Dutch national research agenda

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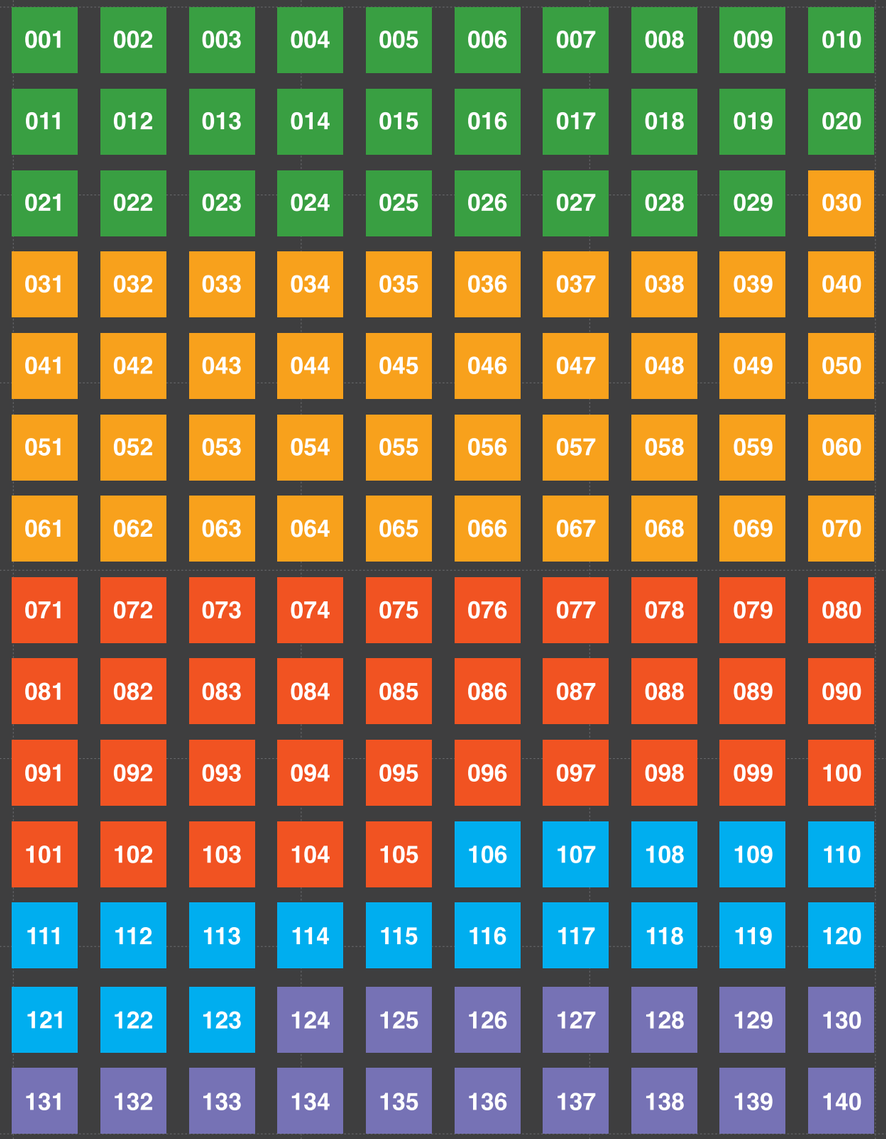
Dutch national research agenda



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Foreword

The Dutch National Research Agenda was drawn up by the Knowledge Coalition[1] and is meant to point the way for Dutch research over the next ten years. It is also a response to the Dutch Government's policy document *Vision for Science*.[2] At the request of the Minister of Education, Culture and Science and the Minister of Economic Affairs,[3] the Coalition – assisted by a Liaison Group[4] – conducted an extensive public consultation procedure and subsequently identified various challenges in fields in which Dutch researchers are likely to excel, and which can further the interests of society and boost the Dutch knowledge economy. The relevant issues reflect the strengths of Dutch research, the challenges facing society today, and the economic opportunities that have presented themselves.

The National Research Agenda, on which many different people have worked, also addresses many different people. It calls on researchers, businesses, the authorities, and civil society to join forces by participating in, funding, and valorising research. It also invites the public to interest itself in research, and it promotes collaboration throughout the entire knowledge value chain. It is therefore an agenda that unifies and builds bridges between many different parties and sectors.

The purpose of the National Research Agenda is to better equip Dutch researchers to find solutions to the challenges of our time and to foster the necessary transitions in such areas as energy use, health care, social and democratic progress, safety and security, and world food security. These are complex issues typified by conflicting values, mounting political pressure, and major economic interests. Such complexity requires the involvement of multiple parties and approaches, as well as innovative new connections and partnerships. The National Research Agenda aims to spur us into forging uncommon alliances and exploring unanticipated relationships.

It does not, however, cover the entire field of science, and is not meant to be a comprehensive agenda for research across the board. The Ministers' message was clear: every matter included in the National Research Agenda should be important, but not every important matter be included in the National Research Agenda. Small-scale, specialist research is no less significant and merits our support and sympathy, but the National Research Agenda focuses specifically on interdisciplinary and multisector challenges. It should generate more synergy in research as a whole and augment the consistency, efficiency and impact of Dutch research.

[1] Consisting of Dutch research universities (VSNU), universities of applied sciences (VH), organisations for applied research (TO2), employers (VNO-NCW and MKB-Nederland), university medical centres (NFU), the Netherlands Organisation for Scientific Research (NWO), and the Royal Netherlands Academy of Arts and Sciences (KNAW).

[2] Ministry of Education, Culture and Science, *Wetenschapsvisie 2025 - keuzes voor de toekomst*, November 2014.

[3] Ministry of Education, Culture and Science, *Opdracht Ontwikkelen Nationale Wetenschapsagenda*, 25 November 2014.

[4] The Liaison Group offered solicited and unsolicited advice, attended conferences, and built relationships with strategic agendas, knowledge-based institutions, and advisory bodies. Its members acted in a private capacity and represented a wide range of different civil society organisations.

Part I Introduction

A gold mine of questions

Questions form the basis for the National Research Agenda. Curiosity starts with a desire for knowledge and the will to do something with it. People ask questions for all sorts of reasons, for example to understand, evaluate, or influence something. Whether change comes in the guise of scientific breakthroughs, economic revitalisation, or social progress, it often begins with a question. The National Research Agenda is an ode to the question – major or minor, hesitant or self-assured, basic or applied.

Other European countries have also begun to develop a national science or research agenda, but the Dutch approach has been genuinely unique. Instead of asking a small group of experts to define the Dutch National Research Agenda, the Knowledge Coalition invited the general public to submit questions, whether out of personal curiosity or on behalf of a group. All questions about science were welcome. This approach, unique in the world, produced 11,700 questions[5] addressing the entire breadth of scientific research – a result that exceeded all expectations.

Multidisciplinary juries made up of top researchers engaged in a series of discussions and workshops to reduce the questions to 140 cluster questions. The public's questions thus served as building blocks and a source of inspiration for the issues that now form the focus of the National Research Agenda.

Assembling the National Research Agenda from the bottom up sparked a great deal of enthusiasm and energy in the general public and generated considerable media interest. Many of those who submitted questions were ordinary people with an interest in science. To help this group communicate with scientists about science, the National Research Agenda website (www.wetenschapsagenda.nl) was furnished with a special function (labelled 'In Conversation') that allows research institutes and other knowledge-based institutions to contact those who had submitted questions without infringing on their privacy. Dozens of meetings and events took place while the National Research Agenda was still on the drawing board. Many people who submitted questions communicated directly with researchers prepared to answer their questions. All this shows how deeply interested the Dutch public is in science, and how willing the research community is to take the public's and the private sector's expectations seriously.

The process of drafting the Dutch National Research Agenda, then, has already led to new interactions between researchers, policymakers, businesses, and the general public. As a result, the National Research Agenda has become a public good that has already gained widespread support.

[5] See Appendix 1 for the figures.

The National Research Agenda focuses on fields in which Dutch research excels and in which we can expect to see considerable progress over the next ten years. In Part II of the Dutch National Research Agenda, we present the 140 cluster questions one by one over the course of five chapters and explain, in each case, their connective power.

For example, all 140 questions call for an interdisciplinary approach. In many cases, they transcend the boundaries of larger research domains (humanities, life sciences, natural sciences, social sciences, and technology and engineering) and require collaboration between two or more of these domains to find answers.

One good example is the question *How can we manage the unpredictability of complex networks and chaotic systems?* It is a relevant problem inmany different fields. Complex networks play a role in communication, information, traffic, transport, finance, energy, the climate, and our brains. The search for answers starts with mathematics, but also branches out to many other disciplines and subdisciplines, including public administration, biology, chemistry, economics, brain research, information science, physics, and spatial planning.

The solutions to many problems lie in a combination of basic, applied, practice-based, and at times policy-driven research, either combined or in succession. The question *Why is biodiversity important and how do we protect it?* is an example of this. It connects basic ecological research with policy-driven and applied ecology. But it also encompasses research carried out by an army of volunteers and in that way serves to engage the public in science ('citizen science projects').

Many questions are multidimensional in nature. They are not only descriptive or explanatory but also have a normative, evaluative, or even a design purpose, for example. The question *What do humans and nature mean to each other and what is the ideal relationship between the two?* expresses a normative quest to ascertain the intrinsic value of nature and the ideal relationship between human beings and nature. But it also involves describing and analysing the impact of human activity on nature, the ethical choices that underpin the development of algorithms, and the design of simulations.

The National Research Agenda offers those active within the science system an ideal opportunity to seek each other out. The website offers visitors information on the research agendas of Dutch research institutes.[6] These institutes represent the supply side of science, and their information makes it possible to compare the issues addressed in the National Research Agenda with the topics and priorities identified by Dutch knowledge-driven institutions. The website also offers information on the policy agendas[7] of organisations that contract research, representing the demand side.

Policy agendas can be found on various geographical orders of scale. Globally, we have the United Nations' Sustainable Development Goals (SDGs). In Europe, the European Commission has identified a number of Societal Challenges in one pillar of the Horizon 2020 Agenda. In the Netherlands, the top economic sectors have formulated Knowledge and Innovation Agendas (KIAs) and our government ministries have strategic knowledge agendas, clarifying the relationship between the National Research Agenda and national policymaking. Finally, provincial and regional authorities develop their own research and innovation agendas, partly in an effort to obtain funding from the European Regional Development Fund (ERDF).

[6] See Appendix 2 for the research agendas.
[7] See Appendix 3 for the policy agendas.

For each cluster question in the National Research Agenda, the website shows which of the many parties on both the supply and demand side of science are working on it in one way or another. These parties may not know each other or be acquainted with each other's work. One party may be tackling the question (or part of the question) from the perspective of basic research, while another is working on it with more practical ends in mind. Pointing out their shared interest may help them get to know each other, coordinate their efforts, and work together in future. The information will spur new alliances between NWO and Academy research institutes, research universities, UMCs, government expertise centres, businesses, universities of applied science, institutes of applied research, ministries, and civil society organisations.

For example, the question *How do we arm ourselves against natural disasters such as earthquakes, volcanic eruptions, and floods?* concerns many different parties, not only in the Netherlands but also elsewhere. As the world population grows, the risk of disasters increases. A better understanding of the Earth as a system requires close cooperation worldwide. Technological progress is vital to our obtaining basic knowledge in this area, but we must also develop the technology to make buildings, bridges, and flood barriers more disaster-proof. The private sector is indispensable in all this. Disasters have numerous implications for local, national, and international aspects (administrative, social, and societal) in which the authorities and civil society organisations are closely involved. If we analyse all these various research and policy agendas, we see that their underlying priorities and themes are well represented in the Dutch National Research Agenda and can be linked to many other questions. A search routine embedded in the National Research Agenda means that it can function as a digital tool for linking broad subcategories of questions to other research agendas and to larger groups of interested parties.

A route map for navigating the research landscape

It was against this background that the idea emerged of plotting 'routes' through the National Research Agenda. Routes help identify a subcategory of interrelated questions concerning a complex theme. They make it possible to tap into and mobilise all the strengths of the Dutch knowledge infrastructure to develop a better approach, for example to the European Commission's Societal Challenges. The routes thus serve as a tool for seeking out new partners. Bringing together important lines of research from disparate scientific disciplines will also reveal new approaches that boost the success and impact of research.

The National Research Agenda has thus become a route map in which the cluster questions bridge the gap between research supply and research demand. Users can perform different types of searches and seek out relationships between differing cluster questions, or between a cluster question and the priorities identified in other agendas. That is what is unique about the route map as a tool: it gives us access to the full breadth of Dutch research. A route may inspire us to come up with new solutions, challenge us to make choices, and suggest the ideal approach to tackling a complex issue.

Part III describes 16 example routes. Each one of these is inspiring and holds out great promise within a culture as open to collaboration as the Dutch research community. The 16 routes outline some key challenges for science. At the same time, they demonstrate how the route tool might mobilise Dutch researchers and what path they must take to bring these challenges to a successful conclusion. The routes are a tangible illustration of the connective power of the National Research Agenda. The Knowledge Coalition selected the 16 routes for their relevance to society, the economy, and science itself. These routes are only a beginning, and important new routes will be added in the course of time. Although the list is incomplete, it nevertheless calls for commitment. It will be up to the Knowledge Coalition itself to add further routes.

With its 140 cluster questions and route tool, the National Research Agenda is creating a framework for more consistency and coordination in research. In that respect, it will serve as a compass with which to fine-tune existing research agendas. It should not, however, be seen as a substitute for those agendas. On the contrary, it supplements them. The compass focuses specifically on interdisciplinary and multisector challenges, pointing the way towards promising alliances. The resulting cross-pollination will generate synergy in the science system as a whole and make the system of direct, indirect, and contract funding more consistent.

For example, the *'Personalised medicine'* route could lead to an alliance between parties in the top Dutch economic sectors Life Sciences and Health and High Tech Systems and Materials, the UMCs, the Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital (NKI/AvL), the Hubrecht Laboratory, TNO and the National Institute for Public Health and the Environment (RIVM), and research universities and bio-tech businesses, with technological, biomedical, and psychosocial research being integrated. That would allow these parties to move into position for EU funding programmes such as (in this case) the Societal Challenge 'Health, Demographic Change and Wellbeing'.

Another example is the route *'Responsible use of big data'*. This route connects mathematics and statistics to economics, law and ethics, connects retail practice with the protection of personal data, joins basic information science and hardware, and involves interested individuals and relevant research groups in all sectors of society. According to a recent report by the Advisory Council for Science, Technology and Innovation (AWTI),[8] developing a consortium along this route would allow the Netherlands to upgrade its own information technology and ICT skills and to take the lead in Europe (for example in response to the Societal Challenge 'Europe in a Changing World' or to the Key Enabling Technologies). A number of promising initiatives have already emerged, such as Commit2data.

The route *'Sustainable and safe food production and health'* also unites a huge number of parties. This route is an excellent example of a worldwide challenge that the Netherlands can address by drawing on its broad scientific, industrial and social traditions. The route touches on a vast number of social and knowledge agendas, for example the report by the Scientific Council for Government Policy (WRR) on food policy *(Naar een voedselbeleid)*, the Agri & Food 2016-2019 roadmaps, the Joint Programming Initiatives 'Agriculture, Food Security and Climate Change', 'Healthy Diet for a Healthy Life', and the Horizon 2020 Societal Challenge 'Food Security, Sustainable Agriculture and Forestry, Marine, Maritime and Inland Water Research and the Bioeconomy'. It is also related to the global food security agenda of the United Nations ('zero hunger', the second of its Sustainable Development Goals), the Ministry of Foreign Affairs, and the associated Food & Business Knowledge Platform. Civil society is closely involved in this issue, with both consumers and the general public making more demands on the quality of products and the way in which they are produced.

[8] ***Klaar voor de Toekomst? Naar een brede strategie voor ICT,*** **AWTI, 2015.**

The final example, the route *'Resilient and meaningful societies'*, affects us all. Globalisation has raised questions to which familiar systems and institutions have no ready answer. The route connects the agendas and strategic themes of the research universities (such as 'Institutions' for Open Societies) and universities of applied science with the KIAs identified by the top economic sectors Water, High Tech Systems and Materials/ICT, Agri & Food, Horticulture & Starting Materials, Life Sciences & Health, Creative Industry, Logistics, and the Social Infrastructure Agenda. It also reflects the WRR's report to the Government on the learning economy *(Naar een lerende economie)*, the Horizon 2020 Societal Challenge 'Europe in a Changing World', and social agendas such as 'Heritage and Space' and 'Connecting Sustainable Cities'. Because it corresponds with a large number of other agendas, the route will gain considerable support.

It is no coincidence that the examples given above all refer to Horizon 2020. Many of the questions posed in the National Research Agenda relate to Horizon 2020 themes. All 140 cluster questions in the National Research Agenda can be grouped into ten themes derived from Horizon 2020.[9] In that sense, the Dutch National Research Agenda is the Netherlands' interpretation of Horizon 2020 showing in which areas Dutch research can best contribute to the EU agenda. The Knowledge Coalition therefore sees promising opportunities to follow up these routes with applications for EU funding.

The start of a process

The completion of the Dutch National Research Agenda is not an end, but a beginning. It is the start of a process of implementation and further refinement in which the Agenda becomes a dynamic tool for generating synergy.

To ensure that the route map remains fit for purpose, information on existing agendas will be updated continuously. At the moment, that information has been taken from the websites of the relevant institutions. Eventually, these institutions – research universities, universities of applied science, research institutes, but also ministries and the top Dutch economic sectors – will be responsible for updating their own information in the National Research Agenda. They will have their own website accounts allowing them to make changes according to a fixed format. It is to their advantage to keep their information up to date; after all, it gives them a public platform and makes them accessible. Quality improvements thus become self-reinforcing, and the impact of the National Research Agenda as a connective force will continue to grow.

In the longer term, the institutions will be able to flesh out their existing agendas by adding more information about the research groups involved and the funding available. Other agendas can also be added to the database, broadening the scope of the National Research Agenda as a route map. *In Conversation* will be made into a permanent function. It can be refined further in order to include new parties. Interested members of the public will be able to register and indicate their topics of interest. In this way, *In Conversation* will ultimately become a powerful channel of communication between science and civil society.

The National Research Agenda is meant to provide a sound basis and inspiration for planning. Individual institutions can polish their own strategic or specialist agenda by comparing it to the National Research Agenda. The Agenda will also help coordinate funding with government bodies. It will contribute to the dialogue between the various ministers, the representative organisations, and individual institutions, helping the latter (i.e. the research universities, UMCs, universities of applied sciences, businesses, institutes of applied research, government expertise centres, and research institutes) coordinate their plans. Institutions will be better able to develop complementary research programmes along the knowledge value chain.

To point the way for Dutch research, the National Research Agenda must function as a reliable compass for refining existing agendas. In other words, the issues it addresses should serve as a long-term frame of reference. At the same time, the stability that the Agenda offers must not become a straightjacket that excludes change. There should be scope for emerging issues of such relevance that they must be added before the next review. The National Research Agenda must adapt and evolve along with trends in society and in science and research. Those active in the science system will therefore be able to use the National Research Agenda in many different ways to prioritise, form alliances, seek funding, valorise research, communicate with other parties, and pursue other aims.

The pressure on the Dutch science system is mounting, owing to sluggish investment within an increasingly competitive international context. Public funding of R&D and innovation will drop off gradually in the years ahead. Private sector investment in R&D is stable but clearly below the European Union average. For some time now, investment in university research has not kept pace with the rise in the number of students in higher education. The percentage of researchers awarded funding has dropped to a new low and the budget for applied research has been cut significantly in recent years. All this is happening at a time when there has been a sharp rise in R&D investment elsewhere. Competition for funding, talented researchers, and a top spot in the international rankings has increased accordingly. It should be noted that Dutch universities have fallen in such rankings.

To ensure that the National Research Agenda achieves its full potential, the Dutch science system needs to be fortified, a project that will require dedicated public and private funding. Completion of the Agenda thus also marks the start of efforts to develop a solid proposal for an investment agenda, which will take the routes described above as their basis. In the first half of 2016, the Knowledge Coalition will organise 'route workshops', focusing in the beginning on the 16 example routes described in Part III of this document. The workshops are meant to forge innovative alliances focusing on complex themes.

The route workshops will make it possible for research universities, UMCs, research institutes, government expertise centres, universities of applied sciences, businesses, and institutes of applied research to bring their own strengths to bear in exploring opportunities for collaboration and in making choices in that context. This process will give rise to new consortiums for interdisciplinary, multisector, and public-private partnerships. It will help remove barriers and generate new cross-sector dynamics. The route workshop participants will choose specific themes for their partnerships and in doing so imply certain priorities, working from the bottom up.

The outcomes of the route workshops will reveal the redundancies and blank spots in the Dutch science system. They can help identify themes regarded as important by many parties and topics that cut across different fields. The Knowledge Coalition will analyse these outcomes and prioritise additional investment in the science system on that basis.

[9] See Appendix 4 for a breakdown of the questions across the ten themes.

The process described above will deliver a key component for an integrated science, innovation, and technology policy. The Knowledge Coalition will use it to draft a joint manifesto and a solid, detailed proposal for an investment agenda that will inform the current and subsequent Government coalitions. The scope of the manifesto and investment agenda will be broader than a simple thematic prioritisation; it will also encompass curiosity-driven research, talent development, and large-scale infrastructure. The manifesto and investment agenda will identify which conditions must be created to boost the impact of the National Research Agenda. They will be submitted to the Dutch Government in mid-2016 and represent an important stage en route to achieving the aims set out in the Government's vision document for science.

The Dutch National Research Agenda has been a successful experiment, thanks to the underlying method. It makes the curiosity of the Dutch people uniquely visible – a curiosity driven by the needs of society, by economic opportunities, or simply by the human determination to know. The next phase will build on the energy that has been unleashed in the public and in the parties that make up the Knowledge Coalition.

Part II Questions

The following section of the Dutch National Research Agenda introduces 140 cluster questions. Each one is a composite of original questions submitted by an extremely wide variety of sources, inspired by both theory and practice and branching into multiple scientific disciplines. Taken as a whole, these questions reveal the diversity and quality of Dutch research and show how the Dutch economy and society are knitted to scientific knowledge.

Each section begins by explaining the background to the question and why it is relevant. All 140 questions require an interdisciplinary approach. The solutions to many issues lie solely in a combination of basic, applied, practice-based and, in some cases, policy-driven research. Many questions are also multidimensional in nature. They are not only descriptive or explanatory, but also have a normative, evaluative, or even a design purpose, for example.

Along with each cluster question, we also show some of the underlying questions, affording readers a glimpse of the enormous depth and variety of queries submitted. All 11,700 questions that we received can be found on the website, each one with its own explanation.

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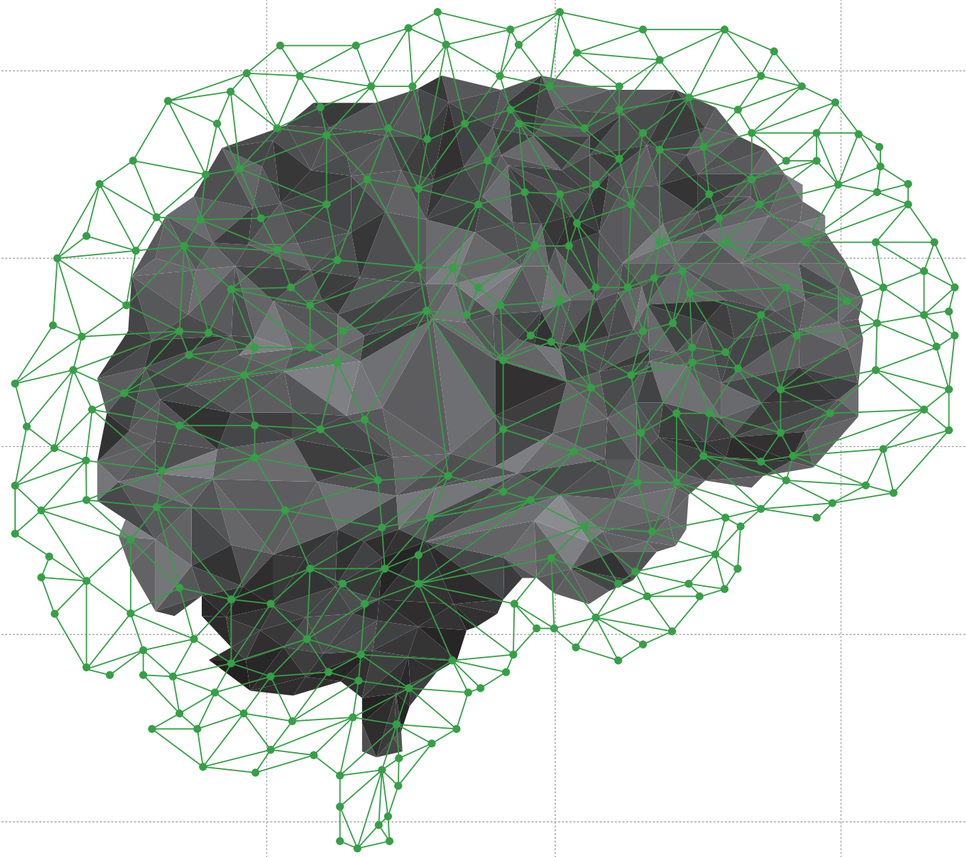
Man, the environment, and the economy



How many people can the Earth sustain?

Submitted questions illustrating depth and connective power

- **To what extent does the Second Law of thermodynamics (entropy) define our planet's capacity to sustain human life?**
- **What are the critical limits and tipping points in social, ecological, and climate systems?**
- **What will happen to life on Earth if we start to run out of one of the basic elements?**

Explanation

To determine the Earth's carrying capacity, we have to take a number of factors into account. The Earth is a system (an eco-system, as it were) that gets its energy from the sun. We can estimate how much of the sun's energy reaches the Earth and what percentage of that energy we are able to capture in various forms. What proportion of that energy do oxygen-producing organisms require to maintain a stable amount of oxygen in the atmosphere? What proportion of that energy do we need for other processes that are essential to the survival of humans and other forms of life? And how much energy do we then have left to create a sustainable society? The above calculation can help us estimate the maximum number of people that the Earth can sustain. But that only addresses one of the underlying questions. In determining the Earth's carrying capacity, we also have to consider such factors as the influence of climate change, biodiversity, social processes, the structure of society, how society differs from one country to the next, and the design of the living environment. Finally, there are other limiting factors, such as the availability of drinking water, raw materials, and food.

Connective power

Fresh insights into the relevant factors can help guide advances in technology, for example in relation to global food security, with a knock-on effect on the economy. Political decisions and international relations will also affect the answer to this question considerably. To understand these interdependencies, we need new research in the social sciences and humanities.

What do humans and nature mean to each other and what is the ideal relationship between the two?

Submitted questions illustrating depth and connective power

- **How are biodiversity and cultural diversity connected?**
- **In what way is biodiversity useful for humans?**
- **Do living creatures other than humans have rights?**

Explanation

Climate change, pollution, loss of habitat, and intensive agriculture and horticulture are putting pressure on ecosystems and placing biodiversity at risk. Modern technologies have given an enormous boost to our productive capacity, but they increasingly raise more fundamental questions about the relationship between humans and nature. How can and how should human beings and the natural world relate to each other? This question has come up in many different disciplines, at many different orders of scale, and in many different forms.

Connective power

To determine the ideal relationship between humans and nature and to develop the right strategies for managing that relationship, we need to improve our understanding of ecological, economic, social, political, and cultural factors. For example, we need to look at the impact of human activity on nature. Part of this examination concerns the irreversibility of processes, which requires us to know about species, systems, and processes as they relate to environmental properties. Another aspect is the purpose that nature serves for human beings. Traditionally, this was as a source of food, but the question of nature's role in physical and mental health is becoming ever more relevant. Nature is also a source of aesthetics and innovation. One good example is biomimicry, with nature serving as a model for artificial systems. Another topic of study is the value of nature. What value do we place on humanity's relationship with nature in general, and with animals in particular? Is loss of biodiversity a problem in and of itself? Do humans have responsibilities in this regard, beyond those based on purely functional arguments? What are those responsibilities based on?
Finally, we must develop both fundamental and practical action alternatives for the relationship between humans and nature. Simulations and scenarios plotted at different temporal and spatial scales can help us explore alternatives and validate choices. Critically important in this context are questions about the factors that determine environmentally friendly or unfriendly behaviour, about how to influence behaviour, and about alternative systems of production and consumption.

Why is biodiversity important and how do we protect it?

Submitted questions illustrating depth and connective power

- **Why is biodiversity declining so rapidly in the Netherlands, specifically migratory birds, insects, amphibians and reptiles, and soil organisms? What sustainable solutions are there for halting this decline?**
- **Does high biodiversity always mean a healthy ecosystem, or can it also indicate deterioration?**
- **Can human beings survive without biodiversity?**

Explanation

The number of people inhabiting the Earth continues to rise, and every person's ecological footprint may be growing at an even faster rate, making it increasingly difficult to satisfy human needs and protect biodiversity at the same time. Biodiversity is declining worldwide, even though we know that high biodiversity keeps an ecosystem healthy. The rapid, widespread loss of biodiversity makes this question a very pertinent one.
Species are not self-sufficient; they interact with other species, whether they live underground, on land, or in the water. Understanding how species interact and how species, systems, and processes relate is crucial to safeguarding biodiversity in the longer term.

Connective power

This question links research on the significance of biodiversity loss to studies exploring the causes of such loss and how we might combat it. We first need to know more about the impact of biodiversity loss on nature itself and on human society. Have we already passed irreversible tipping points? By what standards? The question connects research on species, systems, and processes at a range of scales. It also considers how individual variation contributes to biodiversity and the health of ecosystems. Further, we need to know more about the causes of biodiversity loss. What are the key factors? What is the role of climate change and urbanisation? Can we undo the close relationship in some places between biodiversity and old or obsolete agriculture systems? We need to understand these factors before we can take adequate steps to counteract or restore the loss. This question is related directly to global, European, and national societal agendas that identify the loss of biodiversity as a major issue. It connects basic research in ecology with policy-driven and applied research in that field. Locally, there is a need for evidence-based advice on the ecological impact of urban expansion and infrastructure, with input from the field of law. The question is also linked to research carried out by an army of volunteers and their organisations, in that way serving to engage the public in science ('citizen science projects').

How do ecosystems function and how vulnerable are they to environmental impacts?

Explanation

Ecosystems consist of different interconnected components, for example water and seabed, or surface soil and substrate. Whether or not ecosystems are stable depends on the species that connect these components. Specifically, human intervention puts ecosystems under pressure, for example in the form of climate change, air, soil, and water pollution, changes wrought by farming and urbanisation, and the growing pressure on marine ecosystems. All these factors influence how ecosystems function. We still know very little about the potential impacts on ecosystems of present and future global and regional environmental changes.

Connective power

The challenge lies in conducting multidisciplinary empirical research on populations, organisms, and processes in order to determine how human intervention changes the way ecosystems function. Scenarios studying potential exposure to and the impact of environmental changes on humans and nature should allow us to develop climate adaptation strategies that will protect ecosystems. In order to predict future trends, it is very important to link ecological and evolutionary research on individuals and communities to research on processes. Such research can draw on what we know about how species are currently responding to climate change, for example, and how they did so in the past. This theme is also on the agendas of the Water, Chemistry, and Energy top economic sectors.

Submitted questions illustrating depth and connective power

- **What role do parasites play in the ecology of their hosts?**
- **How can we restore an entire ecosystem so that plants and animals appear (or return) on their own?**
- **Can invasive plants and animals play a positive role in ecosystems?**

What role do micro-organisms play in ecosystems and how can we use them to improve health and the environment?

Explanation

Our planet has more than 10^{30} (thirty zeroes after the one) micro-organisms. Because they play a crucial role in all natural cycles, life would not be possible without them. In natural ecosystems, for example nutrient cycles, micro-organisms remove contaminants from the soil and water, influence the growth, development and health of their hosts, and capture solar energy. In that sense, micro-organisms play a major role in how organisms function and whether they are healthy or sick. Humans have long used helpful micro-organisms in vegetable and animal production processes, and more recently to clean up contaminants and to produce 'green' chemicals and materials from plant waste or directly from sunlight, within the context of the bio-based economy. However, we have yet to identify most of the micro-organisms on our planet. The question is how micro-organisms influence ecosystems, for example by causing disease, protecting against various stress factors such as infections and drought, changing behaviour, and the exchange of genetic material. It is important to understand these processes if we are to predict the behaviour of ecosystems and make sustainable use of helpful micro-organisms.

Connective power

By combining microbial ecology, physiology, and genomics, we can come to understand micro-organisms and their complex interactions and networks. That is important for discovering how infectious diseases spread from animals to humans, or how we can control harmful micro-organisms in the health care sector, livestock farming, and the environment. These questions shift the focus from studying species to a systems-based approach to microbial interactions and their usefulness for human health and the environment. That requires both basic and applied multidisciplinary research.

Submitted questions illustrating depth and connective power

- **What role do bacteria play in the ecology and evolution of their hosts?**
- **Can we use viruses to combat invasive and harmful organisms in the sea?**
- **How can we use CO_2 to produce organic compounds?**

How can we protect and preserve the quality of the subsoil for humans and the environment while leaving room for social and economic development?

Explanation

We want the soil, subsoil, and groundwater to remain useful for every possible purpose, both in the shorter and the longer term, so that the potential for area-specific improvement remains available. How can we learn more about the subsoil to promote safer buildings, improve water management, and increase economic value?
Expertise of this kind can help us answer socially relevant questions such as:
- How can we maintain and improve the soil and groundwater system?
- How can we quantify the impact of interventions in the subsoil?
- How can advances in quantitative research help us take decisions about interventions in the subsoil while also safeguarding the interests of future generations?

The soil is an important basis for sustainable spatial planning, in both the literally and figurative sense. It also serves as the natural custodian of the identity of many areas of nature. It offers opportunities for development, but it also imposes limitations.

Connective power

The Netherlands' search for a sustainable, climate-proof form of spatial planning involves collecting data and expertise on soil use and making what we know available. Topics include underground construction and the multifunctional use of space, but also flood barriers and alternative energy. By building underground, we can improve the quality of public areas above ground. Tackling this issue effectively calls for cooperation between local, regional, and national authorities, businesses, engineering firms, and knowledge-based institutions.

When we apply the results of new research in practice, various questions arise, such as:
- How do we get the right parties working together at the right time?
- What is the spatial, social, cultural, and ecological context?
- How can we optimise and improve the key properties of the soil (actual or potential)?
- What conflicting and shared interests are involved?

Quality is not a uniform concept in spatial planning. Quality depends on the time and the place. It also involves the meaning of a place and its experiential value. The Netherlands already has various organisations that have joined forces on this issue.

Submitted questions illustrating depth and connective power

- **How can we undertake an integrated, spatial approach to the top soil and the shallow (including the groundwater) and deep substrate that strikes a balance between protection and utilisation and allows us to address societal and economic challenges?**
- **How can we efficiently analyse the composition of the sediment up to dozens of metres below the surface?**
- **How can we deal more effectively with the risks and uncertainties related to our use of the substrate?**

How can we measure and model the interaction between ice, atmosphere, and ocean so that we can reliably forecast a rise in the sea level?

Explanation

Climate change reports agree that the sea level is rising, but forecasts of how much it will rise this century vary considerably. Conservative estimates place it at a millimetre a year, but a rise of a metre or even more by the end of the century is not inconceivable. One huge uncertainty in these forecasts is the size of the Greenland ice sheet. If only one percent of the ice sheet were to melt – a relatively small loss – the sea would rise by six centimetres. Small uncertainties therefore have huge consequences. In the past, researchers working on climate modelling studied partial solutions by focusing on the functioning of the atmosphere, or the ocean, or the ice caps. The climate system is not a group of separate compartments: in reality, processes are constantly interacting with each other at all sorts of temporal and spatial scales. Climate sensitivity is the result of feedbacks between land, atmosphere, ocean, sea ice, and land ice. How can we build a model that will simultaneously forecast the future warming of the atmosphere, the melting of land ice, and global sea level rise as part of one and the same system?

Connective power

This question falls into the Earth System Modelling domain. This type of modelling depends on the most powerful supercomputers and requires collaboration between meteorologists, oceanographers, glaciologists, and specialist programmers. The theme corresponds with European and global agendas focusing on climate change and water systems.

Submitted questions illustrating depth and connective power

- **How will the ice caps and the sea level react to a changing climate?**
- **What reliable indicators do we have to detect the melting of Greenland's ice sheet?**
- **Will the rising sea level wipe out the western part of the Netherlands?**

How is the climate changing, including extreme weather, and what impact will those changes have?

Explanation

The climate is changing, the atmosphere is warming. We know the general causes, but there is great uncertainty about how much global warming we can expect in the future. That uncertainty is not only hampering climate change adaptation efforts, for example estimating just how high our dikes need to be, but it also has implications for mitigation policy. How much CO_2 can we emit into the atmosphere without losing control of climate change? Our understanding of the relationship between global warming and the rise in greenhouse gas emissions is imperfect; we do not know what the tipping points are in the climate system and when they will occur. Our projections concerning regional climate change are also inaccurate. Increasingly, extreme precipitation, storms, and drought are attributed to worldwide climate change, turning it into a very tangible but hard-to-predict safety risk. Extreme weather often has a huge impact on everyday reality, stressing the need to tackle this subject in a manner that focuses on the societal dimension. We face various major challenges in this regard, i.e. to map, forecast, and – to the extent possible – reduce the risks associated with climate change and extreme weather on humans and nature, and the impact of migration caused by climate change.

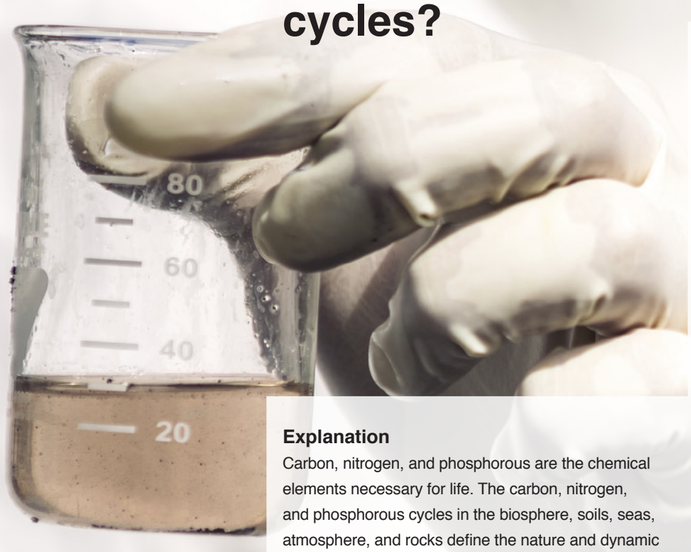
Connective power

Climate change is a complex, global phenomenon with sharply varying regional effects. It requires an integrated, partly international approach that cuts across different orders of scale and disciplines, as well as active collaboration between basic research in the fields of climate physics, hydrology, and mathematics, application-based studies focusing on safety and disaster management, and more practical work. Our climate change adaptation and mitigation efforts and our ability to predict extreme weather would benefit enormously from a better understanding of the causes and processes that underlie climate change. At the same time, applied research and pilot projects can foster innovative approaches that we can then also export as high-value, innovative solutions. The Netherlands has a solid international reputation in such areas as flood safety, coastal defences, building with nature, reliable drinking water supply, and agricultural optimisation. Climate change explicitly requires more research and the adequate monitoring of changes in natural processes and in the living environment. Climate change and extreme weather are phenomena that have a very broad impact on society. Besides protecting vital infrastructure and heritage sites, ensuring good quality of living in our cities (in the delta), and making the necessary adjustments in agriculture, we must also consider the political and administrative aspects of climate change adaptation and mitigation and how to gain public support for implementing the relevant policy.

Submitted questions illustrating depth and connective power

- **Climate change is expected to alter the food chain in the North Sea. So will the Dutch still be eating their traditional raw herring in 2030?**
- **How do we prepare cities for the consequences of climate change, especially peaks in temperature and precipitation?**
- **What ecological and evolutionary impact will climate change have on biodiversity and ecosystem processes?**

How can we make better use of the carbon, nitrogen, and phosphorous cycles?



Explanation

Carbon, nitrogen, and phosphorous are the chemical elements necessary for life. The carbon, nitrogen, and phosphorous cycles in the biosphere, soils, seas, atmosphere, and rocks define the nature and dynamic of life on both a global and regional scale. All sorts of human activity and interventions – for example CO_2 and methane emissions, manuring, and fishing – bring about enormous changes in these cycles. They set off a cascade of biogeochemical processes in soils, in the water, and in the atmosphere; in turn, these processes can have huge, often unexpected effects on ecosystems and may even impact the climate indirectly. It is very important to quantify the total sum of all these processes, which operate at different temporal and spatial scales, so that we can better anticipate the impending changes. There is also the challenge of identifying possible interventions in the various cycles that will allow us to use them to our advantage. For example, can we reduce the concentration of CO_2 in the atmosphere by means of carbon capture and sequestration or by turning CO_2 into new fuels? And how can we recover phosphate from the ocean floor? CO_2 utilisation, sustainable nitrogen fixation, and renewable phosphate are critical research challenges for the Netherlands and internationally.

Connective power

Interventions in the interaction between the carbon, nitrogen, and phosphorous cycles, human activity, and nature at different orders of scale require a broad, multidisciplinary, and internationally coordinated approach, with close cooperation between science, the economy, and policymaking being vital. Progress in this area will depend on technological innovations that permit carbon capture and sequestration, with the end product then serving as feedstock for new processes and products. Achieving this would give the circular economy a boost. Another topic in which technical innovation and basic bioscientific research are complementary is the development of synthetic surfaces that – like leaves – can convert light energy into organic chemical energy and allow us to turn CO_2 into oxygen. We need to find a global solution to the phosphorous shortage. Many natural processes depend on the availability of phosphorous and nitrogen. Most ecosystems are unable to cope with an overabundance of these elements, however, and interventions in their cycles therefore have major, and often negative, environmental impacts on the land and in the water. With more CO_2 being emitted into the atmosphere than the water can absorb, the oceans are gradually becoming more acidic, threatening the biodiversity of calcareous organisms such as coral.

Submitted questions illustrating depth and connective power

- **Can we develop new catalysers that allow for more efficient carbon sequestration and for synthetic photosynthesis that is more efficient than plant photosynthesis?**
- **Is the large-scale conversion of CO_2 into fuel technically and economically feasible?**
- **Can we solve the impending worldwide phosphate shortage that is threatening the agriculture sector before it's too late?**

How can we use new materials, technologies, and processes to lower the cost of buildings and infrastructure and make them safer and more sustainable?

Explanation

It is very important to our society and economy to safely increase the life cycle of existing buildings and infrastructure. There is also a rising demand for sustainable new buildings made of recyclable materials that provide the required functionality. And we want buildings with a pleasant ambience, that help us stay healthy. Designing such future-proof buildings requires a comprehensive approach that serves a major public interest. Right now, however, there are economic and other obstacles preventing the realisation of this development. For example, new, sustainable, smart materials are still more expensive than conventional ones. And truly sustainable building will require changes not only in how we use materials and energy, but also in construction methods. Such innovations also entail new construction processes and a change in the mentality of all the stakeholders.

Connective power

Adaptive building requires new technologies and processes to lower the cost of buildings and make them safer, healthier, stronger, smarter, and more sustainable. Research should initially focus on the relevant technologies and processes, for example new ways of utilising solar energy by incorporating solar cells into roof tiles or paint, or using 3D printers to produce building elements. Next, it is important to study how these technologies and processes and their differing purposes interact. That will lead to a form of design and construction that is itself the subject of basic and applied research. In addition to these dimensions, which focus specifically on building, another important area of research concerns the role and influence of users on the building and the construction process. Relevant questions, for example, would be 'Can a building have a positive effect on an occupant's health?' The societal challenge is to arrive at a liveable built environment not only by continuously adding new structures to it but also by transforming existing ones. This challenge keys into the present discussion about vacant office buildings and retail space, but also touches on the longer term need to build more sustainably. The expertise that the Netherlands is developing to address this problem comprehensively also constitutes an attractive product to export to all major urban areas worldwide.

Submitted questions illustrating depth and connective power

- **Smart sustainable city: what is the ideal combination of ecological, economic, and social sustainability in a city, and how can that ideal combination be achieved? Can we ensure that our homes will adapt to our changing lives?**
- **What composite and other materials can we use to produce buildings with a 3D printer?**
- **How can we design buildings that help people stay healthy or even heal them? And can we train and encourage occupants to use the building as energy efficiently as possible without putting their health at risk?**

How can we ensure proper water governance in the future?

Explanation

Clean water is essential to human life and yet its availability is under threat. Climate change, pollution, waste, and the rising demand for and depletion of finite resources has already led to acute water shortages in many parts of the world. Many other areas will also experience shortages in the foreseeable future, with major implications for arable and livestock farming, horticulture, health, and the overall quality of life. This is not merely a regional problem; it may even threaten relations between entire population groups and states. Advanced water management and water-conservation technologies such as treatment and desalinisation must be further refined so that they can be deployed on a much larger scale for an acceptable price.

Connective power

The demand for forward-looking water governance connects the technical issues of treatment and sanitation with other uses of water and how the water governance system is organised. Water treatment and desalinisation technologies are significant not only in their own right, but also because of their relationship with energy and the recycling of phosphate and other chemicals. The issue of water use is about improving efficiency in existing systems but also about developing new systems that require less water. That may greatly reduce the demand for water in, for example, agriculture. In the case of water governance, the main issue is which new governance systems can link the various parties that use water. Economic measures and legal aspects are also important subjects of study.

Submitted questions illustrating depth and connective power

- **How can we tackle the water shortage problem in African cities in terms of demand and sanitation, availability, the institutional setting, and risk management?**
- **How are countries (in the EU) similar and how do they differ in terms of construction law, regulatory matters and supervision, and what impact does this have on international water governance?**
- **What can we learn about spatial and contextual dimensions from water systems around the world?**

How do the seas and oceans function, and what role will they play in the future?

Explanation

The sea is vital to our future supply of energy, food and raw materials, but we still know very little about the ocean as a system. This is mainly because that system is so enormous and relatively inaccessible. The influence of human activity on the oceans, for example intensive fishing or transport, is growing: acidification owing to the increase in CO_2 in the atmosphere, nutrient-rich pollution killing off life in parts of the ocean, plastic pollution, climate change, and the associated shifts in current patterns. How are these changing conditions influencing the system, including the biology and ecology, the chemical composition of seawater and sediment, physical properties, and the way the ocean interacts with the land and the atmosphere? How can monitoring, experiments, modelling, and reconstructions help us understand the sea better and accurately project how the oceans and seas will change in the future?

Connective power

Seas and oceans require an integrated, multidisciplinary, and often international approach and their unifying capacity is therefore quite exceptional. Close cooperation between scientists, national and international authorities, and business partners is necessary to better understand seas and oceans, monitor them in the longer term, and use them sustainably for a variety of purposes based on sound knowledge.The sea is a source of energy, raw materials, fish, aquaculture, and transport. Therefore it is of immense economic significance to our future, but we also have an obligation to use it efficiently and sustainably. To do this requires not only a sound understanding of biological, ecological, chemical and physical processes, but also stresses the need for new or amended legislation, innovative technological research, and studies exploring the societal implications and socioeconomic frameworks (responsible innovation) for working on and with the sea. Innovative and interdisciplinary research at and between various scales is needed to strike the right balance between protection/restoration and the economic demands of the future. Such research should focus on health issues, for example concerning toxins in the sea-human food chain, societal factors such as the social economy of coastal regions, the sea as a potential threat to heavily populated deltas, and monitoring the state of the marine environment. National and international authorities, the private sector, and science will need to work together closely to uncover the secrets and treasures of the sea in a sustainable, profitable and ethical manner.

Submitted questions illustrating depth and connective power

- **More than 70% of the Earth's surface is covered by seas and oceans. Are there ecologically responsible methods for safely and efficiently extracting raw materials and energy from the sea?**
- **How can we make smarter use of natural processes when protecting coasts and in marine food production?**
- **How can we properly study and monitor the deep sea?**

What eco-friendly methods can we use to protect ourselves against floods?

Explanation

Large parts of the Netherlands only exist because the Dutch have reclaimed land from the water. Flood control is one of the foundations of Dutch society and a vital component of the Netherlands' national identity. But how to cope with rising water levels has become a worldwide problem. Climate change, rising sea levels, and extreme meteorological phenomena will require many places to learn to control, utilise, or prevent flooding. Before this becomes possible, however, we have to understand why and how floods occur. The challenge is to develop and implement solutions that offer protection while optimising sustainability and biodiversity. Societal issues are equally important as problems to be investigated in basic and applied research. The Netherlands is a global leader when it comes to water management research and implementation. Our research infrastructure is unparalleled and the related business sector enjoys world renown. Given that position, the Netherlands must seize and maintain the initiative.

Connective power

The Netherlands has long had a unique, unifying, institutional water management structure. The outcome of cooperation between science, government, and business, that structure has set an example for public-private partnership. It has also allowed the Netherlands to position itself as an international trailblazer. But water management also raises questions about acceptable risk. How and subject to which conditions can we accept the risk of flooding? Are we willing to allow nature to reclaim an area and to adapt our living environment to eco-friendly solutions?

Submitted questions illustrating depth and connective power

- **How will the global risk of flooding change in the future and in which areas will this threaten economic development?**
- **What do we need to ensure that our own major rivers remain safe, sustainable, and robust in the longer term (hundreds (!) of years) while accommodating the needs of shipping, the ecology, and recreation?**
- **What role does Building with Nature play in sustainable coast management?**

How can mimicking plant photosynthesis contribute to a new green revolution?

Explanation

Solar energy is sustainable and virtually inexhaustible. Plants use photosynthesis to store up solar energy and convert it into the components necessary for life on earth. Fundamental and applied research make it possible to mimic photosynthesis and improve on its efficiency, allowing the sustainable production of biomass for food and bio-based fuels, so that the bio-based economy can make a vital contribution to a new green revolution.

Connective power

This research question is highly interdisciplinary in nature and links genetics and physiology with modelling. Research on photosynthesis anticipates the rising worldwide demand for sustainably produced energy, food, and industrial feedstock. On the one hand, it can be a source of basic evolutionary insights; on the other, it offers application-specific reference points for improving survival mechanisms and potential yield improvements in new crops. Knowledge-driven institutions and industrial partners are collaborating closely on nature-inspired engineering and bio-mimicry research (e.g. artificial leaves that can mimic photosynthesis). Plant geneticists are gaining an understanding of how plants function under differing circumstances. By using this knowledge, we can optimise the efficiency of photosynthesis as a process. Such research also raises ethical questions, for example whether society will accept genetically modified products.

Submitted questions illustrating depth and connective power

- **How can our knowledge of plant physiology and development contribute to sustainable food production and the bio-based economy?**
- **Is it possible to develop a super plant that will release oxygen both in the daytime and at night?**

How can we make agricultural production systems more sustainable as the worldwide demand for healthy, safe food continues to grow?

Explanation

The growing world population and changing pattern of consumption make the challenge of supplying the world with enough food – and especially healthy food – one of the biggest that we face in the next few decades. At the same time, more intensive use of natural resources is putting growing pressure on animal and non-animal food production systems and increasingly undermining the quality of our ecosystem, e.g. the quality of the soil and the water, level of salinisation, biodiversity, and fish stocks. Public health is even coming under threat, for example due to zoonoses (diseases transmissible from animals to humans) and overuse of antibiotics. We need new insights to accomplish the transformation to sustainable, resilient production systems that generate high yields and quality products. We also need to minimise external inputs and losses, maximise our use of production waste streams for other, high-value purposes (bio-based economy), and use crop improvement, ICT and other, new technologies. Precision technology can make an important contribution to managing and controlling these production systems. We also need to know more about changing food patterns, especially in relation to protein consumption and malnutrition. To supply the world's growing population with enough protein, we will need to call on other sources, including plant-based ones. To ensure a well-balanced diet, we need to have vitamins, fibre and minerals available to supplement our intake of calories and protein.

Connective power

In the past, basic research led to a wide variety of products that have made agriculture and horticulture more sustainable. This question is about the next stage, in which we combine research from different sectors and scientific disciplines. We need to make new connections between agriculture and horticulture on the one hand and water, high-tech, logistics, and ICT on the other. The extent to which the public accepts and values the relevant applications is also an important factor; consumers must accept new products and technologies. That will require basic but also applied research that transforms evidence-based concepts into innovations suitable for the market. System research involves the integration of technical and socioeconomic dimensions, and that means multidisciplinary cooperation.

Submitted questions illustrating depth and connective power

- **How can we supply the world population with enough safe, healthy, tasty food, produced according to sustainable methods (closed-loop recycling) that do not exert more pressure than the Earth can bear?**
- **Which principles and starting points can we apply towards developing new animal husbandry systems in which production is sustainable in every respect?**
- **How can we optimise the effectiveness of biological controlto combat pest insects so that we can reduce or even discontinue the use of environmentally-unfriendly substances?**

How can we develop healthy new food crops that have higher yields while requiring fewer harmful chemicals?

Explanation

Plants are the most important primary source of food on Earth. They also supply us with important products, such as cotton fibre for clothing, starch for industry, and therapeutic substances used in medicine. The Green Revolution optimised crop cultivation and greatly increased productivity per unit of land. By now, however, the world population is growing so quickly that we need the next Green Revolution – but a revolution that will also undo the harmful effects of the first, such as overuse of fertilisers and pesticides, increasing erosion, and salinisation of the soil. A knowledge of plants and modern plant breeding techniques is vital if we are to engineer the sustainable crops that we require in the future. They will be able to survive on less water and fertiliser than crops today, grow well on marginal land, and convert sunlight very efficiently into energy. They must also be able to resist diseases, pests, and climate-related stressors.

Connective power

To engineer crops that can meet these challenges will require continuous innovation in plant breeding and a combination of genetic, physiological, and phytopathological plant research aided by the latest technological advances in genomics, imaging, and bio-informatics. Also important is the relationship between humans and the environment and the role of micro-organisms, with research focusing on entire ecosystems. The Netherlands plays a leading role worldwide in these disciplines and – thanks to its prominent plant breeding sector – will be capable of coming up with future-proof solutions. To make the best possible use of new findings and new crops, larger organisations, SMEs, and scientists must work together. Good management is required, and the social aspects should also be considered. If properly mobilised, the entire value chain will benefit, all the way from growers who no longer have to spray their plants with toxins, to consumers. Sustainable food crop production has been selected as a priority by the top Dutch economic sector Agri & Food and by the European Commission in its Horizon 2020 Programme. The question corresponds to the government policy domain 'A strong and sustainable agriculture sector'.

Submitted questions illustrating depth and connective power

- **Which plant genes are involved in vulnerability and resistance to biotic and abiotic stress, and how do they interfere with each other and the environment?**
- **How can the development of the 'smart city' help make urban farming more sustainable?**
- **Can refined seaweed cultivation supply humanity with food, raw materials, and energy?**

How can we make chemical and bio-chemical production processes more sustainable, more efficient, and cleaner?

Explanation

Chemicals have improved our quality of life in immeasurable ways. Medicines, synthetics, electronics, clothing, transport: we would have none of these without chemical research and chemical production processes. At the same time, it is clear that our current methods are polluting our environment and exhausting our natural resources, and that the challenge we face in response to a growing demand is to make chemical production processes more sustainable. If we wish to maintain or improve our standard of living and also reduce or even neutralise the impact of human activity, then we will have to make materials and their production processes more ecologically sustainable. This requires a major effort on the part of chemical and biochemical researchers. Can we replace the materials we use today by more environmentally friendly alternatives? Which production methods are best: chemical or biochemical, catalytic or stoichiometric (by means of prescribed ratios between substances)? What can chemical processes teach us about reusing materials or recycling them after use? These questions call for an open approach in which we encourage researchers to explore new and sustainable molecules and materials, their structure and properties, chemical and biochemical production, and separation and reprocessing processes.

Connective power

This question embodies the Netherlands' aim of being at the forefront of the transition to green chemistry. The Netherlands is an internationally acknowledged leader in chemical research, specifically in such areas as sustainable production processes, catalytics and biocatalytics, polymer and materials research, and chemical characterisation. Top research groups have formed various clusters active in different aspects of sustainable production. Sustainability is one of the Horizon 2020 priorities and a main priority for the Chemicals industry, a top Dutch economic sector. The questions that fell into this category related mainly to the Chemical Conversion, Process Technology and Synthesis, and Advanced Materials programme categories. In addition to supplying nutritional and other substances and materials, the chemicals industry is also an enabler of innovation in other sectors. Links with other areas of research therefore go without saying. The question keys into the policy domain 'Sustainability (green economy)'.

Submitted questions illustrating depth and connective power

- **Can we develop new, advanced materials using non-scarce chemical elements?**
- **How can we use metabolic engineering to develop new routes for the production of fuels, fine chemicals, and medicinal drugs based on renewable feedstock?**
- **How do we develop energy-efficient chemical processes for the treatment and desalinisation of drinking water and for the recycling of building materials?**

How can we quickly make our energy supply greener while keeping it affordable and reliable?

Explanation

Converting our current, non-renewable energy supply to a green system is an extremely complex but urgent problem that has many technical, scientific, and socio-economic dimensions. The question is which components we need for an optimised green energy supply system. The urgency of the problem, the reliability of such a system, and the associated costs are also major challenges. In today's competitive energy market, it is difficult for new green technologies to get a foot in the door if they are more expensive than energy derived from fossil fuels. Research in this area is therefore also closely bound up with the associated economic opportunities. In addition, public support for green energy is very important. In a densely populated country such as the Netherlands, it can be difficult to resolve disputes about where to place wind turbines, for example (the NIMBY effect). There are also good opportunities to use ICT to increase energy efficiency, and to match energy generation to energy consumption by means of smart grids.

Connective power

Building a green energy system, including smart energy cities and smart grids, is an important priority in Dutch and other national research and innovation programmes. Access to affordable, reliable, and green energy is one of the biggest global challenges.
To tackle the problem effectively, we need to conduct basic research into alternative sources of energy such as the wind, the sun, bio-based fuels, and the Earth itself (geothermal energy), and to apply the results in the short term within multidisciplinary partnerships. In the end, a worldwide approach to this problem will be required. Combining the effective and efficient spatial planning and organisation of green energy with broad public acceptance will require input from a broad range of different disciplines, including the social sciences. A further point is the timely amendment of legislation. The Netherlands is firmly positioned in research in key areas and plays a pioneering role in various domains.

Submitted questions illustrating depth and connective power

- **How can we optimise the operation of a smart grid by means of local and centralised energy generation, sustainable generation, solar fuels, and local energy storage?**
- **To what extent can the behaviour and perception of green energy consumers and their influence on demand help improve the balance between green energy generation and consumption?**
- **How can we facilitate an integrated approach (i.e. food and fuels) as we transition to biomass as a renewable source of energy?**

How should we undertake the transition to an entirely sustainable energy supply?

Explanation

Our future energy supply should come largely from renewable resources. How do we undertake the transition from fossil fuels to solar, wind, geothermal, or bio-based energy? This question mainly concerns more practical challenges, with the energy supplied to industry being a particular point of concern. A number of other questions address different aspects of this problem.

Connective power

We need to undertake applied research to substantiate the alternative sources of energy (or combinations thereof) that we select and to predict the consequences of our choices. In addition to solar, wind, and bio-based energy, it would be sensible for us to explore the potential of geothermal energy. Efficient energy storage methods are the key to effectuating a breakthrough. If we are to have multiple sources of energy at multiple locations, then we need smart grid technology and technology that can match supply and demand, along with the related (international) pricing methods. Subsidiary questions are how to combine agro-biomass for green energy with the sustainable production of materials and food, and how to set up closed-loop systems for energy and energy resources. Advances in contactless energy transfer would greatly extend the range of electric vehicles and therefore increase public acceptance. As long as fossil fuels are indispensable, rigorous energy efficiency can provide a powerful means to speed up the transition. The design challenges lie in improving energy efficiency in the built environment and industrial processes, in utilising residual heat, and in preventing friction losses. Energy efficiency can also be achieved by changing our behaviour and making smart use of local conditions. Examples include data centres on Iceland cooled by the frigid surroundings, or greenhouses heated by direct sunlight in Spain. Applied social and logistical research can serve to support policy meant to introduce energy-saving interventions.

Submitted questions illustrating depth and connective power

- **How can the Netherlands wean itself off fossil fuels?**
- **How can we harness sources of energy that will remain renewable for the next few millennia, for example geothermal and solar energy? Can we improve the efficiency of plant photosynthesis for large-scale energy generation? How can we mimic photosynthesis?**
- **What will our energy system be like after the energy transition, when energy is generated locally?**

How can the sun meet all our energy needs?

Explanation

The one renewable source of energy that has the greatest potential worldwide is solar energy. It is available everywhere on earth and can be used as a fuel, to generate electricity, and to regulate the temperature. Although we are making increasing use of solar energy, its absolute contribution to the energy supply remains modest. If we want the sun to meet most or all of our energy needs, the conversion of sunlight into useful energy needs to be much more efficient and much less expensive than it now is. The relevant systems must also be durable and, preferably, based on widely available, environmentally friendly components and materials.

Connective power

Given the current state of knowledge and technology, we can only convert a limited amount of sunlight into useful forms of energy. Challenges for basic research lie in utilising more of the solar irradiance spectrum, minimising all the losses, and ensuring stable, long-term functionality. These challenges apply, in various ways, for every type of solar energy conversion, i.e. conversion to electricity, to fuels, and to heat/cold. Key areas of research include designing and synthesising new materials and structures, surfaces, colloids, molecules, and catalysts and improving biological processes and nature-inspired processes that resemble photosynthesis, for example. Advanced, efficient devices such as solar cells and complete systems will have to demonstrate the effectiveness of these components. There is economic potential in developing new product concepts such as electricity-generating roof elements and windows or thin-film solar modules. Integrated conversion and storage also offer new opportunities. Solar fuels are still in their infancy and the challenge is therefore to demonstrate their technical and economic viability. In addition to studying the technology itself, it is also very important to investigate the societal issues associated with the complete switch to solar energy, for example ‘How can the transition to solar energy drive economic activity and create jobs? Which economic models support the transition? What effects will the transition have on our living environment and how can we optimise the positive effects and minimise the negative ones?’ The question also concerns the Netherlands’ position as a production centre. What opportunities and threats does it face in building its position in solar energy? Does it have sufficient quantities of the right raw materials and enough production capacity? Are costs too high? What about patents, logistics, or its visibility as a key player?

Submitted questions illustrating depth and connective power

- **How can we make an ultra-efficient, hybrid solar-energy-conversion device that produces heat, electricity, and fuels?**
- **What research breakthroughs can we achieve and implement so that Dutch commercial parties derive maximum economic advantages from the growth of solar energy (more economic activity, more jobs, and so on)?**
- **Do roof-top solar panels have any harmful effects on the building’s occupants?**

What is the most efficient and sustainable way of converting wind energy into electricity?

Explanation

The wind is an important source of green energy. Research into wind energy covers such aspects as the materials used to make the turbine blades, aerodynamics (including noise production), and the efficiency of the turbines themselves. There are major public interests involved in questions in this cluster, certainly when it comes to selecting sites for wind farms. Given the problems of noise pollution and visual impacts, for example, it is important for countries to cooperate on developing wind farms in remote locations, such as international waters, but that implies transport, conversion, and storage issues. At the same time, potential harm to the environment must be kept to a minimum. Small and low-noise wind turbines are needed to allow wind power to be generated in urban settings. Small-scale wind power systems at multiple locations will require smart solutions that permit flexible interaction with the electricity grid.

Connective power

In terms of technology, we can achieve the biggest efficiency gains by scaling up wind turbines and wind farms. Both basic research and more efficient applications can lead to advances in wind energy, for example the development and use of new materials and the analysis of wind patterns in front of and behind the turbine, increasing their predictability and informing site selection. Big data can play a role in this. However, in addition to breakthroughs in basic research and technology, interdisciplinary and multidisciplinary research is also needed to analyse and surmount the societal, political, and institutional barriers hindering the transition to a sustainable energy supply.

Submitted questions illustrating depth and connective power

- **How can we improve the performance and lower the cost of wind turbines?**
- **How can we measure and model offshore wind farm sites, how can we predict how wind farms will interact with their surroundings, and how can we use this knowledge to optimise offshore wind energy?**
- **Can we produce hydrogen with sea water electrolysis using offshore wind energy?**

What is the most efficient way to use rivers, lakes, seas, and oceans to generate energy?

Explanation

Our future energy supply should come mainly from renewable resources. One idea is to harness the power of rivers and seas. Energy density in water greatly exceeds that in air. Potentially, then, there is much more energy in rivers and seas than in wind. Within ten years, refinements in this form of energy – known as hydropower – could have a major impact on our future energy mix. Many of the questions received address the possibility of combining hydropower with wind and perhaps also solar energy. If we were to utilise the sites of existing wind farms, for example in the North Sea, we would be able to streamline the necessary infrastructure without claiming even more space there. This question is closely bound up with other energy-related questions, specifically concerning wind energy. However, major technical and scientific issues remain concerning the best way to convert energy without this having a negative impact on flora and fauna, on other users such as inland shipping (rivers), and on flood protection systems.

Connective power

The Netherlands has considerable relevant expertise, specifically in the areas of marine and delta engineering (top economic sector ‘Water’) and energy generation (top economic sector ‘Energy’). In addition to technological and physics research, we also need to study the ecological aspects in order to determine the potential of hydropower as a renewable resource. Societal aspects also play a role in the transition to green energy. This cluster therefore connects to questions about the impact of human activity on nature. More fundamental questions concerning the functioning of the oceans are also highly important.

Submitted questions illustrating depth and connective power

- **Would it not be more advantageous and effective to generate electricity from hydropower in our rivers than from wind turbines?**
- **If we were to use tidal energy to meet the whole world’s energy demand, how would this affect the rotation of the Earth on its axis?**
- **Why aren’t we using the massive hydropower generated by the Eastern Scheldt Storm Surge Barrier to generate energy, for example, by positioning turbines below the surface, in front of the openings in the storm surge barrier?**

How can we optimise our use of geothermal energy?

Explanation

We urgently need to meet the rising demand for energy while reducing CO_2 emissions at the same time. One way of doing this is to use geothermal energy. Although current expectations are that geothermal energy will not solve the Netherlands' bigger energy problem, it can solve the issue of building heating and cooling. To determine its actual potential, we need to research the best methods for generating and transporting geothermal energy. For example, there are many questions about which materials or techniques are most suitable for utilising geothermal energy. The expense involved in generating geothermal energy also plays a role; if it turns out to be expensive, then it is unlikely to succeed in the current energy supply market. We must also study the effects of generating and using geothermal energy on the Earth, on groundwater, and on the environment.

Connective power

This question has a large technological component. Ecological, economic, and societal aspects also play a major role, however. This cluster therefore connects to questions about the impact of human activity on nature. The subject also reflects the larger question of how to transition to a sustainable society. The extent to which geothermal energy will be used will also depend on the development of other green energy alternatives, for example wind power or solar energy. Most of the questions in this cluster can be categorised under the heading of applied research. As a result, they could soon have an impact on society or the economy. Underpinning them, however, are fundamental questions concerning the functioning of our Earth and the climate.

Submitted questions illustrating depth and connective power

- **Is it possible to meet a substantial share of our energy needs with geothermal energy?**
- **Can we develop a method that would allow us to design geothermal heating systems for older buildings?**
- **Is it possible to use heat conductors to obtain thermal energy from the Earth?**

How can we use biomass as a feedstock and to generate energy in a bio-based economy?

Explanation

It is important to develop 'clean fossil fuel', as fossil energy sources are becoming depleted, and the burning of fossil fuels releases greenhouse gas carbon dioxide (CO_2) into the atmosphere. We can develop clean fossil fuel by making use of biomass waste, which does not compete with the cultivation of food crops, and can be used in, for example, power plant co-firing systems. To make biomass a truly 'clean fossil' fuel, the CO_2 that it releases must be captured and/or converted into useful products.

Connective power

This question combines many subsidiary questions (both basic and applied in nature) concerning a biopower value chain based on biomass that does not compete with food crop cultivation, and in which the CO_2 emissions can also be used as a feedstock. In terms of basic research, the questions concern new methods for biomass conversion. The questions about temporary carbon sequestration and CO_2 as a feedstock also require basic research. But many of the questions are also applied in nature and concern how new processes can be transformed into practical designs for the value chain. The significance of new value chains for the bio-based economy requires us to evaluate matters at different orders of magnitude. What will the positive and negative effects on the environment be? Potential displacement effects also need to be critically examined.

Submitted questions illustrating depth and connective power

- **How do we develop energy-efficient chemical processes for carbon dioxide conversion and storage, for waste conversion, and for the conversion of biomass into chemicals without producing waste?**
- **Can we develop new catalysers that allow for more efficient carbon storage and for synthetic photosynthesis that is more efficient than plant photosynthesis?**
- **Can renewable biomass replace petroleum as our most important feedstock for the production of chemicals (and fuels)?**

How do we accelerate the development of nuclear fusion, and how can we make nuclear energy safe and clean?

Explanation

Nuclear fusion (joining two atoms) and nuclear fission (splitting an atom) both release vast amounts of energy. Nuclear energy has the potential to contribute to a more sustainable energy system, but before that can happen the technology must be available, affordable, clean, and safe. Nuclear fusion has a few important advantages over nuclear fission technology, specifically with respect to waste and safety issues. Scientists have been working on the development of a continuous nuclear fusion reactor for several decades now, but technical, political, and administrative obstacles have blocked the path to a commercially available product with large-scale potential. That is why nuclear fusion is not usually included in energy supply scenarios. The question is whether its development can be accelerated and, if so, what is required technically and scientifically to achieve this.

Nuclear fission would be more acceptable as a green energy option if convincing solutions could be found for its waste and safety issues. The question is what science and engineering can do to force a breakthrough that will also persuade the public.

The Netherlands has long been an important and valued participant in international nuclear fusion programmes. Dutch scientists are knowledgeable about nuclear technology and safety.

Connective power

Answering this question requires a multidisciplinary effort that combines physics, materials science, mechanical engineering, and other disciplines. Many different high-tech companies are involved in developing nuclear fusion in Europe. The progress they have made has economic potential, but European research depends on European rules and decision-making processes. The relationship between nuclear fission and the arms industry has put the emphasis on uranium at a very early stage of its development. Another option is to build reactors based on thorium. A thorium-based reactor can be made safer and it produces less waste of lower radioactivity than a uranium-based reactor, it is less of a problem for the environment. The theme of nuclear energy necessarily involves issues of public acceptance and interaction with the political world, both domestic and international.

Submitted questions illustrating depth and connective power

- **Is the thorium molten-salt reactor the ideal solution to the energy problem, and can the Netherlands play a key role in its development?**
- **Can nuclear fusion help provide a clean solution to the energy problem within thirty years?**
- **What will scientists accomplish first, nuclear fusion or artificial photosynthesis – and why?**

How can we store, convert, and transport energy efficiently?

Explanation

One crucial challenge related to the large-scale use of renewable energy sources (for example solar or wind energy) is to have the energy available when we need it and where we need it. We need to store energy to even out discrepancies between patterns of supply and demand; this involves dealing with different timescales and locations by using smart grids and smart energy pricing. We can store electricity in batteries and heat in thermal batteries. We can also use kinetic energy, such as in flywheels, or pressure, for example in the form of compressed air or by pumping water to reservoirs at higher altitudes. We can also store energy in the form of fuels or in chemical bonds in general. For example, we can use electricity to produce hydrogen from water, and then turn that hydrogen into other gaseous or liquid fuels that can be stored for longer periods of time and easily transported. New materials underpin the breakthrough technologies that we need to make rigorous transitions. Basic research into materials is also relevant for the societal transition from fossil to green energy, with scientists working closely with engineers and applied researchers on this. The recent discovery of perovskite solar cells is an example of how materials research continues to open up new prospects.

Connective power

Energy storage and supply-demand matching are important priorities in research and innovation programmes focusing on green energy. Researchers are not only exploring new properties of materials but also studying more efficient energy conversion, alternatives to energy-wasting electronics, loss-free energy storage, and grid utilisation. The relevant questions concern catalysis, transparent conductors and semi-conductors, superconducting at high temperatures, replacing scarce and expensive materials such as lithium in batteries and rare-earth metals in magnets, metals and ceramics that can be used in extreme conditions, but also whether piezoceramics can be used to convert kinetic energy into electricity. In addition to technological innovation, influencing behaviour and social adaptation play a major role. The global energy market will offer opportunities for Dutch businesses able to translate their R&D into low-cost product concepts and systems. The question is in line with the policy priority ‘Closed-loop energy, material, and water systems’ and ‘Sustainability (green economy)’.

Submitted questions illustrating depth and connective power

- **How can we alter existing buildings and cities to radically improve their energy performance?**
- **How can we come up with new methods or strategies for linking our natural and cultural heritage with energy-related challenges?**
- **Can we develop materials that will transport energy over long distances with minimum losses?**

What are smarter and greener ways of transporting passengers and goods that make optimal use of all forms of transport?

Explanation

We have access to many different transport options nowadays, each one with its advantages and disadvantages. Seamless connections between forms of transport (modalities) can provide an almost imperceptible and frictionless transportation system that meets the global demand for flexible, inexpensive, and sustainable passenger and goods transport at any given time and under any given circumstance. Although this is a global, or at least European issue, the Netherlands plays an exceptional role in this context owing to its exceptionally wide variety of transport options. In addition, important new technological innovations have emerged, such as the self-driving vehicle, transport chain management facilities, and other advanced technologies that will influence mobility issues for both passengers and goods. Intelligent travel information will grow increasingly popular, and the ratio between the various transport modalities will change. This question therefore covers multiple aspects: smart infrastructure and vehicles, advanced algorithms that enable a high level of control over the entire transport chain, and providing decision-makers with the right ICT support.

Connective power

Passenger and goods transport is increasingly being viewed as an integrated system in which the various transport alternatives influence each other and in which the robustness of the system also depends on the range of different transport modalities available. The challenge for basic research lies in modelling and analysing this integrated transport system. Applied and design research are needed to develop control mechanisms for that system, whether for passengers or goods. Another important challenge for science entails the development of new transport alternatives, for example self-driving cars, but also the relocation of production owing to 3D printing. These questions are technical in nature, but also social, moral, and legal. The way our society functions depends largely on mobility (passengers and goods) and how well we synchronise the various flows. This question therefore also has an important societal component, for example concerning traffic and transport as a source of environmental pollution and the alleviation of traffic congestion, but also the growing individualisation of public transport, finding the right balance between the various transport alternatives, and managing energy consumption in transport. Our need for mobility is expensive. The cost is even higher if we factor in time lost to congestion, the negative impact of emissions and other pollution on health, and the loss and damage of goods and other expenses. Research should result in these costs being lowered while allowing us to maintain an acceptable level of mobility. In addition, there are opportunities to market our expertise concerning mobility system development.

Submitted questions illustrating depth and connective power

- **How will global, European, national, regional, and local trends in goods and passenger transport affect our mainports and national policy targets?**
- **How can Smart Mobility help us make our cities smarter, greener, and more liveable?**
- **How can we improve the logistics of e-commerce so as to reduce the environmental pollution that it causes?**

How can more efficient means of transport contribute to the energy efficiency and environmental-friendliness of the overall transport system?

Explanation

As mobility and transport levels rise, we need transport propulsion systems that are more energy efficient and environmentally friendly. This means a) switching to systems that are inherently greener and more efficient and b) continuing to improve conventional propulsion systems. The latter involves optimising combustion processes to create radically new types of engines. We not only need to adapt existing propulsion systems but in fact to optimise the entire power-train, i.e. the chain that leads from an energy-producing part to a part that converts that energy into a force, and to another part that then applies that force to a part that is meant to move. There are also many different ways to improve the efficiency of the transport system by means of aerodynamics, hydrodynamics, materials, and the design of completely new transport alternatives. Transport can also be streamlined by applying smarter logistics that combine real-time data, applied mathematical models, smart sensors, and the Internet of Things.

Connective power

The research needed to address this question is widely varied: it covers propulsion systems, alternative fuels and efficient energy storage systems, smart logistical models, new materials, coatings, air-vapour mixtures, and methods for accurately testing engine energy efficiency. A knowledge of fluid dynamics is also important for meeting the objectives of efficiency, low energy, and low environmental impact.
It is of huge relevance to society to have an effective transport system made up of safe, sustainable, low-energy means of transport. One significant way to overhaul that system is to innovate the technology and how it is used, while also amending the relevant legislation and considering the role of humans and their behaviour. The Netherlands is a key supplier in many of the relevant equipment manufacturing industries. Its marine equipment industry produces large numbers of complete, often exceptional, vessels. Much of the expertise acquired through research is applied almost directly in these sectors. The Netherlands has developed internationally recognised best practices in smart logistical systems, for example at Amsterdam Airport Schiphol and the Port of Rotterdam. Dutch knowledge-driven institutes and businesses can supply expertise and technology to European and global equipment manufacturers, creating major opportunities for them in transport equipment development. The Dutch position is solid because of the close relationship between knowledge-driven institutes and businesses, for example in the high-tech, marine equipment, and aerospace industries.

Submitted questions illustrating depth and connective power

- **How can we make traffic and transport silent and emissions-free?**
- **How can we come to understand turbulent flows better, describe them more efficiently, and influence them more directly?**
- **The Netherlands is a maritime nation. How can we use transport by water (seas and river delta) to help us meet the climate change targets (lower emissions) and to relieve traffic congestion on land?**

How can we improve traffic and transport safety?

Explanation

Efficient and safe traffic and transport are very important to our society. The public and government have been greatly concerned about the safety of our traffic and transport system for many years. That concern is unlikely to diminish as the setting in which traffic and transport take place grows ever-more complex. The relevant risks are considerable: human lives can be lost, and means of transport and infrastructure can sustain economic damage. In addition, disruptions to traffic and transport flows generally have far-reaching consequences. The public finds transport accidents increasingly unacceptable. The types of accident differ considerably from one category of transport to the next. Road traffic accidents are relatively frequent but minor, whereas marine and aviation accidents are much less common but claim many more victims or cause much more damage. In addition, the setting in which transport takes place is increasingly crowded. That is true of the sea, owing to the construction of wind farms and drilling platforms for oil and gas, not to mention the presence of fishing vessels. But it is also becoming more crowded in the air, on railway lines, on rivers, and on motorways. A further complication is that the Netherlands is responsible for safety in a transport system that foreign parties also use. The vessels in our waters, and, increasingly, the lorries on our roads and aeroplanes in our airspace are not of Dutch origin, or are driven or piloted by foreign personnel. Nevertheless, the Netherlands must ensure the safety of its entire traffic and transport system.

Connective power

This question encompasses a number of different elements. It is about the role of new transport technology, for example autonomous, unmanned transport, and technology that can limit damage, predict accidents, or save victims more effectively. But it is also about the role of humans as participants in traffic, as transport operators, and as stakeholders in a safe transport system. It is also about how society views safety. The latter aspect is expressed in such questions as ‘Can shipping be made even safer?’ and ‘Is flying safer than driving?’. It is up to science to develop new solutions that promote safety in the various transport modalities and to discover the causes of accidents and risk. One example of the latter is to gain a deep understanding of the predictability of traffic flows in aviation, or of the hydrodynamics that determine the stability of vessels. Materials technology can also contribute to making transport safer.

Submitted questions illustrating depth and connective power

- **How can we ensure safe and efficient shipping and aviation in and above the North Sea while intensifying its use (wind farm construction and maintenance, aquaculture, LNG pipelines, and so on)?**
- **How can we improve safety at sea for people, cargo, and the environment by enhancing the interaction between humans and a ship under navigation as a complex system? Is autonomous ship navigation a solution, and in what way?**
- **How can we make a rapid and successful transition to cooperative and autonomous driving?**

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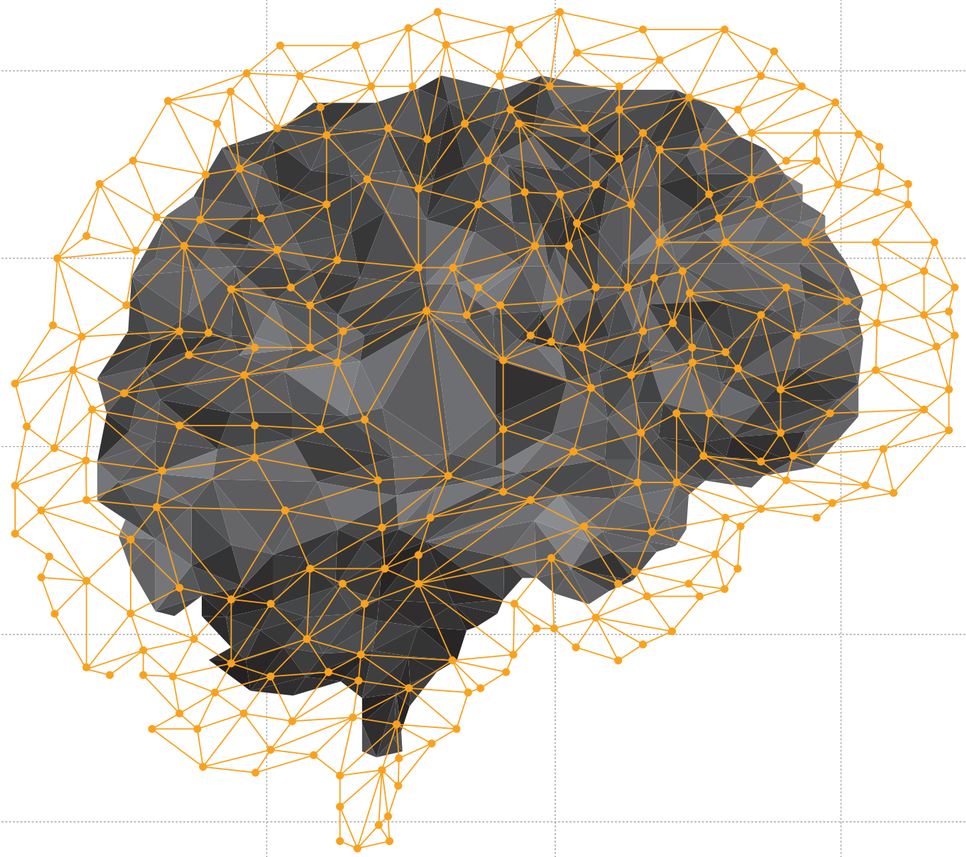
Individual and society



How can we keep our densely populated country liveable?

Explanation

Over the next few years, the Netherlands must come up with a comprehensive response to such challenging issues as population growth, changes in ecological structures (e.g. water management and nature conservation), traffic and transport regulation, and the economic and social welfare of farmers and others. In a densely populated country like our own, it is hugely important to consider all these interests and to find an acceptable balance between investments in infrastructure and facilities (e.g. for water management) and the efficient use of those facilities. Harmonisation and coordination are necessary to keep the Netherlands liveable – both literally and figuratively – and to continue fulfilling our role as the gateway to Europe.

Connective power

Spatial planning involves fundamental questions about the relationship between humans and nature and the way in which economic, social, and cultural functions can be combined or weighed up against each other. Relevant questions include the following:

- What conditions must be in place to improve the quality of the living environment? How can the public and policymakers help create those conditions?
- How can we improve water management in the Netherlands/Europe? Water management has been an overriding concern in the history of the Netherlands and will continue to be so owing to large-scale climate change, mobility, and more intensive use of the available land for a variety of purposes.
- How can we find better solutions to today's and tomorrow's traffic and logistics problems? The Netherlands will remain important as a transport node and gateway to large and important European sales markets. Traffic and logistics issues are therefore extremely important, for example in terms of Gross National Product and prosperity.

Submitted questions illustrating depth and connective power

- How will climate change and new patterns of mobility affect the management and maintenance of our roads, waterways, and rail infrastructure?
- What will the ideal traffic network of the future be like?
- How can we create sustainable landscapes in which nature, farming, recreation, traffic, industry, and housing are not locked in a constant battle for space, but instead are mutually enhancing within a single region?

What does globalisation mean for our cultural identity and for the position of the Netherlands on the world stage?

Explanation

The worldwide migration of art, culture, and knowledge is sparking processes of interculturalisation and fuelling the question of what is 'ours' and what is 'foreign' – a phenomenon that is affecting our national self-image and identity. Throughout history, global cultural transfer and transformation have led to convergence, homogenisation, the loss of variety on the one hand, and greater diversity on the other. Research into past and present interactions and networks helps us understand how the conceptualisationof identity arose, and can explain philosophical, ethical, and aesthetic self-images. An appreciation of these images is important at a time when the Netherlands needs to position itself culturally, economically, and legally in the face of global migration and the process of European unification.

Connective power

The question of our national identity, our national self-image, and how these relate to globalisation is informed by current events that are coloured by issues of nationhood and migration flows. If we regard culture as a product of migration, then research should address such questions as the role of the image as defined by the media, the relationship between the culture of the native country and diaspora cultures, or the role of stereotyping in constructing our national self-image. It is important for the position of the Netherlands in future and for the adaptability of its inhabitants to understand how its relationship with the rest of the world has evolved over time. A striking example is the history of the Dutch slave trade and how that history affects the present day. Research into this question is relevant because it concerns the resilience of our society, where stability is an essential condition for economic and social progress.

Submitted questions illustrating depth and connective power

- Which forms of global cultural transfer and transformation have led, throughout history, to convergence, homogenisation, and the loss of variety? Which have led to greater diversity and/or conflict?
- How can the arts (literature, film, visual arts) help us understand issues of national identity, radicalisation, and terrorism?
- How will globalisation change the role of the nation state in the longer term?

What do Europeanisation and globalization mean for democracy and the constitutional state?

Explanation

Europeanisation and globalisation have put constitutional democracies under enormous pressure. Traditionally, democratic institutions are organised at local and national level, but the big economic, ecological, and social issues of our time – including climate change, migration, cyberwar, and financial crises – are increasingly being tackled and regulated on a European or global scale. In the context of supranational, multi-level governance and regulation, the nation state often loses sovereignty. There is said to be a widening chasm between politicians and ordinary citizens, not only within countries but also in Europe and globally. How is this change in the social order affecting democracies and systems of law as we know them? What is happening to the norms and values that underpin these systems? What new forms of governance are emerging that are better able to regulate supranational challenges?

Connective power

These trends give rise to explanatory, normative, and design questions. What forms of global governance are emerging and to what extent are they legitimate and effective? How can we guarantee the long-term legitimacy and robustness of our constitutional democracy in a globalising economy, and which institutions will that require? In an increasingly interconnected global society, how do we shape and define supranational decision-making, regulatory arrangements, and governance while ensuring the necessary public support? How can we make European and international institutions more democratic and resolute? To what extent will national legislatures and national democratic institutions retain their primacy? We can examine the issue of multi-level governance from the perspective of individual people, nation states, or international systems of law. An interdisciplinary approach is needed that draws together the study of law, the science of public administration, political science, history, European studies, and international relations.

Submitted questions illustrating depth and connective power

- **How can political leaders govern the European Union without losing touch with the public, and without the public losing touch with them?**
- **How can we develop responsible and effective national and international policies, rules, and monitoring systems for public-private partnerships?**
- **How can we develop legislation and governance structures that protect and help implement human and other rights, both now and in the future?**

How robust is democracy, how much confidence does society have in it, and how can we make improvements in both cases?

Explanation

The legitimacy of national representative democracy is under pressure as its institutions face new challenges. Those institutions are now more than one hundred years old. Are they fit for purpose in the 21st century? People today are much better educated than they used to be, more assertive about their needs and wishes, and better organised. Power must be shared with other countries, private parties, and lower tiers of government, all of which are beyond the direct supervision of the national legislature. In addition, the recent financial crises have given rise to 'non-majoritarian' institutions, which take important political decisions without having a direct electoral mandate. Examples include the European Central Bank and numerous other independent market authorities and regulatory bodies. This raises a series of questions about the robustness of democracy and about possible adjustments. Can we improve the performance and legitimacy of democratic institutions by making more use of opinion polls, popular initiatives, referendums, or even appointments by lot? Are there alternatives to political parties and legislative bodies?

Connective power

The robustness of democracy is of preeminent relevance to society. We know a great deal about the waxing and waning of legitimacy in Western societies. For example, the public still believes wholeheartedly in the principle of democracy, but many people in many countries have little confidence in politicians and political parties. We know considerably less about how the aforementioned fragmentation of power impacts legitimacy, even though it represents a major shift in public administration. Are there other ways to speak on behalf of society, for example deliberative forms of democracy, appointment by lot, or online opinion polls? Will the Netherlands still be governable in that case? From what authority do non-majoritarian institutions derive their legitimacy? The relevant research questions are empirical, descriptive, evaluative, and normative in nature, and there are also important design issues involved. What types of institutional reform are possible, necessary, and desirable in representative democracy? In answering these questions, the Netherlands can build on its long tradition of comparative political science and research in the fields of public administration, ethics, history, and the law.

Submitted questions illustrating depth and connective power

- **How can we 'update' the democratic system?**
- **How big must the chasm between politicians in The Hague and the people become before the public rejects politics and rule-making en masse?**
- **Is it possible to have a democracy based on opinion polls?**

How robust is the welfare state, given the changing composition of the Dutch population?

Explanation

The composition of the Dutch population is set to change considerably in the decades ahead. Population decline in certain regions and the ageing of the population are altering the economic structure; the impact of migration is still unknown. It is possible that our trade surplus will become a trade deficit, and that people will save less (for example in a pension fund) and spend more. This new situation has inspired fundamental questions that also have global relevance. The first concerns the robustness of the welfare state and care structure. Can it adequately support the growing population of elderly people financially and in practical terms? What dilemmas will surface? More specific questions concern the relationship between the welfare state and migration. Is migration an opportunity for the Netherlands, or is it aggravating problems? Is international policymaking required? There is a connection here with global trends such as overpopulation, the refugee crisis, and environmental issues.

Connective power

This is an interdisciplinary problem. It is basically an economic issue, but one that has ties with political science, geography, sociology, demographics, history, ethics, health care. Because similar trends are materialising all across Europe, and because this question is related to problems worldwide, it lends itself to international (comparative) research.

Submitted questions illustrating depth and connective power

- **How will the ageing of the population affect the design of the living environment?**
- **How safe are pensions, really? Is there a better yardstick than the fictitious yields based on interest? What interests are involved, and why (politics, e.g. tax income; unions; the elderly; young people; banks/insurers; and so on)?**
- **How do we ensure that population groups originating in other parts of the world are just as healthy as the native Dutch population?**

How can we best design the socioeconomic institutions of the future?

Explanation

The 2008 financial crisis and its lingering effects have made us aware of the need to improve institutional design in the social and economic domains. For centuries, the Netherlands has been one of the most prosperous and just societies in the world. The Dutch appreciate this and consider their lives happy ones. In the longer term, however, the Netherlands will face growing social inequality and global economic competition. There is no guarantee, then, that tomorrow will be as pleasant as today. Many people agree that we must reform the financial sector, make the economy more sustainable, and ensure equal opportunities for all. What that entails is less clear, however; neither do we know for certain how we are to achieve these aims. The free market, public-private partnership, and state intervention are three familiar models, but are any of them actually effective? These questions are not only technical ones, but also imply alternative societal analyses. Differing ethical and political views will also play a major role when implementing solutions.

Connective power

The search for answers to interdisciplinary questions will involve examining issues from different perspectives and disciplines, such as philosophy, ethics, history, the law, political science, economics and the social sciences. The questions include the following:

- Is the free market always the best mechanism of economic production, or is it better to supply certain goods and services according to some other model?
- How has capitalism evolved over time, and to what can we attribute its successes and failures? Are any alternative economic systems conceivable, feasible, and desirable?
- Would a basic income be feasible (politically, financially, socially) and desirable?
- What are the determinants of demographic changes in the shorter and longer term, both locally and globally? What consequences will demographic changes have, and how can we deal with them?
- What is the future of the welfare state? How is decentralisation in the social welfare domain and other changes affecting various groups in society? What does the public think about these effects?

Submitted questions illustrating depth and connective power

- **Alongside Gross National Product (GNP), why don't we introduce a new indicator: Gross National Reference Values Product?**
- **Can we develop a scenario generator for the financial sector?**

How are digitisation, globalisation, a more assertive public, and other changes in society impacting public and semi-public institutions?

Submitted questions illustrating depth and connective power

- **Which forms of public management and professional activity can improve the effectiveness, efficiency, and legitimacy of a public administration that is increasingly relying on popular initiatives and co-production?**
- **How do we design a governance system in which local variation can be used to promote learning and in which decisions are also subject to democratic accountability?**
- **Would appointment by lot to political positions be a good idea for the Netherlands, from a scientific perspective?**

Explanation

A more assertive public, digitisation, globalisation, and other changes typical of contemporary society are putting pressure on traditional forms of organisation, governance, legislation, enforcement, and adjudication. The effects are noticeable both in government and in large non-profit organisations. How are these changes affecting the basic constituents of constitutional democracy, including the voting system and the primacy of popular representation? What alternative institutions might be considered, and how do these compare to the current system of public administration? Innovative forms of regulation ('nudging', public participation, norms embedded into technology) sometimes turn out to offer more effective incentives and control. How can we take advantage of new options to improve the effectiveness, legitimacy, and public acceptance of legal regulations, legislation, court rulings, and enforcement? Cooperative initiatives have also been springing up everywhere in recent years, meeting needs that central government appears less capable of satisfying. Which factors are most important to their success or failure? Which legal frameworks are appropriate? The same changes can be seen in large non-profit organisations such as schools, hospitals, housing cooperatives, clubs and associations. How can these organisations demonstrate social responsibility and organise an appropriate level of public accountability while retaining their private character?

Connective power

This question links internationalisation, information science, informalisation, individualisation, and intensification with the performance of public and semi-public institutions. It is relevant at global, national, and local levels. Research should first examine the precise nature of these trends and developments. How do the underlying technical, social, economic, and institutional factors interact? The question not only lends itself to descriptive and analytical research, but also examines the value of these societal changes. Are they allowing us to make progress towards a better society, or not? For authorities and large institutions, there is also the practical question of how they should respond to these changes. New research results can offer practical support to institutions struggling with these change processes. The question lends itself to transdisciplinary research that unites various disciplines (political science, the science of public administration, the study of law, sociology, history, organisation science, ethics) with non-academic fields. Action research and social change go hand in hand here.

How has the most recent major recession impacted society, and how can financial systems be reformed to avert such crises in the future?

Explanation

A relatively minor shock in the US housing market sent the global financial system to the edge of the abyss. Banks got into trouble and had to be saved. World trade collapsed, throwing many countries into a deep and lengthy recession. Companies failed, employees lost their jobs, and young people were shut out of the workforce. The effects have differed from one country to the next, and each country has responded to the crisis in its own way. What impact will these differences have on their societies, both in the shorter and somewhat longer term? As international networks and interdependencies grow, countries, societies, organisations, and people have become more and more vulnerable to crises of this kind. The question is whether such crises can be prevented in the future, and how.

Connective power

Recessions are not purely economic phenomena. The consequences for people, organisations, and social structures are far-reaching and affect many different aspects of daily life. Research into the causes and, in particular, the effects of crises involves economics, political science, the behavioural and social sciences, and – for example – the health sciences.

- How has this crisis affected the foundations of (Western) economies and how should we examine the financial system, the housing market, the pension system, unemployment, and other factors in that respect?
- How do people cope with dwindling certainties in their everyday lives?
- Should steps be taken to organise supervision, governance, and the accountability of financial institutions and individual bankers in such a way that the individual incentives enjoyed by the banks and bankers are more commensurate with their responsibilities to society and related action?
- Is it desirable and feasible to regulate the financial system or the financial markets?
- What has been the impact at global level, on emerging economies such as China, India, Indonesia, and Brazil, and on the fragile economies of developing countries?

Submitted questions illustrating depth and connective power

- **How do the real economy and the financial sector influence each other?**
- **Can we apply what we know about epidemics and ecology towards designing protocols for stable financial markets?**
- **Why do some societies handle shocks and crises better than others?**

How do we strike the right balance between freedom and responsibility (individual and collective)?

Explanation

Questions about freedom and responsibility go right to the heart of our concept of mankind. The urgency of such questions has increased as society grapples with such crucial issues as climate change, social conflict, the rising cost of health care, and the growing inequality between rich and poor. To what extent are individuals, organisations, and government responsible for doing something about these problems? What does this moral obligation – or the lack of one – mean for the balance between self-reliance and interdependence? And how can we promote both self-reliance and interdependence? We have learned a great deal about how allocating responsibilities promotes cooperation, for example material incentives and sanctions, or social control in informal networks. Informal, formal, and virtual associations are more fleeting now than they used to be, however, whereas many collective responsibilities – keeping the neighbourhood clean or maintaining productivity in a company– require long-term forms of cooperation. The question is how material incentives and social control can be applied most effectively in both fleeting and lasting cooperative relationships to support collective responsibility and cooperation.

Connective power

This question connects philosophy, psychology, sociology, law, the neurosciences, and economics. It addresses the relationship between such concepts as freedom, free will, and responsibility (individual and collective). We also need to know how freedom and responsibility relate to self-reliance and participation. Is it the responsibility of every citizen to manage things for themselves? Am I free to participate, or do I have an obligation to do so? A description of what is morally right is unavoidable in this context, pointing up the normative aspect of the question. The design aspects can be viewed in relation to national policy frameworks. An unequivocal conception of freedom and responsibility is what underpins the vision of society that political parties wish to promote. That vision is recast into policy frameworks in the social welfare and health care domains. Applied and practice-based research in these domains can produce innovative solutions and practical applications that will boost the resilience of both individuals and society.

Submitted questions illustrating depth and connective power

- **How can we encourage moral conduct in the banking industry and quasi-governmental sector (such as housing corporations, schools, and care institutions) and ensure that such conduct is institutionalised?**
- **To what extent can, may, and must government prevent people from fighting boredom with violence if there is less work about for them to do?**
- **How is the Netherlands planning to cope with its growing population of elderly people?**

How can the law and other forms of regulation provide sufficient legal certainty while also responding to opportunities and challenges in society?

Explanation

Society is changing rapidly. Globalisation, digitisation, and the growing influence of private parties are opening up new opportunities for society, for example through innovations in ICT and social media. But they also set challenges that have huge implications for the rights of individuals, for example in the health care system, forms of religious expression, or social security. The law and other forms of regulation are meant to safeguard and enforce these rights, but they must also be flexible and adaptable enough to keep pace with a changing society. How can we combine flexibility and certainty so that the law, regulations, and policies make a positive contribution to social prosperity and our wellbeing?

Connective power

This question invites innovative interdisciplinary investigation of a set of legal/administrative measures that will be flexible and efficient enough to facilitate modernisation while also promoting legal certainty and social wellbeing. By asking evaluative/normative questions, researchers can explore how existing laws and regulations reflect the state of society today. For example, as the average age of the population increases, existing debates about the right to certain medical treatments will soon grow critical. The sharp rise in the number of own-account workers has raised new questions about employment contracts, but also about the claims made on the welfare state. And what is the relationship between national citizenship and European Union citizenship? Solution-driven design questions could lead to new insights into how the law, regulations, and the relevant institutions can better anticipate societal challenges and economic opportunities. For example, they might consider whether a self-correcting capacity can be incorporated into financial regulations, or explore which financial and legal models make road leasing possible. Although initially legal professionals will be most affected by research questions concerning the law, they are not the only ones. Scholarly disciplines such as the study of law, the science of public administration, sociology, and psychology can make an important contribution.

Submitted questions illustrating depth and connective power

- **How can we put a stop to or even reverse the increasing juridification of society?**
- **Is nationality still a suitable reference factor in international family law?**
- **Which current laws need to be amended to make it easier for the elderly to continue living on their own or to make available more informal care in the community?**

How can we improve the effectiveness and legitimacy of legislation, given the global challenges we face with respect to the environment, security, innovation, energy, and climate change?

Explanation

Global society faces a vast number of challenges that will be difficult to manage for various reasons. What role can legislation play in successfully addressing what are often cross-border challenges and problems, specifically those related to energy, security, innovation, the environment, health, and climate change? What set of regulatory and legislative tools can make the most effective contribution, considering the global scale of these challenges and the complexity of the value chains in which people, groups, businesses, and organisations operate?

Connective power

This question covers three related issues concerning the function of legislation in today's society. In the first place, new problems and new solutions lead to new, undesirable human and organisational activity that must be combatted by new legislation. Second, existing legislation is often an obstacle to innovation of all kinds. Third and last, modern advances, for example in ICT, are extremely useful when attempting to improve the effectiveness of legislation and its enforcement.
Research associated with this question focuses on the function and structure of legislation and its impact on society. It is, in part, concerned with generating new knowledge, but it is also a design question. How do we improve legislation? The societal challenges contained in this question encompass the three issues described above: addressing new problems, preventing legislation from obstructing innovation, and using new technology and solutions to improve the effectiveness of legislation. These issues apply in a variety of areas: environmental protection, security, innovation, energy, climate change, mobility, technology, entrepreneurship, organisational forms, development cooperation, and so on. Constructing effective legal frameworks for all these societal issues will give entrepreneurs, consultants, and NGOs opportunities to apply the same solutions towards other societal challenges and in other countries.

Submitted questions illustrating depth and connective power

- **How can we protect our energy system against hackers and others with malicious intent?**
- **How can we use big data to evaluate the effectiveness of government policy, in particular legal and other interventions/sanctions?**
- **To what extent can we resolve the points on which climate change and air quality policies conflict so that emissions mitigation is more effective and a win-win situation arises?**

What is the 'inequality problem'?

Explanation

Inequality is a major priority on the social and political agenda, and not just in the Netherlands but in large parts of the world. Inequality motivates people to put more effort into climbing the social ladder, but in extreme forms it can also be disruptive and undermine economic growth and social cohesion. The post-war reduction of income and capital inequality appears to have been reversed in recent decades; economic inequality is on the rise again in many countries. Inequality leads to inclusion and exclusion, and it is important to know its causes.

Connective power

Equality is one of the core values of modern society. In the reality of everyday life, however, numerous inequalities still prevail, rooted not only in socioeconomic distinctions but also in conscious and unconscious processes of categorisation based on gender, skin colour, sexual preferences, ethnicity, religion, language, mental or physical limitations, age, nationality, and so on. This issue raises empirical, normative, and design-related questions for a whole series of disciplines, including sociology, economics, history, and law. For example:

- Is inequality undesirable in and of itself, or because it is harmful to other values?
- What social and economic inequalities exist in the Netherlands, and what trends do we see in that regard?
- How can we explain the presence of inequalities historically?
- Can we conceive of systems that would offer greater equality and maintain or increase prosperity, or is there an inevitable tension between equality and other aims that we pursue, such as economic growth?
- What are the effects of policy measures and interventions designed to reduce inequality?
- How can lawmakers help promote an inclusive society to which everyone has access?

Submitted questions illustrating depth and connective power

- **How do the pace and nature of economic growth and globalisation impact the development trajectory of societies and the way in which means and resources are distributed between social groups, both locally and globally?**
- **Can the introduction of a basic income (ultimately for everyone) give the Dutch economy (and others) a positive boost? If so, approximately how big should that basic income be?**
- **What is the best way to fight implicit racism and sexism?**

How can we limit poverty and increase wellbeing worldwide?

Explanation

Along with war, poverty is one of the main factors driving international migration. Although economic migration may have huge benefits for both departure and destination countries, migrant populations often fail to integrate, leading to tensions between the new arrivals and the native population. Does the failure to integrate entail a security risk? Is this creating an underclass vulnerable to the allure of international terrorism? Is it best to address such problems with repression, or by supporting and promoting integration? Can we promote international security with certain forms of development cooperation? Over time, governments and private organisations have developed a wide-ranging set of policy measures and related interventions, geared to tackling the causes and/or consequences of poverty. Our challenge now is to understand how effective these measures are so that we know which ones we should be applying in the future. The ultimate aim is to limit poverty and increase wellbeing worldwide.

Connective power

A multidisciplinary approach is needed to answer this question. Economics, international relations, sociology, the study of law, history, and development studies can all help untangle the effects of specific policy interventions, including peace-keeping missions, food aid, partnerships meant to promote security, and investment in the economy or in the establishment of constitutional democracies. The purpose of these interventions is to make a positive contribution to prosperity and wellbeing. One of the challenges for science is to undertake applied/evaluative research on the effectiveness of specific interventions, with comparative research revealing how successful various types of measures are. Researchers must further explore the effectiveness of different types of policy measures, for example communicative, financial and economic, legal, and facilitative. It is also important to conduct evaluative/comparative research on the circumstances in which an intervention succeeds or fails, for instance the degree of political support for certain measures. Another challenge is to conduct strategic/design-based research meant to develop innovative strategies against poverty. It is important to develop interventions that both limit poverty and generate more economic value, leading to greater prosperity. In addition, new insights can be used to develop new types of intervention. We can view this question from both a national and international perspective.

Submitted questions illustrating depth and connective power

- **Which forms of social policy (social safety nets) have contributed to economic growth in developing countries, and which have not?**
- **Can we reduce world hunger if we stop eating meat?**
- **What can we do to involve older migrants in preventive health care and information programmes about healthy diet and exercise?**

What are the causes and consequences of migration, and how can we deal with them?

Explanation

Migration is not a new phenomenon. Europe is to some extent the outcome of a cultural, religious, and socioeconomic diversity that resulted from centuries of migration. Regional conflicts, failing states, globalisation, and European integration are leading to vast and extremely diverse migrant flows to and within Europe. This has opened up deep divisions between different groups in society. The distinction between 'the people' (*dêmos*, as in 'democracy') and 'the others' (foreigners, immigrants) is one of the foundations of the modern nation state. Without borders, there is no national state. The rising flow of international migration is putting pressure on these traditional distinctions, however. In the Netherlands and other countries, 'the people' have long ceased to be culturally or ethnically homogenous, and borders are becoming increasingly permeable.

Connective power

This question links a large number of highly relevant historical, empirical-analytical, evaluative, normative, and design-based questions that are both multi-layered and multidisciplinary in nature. Sociology, history, law, criminology, ethics, cultural studies, and political science are working together to answer the following questions:

- What trends do we see in migration flows, what is the nature of those flows, and what is causing them? What is the connection between the present migration flows and European colonialism and imperialism?
- What conditions facilitate the successful integration of migrants; conversely, how does exclusion arise? How does our society interpret the concept of citizenship, both formally and informally? How can legislation help ensure that migrants and minorities are well treated? How can we ensure that those who are not citizens of the country in which they live and work are heard, in the political and cultural sense?
- How should we appraise migration flows? How will present-day international migration and cultural diversity affect the resilience and sustainability of societies?
- How can we manage migration flows effectively? What are morally just and prudent ways to deal with migration and refugees? What rights and obligations do national majority populations owe minorities? What rights and obligations do nation states owe refugees and asylum seekers? Who are responsible for the many deaths among refugees attempting to reach the European Union? What can we do to prevent these deaths?

Submitted questions illustrating depth and connective power

- **How can we protect our borders while protecting refugees at the same time?**
- **How can we ensure that everyone has an equal opportunity to enjoy good health (in other words, including people with low literacy, the low educated, and ethnic minorities)?**
- **How does sport contribute to quality of living, public safety, and social cohesion in communities and society in general?**

Can globalisation and development be reinvented in a way that, in time, will mitigate differences in prosperity between world regions?

Explanation

Why are there such huge differences in prosperity between world regions, and have those differences altered over time? A thousand years ago, the continents differed very little in terms of prosperity. Since then, they have grown further apart and the differences appear to be permanent: the prosperous West versus the poverty-stricken rest. The rise of Brazil, Russia, India, China, and other emerging economies is recalibrating the relationship between regions. Why is that, what changes are taking place, what consequences will these changes have, and what is the best way for us to respond? People are moving from poor regions to wealthy ones, and these migration flows may contribute to a new equilibrium. It may also be possible to achieve greater equality by improving education in poor regions, by setting up specific investment programmes there, or by undertaking political and administrative reforms. Longitudinal studies of globalisation processes can help us identify successful strategies for dealing with their consequences.

Connective power

Globalisation and development are complex, sweeping processes with historical, economic, political, cultural, and environmental dimensions. Globalisation and development clearly mean different things in India or China than they do in Africa, Europe, or the United States. The social sciences and economics have produced the bulk of theory related to globalisation and development. But we must also study them from other perspectives, for example geography and social geography, history, and ecology. Interdisciplinary questions include the following:

- What do historical fluctuations in the process of globalisation tell us about its future? How should we appraise globalisation? How can globalisation help societies become more resilient? And how can globalisation threaten that resilience?
- What forms of international cooperation between relatively wealthy and relatively poor countries supports the latter's resilience?
- How do global trends and processes relate to regional and local trends, in historical, economic, and cultural terms?
- How can globalisation support biodiversity and the quality of the environment? How can institutional changes encourage long-term investment in developing countries?

Submitted questions illustrating depth and connective power

- **How can we organise international value chains so that they lead to more inclusive and socially and ecologically sustainable economic growth in the southern and northern hemispheres?**
- **Now that societies are becoming increasingly intertwined, how can they respond flexibly and sustainably to the threats posed by globalisation while preserving their own identity and culture?**
- **Why do some parts of the world enjoy more economic growth and wellbeing than others? Why was that the case in the past?**

What are the implications and challenges associated with worldwide urbanisation?

Explanation

Seventy percent of the world population will live in cities in just a few decades. Vast urban regions will increasingly drive economic, social, and cultural development. Tightly packed activity in urban areas can aggravate environmental, logistical, or social problems, but it also offers more potential for resolving these problems. Worldwide urbanisation is a process whose trajectory and implications are not well understood. How can we boost the economic, social, and cultural vigour of cities, and how can we contain conflicts? What makes cities successful, and how can the authorities, businesses, individuals, knowledge-driven institutions, and civil society organisations all contribute to that success? Urbanisation provides a fertile, overarching context for conducting new and pioneering research combining the social sciences, economics, engineering, and history.

Connective power

The implications of urbanisation are relevant in the humanities, science and technology, and the social and behavioural sciences, and combinations thereof. In the humanities, the questions concern the relationship between cities and culture in the broader sense, covering such themes as citizenship and participatory democracy. In science and technology, research involves the urban climate, the urban metabolism, or green features in cities. In the social and behavioural sciences, the questions focus on social cohesion and the city as a source of cultural and technological innovation. But there are also countless subtopics at the interface between the three domains, for example mobility, health, and the quality of living in the city. The link between local phenomena and global processes plays a major role in questions concerning the implications of urbanisation. In exploring these questions, it is important to undertake design-based research that can substantiate specific decisions about urban development and can also help generate images of the ideal city of the future. Lurking in the background are more normative questions, for example concerning rural versus urban values or the issue of urban aesthetics. Research on urbanisation often makes it possible to link action research in communities and neighbourhoods and studies carried out on behalf of municipal governments to theoretical questions exploring ideal forms of urban development. This includes refining and reflecting critically on new urban development concepts such as smart cities, green cities, sustainable cities, sharing cities, and hackable cities.

Submitted questions illustrating depth and connective power

- **How can cities prepare and be prepared for the progressive processes of globalisation and localisation?**
- **What is governable or manageable for the authorities and urban parties?**
- **How does the migration of art, artists, and their ideas influence the development of individual and urban cultural identity?**

What is Europe? Past, present and future

Explanation

For centuries, Europe has regarded itself as the apex of human civilisation. Milestones in the construction of the European self-image are the classical heritage of ancient Greece and Rome, the founding of universities and nations in the Middle Ages, Humanism in the Renaissance, and the 18th-century Enlightenment. The image of an enlightened, civilised Europe was broadcast around the world, often by the harshest means. That history still permeates the post-war project known as the European Union. The preamble of the Treaty establishing a Constitution for Europe referred to inspiration drawn from 'the cultural, religious and humanist inheritance of Europe, from which have developed the universal values of the inviolable and inalienable rights of the human person, freedom, democracy, equality and the rule of law'. Research into the foundations of Europe can create a more realistic image of its emergence and plot out a clearer path for its future.

Connective power

Understanding the foundations of Europe will require a multifaceted array of research in such areas as the law, history, philosophy, economics, sociology, and religious studies. New insights can be used to further the process of European integration, decisive for the future of Europe. If the Dutch people, businesses, civil society organisations, and the Dutch state wish to take full advantage of the opportunities and challenges of the future, it is important for us to know those foundations. That knowledge will make it possible (and easier) to key into international societal and economic issues and opportunities, both now and in the future. Examples of pertinent questions are the following:

- How are globalisation processes influencing our concept of citizenship, sovereignty, nationality, and democracy?
- How can institutions meant to promote freedom and equality, adapt to new trends and developments?
- Can the European experiment with capitalism and democracy sustain itself in the 21st century?
- What role do minorities – whether or not European in origin – play in shaping a multicultural Europe?
- How can the European Union respond decisively to new challenges, crises, and creeping questions such as the ageing population and climate change?

Submitted questions illustrating depth and connective power

- **Why were the Greek philosophers, and especially Plato and Aristotle, so important to European education for so long?**
- **What is Europe and how can the European Union respond decisively to new challenges?**
- **How can Europe confront its colonial past in a manner that allows it to become a truly multicultural continent, and what role can education and research based on post-colonial and globalisation perspectives play in this regard?**

How can we promote social cohesion in a society that is culturally and religiously diverse?

Submitted questions illustrating depth and connective power

- **How do immigrants perceive their own experience of arriving in the Netherlands and settling into Dutch society? What immigration stories have their families passed on?**
- **Which forms of global cultural transfer and transformation have led, throughout history, to convergence, homogenisation, and the loss of variety, and which have led to greater diversity and/or conflict?**
- **How can education encourage social engagement and democratic attitudes?**

Explanation

The cultural and religious diversity of Dutch society has increased in recent decades, owing to secularisation, migration, and the breaking down of ideological and religious 'compartments'. This trend has raised new questions about the nature, scale, and progress of diversity, how we should deal with it, and how we can kerb any societal conflicts to which it gives rise. More specifically, tensions ensue because the values of liberal democracy are incompatible with those of religious fundamentalism. We must identify ways of inviting the relevant individuals and groups to live together in harmony despite their differences. Three types of questions are relevant in this context. The first seeks explanations for the tensions, for example disparities between group or individual values and the values of Dutch society. The second type seeks to find methods for preventing and limiting tensions between groups. Can education play a role, for example, and what options are available to us in that context? Are there any examples from the past that we can revisit? The third type of question seeks to explain and avoid the rise of extremism.

Connective power

Interdisciplinary research is the only way to explore the question of social cohesion in a culturally diverse society. Expertise is needed in such fields as sociology, law, religious studies, history, didactics, philosophy, educational theory, and psychology. The subject itself poses numerous challenges to broad interdisciplinary cooperation of this kind because it entails linking diverse subjects and seeking a variety of different solution strategies. The questions range from basic research, for example into the processes that facilitate group formation, to very practical, applied research. Because it is a question that preoccupies many different societies, international research is essential.

How can we encourage self-reliance and social participation?

Explanation

Increasingly, people feel the need to be actively engaged in society and to contribute actively to both their own health and wellbeing and to social organisations and institutions. We need look no further for evidence than the vast number of questions submitted under this heading. Many questions have been raised about how vulnerable groups – for example the chronically ill, people with psychiatric disorders, but also minority groups – can continue participating actively in our society. Some questions are about seeking solutions in new technology, such as e-health and robotics, and how they can help elderly people live independently for longer, for example.

Connective power

This is a challenging question for researchers, and important to both society and the economy. After all, self-reliance and participation in society lowers government expenditure and stimulates creativity and entrepreneurship. The question has important implications for health care (both mental and physical), for education and training, and for social, economic, and technological progress. It also has descriptive, normative, and design-based dimensions. The descriptive dimensions involve defining the terms self-reliance and participation. The normative dimension involves identifying what is morally right. Design-based dimensions mainly concern education and policymaking. How can education encourage self-reliance and participation? How will greater self-reliance and participation affect policy? But design-based research is also relevant with respect to technological advances. How can technology promote self-reliance?

Submitted questions illustrating depth and connective power

- **What happens when we ask too much or too little of people with a chronic illness or dementia, and how can we assess a person's cognitive capabilities?**
- **Does promoting self-management improve the quality of care, reduce the number of complications, and increase patient satisfaction?**
- **At what point does it become impossible for elderly people to continue living independently?**

How can we ensure that our labour force and labour-market organisations remain robust and resilient as they face the challenges of the 21st century?

Submitted questions illustrating depth and connective power

- **Which jobs will still exist in 2035 and beyond?**
- **How can our education system teach pupils 21st-century skills to prepare them for their role in our future society?**
- **How do new management and organisational strategies contribute to the innovativeness of Dutch organisations?**

Explanation

Human beings are the most important form of capital for a knowledge-driven economy like the Netherlands. How can we ensure that the Dutch labour force and labour-market organisations remain robust and resilient as they face the challenges of the 21st century? People will have longer working lives in the future, and they will switch careers more often. How can they learn and master new skills throughout their careers? Jobs at the lower end of the labour market are not as stable or secure they used to be; the middle segment of the labour market is shrinking; and jobs at the upper-end are requiring more flexibility and adaptability. How can education respond to these changes, which changes are permanent? How do we combine vocational training and general education and prevent a social divide from opening up between low-skilled and high-skilled workers? Skilled workmanship is associated with craftsmanship and tradition, but how can we reinterpret it for the modern economy so that the focus shifts to creativity and innovation? How do we equip the most vulnerable pupils for the labour market of the future? How is the lower end of the labour market changing?

Connective power

This question combines the changes that will affect our society in the century ahead with concerns about our current education system and how to promote employment participation. The structure of the labour market is expected to change fundamentally in the course of the 21st century owing to digitisation, flexible working practices, and organisational change processes. Addressing the question requires socioeconomic analysis and a knowledge of technological advances, which often drive change in our society. The question therefore requires a multidisciplinary approach that builds bridges between different disciplines – including labour and organisation psychology, sociology, didactics, economics, and engineering – to gain a better basic understanding of our changing society in the 21st century. This will give us a better grasp of emerging and future forms of organisation, making it easier to safeguard quality in education, elderly care, employment participation, sustainability, and public security. The relationship between humans and technology plays an important role in this context. The ability to design new organisational forms for work, education, and society also creates new economic opportunities.

What is the secret of a resilient society?

Explanation

The open economy and international outlook of the Netherlands requires Dutch society to demonstrate enormous resilience. Social cohesion and inclusiveness have been put under pressure by new technology, economic globalisation, and migration flows. Robotisation and the international division of labour are causing some sectors and occupational groups to shrink and others to grow. The mass influx of migrants is changing the face of society forever. Events in one part of the world have immediate consequences for events in other areas, in part owing to new media and the internet. Certain traditions seem to be disappearing, and population groups appear to be increasingly divided.

Connective power

The question is whether the above observations are true and to what extent, and if they are, whether and how we can reverse certain processes, promote social cohesion, and mitigate the divisions between population groups. This raises a series of questions with historical, cultural, economic, and social science dimensions. For example:

- What can historical and international comparisons teach us about resilient societies?
- What historical differences can we find between countries, for example with respect to economic growth and social cohesion?
- Which institutions, for example the constitutional state, parliamentary democracy, and the welfare state, determine a society's robustness and cohesion?
- What role do institutions play in social cohesion and cooperation between individuals?
- Can the achievements of the constitutional state, parliamentary democracy, and the welfare state in their current manifestations be maintained, and have those achievements had lasting positive effects on social cohesion?

Submitted questions illustrating depth and connective power

- **How do people perceive reality in a society where general knowledge is growing increasingly complex and abstract, is shared by means of modern communication, and is increasingly based on science and technology?**
- **What role does ideology play in society, past and present?**
- **What role should tradition play in moral and political issues?**

Smart industry– How do we make our factories smarter?

Explanation

A fourth industrial revolution is under way: the transition from industry to a digital world in which ICT is penetrating deep into every facet of the production process. The Internet of Things, the availability of big data, and the coupling of what are now still separate information flows and production phases all play a key role in this. Research on smart industry is not only about technology; it also encompasses the impact on the surroundings, with the expectation being that smart industry will bring about a fundamental change in our society. Online services are already having a huge impact on business models. The ever-present availability of information raises questions about privacy. Another concern is the rising level of robotisation and possible job losses that may result from this development.

Connective power

The technical challenges inherent to smart industry require collaboration between multiple disciplines, including various branches of engineering, materials research, and ICT. Given the huge impact of this question on society, these groups will also need to interact with researchers in sociology and ethics.
The smart industry theme keys into the top economic sector High Tech Systems and Materials, as well as Water, Agri & Food, and Horticulture & Starting Materials. The concept is also promising for production companies and their suppliers and customers, with ample development opportunities for SMEs.
A number of field labs have already been set up in a pilot programme. These are practical platforms in which businesses and knowledge-driven institutions can develop, test, and implement dedicated solutions and in which new research questions can be formulated.

Submitted questions illustrating depth and connective power

- **How can we make mechatronic machine platforms and modules that are faster, more accurate, and more reliable, that use less energy, that have wireless (remote) control, and that use less and more sustainable materials?**
- **How can we organise the logistical processes required for smart industries?**
- **What are the economic implications of ultra-personalised production systems for the structure and operation of Dutch equipment manufacturing? Can these systems be designed to promote the circular economy and support good citizenship?**

How can we create a truly circular economy so that the manufacturing of industrial goods depends less on primary raw materials?

Submitted questions illustrating depth and connective power

- How can we make circular product design the standard?
- How can robotics and automation increase material and energy efficiency?
- How do I measure the recyclability of products and waste streams for a 'minimal footprint' society?

Explanation

The ultimate societal challenge in terms of resources, energy, and materials is to create a circular economy in which nothing is lost and the residue of one process is the feedstock for another. As soon as scarcity drives up the price of raw materials, reuse or recycling becomes more interesting. Initial efforts have focused on closing the loop for processes that use fossil-based materials. Closed-loop systems for partly biodegradable bio-based materials are also becoming increasingly important. Major progress towards sustainability lies in designing structures that are easy to dismantle and recycle. Another solution is to extend the safe useful life of structures. This requires close monitoring of the structure's state of repair throughout its use. Green raw materials and sources of energy should be responsibly produced, i.e. without competing with food crop cultivation and while maintaining agricultural production capacity. After use, they must be recycled or be returned to nature as a food source.

Connective power

The construction industry is one sector in which this question is highly relevant owing to the vast quantities of materials and energy it consumes. Extensive research is needed into processes, e.g. new methods, tendering procedures, materials logistics, new value chains and business models based on life cycle cost estimation, or building with nature. Another important aspect is the sustainable utilisation and effective monitoring and management of the substrate. The top economic sectors Chemistry, Energy, Creative Industry, and Agri & Food also list research on the circular economy in their agendas. The type of research needed is both exploratory and applied, but should also be normative and used to substantiate policy. Besides basic research on self-healing materials that can extend the life cycle of objects, research should, for example, also investigate the use of robotics and automation or alternatives to scarce raw materials. Other challenges involve designing effective incentives, inducements to changing behaviour, and rules for the circular economy. Sustainability research thus benefits greatly from the Responsible Research and Innovation (RRI) approach.

What are the characteristics of a circular economy and how can we achieve it?

Submitted questions illustrating depth and connective power

- How can we use algae to produce plastics and oils from waste water?
- Would it be possible to introduce an economic model that is not based on growth?
- How can bottom-up forces in society be encouraged to implement and support changes towards sustainability?

Explanation

Sustainable methods of guaranteeing future prosperity have been prioritised. Waste does not exist in nature. Every single substance is recycled. Energy from sunlight is converted into chemicals that in turn deliver the energy needed by nature for growth and development. The economy can learn a great deal from ecology in this regard. We will need to carry out a vast amount of pioneering research in the next ten years if we are to transform our linear society into an economy based on closed-loop recycling and waste utilisation – a circular economy. One key part of this challenge is to identify the best scale for closed-loop recycling. In the same context, we must also reconsider our focus on economic growth and on measuring prosperity in terms of growth. Are there other ways to measure prosperity and success? Is it possible to develop models that do more justice to sustainability and *social* prosperity? And there are other challenges. How do we make the transition to a circular economy? How should we organise the transition to 100% green energy? How do we continue feeding a growing world population without damaging the Earth? How do we design a circular economy in which ecology and economy are mutually reinforcing? What do policy initiatives imply for innovation and competitiveness?

Connective power

This question connects ecology with questions in engineering, economics, and the social sciences, both basic and applied. The first important question is what the economy can learn from ecology about recycling. In technical terms, the relevant question is which technologies can contribute to a circular economy and a sustainable society, and how different technologies can be combined to create new systems. In terms of the economics, the question is which economic systems will allow circular technology to mature; in other words, how we can model the circular economy. The question is also linked to the social sciences, which must explore the processes needed to achieve a circular economy and the role of the authorities, businesses, civil society organisations, and the public in those processes.

How do we ensure that the Dutch economy remains competitive?

Explanation

The Netherlands is a small, open economy that tends to expand and contract with the fluctuating European and world economy. How we will earn our keep in the future is a difficult, if not impossible, question to answer. The best strategy for the future seems to involve building on the strengths of the Dutch economy and our traditional crucial trade relations with other countries, and exploiting the opportunities offered by new technologies. But is a small country like the Netherlands really in control of its own destiny? Can we make our economy more sustainable? Research on the strengths and opportunities of the Dutch economy, as well as its weaknesses and the threats it faces in a globalising world, should give us a framework for discussing the direction in which the Netherlands ought to develop.

Connective power

This question focuses on the underlying factors of economic development. What are the structural prerequisites for keying into the world economy flexibly in terms of the built environment and infrastructure, human capital, institutions, data and information, safety and security, and mentality? Many different sub-questions can be conceived in all these domains, but what interests us here is the way in which these factors interact and reinforce or weaken each other. Research can focus on comparisons with the past, on analysing the present, and on projecting into the future, both to get a better grasp of the mechanisms involved and to support government with sound policy recommendations in the practical sense. This question is pre-eminently economic in nature, but it intersects with many other disciplines. Technological disciplines and the social sciences – for example organisation science or business studies – are both important to this problem.

Submitted questions illustrating depth and connective power

- **What is the ideal relationship between institutional stability and reform if the aim is to encourage investment in innovation?**
- **What does human capital contribute to economic growth?**
- **What is needed (in terms of transparency, business assessments, and sanctions) to discourage and fight against ties between the 'straight' world and the underworld?**

How do we protect ourselves against natural disasters (such as earthquakes, volcanic eruptions, and floods)?

Explanation

Disasters caused by nature or by human interference in nature are disruptive for societies. Examples include flooding along coasts and rivers, the earthquakes troubling the Province of Groningen, recent major earthquakes elsewhere, and the 2004 tsunami in the Indian Ocean. As population density increases, so does the risk of disasters, making societies and economies more vulnerable, so does the risk of disasters. Critically, we must improve our ability to anticipate floods as well as earthquakes, volcanic eruptions, landslides, tsunamis, and other geohazards. This will require more insight into the factors that determine the occurrence, force, and scale of such events. With regard to geohazards, we need to recognise and act on early warning signals. To prevent flooding from seas and rivers, we need a good understanding of hydrology and climate as well as close cooperation between the various relevant authorities. Finally, we must make societies and infrastructure more resilient to natural disasters. That will be possible because more and more of the relevant data is available in real time, allowing us to develop new methods for issuing adequate early warnings.

Connective power

There is a real risk of earthquakes, volcanic eruptions, and tsunamis in many parts of the world. If we understood the Earth better as a system, especially the geological processes and structures in the deep substrate, we would eventually be able to predict geohazards of this kind more accurately. Such understanding can only be the result of close international cooperation. Basic research in this field makes serious demands on technology (for example deep drilling into the Earth's crust), data sharing for modelling purposes, and also willingness between regions and countries to join forces and concentrate financial means in order to utilise expensive infrastructure and large-scale sensor networks. The far-reaching impact of many natural disasters calls on us to consider the social and societal aspects, including decision-making and political responsibility. Events such as floods and near-floods, subsidence, and earthquakes owing to natural gas drilling make the urgency of this clear. New technologies are needed that will make new and existing infrastructure such as buildings, bridges, and flood barriers more disaster-proof and that lower safety risks at the same time. By cooperating, the authorities, private parties, and scientists can reduce the risk of natural disasters.

Submitted questions illustrating depth and connective power

- **How will the ice caps and the sea level react to a changing climate?**
- **How can we protect cities and people in the Netherlands and the EU against natural and induced geohazards?**
- **What do we need to ensure that our own major rivers remain safe, sustainable, and robust in the longer term (next few hundreds of years) while accommodating the needs of shipping, ecology, and recreation?**

How can we promote peace, security, and cooperation – and address threats and violations – within and between constitutional states and within and between groups and societies?

Explanation

Individuals, businesses, markets, and nations are becoming more and more intertwined, even across national borders, increasing their economic, societal, and social vulnerability. This manifests itself in many different areas, for instance, in public safety and security - such as jihadism, terrorism, and crime -, and also in employment, the investment climate, sustainability, and technology. Unrest often ensues in the wake of high-risk, hard-to-predict, ungovernable international trends and events, such as the rise of new economies, food safety or financial scandals, an attack, or an epidemic. Such unrest is very difficult to control. However, some individuals, groups, or countries are more successful than others at creating a climate favourable to coping with conflicts and at guaranteeing a certain degree of social tolerance and cooperation.

Connective power

The question of how to promote peace, security, and cooperation is multifaceted and multi-layered. It calls for integrated policy and a multidisciplinary approach that unites many disciplines from the technical sciences, the social sciences and the humanities. Smart solutions to the everyday problems of people living in diversified societies and lasting relationships in the interaction between businesses, authorities, and civil society organisations requires basic insights into the functioning of social and economic systems, as well as insights, into the behaviour of individuals, groups, and institutions, the development of language and culture, and the associated identity formation, education, and personal development of young people. Associated questions are those concerning the role and legitimacy of constitutional democracies, distribution, and equality.

Submitted questions illustrating depth and connective power

- **In guaranteeing a certain level of security, is government responsible for the overall system and, if so, how far does that responsibility go?**
- **What are the neurobiological causes of aggression?**
- **Under what conditions can good, constructive alliances arise and be maintained?**

Can we find the right balance between freedom of information and privacy?

Explanation

Freedom of information has enormous potential for society. For example, it allows us to use big data to track down criminals or to gain access to medical information for research purposes. But it also raises all sorts of new questions, for example who has access to which data and who manages that data? Who owns stored data? How can we prevent abuse? Can we guarantee privacy with a set of legal instruments or with technology? In today's digital era, information use and information management are cross-border phenomena. The questions then are: who is meant to regulate that use and who has jurisdiction in cases of abuse?

Connective power

This question explores the delicate balance between societal and economic opportunities that freedom of information offers on the one hand and the protection of privacy on the other. Applied research can focus on designing innovative technologies or a set of legal and policy measures that promote access to data while protecting data owners at the same time. This is important to society and science, as it can, for example, increase necessary access to medical data. Given the international nature of digital information and the data position of businesses, the question is to what extent we can actually regulate information flows. Legal scholars might focus on the boundaries of international and national law, for example the scope of privacy law. Sociologists and psychologists might explore the changing meaning of privacy in the big data era. To what extent must we or do we wish to protect the right to privacy? These questions require a joint effort by research groups in the social sciences, the study of law, and information science in the field of the protection of privacy and freedom of information.

Submitted questions illustrating depth and connective power

- **How can innovation contribute to 'privacy by design' and thus ensure that we strike the right balance between privacy and security/ investigation?**
- **How should we transform (large-scale) ICT infrastructures to enhance the quality of information security and information-sharing?**
- **How can ordinary people retain ownership of their own data?**

What are the patterns and causes of crime and how can we influence them?

Explanation

Crime leads to feelings of unsafety, which in turn has an effect on societal wellbeing. Fighting crime is therefore an important societal challenge. The changing nature and scale of crime – as demonstrated by new forms like cybercrime and terrorism – means that we can never cease studying its causes and patterns. Investigating existing and new causes and patterns allows us to determine how and to what extent we can prevent or combat different forms of crime. The challenge is to come up with an innovative approach to combat crime that will change as needed over time.

Connective power

Combining research in criminology, psychology, the study of law, and sociology will give us a better understanding of the causes of crime. For example, we can test hypotheses about the link between certain societal features, such as economic stress, and criminal behaviour. New insights into the causes and patterns of crime can serve as input for evaluative research on the effectiveness of existing punitive and/or preventive measures. With the means available to fight crime being limited, it is important to the economy and society to conduct strategic research on the degree to which measures contribute to public security. This makes it possible to set priorities for policymaking in this area. Strategic research can also make a practical contribution to crime-fighting itself, e.g. by asking what steps in the criminal process must be disrupted in order to undermine criminal systems. Given the changing nature of society, basic research in ethics is also appropriate, for example to explore the criminal liability of robots and other automated systems.

Submitted questions illustrating depth and connective power

- How can we relate the impact on society of the various types of crime, so that politicians and the justice system can set better priorities in their efforts to combat it?
- Can we make use of the forms of participation (in crime) defined in national law to hold political and military leaders liable for international crimes?
- How can we help entrepreneurs and others resist being drawn in to the criminal world against their will?

How can we ensure that children and adolescents grow up safe and healthy?

Explanation

This broad question consists of a series of sub-questions about the psychological, physical, social, and cognitive factors that contribute to child and adolescent development and that give rise to developmental problems in them. The questions concern both healthy development and specific developmental problems, including mental illness, child-parent issues, or the impact of extreme circumstances such as child abuse.

For the most part, the complexity of this question can be reduced to the sub-questions below:

- What interventions and therapies are effective at helping children and adolescents become resilient and develop their talents?
- What are the causes and mechanisms that play a role in child and adolescent developmental issues, and what do they mean for diagnostics and treatment?
- How do genetic and environmental factors interact in the occurrence and effects of developmental problems and deficiencies?
- What are the effects of inclusive education, and how can we promote it?
- How prevalent is child abuse, gender-related violence, and bullying? What are the causes and consequences?

Connective power

Child and adolescent development covers many different physical, psychological, social, and cognitive aspects that are influenced by many different interacting factors. These multitudinous aspects and interactions demand a multidisciplinary approach. Disciplines that spring to mind are developmental psychology, didactics, educational theory, and medical science. Many other disciplines are also relevant, however, including human movement science, the study of law, language technology, information science, and engineering. Example questions include the use of serious gaming for skills learning. We are becoming more knowledgeable about child and adolescent development, but countless questions remain. Basic research questions include the role of genetics in brain development; applied research tends to focus on how to optimise child and adolescent development, which tools to use, and under what conditions. To answer the latter, we need to know much more about the mechanisms behind healthy and unhealthy development and how we can influence them.

Submitted questions illustrating depth and connective power

- How do children learn to self-regulate their behaviour, emotions, and thoughts, and how can parents, teachers, and care professionals help them do so?
- How can sport help empower youngsters with a disability?
- How do genetic and environmental factors interact in the occurrence of a developmental language disorder?

How do we guarantee our digital freedom?

Submitted questions illustrating depth and connective power

- **How should privacy and other basic rights be guaranteed within the context of the Internet of Things?**
- **What implications do the various legal systems have for the cybersecurity domain?**
- **How can we exploit the potential of big data, for example to improve physical and virtual security, in a way that limits undesirable side effects, such as violations of existing rules and legislation?**

Explanation

New digital technologies, unreliable software, and the growing possibility of processing large quantities of data may well lead to privacy and security problems. More and more things are becoming 'smart' – smart cities is one example, but consider also the vast quantities of medical data involved in personalised medicine. We are surrounded by digital devices and have in fact come to depend on them. We also have digital lives parallel to our 'real-world' lives, and the boundaries between the two are fading rapidly. Consider, for example, the influence of smartphones, smartwatches, or smart implants. But our digital lives have also made us more vulnerable, for example to infection by malicious software, which is relatively easy to do. We are moving towards a system in which our real-world and digital lives will be more closely integrated, but we must be able to depend on digital components that operate securely. In the same way that the human body has an immune and repair system, our digital counterpart must be able to protect and keep itself healthy. Social, ethical, legal, technological, economic, and political factors can play a role in this context. This question mainly concerns how to protect people with technological innovations, both hardware and software.

Connective power

The question is important in all the top economic sectors owing to progressive digitisation and its implications for security. Innovations are necessary to make the digital infrastructure safer. This question is linked to such subjects as big data, quantum computers, and a quantum internet. Recent advances in quantum computing offer new opportunities, but they also represent a threat. On the one hand, the quantum computers of the future will have no trouble cracking all existing internet codes. On the other hand, quantum communication will allow us to share codes securely. This theme also touches on the issue of how innovation is aligned with societal and moral values. How does technology influence human existence and social change, and what ethical questions does that raise? The question also intersects with the issue of finding the right balance between privacy, open access to data, and data monopolies.

Are modernity and religion each other's opposites?

Submitted questions illustrating depth and connective power

- **What laid the groundwork in the 16th century for the Enlightenment of the 17th and 18th centuries?**
- **To what extent do the traditional narratives of the major religions, and specifically Christianity, implicitly inform 'secular' decision-making and politics?**
- **Is Islam compatible with the European tradition of liberalism, tolerance, and democracy?**

Explanation

Starting in the Enlightenment, many people thought that modernisation and scientific progress would sound the death knell of religion. Secularisation would diminish the role of churches and religion. We now know that modernisation does not lead automatically to the disappearance of religion. Religion takes on many different forms around the world, and new forms of religiosity and secularity are emerging. Migration and globalisation are also leading to a wide variety of views concerning the relationship between the state and religion, and between religions and ideological convictions. These trends have made the question of religion's role in our post-secularised era more urgent than ever. Research can deepen our knowledge of this subject and promote better understanding between people.

Connective power

This question links religious studies, philosophy, history, the study of law, and the social sciences. It has descriptive and design-based aspects. The descriptive aspects lie in interpreting what modernity and religion mean in modern Western and non-Western societies, both now and historically, and how these concepts are enshrined in our constitutional state. The design-based aspects are reflected in policy frameworks; decisions on public spending, for example in the health care or culture sectors, are often informed by certain opinions about the actual or permissible role of religion in society. Awareness of these opinions can assist in community-building and in garnering support for certain decisions.

How does science operate, what is good science, and how can policy key into it?

Explanation

Science may appear to be a harmonious whole, but it is actually a complex and heterogeneous system whose boundaries are difficult to define. It is also a system that is constantly changing, and so, as a result, is our image of science. Some see science as an objective, independent search for truth; others believe this is an illusion and that society, the business community, politicians, and ordinary people should have input into the science agenda. It is important to understand the historical and philosophical roots of science as a disinterested search for truth, and when and why that image began to change. Answers to these questions can help us form an image of science that does justice to the complex context in which modern science operates. These questions relate to others concerning how science policy can be shaped. The questions we received reveal a broad interest in the process of science itself, the scientist as a person, and the contextual factors that can encourage or impede science. In addition, discussions of integrity raise questions about research practices, whether the current systems suffice, and whether alternative models are conceivable. In addition, there are questions about how to develop an effective science policy.

Connective power

Many of the questions have important societal implications, for example how to ensure that society and politicians learn more and make better use of the facts uncovered by scientific research. There are also questions with economic implications, for example how to prevent a 'brain drain' of top scientists from the Netherlands. Answers to descriptive questions about the historical roots of our present-day university structure will serve as important input for normative questions about the purpose and usefulness of science. Design-based questions with policy implications can build on these foundations. They have implications mainly for science policy, but also for education and the knowledge economy. For example, what other models are conceivable for the pursuit and assessment of science? These questions call for interdisciplinary research with input from philosophy, history, sociology, the policy sciences, political science, economics, and other disciplines.

Submitted questions illustrating depth and connective power

- **Is there a connection between the remuneration that scientists receive and their relevant discoveries?**
- **Can informal science communication – for example science cafes, debate cafes, and knowledge-sharing cafes – support the dialogue between the public and scientists?**
- **What should the university be like in the 21st century?**

How objective are cultural canons?

Explanation

'The Great Figures of Ancient Rome', 'The Grand Philosophers', 'Milestone Events', historical exhibitions and so on emphasise the key events, people, and texts in certain regions and eras – supposedly objectively. They are the canons of a culture. In the past decade, the Netherlands has documented the canons of Dutch culture in short publications recounting the highlights and heroes of Dutch civilisation. But there have always been canons; every culture, every country, and every discipline needs its heroes. Without them, we do not really know what is good, beautiful, true, or important. The canon is therefore a benchmark and a yardstick. It is for this very reason that canons are also controversial. In a diverse society made up of different population groups with different histories and cultures, it is difficult to assemble a canon that unites all.
The study of canons – across disciplines, cultural expressions, and historical periods – can tell us a great deal about the opinions, norms, values, and self-image of a specific time.

Connective power

The study of canons produces information about different norms, values, and opinions. This helps us gain perspective on what we regard as good, beautiful, meaningful, and important. Applying this knowledge in education can help build a society that is open-minded about different values. The study of history, ethics, philosophy, and literature goes hand-in-hand with sociology, educational psychology, or educational theory in this context. To explore this question in all its breadth, we need descriptive research on the nature of canons at different periods in history and normative research on the values and opinions that canons appear to embody.

Submitted questions illustrating depth and connective power

- **What is art, and who decides?**
- **What makes a civilisation?**
- **What can the Resistance during the Second World War teach us about the limits of constitutional democracy?**

How can we develop new testing methods in the social sciences?

Explanation

Research has many different faces. It ranges from basic to applied, and can be carried out using many different methods and approaches (quantitative, qualitative, empirical, theoretical, experimental, and combinations thereof). Not only is the methodology constantly evolving, but so is the subject of social science research, i.e. humans in their social setting. A further point is that new digital technologies and methods are making more and more data available. Describing this data is a complex task, in part because it has been collected for different reasons at different aggregate levels. At the same time, we increasingly expect the social sciences to help us solve complex societal and economic problems.

Connective power

The social sciences are divided into the behavioural sciences and the study of society. Together they represent a very broad spectrum of disciplines, including anthropology, the science of public administration, economics, the study of law, political science, sociology, communication science, psychology, educational theory, didactics, criminology, and social geography. There is almost no societal or economic issue imaginable to which the social sciences do not contribute. But that contribution is only relevant if the methodology is state-of-the-art. It must be clear what is being tested and which conclusions can be drawn from the findings. Social science methodology thus forms the basis for a broad spectrum of basic and applied research and the resulting recommendations for resolving many societal, political, and economic issues.

Submitted questions illustrating depth and connective power

- **How can we measure the performance of health care professionals?**
- **Is crowdfunding a yardstick for the esteem in which art and culture are held?**
- **How can we develop a ‘Google Earth’ for the social sciences, economics, and humanities?**

What should education be like in the future?

Explanation

Education serves many different purposes. It is meant to teach skills and transfer knowledge so that pupils have a good chance of finding employment. It is simultaneously meant to turn them into engaged, enterprising, critical citizens with a sound moral and intellectual compass. And finally, it is also supposed to leave them plenty of room for personal development. Today, human capital is regarded as one of the most important factors of production. That is one of the reasons why the Scientific Council for Government Policy (WRR) focused specifically on education in a recent report on the future of the Dutch revenue model. In that report, the Council argues that education must be adapted to the demands of the 21st century. How that should take place, however, is far from clear. The society of the future will require us to master all sorts of new skills, not least the ability to continually adapt and improve ourselves. The forces of globalisation require people to be able to handle major linguistic, cultural, and religious differences. How can education help pupils develop 21st century skills, especially good citizenship? Which new methods can we use to improve existing skills, such as language proficiency and cultural adeptness? What have been the effects of current innovations? How can education reflect the growing cultural diversity of pupil and student populations and meet their need for individual counselling, for example within the context of inclusive education?

Connective power

Innovative learning environments, instructors with good teaching skills, smart structuring, and the dissemination of research findings should all help make education an inspiring challenge for pupils and students and motivate them to learn. That challenge links fundamental and normative questions about the sort of education that society should provide with design-based questions about what does and does not work. ICT and communication skills are key concepts, but the question also touches on issues of inclusion and exclusion. Research in didactics, educational theory, sociology, and linguistics is as important as social research and neurobiological research on the brain and cognition.

Submitted questions illustrating depth and connective power

- **Why is it so difficult to apply in actual practice what we have learned in the classroom?**
- **Is there any point in playing Mozart for babies? In other words, how can we stimulate brain development in babies?**
- **Does bilingualism lead to contradictory norms and values? How does a child reconcile these contradictions as its sense of judgement and personality take shape? What does that mean for our national language policy?**

Does knowing about materials change the way we think about artwork, tangible cultural heritage, the built environment, and their preservation?

Explanation

The Netherlands leads the way in R&D on self-healing materials, i.e. materials that can repair themselves. They are revolutionising construction and design, but also restoration and heritage preservation. We no longer see materials and substances as purely instrumental; increasingly, they are considered to be actors in their own right, as much a part of and essential to our world as people are. Research into new technologies for heritage preservation makes allowance for the instability of materials. Pertinent questions include ‘Should we restore buildings to their condition just after construction, or after a century of use?’ This question becomes even more pressing if materials are capable of changing or repairing themselves. In that case, what is the original work of art?

Connective power

To understand the relationship between materials (and materials knowledge) and meaningful production, we need interdisciplinary research in which the humanities and the natural sciences join forces to study materials and their properties. For a long time, there was an unbridgeable gap between materials research for art conservation and art historical research. An interdisciplinary approach that combines the study of materials and techniques with provenance research can lead to new insights into the interpretation, conservation, and restoration of cultural heritage. The insights gained in basic research are important for the choices we make when conserving and managing cultural heritage for future generations. Our cultural heritage is of inestimable value in defining our identity and in fostering social cohesion.

Submitted questions illustrating depth and connective power

- **How can we improve our understanding of ancient art objects?**
- **How can we optimise the revenue generated from cultural heritage in a respectful manner?**
- **How much longer can we expect Rembrandt’s *Night Watch* to endure?**

What does art mean to people?

Explanation

The question of what art means touches on the essence of our existence and is critical to the resilience of our society. Cultural awareness is an important tool for any individual living in an increasingly diverse society. Becoming actively involved in the arts and culture offers children, adolescents, and adults opportunities to shape their relationship with the world, with others, and with society, and therefore their own identity. People can shape their identity by participating in culture, leading them to ask more profound questions about art and meaningfulness and about the role that art and historico-cultural artefacts play in their relationship with the world.

Connective power

This subject connects a number of questions that explore what art means to people from differing perspectives. It involves both practice-based and basic research on the relationship between aesthetic experience, knowledge generation, and ethical attitudes, as well as investigations into the role of art consumption and reception and the importance of art for wellbeing. Art can evoke strong emotions, play a role in social interaction, and have a therapeutic effect. The starting point for research in this area can be formalistic or sociocultural, i.e. from the perspective of the arts. It is also possible, however, to seek explanations for the strong emotions elicited by the arts in the brain, as in the relatively new subdiscipline of neuroaesthetics. The question concerns the entire chain, from cultural production to consumption and reception in the very broadest sense. Research is also important from a societal perspective because it echoes the quest – provoked by recent budget cuts in the Dutch culture sector – to identify art’s contribution to society. At the same time, Dutch cultural policy has for many years emphasised cultural participation, because culture is regarded as an element of social cohesion. In more individual terms, the question concerning art and emotion explores the new opportunities that emerge by linking historico-cultural and neurological research.

Submitted questions illustrating depth and connective power

- **How was and is music used in military and social conflicts as a means of expression and communication that regulates emotions?**
- **How do people actively shape their lives by participating in culture, and how does this individual or collective process of interpretation and sensemaking explain the value of art and culture for society?**
- **In what way do artists and designers create specific knowable and experiential perspectives on how people relate to the world?**

How can we promote and utilise creativity and innovation?

Submitted questions illustrating depth and connective power

- What is the neurobiological basis of creativity?
- How do we measure what creativity contributes to innovation? Does creativity in artists and designers differ from creativity in other professions?
- How can government stimulate, facilitate, and utilise creativity in ordinary people, businesses, and lower tiers of government to solve persistent sustainability problems?

Explanation

Creativity is the driver of society. Without imagination, there would be no innovation. The Netherlands has a worldwide reputation in concept development and cutting-edge design. Dutch Design is a good example of this. The Dutch have a strong tradition in creative design in the fields of urban planning, architecture, landscape architecture, and arts and crafts. Artists, architects, and designers make a unique contribution to exposing and resolving societal issues. Their imaginative creations make the technology-driven environment liveable. Creativity also plays a major role beyond the creative sector, of course. In our post-industrial economy and society, a world that hinges on information and information processing, businesspeople, employees, and ordinary citizens are expected to interpret their roles and tasks creatively. The Netherlands has also seen a growing number of innovative start-up firms that help drive social innovation. Many of the questions concern how policymakers can make the Netherlands into a creative and innovative habitat. But although there is widespread consensus and recognition of its importance, we still know very little about the true nature of creativity, making it difficult to promote and utilise effectively. Our knowledge of creativity is the result of research in a broad spectrum of fields, ranging from neurobiology to art history, and they are often unacquainted with each other's findings. Many of the questions we received asked how we can understand and then encourage and utilise people's creativity and innovativeness, and how creativity and innovation can play a role in solving societal problems.

Connective power

Innovative and creative processes always involve making new and unexpected connections. To study this subject properly, then, will itself require creativity and innovation. The main question is how to utilise creativity and innovation as effectively as possible and as much as possible to generate societal and economic value. This question has implications in various policy domains, ranging from economic policy (new businesses) to cultural policy (the arts and culture sector), and to educational policy (can creativity can be learned, and if so, how?). Fundamental questions focus on how the creative process operates in the brain or how creative cooperation functions, or how innovation influences individuals, groups, or a society. Research links various disciplines, for example the neurosciences, psychology, didactics, economics, and philosophy.

What causes language variation and why do we understand each other despite the differences?

Explanation

We use language to communicate, shape our thoughts, and express our emotions. Every day, we hear and speak our native or other languages without asking where the underlying language system comes from, what its features are, and how it is changing. The way groups use language changes just as much as the way individuals do. We know that young people have always been a source of language change. We also know that language changes differently in cities than it does in rural areas. But precisely how does that happen? Which language features ensure that it takes only half a word for us to understand each other in complex situations, despite the enormous variation? And when do things get muddled?

Connective power

The concept of language variation raises questions that are both scientifically and socially relevant, and that involve both basic and practice-based research. Questions of scientific importance and conducive to basic research concern the 'why' of language change and language variation, how language features resist change, the relationship between language development and cognitive development, between standard language and dialects, and between spoken language and gestures, the consequences of language variation for communication, the appraisal of language variants, semantics, or language and wavelength. Such questions are mainly meant to describe and explain. But language variation also raises many normative questions about issues that are often of societal relevance: the positive and negative effects of multilingualism, the value of minor languages, attitudes towards different language variants, gender and language, and language loss. Design-based questions, finally, often have societal relevance as well and address such topics as improving foreign language skills, making language gender-neutral, preventing language loss, optimising language learning for adults, removing language barriers in a society, and communicating with automated systems and robots.

Submitted questions illustrating depth and connective power

- How do communication processes unfold in ultra-diverse cities and what role do the languages spoken there play in those processes? What are the consequences for community-building and for local social cohesion?
- Why are some people so much better than others at learning a foreign language?
- Why do we use so many metaphors in our speech?

Why do we do what we do, are we who we think we are, and what factors influence our behaviour? In other words, how can we understand our behaviour?

Explanation

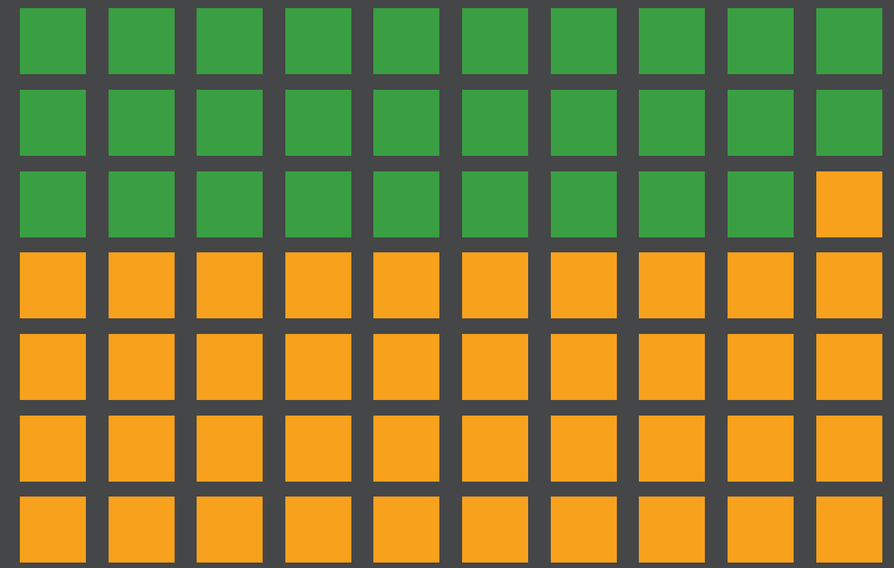
This question concerns human behaviour and perception. Human behaviour is complex. It is determined by the interaction between our genes and our environment, and it defines the quality of our lives to a large extent. How can we process external stimuli – both negative and positive – in a way that benefits us? Do we all perceive things in the same way, or does every person have his or her own reality?

Connective power

Research on behaviour is crucial to understanding society as well as group and individual behaviour. Basic research explores how flexible and controllable our behaviour is, and to what extent behaviour is programmed by evolution/DNA. Behavioural research unites a broad range of research disciplines, including psychology, educational theory, sociology, cultural anthropology, communication science, sport science, and neuroscience. Research on the brain and how it influences human behaviour and society is a vital component of behavioural research. This domain brings together psychiatrists, psychologists, linguists, biologists, and ICT specialists from civil society institutions and businesses.

Submitted questions illustrating depth and connective power

- **Which factors influence the occurrence of NLD (Non-verbal Learning Disabilities), autism, ADHD (Attention Deficit Hyperactivity Disorder), and ADD (Attention Deficit Disorder)?**
- **How does the unconscious / unconscious behaviour affect human behaviour in sport and movement, how can we use that knowledge to encourage people to engage in sport and physical activity?**
- **How do we take decisions in our everyday lives?**



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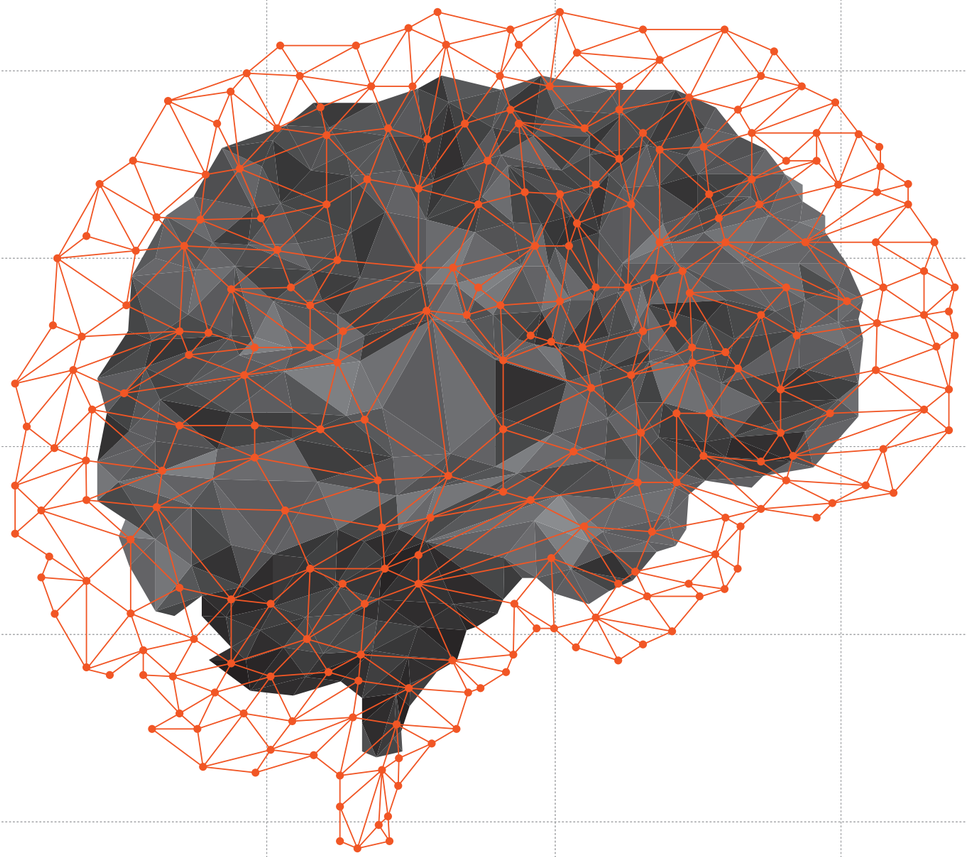
Sickness and health



What do we mean by ‘quality of life’?

Explanation

‘Quality of life’ is becoming a common expression in policymaking and public discourse, but there is considerable confusion about the definition of this term. Everyone agrees that it is not the same as economic prosperity or individual wellbeing, and that it is more than mainly a question of good health. There is no consensus, however, on what it does mean. Conceptual and philosophical analysis can help us define what we mean by ‘quality of life’ and explore whether and how it can be measured. Historical research can show how quality of life has changed over the centuries, and to what extent choosing a particular interpretation of the concept determines how quality of life evolves. By defining quality of life more precisely, we can also find better answers to ethical and political questions, for example to what extent civil society organisations and the authorities should deliberately strive to improve the quality of people’s lives. When does promoting quality of life for employees, consumers, patients, or the general public go too far and become an undesirable form of paternalism?

Connective power

This question links philosophy, history, medical science, sociology, politics, economics, and the humanities. Basic research on the meaning and interpretation of the quality of life concept can provide a basis for addressing societal problems related to ageing, sickness and health, and, for example, migration issues. In addition, society today also requires us to consider the cultural or diversity dimension of the concept. Finally, the way in which we choose to deal with these societal issues has implications for our economic position. The question has descriptive, normative, and design-based aspects. The descriptive aspects concern the meaning and history of the quality of life concept. What role does this concept play in past and present public discourse? And what implications do cultural differences have for its interpretation? The normative aspects concern our understanding or definition of quality of life. The design-based aspects lie in the need for a definition for policymaking purposes, in innovative applications in health care and the workplace, and more generally in innovations that promote a qualitatively sound, healthy life course.

Submitted questions illustrating depth and connective power

- **The quality-adjusted life year (QALY), used to express the value of health outcomes, and the setting of utility values in that context continue to rouse discussion. Can we come up with a better standard method?**
- **How do we measure collective happiness, and how can we structure society to increase wellbeing and happiness?**
- **How can we ensure a good quality of life for everyone in old age, and how do we then deal with the large discrepancies in income, social capital, and care requirements among the elderly?**

How do a healthy lifestyle and wholesome habits promote good health and prevent illness?

Submitted questions illustrating depth and connective power

- **Can we develop innovative behavioural interventions promoting a healthy lifestyle among those who need it most?**
- **How can we structure the home-work-living environment to encourage physical activity automatically without it being perceived as burdensome (healthy buildings)?**
- **How can we use smart technology (e.g. wearables) to promote a healthy lifestyle?**

Explanation

Health care focuses on preventing disease and curing sickness when possible. Many of the health problems we face today can be prevented by changing our behaviour, adapting our surroundings, early detection, or other evidence-based interventions. Nutrition and physical activity play an important role in both the occurrence and treatment of health problems. The rise in the number of lifestyle diseases and the growing number of risk factors for chronic illness, such as overweight and physical inactivity, raises the issue of what people and families can do to prevent or heal sickness and optimise good health. Example questions included ‘How do behaviour and lifestyle, for example physical exercise, smoking, nutrition, and amount of sleep, influence physical and mental health?’ ‘What lifestyles and behaviours affect physical health in children and adults?’, and ‘Can a healthy lifestyle and behavioural interventions have a positive effect on chronic physical disorders?’. Research on the influence of such factors as lifestyle and behaviour on physical and mental disorders helps us understand the mutual causal relationships and makes it possible to develop effective treatments.

Connective power

This question requires basic research on the causes of diseases, and applied research exploring how to develop and evaluate methods to tackle those causes. Multidisciplinary research – for example combining human movement science, epidemiology, and architectural engineering in the case of movement behaviour – is likely to lead to major breakthroughs. The societal and scientific significance of this question is obvious; many different public, economic, and scientific agendas in the Netherlands list these issues as priorities and they have important implications for health care (both mental and physical) and for social, economic, and technological progress. In the interests of the Dutch economy, and given the need to limit the cost of national health care, research should focus on preventing illness so that people stay healthier and are able to work and participate in society for longer. That focus will also help improve quality of life for diverse groups in society.

What effect is the rising 24-hour economy having on human health and performance and how can our knowledge of biorhythms enhance the relationship between the individual and society?

Explanation

Our brains have a built-in circadian rhythm that attunes our behaviour and body to the natural day-night cycle. This biological clock is sensitive to all sorts of external stimuli, for example the influence of light and darkness. That sensitivity allows our biorhythm to be adapted ('entrained') to changes in the 24-hour cycle brought on by seasonal variation, the switch to summer/winter time, or travel to different time zones. Today's society is increasingly active 24x7, putting ever-harsher demands on this biological system. What impact is that having on our health? Increasingly, our work extends beyond the standard 9 to 5 schedule. We are also online everywhere and all the time and receive calls and notifications – both personal and work-related – throughout the entire day. Our computer and smartphone screens emit a bright, very specific blue light that may act as an added stimulant. A well-known negative side effect is that we no longer sleep as soundly as we once did. The growing disturbance of our natural sleep/wake cycle has already been associated with disrupted eating patterns, obesity, and the risk of cancer.

Connective power

Research on biorhythms couples the behavioural sciences, neurobiology, medical and health research, and physiological engineering. Applied research brings other disciplines on board, for example sociology, economics, business administration, and the design disciplines. Technical and IT innovations are bringing about rapid changes in society. The rise of the 24-hour economy is having a sweeping impact on our lives. Now that we are beginning to understand its negative effects on human health, it is important to understand why the disruption of the biorhythm causes problems, precisely which problems it causes, and in whom. This knowledge will also support individual optimisation based on chronotype (morning or evening person), age, and living and working conditions. Businesses are interested in and can benefit from such research because they believe it can help them prevent health problems in their employees and deploy their staff more effectively, with fewer absences due to illness. But there is an equally interesting market for companies that can convert their expertise on biorhythms and the design of the environment into products such as smart lighting, spatial planning, and devices that monitor activity and coach users throughout the day.

Submitted questions illustrating depth and connective power

- **Do adolescents have a different circadian rhythm or needs than children or adults? If so, should we adjust school hours accordingly?**
- **How does the biological clock affect the health of night-shift workers?**
- **How can chronotherapy, a treatment and approach that works with our biological clock, improve our mental and physical health?**

How does sleep affect our health?

Explanation

Sleep influences both mental and physical health. Sleep deprivation leads to poor performance and is associated with various mental disorders, specifically depression and anxiety. The result is a larger burden of illness, absenteeism, and negative consequences for quality of life. But even before a person becomes sick, sleep deprivation can affect his or her emotions and lead to a decline in memory, concentration, articulation, reaction speed, decision-making ability, and immunity to illness. Questions in this research domain focus on both the causes and consequences of sleep loss and how to prevent and cure sleep disorders. The subject is also related directly to questions about the higher mental functions in humans. Scanning technology has improved greatly in recent years, as have animal models of human cognition. We expect a major breakthrough in translational medicine within the next ten years that will link basic and applied expertise in this area.

Connective power

Sleep disorders have negative consequences for both physical and mental health and, as a result, for the economy and society. A growing number of hospitals have already set up units that specialise in sleep-related disorders. New insights from basic research can lead to better methods for helping people with sleep disorders. There is an obvious connection to questions that focus on cognitive and mental disorders, with research looking at both the relationship between sleep deprivation and mental instability and the connection with such factors as age, genetics, educational level, glucose levels, and depression. Cognitive psychology is one of the disciplines that conduct research on the higher mental functions in humans. Studies investigating the neural basis of mental functions use a variety of methods, from MRi imaging and psychophysiological techniques to behaviour genetics, simulations, pharmacology, neurofeedback, and behavioural research. This research is clearly interdisciplinary in nature, as it brings together psychologists, neuroscientists, IT specialists, mathematicians, linguists, and philosophers.

Submitted questions illustrating depth and connective power

- **Would it be advantageous to attune society more closely to individual sleep/wake rhythms of morning and – in particular – evening persons, and if so, how can we best go about it?**
- **How can physical exercise, sleep, and nutrition be used to encourage healthy brain development and preservation?**
- **Does working night shift shorten someone's life?**

How can we use sport, exercise, and nutrition to promote good health and what effects will this have?

Explanation

For a number of years now, more and more studies have been devoted to sport and exercise and how they relate to nutrition and health. We now know, for example, that exercise and nutrition have a positive effect on bone density and on the prevention of diabetes and breast cancer. Exercise is good for you – that much is clear. Nevertheless, various studies have shown that almost half the Dutch population does not get enough exercise. The Netherlands is no exception in that respect, at least not in the West. How can we encourage people to exercise more, and how will that affect health and the societal, social, and economic domains? We need to know more about how injuries and overstraining occur and can be prevented, both in professional and recreational sports. In addition, a host of other positive effects are attributed to sport and exercise that have never been studied properly.

Connective power

More insights into this question and utilisation of this knowledge in interventions and technologies could be advantageous for both the economy and society, for example by promoting a healthy working population and social integration, i.e. greater participation in society, even among the socially disadvantaged. Answers can perhaps be found in basic research on the mechanisms and determinants that underpin movement behaviour and the relationship between nutrition and health, as well as in the development of behavioural theories that promote movement behaviour and a healthy lifestyle in general. In design-based research, the challenge is to experiment with methods and measures that encourage people to adopt healthy exercise and nutritional habits.

Submitted questions illustrating depth and connective power

- **What would be an ideal mobile app encouraging physically inactive people to exercise?**
- **What do sport and exercise mean for youngsters from different backgrounds, and how can sport and exercise contribute to a positive child-rearing environment that promotes children's wellbeing and health in the longer term?**
- **How can nutrition and exercise improve patients' state of fitness in order to speed their recovery?**

What are the consequences of chronic disorders, stress, and disabilities and what is the best way to deal with them?

Explanation

The consequences of chronic mental and/or physical disorders, stress, and disabilities – e.g. chronic diseases, unexplained somatic complaints, and mental disabilities – are enormous for both individuals and society. That makes the question of how patients, care givers, and society deal with these consequences an extremely important one, not only with a view to promoting the health and wellbeing of patients but also in terms of the impact on society and the economy. One in four Dutch people now suffers from a chronic disorder.Therefore, this question could have a very large impact.

Connective power

Research on chronic disorders, stress, and disabilities has important implications for health care (both mental and physical) and for social, economic, and technological progress. We received a large number of questions related to this issue, for example concerning:

- how to analyse the mental and physical consequences for quality of life and participation in society;
- causal, precipitating, and reinforcing contextual factors;
- how to deal with disorders in a way that limits the impact on the individual and society as much as possible;
- how to design societal and economic arrangements that support the long-term and meaningful participation of people with chronic disorders.

Submitted questions illustrating depth and connective power

- **What impact does financial stress have on our ability to learn? How is this harmful to society in economic terms?**
- **Does the immune system also play a psychological role?**
- **How can people with a physical and/or mental disability nevertheless participate fully in society?**

What do non-genetic factors contribute to personal traits and disease processes?

Submitted questions illustrating depth and connective power

- **What is de relationship between DNA sequence, DNA methylation, chromatin structure, gene expression, and protein expression?**
- **Why do some people remain healthy despite having an unfavourable genome (DNA)?**
- **How does the environment influence brain development?**

Explanation

We know more and more about the influence of external factors on our functional performance. Such factors can influence individuals directly or interact with their inborn predispositions. New traits that develop in response to an external factor can even be passed on without there being any change in the DNA sequence. Our environment and our way of life are therefore decisive for how our own cells function but also for how the generations after us evolve. Research in this area is of huge relevance to society. We can expect to see breakthroughs in our understanding of the way the brain and behaviour function. We may also gain a new understanding of how chronic diseases arise, which people are susceptible to them, and what interventions are possible.

Connective power

This question involves e.g. basic molecular, cellular, animal modelling, behavioural and demographic research. Environmental factors such as nutrition, stress, and living conditions can have a big impact on our wellbeing. For example, research has recently established a connection between nutrition, especially gut flora, and brain function. Chronic illnesses such as Crohn's disease have also been shown to be related to nutrition. Longitudinal observational research from the prenatal stage onwards can help us understand these influences better. We can use that knowledge to determine susceptibility to disease and identify early interventions, or to support children's learning. Such research intersects with ethics, as we must decide when and how government and businesses should use what we have learned to influence people, for example in neuromarketing. The question is also important in legal practice, for example in deciding when behaviour is culpable and when it is biologically determined.

How does the built environment affect health and wellbeing?

Submitted questions illustrating depth and connective power

- **How can we design buildings that are healthy (optimal indoor environmental quality) or that can even heal people?**
- **How do we plan a city in a way that enhances its inhabitants' quality of life?**
- **Which plants and trees have a direct and demonstrable positive effect on human health?**

Explanation

Seventy percent of the world population will live in cities in just a few decades. That fact alone makes questions about quality of life in cities increasingly urgent. The relevant research concerns the effects of chemical substances and technology on health, for example emissions, radiation, electromagnetic fields, ultrafine particulate matter, and lighting. It also, however, explores how green vegetation can contribute to a healthy living and working environment. The focus in architectural and interior design is shifting from technology to human beings. The world is increasingly digitised, while people are becoming more individualistic and living longer than they used to. The built environment must be designed to serve both practical/aesthetic and ecological/social aims; buildings must be safe for people to inhabit and set up to allow the elderly to live independently as long as possible. It will be increasingly important in such urban settings to design buildings and living environments that contribute positively to human health.

Connective power

The design of the living environment influences health in general, and more specifically working conditions and productivity. Research in this domain concerns not only the effects of and remedies for exposure to environmental and other background factors, but also the promotion of a healthy lifestyle and social wellbeing. We know that some determinants, for example fine particulate matter, influence public health, but we do not know all the effects on human health of individual determinants. It is also important to look beyond the individual effects and develop additional methods for assessing the risks of combined determinants on human health. This area of study requires collaboration between researchers in the social sciences, environmental sciences, and engineering. In addition to basic research exploring the relationship between the living environment and health, we also need applied research in which evidence-based concepts are transformed into innovations for the design, construction, and furnishing of buildings and public spaces. Research on the living environment is of huge societal and economic relevance. Big cities are a worldwide phenomenon, and an understanding of the problems they face can provide a sound basis for new export products.

What is the impact on human beings of electromagnetic fields (EMFs), for example as emitted by wireless devices and high-voltage power lines?

Explanation

Wireless communication is becoming increasingly ubiquitous. The public is growing more worried about the possible harmful effects of electromagnetic radiation, and we are seeing more and more discussions and questions about the health effects of living near electrical facilities.There have been many studies around the world on the potential health effects of living near high-voltage power lines. They have not assuaged people's fears. Recent discussions about electromagnetic hypersensitivity (EHS) and the IARC's classification of mobile telephone radiation as 'possibly carcinogenic to humans' show that uncertainties still abound when it comes to the real health effects of EMFs. Reliable facts obtained in research are needed to inform the discussion.

Connective power

Research – including longitudinal research – on the biological effects of electromagnetic radiation and EMFs and on the incidence of EHS in populations can help us design and construct safer wireless devices, develop more reliable regulations in this area, and provide a factual basis for the relevant discussions. This subject requires a multidisciplinary approach involving biologists, physicians, biophysicists, and engineers, as well as input from the social sciences. Industry and government are also stakeholders in such research. The question corresponds with the government policy priority 'Human and animal health and welfare'. In the Netherlands, the EMF & Health Knowledge Platform has a good idea of what we already know and what questions have yet to be answered. The Platform brings together relevant institutions and organisations that are in direct contact with the public and employees about this issue.

Submitted questions illustrating depth and connective power

- **How harmful for our bodies are the signals emitted by WiFi, mobile telephones, and other wireless devices?**
- **Investigations into the reliability of standards governing pulsed, unnatural, non-ionising microwaves (RF/HF).**
- **Which ICT technologies can electrical engineers use to advance the energy transition in the built environment?**

Can we gain a better understanding of the factors that play a role in the occurrence and persistence of long-term, medically unexplained physical symptoms, leading to better treatments for them?

Explanation

Medically unexplained physical symptoms (MUPS) are an important cause of sickness absenteeism. MUPS are seen in irritable bowel syndrome (IBS), fibromyalgia, and myalgic encephalomyelitis (ME)/chronic fatigue syndrome (CFS), for example. At the same time, they represent a medical challenge. There is still much confusion about how MUPS develop and persist. A better understanding of the underlying physiological, psychological, and environmental factors would allow us to develop more successful treatments, mitigating personal suffering and reducing absenteeism and the associated cost to society. Research should focus on identifying the causes of MUPS and on improving patient care.

Connective power

Most people who consult their GP have symptoms with no clear somatic cause. Many of these symptoms simply disappear on their own. Some persist, however, and they account for a large proportion of medical care consumption as well as absenteeism in education and the workplace. Very often, physicians confine themselves to searching for a somatic cause. The underlying problem is that many of them still adhere to a Cartesian distinction between body and mind, whereas it has already become clear that unexplained symptoms are the result of a complex combination of physical, behavioural, and environmental factors. The multidisciplinary quest to find causes and improve treatment embraces basic genetic, molecular, and neurobiological research as well as physiological, psychological, and behavioural research. This research can also explore the little understood connection between physical complaints, such as pain and exhaustion, and chronic illness. The question also overlaps with the way care is organised and physicians' attitudes towards MUPS, and with legal questions concerning the legitimacy of medical complaints, for example in connection with absenteeism or sickness benefits, when there is no identifiable medical cause. In addition, the societal pressure to eradicate disease as much as possible raises questions of a sociological nature. This question ties in with the government policy domains 'Work, care, and self-reliance' and 'Anticipating changing care demands in a transparent environment: Providing a different type of care'.

Submitted questions illustrating depth and connective power

- **How does neuro-inflammation influence myalgic encephalomyelitis (ME)/chronic fatigue syndrome (CFS)?**
- **How can we minimise the negative effects of MUPS in children on their health and development?**
- **What circumstances are most conducive to recovery from acute and chronic physical complaints?**

How will our knowledge of genetics play a role in analysing, screening for, and treating diseases?

Explanation

Many diseases have a genetic component. Multiple genes often play a role in such cases, complicating the process of identifying the precise cause of the disease and potential treatments. Besides genetics, environmental factors can also determine whether or not a disease manifests itself. It is possible to diagnose a genetic disorder by analysing an individual's genetic material, for example with new DNA sequencing techniques. A family health history can reveal whether a patient's family has a greater chance of developing the same disease; this involves tracing the disease in various family members and creating a family tree based on that information. Additional tests, for example genetic diagnostics, can also be carried out.

One example of screening in children is the test for cystic fibrosis. Infants are now screened at birth for this rare genetic disorder. If treatment commences at an early stage, it is more likely to be successful.

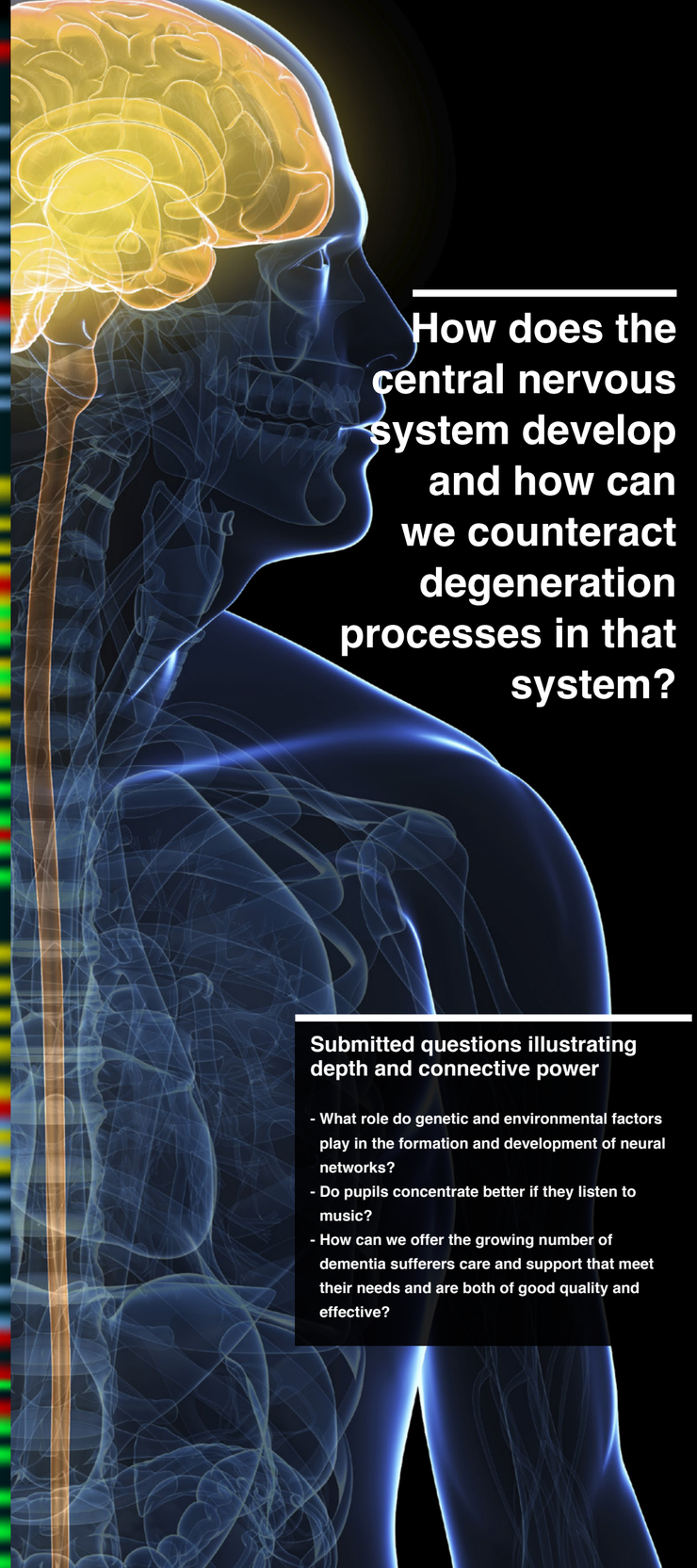
In addition to defects in the genes themselves, gene regulation processes are also partly to blame for hereditary disorders. We still know very little about such epigenetic processes. They probably explain why different people with the same genetic defect respond so differently to the same medication. Cancer research has made these individual variations clear. They mean that the treatment of a seemingly uniform genetic defect must be personalised to be effective. Future research will have to determine whether such epigenetic processes can also be easily screened.

Connective power

The Netherlands is an international leader when it comes to the clinical application of genetic technologies and expertise. For example, the first gene therapy approved in Europe for the rare genetic metabolic disorder lipoprotein lipase deficiency (LPLD) was developed in the Netherlands. The Dutch are especially renowned for their research on hereditary cancer genetics. It is very important from an economic perspective to detect a hereditary disease as soon as possible because early detection can greatly improve the chance of successful treatment and thus cut down on the cost of care. The challenge for science is, first of all, to improve our understanding of genetic and epigenetic complexity and to continue to develop and improve screening technologies. Screening methods must be made simpler, more reliable, less invasive, and less expensive. They must also cover a wider area of application so that we can develop new and effective treatments for a larger number of diseases. Such research connects the interests of science with a societal challenge and also offers economic opportunities.

Submitted questions illustrating depth and connective power

- How do we deal with genetic modification in humans?
- What is the value of next-generation sequencing (NGS) for phylogenetics?
- How will research on the human genome and epigenetic complexity help improve disease prevention and treatment?



How does the central nervous system develop and how can we counteract degeneration processes in that system?

Explanation

Our brain, and in the broader sense our nervous system, remains mysterious to us even today. We are still asking ourselves 'When did humans become conscious beings?' and 'Is there such a thing as collective intelligence?' These questions are not only relevant because they assuage our curiosity. They are also important for exploring how best to develop someone's talent, or to what extent nervous system function can lead to problem behaviour or developmental issues. A better understanding of the nervous system is also very much needed in the case of a degenerative nerve disease. As the population ages, the number of people suffering from dementia is increasing. There are still major questions concerning the occurrence and progression of this disease, including how to improve quality of life for dementia patients. Parkinson's disease, amyotrophic lateral sclerosis (ALS), and muscular sclerosis (MS) raise the same questions.

Connective power

Research focuses on the relationship between the nervous system and how we think and act, and on how to influence that relationship. The many advances in technology have further given rise to a new field of research that images the activity of the nervous system and underlying mechanisms. Major progress can be made by combining expertise in the various subdisciplines, including neurobiology, psychology, didactics, and ethics. Issues related to nerve degeneration and the associated diseases call for basic research on neurological processes. Applied research is also important, focusing on both the perceptions and capabilities of people suffering such degenerative conditions, as well as how families and society can best support them. This is pre-eminently multidisciplinary research, ranging from the study of meaningfulness to the design of a residential setting in which people can live independently for as long as possible. The Dutch government, businesses, scientists, patient organisations, care providers, and insurers have formed solid alliances in which they share the work of building and applying new knowledge about dementia and Parkinson's disease.

Submitted questions illustrating depth and connective power

- What role do genetic and environmental factors play in the formation and development of neural networks?
- Do pupils concentrate better if they listen to music?
- How can we offer the growing number of dementia sufferers care and support that meet their needs and are both of good quality and effective?

How do neurological, psychiatric, and mental disorders arise, and how can we prevent, mitigate, or cure them?

Explanation

Neurological, psychiatric, and mental disorders such as Alzheimer's disease, Parkinson's disease, muscular sclerosis, depression, anxiety disorders, burn out, or ADHD are common in every phase of the life cycle. The incidence of some of these disorders is expected to increase. Many questions about causes, treatments, and the consequences for society remain unanswered, however. They include:

- What causal factors play a role in mental disorders such as depression, anxiety, post-traumatic stress syndrome (PTSS), schizophrenia, ADHD, addiction, and so on? What causal factors play a role in neurological disorders such as muscular sclerosis, Alzheimer's disease, and Parkinson's disease?
- What neurological and mental processes underpin negative emotions (such as sadness or jealousy) or cognitions (such as worrying), and how do these processes influence long-term health?
- What is the best way to treat neurological and mental problems (for example with behavioural interventions, prevention, medication)?
- How can we best equip municipal mental health and other care facilities to deal with these problems?

It is very important for Dutch society in general and, of course, for patients and their families in particular to understand and be able to predict neurological, psychiatric, and mental disorders.

Connective power

At the moment, it is often difficult to treat neurological, psychiatric, and mental disorders. That has consequences for the economy, for example in terms of lost labour. A transnational approach is required to develop treatments, and the first steps have already been taken. Major advances are expected in the next ten years. The questions we received require input from the life sciences, but to improve our understanding of the neurobiological and psychological basis of psychiatric and mental disorders and how to treat them also calls for contributions from the humanities (for example philosophy). Basic genome research concerning the causes of such disorders will help us identify the best methods for treating and preventing neurological, psychiatric, and mental disorders. The best way to understand these disorders is by means of translational research. This question ties in with the top economic sector Life Sciences and Health and the policy domain 'Human and animal health and welfare'.

Submitted questions illustrating depth and connective power

- **Are people with an auto-immune disease at greater risk of developing multiple psychiatric disorders (e.g. an eating disorder, autism, an anxiety disorder, or ADHD)?**
- **Why does insomnia lead to so many mental and physical problems?**
- **What causes addiction and what can we do about it?**

What is the best way for us to analyse and prevent the problem of overweight and obesity?

Explanation

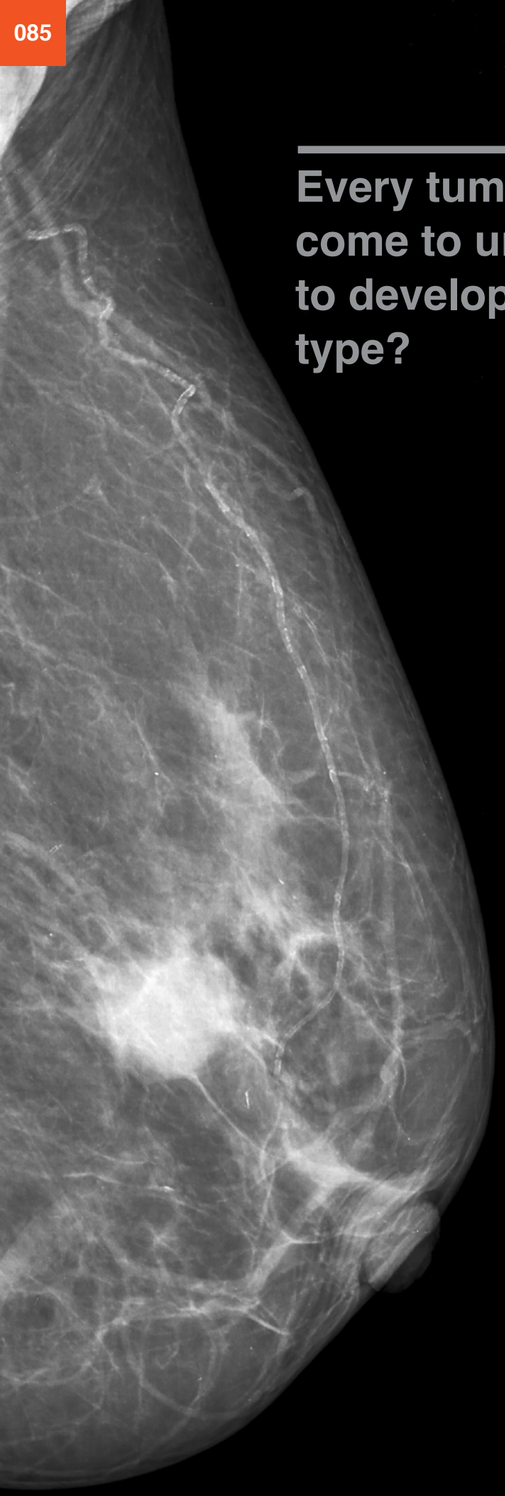
More and more people in the Netherlands are overweight, even obese. Heavy body weight is associated with numerous serious disorders, including diabetes, cardiovascular diseases, cancer, degenerative joint disease, back complaints, as well as obstructive sleep apnoea and other breathing problems. Overweight is not only a problem among older people; what is perhaps even more alarming is that more and more children are seriously overweight. Obese children often develop serious health problems in adulthood. Timely prevention, for example nutritional advice, more exercise, and other lifestyle interventions, can obviously make a big difference in such cases. The Netherlands has various cohorts of children and adults who are being tracked over time, producing important data that can improve our understanding. We would also be able to tackle obesity more successfully if we understood why one person gains weight easily while another does not.

Connective power

Researchers study obesity from different perspectives, ranging from basic to applied research. Obesity research examines energy metabolism, eating habits (including the associated cognitive mechanisms), cultural influences, and exercise and lifestyle interventions. Another important line of research looks at how genetic factors interact with environmental factors. Knowing more about how genes and the environment influence obesity will help us understand this disorder better. Obese people have a higher risk of developing such disorders as cardiovascular diseases, diabetes, and cancer. They can also suffer side effects, including arthritis, sleep disorders, and breathing difficulties. That is why this question is linked directly to these areas of research.

Submitted questions illustrating depth and connective power

- **How can we improve the success rate of treatments for eating disorders and obesity?**
- **Why are some overweight or obese people more likely than others to develop diabetes or cardiovascular disease?**
- **What do children think of child obesity? What do they think causes it and what do they see as successful preventive measures and treatments?**



Every tumour is different, so how can we come to understand cancer well enough to develop a treatment for each and every type?

Explanation

Every year some 45,000 people in the Netherlands die of cancer, despite improvements in treatment. It is the number one cause of death in our country. Every year, 100,000 people are diagnosed with cancer. Cancer – the uncontrolled growth of cells – is caused by genetic mutations in cells. The mutations cause problems in a whole range of essential biological systems and processes, such as the patient's metabolism, signal transmission, and protein transport, leading to changes in their sensitivity to medication. Tumours are seldom identical. It is important to know the genetic make-up and the tumour's traits so that we can recognise them earlier on and provide patients with more personalised treatment.

Connective power

Cancer raises many questions not only in medicine itself but also about care and quality of life. What we ultimately want is to eradicate cancer altogether. Failing that, we want to be able to treat cancer as a chronic disease and provide appropriate care and follow-up while maintaining quality of life for patients.Many different disciplines are involved in answering the medical questions associated with cancer. In-depth molecular research exploring the complex functioning of cells and stem cells is needed to understand how genetic mutations give rise to tumour cells and cause them to be resistant to conventional medicines. It is also needed to develop better personalised, cost-effective treatments once cancer develops. Such treatments might consist of new precision medicines (singly or in combination) in addition to more refined surgical, imaging, and radiation techniques. One of the biggest challenges will be to determine the most effective therapy combination for specific patients with their specific genetic backgrounds – and specific tumours. Developing tumour stem cells, known as organoids, makes it possible to screen the effectiveness of large numbers of potential drugs without having to test them on the patient. In addition, relatively new non-tumour-specific immunotherapies are promising; they stimulate the patient's immune system in general, leading to a better immune response against cancer cells.

Submitted questions illustrating depth and connective power

- **Can we use viruses to prevent different forms of cancer?**
- **How does stress contribute to cancer and ageing and can we slow down this mechanism?**
- **Every tumour is unique and so is every patient. What is the best and most cost-effective way to decide who should receive treatment, when, and using which therapy?**

Intestinal disorders, and specifically the relationship between gut flora and health: what can we do to benefit our gut flora?

Explanation

The intestines are the largest organ in the human body. They are also an extremely dynamic organ. Their cells have a renewal rate of three days, and they absorb all the nutrients we ingest and separate out the waste products. From birth, our intestines are colonised by a complex microbial ecosystem that is increasingly thought to be connected to sickness and health. We have more than a thousand different types of micro-organisms in our intestines. The precise composition of this ecosystem is unique for every person. Despite the wide variety of bacteria present in the intestines, gut flora are well balanced in healthy persons, but that delicate balance can also be disturbed by antibiotic use, nutrition, and ageing. The composition of gut flora – now often referred to as gut microbiota or gut microbiome – can predict diabetes, rheumatic diseases, irritable bowel syndrome (IBS), and abnormal behaviour.

Connective power

Research on the interaction between micro-organisms in the gut and between gut micro-organisms and their host can help us link good health (or poor health) to the composition of the microbiome.

We need new analysis methods to learn more about gut flora. We also need to study whether gut flora transplants constitute a possible treatment for intestinal and other disorders and what consequences that treatment would have. One key question is which bacteria are found in a healthy ecosystem, what their function is, and how we can use this knowledge to develop new forms of treatment. Personalised preventive and curative interventions based on that knowledge can help keep the intestines healthy. We also need to study the possibility and consequences of using gut flora transplants and bacteriophage therapies (viruses that kill bacteria selectively) as a possible treatment for intestinal and other disorders. This area of research, which is largely unexplored, is important for both the general and specialised food industry and for pharmaceutical firms. It therefore represents an interesting link between two business domains that have so far been largely separate. The challenge is for researchers to explore this complex but promising subject in partnership with physicians and product developers.

Submitted questions illustrating depth and connective power

- **What is the relationship between our gut flora and sickness/health and how can nutrition, for example probiotics, and faecal transplantation or bacteriotherapy (single bacterium or a combination) have a beneficial effect on gut flora?**
- **What causes Crohn's disease or ulcerative colitis and how can it be prevented?**
- **Why can't we transplant the intestines?**

What causes type 1 and type 2 diabetes, how can we detect them sooner, and how can we treat them on an individual basis?

Explanation

Diabetes is caused by an insulin deficiency or insulin resistance. Insulin is produced by the pancreas. In type 1 diabetes, the immune system mistakenly attacks cells in the pancreas, destroying its ability to produce insulin. Type 2 diabetes is usually precipitated by insulin resistance, often the result of overweight, with the pancreas being unable to produce enough insulin to overcome that resistance. Insulin plays a role in blood glucose regulation, but also in many other metabolic processes. Diabetes not only disrupts blood glucose levels and other metabolic processes but can also soon lead to serious vascular complications. Microvascular complications can result in eye or kidney problems. Macrovascular damage can lead to heart disease, among other things.

Connective power

Dutch researchers have devoted considerable effort to studying diabetes. Their excellent work combines very basic, experimental, and patient-based approaches. Diabetes research focuses on many different facets of the disease. In terms of causes, for example, it looks at the immune response that leads to type 1 diabetes. In terms of treatment, one promising avenue consists of continuous glucose monitoring using a smart sensor inserted under the skin and combined with micro insulin pumps. Another area of research involves the treatment of diabetes-related organ damage. Researchers are also studying prevention, for example by influencing people's nutritional habits.

Submitted questions illustrating depth and connective power

- **What same underlying mechanisms give rise to the ageing of the reproductive system, type 2 diabetes, and cardiovascular diseases?**
- **Is a pancreatic transplant a possible cure for type 1 diabetes? Is an artificial pancreas a realistic option?**

How can we predict, prevent, and treat cardiovascular diseases (atherosclerosis, heart failure, heart arrhythmia, and thrombosis) in individuals at an early stage?

Explanation

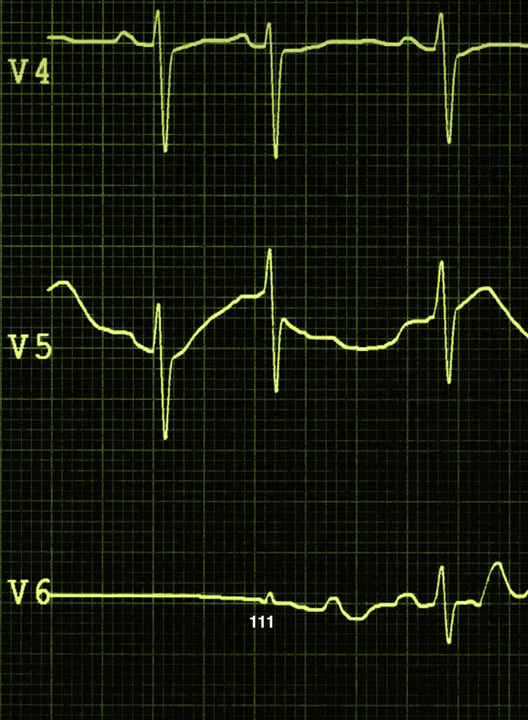
Cardiovascular diseases are common in the Netherlands. Obesity, ageing, and an unhealthy lifestyle are factors with a negative impact on the cardiovascular system. Congenital heart defects are also common in the Netherlands. The challenge is to diagnose and treat cardiovascular diseases before they manifest themselves. This does, however, involve issues of responsibility and the cost of health care. Is it a good idea to screen healthy people to prevent illness? This question also looks at the genetic risk factors of cardiovascular diseases and the underlying causes of abnormal cardiovascular function.

Connective power

One of the typical features of cardiovascular research in the Netherlands is that it is organised from the bottom up. Knowledge-based institutions, industry, and civil society organisations work together on projects meant to improve the quality of Dutch cardiovascular research. Patients also have the opportunity to give their input. The research is basic as well as translational and clinical in nature. It focuses on detecting cardiovascular diseases early on, how these diseases differ between men and women, the treatment of heart arrhythmia and heart failure, rapid treatment in the case of strokes, and innovative methods for helping people achieve and maintain a healthy lifestyle. The latter has a direct relationship with technological research involving self-management strategies, apps, and gaming.

Submitted questions illustrating depth and connective power

- **How do men and women differ when it comes to the symptoms, risk factors, causes, progression, diagnosis, and treatment of cardiovascular diseases?**
- **How can we improve the treatment for heart arrhythmia and heart failure and lower its cost?**
- **What role does the immune system play in the recovery of the artery wall after atherosclerosis surgery?**



How can we improve our understanding and treatment of pulmonary diseases?

Explanation

Pulmonary diseases are among the most common disorders, both among children (asthma) and the elderly (chronic bronchitis and emphysema).
In children, asthma is caused by an excessive immune response. Treatment is usually effective, but the disease can also take on very serious forms.
A better understanding of the underlying causes and mechanisms would lead to improved medication and management. Environmental factors such as air quality may also play a role. Chronic bronchitis and emphysema are caused by smoking and are very difficult to treat; enormous progress is still possible in this area.

Connective power

Research on pulmonary diseases ranges from basic to applied and focuses on preventing and understanding the relevant disorders, developing new or improving existing drugs or vaccines, and transplanting or even repairing impaired lungs. Longitudinal population studies are needed to identify at what point a person develops a lung disease and which factors play a role. Input by patients is an indispensable part of such research.

Submitted questions illustrating depth and connective power

- **How can we develop better medicines to combat viral and bacterial respiratory infections?**
- **What happens to children's lungs if they grow up surrounded by serious air pollution?**
- **How can we get lungs to regenerate?**

What causes chronic kidney disease, how can we detect it sooner, and how can we treat it on an individual basis?

Explanation

When people suffer from chronic renal failure, their kidneys function insufficiently over a longer period of time. Usually this happens because they have high blood pressure, diabetes, or another renal disorder. Most people who have chronic renal failure are not troubled by it at first. In some cases, they may only have a few vague symptoms. Chronic renal failure is incurable. Damaged renal tissue does not recover. The symptoms ultimately become serious and include anaemia and cardiovascular diseases. Early diagnosis of chronic renal failure is vital to preventing irreparable kidney damage.

Connective power

Research on kidney failure focuses on the many facets of the disease: causes and treatment, prevention, and the treatment of associated organ problems. Research is needed on biomarkers that can predict kidney damage in the early stages of the disease, before any symptoms have appeared. Research is also required on the molecular mechanisms leading to kidney damage so that personalised treatment can be developed. Finally, we need to improve quality of life for kidney patients by studying how kidney disease impacts other essential bodily functions and how to avoid that impact.

Submitted questions illustrating depth and connective power

- **Do age, gender, and lifestyle influence the occurrence of kidney disease?**
- **Can new biomarkers help us detect kidney cancer sooner?**
- **Will researchers ever create an artificial implantable kidney?**

Pregnancy, childbirth and menopause: can enhanced insight into these processes contribute to a more comfortable experience?

Explanation

Pregnancy, childbirth, and menopause are major events in a woman's life. Childbirth is one of the most perilous moments in the life of both the mother and the child. If something goes wrong, it can have a lifelong impact on the mental and physical wellbeing of both. Basic research questions concern the complex physical processes involved in conception, implantation, and foetal development in close interaction with the mother's body until birth, the transition of the foetus into an autonomous individual, and the physiological and mental effects of labour on a woman. Other factors that significantly affect the quality of the pre-pregnancy stage, the prenatal stage, and birth are sexual orientation, choice of partner, fertility (or infertility), nutrition and behaviour, drug use, and safety risks posed by environmental factors during pregnancy. The ethical dilemmas associated with diagnostic screening and unplanned pregnancy are also important facets. Women who wish to avoid pregnancy can take the pill, but there is no pill for women who are troubled by menopause. Can something be done for them? Would a better understanding of the underlying physiology at molecular, cellular and organism level ease the stress of these events in a woman's life?

Connective power

Dutch health care is excellent, thanks to the superb quality of hospital care, pioneering research at Dutch university medical centres, and their cooperation with university research groups. This puts us in an excellent position to make important contributions to solving various problems in this socially highly important domain over the next ten years. New interventions based on studies of the underlying processes will improve quality of life and help build a healthy, stable society. The arrival of new diagnostics and technologies is also raising numerous ethical questions, for example deciding when treatment is still in the patient's interest. For prevention, public information, counselling, and individual guidance are important support activities that can help avoid physical and social problems, and the associated health care costs. That will also deliver real benefits for the Dutch economy, for example by reducing sickness absenteeism.

Submitted questions illustrating depth and connective power

- **Why is there no effective remedy for hot flushes?**
- **What role does nutrition play in the development and performance of the immune system during embryogenesis?**
- **Why is it that a pregnant woman's body does not reject her baby but would reject a transplanted kidney donated by the baby's father?**

Can we combine mainstream and complementary therapies, leading to integrative health care that allows for the many differences between patients?

Explanation

Complementary and alternative medicine (CAM) – for example Ayurveda, acupuncture, homeopathy, reflexology, orthomanual therapy, traditional Chinese medicine, but also the paleo diet, meditation, and mindfulness – is growing increasingly popular. Some people believe they benefit from it, whereas others consider it a sham. Unless we devote enough scientific research to studying CAM, we will never know whether it produces a placebo effect or genuine physiological results. While we are all familiar with the placebo effect, we know very little about the mechanisms behind it and how it can be used in other contexts. Sub-questions include:

- Is there scientific evidence for the beneficial effects of CAM?
- What role can CAM play in health care?
- Based on what we know about the effectiveness of placebos, can we identify any principles or mechanisms for developing an alternative, perhaps only partially applicable, form of healing that involves fewer or no drugs?

This is an issue of considerable interest to the public.

Connective power

This question relates to various other questions, for example about treatment methods for certain diseases, sickness prevention, the influence of nutrition and lifestyle on health, and the role of the immune system. Various research groups and institutes, ranging from basic to applied in nature, are actively investigating topics that touch on this question, including prevention and healthy ageing. To arrive at answers to these questions, integrated medical, behavioural, and sociological research is needed. The theme keys into the top economic sector Life Sciences and Health and a number of government priorities, i.e. 'Anticipating changing care demands in a transparent environment: Providing a different type of care', 'Creating a suitable health care system: Promoting all-round cooperation and efficiency', 'Choosing collective priorities: Affordable collective health care and assistance'.

Submitted questions illustrating depth and connective power

- **Can we combine mainstream and complementary therapies, leading to integrative health care that allows for the many differences between patients?**
- **Why is medicinal cannabis more or less neglected even though there's worldwide evidence that it is an excellent medicine with no negative side effects in humans?**
- **How powerful is the force of persuasion (placebo/nocebo effect) in medical science (e.g. pain, depression), the behavioural sciences (e.g. anorexia, bulimia), and religion (e.g. jihadism, belief in a God)?**

How can we promote innovativeness, quality, and accessibility in institutionalised and informal forms of care?

Explanation

New and sweeping changes have recently been introduced in Dutch health care financing. Changing insights into self-reliance, participation in society, and their relationship to health have also given rise to major transformations in health care. We are not out to solve people's problems for them but instead want to encourage self-care and resilience so that every individual can achieve the right physical, social, and emotional balance for themselves. Organisations face the task of setting up new care processes and helping staff adapt their values and professional attitudes to the new situation. The question is how we can promote the quality and accessibility of institutional and informal care, for every age group, under the new financing and value systems.

Connective power

This question consists of a number of sub-questions:
- How can we best promote self-care and care in the community?
- How can innovations in technology improve the quality and accessibility of care?
- How should the new approach to health care be financed?

The challenge that this question poses for researchers lies in developing and applying evidence-based methods in all sorts of care-related areas, and in developing new care processes that support the transition to prevention, self-reliance, and accessibility. In addition, researchers also face major questions concerning the effective deployment of advanced and low-threshold technology in health care, both in institutional and home settings. Societal challenges lie mainly in financing care-related activities and training care professionals to deal skilfully with new care processes and technologies. The economic opportunities lie in using the associated cost savings to finance some of the health care reforms. This is in fact a design-based issue, i.e. the need for a financing model that is sustainable and effective and that supports continuous innovation in health care.

Submitted questions illustrating depth and connective power

- **Gaming and health: How can we use serious gaming in the field of health and health care?**
- **Are people getting the care they need, and how can they influence that?**
- **How can we integrate e-health into physiotherapeutic practice and what would we gain by doing so?**

How do we improve the quality of health care as much as possible while keeping it affordable?

Explanation

Health care systems all around the world are under tremendous pressure. Advances in technology, ageing populations, new health risks, and cultural trends are driving up the demand for care and the cost so fast that current financing systems cannot keep up. More and more aspects of care are regarded as an individual responsibility, putting greater pressure on family care givers, for example. Research can help solve this problem in various ways. Research on new treatment methods can help professionals do their work more efficiently. Organisational studies can help institutions operate more efficiently. Health economics research can help policymakers make the right decisions.

Connective power

Multidisciplinarity is the key to health care research. Researchers in health economics, health care law, organisation science, public administration, medical sociology, ethics, anthropology, and other disciplines work together closely on health care-related questions. They will also need to cooperate with technology researchers, since technology can lead to cost savings. The use of ICT is frequently cited as a tool for streamlining the organisation of health care. Some of the questions involve basic and others applied research. Many questions have an ethical dimension. Cooperation with civil society organisations, for example patient interest groups, is emphasised in this research, guaranteeing its ongoing relevance and applicability.

Submitted questions illustrating depth and connective power

- **How can we assess Dutch medical guidelines on their effect, usefulness, and cost-effectiveness?**
- **How can technology help improve the quality and lower the cost of health care?**
- **To what extent does value-based health care (care based on value creation as defined by patients) improve outcomes in terms of survival and quality of life?**

How can we personalise health care, for example by using biomarkers?

Explanation

Medicines and treatment methods are not always as effective as they could be. In the case of drugs, 25 to 60% of patients have only a slight or no response at all to treatment. Other treatment methods also appear to be based on the average patient rather than the specific individual. There is broad consensus about the importance of what is known as personalised (or precision) medicine and health care, something that is playing an increasingly significant role in policymaking and research. Personalised health care involves administering the right drugs in the right dosage to the right patient at the right time. The key to this approach lies in molecular biomarkers, which can tell us whether a treatment is likely to be successful for a specific patient. Biomarkers have yet to be discovered for many diseases. The ultimate aim is for medical care, prevention, diagnosis, treatment, and follow-up to be based on the patient's individual traits. Personalised care must also be mentioned in that context.

Connective power

The more we learn about the human body's functional performance at the molecular level, the clearer it is that each and every individual has a slightly different genetic make-up. That implies that the drug action pathways may also differ from one individual to the next, so that the effect of a specific drug may differ from person to person. Recent cancer research in the Netherlands shows that there is a connection between genetic variation and the effecti-veness of treatment, and that a cocktail of drugs, each one taking a different action pathway, is needed to fight cancer cells successfully. The precise relationship between genetic variation and drug effectiveness is not well understood, however, and requires comprehensive multidisciplinary research involving molecular biologists, biotech IT experts, medical specialists, and pharmaceutical scientists. Factors beyond those based on genetic variation will also become more personalised, whether or not at the patient's request. The financial effect of such personalised approaches is still largely unknown and will be an important factor when it comes to controlling the cost of care.

Submitted questions illustrating depth and connective power

- **How can we ensure that information about biomarkers, drug use, and physician and patient observations are combined and made accessible, thereby improving the treatment of chronic diseases and lowering the cost of care?**
- **Is it possible to predict an individual patient's risk of complications after a medical intervention?**
- **How can we finance the upcoming trend towards personalised medical treatment?**

How can we improve diagnostics, treatment, and vaccines for immunodeficiencies and infectious diseases?

Explanation

The old adage that an ounce of prevention is worth a tonne of cure is certainly true of infectious diseases. This question explores how to determine the nature of an infectious disease as well as how to treat it. How complicated is it to diagnose an infectious disease, and what role do GPs and specialists play in this process? Vaccination is a highly successful way of preventing infectious diseases. Vaccines have made it possible to contain serious large-scale epidemics, including smallpox, cholera, and diphtheria. Nevertheless, research is still needed on diseases for which we have yet to identify an effective vaccine, such as HIV, malaria, tuberculosis, or hepatitis C. In addition, it has become increasingly apparent in recent years that vaccination can be useful in treating or preventing diseases other than infectious ones. For example, it seems that vaccines will eventually play a useful role in the personalised treatment of cancer patients. In fact, a vaccine against cervical cancer is already being administered. Medical researchers also speculate that vaccination may help fight nicotine addiction, diabetes, or dementia. Autologous stem cell transplantation is sometimes used to treat serious auto-immune diseases. Considerable research is needed in that area.

Connective power

Infectious diseases are caused by pathogenic micro-organisms such as bacteria, viruses, moulds, or parasites. They are transmitted by people or animals. An unusually serious infection or one caused by an abnormal pathogen may lead to immunodeficiency, in other words compromise the immune system's ability to fight off infectious disease. Much of the research on immunodeficiency is diagnostic in nature and focuses on describing the disorder, its genetic causes, and its symptoms. The specialisms that play a role in such research include clinical infectology, immunology, medical microbiology, and virology. These areas of expertise illustrate the broad, diverse scope of research on infectious diseases, which encompasses basic, translational, and applied clinical research. The Netherlands is a trailblazer in vaccinology, especially in basic research. Large university medical centres are involved in this field, as well as private companies that conduct their research in the Netherlands.

Submitted questions illustrating depth and connective power

- **How can we improve the personalised treatment of patients with an immunodeficiency?**
- **What environmental and interaction factors play a role in the dispersion of pathogens?**
- **How do vaccinations affect child development and health?**

How can we control micro-organisms in health care, livestock farming, and the environment?

Explanation

One of the biggest advances in medicine and health care was the discovery of antibiotics, crucial to the fight against bacterial infections. Unfortunately, bacteria soon began to develop antibiotic resistance. The widespread and frequent use of antibiotics in both human and veterinary medicine has led to a precipitous rise in antimicrobial resistance (AMR) since the 1980s. Some strains of *Staphylococcus aureus* (MRSA), *Klebsiella pneumoniae* (pneumonia) and *Mycobacterium tuberculosis* (TB) are resistant to virtually all known antibiotics. In addition, AMR is a growing problem in the battle against parasites, viruses, moulds, and other micro-organisms, malaria being a notorious example. AMR is therefore one of the greatest threats to public health owing to the increasing cost, health problems, and efforts needed to control and prevent it in health care, agriculture, and the environment.

Connective power

To control pathogenic micro-organisms, we need to conduct in-depth multidisciplinary research that focuses both on developing new drugs and on preventing resistance. Improved diagnostics are needed to quickly identify the pathogenic micro-organisms causing infection in patients as well as the associated resistance profile. The vast majority of antimicrobial drugs were originally derived from micro-organisms. Ninety-nine percent of microbes cannot be cultivated as yet and form a potential rich source of new antimicrobial drugs. Advances and applications in synthetic biology, genomics, metabolomics, and other technologies are essential to the development of new drugs. Since R&D expenditure on new antibiotics is difficult to recover, it will be necessary to develop new revenue models in the public-private setting. Another point of attention is the responsible use of antimicrobial drugs in humans and animals and preventive hygiene in hospitals and nursing homes. It is vital to involve the agriculture sector in such studies, given our intensive livestock farming systems, the way various production and sales chains are organised, and hygiene practices in farming. Waste water flows are a significant source of AMR dispersion and should therefore be mapped out in detail.

Submitted questions illustrating depth and connective power

- **What role does the environment play in the dissemination of antibiotic resistance?**
- **How do we find new sources of antibiotics if industry is unable to discover new ones despite a herculean effort?**
- **Is it possible to replace all the antibiotics used in livestock farming by secondary metabolites from plants while maintaining economic performance?**

How can we use breakthroughs in basic biomedical research to develop new medicines?

Submitted questions illustrating depth and connective power

- **How can we predict which drugs will be effective and safe for children?**
- **How can we amend the rules governing drug registration so patients who wish to take them can do so at an early point in the testing process?**
- **Why doesn't government cooperate with research centres and insurers to develop drugs on a non-profit basis?**

Explanation

Drug discovery and development is a complex and labour-intensive process that takes about ten to fifteen years. The cost of R&D can exceed a billion euros. Owing to patent terms, data protection, and market exclusiveness, these costs need to be recouped within about ten years. This makes drugs expensive, especially if the patient population is small. Various breakthroughs in biomedical research are expected in the coming years that will have a major, positive impact on drug discovery and development, for example:

- next-generation DNA sequencing, for faster collection of more patient data;
- progress in such advanced therapies as gene therapy, immunotherapy, stem cells, and organoids;
- more knowledge of biomarkers, improving early detection and tracking of disease processes;
- advances in ICT, leading to faster, smarter learning from practice and on the job.

One key challenge in the years ahead is to guarantee patients rapid access to innovative therapies at an affordable cost to society. Various innovative solutions are conceivable, for example new revenue models, more effective methods for producing and administering drugs, shorter development and registration procedures, and close cooperation between public and private parties.

Connective power

Dutch universities, knowledge-based institutions, and university medical centres cover the entire value chain, have superb networks in European research programmes, and benefit from each other's geographical proximity. In terms of private initiatives, the number of successful, innovative Dutch biotech firms has increased rapidly in recent years. We can continue and boost this trend by clustering biomedical research in a national/international setting that involves private parties, including innovative hi-tech or biotech firms, insurers, health research funding organisations, and non-profit organisations. Besides continuing to support basic and applied ICT research, it is important to improve the Dutch research infrastructure and to implement relevant, cost-effective e-health applications in the real world. This not only means setting up practical, up-to-date training programmes but also getting ICT and medical specialists to collaborate closely. In addition, explicit attention must be given to the privacy and accountability concerns associated with the general availability of medical and, therefore, highly personal data. Close cooperation between data-generating (medical equipment, sensors, robots) and data-processing systems will also lead to a more efficient use of resources.

How can a broader definition of ‘life’ help us identify new targets for molecular therapies, antibiotics, and antiviral drugs?

Explanation

The questions in this cluster concern the use of innovative technologies in drug research. One example is the lab-on-a-chip, i.e. integrating various laboratory functions on a single chip. This technology can reduce the amount of time and the costs involved in blood, saliva, or urine tests, for example. Developing countries are interested in this technology because such tests do not require a highly complex infrastructure. The cluster focuses specifically on how innovative technologies might improve our basic understanding of molecular and physiological processes. Knowing more about them could open up new avenues in drug research. Another important factor is the development of new laboratory models for studying the human body.

Connective power

This question has a close relationship with the top economic sector Life Sciences and Health. It is also clearly linked to the Chemistry top economic sector. The emphasis in basic research is on how innovative technologies, for example stem cell technology, can support the development of new drugs and therapies. Applied research explores how to improve the efficiency and effectiveness of the drug development process. Some of the questions we received focus on the potential for producing drugs and other substances sustainably. Cooperation between the disciplines of chemistry, biology, medicine, and ICT or fundamental physics is very important in this cluster.

Submitted questions illustrating depth and connective power

- **How can we use the rapid development of lab-on-a-chip technology to improve the quality of biomedical data and to gain continuous insight into pharmaceutical processes?**
- **How can the phenomenal increase in computing power (Moore’s law) best be used in health/medical research?**
- **How can we use metabolic engineering to develop new routes for the production of fuels, fine chemicals, and medicinal drugs based on renewable feedstock?**

How can we use cells, stem cells, and biomaterials to engineer and regenerate tissues and organs?

Explanation

Regenerative medicine – functional recovery in damaged organs and tissues – is about to undergo a revolution, given the potential of using stem cells and tissue engineering in new healing methods. Stem cells are the basic material from which all tissues and organs develop. But how do they work and how do they know what they are supposed to do? To turn stem cells into specific tissues and organs, we need to know more about how stem cells function, and about the relationship between different tissue types in an organ in a three-dimensional context. Regenerative medicine and treatments that enhance tissue or organ self-repair can also reduce the demand for donors, a very desirable outcome given the serious shortage of donor organs.

Connective power

Stem cell technology and tissue engineering make it possible to grow tissue from autologous cells. Pluripotent stem cells have the potential to differentiate into almost any specialised cell in the body; multipotent adult stem cells can differentiate into a limited number of specialised cells with specific functions, but they are safer. Over the next ten years, research should show which of these is best for repairing human tissues and organs. We need to develop biomaterials that adapt to their host, that do not induce an immune response leading to organ or tissue rejection, and, ideally, that stimulate autologous tissue to self-repair. In some cases, it may be possible to repair tissues by intervening at the molecular level. It may even become possible at some point to create tissues by 3D printing.

Submitted questions illustrating depth and connective power

- **How can we combine natural and synthetic biomaterials with nanotechnology to influence cells and tissue such that 1) they retain or recover their function, and 2) we can stop disease processes?**
- **Will we be able to reverse the ageing process in the future by regrowing young cells?**
- **Would it be possible to live forever by constantly replacing damaged organs?**

Can we model the human body and use smart technologies for health, nutritional, and toxicity research, drastically reducing the use of laboratory animals at the same time?

Explanation

The cost-effectiveness of the pharmaceutical industry is declining steadily. One important reason is that, after a lengthy development process, many drugs end up not being effective or having negative side effects. A similar problem has arisen in the nutrition and food industry, where it is difficult to demonstrate cost-effectively that innovative products are safe and healthy. And then there is the chemicals industry, which faces the challenge of determining the toxicity of large numbers of substances — something that requires a great deal of animal testing, according to current protocols. Realistic laboratory models of organs based on cultivated tissue can make a unique contribution to research on diseases, toxicity, drug development, and personalised medical treatments. Besides its obvious biomedical relevance, human and animal laboratory modelling also meets the societal demand for alternatives to animal testing. Organs-on-chips are examples of laboratory models based on the use of cellular material in microdevices. Technology makes it possible to create chips in which we can control the biochemical, mechanical, and physical environmental factors to perfection. The next step is to grow tissues in conditions that mimic those of the human body, and to have those tissues function the way our organs do.

Connective power

Cultured models of human organs on chips can certainly be developed within the next ten years, especially given the huge advances within reach of Dutch researchers in such areas as stem cell biology, microfluidics, nanotechnology, materials science, 3D printing, and genetics. Sources of human tissue are needed, but obtaining tissue in the Netherlands will require us to investigate the relevant legal and ethical aspects. As yet undiscovered applications combining human tissue and electronics and the early and accurate prediction of diseases also raise ethical questions. Synthetic biology is a fast-developing area of research, including cell or organ fabrication and the related chip-based detection and analysis systems. This area is included under the theme ‘Regenerative medicine’ in the Life Sciences and Health top economic sector and under ’Chemical nanotechnology & devices’, one of the programme categories in the Chemistry top economic sector. The relevant research is well in line with the BRAIN Initiative and other major programmes in the USA and with the European Union’s Human Brain Project.

Submitted questions illustrating depth and connective power

- **Can we develop new medicinal drugs without using laboratory animals?**
- **Can we 3D print the human brain on a chip?**
- **Will nanotechnology someday allow us to track down and cure defects and diseases in the human body?**

How can we develop new drugs and treatment methods that will keep us as healthy and vigorous as possible?

Explanation

Over the past century, drug development, better nutrition, and improved hygiene have increased the average life expectancy by dozens of years, especially in the West. In 2050, 20% of the world population will be older than 60 and the number of people above the age of 80 will have tripled. A major effort is required not only to improve quality of life in an ageing society but also to maintain the current standard of living. The question is: How far can we go? And how far do we want to go?

Connective power

Providing for a healthy and vigorous old age will require input from across the health sector. Our ageing society faces an increase in age-related chronic diseases, including type II diabetes, cardiovascular diseases, dementia, and cancer. Today’s unhealthy lifestyle, which leads to overweight and obesity, will raise the incidence of these diseases. Conceptually, it is possible to tackle age-related diseases as a group, and not as individual illnesses. Early diagnostics is essential in this respect. In addition, we need new drugs and treatments to keep the population healthy and active as it ages. Molecular disease research provides the basis for new methods of treatment. The future, however, lies in translational research, which applies research findings in real-life contexts. Whether or not individuals are healthy in old age depends on the interaction between their genetic make-up, their environment, and their lifestyle. Other crucial factors include innovations in preventive behavioural interventions, housing, nutrition, ICT, e-health and mobile health, medical devices, and innovations in the care sector. The quest to develop innovative products and services depends on close collaboration between research institutes, businesses, and the authorities in such areas as genomics, clinical research, epidemiological research, and behavioural research, preferably in public-private partnerships. One of the challenges is to combine such research with developments in architecture, the creative sector, and the nutrition and medical devices industries. Besides serving an obvious public interest, this subject is also economically advantageous.

Submitted questions illustrating depth and connective power

- **How do we ensure that young children who undergo serious medical treatment enjoy good health in old age?**
- **What combination of indicators (biological age, functional geriatric tests, measures of physical and mental wellbeing) is most accurate when monitoring the effectiveness of preventive and clinical interventions in the elderly?**
- **What lifestyle offers the best chance of living as long as possible?**

How can we understand and assess the potential and limitations of medical progress?

Explanation

Medicine has traditionally focused on how diseases or defects influence the functional performance of the human body. Its purpose is to return the body to a good state of health, alleviate symptoms, or avoid a pathological condition. However, advances in medical science raise all sorts of social and moral dilemmas. Medicine is infiltrating deeper than ever into our lives, carried there by cultural trends and technological progress. It plays a role during birth, sickness, and death, and increasingly in the intervening periods. Medical science and technology are advancing rapidly, and social norms and values are also in a constant state of transition. Social mechanisms, cultural patterns, and normative issues shape our concepts of health and care, but are in turn also influenced by them. This question broadly considers how research in the social sciences and humanities can inform the debate about quality care and medicine. Within that context, many of the questions focus on the ethical dilemmas raised by medical progress. New methods, for example that extend life or allow prenatal testing, raise questions about quality of life, privacy, and freedom of choice. Is everything that is medically possible automatically desirable? There is also a host of questions about society's perception of diseases, disorders, and disabilities. These concern the influence of a culture and a society on the way people experience and interpret health problems, address their health, and respond to health care interventions.

Connective power

The answers to these questions are situated at the interface between the humanities, the social sciences, and medical science. Conceptual, theoretical, and normative analyses make it possible to view assumptions, classifications, and judgements in medical science from a broader perspective. That requires some insight into societal perceptions. What do we think of diseases and disabilities, and what do we consider important when it comes to healing or care? What does the organisation of the health care system tell us about this? Descriptive, historical, and transcultural studies can help us learn from the approaches to these issues taken in different countries and in different epochs.

Submitted questions illustrating depth and connective power

- **Is there an ethical way of inducing people to use new technology that 'nudges' them to consume less energy, adopt a healthier lifestyle, drive safely, and so on?**
- **How do dementia sufferers, especially those in the advanced stages, experience reality and their surroundings?**
- **What will happen if human beings continue to live longer and become more or less immortal?**

How do we develop minimally invasive techniques and interventions for diagnosis, prognosis, and treatment?

Explanation

Medical care will continue its rapid transition from invasive to minimally invasive treatment in the years ahead. As minimally invasive techniques become more refined and are used in combination, more effective and efficient diagnosis and treatment become possible without the burden of surgical intervention. Minimally invasive techniques combined with image-guidance tools have revolutionised vascular medicine, for example in percutaneous angioplasty or the insertion of a stent. In the next few decades, a similar revolution is set to take place in the treatment of cancer and neurological and orthopaedic disorders. Current diagnostic techniques that allow us to look inside the human body are either damaging or expensive. Visible light is a benign and inexpensive alternative. Without adaptation, however, light does not penetrate very deep into the body and is easily scattered. Recent Dutch breakthroughs have demonstrated that we can adapt the light wave pattern to infiltrate deep into the body. A further breakthrough is expected in the next ten years.

Connective power

Molecular diagnostics, imaging, and image-guided intervention are important themes in the Life Sciences and Health top economic sector. This question also ties in with research priorities in the Chemistry top economic sector, the Advanced Instrumentation roadmap in the High Tech Systems and Materials top economic sector, and the COAST Analytical Science and Technology roadmap. There are many opportunities for cooperation with medical technology firms and for medical technology spin-offs. Within the context of health care, minimally invasive techniques are beneficial because recovery is likely to be faster.

Submitted questions illustrating depth and connective power

- **How can we heal the body without opening it up?**
- **How deep under the skin's surface can we see with light?**
- **How can we incorporate the most advanced microscopy techniques into miniature tools for minimally invasive diagnosis and treatment?**

How can big data and technological innovation (e-health) contribute to health care?

Explanation

The use of large quantities of data is rapidly becoming common practice in the medical sector. This is partly owing to the digitisation of medical data, but also because of rapid advances in smartphone, sensor, and medical device technology for tracking an individual's health, behaviour, and environmental factors. Thanks to these advances, it is growing easier to adapt health recommendations, drugs, and care to individual needs, which we refer to as personalised medicine and e-health. The health care sector will increasingly be data-driven, especially as the cost of collecting, storing, and processing data falls and GPs, hospitals, home care organisations, community caregivers, and patients can easily share information with one another. The big data revolution also makes it possible to shorten the time spent on medical research by combining information from all relevant databases. One important challenge is to ensure that such data is FAIR (Findable, Accessible, Interoperable and Reusable) in health care and research. That involves making appropriate arrangements about such matters as standardisation, user ease, sustainable storage, ownership rights, and privacy throughout the health care sector. These trends will require the development of new concepts, methods, and software that allow for the appropriate analysis and interpretation of vast quantities of health-related data and expertise, and their adaptation into personal health recommendations.

Connective power

Besides continuing to support basic and applied ICT research, it is important to improve the Dutch infrastructure and for caregivers to actually implement relevant, cost-effective e-health applications in clinical settings and the everyday home environment. This not only means setting up practical, up-to-date training/retraining programmes but also getting ICT and medical specialists to work together closely. In addition, explicit attention must be given to the privacy and accountability concerns associated with the widespread availability of medical and, therefore, highly personal data. Close cooperation between data-generating (medical devices, sensors, robots) and data-processing systems will also lead to a more efficient use of resources. The Netherlands is a leader in terms of available ICT infrastructure, FAIR data, and the development of digital image-processing equipment, and there are opportunities for it to continue building its position within Europe and internationally.

Submitted questions illustrating depth and connective power

- **Does our modern, communication-driven society require a new kind of physician/specialist?**
- **How will we go about guaranteeing privacy in the health care sector, especially in view of the rise of big data?**
- **To what extent can social robotics make robots more effective and accepted in care settings?**

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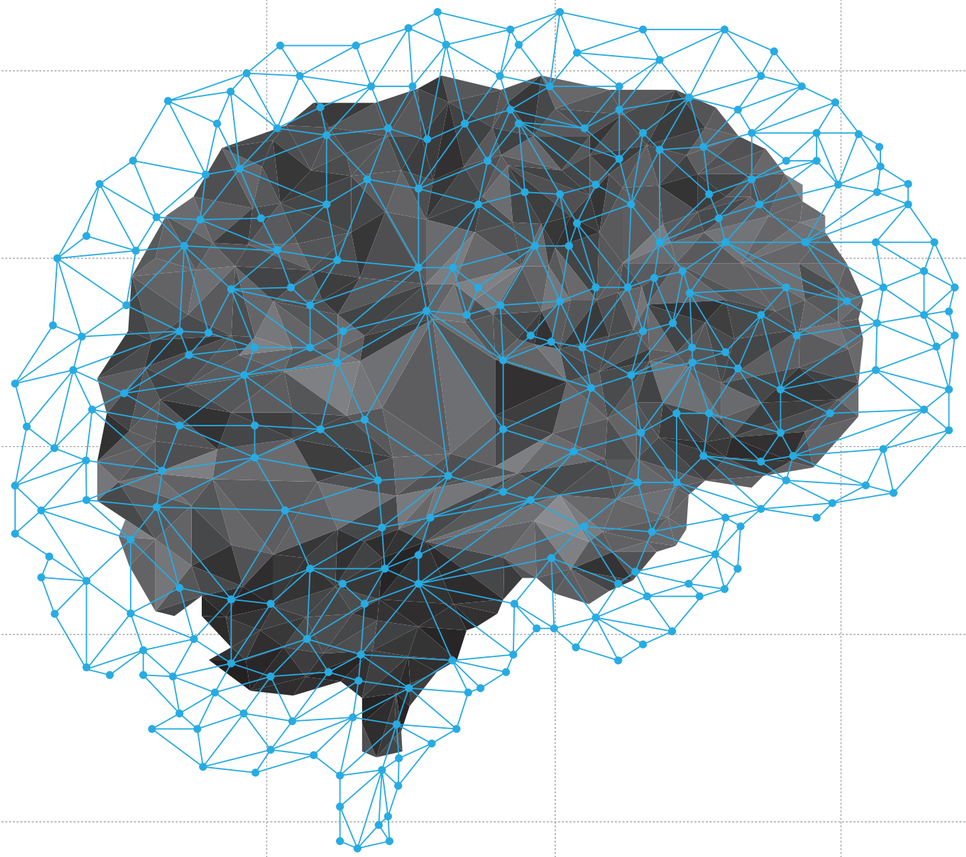
Technology and society



What transformation will we see in the manufacturing, service, and maintenance industries, and which technological innovations will make this possible?

Explanation

Sensor networks, the Internet of Things, and advanced modelling will lead to enormous efficiency gains in the long-term management and maintenance of our extremely costly infrastructure. New advances in technology (including sensors, smart materials, and 3D printing) and sustainable materials use can help keep Dutch manufacturing financially healthy and competitive. This will require not only new design tools but also new business models and organisational chains tailored to the technology.

Connective power

Combining emerging technologies – the Internet of Things, microsensors, autonomous sensor networks, robotics, big data, and so on – makes entirely new products and services possible. One requirement, however, is that we simultaneously develop the necessary ICT to share information along the chain and adapt production, distribution, and service processes accordingly. These are the technologies that will make industry smarter and more competitive, and ensure that employment levels in industry hold steady. Industry itself considers this a 'fourth industrial revolution'. 3D printing may represent a paradigm shift for manufacturing, with production shifting from enormous factories to 'container companies' and corner 3D copy shops. Things are changing rapidly and at multiple orders of scale all at the same time, from the design of new materials to food, biomedical materials, and entire houses. Numerical tools for creating ready-to-print designs have yet to become available, especially for more complex materials. Progress in this area depends on basic research that combines numerical modelling with materials research and materials characterisation. The Netherlands has a robust knowledge infrastructure firmly rooted in the industrial setting. This question complements various top economic sectors – specifically High Tech Systems and Materials, Chemistry, Life Sciences and Health, Creative Industry, and Logistics – and the policy domains 'Deploying new technologies', 'A strong and Innovative Green Knowledge Economy', and 'New technologies for defence purposes'.

Submitted questions illustrating depth and connective power

- **Will we all have 3D printers at home someday, and what will that mean for the economy?**
- **How can we develop a new generation of adaptive, self-learning, interlinked robotic systems (known as 'Future Production Systems') for the manufacturing industry, with robots taking over physically demanding, unhealthy, or monotonous work?**
- **How can advances in technology (sensors, smart materials, sustainable materials use) support long-term management and maintenance?**

How can we anticipate the impact of new technologies on humans and society, and understand and evaluate the influence of existing technologies?

Submitted questions illustrating depth and connective power

- **How can we align technological innovations more closely to key societal and moral values?**
- **How can we create robots that assist care staff and heal patients (rather than replace care staff and frighten patients)?**
- **Can we use serious gaming and gamification to teach 21st century skills?**

Explanation

Technology is advancing at an increasingly rapid pace and impacting human existence more and more. That sometimes puts pressure on core societal and ethical values, for example our responsibility for the environment, respect for privacy and security, autonomy, attention and concentration, and the quality of social relationships. New technologies raise questions about privacy, quality of life, the possibility of superintelligent robots making human beings redundant, and the issue of who is responsible if a self-driving automobile takes the wrong decision. This question focuses on three aspects. The first is how we can anticipate the societal impact of future technologies. This aspect concerns both the features of specific technologies and the process of technological development, and the use of technology. The second aspect is to understand how existing technology impacts society. The third and final aspect is to learn to evaluate that impact. Anticipating and describing the impact of technology on humans and society can provide input for the normative and ethical evaluation of technology.

Connective power

This question links historians, philosophers, sociologists, and legal scholars with technology researchers, designers, and engineers. Describing and evaluating the impact of technology on society can provide input for policymaking, business operations in technology firms, and the methods used by technology researchers or engineers. Methodology issues, for example how best to analyse the impact of technology, will inform evaluative questions about the wished-for impact. Serious gaming is an example of an interesting method for simulating projected changes in technology and their impact on society. Many questions are normative in nature and require a study of ethics. Medical or health care technology, for example, often raises questions about responsibility. Once the norm has been established, the question is how to design technologies that achieve the wished-for impact. The answers to these questions then provide input for designing legislation or policy ensuring broad adherence to those norms. In terms of applied research, the answers can be used almost immediately to guide innovation processes. Finding these answers means first exploring a host of basic research questions concerning the relationship between humans and technology.

What social changes are imminent owing to advancing technology and how will they affect prosperity?

Explanation

Technology is a potential source of prosperity. However, its positive effects, e.g. greater productivity and affluence, often only manifest themselves in the longer term. People often worry about the consequences of rapid and far-reaching technological change because it alters the relationship between humans and machines without the outcome being known. Jobs are disappearing, new jobs are being created, and markets are being shaken to their core, giving rise to new relationships. In many cases, these changes affect the daily lives of ordinary people. What does that mean for society, and how will things turn out in five, or ten, or twenty-five years' time? Who will gain from new opportunities, and who will lose out and perhaps have to hunt for another job? How much is our privacy worth to us?

Connective power

The questions we received on this subject cover many different domains. They included questions about jurisprudence, food supply, health care, learning and development, social systems, big data, trust in institutions, the smart city, gaming, child development, liability, democracy, labour market trends, and industry. They ranged from basic ('What impact do societal and technological changes have on child development?') to applied research ('How can we use the digital data that we generate to improve our health?). Technology now affects every aspect of people's lives and the societies and economies in which they live. Current changes offer numerous exceptional opportunities in many different domains.

Submitted questions illustrating depth and connective power

- **How do we generate synergy between the physical and digital world to make life safer, healthier, 'wealthier', and better worldwide?**
- **Can technology make us more humane?**
- **How can big data contribute to sustainability?**

How are new technologies and big data impacting the effectiveness of public administration and the constitutional state?

Explanation

The rise of ICT and, more recently, the growing interest in the potential of big data have already had far-reaching consequences for the apparatus of public administration. Public services have been digitised, databases are now linked, and pattern recognition software is helping to detect fraud. Big data also has huge potential when it comes to public acceptance of legislation and jurisprudence and innovations in these areas. We still know very little about the way in which technology impacts the effectiveness of public administration and constitutional democracy or the trust the public places in them. Policymakers assume that it has a positive impact, but their optimism is not always justified. We must study how public administration and constitutional democracy can deal even-handedly with and offer a transparent legal framework for advances in digitisation, big data, genetics, biotechnology, nanotechnology, and the cognitive sciences. Finally, law enforcement can also benefit enormously from new technologies.

Connective power

This question consists of three related issues concerning public administration and constitutional democracy in today's society. In the first place, new issues and new solutions lead to new, undesirable human and organisational activity that must be combatted by new legislation. Second, existing administrative procedures and legislation are often an obstacle to innovation. Third and last, modern advances, for example in ICT, are extremely useful when attempting to improve the effectiveness of public administration, legislation, and enforcement. Research associated with this question focuses on the function, structure, and impact of administrative processes, legislation, and enforcement on society. These issues apply in a variety of areas: environmental protection, security, innovation, energy, climate change, mobility, technology, entrepreneurship, organisational forms, development cooperation, and so on. Constructing effective legal frameworks for all these societal issues will give entrepreneurs, consultants, and, for example, NGOs tremendous opportunities to apply the same solutions towards other societal challenges and in other countries.

Submitted questions illustrating depth and connective power

- **How can we use big data to evaluate the effectiveness of government policy, in particular legal and other interventions/sanctions?**
- **What role does national legislation play in our rapidly developing and changing context?**
- **How will we deal with crimes committed by machines (or human-machine interfaces) rather than people?**

How do the old and new media influence individuals and society?

Explanation

The media are the gatekeepers between individuals and society. That was true of the traditional media – the print media, radio, and television – and it is even truer of the new online media. They have an important artistic dimension in that design, images, and music now play a major role in how messages are packaged and received. Taken as whole, the media in fact fashion the way in which we experience the world. On the one hand, this question focuses on the influence of traditional and new media on child development and the opportunities and threats that they represent for young people. On the other hand, it also summarises many questions about the rise of social media and other new technologies and how they can improve the problem-solving ability of individuals and society. A third set of questions asks how we can make media communication more effective.

Connective power

ICT innovations provide the basis for new, mobile means of communication and for social networks that connect people regardless of time and place. Today's generation is all about 'bonding', i.e. assembling a group of like-minded individuals consisting of 'friends', 'followers', and 'likes'. The flood of information available online is also feeding a strong inclination towards selective exposure, with people limiting what they see, hear, and discuss to communications that confirm their existing attitudes and preferences. At the same time, questions on both the micro and macro level – for example about health, the environment, democracy, or innovation – have become more complex than ever. Solving such complex problems requires not only bonding but 'bridging', i.e. bringing together groups who have differing interests and levels of expertise and who hold differing opinions. How can the bonding and bridging processes created by new technology generate information capital alongside financial and social capital? And how do these new technologies relate to the arts and the way they encourage us to reflect on society? After all, artistic interventions in the form of images or narratives can contribute to processes of social inclusion, social exclusion, or technological change, or they can play a role in social cohesion or serve as a guiding factor in society in some other sense. To understand how that process unfolds, we need to know more about how web services allow people to share information and influence communication in turn.

Submitted questions illustrating depth and connective power

- **How do social media and other new communication formats affect the quality of the moral and political discourse and of societal decision-making?**
- **How 'social' are social media? Children appear to be glued to social apps. Do they actually make them more social? How meaningful are their relationships with online 'friends'? Are they exposing their whole lives – and the lives of their friends and family members – to public scrutiny? What should parents, teachers, and lawmakers do?**
- **How can we show how creativity and the arts contribute to solving societal problems?**

Will digitisation save our cultural heritage?

Explanation

Until recently, the public had very little access to museum depositories and archives. Only the connoisseurs really knew what they contained. Digitisation has helped make many archives and collections more searchable and put them online, but in turn that has led to a flood of difficult-to-navigate data. The field of digital humanities faces the enormous challenge of linking multiple complex sources, in that way adding value to our historical and cultural heritage. The data is often fragmented and complex, and the context that would render it meaningful is unknown in many cases. Digital techniques make it possible to combine fragmented data, track down missing pieces of the puzzle, and paint a clearer picture of the general context.

Connective power

This question connects art history, musicology, media studies, and other disciplines in the humanities with computer science. It is explanatory in nature to the extent that it addresses coherence in cultural heritage. New data can help us search systematically for answers to questions about cultures and their tangible legacy. It can also help us understand the relationship between tangible and intangible heritage. Design-based aspects also play a role in connection with source accessibility. For researchers, meaningful interpretation of heritage depends on efficient data and text mining techniques and methods. Visibility is also important, however; research findings must be used to develop innovations that reach a broader public but also meet the needs of heritage sector professionals. Finally, heritage digitisation offers numerous new opportunities for shaping cultural policy.

Submitted questions illustrating depth and connective power

- **How can we ensure that museums and their collections – the custodians of our national heritage – remain relevant in the future?**
- **How can we guarantee that digital cultural heritage and other sources of digital data will be preserved and remain accessible in the future?**
- **How do we improve the availability of and simplify access to our cultural heritage?**

Can we use big data and big data collection to define values, generate insights, and get answers?

Explanation

Gigantic datasets, known as big data, are becoming increasingly important in a growing number of fields, from climate science, health care, and finance to astronomy, particle physics, and energy systems. Big data is challenging in many different ways. How do we collect it, how do we store it, how do we make it accessible, how do we get all the information we need from it, how do we protect it, and what changes is it bringing about? It is not as if we could read the databases themselves. We have to visualise and 'translate' it into objects, stories, games, or graphs that we understand and can use. The rise of big data is forcing us to reorganise our knowledge and to retell stories in a new way. This question focuses on the problems inherent to working with big data, on general big data applications, and on the impact of big data on society and the economy. Privacy and freedom of information are important factors in this context.

Connective power

Research on big data links all sorts of questions. The key to creating applications lies in algorithms, mathematical equations that make it possible to search data rapidly and to order, process, and use it, in many cases online and in real time. Efficiency, quality, validity, and reliability are crucial aspects. Mathematics and IT go hand in hand in tackling the big questions about algorithms, for example concerning distributed/streaming technologies. Data analysis and visualisation are the priorities for present and future ICT research. Tags include business intelligence, data mining, machine learning, artificial intelligence, visualisation, visual analytics, and the integration of data science and geo-information. This question also involves research addressing issues of privacy, transparency, and freedom of information, as well as whether big data will change our general understanding of the world. The Netherlands has a broad users community in various domains that generate vast quantities of data. It also has an e-infrastructure that makes big data research possible. Given the importance of big data for virtually every sector of the Dutch economy, there are many contexts in which businesses – including SMEs – can collaborate with knowledge-based institutions on innovations.

Submitted questions illustrating depth and connective power

- **Is it useful to mine big data if no hypothesis has been put forward concerning the relationship between the individual pieces of data?**
- **How is the rise of new technologies (including social media) influencing the social structure and dynamism of society and the problem-solving ability of individuals and society?**
- **How can we use big data to improve the physical condition of the Dutch population?**

Can we develop human language technology (HLT) that allows us to communicate with our computers (smartphones, tablets)?

Explanation

It's hard to imagine going through even a single day without computers. Technology is inevitably becoming our constant companion in almost every aspect of our lives. That is why we are always searching for ways to integrate computers as seamlessly as possible into our activities. Human language technology (HLT) and speech technology play a major role in that search because advanced techniques will make it easier to communicate with computer systems in natural language. Once computers also learn to speak our language, we can make huge strides in refining and seamlessly integrating and using automated systems in everyday life, aided by better HLT and better speech recognition of different language variants. Along with language and visual communication, computers could also learn to process our other senses, i.e. touch, smell, and taste.

Connective power

This subject requires interdisciplinary research on human-machine interaction, with input from psychology, artificial intelligence, and HLT and speech technology. Basic research in this area faces many questions related to HLT and speech recognition, synthesis, and modification, for example how to surmount the problems caused by online multilingualism. We need to develop intelligent search engines for international information-sharing, cooperation, and trade contacts. They should make it possible to forecast trends in markets or in society based on research involving big data. The use of HLT in businesses and organisations can also streamline knowledge and information flows. Speech recognition can be used to make intelligent access control possible in the aviation sector. Another public interest would be served by using HLT and speech technology in e-health applications that help treat and support people with a communication disorder or autism.

Submitted questions illustrating depth and connective power

- **How can we teach robots that will become part of our society to communicate with us?**
- **How does information work, and what consequences does digitisation have for the way people obtain information, learn, entertain themselves, and are swayed to think or do something?**
- **How does the brain process language, and how can we use this knowledge to improve the way computers process language?**

How can we connect ‘things’ (hardware) all the time and everywhere and boost processing speed while using less energy?

Explanation

Our society is increasingly turning into a digital communication network. That requires hardware innovations, for example in fibre-optics and wireless communication, allowing our devices and systems (such as sensors) to communicate with each other with greater speed, intensity, interactivity, reliability, and flexibility. Various names have been coined to describe this phenomenon, such as ‘The Network Society’ and ‘The Internet of Things’. Other hardware innovations are needed for faster, more energy-efficient computing. Although the emphasis is on innovating hardware, the huge quantities of data being generated and shared also require advanced software capable of processing that data and converting it into information that is useful in real time. Another subject worth studying is what the increasing speed, density, and compatibility of data mean for society.

Connective power

Various disciplines can assist in answering this question. ICT, for example, plays an important part, although mainly in cooperation with other disciplines. Basic quantum physics research naturally plays an important role in the field of quantum computing, but also the basic humanities question of the relationship between humans and technology. Applied research is concentrated in mechanical engineering and other design-based disciplines and considers how to actually give shape to the Internet of Things. The Netherlands has a robust ecosystem of industrial and research groups active in this domain and ranked among the best in the world. The same can be said of the Dutch telecom infrastructure and e-infrastructure. There is a growing market for networked products and services. The expectation is that many new SMEs and other forms of business activity would emerge if the Netherlands were to take the lead in this field. A robust infrastructure also attracts foreign businesses and investors.

Submitted questions illustrating depth and connective power

- **Can miniaturisation and the integration of electronic devices help us develop new functions for detection and information processing and for low-energy data storage and processing?**
- **Could we design a new or different model of the internet without all the disadvantages of the existing one?**
- **It looks as if conventional computers and networks are gradually reaching the end of their development cycle. Radical new systems are emerging. How do we make the transition?**

How can we build and maintain future-proof software?

Explanation

The rapid advances in technology mean that software quickly becomes obsolete. At the moment, this is mainly a problem in sectors that computerised early on, for example the banking industry. Obsolete software affects the sustainability and reliability of our digital infrastructure. It also makes that infrastructure vulnerable to malicious external attacks. It can further be very complicated and expensive to maintain obsolete systems. Last but not least, the state of technology influences the way in which new software is developed. As ICT projects have grown more complex, software has become less reliable. It is also becoming more difficult to predict how certain software projects will ultimately turn out. At the same time, software will play an increasingly important role in our society, with a growing number of everyday systems running on software that allows them to function autonomously.

Connective power

Software obsolescence and the efforts required to maintain obsolete systems are, first of all, important societal challenges. They can be addressed by research that focuses on mapping digital infrastructures, redesigning generic, non-system-specific data structures and information models, and drawing up agreements about optimising the performance of complex distributed software systems. Such research should lead to a future-proof virtual infrastructure. There are challenges for researchers in creating new software development systems, in developing self-repairing software, in studying the adaptivity and configurability of systems, and in discovering and using new methods for detecting software vulnerabilities and bugs. Economic opportunities lie in designing and building innovative methods and techniques and in controlling the cost of software development and systems maintenance. There has been much bad press recently about the spiralling cost and lead time of various software projects, both in the public and private sectors. This is ultimately bad for our economy because the money budgeted for such projects could have been spent more effectively elsewhere, and the organisations involved lose productivity during the transition period.

Submitted questions illustrating depth and connective power

- **How do we ensure that today’s and yesterday’s software continues to work in the future?**
- **Can software repair and upgrade itself?**
- **What should a future-proof virtual infrastructure look like?**

Can we extend Moore's Law in the post-silicon era?

Explanation

Today's silicon-based semiconductor technology is the foundation of all modern electronics, including PCs, laptops, tablets, telephones, and sensors. But that technology is reaching its physical limits, and we are approaching the end of the steady progress described by Moore's Law. To improve the speed and efficiency of computing power in the future, we will need to explore entirely new materials and concepts, for example based on electron spin, brain architecture, or the manipulation of light.

Connective power

Basic research questions mainly concern new material concepts and properties, for example discovering, understanding, and creating new molecular, organic materials and ultrathin, two-dimensional materials such as graphene with the right optical and electronic properties. The Netherlands is at the forefront of international research in the relevant fields of basic physics and chemistry. Applied research is needed to create these materials in a form that permits industrial production. We also need to integrate new functionalities – in the sense of new optical, magnetic, chemical, and electronic properties – with existing semiconductor technology at nanoscale. As was the case with micro-electronics, these new materials and techniques will make it possible to design and develop all sorts of new devices (such as bionic implants). Applied research is needed to develop techniques that allow us to study the form and the chemical, electronic, or optical properties of such ultrasmall structures at atomic scale. Nanoscale production will also require specialised expertise. This will lead not only to new products that address societal problems, but also to a new generation of products (instruments and machinery) for existing and new industrial businesses. A number of successful public-private partnerships have been set up in this area in the past decade. This network provides a solid starting point for further innovation and for also involving SMEs.

Submitted questions illustrating depth and connective power

- **Can photonic integrated circuit technology play the same role in photonics as electronic integrated circuit technology in electronics?**
- **How do we take 'nano' from lab to app?**
- **Can a computer develop a computer?**

What will quantum computing and the quantum internet mean for our future?

Explanation

Both scientists and the general public have long been fascinated by quantum computers, but is it even possible to build one? And if so, what impact would quantum computing have on our everyday lives? Recent breakthroughs, including in the Netherlands, have revealed which crucial steps are necessary to build a real quantum computer. The next five years should show whether we can take those steps, and how. The basic principles of quantum computing differ from those of conventional computing. Quantum computers do their calculations with quantum bits or qubits, which can store both zero and one and can be entangled even over long distances. Thanks to its unusual quantum properties, a quantum computer can solve hugely complex computing problems in mathematics, physics, chemistry, and materials science. But what will that mean for everyday life? Will quantum computing boost innovation dramatically? Will quantum computing erode online security, or will it make the internet safer? In 2014, the Dutch Government designated quantum technology as one of the Netherlands' four National Icons.

Connective power

The quest to control large-scale quantum behaviour is an exciting scientific and technological challenge. Basic research is needed to understand qubits, for example in order to come up with effective protection against decoherence, i.e. the loss of entanglement due to external influences. What is the ideal building block for the qubit: a photon, an electron, or the Majorana particle? How can entangled qubits be separated and used to communicate faster than the speed of light across a quantum internet? New materials, chip structures, software, and mathematical algorithms are needed to answer these questions. The race to crack the problem of quantum computing raises a wide range of questions. We must also consider in advance the societal and economic opportunities that this technology will create. New fields of research, for example bio-quantum computing, could emerge and dramatically accelerate drug discovery and development, among other things.

Ingediende vragen die rijkdom en verbindend karakter illustreren

- **Can we build a quantum internet that rules out 'eavesdropping'?**
- **How can we program a quantum computer?**
- **Can quantum computers design materials with specific functionalities?**

How can we develop the stable and selective catalysts that we need to make the transition to sustainable energy and production systems and a bio-based economy?

Explanation

Catalysts make processes cleaner and more efficient. Catalysis has solved the problem of acid rain and contributed to our prosperity by making fertilisers, polymers, clean petrol, and many other products possible. Catalysis can help us convert CO_2 into practical materials, transform biomass into chemicals and fuel, and create new materials that increase prosperity and spare the environment. It can also help us convert waste into useful feedstock and semi-manufactures. Catalytic processes are behind about 90% of all chemical products. In the transition to a sustainable society, one of the priorities is to develop efficient methods for energy generation, transport, and storage. It will only be possible to switch to biomass as feedstock in the chemicals industry if we develop new organic, homogeneous, or heterogeneous catalytic processes. Catalytic reactions are femtosecond surface reactions that take place on the atomic scale (a femtosecond is a billionth of a second), but they also play a role in large-scale reactors and processing installations. We currently create industrial catalysts by a process of trial and error and know very little about why a certain catalyst is suitable for a specific chemical process.

Connective power

Physical-chemical research is vital to our understanding the nature of catalysis. That knowledge could play a major role in industry, for example in the energy sector, manufacturing, and waste processing. Applying the same knowledge to create products and processes also supports sustainable development. Catalysis and the bio-based economy are frequently cited topics of interest in the Chemistry top economic sector. This question links scientific, economic, and societal challenges.

Submitted questions illustrating depth and connective power

- **How can we activate carbon dioxide, oxygen, water, methane, nitrogen and other small molecules?**
- **How can we develop new catalysts for N_2 activation?**
- **Can we develop new chemicals that allow us to produce electricity in advanced fuel cells based on inexpensive and sustainable catalytic electrodes?**

How can we remove fine particles, harmful gases, and pathogens from the air and keep it clean?

Explanation

Clean air is of huge importance to human health. We can control air pollution levels to a considerable extent by utilising technologies that limit harmful emissions and by optimising combustion processes. In addition to emissions standards, technical adaptations (such as better filters for flue gases) and new materials (for tyres, asphalt and so on), we also need better testing methods. However, the biggest gains will come by improving the efficiency of combustion processes. Combustion methods have improved vastly over the past 15 years and further refinements are likely to improve emissions even more. It's only a matter of time until flue gases contain fewer particles than the atmosphere that surrounds us. Once that happens, our engines will no longer pollute the air, but clean it.

Connective power

On the one hand, this question concerns the development of efficient combustion processes and efficient methods of reducing particle and other harmful and pathogenic emissions. On the other, it addresses the development of inexpensive and sensitive tests for tracking harmful particles, gases, and pathogens. We derive 80 to 90% of our current energy supply from combustion processes. Owing to the sharp rise in the demand for energy, that percentage is unlikely to fall in the decades ahead, even if we make more use of solar power and other renewable sources of energy. Fine particles produced by combustion processes cause a serious deterioration in air quality, especially in densely populated areas. Although there are prospects for developing combustion processes without emissions, it remains important to test for the presence and severity of pollution. We now use a combination of modelling and testing to measure air pollution levels. We need more real time data, for example to alert asthma patients to hourly air quality levels in their direct environment. There are opportunities here for 'citizen science', with members of the public using relatively simple techniques to test the air quality in their immediate surroundings.

Submitted questions illustrating depth and connective power

- **How can we improve combustion processes to the point where emissions are cleaner than the air we breathe?**
- **Can we develop an inexpensive sensor that runs on an independent power supply and measures ultrafine particulate matter and NO_2 levels?**
- **How can we prevent the airborne transmission of infectious diseases?**

Can we design smart materials and structures that have new and advanced properties?

Explanation

The design of new materials can have an enormous impact on our lives and our living environment. Responsive, adaptive, self-repairing, smart, energy-saving, and reusable materials hold out unique promise. There is also a need for materials that can withstand extreme conditions, for example during space travel or deep sea mining. It will take an entirely new design philosophy to discover such materials. Our growing understanding of nanostructures, nanofabrication, and nanocharacterisation tools has made nanoengineering possible. The focus in materials science has simultaneously shifted to functional materials. The challenge is to combine materials research at different orders of scale with the search for active functions. By combining advanced computer simulations and modern experimental techniques, we may be able to design materials on the drawing board rather than discover them by trial and error.

Connective power

Smart materials will play a growing role in integrating technologies into all sorts of sectors, from medicine to IT. The materials of the future will be the result of collaboration between scientists who specialise in polymers, composite materials, semiconductors, biomaterials, soft materials, and numerous other areas of expertise. Dutch materials research has an outstanding international reputation, whether in academic, applied, or public-private alliances. It can be of enormous benefit to society and the economy, as the many different practical applications make clear. We received questions about smart windows that react to light, self-repairing building materials, synthetic cells, bio-electronics compatible with the human body, materials for generating, storing, and converting energy, materials that protect against accident and attack, materials for self-assembling nanomachines, materials for new medicinal drugs, foldable surfaces that are luminescent or responsive, and materials that react to climatological stimuli. New materials are the key to addressing societal challenges in such areas as energy, mobility, the built environment, communication, health, security, and sustainability, and they will lead to totally unforeseen products in forthcoming markets.

Submitted questions illustrating depth and connective power

- How can smart materials integrated into systems and products (e.g. transport vehicles, buildings, and clothing) harvest energy, for example from heat or vibrations?
- Can we develop new nanomaterials and synthesising techniques to generate and store solar energy efficiently and cheaply?
- Can we mimic Mother Nature to create new bio-inspired materials?

Can we design electronic or bio-electronic systems that communicate directly with our bodies as well as materials and technology that restore or support human body functions?

Explanation

New technology that can communicate directly with the human body could lead to entirely new ways of promoting health and combatting disease. Implantable and wearable devices, for example, can be used to restore physical and cognitive functions or to track down and treat diseases. We can also formulate questions concerning bio-electronics and added-value materials or systems, including technologies that can serve as extensions to the human body, systems that translate human and animal biological functions into hardware and software for specific purposes (for example scent or freshness indicators), or inventions leading to guidance tools for social networks. Human-centred design of materials and systems is naturally a must when optimising the relevant functions. To refine this technology, we need to thoroughly understand the interaction between bio-electronic and nanotechnological components and human cells, tissues and organs. There are also overlaps with the field of human-computer interaction, which is in turn part of the investigation of artificial intelligence and data science. There is also a philosophical component to the proposed subjects and approaches.

Connective power

The Dutch nanotechnology network is robust and rooted both in academia and industry. This network is pre-eminently suited to tackling the relevant interdisciplinary and biotechnology challenges. It is an ecosystem that joins basic and more applied research, ultimately leading to technical applications. Medical research points the way for technology development. Research in biology, sensorimotor physiology, and sociology will also drive the development of tools that extend the functions of the human body and stimulate interactions, for example non-invasive monitoring or self-monitoring devices. There is also the potential for knowledge-intensive spin-off in the medical sector. Research findings provide a firm basis for many start-up activities. The products to which these activities give rise are of direct interest to society.

Submitted questions illustrating depth and connective power

- What is the best way to connect an organic human nerve cell to an electronic device?
- What sort of bionic implants will be possible if we can create soft, elastic electronics resembling biological tissue and allowing seamless integration into the human body?
- What is the ideal number of keys for a computer keyboard?

Can we build a synthetic cell?

Explanation

Living cells have complex, dynamic reaction networks consisting of proteins and nucleic acids. They consume a continuous supply of energy and substances and the reactions take place far beyond equilibrium. We have mapped almost the complete cellular composition of the *Escherichia coli (E. coli)* bacterium, for example. What we lack, however, is a blueprint for building a cell from individual biomolecules. The combined expertise of biologists, chemists, IT experts, and physicists will take us one step closer to building a cell.

Connective power

It is an enormous challenge for basic research to design and build new systems that resemble cells from the bottom up, but there are also unprecedented practical applications, for example in medicine or regenerative medicine and in the production of drugs and raw materials. The ultimate aim is to build a synthetic cell that grows and in which all sorts of processes evolve. The Netherlands plays a leading role in this field, with numerous top scientists and businesses studying complex dynamic systems. The Netherlands has a good chance of becoming a worldwide hub for such research with all the associated high-tech activity that entails. The theme ties in with various top economic sectors, including Life Sciences and Health and Chemistry. Numerous businesses in all the relevant areas are already actively involved in research and in public-private partnerships with knowledge-based institutions. This question is linked to the way living cells function, what cells can teach us about life processes, and how we can repair, replace, or redesign biological systems. It further touches on how technology changes human existence and on the associated ethical questions.

Submitted questions illustrating depth and connective power

- **How far can we push the boundaries of self-assembly?**
- **If we can build synthetic cells out of individual components, have we created life?**
- **Can we assemble a living cell ourselves?**

How can we manage the unpredictability of complex networks and chaotic systems?

Explanation

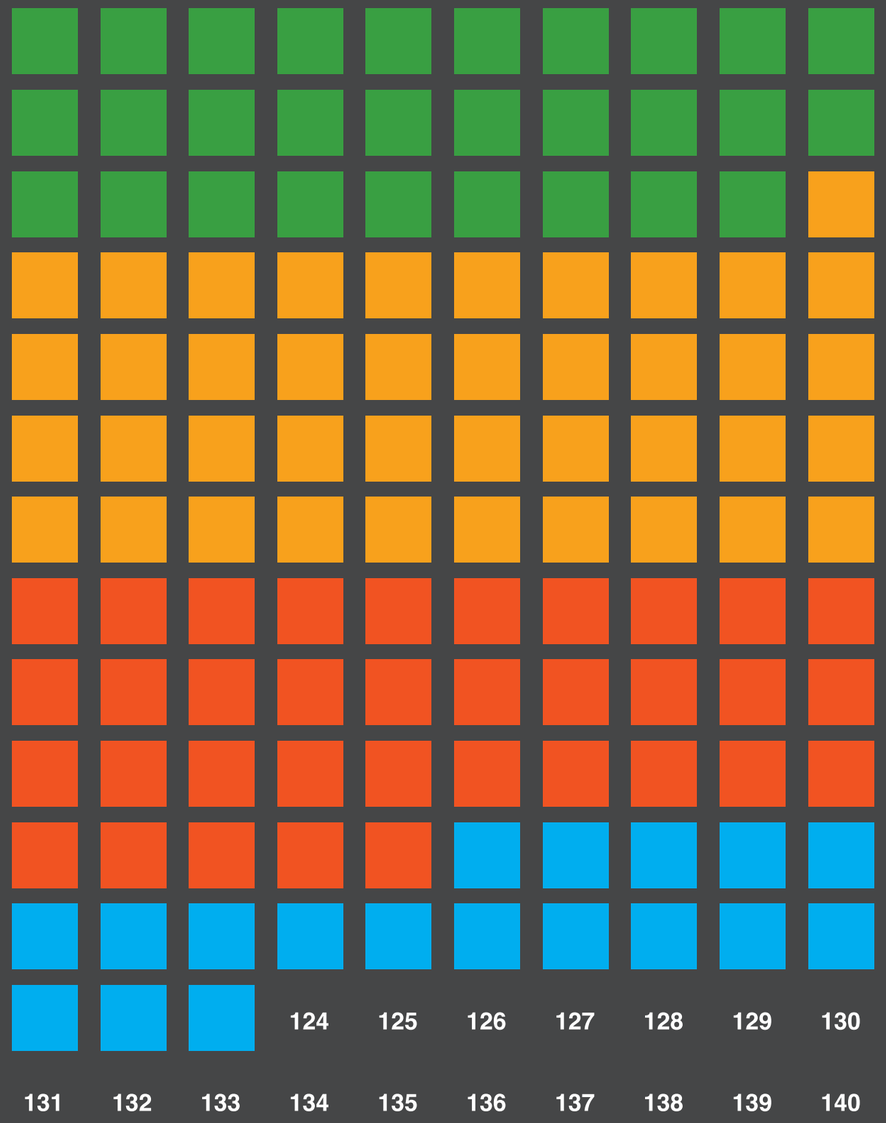
Networks play a vital role in our society. People all around the world depend on large-scale networks for communication, information, traffic, transport, finance, and energy. These networks also contain a great deal of information. It is an enormous challenge to understand, model, control, and optimise a network, especially when we do not know its architecture. Complex networks also play a major role in nature. Examples include the climate, the brain, the cell, and other chaotic, dynamic systems. These networks raise urgent questions about complexity, sustainability, biodiversity, self-organising ability, emergence, and uncertainty.

Connective power

Basic research on the structure, behaviour, and universality of complex systems benefits from mathematics in close interaction with other disciplines. There are challenges in numerous areas, from developing statistical methods for the empirical evaluation of network models and defining reliability margins for conclusions derived from complex datasets to graph theory, algorithm analysis, and matrix operations. New mathematical models are also needed to answer practical questions concerning the structural reducibility of a network based on limited observations, the future of chaotic systems such as the earth in terms of sustainability, human influence, climate change, or biodiversity, and the identification of transition points towards new coherent or emergent behaviour. For example, can we develop neural networks that spontaneously display new behaviour – in other words, computers that possess consciousness? The question of why both natural and non-natural complex systems appear to become more complex as a matter of course is philosophical in nature. Applied research turns models into algorithms for understanding and controlling complex networks. Questions we received mentioned the following: evidence-based choices concerning our future energy supply; avoiding peak loading in traffic, on the internet, and in the energy supply system; modelling regulation in biological networks such as the brain in order to predict Alzheimer's, Parkinson's, and other diseases; or predicting rare events that have an enormous impact on society, such as a financial crisis or flood.

Submitted questions illustrating depth and connective power

- **Can we detect universal organising principles in the behaviour of complex systems?**
- **Can we understand and use the behaviour of complex molecular systems to produce true-to-life, smart materials?**
- **Can we map out the impact of the banking industry's decisions mathematically, and estimate all the associated risks?**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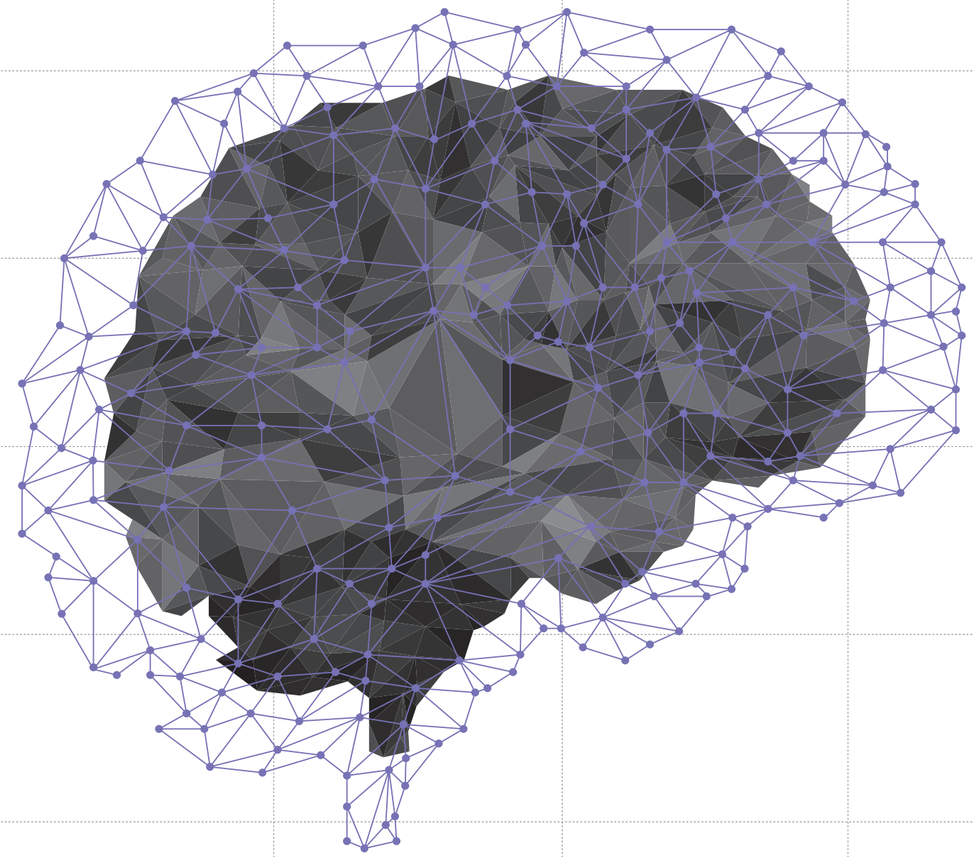
Fundamentals of existence



How can we bridge different scales when modelling dynamic systems, for example fluid and gas flows?

Explanation
Our environment consists of solid, fluid, and gaseous materials. We can simulate the behaviour of these materials at the very smallest scales using molecular dynamics, which studies the physical movement of individual molecules. At larger scales, we use continuum models to study a material as a continuous mass (rather than as discrete particles). However, many practical problems require us to use multiple scales at once. Single-scale problems can be resolved either with a continuum model or a particle model. Multi-scale systems require a combination of such methods. There are many areas of application that would benefit from a better understanding of flows. Examples include weather forecasting, industrial drying processes, the ability to predict high and low tide, micro-electronic cooling, aerodynamics in aviation, the dispersion of pollution in the atmosphere and water, and noise pollution.

Connective power
The challenges of the future require interdisciplinary and multidisciplinary research by academic and industrial scientists active in a variety of fields, such as physics, engineering, mathematics, and information science. Multi-scale modelling is very important in numerous practical areas of great relevance to society and industry. In the former, that includes the ability to predict natural disasters and their impact, a better understanding of interventions in ecosystems, and insight into large-scale weather systems and climate models. In the latter, it includes a better understanding of turbulence, free surfaces and flow separations, large pressure gradients, mixtures of solid, fluid, and gaseous materials, and interactions between fluids and particles, as well as the ability to combine different simulation methods. This question is important to the 'Water and climate' policy area.

Submitted questions illustrating depth and connective power

- **How can we link systems at differing length scales (from molecular to macroscopic and from living to dead matter) in order to develop smart materials and, for example, understand the workings of the brain and climate change?**
- **How can we make bio-related or bio-inspired structures and materials using the basic design principles of life at differing length scales?**
- **How can we understand multi-phase flows so that we have more control over them in industrial applications?**

What symmetries are hidden in prime numbers and how can number theory in mathematics inform theory-building in physics?

Explanation
Symmetry is everywhere in nature, and constitutes the point where mathematics and physics converge. Oddly enough, symmetry also plays a major role in the world of numbers. In the 1970s, mathematician Robert Langlands produced a coherent set of conjectures suggesting that the behaviour of prime numbers is defined largely by hidden symmetries. His conjectures are now known as the Langlands programme. Langlands' ideas are revolutionary and visionary, and suggest that there is a very deep connection between geometry and number theory. This has already led to astonishing discoveries in the latter, the best-known being mathematician Andrew Wiles' proof of 'Fermat's Last Theorem'. A geometric reformulation of the Langlands programme was recently described that builds new bridges between mathematics and physics. The Langlands programme is so challenging and broad in scope that many mathematicians worldwide are working on it. The Netherlands has a unique cluster of experts in the Langlands programme, so it is excellently positioned to make a valuable contribution to this important international research effort.

Connective power
In the first instance, this is a pure research question that builds bridges between mathematics and physics. Prime numbers play an important role in cryptography, for example in the encryption of online banking data.

Submitted questions illustrating depth and connective power

- **Are the Langlands conjectures true, and what do they mean for physics?**
- **Will there ever be a short proof of Fermat's Last Theorem?**
- **Are there limits to symmetry?**

What role does quantum physics play in macroscopic systems and what spectacular new phenomena and applications does it make possible?

Explanation

Quantum physics is important in macroscopic systems in a number of domains. For example, the quantum-mechanical, collective behaviour of electrons gives rise to exotic macroscopic phenomena, such as superconductivity (zero electrical resistance). There is also a growing number of interesting questions related to magnetism concerning quantum effects in macroscopic systems. A series of surprising new discoveries has challenged our theoretical understanding of the collective quantum effect, including certain model systems proposing high-temperature superconductivity. Can we develop materials that validate these model systems? Room-temperature superconductivity would make electricity transmission without losses possible. That would have an enormous impact on the global energy supply.

Connective power

The quest to control quantum behaviour is a major scientific and technological challenge. To achieve this, advances are needed in new materials, switching structures, and IT. There is a relationship here with nanotechnology, optics, microscopic techniques, and plasmonics. The Dutch physics community is excellently positioned to play a leading role in this pioneering avenue of pure physics research. Not only is superconductivity a Dutch invention, but the entire field of quantum matter – as these new types of materials are called – plays a key role in NWO Gravitation programmes.

Submitted questions illustrating depth and connective power

- **What role does quantum coherent dynamics play in life's essential processes?**
- **How can we design and use quantum materials?**
- **How do the principles of quantum mechanics determine the properties of materials at nano, meso, and macro scale?**

What are the origins, history, and future of the universe?

Explanation

Among the oldest questions in human history are those concerning the true nature and origins of our universe. Almost everyone knows about the 'big bang', but it is an event that experts are far from understanding. Did that early condition of extreme heat really arise out of nothing? And what came before it? Or is that the wrong question to ask? And where is the universe going? We know that the universe is expanding at an increasing rate. Eventually, if that expansion continues to accelerate, we will no longer be able to see other galaxies – a very odd prospect. Research that can help us answer these questions focuses on understanding the history of the universe from its birth, and on observations and computer simulations of the very earliest stages of our cosmos. This information will serve as input for theories about the nature and origins of the universe. The knowledge that we acquire by means of observation and simulation can both inspire and referee the theories that we examine.

Connective power

Research on this question is related directly to theoretical physics and astronomy. Besides developing new theoretical concepts, we also need new instruments with which we can make more precise observations in increasingly broader segments of the electromagnetic spectrum. We must also be able to conduct the necessary large-scale simulations. The relevant technological advances will also lead to applications beyond the field of astronomy, and they therefore represent economic opportunities for the businesses involved. The development of the necessary instruments also requires research.

Submitted questions illustrating depth and connective power

- **What was there before there was the universe?**
- **How are the smallest and largest structures in the universe connected?**
- **Is the universe a computer, and if so, is there a programmer?**

Have we identified all the elementary particles of matter?

Explanation

The Standard Model describes all the elementary particles known to us. It resembles a Periodic Table of the Elements, but is much smaller. It is astonishing to think that such a small number of elementary particles can explain all known forms of matter. The maximum number of elementary particles is defined by certain symmetries that we impose on the model. However, we still do not know why the model works and what gives rise to this symmetry structure, and therefore to the small number of elementary particles. Like other grand phenomena in physics, such as the general theory of relativity and quantum mechanics, it is possible that the symmetry structure can also manifest itself at macroscopic scale and lead to revolutionary applications. Another possibility is that the model is incomplete, and that there are other, as yet undiscovered elementary particles.

Connective power

This question links very basic questions about the origins of the universe and the elementary particles of matter. Pioneering technology is needed to answer these questions. Breaking through the relevant technological barriers could give rise to numerous new spin-offs, with opportunities for businesses, and specifically for SMEs. Although applications from unexpected sources are difficult to predict, we received questions about using energy from the Higgs Field or muons for scanning high-mass objects. Another question was whether we could scan the entire earth with neutrinos. The Dutch research community is in the vanguard when it comes to the search for the elementary particles of matter. The coming decade will be a crucial time in this voyage of discovery.

Submitted questions illustrating depth and connective power

- **Do we understand how the fundamental laws of nature for elementary particles can lead to qualitative new macroscopic phenomena?**
- **Is there a limit to the divisibility of elementary particles?**
- **Why is there no antimatter in our universe?**

What is the true nature of gravity, space, and time and what can we learn from black holes?

Explanation

Einstein's theory of relativity links space and time and explains gravity as a distortion of spacetime. That makes gravity fundamentally different from the other forces of nature. But Einstein's theory has not been tested to the limit. That can only happen out in the universe, where black holes and neutron stars bend space so much that they produce exotic phenomena. Studying these objects therefore offers unique insight into the laws of nature that underpin our basic understanding of the essence of space and time. The challenge is to detect these phenomena with extremely sensitive instruments that allow us to observe gamma rays, x-rays, radio waves, and gravitational waves. This will become possible in the next few years. Theoretical work is also essential. Is gravity in fact holographic and emergent, as suggested by string theory, and what does that say about the true nature of space and time?

Connective power

Dutch researchers play a leading role in these areas worldwide. That is clear not only because the Netherlands has various relevant research programmes (at top research schools), but also because of its extensive involvement in international ground-based and space-based facilities with their unique instruments. Advanced instrument technologies are essential to this type of research, and knowledge-based institutions are involved in their development, often working with high-tech SMEs.

Submitted questions illustrating depth and connective power

- **How can ultraprecise measurements be used in basic physics research and to develop new technologies?**
- **What's at the centre of a black hole?**
- **Where did gravity come from?**

What is dark matter and what is dark energy?

Explanation

We can explain only 4% of the universe in terms of the familiar elementary particles and their four fundamental interactions, i.e. electromagnetic, weak nuclear, strong nuclear, and gravitational force. We see the effects of the remaining 96% of the energy in the universe, but we do not know what that energy is. Some of it is ‘dark matter’, but most of it is referred to as ‘dark energy’. Gravitational force caused by dark matter holds galaxies and galaxy clusters together. Dark energy, on the other hand, is behind the accelerating universe (i.e. expanding at an increasing rate). Researchers search for this unknown matter and energy by mapping the movements of celestial bodies and by conducting sensitive physics experiments. Theoretical physics also plays an important part in this quest. There are major international research programmes, including a large-scale European satellite project, focusing on the composition of dark matter and the ‘equation of state’ of dark energy. Solving the riddle of the dark part of the universe is one of the greatest challenges of basic research, and the Netherlands can play a decisive role.

Connective power

This question first requires basic research, which is being undertaken at CERN and within other close international alliances.Part of the research depends on all sorts of instruments, and the high-tech industry faces the challenge of developing the appropriate equipment. Much of the practical knowledge gained in doing so will be useful in other fields as well, generating new economic opportunities. To develop the most appropriate equipment, businesses must work closely with astronomers, physicists, and other specialists in multidisciplinary alliances.

Submitted questions illustrating depth and connective power

- **What are the fundamental building blocks of our universe?**
- **Can we measure dark matter directly?**
- **Why is the universe expanding at an increasing rate?**

How are galaxies, stars, and planets born and how do they evolve?

Explanation

The universe has a complex structure in which the cosmic void contrasts starkly with dense concentrations of mass in the form of galaxies, stars, planets, and ultimately human beings. All this evolved from relatively simple beginnings fourteen billion years ago. The universe was then filled with evenly dispersed gas of rudimentary structure which we can still detect in cosmic microwave background radiation. Gravitational force strengthened that structure by concentrating both normal and the mysterious dark matter. Some hundreds of millions of years later, the first stars and galaxies began to glimmer in this cosmic dawn. The first stars produced new elements that gave rise to other new stars with planetary systems. We can use large telescopes to observe all these processes and simulate them with powerful supercomputers to ultimately discover where all the matter, energy, and forces in the universe come from and how they will evolve. For example, astronomers are using the international LOFAR radio telescope, located partly in the Dutch Province of Drenthe, to search for effects of the first light after the big bang. Several strong groups of Dutch astronomers and cosmologists, united in NWO and top research school programmes and affiliated with international partnerships, are spearheading worldwide research on cosmic structures.

Connective power

This question covers much of the field of astronomy and therefore fits in with the Dutch Astronomy Sector Plan. Instrumentation plays an essential role in this research, which is closely related to the fundaments of physics. The challenge of developing the necessary instruments offers the high-tech industry new spin-off opportunities and partnerships with other businesses. Development programmes also often lead to innovative spin-offs, with connections to the top economic sector High Tech Systems & Materials. There is clearly also a relationship with astrochemistry, IT, and mathematics, as well as overlaps with the theme of self-organisation. Big data, the large-scale collection of data, evidently is another related theme.

Submitted questions illustrating depth and connective power

- **If a distant galaxy were composed solely of antimatter, would we be able to observe this from the Earth, and if so, how?**
- **Why is there water on Earth?**
- **What mechanisms cause galaxies to take on different shapes during their formation, for example lenticular, spiral, and – even odder – barred spiral galaxies?**

How can spacecrafts and telescopes help us learn more about the universe and explore our own solar system?

Explanation

The technological innovations that give rise to ever-more-advanced telescopes and spacecraft are deepening our understanding of the universe and interplanetary space and making that space increasingly useful to humanity. A world without weather and communication satellites and GPS has become almost unimaginable. To unlock the secrets of nature and someday even monetise our exploration of the solar system, we must continue to push the relevant technology forward and come up with new applications. The spin-off will resonate throughout society. The Netherlands can make an important contribution to international scientific progress in these areas. Dutch institutes specialising in astrotechnology and space exploration technology are highly prominent in international research, especially in view of their relatively small size.

Connective power

Interplanetary exploration requires research and coordination between a wide range of disciplines and technologies. Innovative telescopes are the product of new technology, which then turns out to be useful in other areas. The technology developed to study and explore space is highly innovative because it must operate in extreme circumstances and because space instruments are subject to exceedingly strict reliability and life-cycle criteria. In the past, space exploration produced innovations that had societal and economic impacts. Going forward, we can expect to see similar spin-offs with potential benefits for society and Dutch industry.

Submitted questions illustrating depth and connective power

- **Which instruments will we use to study the very smallest and the very largest components of our world (our universe)?**
- **How are we going to clean up and prevent space clutter?**
- **What can 21st century space travel contribute to solving the major scarcity problems that our world is facing, such as our dwindling supply of raw materials, energy, and drinking water?**

Is there life beyond our Earth?

Explanation

Are we alone in the universe or is there life elsewhere? It's an age-old question. Thanks to powerful new telescopes, we are finally figuring out how science can tackle this question. For the first time ever, it is possible to observe what happens on planets beyond our own solar system and to look for the formation of molecules that form the building blocks of life. Dutch astronomers have taken the lead in such research worldwide. Supersharp images allow them to spot planet systems being born and to simulate cosmic chemical processes in the laboratory.
In the successful quest to discover planets outside our solar system – known as exoplanets – astronomers have found planets where liquid water may be present, one of the criteria for life as we know it on Earth. Life of all kinds might betray its presence by leaving behind fingerprints of molecules, fine particles, and vegetation in the exoplanet's light waves. The challenge is to distinguish the faint light of the exoplanet from the blinding glare of its parent star.

Connective power

The search for alien life encompasses basic questions about the nature of life and how we might recognise it. It is related to the study of terrestrial extremophiles. A broad spectrum of disciplines converge in this context, for example the life sciences, earth sciences, and astrochemistry. The Dutch astronomy sector is small but very well organised and coordinated, and that is partly why it has such a good reputation worldwide. The equipment developed to study exoplanets and extra-terrestrial life also has potential for the high-tech industry in other fields, in that way generating new economic opportunities. The Dutch high-tech industry – both large companies and SMEs – is involved in developing such equipment and will take advantage of opportunities for technological innovation, further boosting its economic position. This question fits in with the Strategic Plan for Dutch Astronomy and ASTRONET's roadmap for European astronomy.

Submitted questions illustrating depth and connective power

- **Why do we assume that water is essential for alien life to exist?**
- **If evolution were to take place on a different planet based on organic processes and matter unknown to us, would we recognise living beings from that planet as such?**
- **Did life really begin on Earth, or could it have arisen elsewhere?**

How did life arise and how does evolution work?

Explanation

How life arose and evolved on Earth is one of the biggest questions in the natural sciences. There are millions of plant varieties and animal species, from microscopic to gigantic. Natural selection plays a vital and continuous role in speciation (the formation of new species), and it has led to a huge variety of life forms. So far we have only managed to describe and understand a small percentage of them. We are far from knowing how many species there are and how many mechanisms play a role in speciation, species segregation, and species-specific reproduction. The underlying questions range from the origins of the genetic code to the adaptation of individual species and ecosystems to changes in their immediate habitat and the environment. A better understanding of evolutionary processes will not only help us comprehend the way ecosystems, organisms, organs, and even cells function; it will also teach us about the impact of diverse environmental factors and how we can influence them in favourable ways.

Connective power

To understand complex systems of living organisms, it is important to study the dynamics of speciation and interaction between species. If our aim is to exploit species for the benefit of mankind, then we need to understand the stability of these systems under variable conditions and environmental stresses. Research on the underlying principles and mechanisms of complex systems can also help us develop useful tools for R&D and applications. Dutch and European biodiversity research programmes attest to the importance of such research.

Submitted questions illustrating depth and connective power

- **How does life sustain itself at the bottom of the ocean?**
- **Where does biodiversity come from? How have speciation processes contributed to biodiversity?**
- **How is it possible for life to arise from inanimate matter?**

How can we learn more about molecular properties, functions, and interactions in living systems, so that we can develop life-inspired systems ourselves, for example?

Explanation

We still do not understand how biomolecular interactions lead to living organisms. What we do know is that the molecules present in living organisms recognise each other, react to form new molecules, interact with each other, and undergo many complex processes as they assemble themselves into structures. These molecular processes are essential for chemical reactions and for the proper functioning of biological systems that consist of two parts, for example enzyme and substrate, virus and host, and antigen and antibody. Research on such complex molecular systems and the possibility of controlling them to our advantage provides a framework for tackling environmental, energy, and health issues. Over the next ten years, our challenge will be to learn to control molecular self-assembly (spontaneous ordering into structures). We can do this, for example, by designing and assembling molecular motors, modelling biological systems, designing dynamic biomaterials that repair human tissue, or regulating catalytic processes in living cells. Eventually, we may even be able to build synthetic molecular systems and materials that can carry out autonomous functions, generating a completely new chemical world.

Connective power

The core concepts of this question concern evolution, life functions, and explaining complex processes at different length and time scales. Practical applications and economic opportunities can be found in such areas as medicine, food, and materials. We received questions concerning prosthetics, synthetic tissue and organs, life-like smart materials, new medicinal drugs, nanorobots, molecular electronics, new target proteins for molecular therapies, antibiotics and antivirals, the creation of a synthetic cell, cancer treatment, and sustainably produced proteins. Research is needed into complex molecular systems, unequilibrated systems, and functional molecular architectures. Subthemes touch on such fields as microbiology, chemical immunology, functional molecular systems, and matter at various length scales.

Submitted questions illustrating depth and connective power

- **How do atoms find each other and how do they combine to form large biomolecules? How do molecules react with each other and how do they form living matter, organs, and organisms?**
- **Can we use assembled or self-assembled molecular layers to develop metal-molecule interfaces on surfaces or in systems in order to create advanced materials?**
- **Will we ever understand how catalytic processes (enzymatic, heterogeneous, or homogeneous) work in molecular reactions?**

Cells are the building blocks of life. How do they work and what can they teach us about life processes?

Explanation

The human body is made up of more than a hundred trillion cells. They perform all the body's functions, making them the most basic building blocks of life. Every living cell harbours a network of more than a thousand different chemical reactions responsible for converting nutrients into energy and assembling the components for a new cell. They also fuel essential processes such as DNA replication and transcription and protein synthesis. Cells are also capable of dividing themselves, and of receiving and processing external signals (signal transduction). After many years of biochemical research, we have identified these networks and the enzymes and regulatory circuitry involved, but we are still in the dark as to how and why the networks function at all. As a result, all current successful interventions into metabolism, gene expression, and signal transduction in relation to disease and industrial biotechnology have been based mainly on trial and error. Research in this area is crucial to further advances in many medical and biomedical fields.

Connective power

A better understanding of how cells work will allow us to develop better precision and other drugs, sustainable production methods for chemicals, foods, and energy, and diagnostic tests and other medical aids. Research on the genetic and metabolic networks of cells can help us identify methods to treat or prevent diseases in which metabolism plays a major role, such as diabetes and cancer. It will also clear a path to new strategies for combatting infectious diseases and, potentially, allow us to design cell factories that will support the bio-based economy. The Netherlands already has a robust R&D chain in cellular physiology. Evidence can be found in the growing number of public-private partnerships between knowledge-based institutions and innovative large and small businesses, and in investors' increasing interest in this field. By studying the cell system as a whole, researchers anticipate being able to develop a variety of predictive models, reprogram cell systems to carry out specific functions, or design new systems based on advances in synthetic biology. This will necessitate close cooperation between the relevant disciplines in the life sciences and natural sciences. The potential ethical and social consequences will also require input from the humanities and behavioural sciences.

Submitted questions illustrating depth and connective power

- **How is it that a single genome gives rise to so many different cells? Why are different genes switched on or off in different cell types?**
- **Will we ever understand cells as a comprehensive system in which we link the properties of enzymes and nucleic acids to the function of the organism?**
- **Ten years from now, will we be able to predict and influence the way in which metabolism and information exchange function in a living cell.**

How does a zygote (a fertilised egg cell) develop into a complex organism with various specialised tissues and organs?

Explanation

An adult has more than 10^{13} specialised cells. These cells do not act individually but instead work together in functional tissues and organs. And yet they all developed from a single zygote. Which signals cause the zygote to develop into different types of cells that know precisely when to divide or differentiate and then organise themselves into complex, three-dimensional tissues? Errors that arise during the first round of cell division can lead to a miscarriage or genetic defects. Research on normal cell division and what causes errors in that process may help prevent birth defects. The Netherlands has a long research tradition in developmental biology. Over the next ten years, Dutch researchers could very well make a significant contribution to answering questions about the normal and abnormal development of human and animal embryos.

Connective power

Developmental biology focuses on understanding the biological processes by which a zygote develops into a new-born. It explores the underlying regulatory mechanisms that are responsible for the development of living organisms. Basic research in this area is related directly to the study of congenital defects caused by genotype and environmental factors. The questions that developmental biology addresses are closely related to stem cell biology research. A basic understanding of biological development processes could lead to cell therapies for treating defects and diseases. The question also overlaps with regenerative medicine, which focuses on replacing, engineering, or regenerating tissues. The study of cell division errors that lead to abnormalities also has societal implications, for example questions about screening for potential birth defects.

Submitted questions illustrating depth and connective power

- **What is the relationship (potentially modifiable) between early embryo development and health in adulthood and old age?**
- **What are the long-term effects of severe congenital anomalies in new-borns?**
- **Gene-environment interaction during embryonic development is decisive for individual form and function and influences the risk of disease. How does that work?**

How and why do animals do what they do?

Explanation

Animal behaviour continues to fascinate us. One of the most challenging questions of the present moment is whether animals have consciousness. A better understanding of animal behaviour is essential to animal welfare research. Such research can produce insights important to the public discourse about factory farming and the ethics of animal testing. Questions about how animals interact with their habitats and, as a result, with humans and human activities are also important for the relationship between humans and animals. Other questions focus more on evolution and explore how their behaviour helps animals survive.

Connective power

This question calls for cooperation between ecologists, biologists, agricultural scientists, veterinary physicians, and planning specialists. Research on the ethology of both wild and domestic animals can inform our understanding of a range of different issues. It may concentrate on animal behaviour in natural habitats, the preservation of biodiversity in urban settings, how animals interact with man-made environments, or the spread of disease by animals or humans. Other questions that also require cooperation between different disciplines concern the meaning of animal ecosystems for crop and livestock production systems, and the improvement of animal welfare in zoos, animal parks, and livestock production systems. Research on animal behaviour in populations or subpopulations under wide-ranging conditions, for example in the presence of stress factors, can also produce valuable insights about abnormal behaviour in human populations or subpopulations.

Submitted questions illustrating depth and connective power

- **How does animal behaviour influence population and community dynamics on both an ecological and evolutionary scale?**
- **Does extremism occur in the animal kingdom?**
- **How can we prevent infectious and other diseases from being transmitted from animals to humans (zoonosis, One Health concept)?**

How does our brain process and retain information, and what role do plasticity and networks play at different microscopic and macroscopic levels?

Explanation

We know a great deal about the anatomy of the nervous system, and we have also made great strides in neurodiagnostics. It remains difficult, however, to predict the course of a neurological disease and to understand the underlying mechanisms. Neuroscientists have increasingly come to regard the brain as a network, and not as a collection of individual regions, each with its own function. A dysfunction in a certain region of the brain does not seem to matter that much; what is important is how it affects the entire brain network. Current brain research therefore focuses on understanding information processing in the brain network and the plasticity (i.e. adaptability) of the brain.

Connective power

Brain research touches on major societal issues. Mental disorders are common. The brain also plays an important role in how people respond to sickness and health. Impaired brain function can interfere with child development and children's learning capacity. The brain controls our emotions and therefore influences our wellbeing and productivity. It can also be a source of antisocial behaviour, such as violence and substance abuse. By studying the brain in old age, we can learn how to live healthier, independent lives for longer. Brain research unites many different disciplines, including medicine, physics, chemistry, biology, behavioural science, nutritional science, engineering, criminology, decision theory, and educational theory. This question covers a broad spectrum including basic research, for example brain function at molecular and genetic level, as well as applied research, for example the potential for influencing behaviour.

Submitted questions illustrating depth and connective power

- **How is brain activity related to human wellbeing?**
- **How can we support or repair specific brain functions? And what is the ideal way to do this?**
- **Is consciousness the result of an increase in the complexity of the neural network?**

As human beings, what are we capable of knowing about ourselves, God, and our place in the cosmos, and to what extent can science help us in this respect?

Explanation

For centuries, mankind has pondered what makes humans what they are, what place they occupy in the cosmos, and whether there is more to existence than the material world. New research, for example on the brain, has altered our concept of mankind dramatically in recent years. The question is, what impact will this new concept have on our relationship to God and our view of mankind's place in the cosmos? And can science even answer this question?

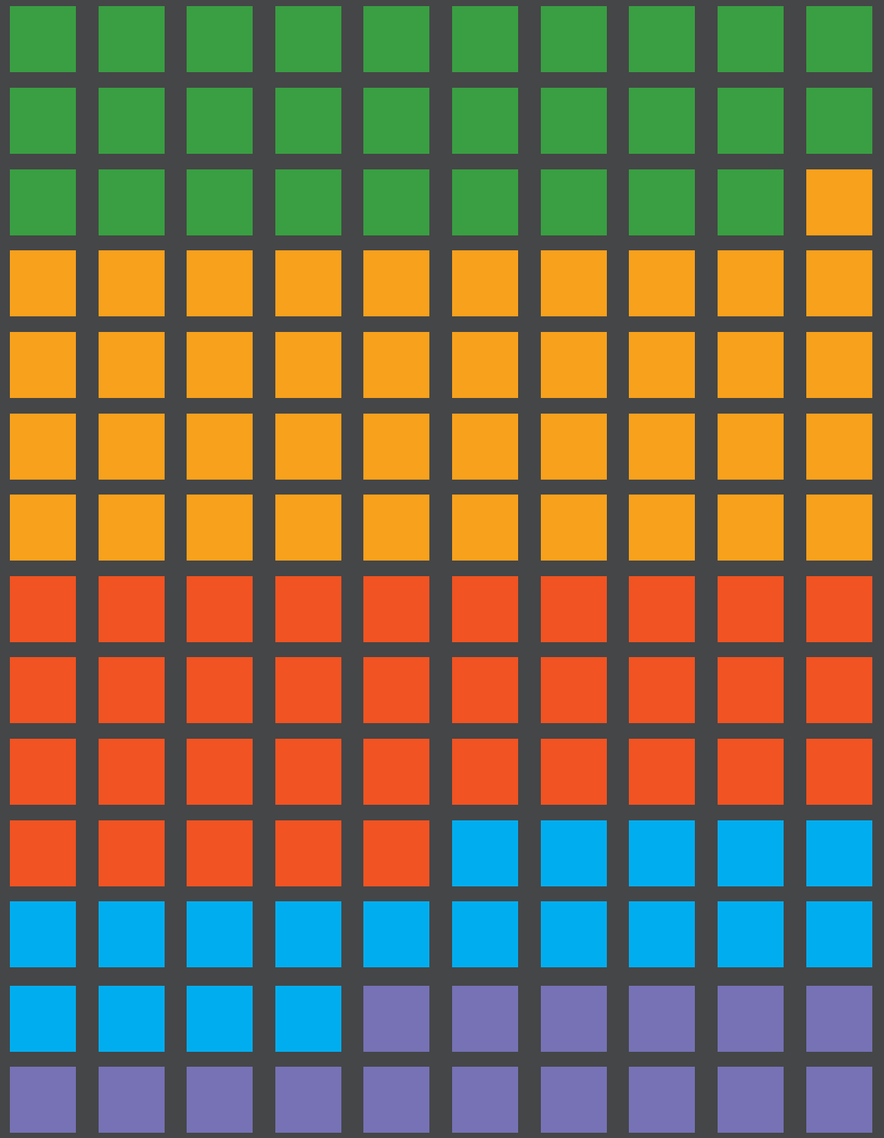
Connective power

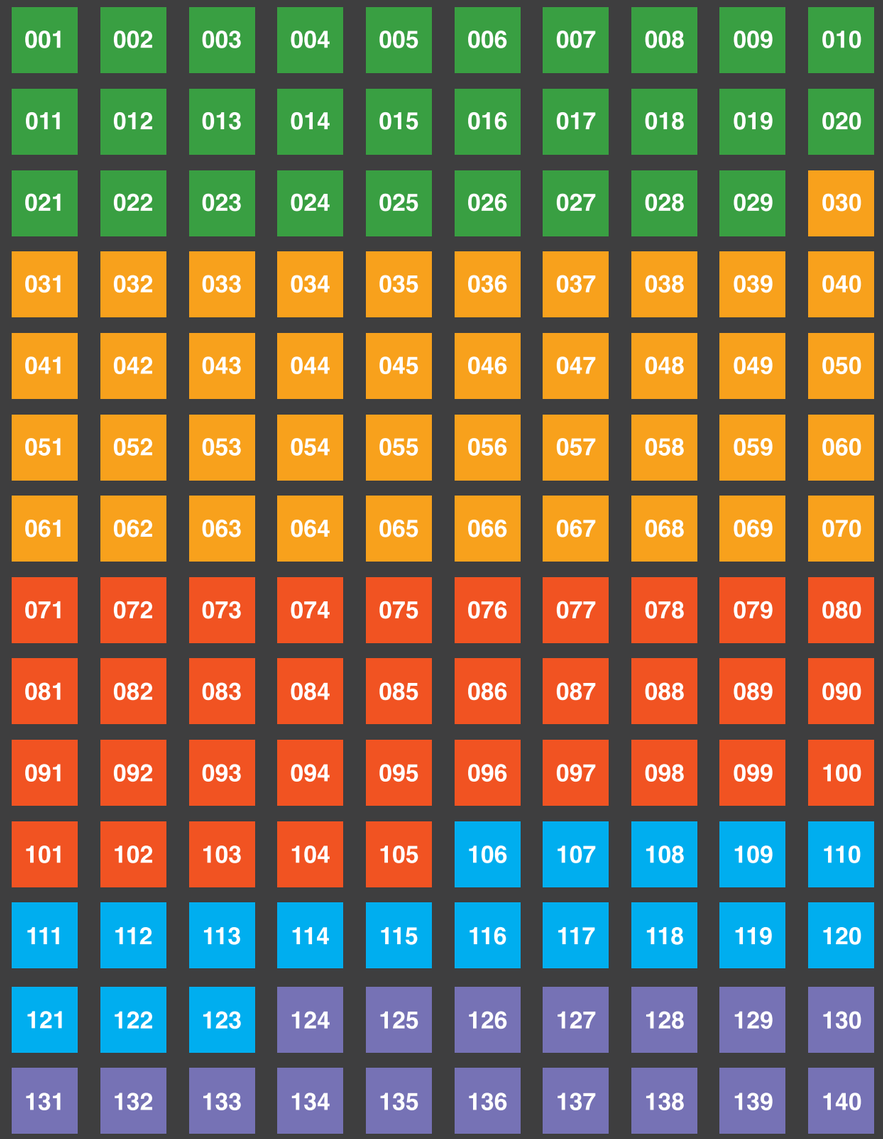
This question connects philosophy, religious studies, theology, and history. It has descriptive, evaluative, and design-based aspects. To answer it, we must first describe our present concept of mankind and how that concept has evolved in the course of history. Historical, philosophical, and religious perspectives are needed to understand the impact of that changing concept on our relationship to divine forces and on our view of mankind's place in the cosmos. To ask whether science can even answer this question forces us to examine the scope of our knowledge and probe the very limits of what science can tell us. Philosophy can help us determine what that scope is. The design-based aspect addresses different areas:

- Science communication: a better understanding of what is and is not scientific will help us communicate which results we can and cannot achieve with science.
- Science policy: a good understanding of the limits of our knowledge can help us bring our research efforts into line with what we actually need to know to shape our world, for example through politics and economics.
- Administrative policy: decisions on public spending, for example in the health care or culture sectors, are often informed by a certain concept of mankind. Explicit awareness of that concept can assist in community-building and in garnering support for certain decisions.

Submitted questions illustrating depth and connective power

- **Does science rule out religion?**
- **What are the limits of human intelligence?**
- **Can we establish the existence of an incorporeal soul empirically using brain scans of near-death experiences?**





Part III Connections and prospects

The following section of the Dutch National Research Agenda presents 16 example routes. Routes help identify a subcategory of interrelated questions concerning a complex theme. They take us on a 'tour' of various cluster questions and help us identify the most relevant ones as we search for an effective way to tackle a complex problem. Routes reveal theoretical and practical relationships that can lead to closer contact and coordination between the parties that make up the Knowledge Coalition and the organisations they represent.

The Knowledge Coalition selected the 16 routes for their relevance to society, the economy, and science itself. Other routes are of course possible, and website visitors can plot out routes that will help them find potential partners and set priorities for research programmes and partnerships. But the Knowledge Coalition will only consider routes that focus on fostering broad, innovative alliances, in keeping with the spirit of the Dutch National Research Agenda.

Research Agendas

Universities

Medical centres

UAS

Research institutes and expertise centres

Policy Agendas

Research funding bodies

Ministries

Top economic sectors

International

Personalised medicine

Importance of route

People want affordable health care that is tailored to the individual as much as possible. The future of health care will increasingly depend on our ability to identify and correctly interpret the earliest signs of susceptibility to disease, so that we can prevent or intercept sickness in individuals even before symptoms appear. As a result, people will live longer and remain healthier into old age. Personalised medicine (or precision medicine) plays a key role in this development; it involves identifying the most successful treatment based on a patient's individual characteristics (for example genetic blueprint or protein expression) or specific disease traits (for example tumour mutations). The aim is to treat the patient successfully and to avoid unfavourable side effects. Personalised medicine even allows us to identify which individuals have a higher risk of certain disorders, and offers unprecedented opportunities for sickness prevention.

Potential new connections

At the moment, research in such disciplines as biotechnology, molecular genetics, and physics is driving progress in medicine and health care. For personalised medicine to flourish, innovation and technology are vital. For example, early detection and imaging are hugely important in this context. Given the vast amount of data that personalised medicine generates, it is particularly important to consider the role of IT. Data management and analysis (big data) and the right tools to evaluate decisions and interventions are also essential. The challenge that we face in the decades ahead is to take all these new insights and use them to improve preventive medicine, diagnostics, and treatment. That will require new strategic partnerships. In terms of research and innovation, the Netherlands has secured a favourable place for itself in the global Life Sciences & Health sector. By offering a unique combination of expertise and skills, this sector is a promising one for the Dutch knowledge economy. Now is the time for the relevant parties to agree on a shared agenda. There are new opportunities for collaboration with tech businesses that also focus on health, such as Philips, and information processing companies such as Google.

Cluster questions illustrating scope and connective power of route:

- Can we convert big data into value, insights, and answers?
- Every tumour is different, so how can we come to understand cancer well enough to develop a treatment for each and every type?
- How can we personalise health care, for example by using biomarkers?
- How can we predict, prevent, and treat cardiovascular diseases (atherosclerosis, heart failure, heart arrhythmia, and thrombosis) in individuals at an early stage?
- What causes chronic kidney disease, how can we detect it sooner, and how can we treat it on an individual basis?
- What causes type 1 and type 2 diabetes, how can we detect them sooner, and how can we treat them on an individual basis?
- How can big data and technological innovation (e-health) contribute to health care?
- Can we design smart materials and structures that have new and advanced properties?

This route connects the research and policy agendas of the following institutions:

Universities: EUR, RUG, RU, TU/e, TUD, UL, UM, UT, UU, UvA, VU, WUR, 3TU
Medical centres: AMC, Erasmus MC, LUMC, MUMC, NFU, NKI/AvL, Radboud UMC, UMCG, UMCU, VUMC
UAS: Arnhem and Nijmegen, Fontys, Inholland, Leiden, Stenden, Utrecht UAS of the Arts, VHL, Windesheim, Zuyd
Research institutes and expertise centres: AMOLF, Biomedical Primate Research Centre, CWI, KNAW Hubrecht Institute for Developmental Biology and Stem Cell Research, KNAW Huygens ING, KNAW Meertens Institute, KNAW NIN, KNAW Rathenau Institute, Mulier Institute, Netherlands Youth Institute, (TO2) ECN, (TO2) TNO, RIVM, Trimbos Institute, Veiligheid NL, VILANS
Research funding bodies: NWO, ZonMw
Ministries: Economic Affairs; Health Welfare and Sport
Top economic sectors: Chemistry, Creative Industry, Life Sciences & Health, Agri & Food
International: Horizon 2020, UN SDGs
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This route connects the following questions:

072, 073, 075, 080, 085, 086, 087, 088, 089, 090, 094, 095, 101, 104, 105, 112, 120

Personalised medicine

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101	102	103	104	105	106	107	108	109	110
111	112	113	114	115	116	117	118	119	120
121	122	123	124	125	126	127	128	129	130
131	132	133	134	135	136	137	138	139	140

13	10	9	16			2	2	4	2

Regenerative medicine

Importance of route

Regenerative medicine focuses on developing new treatments that make smart use of our body's self-healing ability. These treatments are meant to permanently restore normal function in tissues or organs affected by disease or injury, without causing side effects. Researchers have high hopes for regenerative medicine. The years ahead will see new clinical treatments emerge. Regenerative medicine will, for example, lead to new therapies for neurological, musculoskeletal, and cardiovascular disorders.

Potential new connections

The restoration of normal function in impaired organs and damaged tissues and the engineering of new organs or tissues for transplantation or research represent a relatively new multidisciplinary field. To be able to grow tissues or even complete organs at will, whether in vivo or ex vivo, requires a combined knowledge of cell biology, biomaterials, modelling, and imaging. Organs or parts of organs that we grow on command can be used not only to repair damage but also to test drugs, eventually obviating the need for laboratory animals. Interdisciplinary cooperation between clinicians, scientific researchers, and spin-offs is crucial to the engineering of an organ or tissue that can be used to tackle unsolved clinical problems.

Cluster questions illustrating scope and connective power of route:

- How can we use cells, stem cells, and biomaterials to engineer and regenerate tissues and organs?
- Can we design electronic or bio-electronic systems that communicate directly with our bodies as well as materials and technology that restore or support human body function?
- Can we model the human body and use smart technologies for health, nutritional, and toxicity research, drastically reducing the use of laboratory animals at the same time?

This route connects the strategic agendas of the following institutions:

Universities: EUR, RU, TU/e, TUD, UL, UM, UvA, UvT, VU, WUR
Medical centres: AMC, Erasmus MC, LUMC, MUMC, NFU, NKI/AvL, Radboud UMC, UMCG, UMCU, VUMC
UAS: Arnhem and Nijmegen, Fontys, Hanze UAS Groningen, Leiden, Rotterdam,Viaa
Research institutes and expertise centres: AMOLF, KNAW Hubrecht Institute for Developmental Biology and Stem Cell Research, KNAW NIOO, Movisie, NIVEL, RIVM, Sanquin, (TO2) TNO, VILANS
Research funding bodies: NWO, ZonMw
Top economic sectors: Life Sciences & Health
International: Horizon 2020

This route connects the following questions:

100, 101, 121

Regenerative medicine

001	002	003	004	005	006	007	008	009	010
011	012	013	014	015	016	017	018	019	020
021	022	023	024	025	026	027	028	029	030
031	032	033	034	035	036	037	038	039	040
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051	052	053	054	055	056	057	058	059	060
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101	102	103	104	105	106	107	108	109	110
111	112	113	114	115	116	117	118	119	120
121	122	123	124	125	126	127	128	129	130
131	132	133	134	135	136	137	138	139	140

10	10	6	9			2	-	1	1

Health care research, sickness prevention, and treatment

Importance of route

A number of major challenges lie ahead in the field of medicine. The elderly population is growing and the labour force is shrinking. Since most chronic diseases become manifest later in life, the pressure on the health care system is growing. At the same time, the number of staff providing bedside care is declining. The development of new, successful, but often expensive treatments for chronic and other diseases can extend and improve quality of life, but such treatments also drive up the cost of care. The number of people suffering 'diseases of prosperity' (e.g. metabolic syndrome, a combination of hypertension, diabetes, high cholesterol levels, and overweight), arthritis, and cardiovascular diseases is growing across age groups. The number of people who suffer mental and psychiatric problems is also on the rise. Infectious diseases remain a threat to public health, with new diseases such as Q fever, SARS, and MERS-CoV cropping up. Some pre-existing diseases are becoming more contagious, sometimes taking the form of an epidemic. With the population ageing and life expectancy increasing, there are more elderly people in the population with lower resistance to disease. New treatments for cancer or rheumatologic disorders also increasingly involve activating or deactivating the immune system. There is a growing focus in medicine on the prevention, early diagnosis, and effective treatment of chronic diseases. Nutrition, 'personalised nutrition', and a healthy lifestyle are also important to prevention. All this is improving quality of life for people, allowing them to participate fully in society. The challenge is to keep health care affordable, accessible, and of good quality at the same time.

Potential new connections

Sustainable health care requires a multidisciplinary approach involving all stakeholders and supported by technology and data-sharing. In addition, the fight against infectious diseases does not stop at our national borders; it requires a coordinated international effort. Microbiology, virology, veterinary medicine, and other disciplines must work with experts in such areas as health care promotion, psychology, and sociology to advance the fight against infectious diseases.

Cluster questions illustrating scope and connective power of route:

- How do a healthy lifestyle and wholesome habits promote good health and prevent illness?
- What is the best way for us to analyse and prevent the problem of overweight and obesity?
- Can we combine mainstream and complementary therapies, leading to integrative health care that allows for the many differences between patients?
- How do we improve the quality of health care as much as possible while keeping it affordable?
- How can we control micro-organisms in health care, livestock farming, and the environment?
- What role do micro-organisms play in ecosystems and how can we use them to improve health and the environment?
- How can a broader definition of 'life' help us identify new targets for molecular therapies, antibiotics, and antiviral drugs?

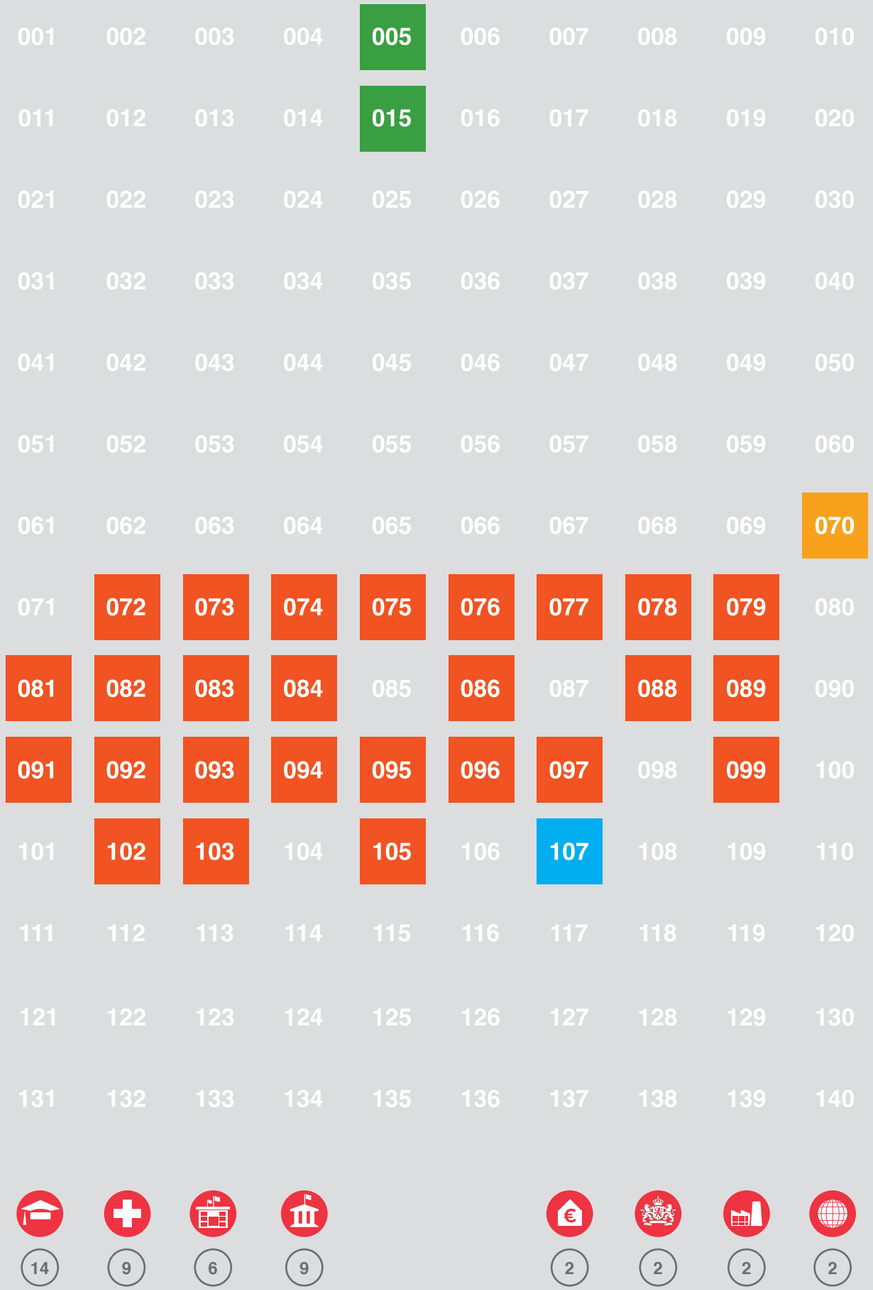
This route connects the agendas of the following institutions:

Universities: EUR, RUG, RU, TU/e, TUD, UL, UM, UT, UU, UvA, UvT, VU, WUR, 3TU
Medical centres: AMC, Erasmus MC, LUMC, MUMC, NFU, NKI/AvL, Radboud UMC, UMCU, VUMC
UAS: Avans, Christian UAS Ede, Fontys, Hanze, Leiden, Windesheim
Research institutes and expertise centres: KNAW Hubrecht Institute for Developmental Biology and Stem Cell Research, KNAW NIN, KNAW NIOO, RIVM, SRON, (TO2) NLR, (TO2) TNO, (TO2) WUR, VILANS
Research funding bodies: NWO, ZonMw
Ministries: Infrastructure and the Environment; Health, Welfare and Sport
Top economic sectors: Agri & Food, Life Sciences & Health
International: Horizon 2020, UN SDGs

This route connects the following questions:

005, 015, 070, 072, 073, 074, 075, 076, 077, 078, 079, 081, 082, 083, 084, 086, 088, 089, 091, 092, 093, 094, 095, 096, 097, 099, 102, 103, 105, 107

Health care research, sickness prevention, and treatment



The origin of life – on earth and in the universe

Importance of route

This route encompasses pure research questions that are as old as humanity itself. How did life arise? What is consciousness? Are we alone in the universe? The search for answers often leads to astonishing new insights. The route begins at the origin of the universe and the formation of habitable planets. It proceeds to the origin and evolution of life on Earth and then moves on to the brain and consciousness. It concludes by asking whether we will ultimately be able to control biological systems, for example in the form of a synthetic living cell.

Potential new connections

This route links questions that address the origin of life as well as the brain, cognition, and meaningfulness. The search for answers involves not only basic research on the origin of life but also applied research on the model systems designed and used to promote human wellbeing. And it naturally addresses the eternal question of whether there is life beyond the Earth.

Cluster questions illustrating scope and connective power of route:

- As human beings, what are we capable of knowing about ourselves, God, and our place in the cosmos, and to what extent can science help us in this respect?
- Cells are the buildings blocks of life. How do they work and what can they teach us about life processes?
- How did life arise and how does evolution work?
- Is there life beyond our Earth?
- How can we learn more about molecular properties, functions, and interactions in living systems, so that we can develop life-inspired systems ourselves, for example?
- What are the origins, history, and future of the universe?

This route connects the agendas of the following institutions:

Universities: RUG, RU, TU/e, TUD, UL, UM, UT, UU, UvA, UvT, VU, WUR, 3TU
Medical centres: AMC, Erasmus MC, LUMC, MUMC, NFU, Radboud UMC, UMCG, UMCU, VUMC
UAS: Ede, Fontys, Hanze, Leiden, Windesheim
Research institutes and expertise centres: AMOLF, ASTRON, KNAW Hubrecht Institute for Developmental Biology and Stem Cell Research, KNAW NIN, KNAW NIOO, Max Planck Institute for Psycholinguistics, Nikhef, Netherlands Research School for Astronomy, NIOZ, SRON, (TO2) NLR, (TO2) TNO, VILANS
Research funding bodies: NIHC, NWO
Ministries: Health, Welfare and Sport
Top economic sectors: Life Sciences & Health
International: Horizon 2020

This route connects the following questions:

082, 099, 100, 101, 121, 122, 124, 127, 131, 132, 133, 134, 135, 136, 137, 139, 140

The origin of life – on earth and in the universe

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051	052	053	054	055	056	057	058	059	060
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071	072	073	074	075	076	077	078	079	080
081	082	083	084	085	086	087	088	089	090
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101	102	103	104	105	106	107	108	109	110
111	112	113	114	115	116	117	118	119	120
121	122	123	124	125	126	127	128	129	130
131	132	133	134	135	136	137	138	139	140

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Building blocks of matter and fundaments of space and time

Importance of route

The 21st century will be the century of new materials (meta-materials) that do not exist in nature but that we have engineered from elementary particles. Before we can do that, however, we need an in-depth understanding of the particles themselves and the various forms that matter takes. Bear in mind that we can explain only about 4% of the matter in the universe. The other 96% – known as 'dark matter' and 'dark energy' – remains a mystery to us. Dutch research suggests that the dark part of the universe is closely connected to the origins of space and time in black holes. For centuries, the question of the origin of time was purely philosophical in nature. Now, however, it may be physicists who ultimately provide the answer.

Potential new connections

The search for new forms of matter and materials with new properties is driven by basic scientific curiosity and by the quest for new applications, for example in the energy sector. In the past, the search proceeded mainly through a process of trial and error, but today it is becoming increasingly model-based. Once we have developed quantum computers, the speed at which we can design new materials with new properties will increase dramatically.

Cluster questions illustrating scope and connective power of route:

- What is the true nature of gravity, space, and time and what can we learn from black holes?
- What is dark matter and what is dark energy?
- Have we identified all the elementary particles of matter?
- Can we design smart materials and structures that have new and advanced properties?
- As human beings, what are we capable of knowing about ourselves, God, and our place in the cosmos, and to what extent can science help us in this respect?
- How can we store, convert, and transport energy efficiently?

This route connects the agendas of the following institutions:

Universities: RUG, RU, TU/e, TUD, UL, UT, UvA, UvT, VU, WUR, 3TU
Medical centres: AMC, LUMC
UAS: Amsterdam, Avans, Den Bosch, Fontys, HKU, Inholland, Rotterdam, The Hague, Utrecht, VHL, Vilentum, Windesheim, Zeeland, Zuyd
Research institutes and expertise centres: AMOLF, ASTRON, CWI, DIFFER, Nikhef, NOVA, SRON, (TO2) ECN, (TO2) NLR, (TO2) TNO, WRR
Research funding bodies: NWO
Ministries: Economic Affairs; Security and Justice
Top economic sectors: Agri & Food, Chemistry, Creative Industry, Energy, High Tech Systems and Materials, Life Sciences & Health
International: Horizon 2020, UN SDGs

This route connects the following questions:

009, 010, 018, 019, 025, 026, 052, 117, 118, 120, 124, 125, 126, 127, 128, 129, 130, 131, 132, 140

Building blocks of matter and fundaments of space and time

001	002	003	004	005	006	007	008	**009**	**010**
011	012	013	014	015	016	017	**018**	**019**	020
021	022	023	024	**025**	**026**	027	028	029	030
031	032	033	034	035	036	037	038	039	040
041	042	043	044	045	046	047	048	049	050
051	**052**	053	054	055	056	057	058	059	060
061	062	063	064	065	066	067	068	069	070
071	072	073	074	075	076	077	078	079	080
081	082	083	084	085	086	087	088	089	090
091	092	093	094	095	096	097	098	099	100
101	102	103	104	105	106	107	108	109	110
111	112	113	114	115	116	**117**	**118**	119	**120**
121	122	123	**124**	**125**	**126**	**127**	**128**	**129**	**130**
131	**132**	133	134	135	136	137	138	139	**140**

11	2	14	12			1	2	6	2

Resilient and meaningful societies

Importance of route

Globalisation is exposing societies to rapid change and new threats. As the world grows increasingly networked, global issues – whether they concern climate change, contagious diseases, disruptive technologies, geopolitical transitions, violent conflicts, ideologies, or computer crime – are forcing their way into everyone's lives. The familiar systems of local, national, and worldwide institutions no longer offer enough protection against these global forces. Societies and their citizens will therefore need to respond to change with more adaptability and creativity. They will become more flexible as a result, and less dependent on slower-moving rules and institutions. This transition requires innovation and creativity, as well as close cooperation between many different research disciplines.

Potential new connections

This route combines a large number of more or less pure research questions concerning pressing societal issues with questions relevant to improving the competitiveness of the Netherlands. It links research questions concerning migration and statecraft, wellbeing and culture, social cohesion and quality of life, vigorous and self-reliant individuals, climate change and the circular economy, technology and 21st century skills, and the economy and infrastructure. The result is a better understanding of the dynamic and complex nature of our rapidly changing world. The questions are also relevant to the design of technical, economic, social, and cultural innovations that may, for example, help solve health care and sustainability problems, foster a better climate for enterprise, or offer an adequate response to public security issues. The research results will be useful for domestic and international policymaking and enhance the position of the Netherlands in a changing world. Different scientific disciplines and perspectives are needed for this, necessitating an interdisciplinary approach in which science and technology, the humanities and social sciences, and the earth and life sciences work together to address these questions. The route also offers various interfaces for different policy and research agendas.

Cluster questions illustrating scope and connective power of route:

- What do Europeanisation and globalisation mean for democracy and the 'constitutional state' (i.e. a state governed by the rule of law)?
- What are the causes and consequences of migration, and how can we deal with them?
- What do we mean by 'quality of life'?
- How can we ensure that our labour force and labour-market organisations remain robust and resilient as they face the challenges of the 21st century?
- What are the features of a circular economy and how can we achieve it?
- How can we promote and utilise creativity and innovation?

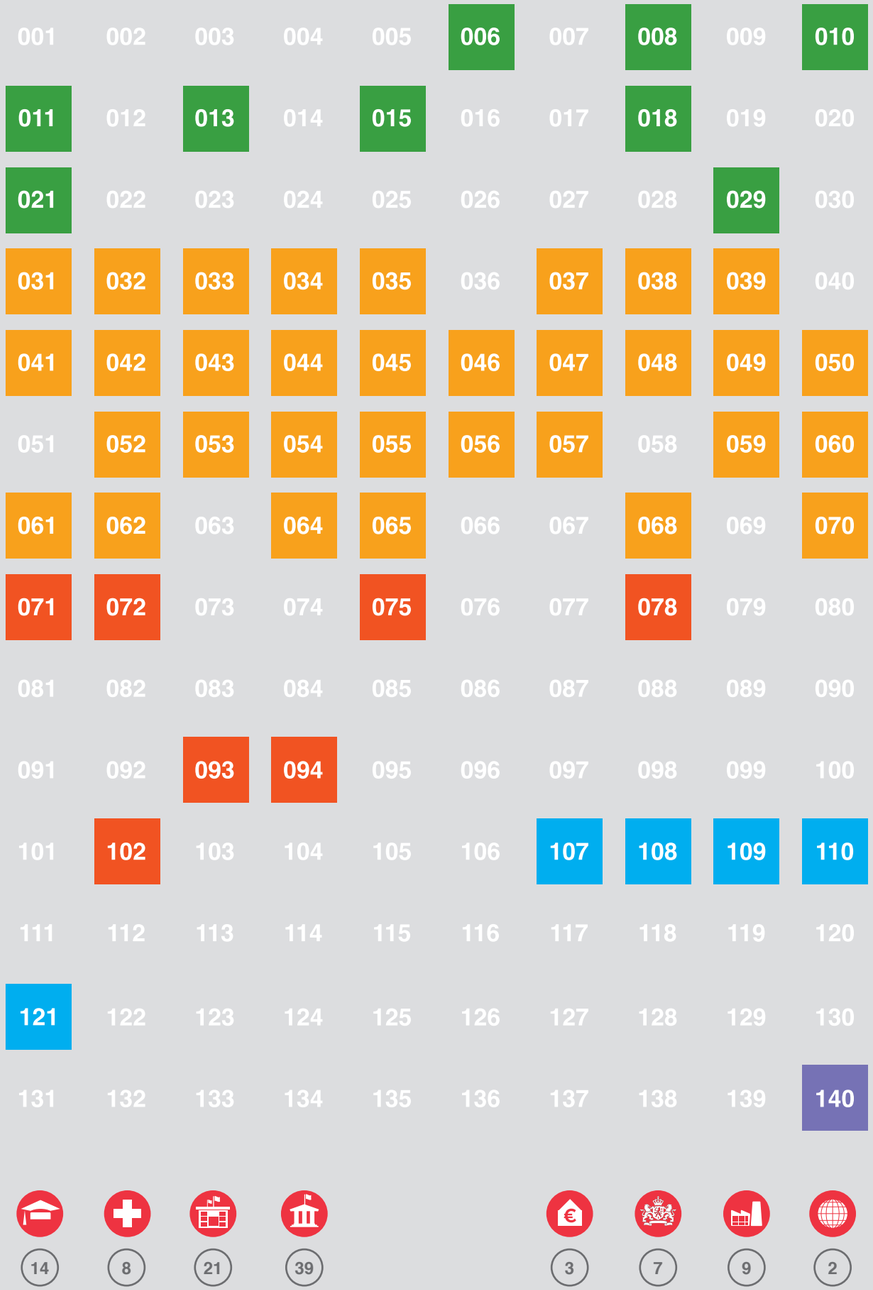
This route connects the agendas of the following institutions:

Universities: EUR, RUG, RU, TU/e, TUD, UL, UM, UT, UU, UvA, UvT, VU, WUR, 3TU
Medical centres: AMC, Erasmus MC, LUMC, MUMC, Radboud UMC, UMCG, UMCU, VUMC
UAS: Amsterdam, Amsterdam University of the Arts, Arnhem and Nijmegen, Avans, Christian UAS Ede, Den Bosch, Fontys, Hanze, Inholland, Leiden, Rotterdam, Stenden, The Hague, Utrecht, Utrecht UAS of the Arts, Viaa, VHL, Vilentum, Windesheim, Zeeland, Zuyd
Research institutes and expertise centres: ASTRON, Biomedical Primate Research Centre, Boekman Foundation, CBS, Clingendael, CPB, CWI, IFV, KiM, KNAW Hubrecht Institute, KNAW IISG, KNAW KITLV, KNAW Meertens Institute, KNAW NIDI, KNAW NIN, KNAW NIOO, KNAW Rathenau Institute, KNMI, Max Planck Institute for Psycholinguistics, Movisie, Mulier Instituut, Netherlands Youth Institute, NFI, NIVEL, NIOZ, NSCR, PBL, Police Academy, Research and Documentation Centre - WODC, SCP, SRON, SWOV, (TO2) ECN, (TO2) NLR, (TO2) TNO, (TO2) WUR, Veiligheid NL, VILANS, WRR
Research funding bodies: NRPO SIA, NWO, ZonMw
Ministries: Defence; Economic Affairs; Education, Culture and Sience; Foreign Affairs; Health, Welfare and Sport; Security and Justice; Social Affairs and Employment
Top economic sectors: Agri & Food, Chemistry, Creative Industry, Energy, High Tech Systems and Materials, Logistics, Life Sciences & Health, Horticulture and Starting Materials, Water
International: Horizon 2020, UN SDGs

This route connects the following questions:

006, 008, 010, 011, 013, 015, 018, 021, 029, 031, 032, 033, 034, 035, 037, 038, 039, 041, 042, 043, 044, 045, 046, 047, 048, 049, 050, 052, 053, 054, 055, 056, 057, 059, 060, 061, 062, 064, 065, 068, 070, 071, 072, 075, 078, 093, 094, 102, 107, 108, 109, 110, 121, 140

Resilient and meaningful societies



Between conflict and cooperation

Importance of route

Despite the initial optimism, the world has become more volatile since the end of the Cold War. Its instability first manifested itself in international relations, but the rise of terrorism has added a domestic dimension. Climate change and the global financial crisis have aggravated the problem. The flood of refugees is only one, very dramatic, symptom. Security has become one of the biggest concerns of government, businesses, and the public. Research in the social sciences, engineering sciences and technology, the natural sciences, and the humanities can help individuals, states, and the world as whole move away from conflict and towards greater cooperation.

Potential new connections

The scale at which the problem has manifested itself calls for cooperation; that, in turn, requires an understanding of the value systems of differing groups in society. Big data, media research, and religious studies play an important role here. The Dutch system of government is changing under the influence of Europeanisation and globalisation, compelling us to find new perspectives on prosperity and equality. That is the only way to promote peace, equality, and cooperation, both at home and internationally, and to understand the causes and consequences of migration issues. In turn, this will require research on social cohesion in a society in which cultural and religious diversity is on the rise. Public security, a prerequisite for wellbeing and economic growth, depends in part on individual features. Aggression, for example, may result from the interaction between genetic factors and personal traits or patterns of individual behaviour. A sustainable future requires worldwide cooperation in the transition to a circular economy. Moreover, we cannot limit ourselves to the national context when it comes to battling floods, earthquakes, volcanic eruptions, and other natural disasters. All these issues require close collaboration between researchers who study the climate, migration flows, conflict management, international diplomacy and cooperation, internal and external security, technology, and the organisation of security. There are also links to research on such matters as physical safety and online security, or aggressive behaviour, social inequality, and terrorism.

Cluster questions illustrating scope and connective power of route:

- Can globalisation and development be reinvented in a way that, in time, will mitigate differences in prosperity between world regions?
- What are the causes and consequences of migration, and how can we deal with them?
- How can we promote peace, security, and cooperation – and address threats and violations – within and between constitutional states and within and between groups and societies?
- How can we ensure proper water governance in the future?
- How can we promote social cohesion in a society that is culturally and religiously diverse?
- How do we guarantee our digital freedom?

This route connects the agendas of the following institutions:

Universities: EUR, RUG, RU, TU/e, TUD, UL, UM, UT, UU, UvA, UvT, VU, WUR, 3TU;
Medical centres: AMC, MUMC, NFU, UMCU
UAS: Amsterdam, Arnhem and Nijmegen, Avans, Den Bosch, Ede, Fontys, Hanze, HKU, Inholland, Rotterdam, Saxion,The Hague, Utrecht, VHL, VIAA, Vilentum, Windesheim, Zeeland, Zuyd
Research institutes and expertise centres: Boekman Foundation, Clingendael, CPB, CWI, Institute for Physical Safety - IFV, KiM, KNAW Huygens ING, KNAW IISG, KNAW Meertens Institute, KNAW NIN, KNAW NIOO, KNAW Rathenau Institute, KNAW NIDI, KNAW NIOD, KNMI, Movisie, Netherlands Youth Institute, NFI, Nikhef, NIOZ, NSCR, SRON, Police Academy, PBL, SCP, Trimbos Institute, SWOV, (TO2) ECN, (TO2) MARIN, (TO2) NLR, (TO2) TNO, (TO2) WUR, WODC, WRR
Research funding bodies: NWO
Ministries: Defence; Economic Affairs; Education, Culture and Science; Foreign Affairs; Health, Welfare and Sport; Security and Justice; Social Affairs and Employment
Top economic sectors: Agri & Food, Creative Industry, Energy, High-tech Systems and Materials, Logistics, LIfe Sciences & Health, Horticulture & Starting Materials, Water
International: Horizon 2020, UN SDGs

This route connects the following questions:

006, 008, 010, 011,013, 029, 031, 032, 037, 039, 040, 041, 042, 043, 044, 045, 046, 047, 055, 056, 057, 058, 060, 077, 107, 108, 109, 110, 112

Between conflict and cooperation

001	002	003	004	005	006	007	008	009	010
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131	132	133	134	135	136	137	138	139	140

14	4	19	34			1	7	8	2

Brain, cognition, and behaviour: learning, development, and self-improvement

Importance of route

People who can develop to their full potential, who improve themselves, and who adapt to changing circumstances, are happier, feel healthier, and contribute more to society. Recent research on the complex relationship between the brain, cognitive functions, behaviour, and environment could lead to many innovations: in health care, to help us remain vigorous and independent for as long as possible; in education, to attune learning pathways to children's or adults' various talents; and in public safety, for example by finding effective ways to treat adolescents who are at risk of developing or consistently exhibit antisocial or aggressive behaviour.

Potential new connections

This route will produce pioneering insights into the relationship between genes and behaviour. Dutch research in the cognitive and behavioural sciences and the neurosciences is highly interdisciplinary and very broad in scope, ranging from clinical, cognitive and epidemiological studies to molecular research, computer modelling, and big data analysis. There is vertical integration, with molecular research being linked through a series of intermediate stages to studies on human interaction. These broad foundations are an excellent breeding ground for new applications and the valorisation of advanced methods, in cooperation with private and civil society parties. That makes it possible to work on a set of educational and training tools appropriate at every stage of the life cycle and attuned to the competences that pupils and employees need. In terms of health care, early markers for anxiety disorders, uncontrolled behaviour, aggressiveness, depression, cognitive decline, or neurodegeneration can help prevent or at least control the limitations associated with them.

Cluster questions illustrating scope and connective power of route:

- What should education be like in the future?
- Why do we do what we do, are we who we think we are, and what factors influence our behaviour? In other words, how can we understand our behaviour?
- How do a healthy lifestyle and wholesome habits promote good health and prevent illness?
- How can big data and technological innovation *(e-health)* contribute to health care?
- How does our brain process and retain information, and what role do plasticity and networks play at different microscopic and macroscopic levels?
- What effect is the rising 24-hour economy having on human health and performance and how can our knowledge of biorhythms enhance the relationship between the individual and society?

This route connects the agendas of the following institutions:

Universities: EUR, RUG, RU, TU/e, TUD, UL, UM, UT, UU, UvA, UvT, VU, WUR, 3TU
Medical centres: AMC, Erasmus MC, LUMC, MUMC, NFU, NKI/AvL, Radboud UMC, UMCG, UMCU, VUMC
UAS: AHK, Amsterdam, Arnhem and Nijmegen, Avans, Ede, Fontys, Hanze, HKU, Inholland, Leiden, Rotterdam, Saxion, Stenden, The Hague, Utrecht, VHL, VIAA, Windesheim, Zeeland, Zuyd
Research institutes and expertise centres: Biomedical Primate Research Centre, Boekman Foundation, CPB, CWI, IFV, KiM, KNAW Huygens ING, KNAW Meertens Institute, KNAW NIAS, KNAW NIDI, KNAW NIN, KNAW Rathenau Institute, Max Planck Institute for Psycholinguistics, Movisie, Mulier Institute, Netherlands Youth Institute, NIVEL, NSCR, PBC, Police Academy, Research and Documentation Centre – WODC, SWOV, (TO2) Deltares, (TO2) TNO, Veiligheid NL, VILANS, WRR
Research funding bodies: NWO, NIHC, NRO, ZonMw
Ministries: Economic Affairs; Education, Culture and Science; Health, Welfare and Sport; Infrastructure and the Environment; Security and Justice; Social Affairs and Employment
Top economic sectors: Chemistry, Creative Industry, Energy, High Tech Systems and Materials, Logistics, Life Sciences & Health, Water
International: Horizon 2020, UN SDGs

This route connects the following questions:

048, 050, 056, 059, 065, 068, 069, 070, 072, 073, 074, 075, 076, 081, 083, 084, 095, 101, 102, 103, 104, 105, 107, 113, 136, 139.

Brain, cognition, and behaviour: learning, development, and self-improvement

001	002	003	004	005	006	007	008	009	010
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071	072	073	074	075	076	077	078	079	080
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091	092	093	094	095	096	097	098	099	100
101	102	103	104	105	106	107	108	109	110
111	112	113	114	115	116	117	118	119	120
121	122	123	124	125	126	127	128	129	130
131	132	133	134	135	136	137	138	139	140

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14	10	20	27						

Using big data responsibly – searching for patterns in large databases

Importance of route

We can scarcely overestimate the implications of the enormous flood of data that ICT permits us to collect, store and analyse in every conceivable domain. The stockpile of instruments producing that continuous stream of data is still growing, both in science and in society. Parallel advances in hardware and software for data processing and data analysis are leading to unprecedented opportunities and challenges. Researchers, businesses, governments, civil society organisations, and the public alike are all affected.

Big data refers to terabytes or even petabytes of data generated almost in real time. The nature and structure of this data varies considerably. It is not confined to research data but includes data collected by other parties, for example through social media or customer loyalty cards. Data is also collected in every imaginable discipline, from astronomy to genetics and epigenetics, from IT to statistics, and from history to linguistics.

Big data challenges us to develop new approaches to producing scientific knowledge, to come up with and implement new statistical analysis methods, and to reassess the boundaries between private life and the public domain.

Potential new connections

The subject of big data is interesting in a large number of areas, from agro production and health to military intelligence and security, from transport and logistics to climate and environment, and from history and cultural heritage to biological evolution and ecosystems. This route links such disciplines as criminology, psychology, art history, genetics, electronics, information science, biology, chemistry, ethics, law, and mathematics. It is of relevance to governments, businesses, civil society organisations, and the public alike. In a recent report, the Advisory Council for Science, Technology and Innovation emphasises the unifying power of ICT in this area (AWTI, 2015).

Cluster questions illustrating scope and connective power of route:

- Can we use big data and big data collection to define values, generate insights, and get answers?
- How can we anticipate the impact of new technologies on humans and society, and understand and evaluate the influence of existing technologies?
- How do the old and new media influence individuals and society?

This route connects the agendas of the following institutions:

Universities: EUR, RUG, RU, TU/e, TUD, UL, UM, UT, UU, UvA, UvT, VU, WUR, 3TU

Medical centres: AMC, Erasmus MC, LUMC, MUMC, NFU, NKI/AVL, Radboud UMC, UMCG, UMCU, VUMC

UAS: Amsterdam, Arnhem and Nijmegen, Breda, Fontys, Inholland, The Hague, Utrecht, VHL, Windesheim, Zeeland, Zuyd

Research institutes and expertise centres: ASTRON, Boekman Foundation, Collaborative organisation for ICT in Dutch education and research - SURF, CWI, KNAW DANS, KNAW Hubrecht Institute for Developmental Biology and Stem Cell Research, KNAW Huygens ING, KNAW Meertens Institute, KNAW NIN, KNAW NIOO, KNAW Rathenau Institute, KNMI, Max Planck Institute for Psycholinguistics, NFI, NLeSC, Nikhef, NIOZ, NOVA, NSCR, SRON, Police Academy, (TO2) Deltares, (TO2) NLR, (TO2) TNO, (TO2) WUR, VILANS, WRR, WODC, (TO2) MARIN

Research funding bodies: NWO, ZonMw;

Ministries: Defence; Economic Affairs; Health, Welfare and Sport; Infrastructure and the Environment; Security and Justice

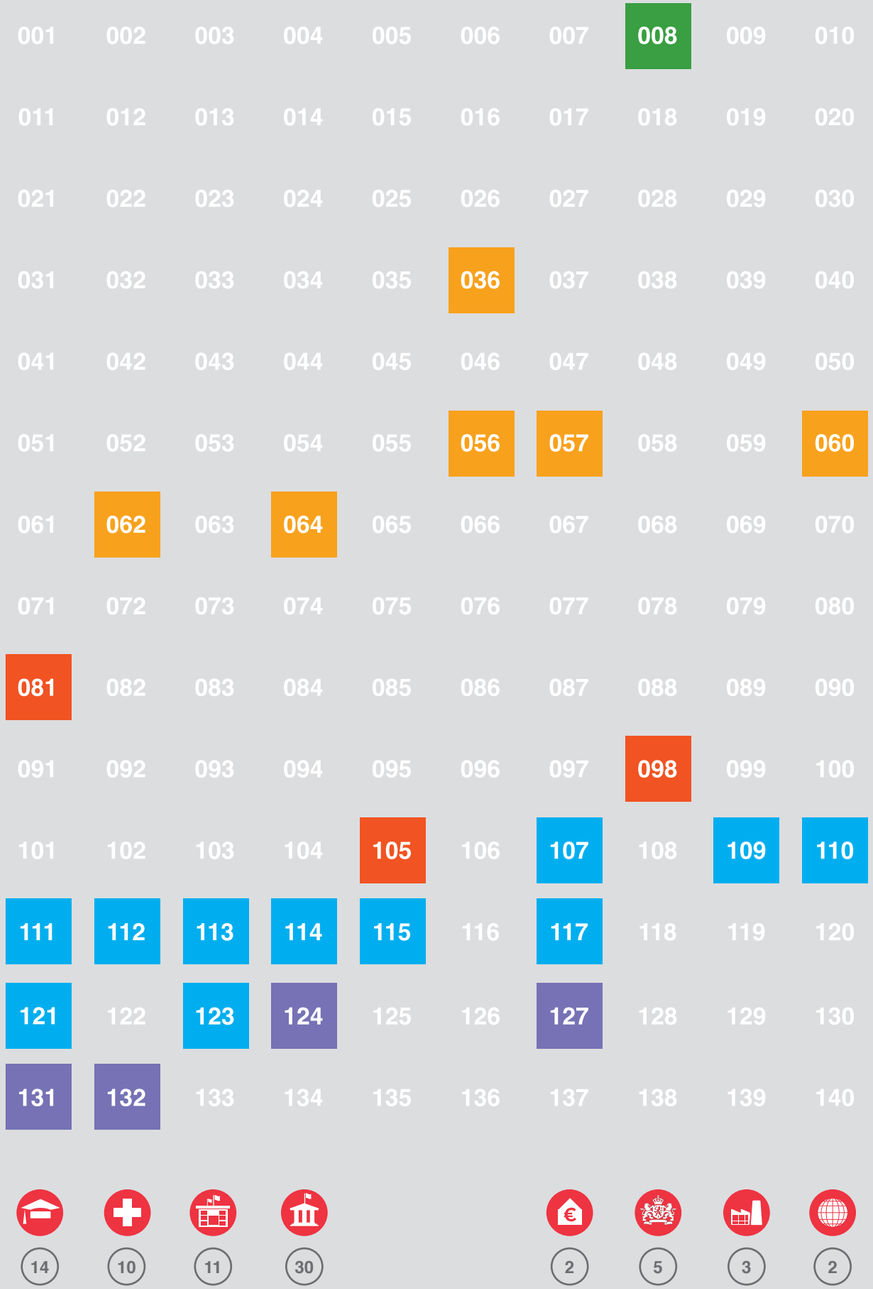
Top economic sectors: High Tech Systems and Materials, Life Sciences & Health, Water

International: Horizon 2020, UN SDGs

This route inks the following questions:

008, 036, 056, 057, 060, 062, 064, 081, 098, 105, 107, 109, 110, 111, 112, 113, 114, 115, 117, 121, 123, 124, 127, 131, 132

Using big data responsibly – searching for patterns in large databases



Smart industry

Importance of route

To maintain our current level of prosperity and wellbeing in the Netherlands, we need to add value to products and services, specifically those intended for export. The Netherlands can only be competitive if we align our strengths with worldwide trends and developments. The products and services of the future will be highly complex and custom-made. They will require multidisciplinary cooperation and we must be able to produce and maintain them on demand, regardless of circumstances. The process of equipping the business sector and the labour market for this future is known as 'smart industry'. Smart industry is about technology, but it is also about the broader impact that these changes will have on tech industry employees and on society as a whole.

Potential new connections

Smart industry offers science many new challenges, ranging from technology and mathematical problems to social, legal, and economic issues. Questions range from 'How do people respond to robots and other new technologies?' to 'What sort of innovation networks play a role?'. Smart industry will have a broad impact on professional practices and on society as a whole. The Smart Industry Science Agenda calls on knowledge-based institutions and businesses to work together to drive innovation forward and foster 21st century skills in the longer term.

Cluster questions illustrating scope and connective power of route:

- How can we anticipate the impact of new technologies on humans and society, and understand and evaluate the influence of existing technologies?
- How can we personalise health care, for example by using biomarkers?
- Can we use big data and big data collection to define values, generate insights, and get answers?
- What should education be like in the future?
- How do we ensure that the Dutch economy remains competitive?
- How can we connect 'things' (hardware) all the time and everywhere and boost processing speed while using less energy?
- How can we create a truly circular economy so that industrial goods manufacturing depends less on primary raw materials?

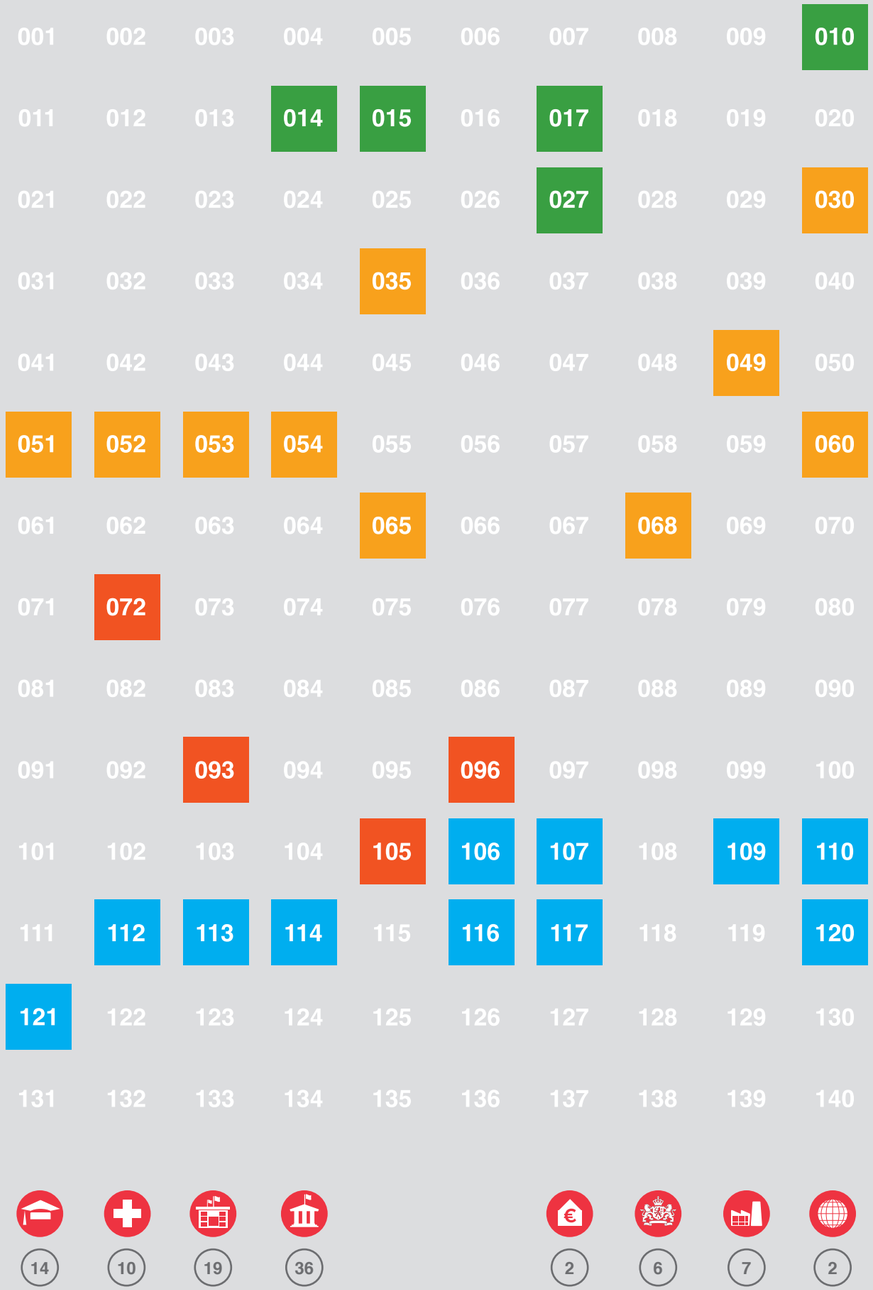
This route connects the agendas of the following institutions:

Universities: EUR, RUG, RUN, TU/e, TUD, UL, UM, UT, UU, UvA, UvT, VU, WUR, 3TU
Medical centres: AMC, Erasmus MC, LUMC, MUMC, NFU, NKI/AvL, Radboud UMC, UMCG, UMCU, VUMC
UAS: AHK, Amsterdam, Arnhem and Nijmegen, Avans, Ede, Fontys, Hanze, HKU, Inholland, Leiden, Rotterdam, Stenden, The Hague, Utrecht, VHL, Vilentum, Windesheim, Zeeland, Zuyd
Research institutes and expertise centres: AMOLF, ARCNL, ASTRON, Boekman Foundation, CPB, CWI, DIFFER, IFV, KiM, KNAW DANS, KNAW Hubrecht Institute, KNAW Huygens ING, KNAW IISG, KNAW Meertens Institute, KNAW NIN, KNAW NIDI, KNAW Rathenau Institute, KNMI, Movisie, Mulier Institute, Netherlands Youth Institute, Nikhef, NIOZ, NSCR, PBL, Police Academy, (TO2) Deltares, (TO2) ECN, (TO2) MARIN, (TO2) NLR, (TO2) TNO, (TO2) WUR, SWOV, VILANS, WODC, WRR
Research funding bodies: NWO, ZonMw
Ministries: Defence; Economic Affairs; Education, Culture and Science; Health, Welfare and Sport; Infrastructure and the Environment; Security and Justice
Top economic sectors: Agri & Food, Chemistry, Creative Industry, Energy, High Tech Systems and Materials, Logistics, Water
International: Horizon 2020, UN SDGs

This route connects the following questions:

010, 014, 015, 017, 027, 030, 035, 049, 051, 052, 053, 054, 060, 065, 068, 072, 093, 096, 105, 106, 107, 109, 110, 112, 113, 114, 116, 117, 120, 121

Smart industry



Smart, liveable cities

Importance of route

Cities are important nerve centres of economic growth, social interaction, innovation, and culture. More than half of the world population lives in cities, a figure that is expected to rise to 70% by 2030. Cities generate almost 60% of global GDP. Urbanisation is vital to sustainable economic growth. At the same time, however, it raises enormous challenges in many different domains: the quality of physical and social living conditions, physical safety and public security, logistics, the use of natural resources, and the pressure on the environment. Problems in urban areas take on a more concentrated form than elsewhere, so that the many different issues are all closely intertwined. They also become evident on different orders of scale, ranging from single-building settings (and thus materials) to neighbourhoods, whole cities, and greater metropolitan areas. In such complex systems, problems can rarely be solved by imposing solutions from the top-down. The aim of this route is therefore to come up with designs and structures that exploit the diversity and vast numbers of interactions in cities. The route is not only about the city and the built environment as such, but also about the relationship between the city and the nation, and the city and the countryside. To tap into their own potential and improve the quality of living, cities need to be smarter about their growth. We can assist them by surveying and analysing the interaction between the many aspects that make up a city and the built environment as a whole.

Potential new connections

We must make buildings and infrastructure more sustainable, and lower costs over the entire life cycle. New technologies and processes can make buildings and infrastructure cheaper, safer, and more sustainable. New buildings will need to be energy-neutral or even energy-producing. Advanced monitoring and modelling technology can improve maintenance. New research and new technology can also improve building materials and make their recycling or reuse possible. Key themes in the built environment include safe building (for example in flood- and earthquake-prone areas), sustainable building, and adaptive building. These aims cover a broad range of subtopics: the development of the built environment; the living environment in the city; urban logistics; the city as a healthy residential area; safe cities and personal safety in the city; the city as an economic system; food supply in cities; the city as an energy-neutral system; and the city as a source of culture. The route also involves elaborating and reflecting critically on new urban development concepts such as circular cities, green cities, sustainable cities, sharing cities, hackable cities, and urban agriculture. Along this route, design-based research can help urban planners in their decision-making and generate ideas for the ideal city of the future. Lurking in the background are various normative questions, for example concerning rural versus urban values or the issue of urban aesthetics. This route is very well suited to transdisciplinary research. It embraces research in the humanities, the social and behavioural sciences, and science and technology, as well as combinations thereof. In the humanities, the questions concern the relationship between cities and culture in the broader sense, covering such themes as citizenship and participatory democracy. In science and technology, research involves the urban climate, urban metabolism, or green features in cities. In the social and behavioural sciences, the questions focus on social cohesion and the city as a source of cultural and technological innovation. But there are also countless subtopics at the interface between the three domains.

Cluster questions illustrating scope and connective power of route:

- What are the implications and challenges associated with worldwide urbanisation?
- How does the built environment affect health and wellbeing?
- How can we keep our densely populated country liveable?
- How can we use new materials, technologies, and processes to lower the cost of buildings and infrastructure and make them safer and more sustainable?
- How can we promote social cohesion in a society that is culturally and religiously diverse?

This route connects the agendas of the following institutions:

Universities: EUR, RUG, RU, TU/e, TUD, UL, UM, UT, UU, UvA, UvT, VU, WUR, 3TU
Medical centres: AMC, Erasmus MC, LUMC, NFU
UAS: AHK, Amsterdam, Arnhem and Nijmegen, Avans, Den Bosch, Ede, Fontys, Hanze, HKU, Inholland, Leiden, Rotterdam, Saxion, The Hague, Utrecht, VHL, Viaa, Vilentum, Windesheim, Zeeland, Zuyd, Zwolle
Research institutes and expertise centres: AHTI, AMS-Institute, ASTRON, Boekman Foundation, CBS, Clingendael, CPB, CWI, DIFFER, IFV, KiM, KNAW IISG, KNAW Meertens Institute, KNAW NIDI, KNAW NIOO, KNAW Rathenau Institute, KNMI, Movisie, NHTV, NIOZ, NIVEL, NSCR, PBL, Police Academy, (TO2) Deltares, (TO2) ECN, (TO2) MARIN, (TO2) TNO, (TO2) WUR, SWOV, WODC, WRR
Research funding bodies: NWO, NPRO SIA, ZonMw
Ministries: Defence; Economic Affairs; Education, Culture and Science; Foreign Affairs; Infrastructure and Environment; Security and Justice; Social Affairs and Employment
Top economic sectors: Agri & Food, Creative Industry, Energy, High Tech Systems and Materials, Logistics, Water
International: Horizon 2020, UN SDGs.

This route connects the following questions:

008, 010, 011, 018, 019, 028, 029, 030, 034, 036, 039, 040, 044, 045, 047, 048, 054, 055, 066, 071, 078, 109, 111

Smart, liveable cities

001	002	003	004	005	006	007	**008**	009	**010**
011	012	013	014	015	016	017	**018**	**019**	020
021	022	023	024	025	026	027	**028**	**029**	**030**
031	032	033	**034**	035	**036**	037	038	**039**	**040**
041	042	043	**044**	**045**	046	**047**	**048**	049	050
051	052	053	**054**	**055**	056	057	058	059	060
061	062	063	064	065	**066**	067	068	069	070
071	072	073	074	075	076	077	**078**	079	080
081	082	083	084	085	086	087	088	089	090
091	092	093	094	095	096	097	098	099	100
101	102	103	104	105	106	107	108	**109**	110
111	112	113	114	115	116	117	118	119	120
121	122	123	124	125	126	127	128	129	130
131	132	133	134	135	136	137	138	139	140

14	4	22	32			3	7	6	2

Circular economy and resource efficiency

Importance of route

Earth Overshoot Day – the calendar date on which our resource consumption for the year exceeds Earth's capacity to regenerate those resources in that year – comes earlier every year (in 2015, it fell on 13 August). For the sake of society, the economy, and the environment, it is vital for us to focus on building a circular economy in which we *use* resources instead of merely *consume* them. That holds not only for the way in which we extract those resources, but also for the design (or redesign) of production processes and products and for the development of new materials and business models. People will need to change their behaviour and use resources and raw materials as efficiently as possible. In specific cases, transitioning to a circular economy will also require research concerning legislation and regulatory matters.

Potential new connections

The enormous pressure that we put on the Earth as a system and the resulting need to build a circular economy makes it necessary to continue integrating the various sub-questions and their related research fields. We can approach the concept of the circular economy from different perspectives, all of which need to be defined more precisely. For example, the agriculture, chemicals (including rubber/synthetics), and energy sectors play an essential role in resource extraction, production processes, and recycling. To optimise biological processes, we need to understand how living systems function and can be engineered. A very important factor in designing closed-loop cycles for natural resources and materials is our understanding of chemical and biochemical matter and processes at both micro and macro scale. Energy use, generation, transmission, and storage are important production factors. The use of alternative means of production in factories and the way we use water and land are also important to this issue. Transport will continue to be crucial in linking the various parts of the chain physically. To facilitate the transition to a circular economy, we must also investigate the extent to which we can influence human behaviour and awareness as well as the necessary legal framework. Another relevant question is how we will position ourselves with respect to the natural world. Because this new information and new technology will be implemented in society and the economy, an important role will be entrusted to a considerable number of top economic sectors.

Cluster questions illustrating scope and connective power of route:

- How can we create a truly circular economy so that industrial goods manufacturing depends less on primary raw materials?
- How can we use new materials, technologies, and processes to lower the cost of buildings and infrastructure and make them safer and more sustainable?
- How can we improve the effectiveness and legitimacy of legislation, given the global challenges we face with respect to the environment, security, innovation, energy, and climate change?

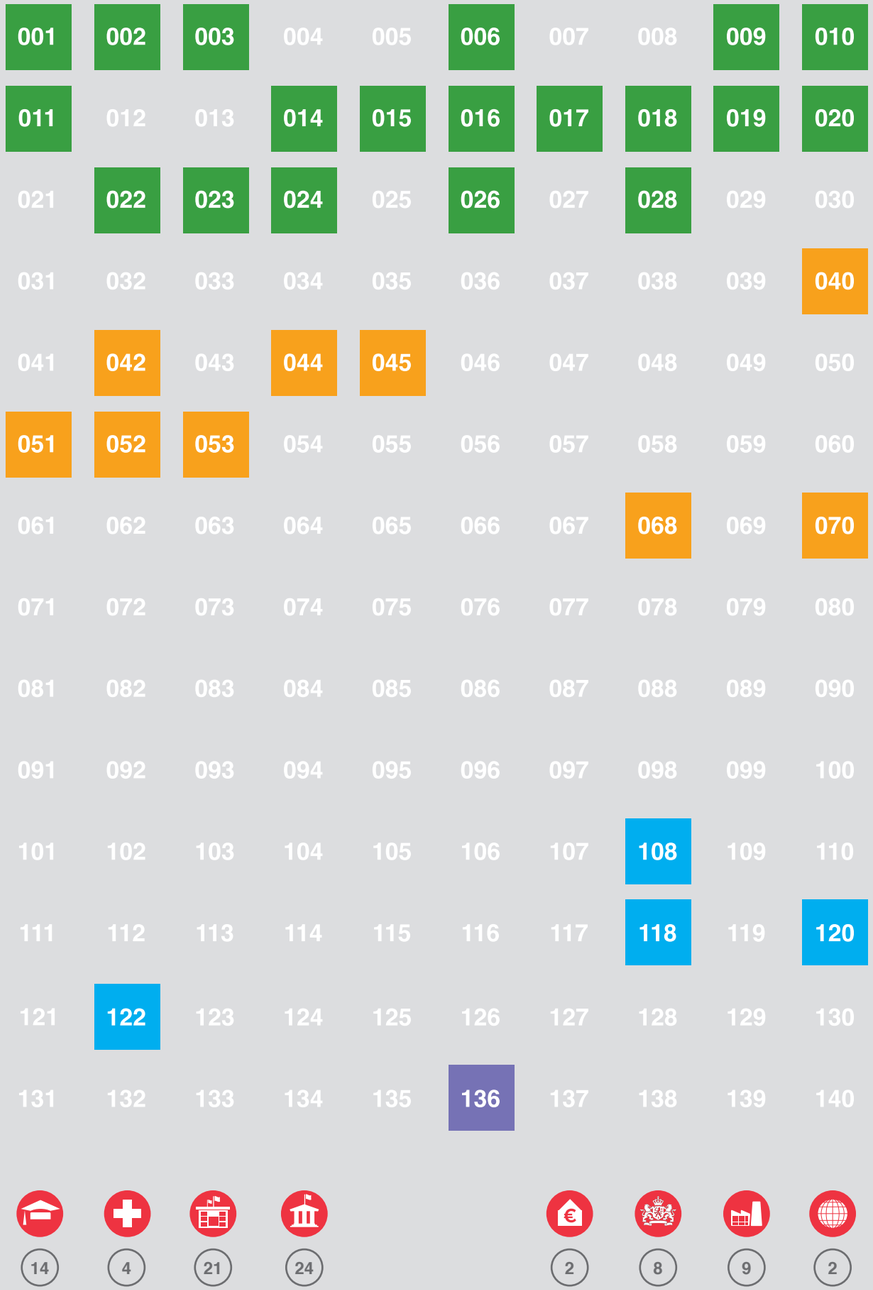
This route connects the agendas of the following institutions:

Universities: EUR, RUG, RU, TU/e, TUD, UL, UM, UT, UU, UvA, UvT, VU, WUR, 3TU
Medical centres: AMC, NFU, NKI/AvL, Radboud UMC
UAS: Amsterdam, Amsterdam University of the Arts, Arnhem and Nijmegen, Avans, Christian UAS Ede, Den Bosch, Fontys, Hanze, Inholland, Leiden, Rotterdam, Saxion, The Hague, Utrecht, Utrecht UAS of the Arts, VHL, Viaa, Vilentum, Windesheim, Zeeland, Zuyd
Research institutes and expertise centres: AMOLF, CPB, CWI, DIFFER, IFV, KIM, KNAW IISG, KNAW NIDI, KNAW NIOO, KNAW Rathenau Institute, KNMI, Movisie, NIOZ, PBL, Police Academy, RIVM, SCP, SRON, WOV, (TO2) Deltares, (TO2) ECN, (TO2) TNO, (TO2) WUR, WRR
Research funding bodies: NWO, NPRO SIA
Ministries: Defence; Economic Affairs; Education, Culture and Science; Foreign Affairs; Health, Welfare and Sport; Infrastructure and the Environment; Security and Justice; Social Affairs and Employment
Top economic sectors: Agri & Food, Chemistry, Creative Industry, Energy, High Tech Systems and Materials, Life Sciences & Health, Logistics, Horticulture and Starting Materials, Water
International: Horizon 2020, UN SDGs

This route connects the following questions:

001, 002, 003, 006, 009, 010, 011, 014, 015, 016, 017, 018, 019, 020, 022, 023, 024, 026, 028, 040, 042, 044, 045, 051, 052, 053, 068, 070, 108, 118, 120, 122, 136

Circular economy and resource efficiency



Sustainable production of safe and healthy food

Importance of route

By 2050, there will be 9 billion people on Earth to feed. As prosperity levels rise, so will consumption, whereas water, land, and energy will grow scarcer. Both consumers and civil society are also making more stringent demands on the quality of products and the way in which they are produced. To guarantee enough safe, healthy food for all, we need sustainable, efficient, safe food production systems. The combined horticulture and agrifood industries – from primary production to food processing, preparation, marketing, and distribution – form the biggest economic sector in the Netherlands and make a significant contribution to the Dutch economy and employment. The Netherlands is the second largest source of horticulture and agrifood export products worldwide. Dutch expertise and Dutch products have a very good reputation, a success that depends largely on the Netherlands' position in expertise and innovation.

Potential new connections

This route connects the reduction of the ecological footprint – with health and product safety being paramount – with personalised nutrition. It will require us to develop efficient production systems, set up sustainable production chains, develop integrated health systems for people, plants, and animals in livestock production chains, and study consumer food-related and food-use behaviour from the perspective of personalised nutrition and lifestyle. Consumers are increasingly selecting food products for evidence-based and measurable personal health advantages. Accurate, evidence-based monitoring of personal health status requires knowledge generation in and integration between the life sciences, diagnostics, and sensor systems (wearable or not). In short, it is very important for the various disciplines to collaborate closely and share their knowledge in this route.

Cluster questions illustrating scope and connective power of route:

- Can we use big data and big data collection to define values, generate insights, and get answers?
- What do humans and nature mean to each other and what is the ideal relationship between the two?
- How can we make agricultural production systems more sustainable as the worldwide demand for healthy, safe food continues to grow?
- How can we use sport, physical exercise, and nutrition to promote good health and what effects will this have?
- How can we develop healthy new food crops that have higher yields while requiring fewer harmful chemicals?

This route connects the agendas of the following institutions:

Universities: EUR, RUG, RU, TU/e, TUD, UL, UM, UT, UU, UvA, UvT, VU, WUR, 3TU

Medical centres: AMC, Erasmus MC, LUMC, MUMC, NKI/AvL, Radboud UMC, UMCG, UMCU, VUMC

UAS: Amsterdam, Arnhem and Nijmegen, Avans, Christian UAS Ede, Fontys, Hanze, HKU, Inholland, Leiden, Rotterdam, Saxion, Stenden, The Hague, VHL, Viaa, Vilentum, Windesheim, Zuyd

Research institutes and expertise centres: CWI, DIFFER, KNAW Huygens ING, KNAW Meertens Institute, KNAW NIN, KNAW NIOO, KNAW Rathenau Institute, KNMI, Movisie, Mulier Institute, Netherlands Youth Institute, NIOZ, NIVEL, NSCR, PBL, RIVM, (TO2) Deltares, (TO2) ECN, (TO2) TNO, (TO2) WUR, WRR

Research funding bodies: NWO, ZonMw

Ministries: Economic Affairs; Education, Culture and Science; Infrastructure and the Environment; Health, Welfare and Sport; Security and Justice; Social Affairs and Employment

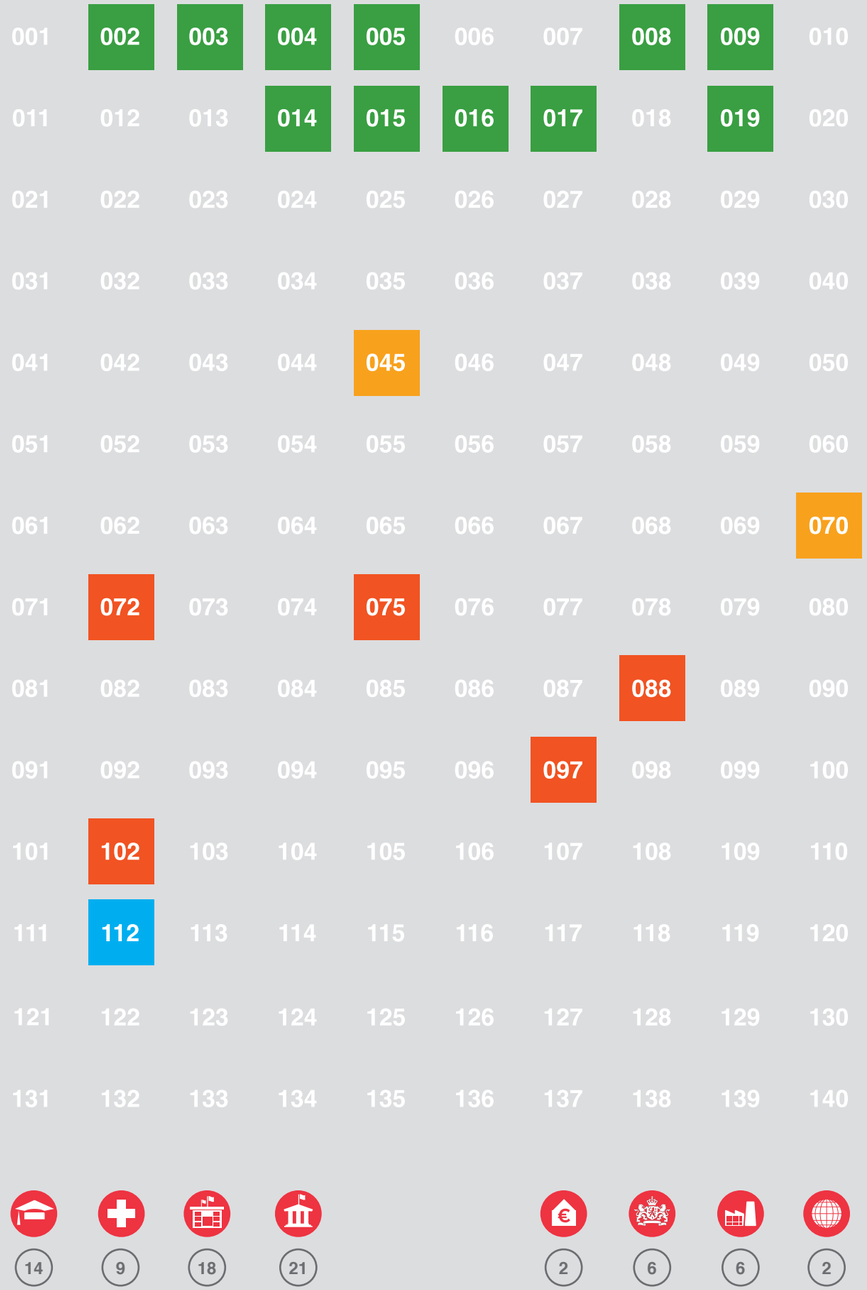
Top economic sectors: Agri & Food, Creative Industry, Energy, High Tech Systems and Materials, Life Sciences & Health, Horticulture and Starting Materials

International: Horizon 2020, UN SDGs

This route connects the following questions:

002, 003, 004, 005, 008, 009, 014, 015, 016, 017, 019, 045, 070, 072, 075, 088, 097, 102, 112

Sustainable production of safe and healthy food



Art: research and innovation in the 21st century

Importance of route

It is human nature to explore creative and artistic ways of depicting reality or an experience we have lived through. We need only consider the Lascaux Caves, the most highly ornamented prehistoric caves that have been discovered to date. Art and imagination are intrinsic forms of human expression, but they also serve as tools for representing culture, politics, economics, education, and science. This route links the power of art and the imagination to various domains, but also uses these new connections to explore the relationship between art/imagination and human existence.

Potential new connections

What does art mean to people? This question focuses on the role that art plays in people's lives, but it is also linked to the issue of creativity and innovation. All too often, we study art as an isolated phenomenon. By asking how we can best promote creativity and innovation, we reveal the relationship between art and education, science, and innovation. A broad range of research questions then becomes possible that touches on virtually every top economic sector and societal challenge. One good example is the question 'What should education be like in the future?' It addresses what is important to society today, in the 21st century. We can approach this from three obvious perspectives:

- Art to facilitate enquiry-based learning
- The role of the artistic imagination in science
- Art, imagination, and perspective in a visual culture

By digging deeper, we can establish a link to the imagined circular economy, but also, more broadly, to the future design of our institutions.

Cluster questions illustrating scope and connective power of route:

- What does art mean to people?
- How can we promote and utilise creativity and innovation?
- What should education be like in the future?
- How do the old and new media influence individuals and society?
- What are the features of a circular economy and how can we achieve it?
- How can we best design the socioeconomic institutions of the future?

This route connects the agendas of the following institutions:

Universities: EUR, RU, TUD, UL, UM, UT, UU, UvA, UvT, VU, 3TU
UAS: AHK, Amsterdam, Avans, Fontys, Hanze, HKDH, Inholland, Utrecht UAS of the Arts, Windesheim, Zuyd
Research institutes and expertise centres: Netherlands Institute for Art History, NSCR, RCE, WRR
Research funding bodies: NPRO SIA, NWO
Ministries: Education, Culture and Science; Security and Justice
International: Horizon 2020, UN SDGs

This route connects the following questions:

063, 065, 066, 067, 068, 071, 110, 111, 140

Art: research and innovation in the 21st century

001	002	003	004	005	006	007	008	009	010
011	012	013	014	015	016	017	018	019	020
021	022	023	024	025	026	027	028	029	030
031	032	033	034	035	036	037	038	039	040
041	042	043	044	045	046	047	048	049	050
051	052	053	054	055	056	057	058	059	060
061	062	063	064	065	066	067	068	069	070
071	072	073	074	075	076	077	078	079	080
081	082	083	084	085	086	087	088	089	090
091	092	093	094	095	096	097	098	099	100
101	102	103	104	105	106	107	108	109	110
111	112	113	114	115	116	117	118	119	120
121	122	123	124	125	126	127	128	129	130
131	132	133	134	135	136	137	138	139	140

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Quality of the environment: the value of nature, landscape, soil, climate, water, and the ecology

Importance of route

This route encompasses all the questions that address the overall quality of the environment. It addresses such topics as nature, landscape, ecology, soil, water, and climate. The quality of the environment is important to society in different ways: it provides feedstock for sustainable production, it is a source of enjoyment and experience, it is a factor in human health, it is important to our physical safety, it is part of our identity, it is a location factor for businesses, and it is valuable in and of itself. When the quality of the environment is satisfactory, it is beneficial in all these different ways simultaneously. On the one hand, this route involves developing new technologies and new production systems that do not damage but rather improve the quality of the environment. On the other, it challenges us to utilise the environment in a way that supports social and economic progress. For example, biodiversity is harmed by some economic trends, but it is also a valuable resource for others.

Potential new connections

The route encompasses a wide variety of interconnected issues that have a major impact on prosperity and wellbeing. They include climate change, water quality, sustainable agriculture and horticulture, the condition of the soil, and biodiversity. Not only are the analytical and technical aspects important, but also experience, perception, and what action the authorities can take. The latter question is highly relevant at the moment because the Dutch government is working on a new environmental planning strategy. This route links applied research questions with questions that are more basic, conceptual, and normative in nature.

Cluster questions illustrating scope and connective power of route:

- What do humans and nature mean to each other and what is the ideal relationship between the two?
- Why is biodiversity important and how do we protect it?
- How can we make agricultural production systems more sustainable as the worldwide demand for healthy, safe food continues to grow?
- How many people can the Earth sustain?
- How can we create a truly circular economy so that industrial goods manufacturing depends less on primary raw materials?

This route connects the agendas of the following institutions:

Universities: EUR, RUG, RU, TU/e, TUD, UL, UM, UT, UU, UvA, UvT, VU, WUR, 3TU
Medical centres: AMC, LUMC
UAS: Arnhem and Nijmegen, Avans, Den Bosch, Fontys, Hanze, Inholland, Leiden, Rotterdam, The Hague, VHL, Viaa, Vilentum, Windesheim, Zeeland, Zuyd
Research institutes and expertise centres: CPB, DIFFER, IFV, KNAW NIOO, KNMI, Movisie, NIVEL, NIOZ, NSCR, RIVM, PBL, Police Academy, SCP, SRON, SWOV, (TO2) Deltares, (TO2) MARIN, (TO2) TNO, (TO2) WUR, WRR
Research funding bodies: NWO, NPRO SIA, ZonMw
Ministries: Defence; Economic Affairs; Foreign Affairs; Infrastructure and Environment; Security and Justice; Social Affairs and Employment
Top economic sectors: Agri & Food, High Tech Systems and Materials, Horticulture and Starting Materials, Water
International: Horizon 2020, UN SDGs

This route connects the following questions:

001, 002, 003, 004, 006, 007, 008, 009, 012, 013, 015, 018, 019, 020, 021, 022, 023, 028, 030, 045, 052, 078, 097, 118, 119, 124, 138

Quality of the environment: the value of nature, landscape, soil, climate, water, and the ecology

001	002	003	004	005	006	007	008	009	010
011	012	013	014	015	016	017	018	019	020
021	022	023	024	025	026	027	028	029	030
031	032	033	034	035	036	037	038	039	040
041	042	043	044	045	046	047	048	049	050
051	052	053	054	055	056	057	058	059	060
061	062	063	064	065	066	067	068	069	070
071	072	073	074	075	076	077	078	079	080
081	082	083	084	085	086	087	088	089	090
091	092	093	094	095	096	097	098	099	100
101	102	103	104	105	106	107	108	109	110
111	112	113	114	115	116	117	118	119	120
121	122	123	124	125	126	127	128	129	130
131	132	133	134	135	136	137	138	139	140

14	2	17	20			3	6	4	2

Logistics and transport in an energetic, innovative, and sustainable society

Importance of route

The Dutch economy relies on efficient, safe, and convenient passenger and goods transport. We still have much to gain in that regard. New technical and logistical systems are vital to our ability to meet the growing demand for transport, minimise the pollution that it causes, and make it safer, more pleasant, and more convenient for those who use it. This is true of each individual form of transport, whether on the road, on the rails, in the air, or on the water. An even bigger challenge, however, is to achieve these aims for the transport system as a whole. The Dutch logistics sector has an added value of 55 billion euros a year and employs 813,000 people. The Netherlands transports 3.7% of all the goods traded in the world, although its populace accounts for only 0.25% of the world population and its manufacturing industry for only 1% of global production.

Potential new connections

Transport and logistics are vital to the timeliness and reliability of arrivals (passengers) and deliveries (goods). The quality of this sector has a direct impact on where businesses position themselves in the market, on the climate for international investment, on employment, and more generally on the economy of the Netherlands and its position in the global economy. A good quality, highly developed transport and logistics sector can boost the Netherlands' position as a credible partner in the logistical management of worldwide goods flows. We face a number of challenges in this regard. In terms of sustainability and quality of living conditions, there is the ecological footprint that transport leaves behind (for example in terms of energy consumption, fine particle and carbon dioxide emissions, and noise pollution). That footprint is relatively large, but it does vary from one form of transport to the next. Solutions range from making more efficient use of existing systems to developing and implementing new systems and techniques. Urbanisation raises questions about the way space is being occupied and used, and it is inextricably bound up with innovative logistical passenger and goods transport systems. Transport and logistics have a huge impact on spatial planning and hence on the social and cultural aspects of society.

Cluster questions illustrating scope and connective power of route:

- What are smarter and greener ways of transporting passengers and goods that make optimal use of all forms of transport?
- How can more fuel-efficient ships, aeroplanes, vehicles, trains and other means of transport contribute to the energy efficiency and environmental-friendliness of the overall transport system?
- How can we improve traffic and transport safety?
- What are the implications and challenges associated with worldwide urbanisation?

This route connects the agendas of the following institutions:

Universities: EUR, RUG, TU/e, TUD, UM, UT, UvA, VU, WUR, 3TU
Medical centres: AMC
UAS: Amsterdam, Arnhem and Nijmegen, Fontys, Rotterdam, Windesheim
Research institutes and expertise centres: CPB, CWI, DIFFER, IFV, KiM, KNMI, NIOZ, (TO2) Deltares, (TO2) ECN, (TO2) MARIN, (TO2) NLR, (TO2) TNO, (TO2) WUR, PBL, SWOV
Research funding bodies: NWO
Ministries: Economic Affairs; Infrastructure and the Environment
Top economic sectors: Energy, High Tech Systems and Materials, Logistics, Water
International: Horizon 2020

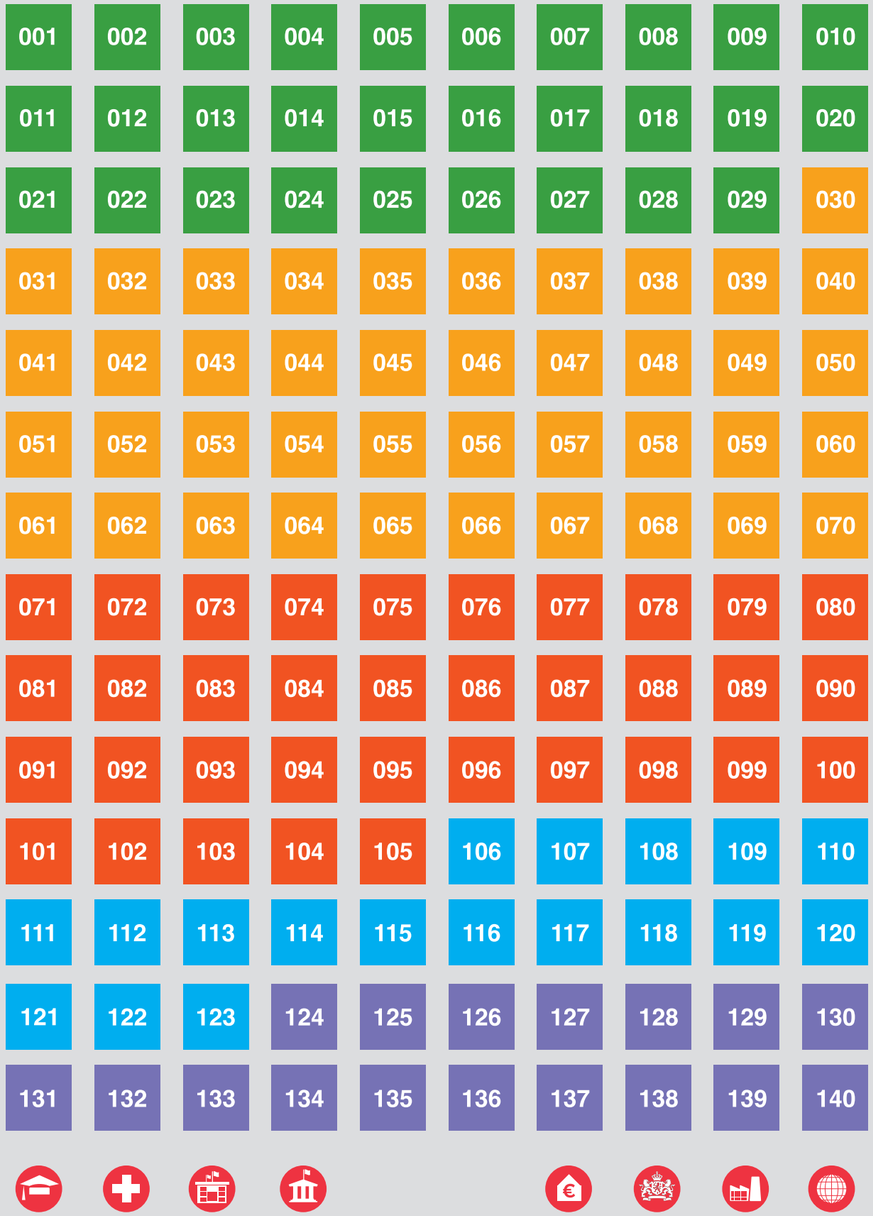
This route connects the following questions:

008, 011, 027, 028, 029, 045

Logistics and transport in an energetic, innovative, and sustainable society

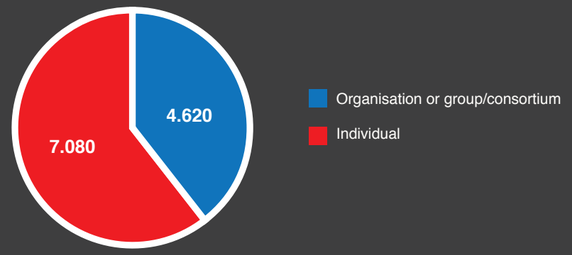
001	002	003	004	005	006	007	**008**	009	010
011	012	013	014	015	016	017	018	019	020
021	022	023	024	025	026	**027**	**028**	**029**	030
031	032	033	034	035	036	037	038	039	040
041	042	043	044	**045**	046	047	048	049	050
051	052	053	054	055	056	057	058	059	060
061	062	063	064	065	066	067	068	069	070
071	072	073	074	075	076	077	078	079	080
081	082	083	084	085	086	087	088	089	090
091	092	093	094	095	096	097	098	099	100
101	102	103	104	105	106	107	108	109	110
111	112	113	114	115	116	117	118	119	120
121	122	123	124	125	126	127	128	129	130
131	132	133	134	135	136	137	138	139	140

10	1	5	15			1	2	4	1

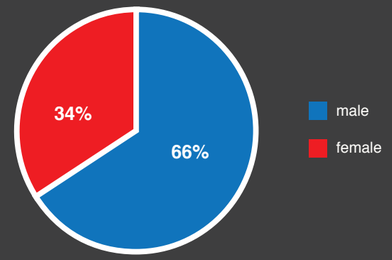


Appendix 1 Characteristics of the submitted questions

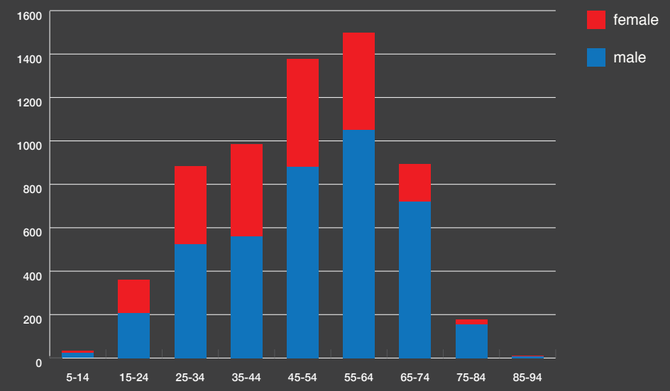
Total questions submitted (11.700) by organisations and individuals



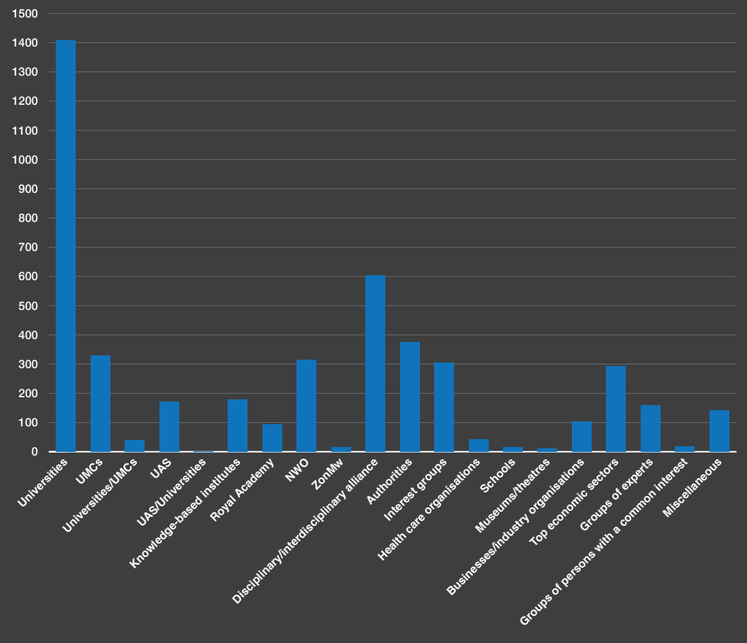
Individually submitted questions by gender



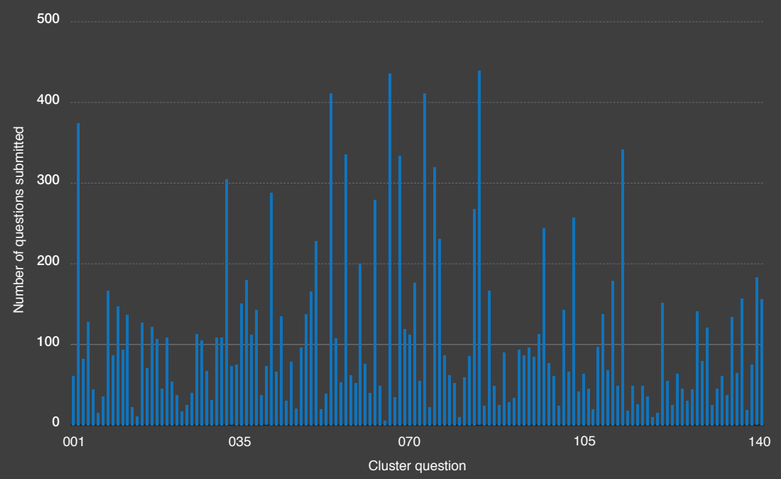
Individually submitted questions by age and gender



Source of the 4620 questions submitted by organisations



Clustering of the 11.700 questions into 140 cluster questions



The 11,700 questions were grouped by subject into 140 cluster questions. The cluster questions therefore represent differing numbers of original questions. The figure above shows how that number varied from cluster question to cluster question. A few questions stand out. The cluster questions about the circular economy, education in the future, health and lifestyle, and mental disorders represent more than 400 original questions. The cluster question about testing methods in the social sciences covers only six original questions, the smallest number of all the cluster questions.

Subject matter of the questions

Appendix 2 Research agendas

Universities
- Utrecht University
- Leiden University
- University of Groningen
- University of Amsterdam
- VU University
- Erasmus University Rotterdam
- Radboud University Nijmegen
- Tilburg University
- Maastricht University
- Delft University of Technology
- Eindhoven University of Technology
- University of Twente
- Wageningen University and Research Centre

University Medical Centres
- Netherlands Federation of University Medical Centres
- University Medical Centre Utrecht
- Leiden University Medical Centre
- University Medical Centre Groningen
- Academic Medical Centre
- VU University Medical Centre
- Erasmus Medical Centre
- Radboud University Medical Centre
- Maastricht University Medical Centre
- Netherlands Cancer Institute Antoni van Leeuwenhoek

Universities of Applied Sciences (UAS)
- Amsterdam
- Amsterdam University of the Arts
- Arnhem and Nijmegen
- ArtEZ Institute of the Arts
- Avans
- Breda
- Christian UAS Ede
- De Kempel
- Den Bosch
- Design Academy Eindhoven
- Driestar Christian University for Teacher Education
- Fontys
- Gerrit Rietveld Academy
- Hanze UAS Groningen
- InHolland
- iPabo Academy of Applied Sciences
- Iselinge
- Leeuwarden
- Leiden
- Marnix Academy
- Rotterdam
- Royal Academy of Art The Hague
- Saxion
- Stenden
- The Hague
- The Hague Hospitality Business School
- Utrecht
- Utrecht UAS of the Arts
- Van Hall Larenstein (VHL)
- Viaa
- Vilentum
- Windesheim
- Zeeland
- Zuyd
- Zwolle

Research institutes and expertise centres

NWO institutes
- Advanced Research Center for Nanolithography (ARCNL)
- Centre for Mathematics and Computer Science (CWI)
- Data Archiving and Networked Services (DANS)

Both NWO and KNAW
- Foundation for Fundamental Research on Matter (FOM *Including Institute for Nuclear Physics and High Energy Physics NIKHEF, Dutch Institute For Fundamental Energy Research DIFFER & AMOLF Institute*
- Netherlands eScience Center (NLeSC)
- Netherlands Institute for Radio Astronomy (ASTRON)
- Netherlands Institute for Space Research (SRON)
- Netherlands Institute for the Study of Crime and Law Enforcement (NSCR)
- Royal Netherlands Institute for Sea Research (NIOZ)

Academy (KNAW) institutes
- Fungal Biodiversity Centre
- Fryske Akademy (FA)
- Hubrecht Institute for Developmental Biology and Stem Cell Research
- Huygens Institute for Netherlands History (ING)
- International Institute of Social History (IISG)
- Meertens Institute *Research and documentation on Dutch language and culture*
- Netherlands Heart Institute (ICIN)
- Netherlands Institute for Advanced Study in the Humanities and Social Sciences (NIAS)
- Netherlands Institute for Neuroscience (NIN)
- Netherlands Institute of Ecology (NIOO)
- Netherlands Interdisciplinary Demographic Institute (NIDI)
- NIOD Institute for War, Holocaust and Genocide Studies
- Rathenau Institute
- Royal Netherlands Institute of Southeast Asian and Caribbean Studies (KITLV)
- Spinoza Centre for Neuroimaging

TO2 Federation
- TNO Netherlands Organisation for Applied Scientific Research
- Agricultural Research Service
- Deltares
- Energy Research Centre of the Netherlands (ECN)
- National Aerospace Laboratory (NLR)
- Maritime Research Institute Netherlands (MARIN)
- Wageningen Univesity and Research Centre (WUR)

Ministerial expertise centres
- Cultural Heritage Agency (RCE)
- Netherlands Bureau for Economic Policy Analysis (CPB)
- Netherlands Environmental Assessement Agency (PBL)
- Netherlands Forensic Institute (NFI)
- Netherlands Institute for Art History (RKD)
- National Institute for Public Health and the Environment (RIVM)
- Netherlands Institute for Social Research (SCP)
- Netherlands Institute for Transport Policy Analysis (KiM)
- Research and Documentation Centre
- Royal Netherlands Meteorological Institute (KNMI)
- Scientific Council for Government Policy (WRR)
- Statistics Netherlands (CBS)

Non-academic expertise centres
- Amsterdam Health and Technology Institute (AHTI)
- Amsterdam Institute for Advanced Metropolitan Solutions (AMS-Institute)
- Biomedical Primate Research Centre
- Boekman Foundation: Study Centre for arts, culture, and related policy
- Clingendael Netherlands Institute of International Relations
- Colaborative Organisation for ICT in Dutch education and research (SURF)
- Geonovum
- Institute for Physical Safety (IFV)
- Movisie
- Mulier Institute, Centre for Research on Sports in Society
- Netherlands Aerospace Centre
- Netherlands Defence Academy
- Netherlands Institute for Art History
- Netherlands Institute for Health Services Research (NIVEL)
- Netherlands Youth Institute
- Police Academy
- Sanquin
- SWOV Institute for Road Safety Research
- Trimbos Netherlands Institute of Mental Health and Addiction
- Veiligheid NL
- Vilans

Appendix 3 Policy agendas

Ministries
- Ministry of Defence
- Ministry of Economic Affairs
- Ministry of Education, Culture and Science
- Ministry of Foreign Affairs
- Ministry of Health, Welfare and Sport
- Ministry of Infrastructure and the Environment
- Ministry of Security and Justice
- Ministry of Social Affairs and Employment

Top economic sectors
- Chemistry
- Creative Industry
- Energy
- High Tech Systems & Materials
- Horticulture & Starting Materials
- Life Sciences & Health
- Logistics
- Water

Research funding bodies
- Netherlands Organisation for Scientific Research
- Netherlands Organisation for Health Research and Development ZonMW
- National Initiative Brain & Cognition NIHC
- Netherlands Initiative for Education Research NRO
- Taskforce for Applied Research SIA

Regional agendas
- European Regional Development Fund - North
- European Regional Development Fund - South
- European Regional Development Fund - West
- European Regional Development Fund - East

International
- United Nations Sustainable Development Goals (Global Goals)
- The EU Framework Programme for Research and Innovation Horizon 2020

Appendix 4 Questions sorted into ten Horizon 2020 themes

Seven of the ten themes are based on the Societal Challenges in the third pillar of the Horizon 2020 Agenda. One theme ('key enabling technologies') corresponds with an important focus area in the second pillar of Horizon 2020. The remaining two themes ('culture and identity' and 'fundamentals of life and the universe') are not referred to explicitly in Horizon 2020, but do come within the remit of the European Research Council in the first pillar. In that sense, each of the 140 cluster questions fits into a European Union slot. That means that the five chapters into which we have divided the 140 cluster questions are also related to the ten Horizon 2020 Agenda themes, as the following table shows.

Themes borrowed from Horizon 2020 Agenda	Chapter heading
Climate action, environment, resource efficiency and raw materials	Man, the environment, and the economy
Food security, sustainable agriculture and forestry, marine and maritime and inland water research and the bio-economy	
Secure, clean and efficient energy	
Smart, green and integrated transport	
Europe in a changing world – inclusive, innovative and reflective societies	Individual and society
Secure societies – protecting freedom and security of Europe and its citizens	
Culture and identity	
Health, demographic change and wellbeing	Sickness and health
Key enabling technologies	Technology and society
Fundamentals of life and the universe	Fundamentals of existence

The following table lists each of the 140 cluster questions under its relevant Horizon 2020 theme.

MAN, THE ENVIRONMENT, AND THE ECONOMY

Climate action, environment, resource efficiency and raw materials

001 How many people can the Earth sustain?
002 What do humans and nature mean to each other and what is the ideal relationship between the two?
003 Why is biodiversity important and how do we protect it?
004 How do ecosystems function and how vulnerable are they to environmental impacts?
005 What role do micro-organisms play in ecosystems and how can we use them to improve health and the environment?
006 How can we protect and preserve the quality of the subsoil for humans and the environment while leaving room for social and economic development?
007 How can we measure and model the interaction between ice, atmosphere, and ocean so that we can reliably forecast a rise in the sea level?
008 How is the climate changing, including extreme weather, and what impact will those changes have?
009 How can we make better use of the carbon, nitrogen, and phosphorous cycles?
010 How can we use new materials, technologies, and processes to lower the cost of buildings and infrastructure and make them safer and more sustainable?

Food security, sustainable agriculture and forestry, marine and maritime and inland water research and the bio-economy

011 How can we ensure proper water governance in the future?
012 How do the seas and oceans function, and what role will they play in the future?
013 What eco-friendly methods can we use to protect ourselves against floods?
014 How can mimicking plant photosynthesis contribute to a new green revolution?
015 How can we make agricultural production systems more sustainable as the worldwide demand for healthy, safe food continues to grow?
016 How can we develop healthy new food crops that have higher yields while requiring fewer harmful chemicals?
017 How can we make chemical and biochemical production processes more sustainable, more efficient, and cleaner?

Secure, clean and efficient energy

018 How can we quickly make our energy supply greener while keeping it affordable and reliable?
019 How should we undertake the transition to an entirely sustainable energy supply?
020 How can the sun meet all our energy needs?
021 What is the most efficient and sustainable way of converting wind energy into electricity?
022 What is the most efficient way to use rivers, lakes, seas, and oceans to generate energy?
023 How can we optimise our use of geothermal energy?
024 How can we use biomass as a feedstock and to generate energy in a bio-based economy?
025 How do we accelerate the development of nuclear fusion, and how can we make nuclear energy safe and clean?
026 How can we store, convert, and transport energy efficiently?

Smart, green and integrated transport

027 What are smarter and greener ways of transporting passengers and goods that make optimal use of all forms of transport?
028 How can more efficient means of transport contribute to the energy efficiency and environmental-friendliness of the overall transport system?
029 How can we improve traffic and transport safety?

INDIVIDUAL AND SOCIETY

Europe in a changing world - inclusive, innovative and reflective societies

030 How can we keep our densely populated country liveable?
031 What does globalisation mean for our cultural identity and for the position of the Netherlands on the world stage?
032 What do Europeanisation and globalization mean for democracy and the constitutional state?
033 How robust is democracy, how much confidence does society have in it, and how can we make improvements in both cases?
034 How robust is the welfare state, given the changing composition of the Dutch population?
035 How can we best design the socioeconomic institutions of the future?
036 How are digitisation, globalisation, a more assertive public, and other changes in society impacting public and semi-public institutions?
037 How has the most recent major recession impacted society, and how can financial systems be reformed to avert such crises in the future?
038 How do we strike the right balance between freedom and responsibility (individual and collective)?
039 How can the law and other forms of regulation provide sufficient legal certainty while also responding to opportunities and challenges in society?
040 How can we improve the effectiveness and legitimacy of legislation, given the global challenges we face with respect to the environment, security, innovation, energy, and climate change?
041 What is the 'inequality problem'?
042 How can we limit poverty and increase wellbeing worldwide?
043 What are the causes and consequences of migration, and how can we deal with them?
044 Can globalisation and development be reinvented in a way that, in time, will mitigate differences in prosperity between world regions?
045 What are the implications and challenges associated with worldwide urbanisation?
046 What is Europe? Past, present and future
047 How can we promote social cohesion in a society that is culturally and religiously diverse?
048 How can we encourage self-reliance and social participation?
049 How can we ensure that our labour force and labour-market organisations remain robust and resilient as they face the challenges of the 21st century?
050 What is the secret of a resilient society?
051 Smart industry – How do we make our factories smarter?
052 How can we create a truly circular economy so that the manufacturing of industrial goods depends less on primary raw materials?
053 What are the characteristics of a circular economy and how can we achieve it?
054 How do we ensure that the Dutch economy remains competitive?

Secure societies - protecting freedom and security of Europe and its citizens

055 How do we protect ourselves against natural disasters (such as earthquakes, volcanic eruptions, and floods)?
056 How can we promote peace, security, and cooperation – and address threats and violations – within and between constitutional states and within and between groups and societies?
057 Can we find the right balance between freedom of information and privacy?
058 What are the patterns and causes of crime and how can we influence them?
059 How can we ensure that children and adolescents grow up safe and healthy?
060 How do we guarantee our digital freedom?

Culture and Identity

061 Are modernity and religion each other's opposites?
062 How does science operate, what is good science, and how can policy key into it?
063 How objective are cultural canons?
064 How can we develop new testing methods in the social sciences?
065 What should education be like in the future?
066 Does knowing about materials change the way we think about artwork, tangible cultural heritage, the built environment, and their preservation?
067 What does art mean to people?
068 How can we promote and utilise creativity and innovation?
069 What causes language variation and why do we understand each other despite the differences?
070 Why do we do what we do, are we who we think we are, and what factors influence our behaviour? In other words, how can we understand our behaviour?

SICKNESS AND HEALTH

Health, demographic change and wellbeing

071 What do we mean by 'quality of life'?
072 How do a healthy lifestyle and wholesome habits promote good health and prevent illness?
073 What effect is the rising 24-hour economy having on human health and performance and how can our knowledge of biorhythms enhance the relationship between the individual and society?
074 How does sleep affect our health?
075 How can we use sport, exercise, and nutrition to promote good health and what effects will this have?
076 What are the consequences of chronic disorders, stress, and disabilities and what is the best way to deal with them?
077 What do non-genetic factors contribute to personal traits and disease processes?
078 How does the built environment affect health and wellbeing?
079 What is the impact on human beings of electromagnetic fields (EMFs), for example as emitted by wireless devices and high-voltage power lines?
080 Can we gain a better understanding of the factors that play a role in the occurrence and persistence of long-term, medically unexplained physical symptoms, leading to better treatments for them?
081 How will our knowledge of genetics play a role in analysing, screening for, and treating diseases?
082 How does the central nervous system develop and how can we counteract degeneration processes in that system?
083 How do neurological, psychiatric, and mental disorders arise, and how can we prevent, mitigate, or cure them?
084 What is the best way for us to analyse and prevent the problem of overweight and obesity?
085 Every tumour is different, so how can we come to understand cancer well enough to develop a treatment for each and every type?
086 Intestinal disorders, and specifically the relationship between gut flora and health: what can we do to benefit our gut flora?
087 What causes type 1 and type 2 diabetes, how can we detect them sooner, and how can we treat them on an individual basis?
088 How can we predict, prevent, and treat cardiovascular diseases (atherosclerosis, heart failure, heart arrhythmia, and thrombosis) in individuals at an early stage?
089 How can we improve our understanding and treatment of pulmonary diseases?
090 What causes chronic kidney disease, how can we detect it sooner, and how can we treat it on an individual basis?
091 Pregnancy, childbirth and menopause: can enhanced insight into these processes contribute to a more comfortable experience?
092 Can we combine mainstream and complementary therapies, leading to integrative health care that allows for the many differences between patients?
093 How can we promote innovativeness, quality, and accessibility in institutionalised and informal forms of care?
094 How do we improve the quality of health care as much as possible while keeping it affordable?
095 How can we personalise health care, for example by using biomarkers?
096 How can we improve diagnostics, treatment, and vaccines for immunodeficiencies and infectious diseases?
097 How can we control micro-organisms in health care, livestock farming, and the environment?
098 How can we use breakthroughs in basic biomedical research to develop new medicines?
099 How can a broader definition of 'life' help us identify new targets for molecular therapies, antibiotics, and antiviral drugs?
100 How can we use cells, stem cells, and biomaterials to engineer and regenerate tissues and organs?
101 Can we model the human body and use smart technologies for health, nutritional, and toxicity research, drastically reducing the use of laboratory animals at the same time?
102 How can we develop new drugs and treatment methods that will keep us as healthy and vigorous as possible?
103 How can we understand and assess the potential and limitations of medical progress?
104 How do we develop minimally invasive techniques and interventions for diagnosis, prognosis, and treatment?
105 How can big data and technological innovation (e-health) contribute to health care?

TECHNOLOGY AND SOCIETY

Key enabling technologies

106 What transformation will we see in the manufacturing, service, and maintenance industries, and which technological innovations will make this possible?

107 How can we anticipate the impact of new technologies on humans and society, and understand and evaluate the influence of existing technologies?

108 What social changes are imminent owing to advancing technology and how will they affect prosperity?

109 How are new technologies and big data impacting the effectiveness of public administration and the constitutional state?

110 How do the old and new media influence individuals and society?

111 Will digitisation save our cultural heritage?

112 Can we use big data and big data collection to define values, generate insights, and get answers?

113 Can we develop human language technology (HLT) that allows us to communicate with our computers (smartphones, tablets)?

114 How can we connect 'things' (hardware) all the time and everywhere and boost processing speed while using less energy?

115 How can we build and maintain future-proof software?

116 Can we extend Moore's Law in the post-silicon era?

117 What will quantum computing and the quantum internet mean for our future?

118 How can we develop the stable and selective catalysts that we need to make the transition to sustainable energy and production systems and a bio-based economy?

119 How can we remove fine particles, harmful gases, and pathogens from the air and keep it clean?

120 Can we design smart materials and structures that have new and advanced properties?

121 Can we design electronic or bio-electronic systems that communicate directly with our bodies as well as materials and technology that restore or support human body functions?

122 Can we build a synthetic cell?

123 How can we manage the unpredictability of complex networks and chaotic systems?

FUNDAMENTALS OF EXISTENCE

Fundamentals of life and the universe

124 How can we bridge different scales when modelling dynamic systems, for example fluid and gas flows?

125 What symmetries are hidden in prime numbers and how can number theory in mathematics inform theory-building in physics?

126 What role does quantum physics play in macroscopic systems and what spectacular new phenomena and applications does it make possible?

127 What are the origins, history, and future of the universe?

128 Have we identified all the elementary particles of matter?

129 What is the true nature of gravity, space, and time and what can we learn from black holes?

130 What is dark matter and what is dark energy?

131 How are galaxies, stars, and planets born and how do they evolve?

132 How can spacecrafts and telescopes help us learn more about the universe and explore our own solar system?

133 Is there life beyond our Earth?

134 How did life arise and how does evolution work?

135 How can we learn more about molecular properties, functions, and interactions in living systems, so that we can develop life-inspired systems ourselves, for example?

136 Cells are the building blocks of life. How do they work and what can they teach us about life processes?

137 How does a zygote (a fertilised egg cell) develop into a complex organism with various specialised tissues and organs?

138 How and why do animals do what they do?

139 How does our brain process and retain information, and what role do plasticity and networks play at different microscopic and macroscopic levels?

140 As human beings, what are we capable of knowing about ourselves, God, and our place in the cosmos, and to what extent can science help us in this respect?