## Nanodentistry

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## Synonyms

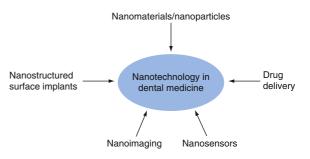
Nanotechnology in dental medicine

## Definition

Nanodentistry is defined as the science and technology of diagnosing, treating, and preventing oral and dental diseases, relieving pain, and of preserving and improving dental health, applying materials structured on the nanometer scale [1]. The nanotechnology considers nanostructures between 1 and 100 nm exhibiting properties and functionalities that fundamentally differ from that of other length scales, as the surface of the nanostructures dominates the material properties usually given by the bulk. The nanomaterials are not only promised to improve the properties and functionalities of dental products but also to lead to the development of innovative, novel products for the benefit of patients. In particular, nanomaterials have been part of engineered products, such as implants, dental and surgical instruments, dental care wares, as well as diagnostics tools.

## **Overview**

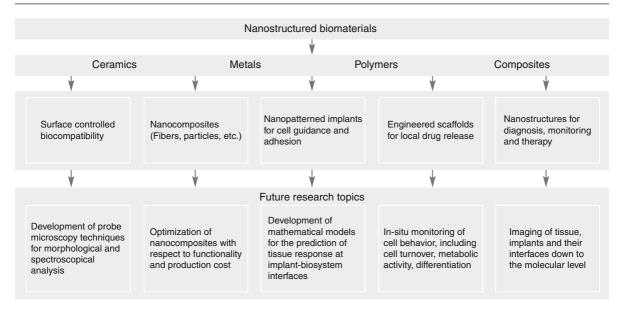
The cover story of R. A. Freitas Jr. in the *Journal of the American Dental Association* more than a decade ago [2] introduced the term *nanodentistry* to a larger community. He developed visions effectively using dental nanorobots for orthodontic realignments, for dentition regeneration procedures and, finally, oral health maintenance. He already elucidated the increasing influence of nanomaterials and the importance of tissue engineering. It has been pointed out that properly configured dentifrobots will recognize and subsequently destroy pathogenic bacteria residing in the plaque and elsewhere.



**Nanodentistry, Fig. 1** Key issues currently related to nanotechnology in dental medicine

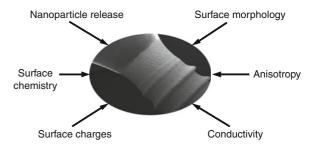
Although most of Freitas' ideas are still science fiction, today many applications of nanometer-scale components are known in the field of dentistry, which include nanoparticles in sensitive toothpastes, nanostructured surfaces of dental implants to improve osseointegration, and to reduce inflammatory reactions of different kinds of drugs (cp. Fig. 1). Further applications still on the research stage are classified into nanoimaging to reveal the nanometer-sized features in human tissues and man-made implants or nanosensors to quantify physical, chemical, or biological parameters within the oral cavity.

Dental materials are ceramics, metals, and polymers or any combination (cp. Fig. 2). Applying the knowledge and experience of nanotechnology to solve problems in the field of dental medicine, nanometersized patterns have been created on surfaces of implants and surgical instruments and incorporated into the bulk of the dental materials to accomplish the dedicated functionality. Nanostructures can improve the biocompatibility of dental implants or carry drugs toward the target within the oral cavity. Reactive nanostructures are going to emerge in diagnosis, monitoring, and therapy to enhance the patient treatments. Diverse activities augment the basic research of bio-nano-materials. Scanning probe microscopy techniques, for instance, enable us to morphologically and spectroscopically analyze hard and soft tissues to understand the structure-function relationship on the nanometer scale. Sophisticated mathematical simulations allow tailoring the material properties by the combination of nanometer-sized components. The outcome also predicts the tissue response and the self-organization at the implant-biosystem interfaces down to the molecular scale. Highly advanced in vivo measurements support cell biologists to determine the cell behavior with



Nanodentistry, Fig. 2 Materials science for nanodentistry

respect to proliferation, differentiation, and metabolism, especially at the interface between the dental material and the surrounding tissues. For this target, high-resolution imaging facilities have become more and more vital to quantify the different kinds of nanostructures with the desired precision.



#### Biocompatibility

Biocompatibility cannot be simply described as a specific property of the selected biomaterial, as well known from mechanical quantities such as Young's modulus. It is a peculiar term and defined as "... the ability of a material to perform with an appropriate host response in a specific application." [3]. This means it not only depends on the material itself but also from the location within the human body where the material is to be placed. Consequently, biocompatibility is not only related to intrinsic material properties. Its classification relies on standards (mainly ISO 10993 [4]). Therefore, the regular updates of these standards may change the status of a material concerning biocompatibility. Natural scientists and engineers are often not familiar with such a practice and, hence, usually terminate their work on such research areas.

The encouraging argument, however, correlates to the experimental observations that biocompatibility of

**Nanodentistry, Fig. 3** Several parameters allow tailoring the biocompatibility of dental implants

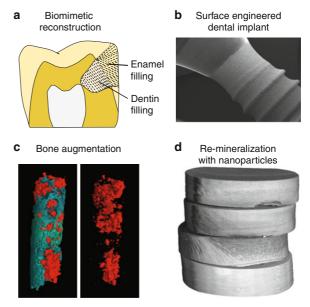
implants can be intentionally manipulated to optimize the clinical outcome. Figure 3 illustrates how some selected phenomena can influence the biocompatibility. For a dental titanium implant, for example, the surface is made rough down to the molecular level by sandblasting and etching procedures to ensure osseointegration and to reduce the inflammatory reactions [5]. Surface morphology can offer certain angles for dedicated protein absorption and activity. In addition, the surface chemistry is commonly tailored concerning oxide thickness, stoichiometry, and normally functionalized to obtain a hydrophilic surface. Further relevant factors are particle and ion release, surface charges, electrical conductivity, and anisotropies as present on patterned surface microand nanostructures. The measurement of the surface roughness on real implants is more than challenging,

since there is no single parameter and no single experimental setup, which allow simultaneously determining roughness on the micro- and nanometer scales.

## **Key Research Findings**

Figure 4 shows representative applications of nanotechnology in dental medicine. The fillers of reconstruction materials, the surfaces of dental implants, the different kinds of bone-augmentation ceramics and glass ceramics, as well as the re-mineralization of hard tissues by means of nanoparticles exploit nanotechnology by now and possess enormous growing potential. Nature-analogue, anisotropic restorations will replace today's dental filling and inlay materials as well as artificial teeth [6]. Researchers are still searching how the anisotropy can be introduced to obtain nanostructures similar to the ones present in healthy human teeth.

It belongs to the key impacts to realize that the ceramic components in dentin are orthogonally oriented to the nanostructures of the same size in enamel (see Fig. 5). This finding well observable in scanning small-angle X-ray scattering could explain why the dentin-enamel junction acts as an effective crack barrier. Small-angle X-ray scattering in scanning mode, as performed at the cSAXS beamline (Swiss Light Source, Paul Scherrer Institut, Switzerland) allows uncovering the mean orientation, abundance, and anisotropy of nanometer-sized components in human tissues over macroscopic areas [7]. It is in general difficult to isolate the contribution of specific components to the scattering signal, see chapter "Imaging the human body down to the molecular level." The collagen in human dentin, however, yields a characteristic signal related to its 67 nm-wide periodicity. Due to the sensitivity of scattering data to periodic structures, it is possible to extract a signal unequivocally related to collagen, thus allowing gathering component-specific information. Several 400 µm-thin slices from a human third molar were examined. Figure 5 shows the processed scattering signal from the features with sizes between 60 and 70 nm. The mean orientation of the scattering signal is coded according to the color wheel. The brightness relates to the abundance of nanostructures, while color saturation matches the degree of the anisotropy. The orientation of the scattering signal in both enamel and dentin is

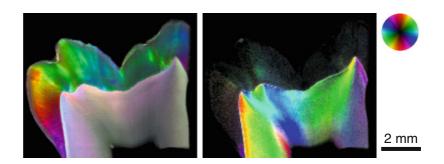


Nanodentistry, Fig. 4 Applications of nanotechnology in dentistry with growing potential

perpendicular to the crystallite orientation. On the left-hand side, the information from the total scattering signal is shown, which is mainly produced by the ceramic components of the tooth. Enamel and dentin can clearly be distinguished due to their different scattering potential. The strong color in the enamel is related to the high degree of anisotropy, that is, the high degree of orientation of the calcium phosphate crystallites, and their strong scattering potential in this range. In the dentin, the anisotropy is less distinct, and decreases with increasing distance from the dentinenamel junction (DEJ). Moreover, a perpendicular orientation of the scattering signal, and thus of the nanostructures, between enamel and dentin is observed. While the crystallites are mainly oriented perpendicular to the DEJ in enamel, parallel to the main direction of mechanical load, the dentin structures appear parallel to the DEJ, perpendicular to the mechanical loading. It is well known that the DEJ acts as an effective crack barrier, impeding the propagation of cracks from the enamel into the dentin. The image on the right in Fig. 5 shows only the signal related to the collagen matrix. Due to the distinctive periodicity of 67 nm along the collagen fibrils, the scattering signal is oriented parallel to the fibrils. No significant signal is found in the enamel. The mean scattering orientation of the collagen is found to be mainly perpendicular to

#### Nanodentistry,

**Fig. 5** Processed small-angle X-ray scattering data in the range between 60 and 70 nm. The mean orientation of the scattering signal is according to the color wheel. The brightness relates to the nanoparticle abundance, while color saturation codes their degree of anisotropy



that of the total signal on the left-hand image, revealing a parallel arrangement of collagen fibrils with the calcium phosphate crystallites. The collagen abundance is maximal near the DEJ and decreases toward the pulp. Abrupt changes in collagen fibril orientation are found along lines connecting the tooth cusps and the pulp. In this manner, the structure of the human teeth along the entire nanometer range is evaluated.

As pointed out above, the part of dental implants to be fixed in the bone is made rough. It contains nanostructures which resemble the apatite crystallites in human bone and therefore offer nanostructures with angles for suitable protein absorption. The suppliers have their secrets for the surface engineering processing, which includes sandblasting, etching, and electrochemical functionalization. Surface-engineered dental implants are very well established and do have a high success rate. During the next decade, we can expect a significant reduction in price so that a broader community of our aging society can benefit from such surface-engineered implants with dedicated nanostructures.

The calcium phosphate phases for bone augmentation gain more and more importance in our aging population. The resorbable calcium phosphate ceramics or bio-glasses do actively support the bone formation. These bone substitutes are combined with autologous bony tissues to repair larger and larger defects arising from cancer surgery, trauma, or just tooth loss.

There are numerous reasons for the demineralization of teeth. The mineral loss, especially owing to attacks of caries bacteria, has a massive effect on lifetime and function of teeth. Therefore, strategies have been developed to at least partially re-mineralize the enamel and dentin as the robust alternative to mechanical removal and conventional filling the defect. Optimized dental hygiene has reached restricted success in small caries lesions. Researchers all over the world use slices of dentin to explore the re-mineralization capacity of a variety of nanotechnology-based ceramics particles. Using a set of slices, a direct comparison of the different materials and procedures has become possible.

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#### **Future Research**

The dental nano-biomaterials have to be investigated to judge the toxicity and the biocompatibility and to pursue the personalized medicine with respect to more and more frequent material incompatibilities. The development of nanocontainers for a variety of drugs aims for targeted delivery preventing undesired side effects. For larger caries regions, which grow fast into the dentin, the collagen network might be still available, but the mineral phase is already dissolved. The return of the calcium phosphates and traces of other minerals into the affected region for restoration purposes is challenging but not impossible, as the collagen network could provide nucleation sites for the re-mineralization.

Bio-inspired dental fillings and inlays have to exhibit the anisotropy and orientation of organic and inorganic nanometer-sized components as found in enamel and dentin. Today, the dentists already use different fillings for dentin and enamel but without oriented anisotropic ceramics. Therefore, scientists and engineers have to discover opportunities to incorporate anisotropic nanometer-sized ceramics into the fillers and to carry them into the desired direction. Hence nature-analogue mechanical properties should be obtained. Based on these oriented nanostructures, one should search for self-repairing materials. Here again the human body provides concepts: the remodeling of bone.

## **Cross-References**

- AFM in Liquids
- Atomic Force Microscopy
- ► Basic MEMS Actuators
- ▶ Bioadhesion
- ▶ Bioinspired Synthesis of Nanomaterials
- ▶ Biomimetics
- ► Biosensors
- Chitosan Nanoparticles
- Confocal Laser Scanning Microscopy
- ► Electron Microscopy of Interactions Between Engineered Nanomaterials and Cells
- ▶ Imaging Human Body Down to Molecular Level
- In Vivo Toxicity of Titanium Dioxide and Gold Nanoparticles
- ► Microfabricated Probe Technology
- ► Nanomechanical Properties of Nanostructures
- ► Nanomedicine
- ► Nanoparticles
- ► Nanostructured Functionalized Surfaces
- Scanning Electron Microscopy
- Selected Synchrotron Radiation Techniques
- Self-repairing Materials

## Nanodevices

Nanostructures for Energy

## Nano-ecotoxicology

► Ecotoxicity of Inorganic Nanoparticles: From Unicellular Organisms to Invertebrates

## Nano-effects

► Physicochemical Properties of Nanoparticles in Relation with Toxicity

## Nanoelectrodes

► Dielectrophoretic Nanoassembly of Nanotubes onto Nanoelectrodes

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# Nanoencapsulation

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## Synonyms

Molecular encapsulation

## Definition

Nanoencapsulation is defined as the entrapping of active ingredients in nanometer-sized capsules.