NanoDialogue
of the German Government

ExpertDialogue

Opportunities and risks of active materials at the nano scale

Institut für Ökologie und Politik GmbH

Content

1 Introduction

1.1 NanoDialogue of the German Government

The ExpertDialogue "Opportunities and Risks of Active Materials at Nano Scale" is organised by the Federal Ministry for the Environment, Nature Conservation, Nuclear Safety and Consumer Protection (BMUV) as part of the 6th phase of the Nano-Dialogue[1]. About 30 participants from different stakeholder groups as well as from ministries and authorities are expected.

The NanoDialogue was launched via the establishment of a NanoCommission in 2006 on the initiative of the Federal Ministry for the Environment. After two dialogue phases (2006 - 2008 and 2009 to 2011), the NanoCommission ended its work, and the dialogue has since been continued in the form of two-day ExpertDialogues.

The upcoming ExpertDialogue will focus not only on nanomaterials that meet the definition[2] proposed by the EU Commission, but also on substances and materials that are larger than 100 nm but still nanoscale. The presentations and discussions at the ExpertDialogue are documented in a summary and published on the Internet.

In addition to a brief introduction to what is meant by active nanoscale materials in the context of the dialogue, this background document contains the abstracts of the planned presentations. A discussion of this document is not intended at the ExpertDialogue.

[1] The documentation of the previous NanoDialogue events can be found on the BMUV website https://www.bmuv.de/themen/gesundheit-chemikalien/nanotechnologie/nanodialog-der-bundesregierung

[2] COMMISSION RECOMMENDATION of 18 October 2011 on the definition of nanomaterials. The proposal is currently being revised.

1.2 Objectives of the ExpertDialogue

The objectives of the ExpertDialogue on active nanoscale materials are:

- To establish a common understanding of what active nanoscale materials are and whether there are typical compositions and/or structures,
- Provide an overview of the functionalities of active nanoscale materials and the (therefore) possible fields of application, including a presentation of products that are already marketed and those that are still in research and development,
- Enable an exchange among stakeholders on the opportunities and potentials of active nanoscale materials and the possible risks from their use that could arise from their type, structure and, in particular, activity,
- Provide and receive input for a discussion on the appropriateness of existing regulations and associated assessment methods for this type of nanoscale materials.

2 Active, nanoscale materials

The ExpertDialogue focuses on materials that are nanoscale, i.e. in at least one dimension smaller than 1000 nm, and that are "active". Activity is assumed if the materials are multifunctional and/or adaptive or if they change their properties reversibly and controllably as reactions to external stimuli.

Another description of active, nanoscale materials refers to the ability to transform energy, e.g. mechanical energy into electrical energy. This process changes either the properties or the structure, composition or functionality of the material (e.g. photochromic and thermochromic materials, electroluminescent materials, piezoelectric materials).

In the ECHA report on so-called nextgeneration[3] nanomaterials, nanomaterials are divided into three generations, of which only the first is passive. The description of the second and third generation can be summarised as follows[4]:

- Second generation: (re)active nanomaterials, nanostructures and nanostructured materials that respond to stimuli and absorb, receive or harvest energy from their environment during use, and use it for a variety of non-equilibrium activities. This changes the energy level of the system and the conformation or molecular structure. The stimuli can be chemical or physical, acting on the surface or the core.
- Third generation (multifunctional nanosystems): Complex chemical reaction networks and synthetic life-like systems and materials built from stimuli-responsive nanoparticles and nanostructures. They are characterised by increased integration between organic and inorganic components.

According to the study, an increase in research activities on active nanostructures has been observed in recent years, although the overall share of nanotechnology research is described as small.

[3] ECHA (2019): A state of play study of the market for so called “next generation” nanomaterials, Hesinki. Available at: https://op.europa.eu/en/publication-detail/-/publication/1b84728b-f6e1-11e9-8c1f-01aa75ed71a1/language-en

[4] ECHA 2019, p. iii ff.

3 Abstracts of the presentations

3.1 Introduction

3.1.1 What are active materials at the nano scale

Dr Bernd Giese, Institute of Safety/Security and Risk Sciences, University of Natural Resources and Life Sciences (BOKU), Vienna

The introductory presentation will first describe and classify the topic for the ExpertDialogue, which is not easy to define on closer examination. After a short historical excursion, possible definitions and differentiations of active nanoscale materials will be presented. This structuring is supplemented by a consideration of their promising properties as well as the possible functionalities that can be achieved with these materials. A look at the spectrum of material types involved shows that, in addition to the inorganic compounds and elements that have been at the forefront of nanotechnology to date, organic chemistry and even biology also play a greater role in the more recent developments of active nanoscale materials. With the help of polymers, which can also be of biological origin, comparatively complex structures are now being created. On this basis, diverse functions are made possible, from the targeted delivery of an active ingredient to information processing. The convergence once predicted by Mihail C. Roco, seems to be realizing in small steps, albeit somewhat later.

3.2 Active materials at the nano scale in medical applications

3.2.1 Active materials at the nano scale in medicines – nano meets bio

Prof. Dr. Aigner, University of Leipzig

Due to their small size, nanoparticles are characterised by physical and chemical properties that can differ significantly from their larger counterparts. This also affects their behaviour in biological milieus and makes them very interesting, e.g. for therapeutic uses.

In medical applications, the activity of nanoscale materials in the biological environment must be considered from two sides:

I. How do nanoparticles interact with biological structures, e.g. when passing through membranes, during their biodistribution in the body and with regard to their uptake in cells, and

II. How are nanoparticles influenced in their properties by a biological environment or can they be made specifically “responsive” to biological triggers?

Both aspects can be exploited in a targeted manner, e.g. for the therapeutic formulation and introduction of active substances with the aim of increasing efficacy and/or avoiding side effects in non-target organs. This approach is of particular importance in the case of active substances that would have insufficient or no efficacy without a nanoparticle formulation because they are too unstable and/or would be too inefficiently distributed in the body and taken up by target cells. RNA-based therapeutics such as small siRNA for specific RNA interference (RNAi)-mediated gene knockdown or mRNA for gain-of-function treatment are important examples of this that have gained considerable importance in recent years. However, the type of 'payload', the therapeutic objective and desired localisation as well as the type of application also place specific demands on nanoparticles in each case, which must be further developed and adapted accordingly. In addition to efficiency, the avoidance of side effects, i.e. a high level of biocompatibility, must also be taken into account as a mandatory property; this can also be achieved through targeted chemical modification, e.g. towards biodegradable nanoparticles.

Literature:

Aigner, A., Perspectives, issues and solutions in RNAi therapy: the expected and the less expected. Nanomed. 14 (21), 2777-2782 (2019)

Liu et al., Non-viral nanoparticles for RNA interference: Principles of design and practical guidelines. Adv. Drug Del. Rev. 174, 576-612 (2021)

Sun et al., Maßgeschneiderte Nanopartikel für den Wirkstofftransport in der Krebstherapie, Angew. Chem. 126, 12520-12568 (2014)

3.2.2 Active materials in pharmacology

Prof. Dr. Andreas Herrmann, DWI RWTH Aachen

DNA is an excellent material for the production of nanostructures. Defined objects can be achieved by folding DNA into the desired shape,[1] by attaching it to inorganic particles[2] or by creating DNA amphiphiles that self-assemble into nanostructures by microphase separation[3]. Single-stranded soft-matter DNA nanoparticles of the latter class of materials can be efficiently functionalised by hybridisation. When equipped with targeting moieties by Watson-Crick base pairing and incorporation of a hydrophobic drug into their interior, they kill cancer cells in vitro[4]. Similarly, they were loaded with anti-biotics by hybridising them with drug-binding aptamers. These DNA-based carriers strongly adhere to the ocular surface and have been successfully used for ophthalmic drug delivery in vivo.[5] When peptide nucleic acids encoding cancer antigens and immunostimulatory DNA sequences are attached to the single-stranded DNA carrier platform, immunological treatment of cancer has been successfully performed in various mouse models.[6] In addition to micelle systems, our group has incorporated DNA amphiphiles into the phospholipid bilayer of vesicles. It has been shown that DNA is specifically aggregated and released from these nanocontainers.[7] Furthermore, amphiphilic oligonucleotides serve as artificial receptors on cell surfaces and facilitate the uptake of vesicles and nanoparticles functionalised with complementary sequences.[8] Finally, polynucleic acids with ultra-high molar mass have been produced by rolling circle transcription and loaded with drugs such as antibiotics. From these carriers, the pharmaceutical agents can be activated by ultrasound as a clinically applied trigger with high tissue penetration depth.[9]

Literature

[1] J. Fu, M. Liu, Y. Liu, H. Yan, Acc. Chem. Res. 2012, 45, 1215.
[2] D. A. Giljohann, D. S. Seferos, W. L. Daniel, M. D. Massich, P. C. Patel, C. A. Mirkin, Angew. Chem. Int. Ed. 2010, 49, 3280.
[3] J. W. de Vries, F. Zhang, A. Herrmann, J. Controlled Rel. 2013, 172, 467.
[4] F. E. Alemdaroglu, C. N. Alemdaroglu, P. Langguth, A. Herrmann, Adv. Mat. 2008, 20, 899.
[5] J. W. de Vries, S. Schnichels, J. Hurst, L. Strudel, A. Gruszka, M. Kwak, K.-U. Bartz-Schmidt, M. S. Spitzer, A. Herrmann, Biomaterials 2018, 157, 98.
[6] J.-O. Jin, H. Kim, Y. Huh, A. Herrmann, M. Kwak, J. Control. Release 2019, 315, 76.
[7] A. Rodriguez-Pulido, A. Kondratchuk, D. K. Prusty, J. Gao, M. Loi, A. Herrmann, Angew. Chem. Int. Ed. 2013, 52, 1008.
[8] H. Li, J. Fan, E.M. Buhl, S. Huo, M. Loznik, R. Göstl, A. Herrmann, Nanoscale 2020, 12, 21299.
[9] S. Huo, P. Zhao, Z. Shi, M. Zou, X. Yang, E. Warszawik, M. Loznik, R. Göstl, A. Herrmann, Nat. Chem. 2021, 13, 131.

3.2.3 Sensors at the nanoscale for optical diagnostics

Wolfgang Fritzsche, Leibniz-Institute of Photonic Technology in Jena

For an effective therapy of infectious diseases, rapid and preferably on-site detection of biomarkers is required. One possible approach is the method of localised surface plasmon resonance, which uses nanoscale metal structures as sensors [1]. These are functionalised with molecules (receptors) that specifically bind the respective biomarker (such as DNA or proteins): The binding of the biomarkers induces a change in the optical properties (shift of the resonance wavelength), which is detected spectroscopically.

The nanosensors used can be synthesised lithographically (top-down) or chemically (bottom-up); we primarily use the latter method. Here, the nanoparticles are produced in solution and immobilised on glass substrates for use [2]. Using the detection of DNA sequences [3], the method and the readout procedures developed for it with the potential for multiplex applications are explained, and examples of applications for protein detection are also given [4].

Literature

[1.] Philosophical Transactions A 369, 3483 (2011).
[2] Analytical and Bioanalytical Chemistry 411, 1537 (2019)
[3] ACS Sensors 4, 335 (2019)
[4] Scientific Reports 12, 836 (2022)

3.3 Active materials at the nano scale in electronic applications

3.3.1 Quantum Dots - a new class of materials for display technologies

Dr. Armin Wedel, Fraunhofer Institute for Applied Polymer research

In recent years, display technologies have constantly evolved. In addition to LCD technologies, which are still used in screens for televisions and computer monitors, OLED technology, in particular, has become increasingly popular, especially for smartphones and tablets. Novel quantum dot (QD) materials have gained new importance as converter materials in the backlights of LCDs. In the future, QDs, also electrically excited, will be found in display applications.

Based on the unique properties of QDs, this will open up new possibilities, especially for the colour saturation of displays (BT2020). Initially, however, QDs will be applied primarily as colour filters. This means that the QDs will be excited by blue (mini or micro) LEDs or OLED and the green and red emissions will be generated by converting the blue light. However, the most promising results in the past involved II-VI semiconductor nanocrystals, including cadmium (Cd). In recent years, these materials have been replaced by less toxic materials. Indium phosphide (InP) based QDs are a promising material among III-V semiconductor nanocrystals.

3.3.2 Nanomaterial based electronic noses – curse or blessing?

Dr Martin Sommer, KIT Institute of Microstructure Technology

A whole range of tasks in daily life in the industry and private life can be solved by determining the respective situations by means of odour analysis. The suitable machine device is the electronic nose ('eNose'), which, following the biological original, consists of several sub-sensors whose essential functional elements - depending on the measuring principle and structure of the eNose - can in turn consist of micro- or even nanomaterials. The benefits of eNoses are undoubtedly very diverse due to their almost universal application possibilities; nevertheless, the expected risks - related to the material - are rather low or non-existent for eNoses with metal oxides as sensitive material. More critical could be the possible misuse of personal or business information caused by the odour analysis itself, which would be simplified by the easy availability due to a low price aimed at in the development of the eNose presented here.

In this presentation, after an introductory example of breath diagnostics, the basic principle of the eNose developed at KIT based on tin dioxide as a sensitive material will be presented. In addition to similarities to the biological model, the difference to conventional, quantitative gas analysis will be explained. Here it is of particular importance that little emphasis is placed on the identification and quantification of the chemical gas components, but rather the recognition of learned overall odours is aimed to determine the current odour situation, which is sufficient for many applications. This type of information acquisition is largely independent of the technical functional principle of the eNose, so that the associated risks (see above) can also be transferred to other eNose types.

Some examples show various possible applications.

Finally, some advantages and risks of this technology are briefly named and discussed. As with the use of other technologies, the same applies here: In conclusion, the user decides whether he or she is doing good or bad with such a device.

Review article:

[1] Karakaya, D., Ulucan, O. & Turkan, M. Electronic Nose and Its Applications: A Survey. *Int. J. Autom. Comput.* **17,** 179–209 (2020). https://doi.org/10.1007/s11633-019-1212-9

3.3.3 Nano-sensors in lightweight construction and high-performance materials

Prof. Robert Böhm, HTWK Leipzig

Carbon-based nanomaterials (Carbon Nano Materials, CNM), e.g. graphene or carbon nanotubes, offer numerous promising potentials for improving high-performance materials in terms of their multifunctionality [1,2]. CNMs are particularly interesting for applications in mechanical and automotive engineering, aerospace, construction, medical technology and many other industries because they can create intelligent component properties, such as integrated sensor technology [3,4]. Such systems are being researched within the EU initiative COST [5] in the EsSENce network [6]. The lecture presents this network and gives an overview of the potentials of CNM-based multifunctional materials based on selected examples.

Literature

[1] Cataldi, P.; et al. Graphene Nanoplatelets-Based Advanced Materials and Recent Progress in Sustainable Applications. Appl. Sci. 2018, 8, 1438.
[2] Zhang, Q.; et al. The Road for Nanomaterials Industry: A Review of Carbon Nanotube Production, Post-Treatment, and Bulk Applications for Composites and Energy Storage. Small 2013, 9, 1237-1265.
[3] Koumoulos, E.P.; et al. Research and Development in Carbon Fibers and Advanced High-Performance Composites Supply Chain in Europe: A Roadmap for Challenges and the Industrial Uptake, Journal of Composites Science, 2019, 3(3), 86
[4] Kumar, V.; et al. Review of Recent Advances in Nanoengineered Polymer Composites. Polymers 2019, 11, 644.
[5] https://www.cost.eu/
[6] http://www.essence-cost.eu/

3.4 Further applications

3.4.1 DNA as construction material for active nanomaterials

Enzo Kopperger, Technical University of Munich

DNA is known from nature mainly as information storage for the production of proteins. Proteins then form the building material and machinery that make the life of organisms possible. In DNA nanotechnology, DNA strands are used directly as a building material for the construction of structures ranging in size from 10 nanometres to several micrometres. For this purpose, the sequences for synthetic

DNA strands are designed with software support in such a way that the desired structure self-assembles itself. The shape and mobility of the structures can be customised for the desired application. In our research group, we are particularly fascinated by mechanical constructs that are based on machine elements from the macroscopic world, such as hinges, freely rotating joints and sliding elements on axes. The design and controlled drive of increasingly sophisticated machine elements should allow them to be assembled into veritable molecular factories in the future. In the near future, applications include, for example, “smart” medical drug transporters, surface coatings and the construction of novel biosensors.

3.4.2 Light against antibiotics resistance: characterization and biological properties of new photoactive materials

Anzhela Galstyan, University of Duisburg/Essen

The demand for antimicrobial nanomaterials is rapidly increasing in various fields of medicine and technology. While tissue contaminations can often be spontaneously cleared by the host's immune defence, infections associated with biomaterials are much more difficult to treat. The proliferation of bacteria at interfaces and the subsequent formation of biofilms is an important step in the pathogenesis of infections associated with engineered materials. In addition, robust antimicrobial materials suitable for large-scale wastewater decontamination are urgently needed. Photodynamic inactivation of bacteria has emerged as a promising alternative strategy to antibiotic treatment. Based on this approach, light-activated anti-infective coatings could be produced by incorporating the photosensitizer into polymer-based materials. The wide variety of polymers available today offers the possibility to select the most suitable ones for a specific application. Novel nanoscale materials with photodynamic antimicrobial activity are presented.

3.4.3 Electroactive Polymers

Ivica Kolaric, Fraunhofer IPA

Since the introduction of the iPhone in 2007, the term “usability” has enjoyed growing public attention and the interaction between humans and the required hardware and software is becoming more and more important. Whether smartphone, car, building or robot, people will interact more and more with machines and digitalised services in the future. The technology required for this is called “Human Machine Interaction” (HMI) and essentially describes the interface between humans and hardware and software. Furthermore, robots are evolving away from being purely a means of production towards becoming a cooperative partner that works together with humans. Driven by the growing demand for cooperative robotics, bio-inspired, soft-robotic solutions are increasingly being developed. Additive manufacturing now makes it possible to efficiently produce complex structures and to process polymer and bio-based materials into organ-like structures.

The three future technologies described are partly based on nanoscale and electroactive materials, such as electroactive polymers (EAP). EAPs offer numerous advantages over traditional electromechanical solutions. They operate silently, require a very low supply voltage, are lightweight and flexible. With all these technical advantages, EAP's are multi-material composite systems and may contain nanoscale additives which raise issues of safety, processing and disposal.

In this talk, EAP sensor-actuator systems and their innovative applications will be presented. Based on a risk assessment, the effects of the materials used and the EAPs on humans and the environment will be considered and accompanying measures to increase safety in handling over the entire life cycle of the EAPs will be presented.

3.5 Regulation and ethical aspects

3.5.1 Regulatory issues regarding active materials at the nano scale in REACH and in the CLP regulation

Lars Tietjen, German Environment Agency

The CLP and the REACH regulation form the core of European chemicals legislation. With the obligations to classify and label hazardous substances and mixtures (CLP Regulation) to register substances, provide safety data sheets for substances and mixtures, and the processes of the identification of substances of very high concern, authorisation and restriction (REACH Regulation), a broad regulatory framework is available.

The topic of the articles will be dealt with in more detail. Here, the obligations of chemicals legislation are limited. The special status of polymers in the context of registration will also be addressed.

This presentation will show whether the instruments of chemicals legislation are also suitable for active nanoscale materials.[5] In addition, it will briefly outline which further developments for REACH[6] and CLP are in preparation within the framework of the EU Chemicals Strategy for Sustainability and whether these could play a role in the context of active nanoscale material

[5] In general, on the current regulatory framework in the context of advanced materials, see Risk Governance of Advanced Materials - Considerations from the joint perspective of the German Higher Federal Authorities BAuA, BfR and UBA; 2021 https://www.umweltbundesamt.de/sites/default/files/medien/479/publikationen/texte_156-2021_risk-governance-advanced-materials.pdf

[6] European Commission, website on the REACH revision
https://ec.europa.eu/environment/chemicals/reach/reach_revision_chemical_strategy_en.htm

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https://www.umweltbundesamt.de/publikationen/the-revision-of-the-reach-authorisation-restriction

Imprint

ÖKOPOL GmbH
Institut für Ökologie und Politik

Nernstweg 32–34
D – 22765 Hamburg

www.oekopol.de
info@oekopol.de

Tel.: ++ 49-40-39 100 2 0
Fax: ++ 49-40-39 100 2 33