S&T&I FOR 2050

Science, Technology and Innovation for Ecosystem Performance – Accelerating Sustainability Transitions

CASE STUDY: ECOSYSTEMS AND MICRO-AND NANO COSMOS

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November 2022

1. INTRODUCTION

The influential narratives about new nano-materials, the threats from micro-plastics and the threats to human and animal health through antimicrobial resistance, have risen attention of policy makers, strong enough to create new topics for established policy fields and research. This case study explores how a strong focus on ecosystem flourishing could change the current thinking about the narrative towards micro-and nano cosmos (MNC).
The search for knowledge about the micro-nano cosmos creates the possibilities for new fundamental understandings as well as new generic technologies. At the same time the knowledge about potential risks and threats to the health of humans, non-human life and flourishing of ecosystems is often lagging. This case study explores the aspects of micro-and nanoscale materials and systems, interacting with biological systems and thus having an influence and drive processes at the ecosystem scale on human and non-human agents. It follows the need for new approaches to understand potential impacts of nano / bio molecular agents in the environment. All this has, or may have, implications for human wellbeing as well as the role of humans in ecosystem stewardship.

The case study provides the following sections:
Status Quo Analysis: It outlines some of the current developments, (1) by sketching the ongoing innovation activities in the micro-nano cosmos and (2) discuss developments on the micro-nanoscale with potential effects threatening ecosystem stewardship and human health.
Scenario Sketching: In this section a range of possible micro-nano-scale scenarios are narrated in the light of the three perspectives of ecosystem flourishing.
Policy Implications: The case study furthermore discusses implications for STI policy to address the Micro-nano cosmos -- to inform programming and implementation of Horizon Europe and future STI frameworks.

2. STATUS QUO OF INNOVATIONS AND ISSUES OF POTENTIAL THREATS

Nanotechnology, the manipulation of nanomaterials for several purposes, plays an ever increasing for human- and non-human agents in ecosystem performance. Applications in the food and agriculture sectors and addressing human health through novel and innovative approaches are taking place on multiple size levels (Nile, S.H. et al., 2020; S.E. McNeil, 2005), which we consider as the scales of the micro- and nano-cosmos (MNC).

With the environmental and health related issues of nanotechnologies and cleaning up micro-plastics in the societal discourse, scientific communities have been drawing more attention on life-forms on those scales. Also, technological developments on the micro-nano scale, from new materials to self-organising and self-replicating cellular robots are expected to shape the micro- and nano-cosmos. Along with the prospects that nanotechnology holds for innovation comes the caveat that this is uncharted scientific territory and may have potential risks and hazards. There is evidence that certain nanoscale particles can have detrimental effects on living organisms (S.E. McNeil, 2005).
In two different parts, we will outline some of the current developments.
In the first part “Innovation in the Micro-Nano Cosmos” ongoing innovation activities are sketched, such as self-replicating materials, organoids, xenobots, bioactive materials, bioeffectors, biostimulants and microbe-assisted crop production, cell factories, bio-inspired materials and plastic-degrading enzymes.
In the second part “Issues of Potential Threats from the Micro- and Nanoscale”, we discuss developments on the micro-nanoscale with potential critical impacts on ecosystem stewardship and human health. We draw on results of the Delphi Study about harms for ecosystem performance and explore issues such as antibiotic resistance, microplastic, micro-flotation processes.
It is not always unambiguous to categorize some of the analysed developments below to either innovation

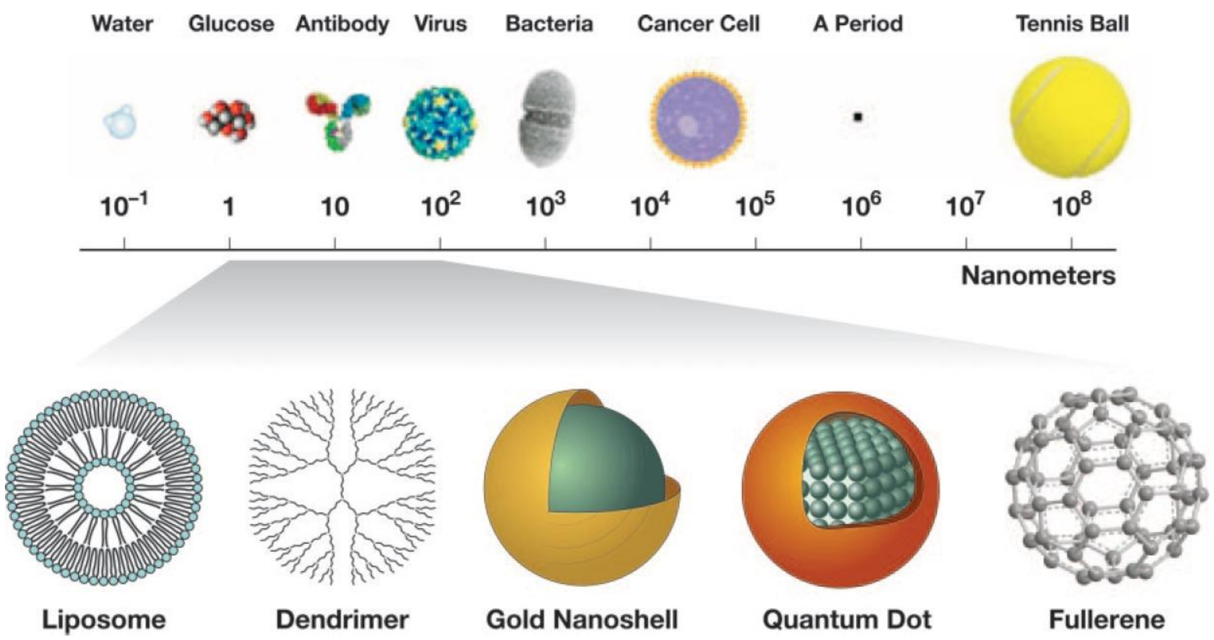


Figure 1 Different sized nanoparticles used in nanotechnologies. This figure was modified and adopted from [S.E. McNeil, (2005). https ://doi.org/10.1189/jlb.02050 74]

activities or potential threats. Hence, for each of the innovation activities and impact issues, challenges and opportunities are discussed.

3. INNOVATION IN THE MICRO-NANO COSMOS

When exploring the micro-nano cosmos, it becomes clear that a major part of innovative activities takes place in the realm of materials, but also touches upon fields of application such as medicine, construction, packaging and food supply. The relevance of nanotechnologies for ecosystem stewardship appears to resemble the seminal work of Roco and Bainbridge (2003) on converging technologies for improving human performance. The following overview provides evidence that converging technologies between nano-bio, nano-bio-computing, nano-robotic etc. also play a role for "ecosystem performance".

STI 2050: Delphi Results:
Several of the STI-direction from STI 2050 -Delphi Report[1] are related to innovation in the micro- and nano-cosmos such as: Graphene membranes that artificially mimic photosynthesis; Water decontamination technologies like filtering products - e.g. graphene filters and nanopowder for removing toxic metal ions; Nanofertilizers and nano chelated iron fertilizers; Nanomaterials to improve plant stress tolerance; Nano-composite films for food packaging; Nano-based precision farming to optimize crop used to produce biofuel; Antimicrobial polymeric bio-nanocomposites for food packaging, drug delivery; tissue engineering; Light weight and eco-friendly bio-nanocomposites to replace non-biodegradable petroleum-based plastics; Engineered nanocomposites for need-based delivery of agrochemicals; Nanocomposites to eliminate bacteria, viruses, and inorganic and organic pollutants from wastewater; Nanocarbon based composites for agriculture, energy storage devices, photocatalysis, water purification; Heavy nanocomposites for gamma shielding; Nanoparticles for dentistry; Nanocomposites as heterogeneous catalysts; Agricultural nanotechnology: e.g. Nano-pesticide delivery; Slow and controlled release of nanoparticles containing biofertilizers or nano biosensors for rapid detection of phytopathogen and other biotic and abiotic stresses; Biocomputers: e.g. microbial nanowires, lipid 'nanotablet' resembling cell membrane to perform Boolean logic operations.

Self-replicating materials

A "self-replicator" is usually understood to be an object of definite form that promotes the conversion of materials in its environment into a nearly identical copy of itself (Sakar & England 2019). The challenge of engineering novel, micro- or nanoscale self-replicators has attracted keen interest in recent years, both because exponential amplification is an attractive method for generating high yields of specific

1 https://www.futures4europe.eu/_files/ugd/ff6ca7_bf90fad2a518441ba4d1f11d3ada3cfc.pdf

products and, also, because self-reproducing entities have the potential to be optimized or adapted through rounds of iterative selection. Substantial steps forward have been achieved both in the engineering of particular self-replicating molecules and in the characterization of the physical basis for possible mechanisms of self-replication (Sakar & England 2019). Other terminology used in this context is molecular manufacturing, self-reproducing machines, exponential manufacturing or in the context of biotechnology artificial life. Most research has been conducted in biological studies concentrating on natural replications investigating the origin of life and the ability of DNA, RNA and other organic molecules to self-replicate. Industrial applications concentrate on space exploration and manufacturing, applying nanotechnology and nano scale assemblers, while in computer science self-reproducing computer programs that infect computers such as computer worms and computer viruses are examples for self-replicating approaches.

Opportunities: Fast progress is being made in these research areas and, as with all new technologies appearing, there is a vivid discussion ongoing between those wishing to exploit these new opportunities as rapidly as possible and those wishing to wait –forever, if necessary–to have it proved absolutely safe. Research on self-replicating systems that will eventually be programmable and enable new manufacturing bases that can produce both small and large objects precisely and inexpensively or even lead to the manufacturing of living objects and thus artificial life, is ongoing. There is a consensus that embedded controls can be integrated in designed systems at many dimensions of design properties. The development of such sensitive systems as self-replicating nano-systems requires close collaboration between policymakers and industry to develop and commercialize a manufacturing industry based on productive nano-systems designed for safety and reliability. For the application of nanotechnology Foresight guidelines[2] have been developed to ensure responsible development and application. Nanotechnology policy will have to balance risks with benefits and distinguish between different classes of risks. Molecular manufacturing and nanotechnology are not one technology, but rather a spectrum of technologies, with radically different risk profiles.

Challenges: The biggest concern about advanced forms of self-replication, after feasibility issues have been addressed, tends to concentrate on the possibility of the technology getting out of control. The risk of accident or malfunction is seen less problematic for new technologies than the dangers of abuse. Fuelled by scenarios by Drexler from 1986 popular science fiction describes molecular robots that are autonomous self-replicating machines or autonomous replicators that evolve beyond human control or cannot stop reproducing. While these scenarios are not entirely impossible, they are not considered as very likely and that other social and ethical concerns deserve more attention (Phoenix and Drexler 2004, Poel, 2016). This heated discussion about these scenarios and the description of popular science fiction on molecular robots is problematic as they draw moral and regulatory attention away from the more important ethical issues in fields.

Organoids

Organoids are so called mini-organs, able to self-assemble in three-dimensional structures that resemble real organs in architecture and function and that are grown in vitro from stem-cells. Human organoids have a huge potential for biomedical research and personalised medicine, as they allow for a detailed study of human cell pathologies and advancements in research related to transplants .

Opportunities: Organoids are regarded as one of the most significant developments in stem cell research and promise a wide range of application in research and in the clinic. Stored in biobanks organoids could contribute to fundamental research, precision medicine, and regenerative medicine, especially to advance the understanding of brain development or to serve as drug-testing tools. They could also help reduce animal testing.

Challenges: Despite the high potential attributed to organoids, a range of challenges remain that will need to be addressed in the future. Ethical issues concern the origin of the cells that are used to produce organoids, i.e., human embryos . This holds especially true for cerebral organoids, that exhibit neural connections and electrical activity, which raises the question of their status as living beings. Also questions of consent, ownership, commercialization, intellectual property rights, and safety come along with the production and use of organoids.

Xenobots

One example for a very recent development in micro-nanoscale R&I is the case of xenobots. Xenobots are living, computer-designed organisms that U.S. researchers have developed with the help of a supercomputer (Kriegman et al. 2020). They derive their name and cells from *Xenopus laevis* (Latin), the African clawed frog. The prefix "xeno" (derived from the Greek *xénos*, meaning "guest", "stranger") refers to the fact that the cells

2 https://foresight.org/about-nanotechnology/foresight-guidelines/

assembled into an organism can perform functions other than those intended by their original genetic blueprint. Propelled by synthetic biology (synbio), xenobots are a first example of an artificially created life form with special properties. They consist exclusively of living animal skin and (heart) muscle cells, which, through their continuous pulsation, allow the organisms limited movements. The living machines can swim, transport small loads, work together in groups and heal themselves. Such artificial organisms are developed with the help of artificial intelligence (AI) methods, i.e., an "evolutionary algorithm” aimed at producing different construction plans in numerous simulations, from which suitable designs are selected. The second generation of xenobots - also known as xenobots 2.0 - differs from the first generation in that the organisms, which develop from stem cells, self-assemble into a spherical body and do not require extra muscle cells to ensure their mobility (Blackiston et al. 2021).

Opportunities: The current focus is on demonstrating the feasibility of this new technology and advancing research on the mechanisms of life. Expectations in terms of societal benefits go in two directions, depending on the cell material used. Xenobots built from animal cells promise a vast potential for application, e.g., in detecting radioactive or toxic contamination in polluted areas or in cleaning the oceans of microplastics. If the artificial organisms are produced from human cells, they could be highly relevant for biomedical research. For example, xenobots that are developed from the body's own cells of a person suffering from cancer, could be used to deliver drugs to the site of the cancer tumour autonomously and in a targeted manner. The process would be similar to clearing calcified arteries of plaque from the inside. An advantage of this technology is seen in the better immune tolerance of the externally introduced organisms, as they could be developed from the affected person’s own body material.

Challenges: Although application is still a very distant, the current development raises far-reaching ethical and social questions. First and foremost, the central question: What are xenobots in the first place and what status would they have in our society? Do they fulfil sufficient requirements to be classified as living beings? And at what point should we consider and protect artificially created living beings as life forms with their own interests (Lavazza and Massimini 2018)? Much of the research on the artificial, living machines is done publicly and with the involvement of legal expertise. Even the source code used to develop the computer-designed beings is free and publicly available. Nevertheless, the question remains open as to how society's awareness of this complex and still immature development and its possible consequences can be raised.

Bioactive nanomaterials

The field of bioactive materials has grown rapidly over the last few decades, in biomedical device design and the development of tissue engineering solutions for cell delivery, drug delivery, device integration, tissue replacement, and more. Bioactive materials are materials that produce physiological response, differentiating it from biocompatible material, which is tolerated by the biological system it comes into contact with.

Bioactive nanomaterials are not a simple miniaturization of macroscopic materials. They exhibit unique bioactivities due to their nanoscale size effect, high specific surface area, and precise nanostructure, which can significantly influence the interactions with biological systems. Nowadays, bioactive nanomaterials have represented an important and exciting area of research (Zhao, Y., et al. (2021).

Opportunities: To improve the biocompatibility and biodegradability of delivered materials natural substrates are used, such as macromolecules native to plants and animals. Biomaterials are widely used in tissue engineering solutions in combination with cells, synthetic materials, and therapeutic molecules to produce advanced therapeutic medicinal products. A three-dimensional polymeric scaffold often provides a support structure for the delivery of cells and biologically actives components. There is an increasing trend in tissue engineering to use naturally occurring macromolecules as a starting material due to their advantageous properties, since such materials are well tolerated, promoting cellular adhesion, and subsequent tissue formation to facilitate body integration while their biodegradability allows for tissue remodelling (Joyce et al., 2021).

Challenges: The rapid expansion in the biomaterials toolkit comes at a cost; a considerable increased risk of adverse reactions to implanted biomaterials which includes allergies, chronic inflammation, susceptibility to infection, collateral tissue damage, and loss of functionality due to immune reactions. Moreover, the highly personalized nature of immune reactions needs to be taken into account while assessing the use of new biomaterials. These concerns have created a general reticence in the medical device industry for the utilization of novel biomaterials and complex, multi-material structures which significantly hinders the advances in the field and also decelerates the introduction of new and potentially transformative technologies to the healthcare system. Thus potential ways out of this conundrum Vrana et al (2019) suggest (i) to improve the capacities in the risk assessment of biomaterials by developing novel in vitro testing systems, preferably in a personalized manner (i.e., using patients' own cells); (ii) to develop new technologies to control the interface between the implanted materials and the host tissues where immune reactions can be either attenuated or directed toward expected outcomes (iii) to achieve systems level understanding of personalized response to biomaterials using the recent advances in high throughput analysis methods available (Vrana et al, 2019).

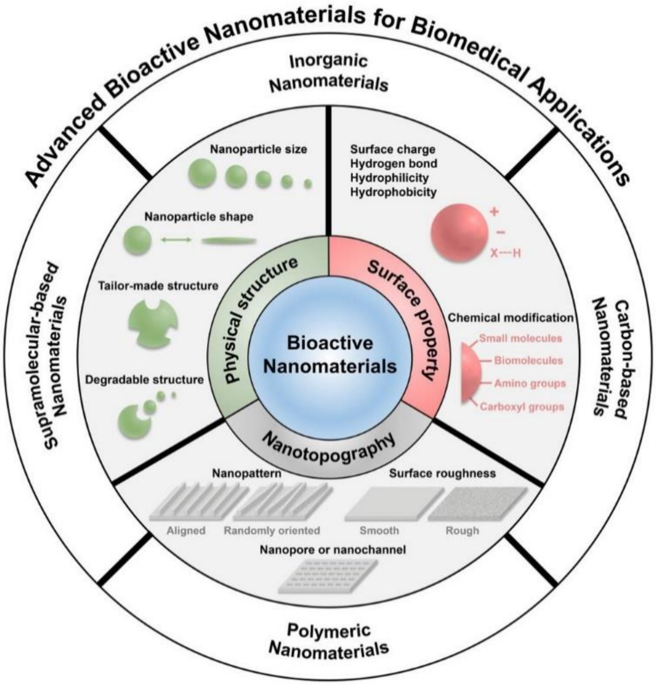


Figure 2 Advanced bioactive nanomaterials for biomedical applications [Zhao, Y., et al. (2021)]

Bioeffectors, Biostimulants and Microbe-assisted Crop Production

Biostimulants include organic compounds and microorganisms that are applied to plants or soils to improve crop yield, quality, vigour, and tolerance to insects, diseases, weeds, or abiotic stresses. Bioeffectors are special microorganisms or active naturally occurring compounds that, in symbiosis with certain other bacteria, contribute to improving crop traits (especially growth) and to the biological control of pathogens (Duque et al. 2019).

To understand the mechanisms by which the microbes enter the plant roots and spread throughout the plant, genetically modified organisms are used in advance under safe laboratory conditions in in vitro experiments and in the construction of control systems in the greenhouse. Plant biostimulants were defined by du Jardin (2015) as follows: "A plant biostimulant is any substance or microorganism applied to plants with the aim to enhance nutrition efficiency, abiotic stress tolerance and/or crop quality traits, regardless of its nutrient content". This definition could be completed by "By extension plant biostimulants also designate commercial products containing mixtures of such substances and/or microorganisms". The definition of plant biostimulants has been rigorously debated over the last decade, and recently under the new Regulation (EU) 2019/1009, which led to the following: "A plant stimulants shall be an EU fertilising product the function of which is to stimulate plant nutrition processes independently of the product's nutrient content with the sole aim of improving one or more of the following characteristics of the plant or the plant rhizosphere: i) nutrient use efficiency, ii) tolerance to abiotic stress, iii) quality traits, or iv) availability of confined nutrients in the soil or rhizosphere" (EU, 2019). (Rouphael Y and Colla G, 2020)

Du Jardin (2012) proposes eight categories of biostimulants, but also states that the functional distinction between them may be overlapping: 1) humic substances, 2) complex organic materials, 3) beneficial chemical elements, 4) inorganic salts, 5) seaweed extracts, 6) chitin and chitosan, 7) antitranspirants, 8) free amino acids and other N-containing substances.

Opportunities: Plant biostimulants including natural substances and microbial inoculants appear as a novel and potential category of agricultural inputs, complementing agrochemicals including synthetic fertilizers, and improving tolerance to abiotic stresses, as well as enhancing the quality of agricultural and horticultural commodities. Consequently, chemical fertiliser application and the use of chemical antimycotics can be reduced. The linking of biobased and digital technologies opens up further development paths, e.g. for new processes in white, red and green biotechnology or for personalised medical applications. Furthermore, the application of microbial and non-microbial plant biostimulants stimulate plant primary and secondary metabolism leading

to the synthesis and accumulation of antioxidant molecules (i.e., secondary metabolites) which are important for human (and animal) diet (Rouphael Y and Colla G, 2020).
Challenges: Legal aspects in terms of defining the diverse field of biostimulants are challenging the development, as currently new regulations are entering into force, which introduce a transitional period that allows industry to adapt.[3] Bioeffectors are also related to the debate on genetic engineering, as the microorganisms used for research can be genetically modified in the laboratory.

Cell Factories

One vision for the future in the production of novel materials is to make extensive use of living cells and their molecular components as cell factories on an industrial scale. To use microorganisms to produce special substances, biotechnology uses the process of metabolic engineering. In this design of customised metabolic and synthesis pathways in a cell, genetic control elements and biosynthesis genes from plants, animals or microorganisms can be combined to turn microbes into efficient cell factories - and use them to produce drugs, for example. Synthetic yeast cell factories are already possible on a laboratory scale, which will be able to produce the potential cancer drug noscapine in the future (cf. Li et al. 2018).
Opportunities: The future potential of cell factories in medicine, in the bio-based economy and in industrial applications is very far-reaching. However, some of the promising cell factories also call into question previous international regulatory approaches: yeast fungi can be modified in such a way that they can produce opium-like substances. This means that in the future highly effective painkillers could be developed from the simplest materials.
Challenges: Technologies for large scale genome editing and the development of strains and processes for production is time consuming and expensive. While novel technologies, such as CRISPR-Cas systems mediated genome editing, third generation sequencing, optimized workflows for genome assemblies, together with predictive models, have positively impacted the progress, there are still numerous challenges to be solved such as regulatory aspects and admission of (gene) modified products.

Plastic-degrading enzymes

A few years ago, a specific type of bacteria was discovered, that is able to degrade plastic. Researchers optimised a variant of this enzyme and are now trying to render it useable for bioinspired recycling of plastics (Austin et al. 2018).
Opportunities: Once the technology is mature, the artificially modified bacteria could help remove microplastics from our ecosystems and therefore have a high potential for the future.
Challenges: Currently, this technology is not yet widely deployable, and technical hurdles still need to be overcome in the near future to demonstrate effective use.

4. ISSUES OF POTENTIAL THREATS FROM THE MICRO- AND NANOSCALE

Newly developed materials need to undergo risk assessment to help evaluate potential environmental and health risks. However, traditional risk assessment frameworks and methods often face significant challenges when evaluating novel materials due to uncertainties and data gaps. Engineered nanomaterials is one prominent example of new, advanced materials whereby scientists, researchers and decision-makers are still discussing best practices to modify and update risk assessment frameworks after nearly two decades of research (Baun & Grieger, 2022).
However, it is not possible to make a generally valid statement on the hazardousness or safety of nanomaterials and other novel materials. For example, available data based on regulatory relevant endpoints focus mainly on acute ecotoxicity whereas long- term data are often still limited. Also, information on actual exposure during the test is often lacking, and thus, quality- assured data on ecotoxicity for nanomaterials remain scarce. Those challenges in reliable aquatic toxicity testing of nanomaterials have already been identified, and solutions by, for example, developing test and assessment strategies were proposed. Exposure estimation is still challeng-

3 https://www.fertilizerseurope.com/agriculture-environment/fertilizing-products-regulation/

ing for nanomaterials. In particular, fate and behaviour processes of nanomaterials differ considerably in comparison to that of soluble (organic) substances. Experts have started to develop various models or tools for allowing realistic exposure estimation for nanomaterials (Schwirn et al, 2020).

Antibiotic Resistance

When considering the micro- and nano cosmos, antibiotic resistance needs to be discussed as a threat and major influencing factor. It is estimated, that more than 1,2 million people worldwide and approx. 33.000 people in Europe die each year as a result of infection by resistant pathogens. So-called multi-resistant bacteria ("superbugs") pose a particular challenge to public health. These are microorganisms that are resistant to several or even all known antibiotics in use (Magiorakos et al. 2012). These include the bacteria Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa and Enterobacter spp. which are summarised under the acronym "ESKAPE" (Pendleton et al. 2013).

Opportunities: One possibility to address the problem of antibiotic resistance is the advancement of diagnostic procedures that support the identification of pathogens, such as rapid antimicrobial susceptibility testing – AST (Vasala et al. 2020). With faster and more efficient identification, more targeted narrow-spectrum antibiotics can be used, reducing the risk of resistance development. Phage therapy; animal-friendly livestock farming and more ecologically compatible forms of agriculture.

Challenges: In addition to the development of resistance, other challenges exacerbate the potential consequences for society: the often lengthy and expensive development of new antibiotics (10-15 years on average), the incorrect use of antibiotics, poor hygienic conditions, the environmental release of antibiotics from industrial producers, and, above all, the widespread use of antibiotics in large-scale livestock farming.

Microplastic

Micro- and Nano plastics (MNPs) are today recognized as emerging contaminants, showing impacts on aquatic and terrestrial biota and most ecosystems on earth, including atmospheric microplastics, with unknown health and environmental significance. MNPs passing through the gastrointestinal tract have been brought in context with disruption of the gut microbiome. Several molecular mechanisms have been described to facilitate tissue uptake of MNPs, which then are involved in local inflammatory and immune responses. Furthermore, MNPs are also considered as potential transporters, vectors, of contaminants and as chemosensitizers for toxic substances (Gruber, E. S., et al. 2022). As a multitude of studies show in that action needs to be taken immediately to reduce plastic use and plastic waste mismanagement to avoid increased microplastic pollution in the future. Progress has been made to reduce the use of certain single-use plastics through legislative actions, but there are few mitigative strategies to reduce sources of microplastic pollution.

Challenges: Most stakeholders (outside of academia) are still unaware of the connections between their use and mismanagement of plastics and the threats posed by microplastic pollution. The lack of strategies to control microplastic pollution could be partly due to the lack of appropriate technologies, but also to our insufficient understanding of the scientific background of the origin, fate and transport of microplastics. This is clearly an obstacle to behavioural change in the public combined with inaction by industry or government. While the benefits of measures against macroplastics often exceed the costs, downstream clean-up measures for microplastics are unlikely to be cost-effective. It must be considered that it is in the interests of those employed in many sectors of the economy to find strategies to reduce marine litter, as this can help reduce social and economic burdens. Examples include tourism and recreation, aquaculture and fisheries, and shipping. In parallel, citizen consumption of goods and services, personal habits (e.g., use of reusable bags and packaging) and waste practices (littering, waste separation) are a key driver of marine litter (GESAMP. 2016, Sarkar, B. et al, 2022).

Opportunities: Innovative approaches to overcome the risks include measures and economic practices such as plastic waste conversion to energy, biotechnological upcycling, conversion of plastic waste to value-added materials (e.g., adsorbents and catalysts), and utilization in construction materials, support the sustainable management of plastic particulates. To improve our understanding of microplastic pollution, it is necessary to involve citizen scientists in monitoring microplastic hotspots and to engage in effective scientific communication with all stakeholders (e.g. civil society, NGOs, government policy makers and industry) about the hazards posed by microplastics and potential opportunities to reduce microplastic sources (Walker, 2022).

Micro-flotation processes - Microbubbles

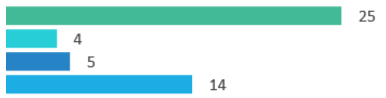
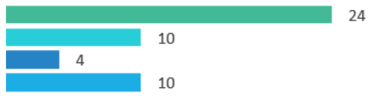
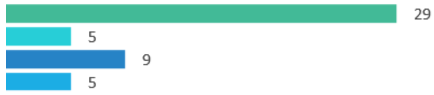
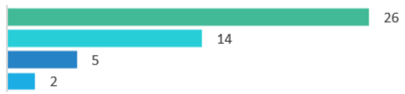
Flotation is a separation technique based on physical and chemical surface properties and density gradients of different materials and was already used in the Middle Ages for mineral processing (Gulden 2019). Simply described, the process works by binding hydrophobic particles to gas bubbles that rise and transport the particles to the surface where they can be easily skimmed off. The bubble size is a key parameter that influences the rate of ascent in the medium, the probability of merging with other bubbles, as well as the interaction with particles further along and the medium itself (Gulden 2019). For the optimisation of flotation processes, the bubble size is therefore central, and the small diameters of microbubbles also give their name to newer micro-flotation processes.

Challenges: Micro-flotation systems work excellently if you put them next to a body of water. You have to pump or isolate water from lakes or seas to purify it. This is great for manageable amounts of water (from municipalities and industrial plants), but for large bodies of water and their huge pollution problems, it has been rather unrealistic until now.

Opportunities: Compact floating rings[4] have a huge potential in terms of cleaning water bodies from e.g. microplastic, especially compared to permanently installed micro-flotation systems, to which the water must be diverted. They form a mist-like cloud of bubbles with a very high bubble density, all of which rise very slowly and attract even the finest microplastic particles like a magnet and carry them to the surface. In this way, water can be freed from microplastics without chemicals, maintenance-free, with very low energy consumption.

Other potential harms

The following table shows statements of the STI 2050 Delphi[5] in which participants assessed, potential harms, which relate to the micro- and nanoscale. The assessment indicated whether they represented significant potential harms to the capability of planetary ecosystems to flourish from now to 2050.

<table>
<tr><td>STI 2050: Delphi Results:</td><td>YES NO It depends on other factors I don't know</td></tr>
<tr><td>The nano-materials that cannot be metabolised are accumulating in the body, generating long term toxicity (e.g. negligence in handling nano-powders may lead to cancer, as a result of inhalation and/or contact with human skin).</td><td></td></tr>
<tr><td>Waste derived nano-particles involves recycling part of the content and renders the remaining material useless, as opposed to using the initial material as such (e.g. the case of used tyres).</td><td></td></tr>
<tr><td>Agricultural nanotechnology runs the risk of introducing nanoparticles in the agri-environment before full assessment of end-of-life effects, leading to unexpected and uncontrollable response from nature.</td><td></td></tr>
<tr><td>Recycling plastic into roads, bricks, clothes can produce micro and nano plastic, which have severe consequences on all elements of the ecosystem.</td><td></td></tr>
<tr><td></td><td>Note: Numbers show count of experts assessing the statement</td></tr>
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5. SCENARIOS

A range of possible micro-nano-scale scenarios are narrated in the light of the three perspectives of ecosystem flourishing from the conceptual framework for society-nature interactions (Warnke et al. 2021).

Error! Reference source not found.1 provides an overview of the scenarios in respect to which perspective on society-nature interaction has been taken and which key questions arise when thinking about the future in 2050.

4 https://www.sprind.org/de/projekte/roland_damann/

5 https://www.futures4europe.eu/_files/ugd/ff6ca7_bf90fad2a518441ba4d1f11d3ada3cfc.pdf

Table 1 Overview of scenarios regarding MNC, informed by the three perspectives

	Using, protecting and restoring	*Co-shaping socio-ecological systems*	*Caring within hybrid collectives*
Scenario title	**Cleaning up Micro- and Nano-Cosmos (MNC)**	**Reflexively and anticipatory aligning with MNC**	**From predation to adaptive and caring human's role within MNC**
Key descriptors on the social construction of society-nature interaction	Ecosystems as provider of goods and services, mainly valuable when benefitting people; Human interventions on micro- and nano-scale seen as alternating between destruction/degradation and reparation/conservation of ecosystems	MNC, ecosystems and humans are moulding each other continuously Humans work in partnership with the dynamics at micro- and nano-scale towards adaptive and transformative capacities of the socio-ecological system	Agency at micro- and nano-scale is blurred, with new hybrid forms of life like nanobots and xenobots. Who animates whom? - is an open question
Implications	-Specific solutions to particular impacts ('half baked sustainability') -principle of "do no harm" is dominating policy making with respect to impacts of MNC on ecosystem performance	- Ecosystem oriented adaptation and management, - applying the "Precautionary Principle" to maintain and safeguard ecosystem services (not only human health) -MNC based solutions support ecosystem stewardship	- The practice of 'collaboration' with microbes and hybrid forms of living - applying the "Stewardship Principle" to wellbeing of all living beings
Limitations	-perpetuation of a separation between the natural and human sphere that cannot support ecosystem flourishing on the long run -inability to radically challenge ('stretch and transform') current regimes with their power concentrations	-if solely the responsibility of innovative businesses based on converging technologies, MNC might not provide solutions for ecosystem stewardship, but create new challenges -the success of these practices is supported/hindered by the narratives of precaution, competition and finding synergies	-challenges in translating into practices and norms the understanding of human-soil relationships as matters of care, marked by spirituality - life-affirming intentions in the MNC can still be overruled by the logic of the macro-cosmos

P1 Scenario: Cleaning up Micro- and Nano-Cosmos

This scenario is assuming the anthropocentric understanding of human/nature interaction as taking from and disposing of residues from societal activities to the natural environment of the separate and dominating sphere of humans. Micro- and Nano-Cosmoses are equally separated and controllable by humans as predators in the ecosystem having the means to exploit the resources of the MNC. Once the pressure of human action on nature is felt as having repercussions on human health or economic performance, reactive action is taken. Depending on the power relations in society, measures taken are either focussing on limiting the unintended pressure on the environment (as reflected in the principle of do-no-significant-harm), regenerating the ecosystems (e.g. by defining protected areas in the macro-, micro- or nano-cosmos) or even reversing the impact of

negative effects, if affecting other human stakeholders (in the macro-cosmos e.g. renaturation of river systems).
The aim of knowledge from science is mainly to monitor the driving-force, pressures and state of human health and environmental related issues, and it provides evidence-based input to for assessing risks. However, the anthropocentric approach still creates tensions in finding agreement on managing the risks. Technology development and innovation in the micro-nano cosmos, aim to provide solutions to limit the impact of harmful human action on the environment stemming from its interventions in the macro-cosmos e.g. by means of end of pipe filtering technologies (e.g., graphene filters for water decontamination), finding new remedies against health threats (e.g. nanopowder for removing toxic metal ions) or by collecting waste (e.g., microrobots to clean up radioactive waste). If such solutions are not in sight, STI might be targeted towards developing reactive ecosystem management measures in the macro-cosmos, e.g. pesticides to cope with monoculture, medication to avoid methane emissions from cows' digestive processes)
A key concept in the environmental policy discourse is understanding society and the environment as unidirectional relation with respect to society threatening the state of the environment. Thereby, reaction to pressure on the environment is the social response to change the future state of environment. Research aims for data monitoring and modelling approaches depicting relations on various scales, which build the basis for environmental impact assessment.
Common to many strategies of this scenario-perspective concerned with the environment is the **understanding of society and human beings as disturbing or managing factor in an ecosystem, which otherwise would be in a stable state.**
Sustainability transition might be achieved by additional resources put into technology fixes and other solutions made possible through undisturbed economic activities. Technological solutions are provided by means of fast response by STI to avoid negative effects on GHG emissions or on achieving other societal aims (. In the micro-nano-cosmos cleaning-up technologies like nano-robots are introduced and energy storage solutions are enabled by means of nanotechnologies.

P2 Scenario: Aligning with MNC *- Reflexively and anticipatory aligning Macro-cosmos with Micro- and Nano-cosmos for flourishing ecosystems (i)*

This scenario is assuming the anthropocentric but reflexive understanding of human/nature interaction as interplay between two intertwined spheres of the material world and the cultural sphere. Humans work in partnership with the dynamics at micro- and nano-scale towards adaptive and transformative capacities of the socio-ecological system. Nevertheless, more emphasis is laid on monitoring the macro-cosmos with its material stocks and flows as well as biodiversity. Even if understood well, knowledge on the micro- and nano-cosmos, are difficult to be used for maintaining or improving ecosystem services and biodiversity.
Common to strategies applied in this scenario is the **understanding of society/human beings as integrated but dominating actor in an ecosystem, which in some worldviews would be in a stable state or could be brought from an instable to a temporarily stable state by human ingenuity.** The precautionary principle is applied to the MNC which implies significant research efforts in understanding and anticipating negative effects of fast-growing applications of nanotechnology.
Society has a responsibility for all living species and the planet. With its capabilities of reflection (e.g. understanding effects of antibiotic resistance) and anticipation (e.g. finding scientific evidence how phenomena on the nano-scale effect ecosystem performance) provided by science, humans shall play a cooperative role in ecosystems and develop and implement innovations and solutions to bring ecosystems (back) into a flourishing state. Anticipatory and reflexive capabilities also aim for ecosystem stewardship having positive effects on SDGs. An example is the application of gene-manipulated microorganisms providing materials sustainably substituting other natural resource-extracting measures (e.g., glue produced from micro-organisms replacing cement), thus putting less pressure on ecosystems otherwise affected by extractive measures.

P3 Scenario: Caring humans within the MNC *- from predation to adaptive and caring humans' role within Micro- and nano-Cosmos*

This scenario is assuming that after a period of crisis of humans' conflicts with each other and with ecosystems, anthropocentrism has been overcome and guarantees ecosystems to flourish.[6] In 2050 there are no predefined categories like nature and culture or human and non-human beings but a wide range of agents[7] with diverse modes of existence and continuously emerging status. Human/nature interaction is taking place in

6 Diving into this scenario is an intellectual challenge as this framework is characterised by the prevalence of relational ontologies and epistemologies. This means they view subjects not as pre-given independent entities, but rather as being continuously(re)produced through interaction processes.

7 Agency is considered not the result of specific entities action but rather emergent from relational network interactions.

critical zones where human agents are on the same level as other living beings. Like bacteria, this encompasses non-human agents in the MNC created by humans such as nano robots, organoids, xenobots, etc., for which it is now shared understanding that they are treated as living beings. In such relations, “care” is recognized and valued as a reciprocal practice among human and non-human beings and ecosystems.

Common to all strategies of this scenario-perspective is the shared **understanding of human beings as integrated actor in an ecosystem. The society has abandoned the role as predator in ecosystems, as multiple crisis since the 2020ies have taught us that with such a worldview, humans are doomed to be in a permanently instable state.** Humans are still assuming that the paradigm shift also has had negative effects on the economy as defined in old days. Nevertheless, by breaking the vicious circle of boundaryless expansion of mankind, humans reached a **sufficient level of wellbeing in those regions that could maintain relatively stable societal structures. To succeed, humans became synergetic agents like other living beings.** Thus, innovations and solutions no longer use predatorial technologies and powers.

The practice of ‘collaboration’ with microbes and hybrid forms of living has been established by applying the “Stewardship Principle” to wellbeing of all living beings. **In “critical zones” in which humans accepted their agency** in a responsible way. As a consequence**, ecosystems have been brought from an instable to a dynamic stable state, guaranteeing an economic system to flourish as well.** With respect to the micro-nano-cosmos this required a leap in understanding of interaction between human and non-human agents e.g, how micro-material interact with living beings, or which nano-level processes produce poisonous outputs.

Humans, as agents **playing a caring role**, have been taking up responsibility and finding alternative ways of coexistence with the aim to increase transformative capacities in critical zones for non-human agents as well. Our capabilities and capacities to communicate with non-human agents helped us to create the knowledge to understand the needs, values, and potentials of other creatures and agents like nano robots, organoids and xenobots on the micro-nanoscale. Solutions provided by STI bring ecosystems into a flourishing state, even in multiple critical zones, which had emerged through climate change.

6. IMPLICATIONS FOR STI POLICY

STI-Themes/directions

Most of the above-mentioned innovation and impact fields are potential STI themes. It is to be expected that future innovation activities involving converging technologies, as discussed above, will influence ecosystem stewardship (e.g. self-replicating materials, organoids, xenobots, bioactive materials, bioeffectors, biostimulants and microbe-assisted crop production, cell factories, bio-inspired materials and plastic-degrading enzymes).

Substantial inter- and transdisciplinary R&D programs combining natural sciences with social sciences and humanities will be needed to clarify the nature, magnitude and likelihood of the potential risks, as well as the options available for dealing with them effectively. This includes, amongst others, issues such as self-replicating materials, antibiotic resistance, microplastic, micro-flotation processes etc..

Threats might arise due to the misuse of those technologies for military or unlawful purposes.

How to do STI? Approaches in designing Instruments and programs

Some of the addressed innovation fields are already advancing and considering a mix of strategies regarding all 3 perspectives might form elements of a transformative STI-policy:

- Developing remedies where damages are already done
- Reflective assessment of developments on the micro-nano scale and taking anticipatory measures to avoid threats to flourishing ecosystems
- Better understanding the micro-nano cosmos and its inhabitants (e.g. how to communicate) and the interaction with the micro-scale (e.g. soils, maritime ecosystems, …) and macro-scales of ecosystems (oceans, air, forests, …)

In the “**Cleaning up MNC” Scenario**, more affordable and accessible innovative technologies would be needed, which are aimed at (a) exploiting the potential of MNC technologies to maximise ecosystem performance (ecosystem services), and (b) reducing negative effects of humans on ecosystems (e.g. search for cleaning-up and filtering technologies).

In the “**Aligning with MNC” Scenario**, research for ecosystem stewardship would contribute to monitoring of the relation of macro-scale with the micro-nano scale and to developing narratives of personal and collective identity connecting the MNC as connected to ecosystem. Policy instruments would include living labs and other experimental instruments to co-create, test and pioneer innovations for ecosystem stewardship applying a precautionary principle on MNC.

In the **Scenario "Caring humans within the MNC",** social science and humanities research are needed for investigating agencies in the MNC. The realms of imagination and metaphysics (spirituality) of hybrid life forms (e.g. xenobots) will be receiving attention in ethics and philosophy. This kind of research will require close interaction with natural sciences and engineering allowing for adequate means of observation of the MNC.

Kind of Knowledge required

Overall, knowledge on the implications and potential threats from the micro- and nanoscale is still lagging behind technological developments. This knowledge gap will require significant activities in inter- and trans-disciplinary research for technology assessment and to inform responsible research and innovation.

On the innovation side, besides scientific knowledge on how to observe at micro-and nano-scales, manipulating on micro-and nano-scales (e.g. producing xenobots), engineering knowledge is required.

As untouched areas of the MNC are "conquered" by humans, knowledge and research on ethical and legal issues are emerging.

In the "**Cleaning up MNC" Scenario**, knowledge has more value, if it can facilitate appropriation and management of resources and is mainly focussing on enabling technoscience.

In the "**Aligning with MNC" Scenario**, knowledge builds on a continuous feedback loop with the material world on macro- as well as micro- and nano-scale. Technoscience may be involved, but is taking into account complexity, scale and time in interactions among constituents, as humans are understood as integral part of the ecosystem and their stewardship is also extending to the MNC.

In the **Scenario "Caring humans within the MNC",** the re-emergence of other codes, sensibilities and practices of relating to MNC, (e.g. in case of critical zones of antibiotic resistance) requires knowledge beyond the dominance of natural science framings. Science would participate to a culture of flourishing ecosystems including the MNC and metaphysics would not be considered as defiant of scientific practice, but as contributor to its enrichment.

STI infrastructures and human resources required

Living labs and other forms of experimental spaces and infrastructures to explore the MNC in a responsible way need to be developed and adapted to the micro- and nano-scale.

Particularly in this field brain-drain can be expected to be an issue, and ethical question might play a role in where academics would find employment.

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