

# A toolbox-set of Nanoparticles

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## ABSTRACT

The unique size, morphology and structure of Nanoparticles (NPs), which determines not only their properties but also their reactivity has permitted the development of Nanotechnology in numerous applications. While there is an urge to determinate if the benefit of NPs is worst the risk and therefore to establish adequate, repeatable and standardized nanotoxicology [1], the use of well-defined material to establish real structure–property and structure–activity relationships is of importance for further industrial applications. When investigating the impact of NPs on biological or material systems, it is important to understand that a change in size and shape often leads to a change in surface state (and reactivity within the surrounding of the NPs) [2]. We are currently developing such “nanoparticles-toolbox” of well-designed shape/size/surface/inner-shell NPs [3-6] from the “1st generation” to the “5th generation” of NPs (Figure 1) [7].

**Keywords:** nanoparticles, design, synthesis, characterization, nanosafety.

## 1 INTRODUCTION. A HOT QUESTION.

A deeper understanding of the inorganic NPs behavior in biological media is needed not only to fully control and develop the potential of these materials but also to increase the knowledge of the physical chemistry of inorganic matter when its morphology approaches to that of molecular (biological) entities. Although this knowledge and control is

not yet entirely acquired, industry and society are beginning to use nanomaterials in greater quantities and in consumer products. As normally happens when something new arrives to society, the interest in the broader implications of this emerging technology has grown together with unfounded “nanoeuphoria” and “nanoscars”. On the one hand, nanomaterials (NMs) have received enormous attention since, due to the control being acquired over their properties, they can be applied in biomedicine for diagnosis and therapy, in catalysis, energy production and storage and in environmental remediation among others. But on the other hand, their unique bio-interacting behavior may be associated with potential toxicity.

It is known that not only bacteria, viruses and parasites can be the cause of various pathologies, but also inorganic foreign bodies can lead to health-related problems such as silicosis, asbestosis and inflammatory reactions due to debris from worn out prostheses or related to diesel exhaust particles (DEPs), etc. Similar problems account when considering environmental applications [8]. The use of NPs could help to reduce the cost of environmental remediation but the benefit obtained has to be balanced with the potential risks of introducing large amounts of NPs in the environment [9]. Summarizing, a present hot question is whether the unknown risks of engineered NPs outweigh their benefits for the society. To solve it, many efforts are devoted by laboratories and companies worldwide, and also by national and supranational organizations, and this is also where the CNBSS makes its contribution.

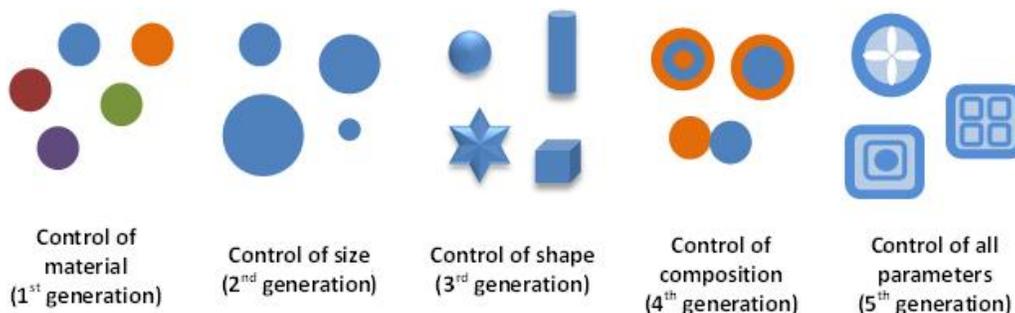


Figure 1: Evolution of the parameter control in the design of inorganic NPs.

## 2 NANOPARTICLE FULL LIFE CYCLE RESEARCH

To address these issues, the knowledge of NPs behavior in different biological media, i.e., their life cycle in those environments and their biological impact, is key to design NPs with improved safety profiles. When facing this challenge, we do not start from scratch. NPs are not a completely new class of materials. In fact, some incidental NPs are central to many natural processes, from marine aerosols to volcanoes and forest fires [10-11]. And they do not have a great effect on health, as we have evolved in their presence. It has been also observed that some nanomaterials, as fullerenes, are produced naturally as unintentional byproducts of combustion processes and burning paraffin and diesel produces carbon nanotubes (CNTs) [12]. NMs can also be found perfectly integrated into biological structures. For example, biogenic magnetic NP occur naturally in many organisms ranging from bacteria to protozoa and to animals [13-15]. A biological model of coated NM also found in humans is ferritin, an iron storage protein of approximately 12nm in diameter that contains 5 to 7nm hydrous ferric oxide inside a protective protein shell [16]. Similarly, man-made inorganic NPs have been in contact with humans since ancient times, *e.i.*, in creams for cosmetics [17]. Also, different food additives are already consisting on inorganic NPs (E-171 consist on ultrafine titanium dioxide, E-172 is iron oxides [8]). Finally, over the last century, human exposure to airborne nanosized particles has increased dramatically due to anthropogenic sources such as internal combustion engines, power plants, and other sources of thermodegradation of organic matter.

The health-related effects of these minute inorganic matter has been studied during last decades and a significant body of research on the effects of natural and incidental NPs has been acquired. However, these studies with engineered NMs are still at early stages and along with contradictory data. For example, on one hand, reports on strong biopersistence and accumulation of NPs for months to years and, on the other hand, reports on their rapid expulsion, including renal clearance of too large NPs coexist in the literature. Furthermore, while reactions of cells and organs to NPs have been observed, the long term consequences of such effects are still not known. Also, reports about NP crossing tight-junctions (as the blood brain barrier) and mucosal barriers are also still unclear and under controversy.

All this has raised concerns to public bodies, industry and society since some nanomaterials are already in the market, the use of NMs is expected to be broadly widespread in the coming years and, moreover, because of the fast development of new NMs for a wide range of applications. During the first decade of this century, the efforts to design and produce monodisperse collections of

inorganic NPs and carbon nanostructures has rapidly grown and an increased number of different types of NPs of increasing complexity and more artificial with time are being produced [3]. The main differences between natural, unintentional NPs and anthropogenic, intentional NPs are: i) the polydisperse and chemically complex nature of the former in contrast to the monodisperse and precise chemically engineered characteristics of the latter; ii) the particle morphology, often a branched structure from combustion particles is in contrast with spherical forms of engineered NPs, and, of course, other intended geometrical figures that are appearing in the scientific literature, including tubes, wires, rings, disks, boxes, double boxes, hollow NPs, etc [3, 5], and iii) “natural” NPs tend to dissolve or agglomerate rapidly to minimize their increased surface energy, but engineered NPs are synthesized to be stable over a much longer time.

However, despite these differences, the same physicochemical principles are likely to be applied to both types of NPs in order to understand the behavior of this class of materials. The reason is that all them are often out of chemical equilibrium, in a metastable phase, and their final fate is the disintegration or agglomeration towards more stable phases. And, in the way of becoming a collection of individual atoms or a larger particle, intended and unintentional NPs follow similar physicochemical processes which have a key role on their impact towards biological systems, such as molecular components of the cell, cellular compartments, cells, tissues, organisms and, going to the basis, the ecosystems. Taking into account all these considerations, to examine the NPs characteristics and evolution during their full life cycle in biological media, and to assess their impact on biological systems we focus our attention in:

i) The stability of the core of the NPs: metallic cations released when NPs corrode can be a source of detrimental health effects. In this context, patterns of cation release are studied and the potential impact on biological systems discussed.

ii) The stability of the surface of the NPs: while much of the NPs functions are due to their core composition, the surface coating defines more likely their bioactivity. NPs never travel alone, but they are constantly surrounded by a coating of different molecules, intended for a further application and/or spontaneous due to molecules present in the environment. This spontaneous coating is not immediate but develops as time progresses enabling different biological responses at different times of exposure [18].

iii) Agglomeration and aggregation of the NPs: their colloidal stability determines their proper interaction with biological entities, e.g., the higher cytotoxicity of unstable

colloidal preparation of NPs are not due to the material but rather its final micro or macrometric size.

iv) The impact towards living systems of either NPs themselves or of these changes in size, shape and surface state. Main questions to solve include how immune system react towards them, how they affect biological barriers and membranes, the Reactive Oxygen Species production derived from NP reactivity, or whether NPs may pose intrinsic risks or they may increase or decrease toxicity of other molecules, by absorbing and trapping them, among others.

### 3 INORGANIC NANOPARTICLES

As a consequence of what has been presented so far, the proper understanding of this fundamental knowledge is essential for the production of NPs with a low risk index. In this context, the CNBSS accompany the development of a "toolbox-set" of nanoparticles ready to be used in a wide range of applications such as materials science, catalysis, medicine, energy and remediation. This "toolbox-set" include NPs with controlled composition, size, shape, surface state (Figure 1).

Before presenting the list, it is worth defining what engineered NPs are. Of course, inorganic NPs are considered as *NPs* not only for their sizes. If NPs are of great scientific and commercial interest it is because they are effectively a bridge between bulk and atomic or molecular structures. This means that, at the nanoscale, material properties change abruptly in respect to those displayed by either a material of the same composition but larger ("bulk"), or the single atom solated (ion), or the single atom forming part of a molecule. And, while a bulk material should have constant physical properties regardless of its size, this is often not the case at the nanoscale. Materials properties change as the percentage of atoms at their surface becomes significant. Size-dependent properties observed for NMs include, among others, quantum confinement in semiconductor NPs, surface plasmon resonance in some metal NPs and superparamagnetism in magnetic materials. Thus, as discussed in our review [8], a NP could be considered as a small particle which present novel properties that differ from the bulk material. Obviously, there is no a strict dividing line between NPs and non-NPs.

Beyond size discussion, another important feature that distinguishes engineered NPs from other particulate matter is their monodispersity. In this sense, it is useful to consider NPs as molecular entities, despite their structural dispersion when compared to truly molecular materials. Thus, what qualifies NPs to be considered molecules is their reduced size and size and shape depending properties (as in the case of biological macromolecules and their Structure-Activity Relationship) and also their

monodispersity. Without entering into a discussion about the physical limit of monodispersity i.e. which standard deviation treshold respect the mean size determines that a collection of NPs should be considered monodisperse, from a practical point of view two NPs can be considered monodisperse if they respond undiscernibly to a determined test. This means that, as in the case of molecules, in one mole of NPs, every NP behaves indistinguishable respect to the others respect to that test and using the current characterization techniques.

Last but not least, to provide an accurately description of the concept of NM, it is important to note again that many of them are independent nanometric units once produced, but they tend to aggregate rapidly into micro or macrometric particles, thus loosing nanoscale properties. Therefore, if engineered NPs need to be kept separate from each other, it is required surface engineering in order to provide them with repulsion forces to prevent aggregation. This can be done either by electrostatic repulsion, *e.i.* allowing the formation of a double electrical layer of inorganic ions around the surface of the NPs, or by steric means, *e.i.* through the conjugation of organic or biological molecules. This has been several times undeservedly neglected in the discussion about the concept of NMs and is a key point to understand what we are dealing with: a NP must be understood not as a bunch of atoms that display different properties in respect to other formats of the same material, but as this bunch of atoms (inorganic core) together with the sabilization layer (inorganic or organic shell) that prevents its agglomeration or aggregation into something bigger.

### 4 A "TOOLBOX-SET OF NANOPARTICLES"

Taking into account all these considerations and regarding production of nanomaterials, the CNBSS is offering which below is summarized:

**NP Composition:** The list of materials CNBSS is offering include (see Figure 2):

Metals: Ag, Au, Co, Fe, Ni, Pd, Pt.

Metal Oxides: CeO<sub>2</sub>, CoO, FeOx, NiO, SiO<sub>2</sub>, TiO<sub>2</sub>, ZnO

Semiconductor: CdSe, ZnS

Hibrids and Heterodimers: Ag/CeO<sub>2</sub>, CdSe/Au, CdSe/Pt, Au/Pt, Co/Pt.

Core-shells and core-shell-shell: Au@Ag, CdSe@CdS@ZnS.

## 5 CONCLUSION

The CNBSS is currently developing a “toolbox” of well-designed shape/size/surface/inner-shell NPs ready to be used in numerous of applications such as materials science, catalysis, medicine, energy and remediation. During investigation on NPs and their development at the industrial level, the CNBSS is also carrying out research on the NP full life-cycle, since NP shape, size and structure may be altered in the application media and, consequently, their reactivity is affected. Thus, the proper knowledge of NPs modifications in those environments is key to properly design performing and safe NPs.

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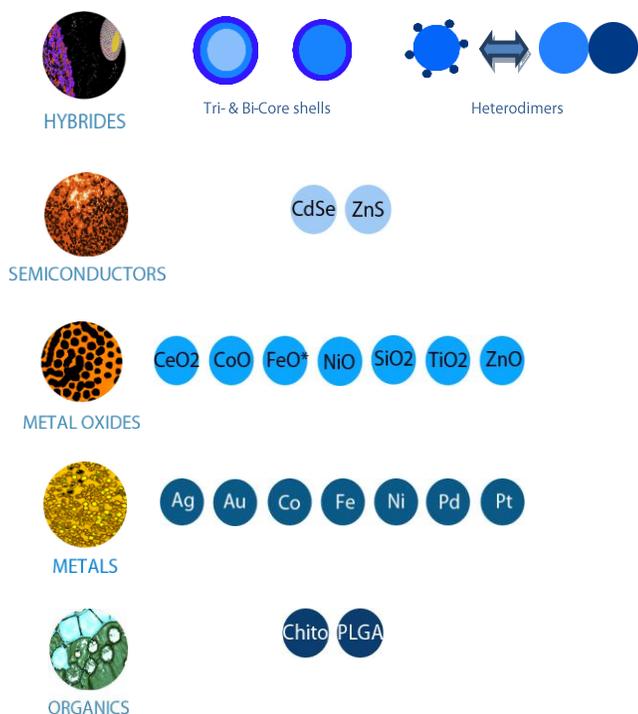


Figure 2: An overview of the NPs provided by the CNBSS.

**NP shape:** depending on the type of NPs, range from spheres, cubes, rings, disks, wires, to hollow nanostructures as boxes, cages and tubs.

**NP surface state:** Also, depending on the desired application, NPs are dispersed either in aqueous or organic solvents and stabilized with a broad range of stabilizers and surfactants such as organic and biologic (PEG (polyethyleneglicol), PVP (polyvinilpirrolidone), mercaptoacids and mercaptoamines, proteins and protein derivatives as antibodies, etc) and inorganic stablizers (trisodium citrate, ascorbic acid, tannic acid, ammonium salts, etc).

**Applications:** These NPs can be applied in a variety of industrial sectors and commercial products including bactericides chemical catalysis, CO<sub>2</sub> capture, imaging, photo-catalysis, sensors, spectroscopy, thermo-catalysis, vectorisation and drug delivery, etc.

**Characterization:** Finally, reproducibility and homogeneity are the key-strength of the CNBSS to permit the best traceability. Thus, NPs can be fully characterized (depending on the requeriments of the sample) by standard techniques such as Electron Microscopies (TEM, SEM), Electron Dispersive X-Ray Spectroscopy (EDS), X-Ray Diffraction, UV-Visible Spectroscopy, Zeta Potential, Dynamic Light Scattering, ICP-MS and by high-resolution characterization techniques such as advanced electron microscopies (HRTEM, EELS).