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# MODERN

MODELING THE ENVIRONMENTAL AND HUMAN HEALTH  
EFFECTS OF NANOMATERIALS

Collaborative Project

Topic NMP.2012.1.3-2: Modeling toxicity behavior of engineered nanoparticles

## D1.1

**Conceptual approach to enable structure-activity modeling for  
nanoparticles**

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**Abstract:** This Deliverable shortly sketches the efforts undertaken to apply quantum-chemical methods for the modeling of iron oxide nanoparticles. At the current state, models for still rather small building blocks are being developed. These blocks will be subsequently enlarged and eventually used to model full nanoparticles.

**Keywords:** Iron oxide nanoparticle, QSAR, quantum chemistry, Density Functional Theory (DFT), Hartree-Fock (HF)

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## **INTRODUCTION.**

Modeling the physicochemical properties of nanoparticles is particularly challenging in comparison to normal molecules with regard to three aspects.

1) While ecotoxicological and toxicological endpoints may be comparable more or less, this holds not true for physico-chemical properties. Several properties as well as several descriptors used in modeling have been identified to be important.

2) Nanoparticles are hard to be modeled as a whole due to their size. Albeit being small on the micro scale of experimental physics, they are huge in comparison to organic and inorganic molecules normally considered for modeling on an atomic scale. An approach to make nanoparticle modeling feasible is to divide the structures into building blocks. Then in a two-step process, these building blocks are handled by conventional modeling in the first step, and secondly the gained information is extrapolated and applied to the nanoscale.

3) Real-world nanoparticles are non-unique with respect to their structural variability. Not only there is a great variance in chemical composition due to core configuration and surface modifications, but even in the case of homogenous chemical composition there is a great variance in size and shape of the resulting particles. Therefore, nanoparticles are very different from ordinary pure substances in the context of physicochemical modeling, and behave to some extent as mixtures.

Within MODERN, it was originally intended to start with whole nanoparticles. However, soon in the beginning this turned out to be less favorable. We decided to start, as described above, with the modeling of particular building blocks, and later on to develop the framework for combining the individual (informational as well as molecular) building blocks while addressing variability. The advantage of this course of action is to maintain chemical flexibility as well as computational feasibility by replacing the modeling of exuberantly huge molecules and inhomogeneous mixtures with size dependent extrapolation and statistical treatment.

The current Deliverable roughly sketches our first modeling efforts. Due to the public dissemination level, detailed preliminary results cannot be disclosed. These are documented separately and could be discussed within the consortium based on bilateral agreements, if appropriate. Details on first results will also be part of the yearly progress report.

## **TARGET TYPES.**

The first decision to be made was the selection of the type of nanoparticles to start with. Generally, the term “nanoparticles” refers to particles with nanoscale dimensions. Nanoscale is a distance between 1 and 100 nm [1]. To be a nanoparticle, normally all three dimensions of the particle need to be within that scale. However, our research is envisaged to also address nanoplates and nanofibers. Nanoplates are larger plates with their thickness within the nanoscale, and nanofibers resemble strings with elliptic nanoscale diameters. The section of the fibers should not deviate from circles too much. The ratio of the largest to smallest dimension should not fall below three.

Generally, all nanoparticles contain a core. This core may be surrounded by a shell, and may further be coated. The function of the shell and of the coating of nanoparticles is to tailor their properties to their intended application.

Structure-activity modeling needs to address all three parts. Conceptually, the first step is to model the core properties by means of building blocks. Even this step has to handle variability within and outside of the building blocks already.

Basically, nanoparticle cores can either be organic or inorganic. Examples for organic nanoparticles are fullerenes and single-wall and multi-wall carbon nanotubes. Inorganic nanoparticles may have a pure metal or metalloid core (as Ag, Al, Au, Cu, Fe, Ti, Ni, and Si), or a metal oxide core (as CeO<sub>2</sub>, Fe<sub>2</sub>O<sub>3</sub>, Fe<sub>3</sub>O<sub>4</sub>, SiO<sub>2</sub>, TiO<sub>2</sub>, ZnO). Furthermore there are quantum dots like CdSe. These particles are crystalline and possess size-depend properties because of quantum-confinement-effects to the electronic states.

In agreement with the other research activities within MODERN, we decided to start with the modeling of inorganic Fe<sub>2</sub>O<sub>3</sub> particles, and later to include nanoparticles with Ag, SiO<sub>2</sub>, and TiO<sub>2</sub> cores.

## **PROPERTIES.**

According to the literature [2], the most important physicochemical properties of nanoparticles are size (diameter, volume, surface, surface/volume ratio, ovality), surface area, surface charge in terms of the zeta-potential, surface and particle composition, state of agglomeration and aggregation, and solvent interaction properties (hydrophilic, hydrophobic, lipophilic etc.). Further potentially interesting

properties are the shape and the type of the nanoparticle (i.e. nanoparticle, nanofiber, nanorod, nanotube, quantum dot etc.).

## **MODELING TECHNIQUES.**

Up to now, the general strategy of our approach is to start with the quantum-chemical characterization of the building blocks. To this end, we apply Density Functional Theory (DFT) and the Hartree-Fock (HF) methods through Gaussian09 [3]. At startup, calculations for very small building blocks of (e.g.  $\text{Fe}_2\text{O}_3$ ) nanoparticles being previously described in the literature are being reproduced. These building blocks then will be subsequently enlarged by adding additional atoms as far as feasible. Later on, these building blocks will be combined by statistical methods to address the variability as well as to approach the nanoscale.

## **FIRST MODELING EFFORTS.**

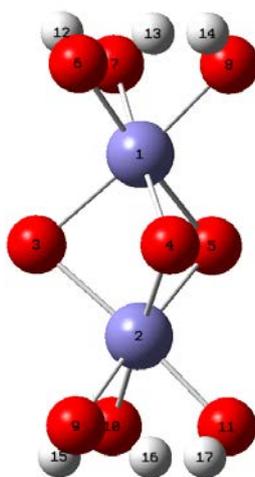
As a starting point, modeling efforts have been undertaken by quantum-chemical characterization of a building block consisting of one iron and one oxygen atom ( $\text{FeO}$ ). This molecule was saturated by adding water molecules to the analyzed iron oxide molecule, because water is ubiquitous under standard conditions [4]. In this case one water molecule was added to the system, so the resulting and saturated molecule was  $\text{Fe}(\text{OH})_2$ . (Fe is saturated by  $\text{OH}^-$ , O is saturated by  $\text{H}^+$ ).

Next, the building block was extended to contain one Fe and two oxygen atoms ( $\text{FeO}_2$ ). After saturation with two water molecules, the resulting molecule was  $\text{Fe}(\text{OH})_3 (+ \text{OH}^-)$ . The second hydroxide anion was neglected and not included in the modeling process. The obtained results showed no substantial deviation from the literature results [5], proving the validity of our calculation protocols.

The next major step is to add a second iron atom to the system. So in this case, the analyzed system consists of two iron and two oxygen atoms ( $\text{Fe}_2\text{O}_2$ ). Adding of two water molecules to the iron oxide molecule, the resulting building block is  $\text{Fe}_2(\text{OH})_4$ , thus the oxidation number of both iron atoms is +2. These calculations are still in progress.

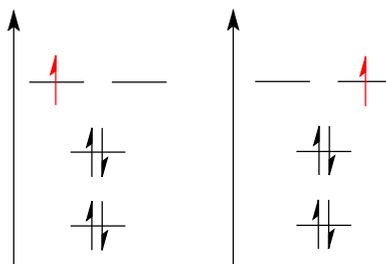
In order to further extend the building block, the next step is the modeling of an increased part of the  $\text{Fe}_2\text{O}_3$  crystal structure. It consists of two iron atoms, three bridge-bonded oxygen atoms, and six hydroxide-ligands (three per iron atom, saturation included). The building block is shown in Fig. 1.

By adding a second iron atom, some particular complications have to be addressed. The spin multiplicity of the iron atoms and therefore the occupation of the electronic levels is not observable from first principles. In the iron atom, the d-orbitals are partially occupied. I.e.  $\text{Fe}^{2+}$  has a  $d^6$ , and  $\text{Fe}^{3+}$  has a  $d^5$  valence electron configuration, respectively. So for both ions a high-spin and a low-spin state is possible. Thus, the spin multiplicity in the combined molecule is not known and depends solely on the resulting total energy. Therefore, a series of calculations accounting for all possible (and reasonable) spin states has to be performed.



**Fig.1.**  $\text{Fe}_2\text{O}_3$  building block, consisting of two iron atoms (1, 2), three bridge-bonded oxygen atoms (3-5), and six hydroxide-ligands (O atoms 6-11 and H atoms 12-17).

Additionally, ambiguities with regard to the occupation of degenerated molecule orbitals may occur (Fig. 2), resulting in difficulties within SCF convergence and geometry optimization. This may be an explanation for the observed critical energy alternations during our geometry optimizations, thus preventing the achievement of convergence.



**Fig. 2.** Ambiguous orbital occupation. In the case of degenerated orbitals, multiple electron configurations (shown in red) may exist, each being represented by a single Slater determinant and contributing with distinctive amplitudes to the resulting multi-determinant ground state. Thus single-determinant approaches such as standard Hartree-Fock and DFT methods are insufficient in describing these kinds of electronic systems, which may result in bad SCF convergence.

There exist solutions to the above mentioned problems, however, all of them are computationally expensive even for small molecules, and thus may not be feasible for the envisaged nanomaterial modeling.

Our current research focus is on overcoming the sketched problems. A promising way forward could be the application of particularly adapted basis sets, adjustments to the SCF options and (if everything else fails) multi-reference approaches.

## OUTLOOK.

The next steps will be to further extend the building blocks up to a reasonable level. Then, protocols for combining building block based information into nanoparticle models have to be developed. From them, nanodescriptors will be derived to model properties. The results will be augmented with and compared to strings based modeling approaches. The non-unique character and variability will be addressed by introducing distribution functions via statistical analysis. The models will be validated by synthesized and characterized particles.

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