Bio-inspired and Biomimetic Nanomaterials

Introduction

Biomimetics is learning from living nature for problem-solving in technology, science, architecture and industry. In recent years biomimetics has seen a massive upswing, facilitated by breakthroughs in the fields of nanoscience and nanotechnology. Many of the functional aspects of extraordinary biological materials, structures and processes are based on properties in the nano-range and can therefore in many cases only now be studied and understood in detail. The objective of biomimetics is to investigate and understand these functional aspects of organisms and ecosystems, to abstract their basic principles and transfer them to human applications. Bioinspiration is understood more broadly than biomimetics, also including mere copies of form. Everything which is biomimetic is also bio-inspired, but not everything which is bio-inspired is also biomimetic.

Terminology

A suitable framework for biomimetic work is provided by the guideline VDI 6620 “Biomimetics – Conception and Strategy” of the Association of German Engineers. According to this guideline, the central element of biomimetics is the concept of transferring from biology to technology. This is described in detail and regulated in the standard DIN ISO 18458:2015 “Biomimetics – Terminology, Concepts and Methodology”.

It should be noted that there is a fundamental difference between “biomimetic” and “bio-based/biogenic”. A bio-based/biogenic material is derived directly from a natural material, whereas a biomimetic material can be made naturally or synthetically, but is in any case inspired by principles from living nature.

Within this dossier the technical terms and definitions for nanotechnology are used according to ISO/TS 80004-5:2011. This is a standardized vocabulary for technical terms at the interface between nanomaterial research and biology. It is intended to enable different interest groups to communicate about the use of nanotechnology in biology or biotechnology and the use of biological matter or biological principles in nanotechnology.

The importance of this interface between biology and nanotechnology is emphasized within the foreword of ISO/TS 80004-5:2011. It represents an exceptionally interesting and technologically promising border area of modern science. Current research is concerned with medical and pharmaceutical applications, with an improved understanding of the uptake and distribution of nano-objects in the organism (especially with the targeted delivery of pharmaceuticals at certain points in the human body), highly sensitive and highly selective sensors and new advanced methods to counteract pollution. The great potential of “natural nanotechnology” can be seen, for example, in the bone, where structures on the nanoscale contribute greatly to its overall functionality.

Two prefixes that are used at the interface between “nano” and “bio” are “nanobio-” and “bio-nano-”. The prefix “bionano-” indicates, that the biological domain affects the nano-domain, while “nanobio-” indicates that the nano-domain affects the bio-domain. If neither direction predominates or the direction is unimportant, the term bio/nano interface is used.

Smart nanomaterials (also known as intelligent materials) are, in the narrow sense, materials that can (independently) react to changing conditions. This includes changes in temperature, changed mechanical loads (i.e., external stresses that act on the material, such as pressure, tension, shear, bending or twisting) or changes in the pH-value. In a broader sense, smart nanomaterials include all substances that can be influenced by active control, such as applied electrical voltages, in a way that is not possible with ordinary materials.

The definition of stability of nanoparticles depends on the desired size-dependent property that is exploited and can only exist for a finite period of time, since all nanostructures are inherently thermodynamically and energetically unfavorable compared to bulk materials, which have constant properties regardless of size. As such, nanomaterial phases can be considered metastable, i.e., in a short-lived energetic state relative to materials at the macro-level.

Summary

This dossier explores bio-inspired and biomimetic nanomaterials, differentiating between bio-inspired or biomimetic nanotechnology and bio-nanotechnology. Following a clarification of these terms, the basics of bio-inspired and biomimetic nanomaterials are then presented. Subsequently, a systematic classification of synthetic methods of bio-inspired and biomimetic nanomaterials is demonstrated. This classification is based on the method of manufacturing and not on the functionality of the materials. This enables a more coherent correlation with security aspects, which are yet to be defined in many cases. Due to the great variety, a categorization according to material properties or material compositions is not considered practical. In addition to chemical properties and behavior, physical parameters such as size, structure and surface quality also play an important role in the categorization. In summary, it can be said that bio-inspired and biomimetic nanomaterials represent important base materials as so-called functional advanced materials in research, development and industry – provided that the material development is accompanied by a corresponding safety and sustainability-oriented technology assessment.

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A composite material consists of two or more components with significantly different physical or chemical properties, which when combined result in a material with properties that differ from those of the individual components. The individual components remain separate and different within the finished structure.

Advanced materials are materials with better performance in one or more properties compared to conventional materials or materials possessing entirely new properties. Very often – but not always – these properties are based on nanoscale functionalities.

Bio-Inspired Nanomaterials

Organisms contain many substances and structures that can serve as inspiration for materials in technical applications. Biological materials are complex, multifunctional, hierarchical and change depending on the environmental conditions. In most cases, effects on the macro scale are due to functionalities on the nanoscale.

Materials in nature are characterized by diverse, highly complex and hierarchical structures. Especially on the micro- and nanometer scale (1 μm = 1,000 nm, 1 mm = 1 μm = 0.001 mm, 1 nanometer = 1 nm = 1/1,000 μm) biological structures show sophistication that far exceeds current artificial materials and structures.

Researchers and engineers have always been inspired by extraordinary phenomena in living nature. Some could be easily transferred to technology\(^5\); but for others the underlying principles have not yet been understood, even with rapid advances in nanotechnology. In some cases, such as for photosynthesis and the navigational ability of birds, one must use quantum theory to gain a basic understanding of the underlying principles. It is likely that some of the wonderful materials, structures and processes of living nature will never be fully understood. Although we can perceive extraordinary properties, we are far from fully understanding such highly complex "biological technologies". Biomimetics researchers thereby also look at the possible, but not (yet) transferable.

According to Steven Vogel, an esteemed American biomechanics expert, the mechanical sciences on the nanoscale hold great potential for biomimetic approaches. In this sense, materials science and nanotechnology appear to be the most promising areas. Shapes and materials in living nature are built in a bottom-up manner through a combination of building blocks on the micro- and nanometer scale. This provides the organism with a variety of hierarchically organized materials with a wide range of possible properties. According to Vogel, promising biomimetic innovations can be expected especially in the fields of composite materials and advanced materials. Among other promising areas Vogel mentions muscle-like actuators converting chemical energy directly into mechanical energy, robotics, walking vehicles, floats that move with the help of flexible materials through bending and novel prostheses with materials and structures closely resembling the original limbs\(^6\).

Biomimetic Synthesis Methods

There are various ways to categorize synthetic methods of biomimetic and bio-inspired nanomaterials. For this NanoTrust dossier, the categorization according to Zan and Wu\(^7\) was chosen because it is process-oriented (as opposed to function-oriented) and therefore enables a correlation with safety aspects. The five main categories of biomimetic synthesis methods are: 1) elementary biomimetic synthesis of micro- and nanostructures via biological templates; 2) biomimetic synthesis through the combination of soft and hard membranes; 3) intelligent biomimetic synthesis through liquid membranes with carriers; 4) biomimetic synthesis by living plants or microorganisms; 5) bio-inspired synthesis with the aid of biomacromolecules.

The bio-inspired material synthesis of nanoparticles pursues a bottom-up strategy\(^8\) and allows the low-temperature production of particles of reproducible size, crystallography, structure, with controllable density of the crystallization nuclei and the possibility of self-assembly.

Materials, structures and processes within living nature are relevant for the bio-inspiration of nanomaterials. The pursuit of mild (i.e. at room temperature, at pH values near the neutral point), efficient and environmentally friendly synthesis methods promises products which do not harm people or the environment. One can learn from plants even for mining applications\(^9\).

Such methods are often more environmentally friendly than the conventional production of nanoparticles, which often uses strongly reducing agents, surface-active substances and organic solvents\(^10\). The microbial as well as the cell-free enzymatic synthesis of nanoparticles from gold, silver, palladium, platinum, selenium, iron, silicon, tellurium, uranium and zinc offer a “green” chemical process approach\(^11\).

The five categories of synthetic methods of bio-inspired and biomimetic nanomaterials are presented below, including concrete examples from current research and development.

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**Table 1:**

**Definition of fundamental terms of bio-inspired nanomaterials based on standard ISO/TS 80004-5:2011(en).**
Elementary Biomimetic Synthesis of Micro- and Nanostructures via biological Templates

A template has desired nanoscale features which allows transfer of structures, shapes and properties of nanomaterials that are otherwise difficult to obtain. By using a biological model, structural aspects can be adopted directly in the elementary biomimetic synthesis of micro- and nanostructures via biological templates.

Specific plant structures can be used, for instance, to produce nanomaterials with a certain morphology, such as microcoils of magnetically powered microswimmers with a diameter of ten to sixty micrometers. As Gao and coworkers showed, a single short petiole (which is the stalk that joins a leaf to a stem) can produce over a million helical microswimmers that can move in human plasma at speeds of around 250µm/s.

The beautiful, hierarchically structured, functional structures can be adopted directly in the elementary biomimetic synthesis of nanomaterials. Both structures and liquid crystals, examples of hard templates are carbon nanotubes. Combined templates (combination of soft and hard membranes) are porous structures with functional groups on the pore wall. These membranes possess rigid structures and capabilities to confine space that are similar to hard templates; on the other hand, the functional groups on the pore walls grant them the soft template characteristics of modifiability and template-inducing effects. Combined templates exhibit the advantages of both approaches. These combined membranes can be artificial or natural. The pore size and membrane thickness can be controlled for artificial membranes, while natural membranes offer high complexity which cannot be produced artificially. In this way, nanotubes, ultra-thin metal films and various nano-superstructures can be produced. Liu and others have synthesized a flower-like calcium oxalate structure using a supramolecular template. The calcium oxalate was then converted into a core/shell CaC₂O₄/CaWO₄ nano-composite with some new optical properties, such as fluorescence, while maintaining its structure.

One of the best known naturally combined membranes is the eggshell membrane: semi-permeable with a woven protein fiber network structure. There are various attempts to reproduce its structure. There are different membranes in different morphologies in ambient conditions. For instance, silver and gold sols can be used to produce silver spheres with a diameter of 11nm. The combination of the respective metal solutions with tansy waste can be used to produce metallic nanoparticles. Here, especially plant hyperaccumulators of heavy metals are used, which are non-toxic for these plants themselves. Of particular interest is also the synthesis of metallic nanoparticles using plant extracts, e.g. from fruit peels which would otherwise be waste.

Biomimetic Synthesis through the Combination of Soft and Hard Membranes

Normally, hard templates provide uniform and predictable structures, whereas soft templates allow the production of unique and specific nanostructures, with the disadvantage of a decreased ability to control uniformity and size. Examples of soft templates are micromelions and liquid crystals, examples of hard templates are carbon nanotubes. Combined templates exhibit the advantages of both approaches. These combined membranes can be artificial or natural. The pore size and membrane thickness can be controlled for artificial membranes, while natural membranes offer high complexity which cannot be produced artificially. In this way, nanotubes, ultra-thin metal films and various nano-superstructures can be produced. Liu and others have synthesized a flower-like calcium oxalate structure using a supramolecular template. The calcium oxalate was then converted into a core/shell CaC₂O₄/CaWO₄ nano-composite with some new optical properties, such as fluorescence, while maintaining its structure.

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Biomimetic Synthesis via Living Plants or Microorganisms

Plants, microorganisms, viruses and even enzymatic extracts can be used to produce metallic nanoparticles. Here, especially plant hyperaccumulators of heavy metals are used, which are non-toxic for these plants themselves. Of particular interest is also the synthesis of metallic nanoparticles using plant extracts, e.g. from fruit peels which would otherwise be waste.

Organic waste is increasingly considered by industry and research as a source of bioactive substances, with the help of which high-quality nanoparticles can be synthesized using water-based chemistry at room temperature and under ambient pressure. For instance, silver and gold solutions with tansy waste can be used to produce silver spheres with a diameter of 16 nm and gold triangles with a side length of 11nm. The combination of the respective metal solutions with banana peels, lignin, coffee and tea extracts, can produce nanoparticles from silver, gold, iron oxide, copper oxide, magnesium oxide and manganese oxide which are consistent in shape.
For this, the solution with the metal salts is mixed with the organic waste solution at room temperature. This starts the process of bioreduction and the formation of the nanoparticles, often recognizable through a change of color of the solution due to the change in oxidation number.

The organic waste molecules also act as natural surfactants and promote growth along specific crystal axes. Important parameters that can influence the size and shape of the nanoparticles are the type and concentration of the organic waste in the solution, the metal concentration in the solution, the temperature of the mixed solution and the reaction time.

Smart nanomaterials with good biocompatibility and functional properties, superstructured nanomaterials and nanomaterials in metastable phases can be produced in this manner.

Biomimetic Synthesis
By Regulating Organic Macromolecules

Biomineralization is fascinating. Plants, animals and microorganisms produce highly controlled hierarchical and complex structures out of various materials such as silica, calcite or magnetic materials under ambient conditions (normal temperature, normal pressure)³ (Fig. 1-3).

This is often done with the help of pre-structured supramolecular templates or organic aggregates. With the exception of their simple forms, i.e., in the case of precipitation and oxidation reactions and reactions in which perfectly crystallized minerals are produced, highly complex proteins are used for biominalization, which control or induce crystal growth and which, when used as additives in technical production, allow a controlled crystal formation. Purely synthetic, bio-inspired macromolecules that simulate biomineralization have also been created, for instance for the production of inorganic, organic or hybrid nanomaterials and nanostructures.

Examples of biomaterials and the respective proteins which are involved in biomineralization, include collagen (which controls the formation of apatite), shell proteins (which control the formation of mother-of-pearl, Fig. 2), silaoproteins (which produce dentin) and tuftelin as well as enamelin (which produce tooth enamel) in teeth. Furthermore, ice-binding proteins control the shape and size of ice structures in plants, animals, fungi and microorganisms and Cytochrome c controls the formation of gold and uranium nanoparticles⁹. More and more of such proteins are being described and used. Currently, 80 different proteins have already been researched regarding the formation of hydrated silicon dioxide structures, such as occur in diatoms and glass sponges (Fig. 1)²³.

Figure 1: Diatoms biomineralize micro- and nanostructured hydrated silicon dioxide. The image shows the fossil shell of the diatom Solium exsculptum ((a) whole shell, (b) and (c) magnifications). Solium exsculptum is functionally nanostructured. © Friedel Hinz, AWI Bremerhaven. Image reproduced with kind permission²⁰.

Figure 2: Pearls. Mother-of-pearl is a natural nanocomposite that is biominalized with the help of proteins and mineral building blocks. © Masayuki Kato. Image reproduced with kind permission²¹.

Figure 3: (a) A magnetotactic bacterium. Scale bar 200 nm. (b) Morphology of magnetosome crystals that are biominalized with atomic precision, using proteins and mineral building blocks. © 2004 Nature Publishing Group. Image reproduced with kind permission ²².
Due to their excellent biocompatibility and biodegradability, the macromolecules occurring in biomimeralization are also of great interest for the synthesis of biomedical (nano)materials, even those with hierarchically arranged complex architectures. Peptides in the form of the secondary structure of proteins are also used as a framework for crystal nucleation and crystal growth. They can be designed to arrange themselves in a wide variety of nanostructures. In this way, predictable and programmable materials are made possible. Due to their unique properties, DNA, RNA and polysaccharides are also used as templates in the biomimeralization of nanostructures.

Notes and References
8 Quednau M. (2017): Geomikrobiologie Band 2: Anwendungen: Von Urban Mining bis Nanogeoscience (de Gruyter Studium), de Gruyter, Kapitel 2.1. (in German)
20 Image source: The sample is from the Hustedt Collection in Bremerhaven, Germany, # E1761.