additional factor is that citizens, whether or not patients, are increasingly demanding to be better informed about the research that their data, images or body materials are being used for. The Netherlands Twin Register has taken the first steps with their MyBiobank project, an internet portal that



involved parties can use to add to or improve their data and assert their rights. It is extremely important that this concept is expanded to include other biobanks in order to maintain and reinforce support within society.

More than 200 biobanks and cohorts are working together in BBMRI to make their data, images and body materials accessible and exchangeable. Together with ELIXIR-NL (page 73), EATRIS-NL, DTL (Dutch Techcentre for Life Sciences), Health Holland and the Netherlands Federation of University Medical Centres (NFU) BBMRI has launched an initiative to establish a nationally standardised infrastructure for research on health and disease, HEALTH-RI.

This facility is part of the ESFRI facility 'Biobanking and BioMolecular Resources Research Infrastructure – European Research Infrastructure Consortium' (BBMRI).

BSL3

Alertness to control infectious diseases

In the *High Containment Research Facility* (HCRF) BSL3 (Biosafety Level 3), scientists can conduct research on infectious diseases with full control of any risks to themselves or the environment. The facility operates at the second-highest possible safety level. Here researchers can examine the agents causing potentially serious infectious diseases.

Recent outbreaks of bird flu and SARS have demonstrated that the threat of infectious diseases is not a thing of the past. On the contrary, as a result of international trade, tourism and climate change, humans and animals are coming into contact with novel pathogens.

In addition to personal suffering – and sometimes societal disruption – infectious diseases cause considerable economic damage. The severity, size and spread of an outbreak is largely dependent on the readiness of and collaboration between researchers, health-care professionals, health-care authorities and supra-national organizations. Safe laboratories are therefore indispensable to investigate exactly which pathogen is involved, where its origin lies and how it spreads.

In addition to research on current outbreaks and meeting the challenge of curtailing them, there is a great need for long-term research into the causes of outbreaks, the (changing) characteristics of pathogens and pathogen–host interaction. The insights provided by experimental research are important for innovative diagnostics, for the development of new or better vaccines and for the treatment of chronic infections.



The BSL3 is part of the *Erasmus Dierexperimenteel Centrum* (the Centre for Laboratory Animal Experimentation) and has extensive facilities for research with class 3 microorganisms. Agents thus classified cause serious diseases such as polio, tuberculosis, and typhoid, but can be prevented by vaccination or treated with medicines, should the need arise. The research is conducted with both culture media and various types of laboratory animals, and several studies can be carried out simultaneously.

The facility was designed to meet the latest international standards and guidelines for *biosafety* and *biosecurity* (including WHO, CWA15793) to safely manage and work with hazardous agents. The safety provisions consist of a special system for air treatment that ensures negative room pressure, airlocks and systems for disinfection and sterilisation.

BSL3 is an initiative of the Erasmus University Medical Center. For research into infectious diseases, BSL3 works at the national level with the National Institute for Public Health and the Environment (RIVM), Wageningen Bioveterinary Research, universities, medical faculties and the veterinary faculties.

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Cluster: ELIXIR-NL

Data infrastructure for the life sciences

As a national focal point in the European network ELIXIR, the Dutch node ELIXIR-NL aims to build the digital environment to make data generated by the life sciences accessible and exchangeable for analysis. The initial emphasis is on biomedical data, as part of the Health-RI initiative, but the plan is to have the infrastructure function as a broad Life Sciences Data Exchange.

Scientific research generates a wealth of data, but in many cases these data are not available to other researchers. And where scientist find each other, their dataset are often incompatible. Recent research shows that 50 to 70 per cent of the supplementary data of scientific papers cannot be retrieved three years after publication. It is even more difficult for researchers in other fields, who read other journals, because they are often not even aware that the data exists.

In order to be (re)usable and exchangeable, data must be treated according to the FAIR principles, drafted in the Netherlands and now adopted worldwide. The acronym stands for *Findable, Accessible, Interoperable and Reusable*. FAIR means that computers must be able to 'understand' these data. Metadata in particular are important so that the computer understands the nature of a dataset. Metadata provides information about the researchers that generated the data and about the equipment, materials and measuring conditions that have been used. The European Commission has allocated two billion euros until 2020 for the development of a European Open Science Cloud based upon the FAIR principles.



ELIXIR is building an intelligent and responsive system that provides researchers with access to collections of life sciences data stored and managed in various places across Europe. A second goal is to provide researchers with the tools and skills required to retrieve these data and use them for their own research. The Dutch focal point adheres to this goal as well to develop a national life science data infrastructure, in which all research organisations can exchange data. In addition, ELIXIR-NL has accepted the task of applying the 'FAIR principles' to the management and use of data files in the life sciences.

In addition to possibilities for reuse, the integration and thus the accessibility and exchangeability of data will change the way science is conducted. Now, researchers still formulate an hypothesis and then collect data to confirm or reject it. In the future, researchers will use clever algorithms that search for patterns and, based on that, generate the hypotheses that are subsequently tested in experiments. As a result, the borders between fields will blur because algorithms base their data on all components of the life sciences. Because the basic FAIR principles



are increasingly adopted in other domains as well, data exchange with other fields is imminent.

In addition to making data exchangeable according the FAIR principles, ELIXIR-NL also intends to create a digital research environment. It could provide researchers with efficient and customised help when storing and managing the data that they submit, and when searching and analysing the data that they need for their research. A third spearhead is training a new generation of researchers in bioinformatics and the life sciences who are committed to using data according to the FAIR principles.

Essentially the ELIXIR-NL infrastructure is accessible to anyone with a computer and an internet connection. There are some conditions, of course, both for suppliers and users of the data. Any data submitted, as mentioned, must be FAIR, and therefore have to meet certain specifications. At the international level, research councils thus have a hand in how to make research data reusable. In terms of the use of the data, the Open Access principle applies, as much as possible. However, the A in FAIR assumes that the Accessibility takes place under transparent conditions. In other words, data will not simply end up on the street. Strict requirements are in place regarding the protection of personal data, especially in the biomedical field, and companies can also allow their IP-sensitive data 'to talk' safely with the international scientific data.

Initially ELIXIR-NL has emphasised the integration of data sources that are important for the development and application of knowledge in human biology and health aimed at individuals, such as illness prevention and care (personalised



health & precision medicine). Importantly, other sectors from the life sciences will be involved in ELIXIR-NL from the outset as well. The plan is to develop a Life Sciences Data Exchange, a platform for exchanging data from all kinds of different fields, ranging from agriculture and nutrition to microbiology and research on biodiversity.

ELIXIR-NL is part of the ESFRI facility ELIXIR – 'A distributed infrastructure for life-science information'. The Dutch node is coordinated by DTL (Dutch Techcentre for Life Sciences), an open platform with over forty partners: universities, university medical centres, institutes and companies. In developing an e-infrastructure for personalised health & medicine, there is also intensive cooperation with other clusters in the life sciences, such as BBMRI-NL (biobanks and cohorts, page 67), MRI and Cognition (page 82), NL-Bioimaging-AM (page 97) and X-omics (page 115) and with SURF.

ISBE

Computer models of life

***Infrastructure Systems Biology Europe* (ISBE) provides researchers in the life sciences with the expertise and the tools to integrate different types of data into computer models. As a result, they can explain and predict the behaviour of biological systems – from cell to ecosystem.**

New techniques that can map the relationship between hereditary information (genotype) and actual observable properties (phenotype) and analyse biological processes are generating an explosion of data in the life sciences. These data can be integrated into computer models that mirror the complexity of biological systems. This has made it possible to predict the behaviour of biological systems (cells, tissues and organism) as environmental factors change or when there are disturbances in the system itself.

Concretely, this means that a systems biology approach can put researchers in a position to use models to predict what the effect of a medicine will be on how an organism functions, for example. Or how crops and their 'microbiome' in the soil will react to artificial fertilizers and crop protection products. The models can also predict which organisms are most suitable for the production of chemicals from plant-based raw materials or what the effect of a certain intervention will be on an ecosystem.

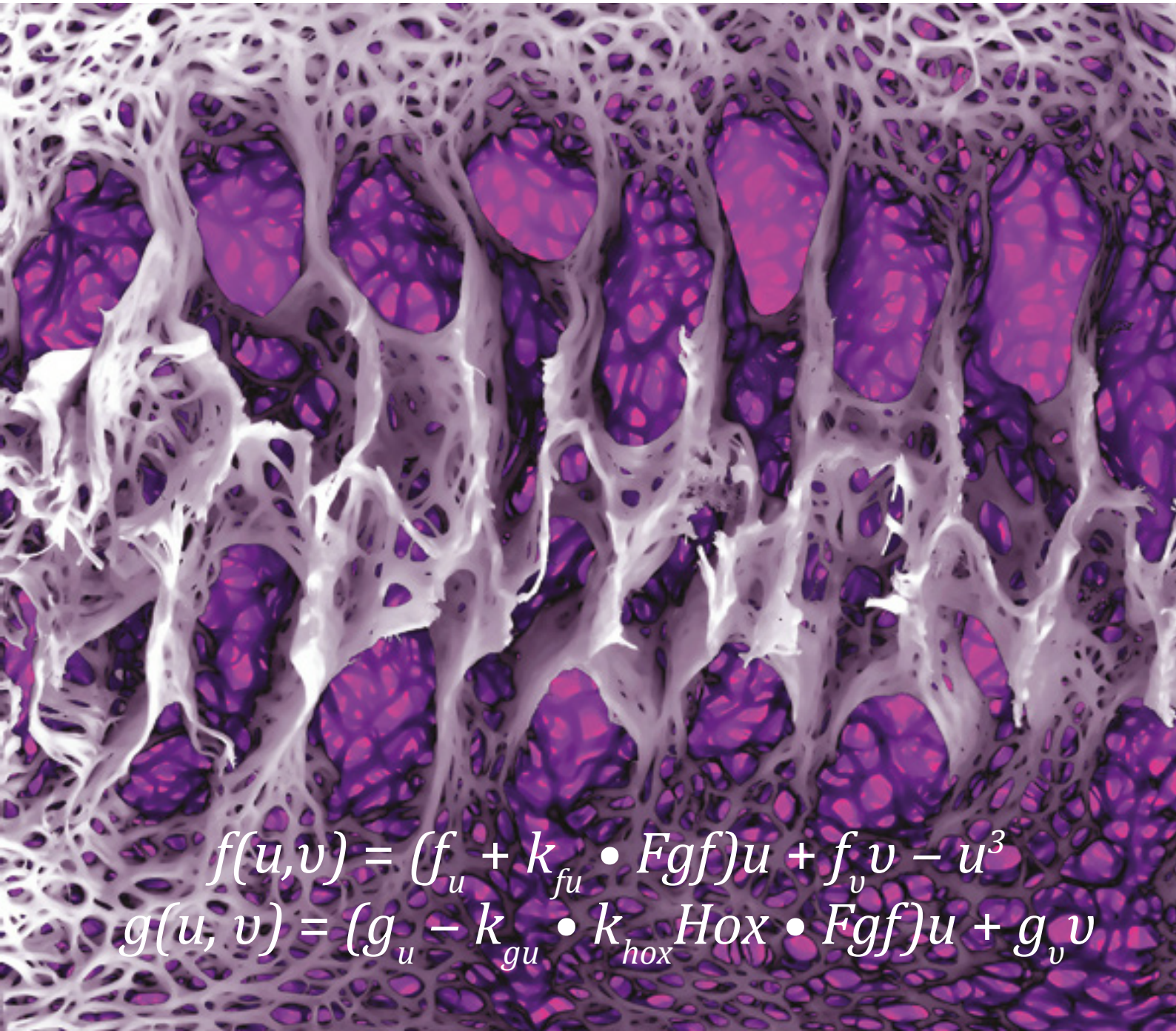


Though the methods of systems biology have great potential, their introduction is going slowly. The main reason for this is that the expertise in this field is not easily accessible everywhere. ISBE should solve this problem in Europe. The aim is to give the academic world, medical institutes and industry easy access to Europe's best expertise and resources, and open up educational and training opportunities. ISBE is also participating in FAIRDOM, an initiative to make data, operating procedures and models FAIR: *Findable, Accessible, Interoperable and Re-usable*. That is essential for the development, validation and expansion of computer models of biological systems in the long term.

ISBE is a decentralised European research infrastructure. The Dutch Techcentre for Life Sciences (DTL) acts as the Netherlands' link to the European ISBE matrix. A web portal is being developed for access to the services that will enable researchers, wherever in Europe they may be, to find the required expertise quickly and efficiently.

The Dutch ISBE Centre consists of research groups from Wageningen University and Research, the University of Amsterdam, VU University Amsterdam, the Delft University of Technology, Erasmus University Rotterdam, Utrecht University, Eindhoven University of Technology, Radboud University Nijmegen, Maastricht University and Leiden University, as well as the NKI and the NWO institute CWI, both situated in Amsterdam.

This facility is part of the ESFRI facility Infrastructure for System Biology Europe (ISBE).


$f(u,v) = (f_u + k_{fu} \bullet Fgf)u + f_v v - u^3$
$g(u, v) = (g_u - k_{gu} \bullet k_{hox} Hox \bullet Fgf)u + g_v v$



Cluster: MCCA

Imaging ageing and disease

The *Mouse Clinic for Cancer and Aging* (MCCA) provides researchers with the opportunity to monitor the aetiology and development of cancer and other age-related diseases with a range of imaging techniques. For this purpose, they use specially developed mouse models and human tissues.

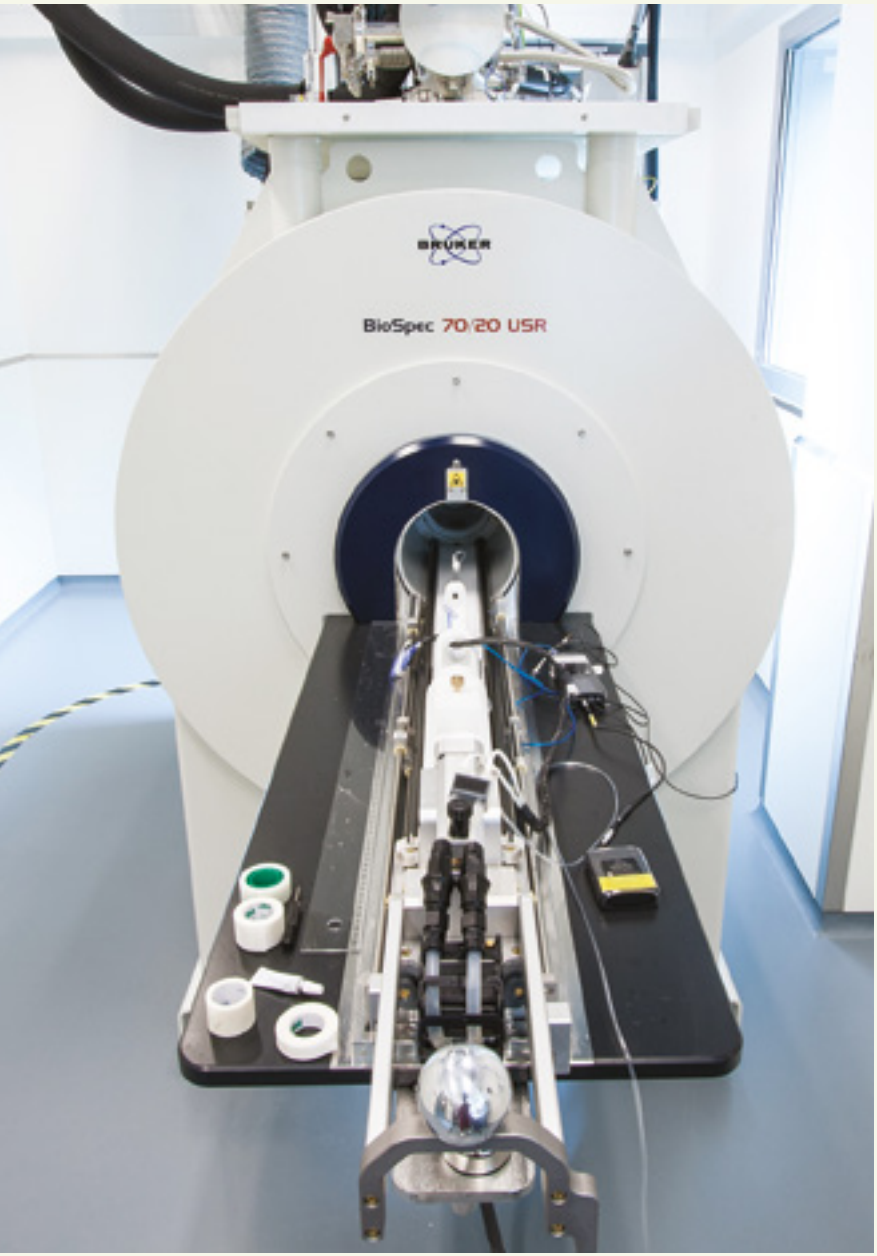
The population in Western countries is ageing, and as a result the number of people with cancer and other age-related diseases is increasing. In order to develop effective therapies, we need more insight into the aetiology and development of these diseases. In many cases, researchers use genetically modified mouse strains that are particularly sensitive to a certain type of cancer or other affliction.

Mice are an excellent model to study the impact of heredity and environmental factors on the aetiology of cancer. Researchers can also use mice to monitor the ageing process in intact organisms. The research on mice has already generated important new insights. That is why the Netherlands Cancer Institute (NKI) and the European Research Institute for the Biology of Ageing (ERIBA) have established the MCCA.



The MCCA forms a cluster with the facility for Applied Molecular Imaging Erasmus MC (AMIE). Researchers can make the aetiology and development of cancer and ageing visible with a wide range of imaging techniques. What is special about these techniques is that researchers are using so-called biomarkers. These are radioactive, light-emitting or fluorescent atoms that attach themselves to substances found naturally in the body. As a result, you can monitor biochemical processes in a living organism or in living tissue and see how organs function. The images of these processes and organs are created by a variety of techniques, including MRI, PET, SPECT, ultrasound, infrared radiation and different types of microscopes.

Together the MCCA and AMIE have four facilities, operated by NKI, the Erasmus Medical Center and the University Medical Center Groningen respectively. In Amsterdam, Rotterdam and Groningen, researchers have various imaging techniques at their disposal for both fundamental and preclinical and patient-related research. There are also dozens of mouse and other animal models available for research in many areas at these locations. These vary from cancer, cardiovascular disease, autoimmune diseases and ageing to microbiology and developmental biology. Because the various imaging techniques are clustered, researchers can get the maximum amount of data out of their experiments and use as few laboratory animals as possible.



The NKI also has a facility where mice can be genetically modified to serve as models for human afflictions. This transgenic facility is capable of rapidly and efficiently developing new mice models using modern techniques. These include the genetic modification of fertilised ova via CRISPR/Cas9 and the modification of embryonic stem cells from regular or genetically modified mice strains. This makes it possible to create mouse models that are tailored to the needs of researchers.

The third facility is the Mouse Cancer Clinic, also located at the NKI. There scientists can conduct preclinical pharmacological research on new medicines or combination of medicines. It primarily involves the processes that active substances undergo or set into motion in the body. Research is also being conducted at the cancer clinic for mice on therapies to combat tumours. These could be interventions in genetic material, but also tumour-specific medicines (targeted drugs) either in combination with chemotherapy or targeted radiation therapy.

The University Medical Center Groningen has an Aging and Phenotyping Facility. This is a facility for research on the relationship between ageing, heredity and environmental factors. The facility also has the capacity to quickly create ageing variants of most mouse strains used in research. And finally, the facility in Groningen has a biobank with a large number of tissues from older mice. The facility works closely with Brains Online, a company specialised in preclinical research on new active substances in living mice.



MCCA is the Dutch hub in the European Mutant Mouse Archive (EMMA) and the Dutch partner of the European infrastructure for ESFRI's Mouse Phenotyping and Archiving Research (INFRAFRONTIER). Furthermore, the cluster is linked to various other European large-scale infrastructures, such as EATRIS and BBMRI (page 67). It is also a partner in various European projects and platforms for research on cancer and ageing. The ultimate goal is to establish a network infrastructure for Small Animal Research Technology (SMART-NL).

Cluster: MRI and Cognition

Images of the brain

***Magnetic Resonance Imaging* (MRI) provides researchers and clinicians with data about the structure (anatomy), the functioning (physiology) and the biochemical processes (metabolism) in the brain and other parts of the body. As such, it is an important tool for researching illness and health, behaviour, learning and development.**

Unique chemical and physical processes occur in the human brain. They not only make it possible for us to respond to stimuli inside and outside our body, but also to reflect on our own and other people's behaviour. Current cognitive research focuses mainly on large groups and often fails to address individual differences. To better understand the development and behaviour of an individual, we need a more personalised approach. This kind of approach would need to take into account hereditary characteristics, experiences, neurobiological limitations and social influences – in short, everything that makes an individual a person.

MRI technology is ideal for precision cognition, the personalised approach for monitoring and understanding the development and behaviour of individuals. MRI is a non-invasive, safe way of studying how the brain works on a scale that corresponds to that of populations of neurons. These populations are behind our behaviour and brain function. The research will provide more insight into the biochemical basis of our thinking and behaviour and will make it possible to precisely pinpoint certain brain functions (and corresponding disorders) and, if possible, to help treat them.



The use of MRI to create images of the brain has many applications. In the clinic, MRI images are used in real time to launch a targeted attack on tumours with ultrasound, ionising radiation or – in the near future – with protons. The big advantage of this targeted intervention is that a high dose of radiation can be administered locally, while inflicting less secondary damage. MRI imaging is also important for the accurate placing of electrodes in deep brain stimulation. Doctors can use it to combat the symptoms of Parkinson's disease.

In another area, MRI can be used to study potential deviations in the metabolism of nerve cells. On the one hand, that generates leads for the development of new medicines to compensate for these deviations. And on the other hand, it creates new opportunities for personalised medicine, by offering patients therapies that are carefully designed to combat their disease.

Because MRI is safe and non-invasive, it is also suitable for research on how the brain works with large groups – cohorts – children, young adults and adults. For example, it can correlate brain activity in certain



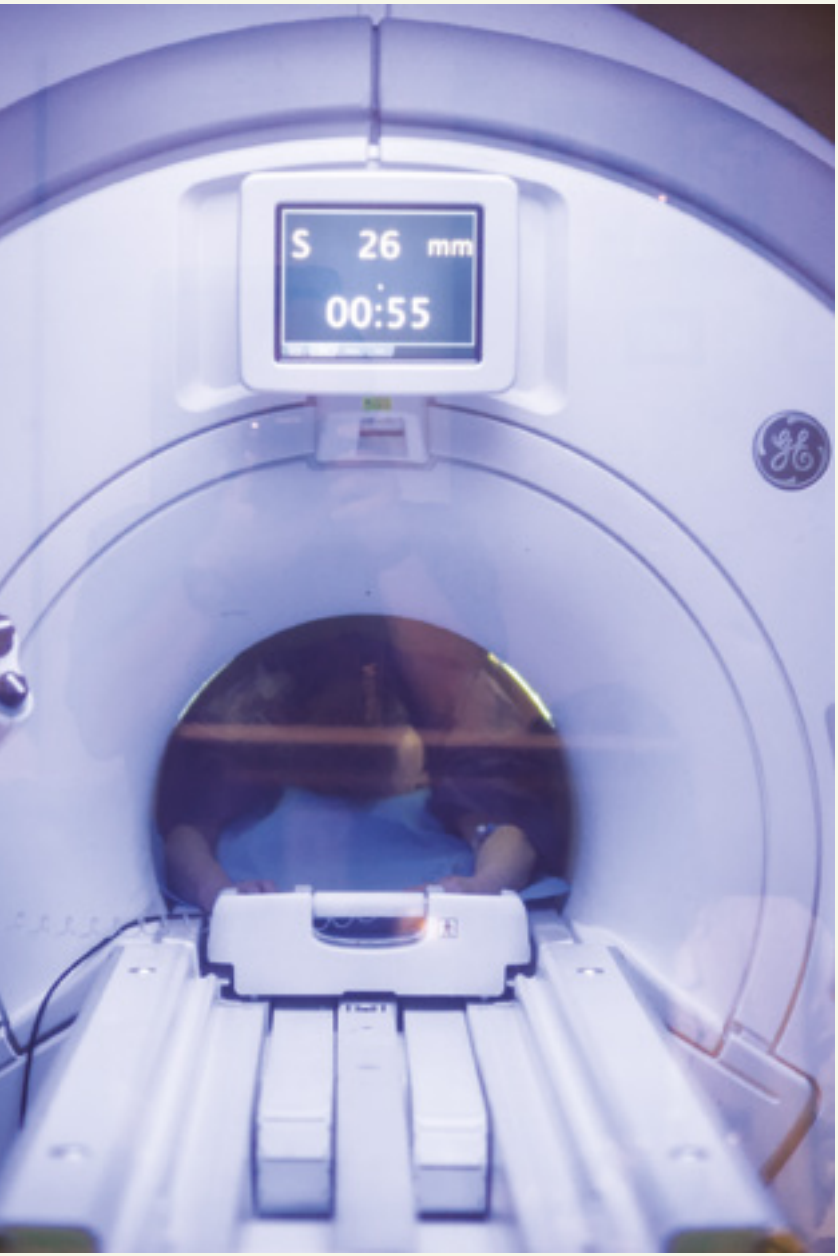


areas to response speed, memory, social interaction and language use. In combination with other data, such as heart rhythm, skin conductance and facial expression and data about lifestyle, education and socio-economic class, it provides opportunities to link cognitive behaviour to neurological data.

The Netherlands has a long tradition of using MRI for cognitive research. Many cohort studies have been conducted in the life sciences in which researchers used data generated by MRI scans. Dutch researchers also play a major role in the use of MRI to administer real-time therapy to treat diseased tissue. They use a well-developed infrastructure consisting of MRI systems with different field strengths.

Systems are installed in various place in the Netherlands (Leiden, Utrecht, Maastricht and Amsterdam) with a high (7 tesla) and ultra-high (9.4 tesla) field strength. Radboudumc and the Donders Institute in Nijmegen work together with the 7 tesla MRI group at the Erwin L. Hahn Institute of the University of Duisburg-Essen. In addition to systems with high field strength these institutes also have MRI systems with a field strength of 3 tesla, which are frequently used for cohort studies. In addition hybrid systems with low field strength (1.5 tesla) are used to treat patients with radiotherapy or ultrasound.

The use of MRI installations in cognitive research is not only scientifically and clinically important, but it is also important for the further development of MRI as an imaging technique. Many institutes act as a beta or development site for new components and installations. Conversely, suppliers of these installations, including Philips, Siemens and other companies and start-ups, regularly use the knowledge and experience and the findings developed by these academic institutes.



The MRI and Cognition cluster comprises the Radboud Imaging Centre and the Donders Institute for Brain, Cognition, and Behaviour in Nijmegen; the Centre for Image Sciences of the UMC Utrecht; the C.J. Gorter Centre for High-field MRI in Leiden; the KNAW Spinoza Centre for Neuroimaging in Amsterdam; the VUmc Imaging Centre, also in Amsterdam and Scannexus-Brains Unlimited of Maastricht University and the Province of Limburg. The MRI and Cognition cluster is part of the HEALTH-RI initiative.

This facility is part of the ESFRI facility 'European Infrastructure for Translational Medicine' (EATRIS).



MRUM

Measuring human metabolism under controlled circumstances

The *Metabolic Research Unit Maastricht* (MRUM) provides the opportunity to conduct research on the metabolism of the human body as a whole or of organs and tissues in a closely controlled environment.

Our modern lifestyle, which entails a high intake of food and little exercise, is one of the causes of (chronic) metabolic diseases, such as obesity, type 2 diabetes and cardiovascular disease. Even though all involved parties acknowledge the problem, they have yet to succeed in finding an adequate answer in terms of successful interventions. It is becoming increasingly clear, however, that other factors connected to our lifestyle have an impact on metabolic diseases. Examples include disturbances in our biological clock, insufficient exposure to the cold and a predominantly sedentary way of life. There is also more evidence that metabolic disturbances play a part in the onset of aging-associated diseases, such as Alzheimer's and certain types of cancer.

More knowledge is needed to study the connection between lifestyle and metabolism and to identify opportunities for interventions and medicines. It mainly concerns knowledge at the tissue and organ level as well as the entire human body. The MRUM consists of 20 metabolic research laboratories for test subjects. There researchers can make highly detailed measurements in a closely controlled environment of the subjects' metabolism, their sensitivity to insulin and their vascular function. These types of measurements are not only clinically important but are also important for medical research in sports and movement analysis.

In the coming years, the MRUM will be equipped with imaging equipment, including MRI (magnetic resonance imaging), MRS (magnetic resonance spectroscopy) and PET (positron emission tomography). That will make it possible to conduct non-invasive research on tissue-specific metabolic processes in the heart, liver, brown adipose tissue, the brain and muscles. The MRUM will also be expanded with time-isolated, climate-controlled metabolic units where researchers can study the other lifestyle factors mentioned above. These include sleep-wake rhythm, ambient environment, long-term sitting behaviour, and frequency and time of food intake.



MRUM is part of Maastricht University. A great deal of research is conducted with other institutes, including Wageningen University and Research and the medical faculties of Leiden University, the University of Groningen and the University of Amsterdam's Academic Medical Center. The food and medical industry also make use of the facility.

Cluster: NEMI

Watching with electrons

Technological developments have instigated a revolution in the more than eighty-year-old field of electron microscopy (EM). *Netherlands Electron Microscopy Infrastructure* (NEMI) provides researchers with an opportunity to actually see how individual atoms and molecules behave and organise themselves in biological and non-biological materials. At the same time, Dutch research institutes and companies can continue to operate on the front of the latest developments in electron microscopy.

An electron microscope uses a beam of accelerated electrons as imaging probes. Because the wavelength of electrons is much lower than that of the photons in visible light, the resolving power is about 5,000 times higher than that of a light microscope.

The life sciences have traditionally used electron microscopes to study sub-microscopic structures, such as viruses and cellular organelles, the compartments of a living cell. New techniques make it possible to study tissues, such as tumour or brain tissue, as well as organs and even molecules down to the smallest details and in three dimensions.

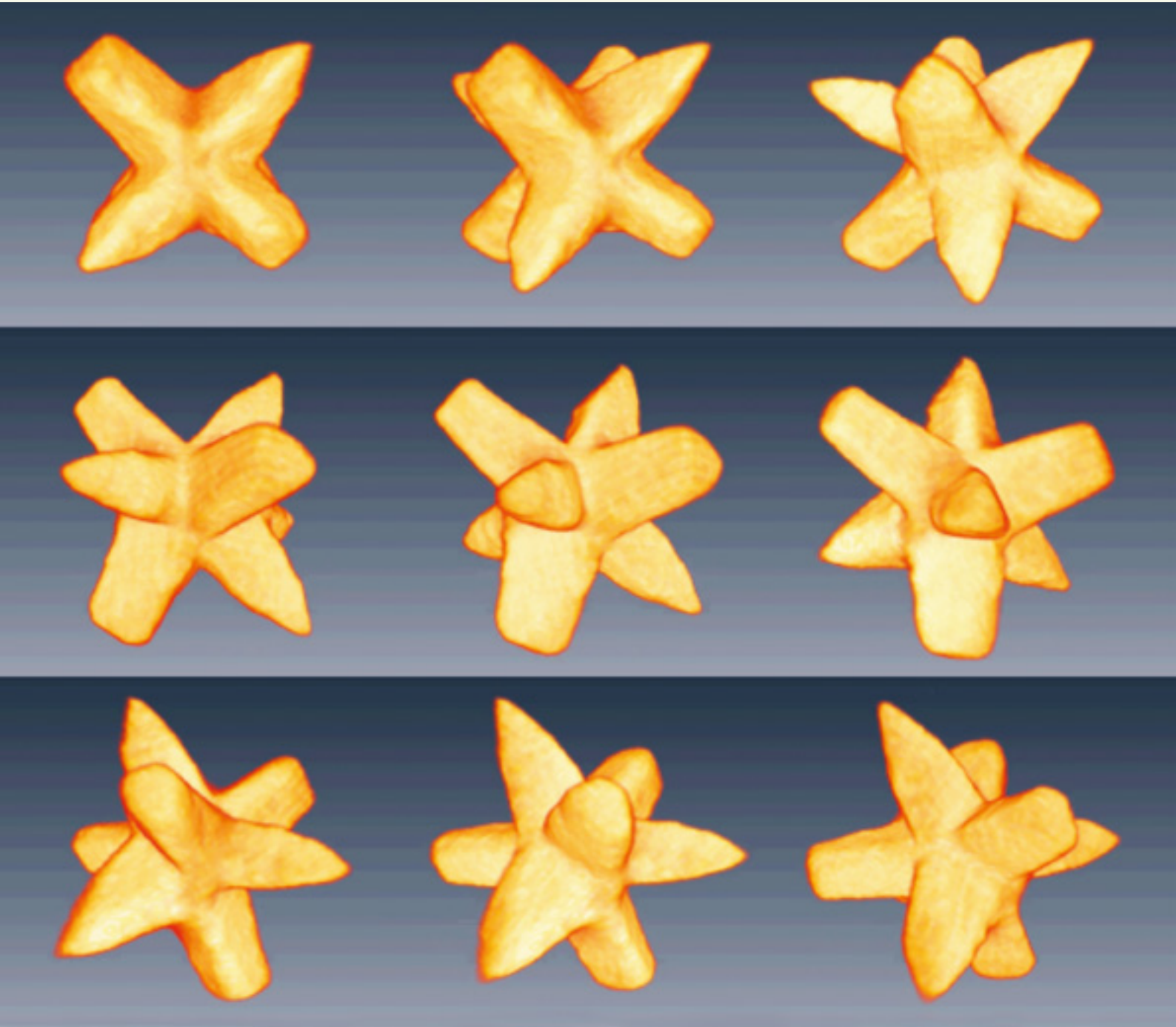
Cryo-electron microscopy (cryo-EM), for example, allows researchers to map three-dimensional structures of biological macromolecules. It increasingly replaces X-ray diffraction for structure determination of isolated biomolecules, in particular for large ones. It is important for fundamental research on these kinds of molecules and for the analysis of potential drugs and of enzymes that are used in industrial fermentation processes.

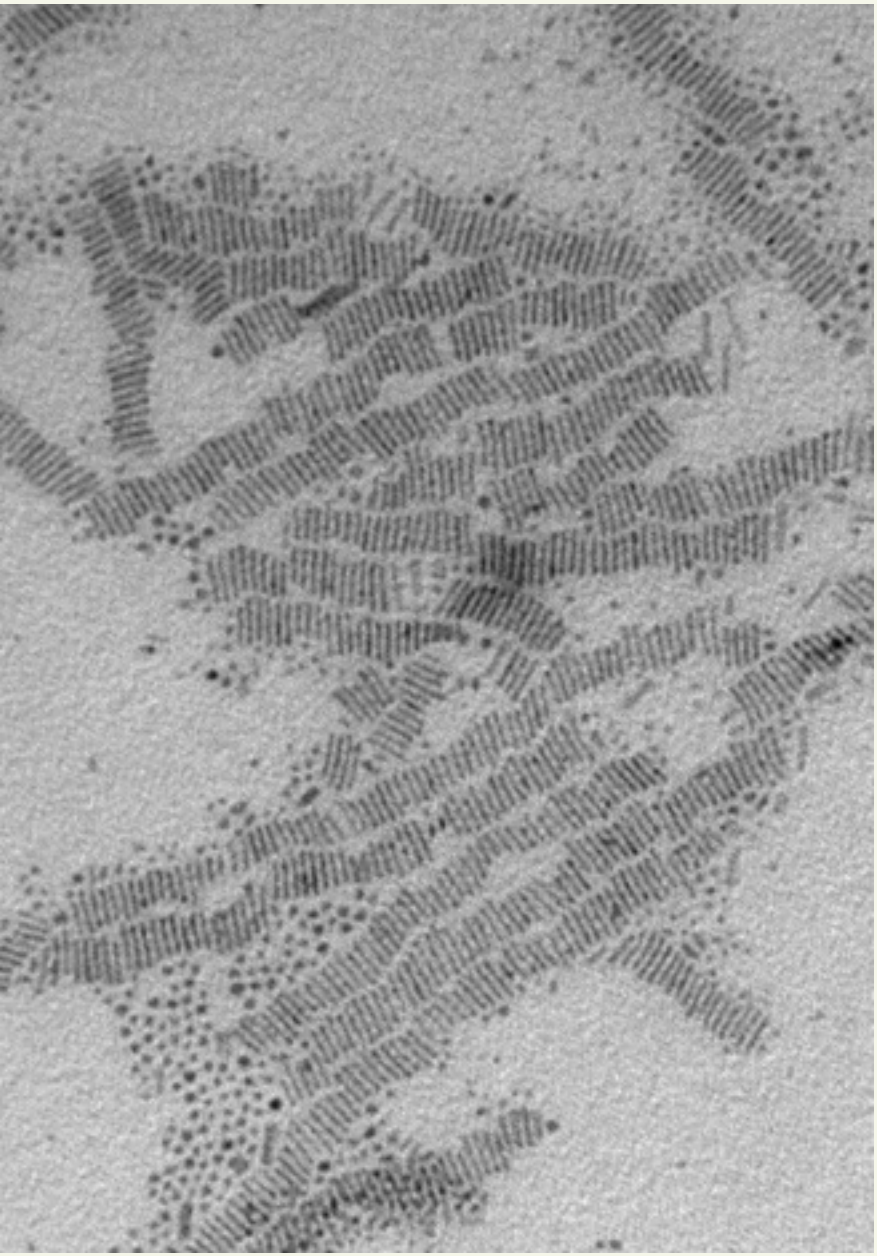


Cryo-electron tomography (cryo-ET) goes a step further. This technique makes it possible to observe the behaviour of biological macromolecules in their natural environment, namely the cell. By combining a number of snapshots from different views, researchers gain insight into biological processes, such as the binding of a virus to a receptor molecule on the cell wall and, vice versa, the binding of an antibody to a virus.

Another new development is the combination of electron microscopy with light microscopy. In Correlative Light Electron Microscopy (CLEM), researchers use a light microscope in combination with fluorescent tags (fluorescence microscopy) to identify interesting parts of a biological system – a tissue, organ or molecule. Subsequently they can examine them in more detail with the electron microscope.

In addition to biological molecules, electron microscopes are also used to analyse and manipulate non-living matter, currently up to the level of individual atoms. Applications include the development of new





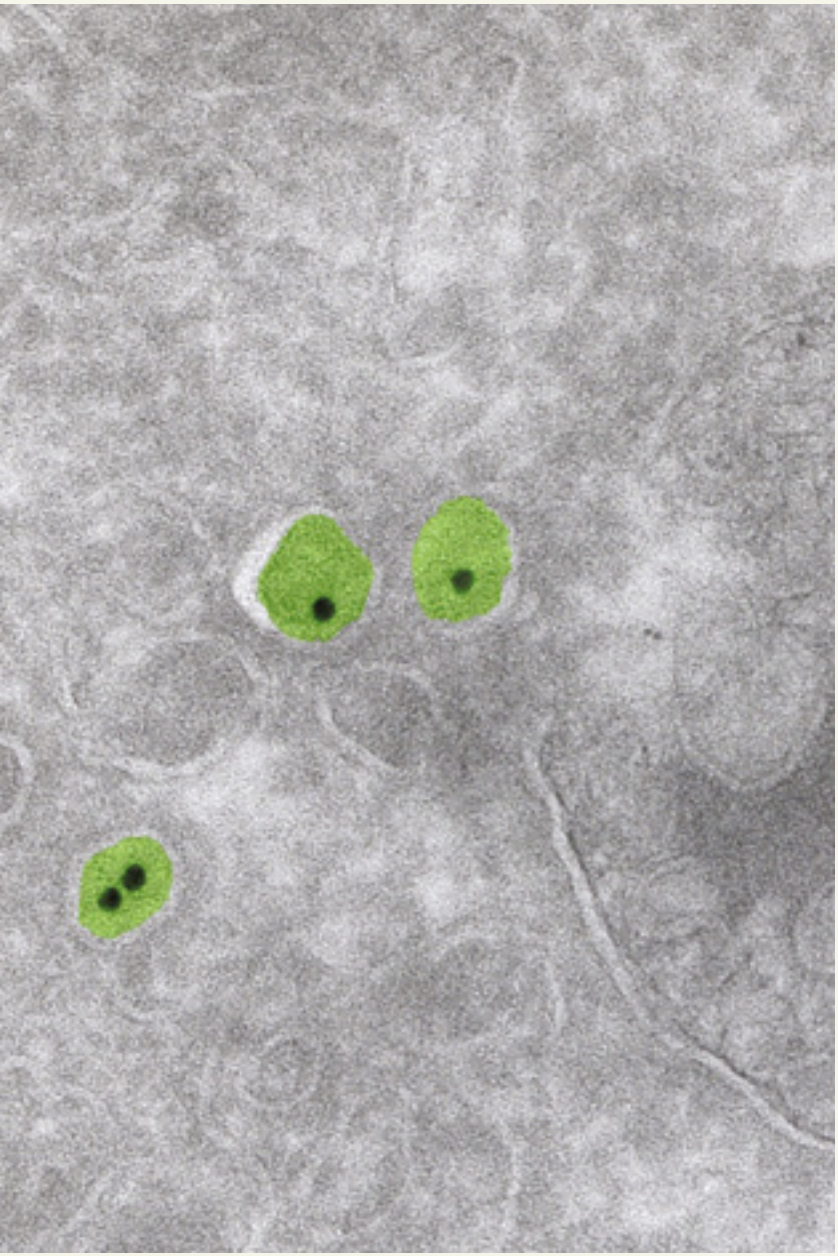
nanostructured catalysts and semiconductor nanomaterials for solar cells and batteries.

The electron microscope is not only used to characterise materials, but also to record chemical, electrical and optical properties. It is also possible to monitor chemical reactions in minute detail in a so-called nanoreactor (in situ electron microscope). Researchers are therefore able to monitor the binding of hydrogen to a metal oxide at the atomic level, for example. These insights may ultimately lead to more efficient methods of producing and storing hydrogen as a fuel.

For decades the Netherlands has played an important role in the development of electron microscopes and corresponding instruments for the preparation of objects and the analysis and processing of data. Indeed, Dutch researchers are at the forefront of the development of time series, in which micrographs are taken by the electron microscope with time intervals of a billionth of a second. This enables researchers to make an extremely detailed 'film' of changes in the structure of materials, for example the binding of a hydrogen atom to a catalyst.

The electron microscopy of living and non-living matter have traditionally been two separate worlds. Research on biological specimens requires a completely different approach than research on hairline cracks in metals. That separation is disappearing, in part because increasingly research is being conducted on soft and hybrid materials, such as fibre-reinforced plastic, and because there is more and more interest in monitoring the behaviour of materials through time.

The union of electron microscopy of living and non-living matter is providing researchers with many mutual benefits. This is true for both the preparation of objects and the actual



observation and processing of data. NEMI caters to the need for a national infrastructure of state-of-the-art equipment and a critical mass of experts who know how to get the most out of it. The Netherlands can thus continue to play a leading role in the development of electron microscopy and its various applications in the life sciences and materials science.

NEMI is a network of regional hubs, each with their own specialism. The pillars include NECEN (Netherlands Centre for Electron Nanoscopy) in Leiden and M4I (Maastricht MultiModal Molecular Imaging Institute). NEMI works together with Dutch and international companies and is affiliated with NL-BioImagingAM (page 97), NanoLabNL (page 51), EPOS-NL (page 32). DTL (Dutch Techcentre for Life Sciences) and Health RI (the national infrastructure for personalised medicine and health).

Part of this facility is part of the ESFRI facility 'Integrated Structural Biology Infrastructure' (INSTRUCT) and ESFRI facility European Research Infrastructure for Imaging Technologies in Biological and Biomedical Sciences (EURO-BioImaging).

Cluster: NIEBA

Diversity and functioning of natural systems

***Netherlands Infrastructure for Ecosystem and Biodiversity Analysis* (NIEBA) provides researchers with easy and remote access to an abundance of validated data about life on Earth. The infrastructure also provides options for analysing and modelling, using these data.**

Living in a technological environment – a technosphere – we do not always realise how much we depend on natural systems. Indeed, nature is much more than a reservoir of wild animals and rare plant species. It is also a complex system that provides us with a wealth of products and services: food, obviously, but also wood as a construction material, fresh water for us to drink and plant and other natural compounds that serve as a basis for medicines.

Natural systems keep water clear, air clean and soil fertile. They provide protection against flooding (think of dunes and mangroves) and store water for dry seasons. They also provide space for recreation and reflection and are a source of natural beauty. In short, natural systems comprise the biological capital from which we reap the fruits in the form of a wide range of products and services.

In order to gain more insight into how ecosystems function, for example how systems respond to change caused either naturally or by humans, we need observations, experiments and models. To achieve that, we need to correlate our knowledge about species, their traits and interactions to ecosystems and their related processes and, ultimately, to global processes such as the cycles of carbon, nitrogen and water and the global distribution of introduced species and pathogens.

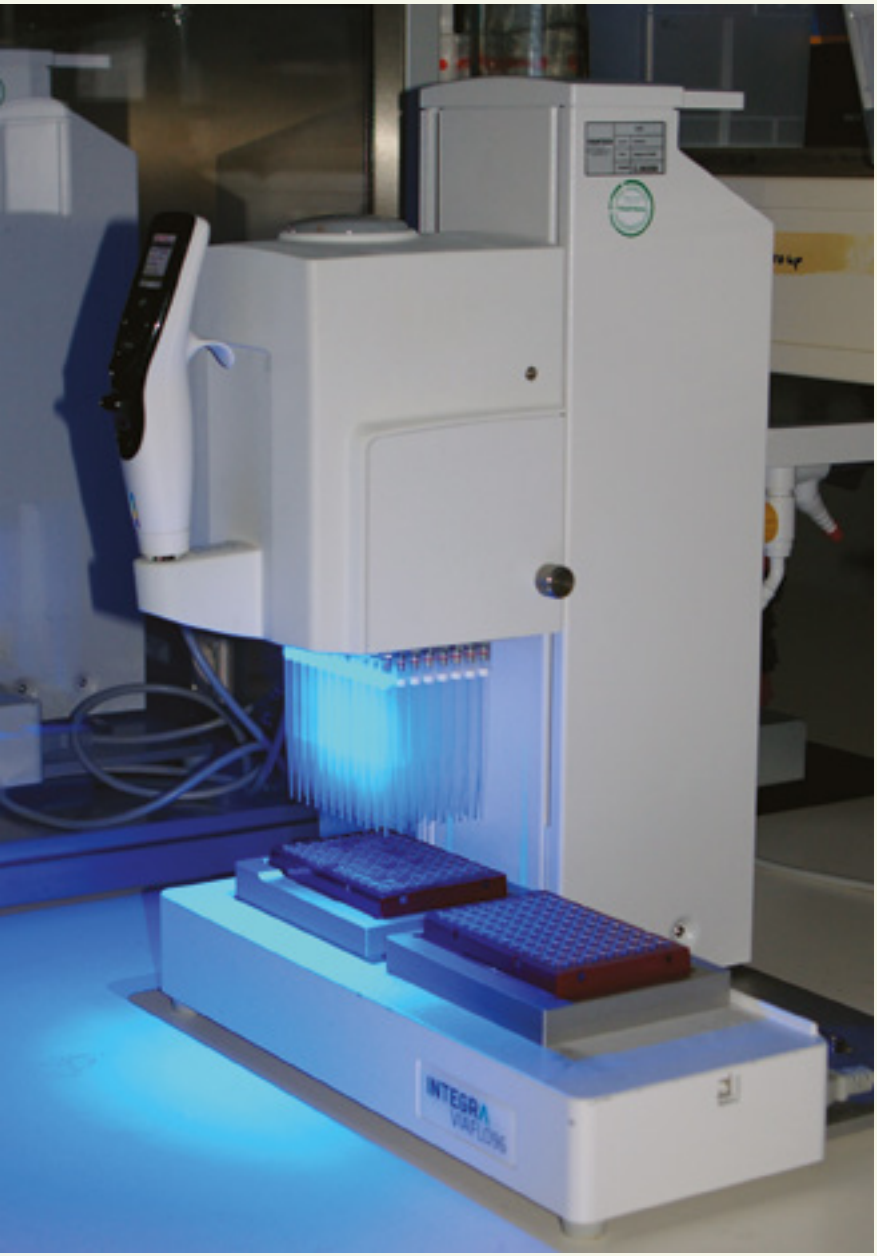


In addition, more knowledge and insight is required on the way in which ecosystems adapt to change. On the global scale, adaptation relates to climate change and its potential impact, such as drought, severe rainfall and the shifting of climate zones. On a local and regional scale this means adaptation to changes in land use, for example urbanisation, land reclamation, deforestation and reforestation, and the intended or unintended introduction of alien species.

What is essential is that we identify the driving forces behind so-called regime shifts: tipping points in an ecosystem that are difficult to reverse. If we gain more of an understanding about this we will be able to predict whether, and if so when, species and species interactions occur and ecosystems are likely to collapse, as a result of which important products and services will vanish. Conversely, more insight may result in more targeted actions that will help us to maintain and "repair" ecosystems.

At the species level are already quite some data available about occurrences, traits and interactions. In the past few hundreds of years we have built huge collections of plants, animals and – more recently –





microorganisms serving as a reference for scientific research. Thanks to new analytical techniques the collections are also a source of new information about former environmental conditions, interactions, evolution and more.

Since a few decades these collections are being digitised. Digitisation includes, apart from recording external features, physiological, biochemical and internal characteristics also hereditary features such as DNA barcodes or whole genomic information. With support of various sensors, researchers have access to new data on the location of individual organisms occur, on how organisms move, and on their activities. Remote sensing techniques are adding information layers by mapping changes in land use and ecosystem characteristics with increasing precision.

Scaling up from species' properties to the functioning of complete ecosystems, researchers want to compile, integrate, analyse, and evaluate data from various sources. Ultimately that will lead to more detailed and reliable models, allowing scientists predict about how the response of species and ecosystems to natural- or human-induced changes. The challenge is to generate knowledge about the occurrence and interactions of species in relation to ecosystem function, and finally how me might manage the natural environment and use it sensibly. This knowledge will contribute to the nature-based solutions for coastal defence, sustainable agriculture and fisheries, liveable cities and human wellbeing.

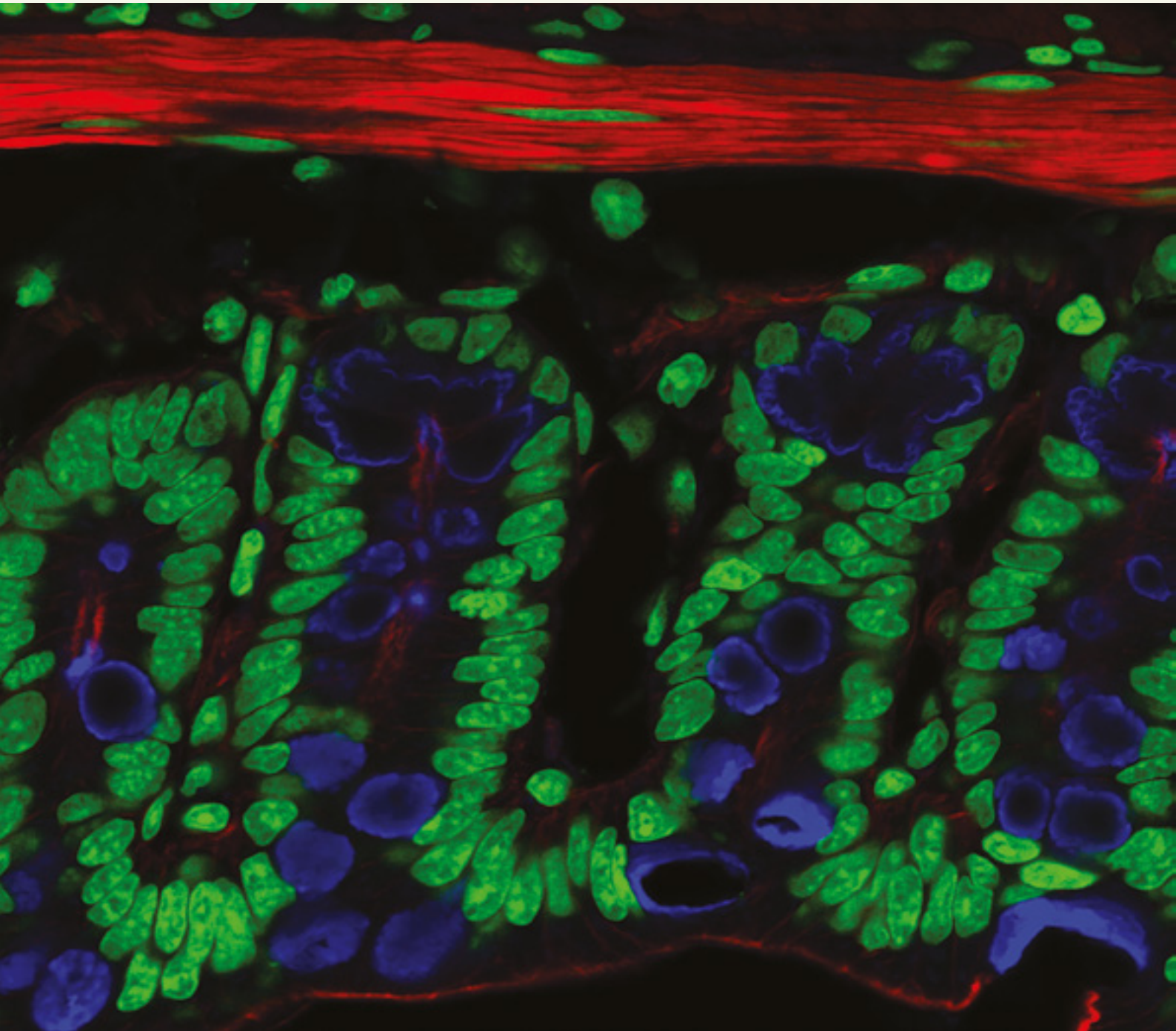
To achieve all this, a national infrastructure has to provide remote access to digital information from biodiversity collections and databases from the Netherlands and other European countries; an infrastructure that provides a virtual research space for the integration, analysis, modelling and evaluation of data. The Naturalis Biodiversity Center and the



Fungal Biodiversity Centre of the CBS-KNAW digitised part of their collections and opened these up for researchers. NIEBA is building on this.

Naturalis also launched an initiative to make scientific collections elsewhere in Europe accessible. This Distributed System of Scientific Collections (DiSSCo) dovetails well with Life Watch, a European infrastructure (ESFRI), providing researchers access to virtual research environment with tools to analyse and model biodiversity patterns and processes using a range of different sources. The Netherlands is playing a leading role in this process.

NIEBA, the national infrastructure for the analysis of ecosystems and biodiversity, is building the facilities for addressing the above challenges. It is an initiative of the University of Amsterdam, the Naturalis Biodiversity Center and the Fungal Biodiversity Centre of CBS-KNAW. It gives researchers access to large collections and corresponding physical and on-line facilities for research. NIEBA is a central hub in the European (ESFRI) infrastructures LifeWatch and DiSSCo.



Cluster: NL-BioImaging AM

Directly observing biomolecules in action

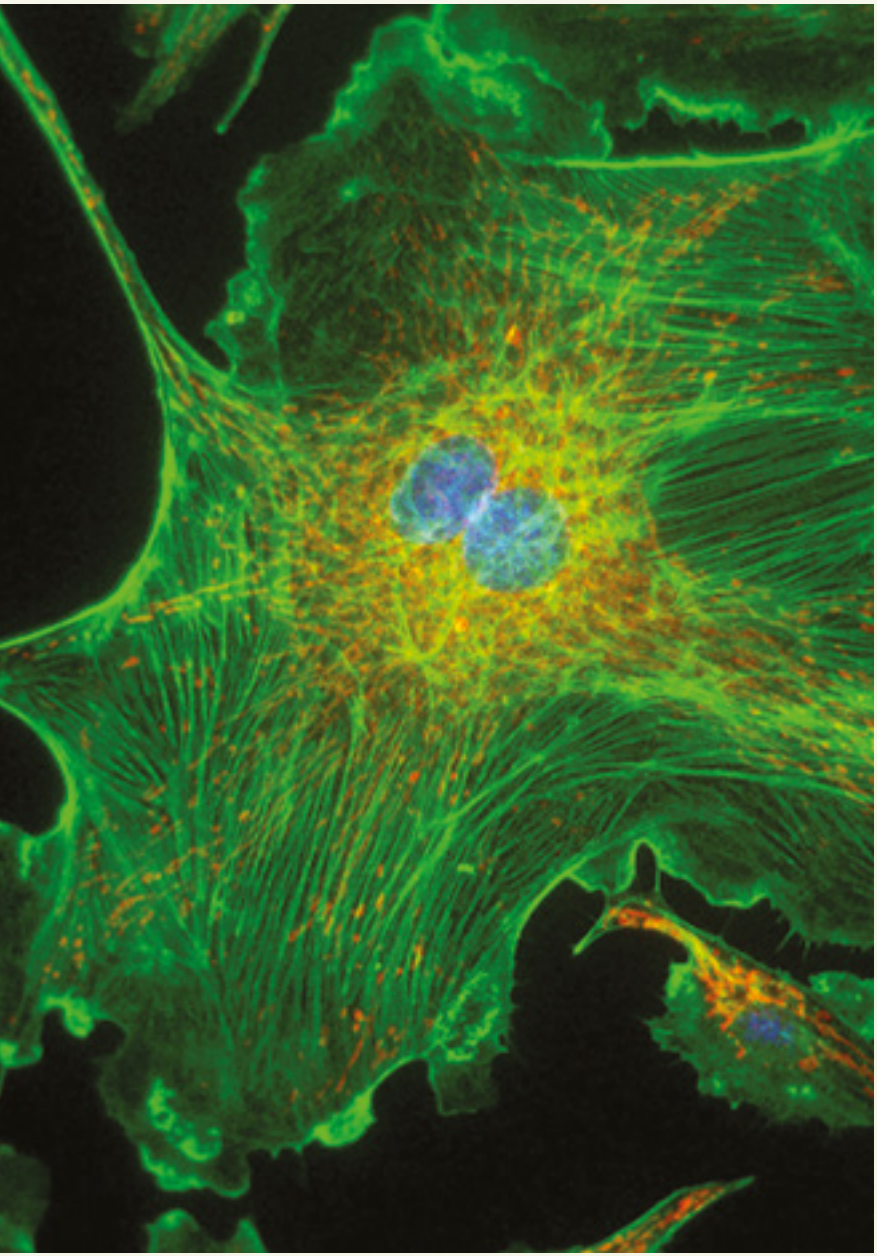
Netherlands BioImaging Advanced Microscopy **(NL-BioImaging AM) develops advanced microscopic techniques to directly observe biological processes in action in cells, tissues and organisms. Moreover, the consortium makes these techniques accessible to other scientists.**

In the three and half centuries that have passed since Antonie van Leeuwenhoek observed 'tiny creatures' through his self-assembled microscope, microscopy has gone through enormous developments. Indeed, these developments have accelerated in recent years thanks to innovative techniques such as functional imaging and super resolution microscopy. That, in turn, has led to a paradigm shift in the life sciences. For the first time ever, it is now possible to observe biological mechanisms in living cells directly at the molecular level. The revolutionary character and significance of (fluorescence)microscopy is further underscored by recent Nobel Prizes for research on fluorescent protein (2008) and super-resolution (2014).

This microscopy revolution is generating fundamental scientific insight into the functioning of cell organelles, cells, tissues and even complete living beings. In addition, it is also important for a better understanding of the aetiology and treatment of diseases, the improvement of food supplies and the development of new, better biomaterials. Increasingly, scientists working in bio-informatics, for example, have access to microscopic data. They combine this with data from other disciplines – such as biochemistry and genomics – in order to explain cell and tissue function. Moving 3D images are laying the foundation for (computer) models of the living cell and a better understanding of the origin of life. Industrial partners are using the facilities for research in the areas of pharmaceuticals, nutrition and materials and to develop new microscopic instruments and the corresponding software.



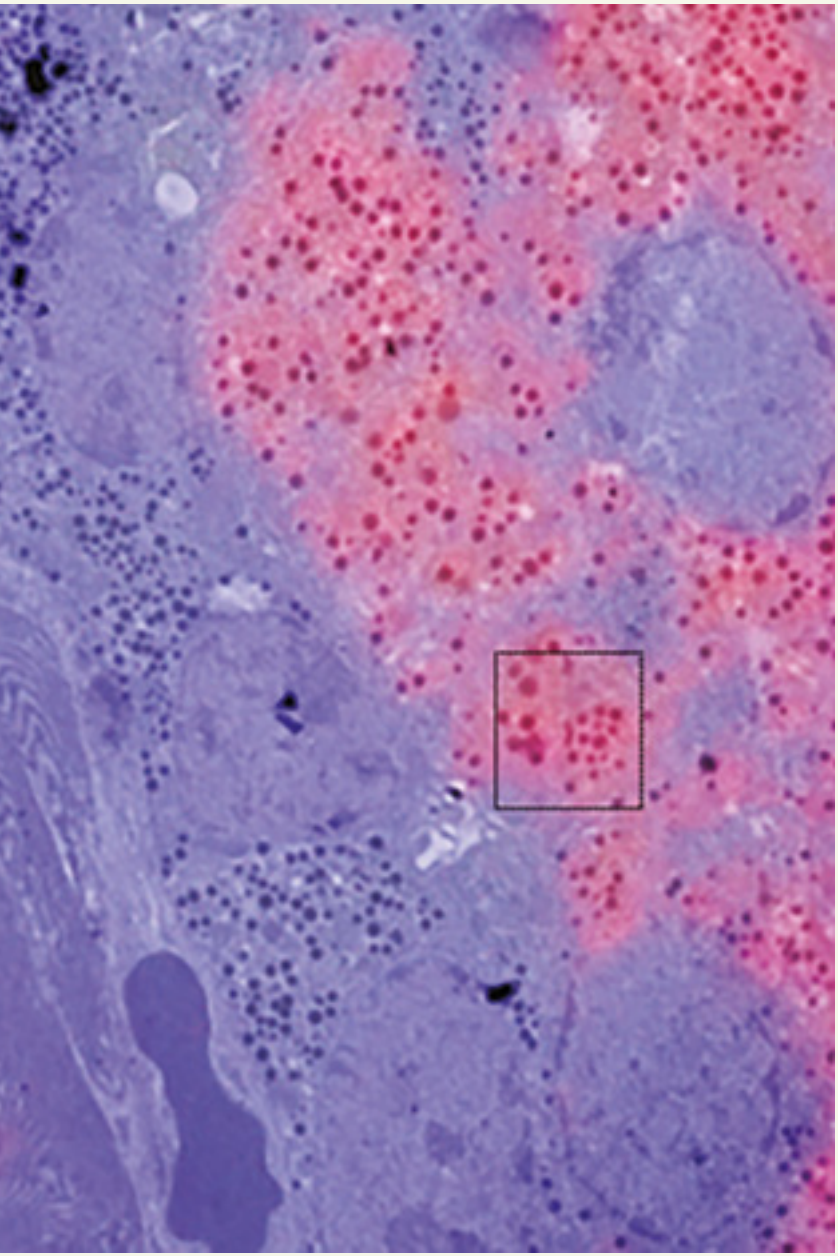
NL-BioImaging AM is a partnership of advanced microscopy centres in the Netherlands. Seven innovative research centres ('flagship nodes') were nationally selected to develop and use advanced microscopic techniques for a variety of applications. These leading research centres – scattered across the country – also act as a gateway for researchers and companies from the Netherlands and abroad who want to use the facilities. They have been branded as centres of excellence by an international committee of independent experts and recently ratified in Euro-BioImaging, an ESFRI network infrastructure in-the-making for imaging in the biological and biomedical sciences.



The research centres in question are: Van Leeuwenhoek Centre for Advanced Microscopy (LCAM)-Functional Imaging Dutch Flagship node, (Amsterdam, single-sited); PRIME-Hubrecht Molecular Imaging Dutch node for Intravital Microscopy (multi-sited); Correlative Light Microscopy Dutch Flagship node (multi-sited); High Throughput Microscopy Dutch Flagship node (multi-sited); Erasmus MC OIC, multimodal advanced light microscopy node, (Rotterdam, single-sited), WISH multimodal advanced light microscopy & molecular imaging (Wageningen, single sited) and Facility of Excellence in Imaging, multimodal advanced light microscopy & molecular imaging, (Maastricht, single-sited).

These seven flagship nodes connect activities taking place at the AMC, Erasmus MC, Hubrecht laboratory, LUMC, NKI, Radboudumc, UL, UMCG, UMCM, UMCU, UU, UvA and Wageningen UR, and are directly accessible for (inter) national researchers. In anticipation of funding linked to the National Roadmap, international access to these seven nodes is currently granted on an interim basis, often with in-kind funding, yet based on the open access principle and with an independent guarantee of the scientific quality of the users' research projects. From June 2016, this will be coordinated via the interim Euro-BioImaging hub and user portal in Finland. In addition to these seven flagship nodes, there is also a strong connecting general-access activity that links all 19 participating Dutch microscopy centres, in which training, data management and image processing are nationally synchronised and coordinated.

NL-BioImaging AM has a governance structure in which strategic decisions are made for national investments in advanced microscopy via national consensus in the National



Steering Committee (NSC). All 19 microscopic centres from universities, institutes and academic centres are represented in the NSC. The executive body is a project management team consisting of six people chosen by the NSC and chaired by professor T.W.J. Gadella.

As co-founder of DTL (Dutch Techcentre for Life Sciences), NL-BioImaging AM has been consulting about content and strategy for some time now with other life sciences infrastructures in the Netherlands, such as BBMRI-NL (page 67), MRI and Cognition, (page 82), ELIXIR-NL (page 73), E-science, X-omics (page 115) and the recently launched Netherlands Electron Microscopy Infrastructure NEMI (page 88). A key focus of this endeavour is to translate European standards and agreements between umbrella ESFRI initiatives, such as the ELIXIR::Euro-BioImaging agreement about data use and stewardship, to the Dutch situation. Finally, the infrastructure of NL-BioImaging is part KNAW 2025 horizons/ roadmaps Bioscopy and HEALTH-RI.

This facility is part of the ESFRI facility European Research Infrastructuur for Imaging Technologies in Biological and Biomedical Sciences (EuroBioImaging).


HighRes

NL-OPENSCREEN

Searching for drug candidates

NL-OPENSCREEN provides researchers with a library containing tens of thousands of compounds plus the facilities to test their biological impact quickly and efficiently.

The unravelling of the human genome has enabled molecular biologists to discover on an almost daily basis new proteins that play a role in biological processes in and between cells. Proteins that cease to function or function sub-optimally can cause diseases and afflictions, such as cancer, Alzheimer's, autoimmune diseases and diabetes. These proteins are consequently an interesting focal point for the development of drugs.

Research on the functioning of these proteins occurs by exposing them to many tens of thousands of compounds ('small molecules'). This *screening* is conducted using many hundreds of compounds simultaneously in an automated process known as *ultra-high-throughput screening*. A number of these small molecules will interact to a greater or lesser degree with the protein (referred to as *hits*). Often these molecules are subsequently chemically modified to see if the effect can be further enhanced. These molecules provide insight into the functioning of the protein in question and the physiological process that it is part of. They can also be the point of departure for the development of new drugs.



NL-OPENSCREEN is building on the existing activities of the Pivot Park Screening Facility in Oss and the Netherlands Cancer Institute (NKI) in Amsterdam. The screening facility in Oss is currently the beating heart of the European Lead Factory (ELF), a programme in the framework of the European Innovative Medicine Initiative, which is scheduled to run until 2018.

The launch of another European initiative, EU-OPENSCREEN, which aims to provide a pan-European infrastructure of screening facilities for chemical-biological research, is scheduled to be launched one year before the end of ELF. In that framework, new libraries of compounds will be created in addition to the existing library of 200,000 small molecules. New tests will also be developed to measure the efficiency of these compounds.

NL-OPENSCREEN is an initiative of Leiden University, Leiden University Medical Center and the Pivot Park Screening Centre, which cooperates with Dutch chemists.

This facility is part of the ESFRI facility European Infrastructure for Open Screening Platforms for Chemical Biology (EU-OPENSCREEN).

Cluster: NPEC

Research on plants in their environment

***Netherlands Plant Eco-Phenotyping Centre* (NPEC) provides scientists with next generation growth platforms to enable research designed to unravel to the interactions between plant genes and the environment. These interactions determine the growth, the health and other observable characteristics – the phenotype – of plants.**

In order to meet the growing demand for food and for (green) raw materials for construction, industry and energy supplies, agricultural production will have to double in the coming decades. Moreover, this production will have to be climate resilient and become more sustainable in order to reduce the environmental burden.

The Netherlands has traditionally played a prominent role in research on plant breeding to increase yields and improve resistance to disease, plagues and other stress factors. In practice, however, there is still a sizable gap between the theoretical yield, which is largely determined by the genetics of the plant, and the actual yield. In order to bridge this yield gap, we require a far more complete and integrated understanding of how environmental factors impact on the growth of plants.



In the past decade, rapid technological advances have led to major breakthroughs in the analysis of the DNA sequences (genomes) of wild and domesticated plant species (agricultural crops). However, it still remains difficult to correlate hereditary traits – the genotype – to observed traits and physiological properties – the phenotype – such as, for example, plant vigour, leaf shape and resistance to various stress factors.

In order to examine and optimise these traits, we clearly need to map the impact of environmental factors more accurately. Abiotic environmental factors, such as the composition and structure of the soil, soil moisture and nutrient levels, and weather and climate, all impact plant growth. At the same time, biotic factors such as interaction with the phytobiome – the (micro)organisms in, on and in the vicinity of the plant – also affect plant development.

Research on the impact of environmental factors on the plant phenotype is being conducted on different scales. By cultivating model plants in highly-controlled environmental chambers, researchers are able to simulate precise environmental factors, such as the amount and colour of light, the amount and composition of nutrients, temperature, moisture level and CO_2 level. Subsequently, each plant can be examined in real time to track the impact of these factors are on visible plant traits, physiological and biochemical changes and responses within the





associated microbiome. Based on the data that is generated and theoretical models, the researchers can make predictions that they can test with crops in greenhouses and in the open field.

At the level of greenhouse and open field experiments, plant measurement are more related to the crop – the agro-ecosystem – and the impact that environmental factors have on plant and ecosystem health. Different crops are cultivated in precision greenhouses and in fields fitted with *in situ* monitoring technology to track plant growth and other traits, from the time of sowing or planting to harvest. The difference in environmental chambers is that the environment in greenhouses is more difficult to regulate. It is even more difficult in the open field, where the impact of the climate – rain, wind and sun – and of diseases and plagues is at its maximum. The fundamental outcomes of the research on plants in environmental chambers can therefore be tested and applied in practice.

In addition to environmental chambers, greenhouses and trial plots – with their corresponding installations for climate control, irrigation, fertilisation –automated systems to conduct precise measurements on the plants are required. Growth, shape and other traits are measured using regular and infrared cameras and fluorescence monitoring in order to determine, for example, the effectiveness of the photosynthesis.

Measurements at both the micro and macro levels generate large of data that serve as the basis for modelling plant growth and responses to changes in their environment. It is therefore critical that protocols for data storage and processing be standardised to ensure that the data generated from



the environmental chamber, greenhouse and the open field experiments can be readily compared.

A better quantitative and qualitative insight into the growth and development of plants and the factors that influence these processes is a necessary step toward the development of better crop cultivation methods and strategies to fully benefit from the advantages of precision farming. Such knowledge is key to the development of new crop breeding strategies that seek to, for example, combine a high yield characteristics with efficient use of water and nutrients, and better resistance to (changing) environmental pressures.

NPEC is a partnership between Utrecht University and Wageningen University & Research, and also includes affiliated groups from Leiden University and the University of Amsterdam. NPEC will become a part of the ESFRI facility European Infrastructure for multi-scale Plant Phenomics and Simulation (EMPHASIS) through the national PhenomicsNL platform. NPEC will also become part of the FoodNexus consortium for the Food KIC-proposal – EIT Food4Future.



Cluster: UNLOCK

Unlocking Earth's microbial life

UNLOCK provides scientists with an opportunity to accelerate how we map microorganisms and their ecosystems from all corners of the Earth. The insights that this will generate will shed light on many potential applications, for example in agriculture and nutrition, health and environmental health and for new processes and products in the industry.

Microorganisms, an umbrella term for archaea, bacteria, yeast and moulds, are the oldest and by far the most common form of life on Earth. They live in the deepest depths of the oceans near hot water sources as well as in the thin air in the peaks of the Himalaya and everywhere in between. Approximately one and a half kilos of microorganisms live in our large intestine. There they play an important role in our digestion and help to keep our immune system alert. An equally complex microbiome – a microbiological ecosystem – keeps soils fertile and plants healthy.

Antonie van Leeuwenhoek was the first researcher, 340 years ago, to observe microscopic bacteria and algae in the Delft canal waters through his self-assembled microscope. A few hundred years later, in the late 19th century, Louis Pasteur proved that microorganisms were the cause of infectious diseases, but also of fermentation processes, such as those used to prepare beer, wine, yoghurt and vinegar. It has only recently become clear what a great diversity of microorganisms there is and how many – important – biological functions they fulfil.



What is also becoming increasingly clear is that so far we have only mapped a fraction of the total diversity of microorganisms. An analysis of the total DNA in a soil or water sample, for example, shows that when attempting to cultivate them in the lab we get to know only a few per cent of what are probably thousands of different microorganisms in the sample. The other approximately 95 per cent constitute the 'dark matter' of biology. Researchers know the letters and sometimes the words and part of a sentence of their DNA. But they do not know exactly which species they are dealing with and in what kind of an ecosystem they function.

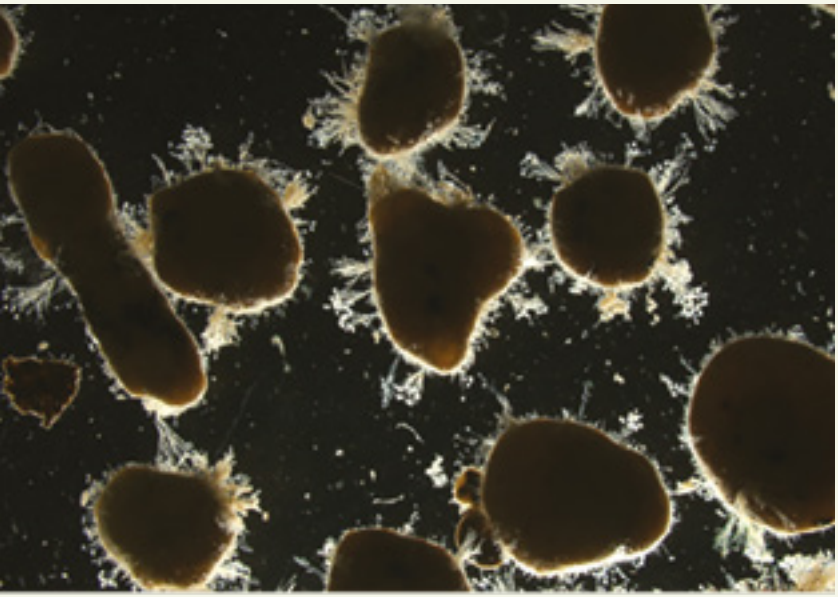
Mapping this microbial diversity, in terms of genes, species and ecosystems, provides interesting leads for a variety of applications. For example, researchers recently determined that plants affect microbial ecosystems in the soil through their roots. Conversely, the microorganisms provide sufficient nutrients for the plants and protect them against diseases and plagues. Growing mixed or successive crops can improve the microbial ecosystem in the soil, which consequently increases yield and decreases the cost of combatting disease and plagues.

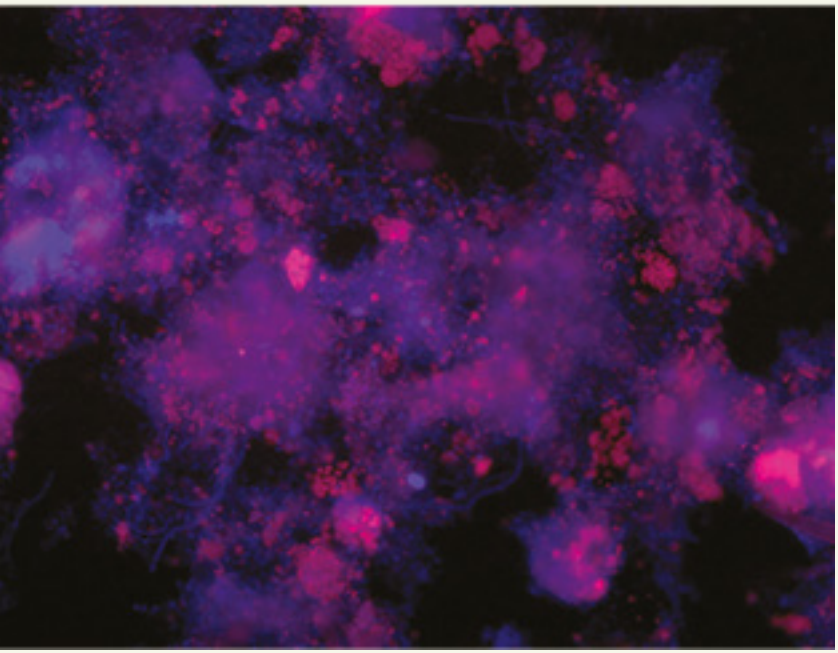


As mentioned, there is still a great deal we do not know about microbial systems, where they may be found and what their relationship is with their hosts, including us humans. New techniques are being developed in the meantime to map microbial ecosystems. Researchers can use automated processes to simultaneously determine entire DNA sequences, which they can also automatically 'translate' into the corresponding genetic traits. Scientists have made great strides in recent years in these areas, namely high throughput technologies, modelling and bioinformatics.

It is more difficult, however, to trace these DNA sequences and genetic traits to species and their mutual relationships. And that, in turn, makes it difficult to explore and exploit the microbial diversity of species and ecosystems. For example, how can we manage the evolution of a microbial ecosystem in the soil in such a way that crops increase their yield and protect themselves better against diseases and plagues? Is it possible to regulate the microbial system in the large intestine with probiotics and prebiotics, so that people have less or no allergic reaction to substances in their environment or in their food? Can we develop microbial ecosystems and used them to create closed cycles of water and raw materials – for example, to remove medical residue from wastewater or to recycle raw materials from waste?

UNLOCK provides researchers with the facilities to enter the *terra incognita* of microbial diversity, to discover how different species of microorganisms coexist and to find out which factors affect the evolution of these ecosystems. Furthermore, they can use high throughput systems to analyse and characterise





this microbial diversity at the DNA level. Using design and analysis methods from synthetic biology, the researchers can subsequently translate the diversity at the DNA level to diversity at the species and ecosystem level.

UNLOCK is an initiative of Wageningen University and Research and the Delft University of Technology. The facilities, including equipment for high throughput research and for computer-driven analysis and design, are located at both sites. UNLOCK acts as the Dutch hub in the European IBISBA network (Industrial Biotechnology & Synthetic Biology Accelerator, www.ibisba.com).

The Permanent Committee has introduced an additional condition for this facility: The facility should reach out to ESFRI facilities Mirri, ISBE and/or ELIXIR.

Cluster: uNMR-NL

Magnetic atomic nuclei unravel molecules and (bio)materials

The ultra-high field magnets at the NMR-NL facility makes it possible to study complex materials, biomolecules and living organisms in even greater detail than previously.

Nuclear Magnetic Resonance Spectroscopy (NMR) and Magnetic Resonance Imaging (MRI) have become versatile and indispensable techniques in recent decades in areas such as materials research, chemistry, biology and the biomedical sciences. Magnetic resonance techniques use the properties of atom nuclei that are vibrated in a strong magnet.
Researchers are using this technique intensively in a range of areas in fundamental and applied research. That varies from developing new medicines to understanding the molecular mechanisms that lead to the process of photosynthesis. These techniques are also important for research on the strength of plastics and the development of efficient batteries.

The greater the magnet's field strength, the more opportunities there are to use NMR to study increasingly complex systems in more and more detail. Thanks in part to developments in the area of superconductivity and hybrid magnet technology, field strengths of more than 22 tesla (ultrahigh-field NMR) are now possible.



In 2011 five university NMR centres established a consortium with TI-COAST, the public–private community for analytical science and technology. This consortium's objective is to manage the use of their NMR facilities and develop NMR with ultra-high field strengths in the Netherlands. In 2015 an NMR facility was installed in Utrecht with a field strength of 22 tesla and a proton frequency of 950 MHz. It is intended to be used for fundamental research in the area of structural biology and (bio)materials. This system can be used for research on both solution state and solid state NMR, but also for modern MRI research. A magnet with a field strength of 28 tesla (1.2 GHz) is currently in development. In the next phase of the uNMR-NL project – the period until 2018 – a similar system will be installed in Utrecht.

What is special about how uNMR-NL has been designed is that the five original individual NMR centres have united in a consortium that is devoted to providing Dutch and international scientists with access to high-field NMR equipment. They also jointly founded the Netherlands Magnetic Resonance Research School (NMARRS), and agreements have been made within the consortium about the distribution of tasks and specialisations.





NMR research in Leiden, for example, concentrates on understanding the structure and dynamics of proteins and DNA in relation to their function. In addition, new methods are being developed to study protein–protein interaction and very large protein–DNA complexes. The researchers in Leiden are also mapping the quantum–chemical processes and molecular mechanisms that are responsible for photosynthesis and its regulation. NMR is subsequently combined with Electron Microscopy (EM) and computer models. The researchers thus hope to translate these natural processes into artificial photosynthesis, a potentially clean source of energy for the future.

The in-situ analysis of molecules is one of the spearheads of the NMR facility in Utrecht. An example of this is the study of the structure and dynamics of growth factor receptors, which play a role in many types of cancer, in their natural environment. Research on protein–DNA interaction, which is important for gene regulation, is another important research focus here. Furthermore, for several years now scientists have been working on the development of technologies and the preparation of samples to increase NMR sensitivity, and on software to model biomolecular complexes.

The main focus of research in Nijmegen is new functional materials. The emphasis is on materials that store (batteries) and convert (solar cells) energy and on polymers: from industrially relevant engineering plastics to hydrogels for biomedical applications. NMR is therefore making it possible to unravel the properties of materials up to the molecular level. Advanced measurement technologies are being developed for this purpose, which focus on miniaturisation and hyperpolarisation methods to be able to detect extremely small sample volumes, interfaces or very low concentrations of a molecule.



Scientists at the Wageningen NMR Centre are developing NMR and MRI hardware and methods. These will be used to study nanoparticles, plants and nutrition, but also to analyse bodily fluids to learn more about the relationship between food and health. The 3T MRI scanner for intact plants and trees is unique in the world. It is also possible to study a single cell using the extremely small NMR electronics that have been developed.

uNMR-NL also provides access to Magnetic Resonance Imaging (MRI) and spectroscopy instrumentation (MRS) through the biomedical group at TU Eindhoven. Research is being conducted here on MRS/MRI methods for the diagnostics of cardiovascular disease, diabetes and cancer, for example. In the near future, the MRI/MRS part of uNMR-NL will be reinforced with research groups in the field of preclinical imaging and MRS/MRI method development.

Private parties from different sectors have access to uNMR-NL's facilities through TI-COAST. In addition, COAST manages a range of other largely complementary rare or unique analytical facilities that are available to the public and private participants in the community.

uNMR-NL is a consortium in which the NMR centres of Utrecht University, Leiden University, Wageningen University and Research and the Eindhoven University of Technology, as well as TI-COAST, work together.

This facility is part of the ESFRI facility Integrated Structural Biology Infrastructure (INSTRUCT).


700
500
400
BORO
3.3
1000 ml

Cluster: X-omics

In search of the molecular basis of life

The X-omics cluster (pronounced: cross-omics) provides researchers at universities, academic hospitals and companies with access to advanced facilities to study the building blocks of life in their natural environment: cells, tissues and bodily fluids.

Many of the major social challenges of our time are related to the functioning of our biological systems. That varies from maintaining and improving our health to ensuring sufficient and safe food, improving the quality of the environment and the transition to a chemical industry based on biological raw materials. Biological systems, however, are extremely complex in terms of composition, structure and function. For a fundamental understanding of biological systems we need to return to the building blocks: DNA (the carrier of genetic information), RNA (the regulating system), proteins (the workhorses) and metabolites (the intermediate products of reactions taking place in a cell).

A better understanding of how these biomolecules function in interaction with each other is the key to a better understanding of biological systems. These include for example the aetiology and development of diseases, the growth and development of agricultural crops, the action of enzymes in the conversion of biomass into useful products and many other processes that are important for health, well-being and the economy.



Research on different kinds of biomolecules is often designated by the suffix -omics:

- *Genomics* focuses on the study of DNA and RNA. It not only involves determining the basic sequences and the variation therin, but also the question of which parts of the DNA are activated and how this is regulated and how the billions of letters of DNA 'translate' into individual traits and disease.
- *Proteomics* concerns the study of the structure and function of proteins and their interactions, both in the manufacture and breakdown of cells and reactions in the cell. Every gene can lead to multiple forms of the same protein, which is one of the reasons why biological systems are so complex. In addition to the regulation of protein expression there is also the important question of how new proteins are modified so they can perform their function.
- *Metabolomics* focuses on metabolites, the intermediate or end products of biochemical reactions in cells, tissues, organs and entire organisms. The classic method has been to study blood and urine, but today the composition and concentration of hundreds to thousands of metabolites in the body can be measured simultaneously.

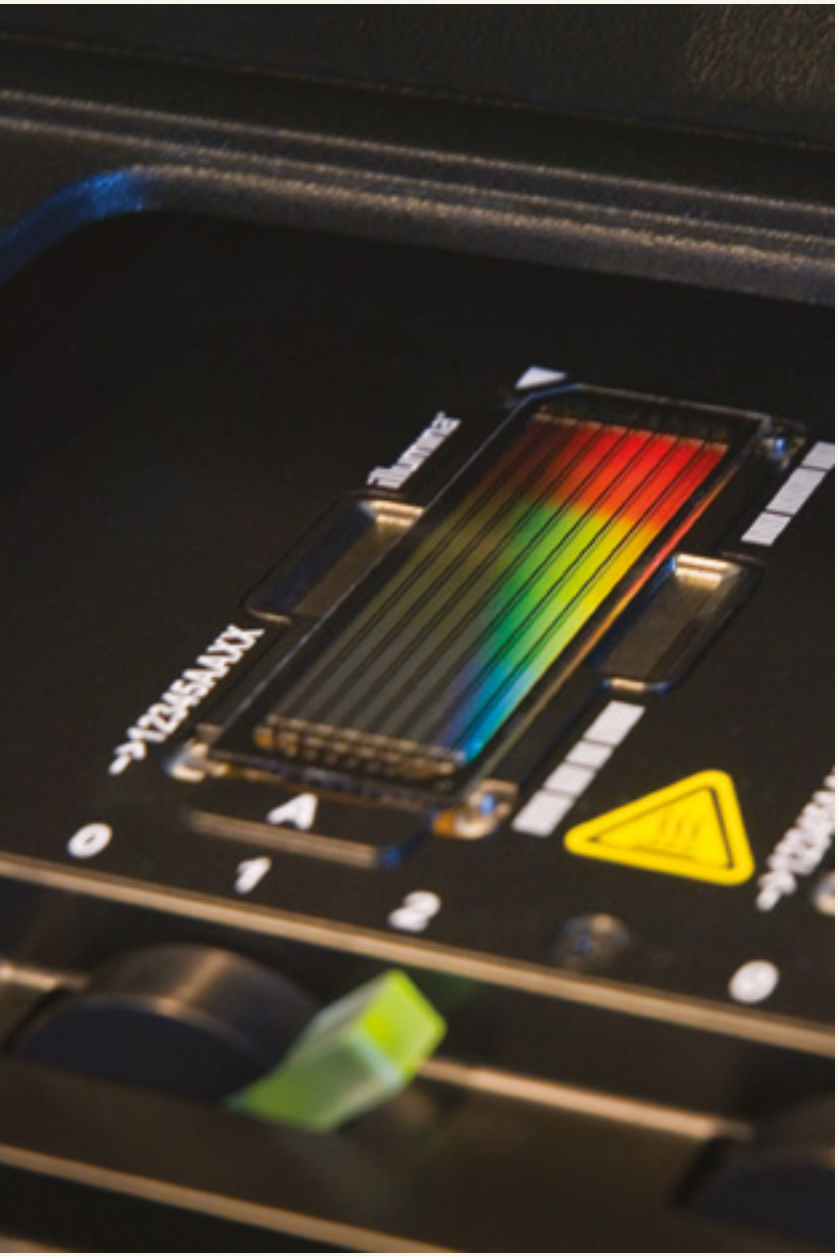


-Omics research uses many different methods and techniques, individually and in combination. Nowadays, DNA sequencing occurs (almost) completely automatically, as robots isolate and offer the DNA to 'sequencers', which determine the sequence at high speed, after which it is analysed with sophisticated algorithms and information from DNA databases. In addition to new insights about the relationship between DNA and traits, *genomics* is also clinically important for tracing hereditary diseases and personalizing treatment, e.g. for cancer.

In *proteomics* scientists analyse proteins – intact or cut into pieces – e.g. in a mass spectrometer that maps with great accuracy both the protein sequence and modifications to it. This enables researchers to detect abnormalities in proteins and disruption of protein-protein interaction.

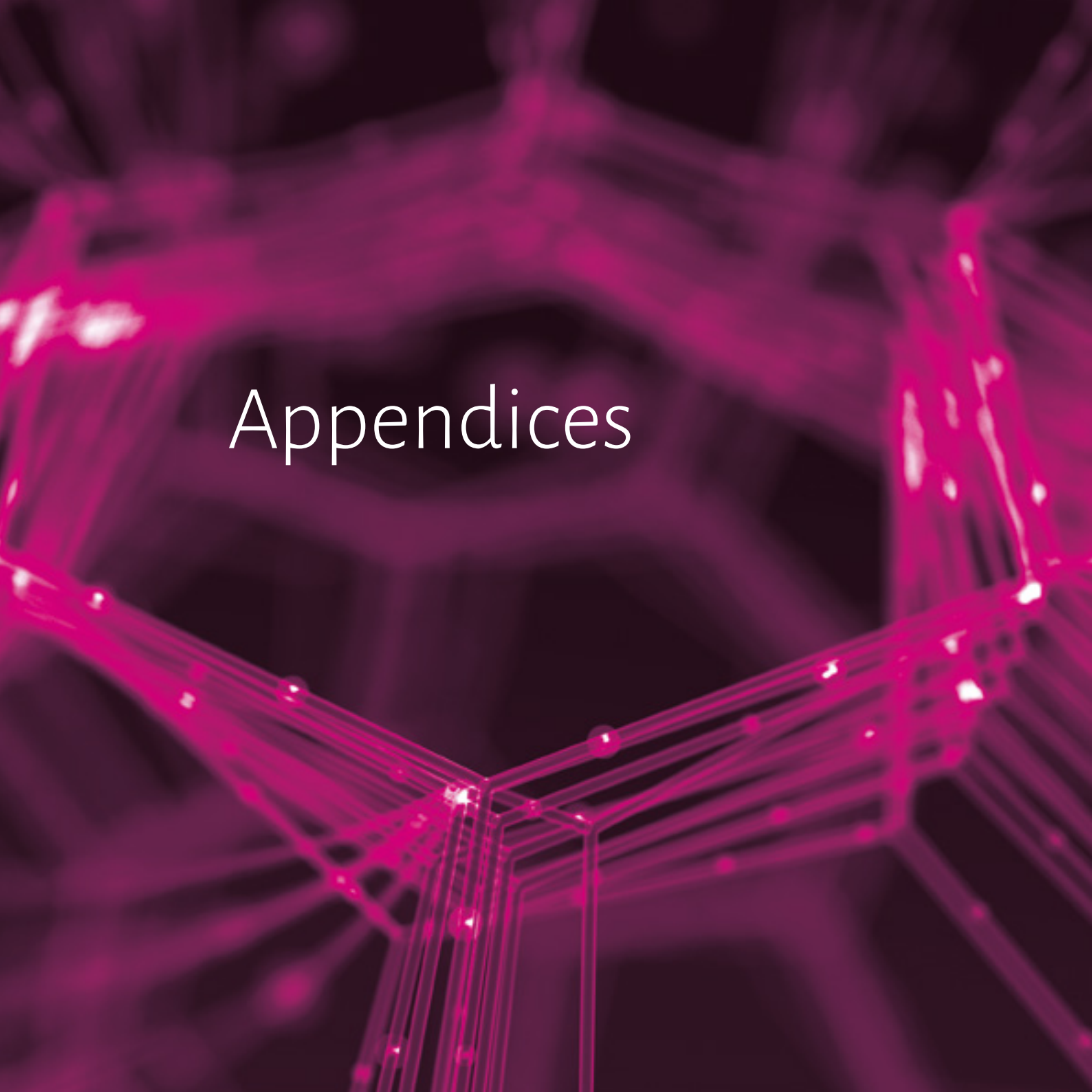
Metabolomics uses a range of analytical techniques, often automated, to map the metabolome (the full set of metabolites) of organisms. As a result, abnormalities that could potentially affect the health of humans, animals and plants can be identified at an early stage. Another application is the identification of substances in plants – secondary metabolites – that could be at the basis for new medicines.

The X-omics cluster provides researchers with direct access to a range of the best facilities in the fields of *genomics*, *proteomics* and *metabolomics* in the Netherlands. The virtual clustering of these fields is important in order to respond optimally to rapid technological developments in –omics research. Specialised expertise can also be further developed in an efficient way in this cluster, such as research design, sample preparation, the preparation of samples, how to operate the equipment and how to interpret results. -Omics research generates large amounts of data, and the linking, integration and analysis



of these data will benefit from bringing together the best expertise in the Netherlands.

The X-omics cluster is spread across facilities at UMC Utrecht and Radboudumc in the area of genomics; at Utrecht University, the University of Groningen, UMC Groningen, Radboudumc and ErasmusMC in the area of proteomics; and at Leiden University in the area of metabolomics. At the national level there are links with Health RI and Bioscopy. At the international level there are links with ESFRI-Landmarks for biobanks (BBMRI, page 67), bio-informatics (ELIXIR, page 73), translational medicine (EATRIS), the ESFRI facility Integrated Structural Biology Infrastructure (INSTRUCT) and the ESFRI preparatory phase in the area of systems biology (ISBE, page 76).



Appendices

Appendix 1: Aligment with the NWA

Facilities	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
Humanities/Social Sciences																									
CLARIAH-PLUS (cluster)						✓	✓	✓	✓	✓	✓	✓		✓	✓									✓	✓
ODISSEI (cluster)	✓		✓			✓	✓	✓	✓	✓	✓	✓			✓	✓			✓		✓	✓		✓	✓
Science/Technology																									
ATHENA					✓																				
CESAR						✓	✓		✓	✓	✓	✓	✓		✓	✓	✓								
DUBBLE	✓	✓	✓	✓	✓	✓		✓	✓		✓	✓		✓	✓		✓	✓	✓	✓	✓		✓	✓	✓
E-ELT				✓	✓				✓	✓															
EPOS-NL (cluster)						✓	✓		✓	✓	✓	✓	✓		✓	✓	✓		✓	✓			✓		
ESS	✓	✓	✓		✓					✓	✓	✓	✓	✓			✓						✓	✓	
ET				✓					✓									✓					✓	✓	
HFML/FELIX (cluster)	✓		✓	✓	✓			✓	✓	✓		✓	✓		✓		✓	✓					✓	✓	
ICOS-NL				✓		✓					✓	✓								✓				✓	
KM3Net					✓																				
LHC detector upgrades			✓	✓	✓				✓															✓	
NanoLabNL (cluster)	✓	✓		✓	✓			✓		✓	✓					✓	✓	✓	✓				✓	✓	
NC2SM						✓					✓	✓		✓	✓		✓	✓	✓	✓			✓	✓	✓
RV Pelagia/ NMRF				✓		✓	✓		✓	✓		✓	✓		✓	✓				✓					
SKA				✓	✓				✓	✓	✓							✓					✓	✓	
Solar Cells (cluster)										✓	✓	✓			✓		✓	✓	✓				✓		

Facilities	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
Medical/Life Sciences																									
BBMRI (cluster)	✓	✓	✓	✓	✓	✓		✓	✓		✓				✓	✓				✓	✓	✓		✓	✓
Bioimaging AM (cluster)	✓	✓	✓	✓				✓										✓	✓	✓	✓		✓	✓	
BSL3	✓		✓				✓	✓	✓															✓	
ELIXIR-NL (cluster)	✓	✓	✓	✓				✓	✓	✓		✓	✓				✓					✓		✓	
ISBE	✓	✓	✓					✓	✓	✓			✓		✓		✓		✓	✓			✓	✓	
MCCA (cluster)	✓	✓	✓					✓	✓															✓	
MRI and Cognition (cluster)	✓	✓	✓					✓	✓												✓	✓		✓	
MRUM	✓		✓								✓				✓									✓	
NEMI (cluster)	✓	✓	✓	✓	✓			✓	✓	✓		✓					✓	✓			✓	✓	✓	✓	
NIEBA (cluster)				✓					✓		✓	✓	✓		✓				✓	✓		✓		✓	
NL-OPENSCREEN	✓		✓																						
NPEC (cluster)											✓	✓	✓		✓		✓		✓	✓				✓	
UNLOCK (cluster)	✓	✓	✓	✓	✓				✓	✓	✓	✓	✓		✓		✓		✓	✓			✓	✓	
uNMR (cluster)	✓	✓	✓	✓	✓							✓	✓				✓	✓					✓	✓	
X-omics (cluster)	✓	✓	✓	✓		✓		✓	✓			✓	✓							✓	✓	✓		✓	

Route and description

1 Personalised medicine
2 Regenerative medicine
3 Health-care research, prevention and treatment
4 The origins of life – on earth and in the universe
5 The building blocks of matter and the origins of space and time
6 Resilient and sensible communities
7 Between conflict and cooperation
8 The brain, cognition and behaviour: learn, develop and build
9 Using big data responsibly – searching for patterns in big databases
10 Smart industry
11 Smart, liveable cities
12 The circular economy and resource efficiency
13 Sustainable production of safe and healthy food
14 Art: research and innovation in the 21st century
15 Environmental quality: the value of nature, the landscape, soil, the climate, water and the environment
16 Logistics and transport in an energy-innovative and sustainable society
17 Energy transition
18 The quantum/nano-revolution
19 Sustainable Development Goals
20 The Blue Route: water as a path to innovation and sustainable growth
21 Sport and exercise
22 Youth and education
23 Materials – Made in Holland
24 Measure and detect: always, everything and everywhere
25 The Living past: the significance of the past in an innovative society

Appendix 2: Definition of Large-Scale Scientific Infrastructure

Large-scale scientific infrastructures are facilities, resources and services that a research community uses to conduct research and promote innovation in its field. Where relevant, the infrastructure can also be used for other purposes than research, for example education or public services. Among other things, it concerns important scientific equipment or collections of instruments; knowledge-based resources such as collections of natural specimens, archives and collections of scientific data; e-infrastructure such as (interlinked) data files, and computer systems and communication networks; and any other unique infrastructure that is critically important for achieving excellence in research and innovation. This could refer to infrastructures situated in a single location, or virtual or distributed infrastructures (in the Netherlands or abroad).

The following points apply for distributed scientific infrastructures – to which the National Roadmap clusters also belong:

- They must provide one central access point for researchers and external organisations, even if the infrastructure is spread across multiple locations;
- They must have one management board responsible for the entire infrastructure as well as a legal structure;
  OR
- They have committed their partnership in a consortium agreement.[1]

An infrastructure in the Dutch Landscape for Large-Scale Scientific Infrastructure must pursue a policy of access for research according to the European Commission's European Charter for Access to Research Infrastructures.[2] This charter defines three modes of access:

- Access based on scientific excellence
- Access based on pay-for-use
- Broad access

At the very least, an infrastructure that is also part of the National Roadmap for Large-Scale Scientific Infrastructure must provide access based on scientific excellence or promote a broad access policy. Infrastructures in the National Roadmap are forbidden to provide access based exclusively on pay-for-use.

The size of the infrastructure, in terms of total capital investment[3] and operating costs for 5 years, amounts to at least 10 million euros. These costs do not include accommodation costs for the facility. The operating costs pertain exclusively to the costs needed to make the facility accessible. In other words, they do not include the costs for the research programme.

[1] This consortium agreement contains, at the very least, the following points:
- Who is participating in the consortium?
- What are the consortium's objectives?
- How is governance arranged?
- Agreements about determining priorities (how are priorities determined and how does the consortium handle situations in which there is a lack of consensus?)
- Agreements about funding the investments (e.g. matching)
- Agreements about access to the facilities (for consortium parties and external parties)
- Agreements about IP rights

[2] The complete text of the charter can be found https://ec.europa.eu/research/infrastructures

[3] Capital investment is intended for the development, purchase/construction of the infrastructure in question, or the cost of adapting an existing infrastructure so that it can be used to make scientific breakthroughs.

Appendix 3: Composition of the Permanent Committee for Large-Scale Scientific Infrastructure

Chair

Hans van Duijn (1950)) is former rector magnificus of the Eindhoven University of Technology (TU/e). He held this position from April 2005 to April 2015. He is also a professor at TU/e and Utrecht University (UU). He is a member of the Supervisory Board of Erasmus University Rotterdam, chairman of the board of the J.M. Burgerscentrum and scientific director of the UU-TU/e Darcy Center.

Van Duijn studied applied physics at the former Technical University of Eindhoven and obtained his doctorate in 1979 in mathematics at Leiden University. He has worked, among other places, at the Delft University of Technology (TUD) as university (senior) lecturer and later as part-time professor in combination with a position at the Centrum voor Wiskunde en Informatica (CWI) in Amsterdam. In 2000 Van Duijn was appointed professor of applied analysis at TU/e.
In 1996 he received the Best Professor Award from TUD and in 1998 the Max Planck Award from the German government.

Committee members

Humanities/Social Sciences (3 members)

Ans van Kemenade (1954)) is professor of English linguistics at Radboud University Nijmegen (RU). Her research interests include grammatical variation and historical changes in West Germanic languages. Van Kemenade has extensive executive experience, including a period on the NWO Humanities Divisional Board where she was responsible for the infrastructure portfolio. Van Kemenade was recently research director and vice-dean of research at RU's Faculty of Arts.

Kees Aarts (1959)) is professor of political institutions and behaviour and also dean of the Faculty of Behavioural and Social Sciences at the University of Groningen (RUG). He conducts research on how democracies function, elections and electoral behaviour, both in the Netherlands and from a comparative international perspective. Aarts is closely affiliated with long-term and internationally coordinated projects such as the Dutch Parliamentary Electoral Studies and the European Social Survey. Aarts is also chairman of KNAW's Big Data foresight committee and chairman of the scientific advisory council of DANS.

Sally Wyatt (1959)) is professor of digital cultures in development at Maastricht University (UM). She conducts a great deal of research on the social aspects of digital technology, including how people use the internet to find health-related information. Wyatt is also programme leader of KNAW's eHumanities group and director of the Science, Technology and Modern Culture (WTMC) research school.

Medical/Life Sciences (3 members)

Folkert Kuipers (1957)) is professor of paediatrics at the University of Groningen (RUG). He specialises in the physiology and pathophysiology of the liver and intestines in congenital and developmental metabolic diseases in children. From 2008 to 2016 Kuipers was dean of the Medical Faculty of the University of Groningen/ University of Groningen Medical Center (UMCG) and vice-chairman of the Board of Directors of UMCG. On 1 March 2016 he returned as head of the Paediatrics Laboratory at UMCG to continue his scientific career.

Titia Sixma (1962) is head of the Biochemistry Section at the Netherlands Cancer Institute (NKI) and also professor by special appointment at Erasmus Medical Center Rotterdam. Sixma does research into protein signal transduction and DNA damage recovery in cancer. She is a member of various advisory boards and user committees in the context of biomedicine and structural biology. Sixma is a member of the NWO Chemical Sciences Divisional Board. She is also a member of the European Molecular Biology Organization (EMBO) and a member of Academia Europaea and KNAW.

Iris Sommer (1970)) is professor of psychiatry at Utrecht University (UU). She conducts research on brain processes that lie at the basis of hallucinations and other symptoms of schizophrenia, including hearing voices in the head. Sommer is a member KNAW's Young Academy. She is also a member KNAW's Committee for Large-Scale Research Facilities and the Netherlands Board on Research Integrity (LOWI).

Science/Technology (2 members)

Frank Linde (1958)) is professor of experimental high-energy physics – elementary particle physics – at the University of Amsterdam. He has worked on experiments at large particle accelerators such as LEP (Z and W bosons) and CERNS's LHC (discovery of the Higgs boson) in Geneva. From 2004 to 2014 he was director of the National Institute for Subatomic Physics (NIKHEF). He is chair of APPEC Astroparticle Physics until 2018. Linde has extensive hands-on and managerial experience with large scientific infrastructures, for example with the detector in the L3 experiment of the large particle accelerator LEP and the large muon spectrometer of LHC's ATLAS experiment.

Ewine van Dishoeck (1955)) is professor of astronomy at Leiden University. She specialises in molecular astrophysics, especially the chemical processes that occur in clouds where new stars and planets are born. She was closely involved in the creation of several large telescopes, in space and on Earth. Van Dishoek is chair of the KNAW Committee for Large-Scale Research Infrastructures. She is also a member of KNAW, a foreign member of the American National Academy of Sciences and a member of the German National Academy of Sciences, *Leopoldina*. Van Dishoeck received an NWO Spinoza Prize (2000) and an Academy Professor Prize.

Technical and Applied Sciences (3 members)

Gerard Beenker (1954) was scientific director of NXP Semiconductors until 2014. He is currently affiliated with the Eindhoven University of Technology as advisor of strategic partnerships in the area of the development of high-tech systems. Beenker has worked in various committees and boards: he was a major driver for the Components and Circuits roadmap in the High Tech (HTSM) top sector, a member of the technology and innovation committee of the employers› organization VNO-NCW, and a member of the board of STW.

Jan Willem Kelder (1949) is vice admiral and former commander of the Royal Dutch Navy (2005 to 2007). As chairman of the Board of Admiralty he was responsible for implementing the defence and navy policy, managing and preparing, whether for combat or not, the staff and units of the Royal Dutch Navy. After early retirement in 2008, he became a member of TNO's Executive Board and chairman of the Council for Defence Research (2009 to 2103). As a board member of TNO Kelder was responsible for TNO's infrastructure policy and delivery.

As chairman of the Council for Defence Research Kelder was responsible for the planning and implementation of research at TNO commissioned by Defence. Subsequently he was acting CEO of TNO's Executive Board until his retirement in March 2015.

Andrzej Stankiewicz (1954) is professor of process intensification at the Delft University of Technology and director of the Institute of Process Technology at TUD. Stankiewicz conducts a wide range of research on sustainable and efficient processes and devices, which use green electricity as a primary source of energy. He was the founder and first chair of the Process Intensification workgroup at the European Process Intensification Centre. Stankiewicz is currently chairman of the board at the European Process Intensification Centre (EUROPIC).

Credits

Foreword: *Photographer: Ivar Pel* page 3

Introduction: *Photographer: Kick Smeets* page 5

Interview with Sander Dekker: *OCW* page 10

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EPOS-NL: *Photographer: Ed van Rijswijk* page's 33-35.
ESS: *European Spallation Source ESS* page 37.
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RV Pelagia/NMRF: *NIOZ* page 56.
SKA: *SKA Organisation* page 58
Zonnecellen: *Photographer: Mark Knight* page's 61-63.

BBMRI: *Humane Genetica LUMC* page's 66-68.
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Colophon

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