# ProtoNANO: assessing the toxicity of inorganic nanomaterials using nano-QSAR models

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## 1. Introduction

Development of new chemicals and materials focuses in enhancing a few properties of interest, such as potential therapeutical effects (pharmaceuticals) or tribological properties (lubricants). However, it is essential to assess the risks that those materials pose for the safety of humans and the environment. Computational assessment is a very convenient way to consider the safety of substances with reduced economical, ecological and ethical impact. Among those methods, the most outstanding are mathematical models to relate the structure of chemicals with a biological/physicochemical property or activity: the QSAR models (from Quantitative Structure-Activity Relationships). QSARs for discrete organic molecules are widely used and are accepted for regulatory purposes. In recent years, QSAR models on nanomaterials (NMs), from herein labelled as nano-QSARs, are being developed and improved [1].

## 2. Nano-QSAR

Usually, QSAR models describes substances by their chemical structure, often represented by the SMILES code. However; this approach is insufficient for NMs, because a key component of their definition is their size. Furthermore, often they are characterised by complex compositions which affect their physicochemical and biological behaviour. In addition to develop specific calculated descriptors for NMs, experimental properties and/or conditions are being used as descriptors, due to their ability to capture insights on the real structure. We recently reviewed the range of numerical descriptors used in the literature for NMs [2], and proposed a classification for descriptors considering if they are direct descriptions of the structure (composition of the core/surface and geometry of the particles) or indirect experimental parameters (related to the NM properties, its synthesis or the endpoint measurement). However, the use of experimental data creates another challenge for the nano-QSAR models, the lack of consistence among the methods and parameters used to characterize and evaluate NM in the literature that hinder the creation of modelling databases.

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ProtoNANO [3], which is one of the modules in the *in silico* prediction server ProtoPRED®, facilitates the use of a series of nano-QSAR models developed for different inorganic NMs, such as noble metals, metallic oxides and quantum dots (QDs). The models concern toxicity (to humans through *in vivo* or *in vitro* models, such as *E. coli* or *cell-lines*), ecotoxicity (adverse effect on plants and animals) and physico-chemical properties. The later includes those with a key role in risk assessment (related with physical hazards or with exposure and environmental fate, such as partition coefficient) but also properties used to characterize and group materials, such as the Zeta potential.

## 3. Case study: Cytotoxicity of QDs

From the different models existing in ProtoNANO, this presentation will use the cytotoxicity of QDs to exemplify the particularities of applying this technique to nanomaterials. In this case, we will explore the dataset compiled by Bilal et al.[4] which includes cytotoxicity data against both tumoral-based cell-lines and primary cells. QDs are a particular group of materials which are characterized by their unique optical and electronic properties caused by their semiconductor nature which makes noticeable certain quantum mechanics (QM) behaviours. For example, their discrete electronic levels lead to UV-visible emission patterns which depend on the size of the particle (Figure 1). In this case, the database describes inorganic, Cd-based QDs which composition is distributed among four different categories: core, shell, ligands and modifications. Interestingly, the database also provides information on experimental data such as the size, wavelength of emission and experimental conditions.

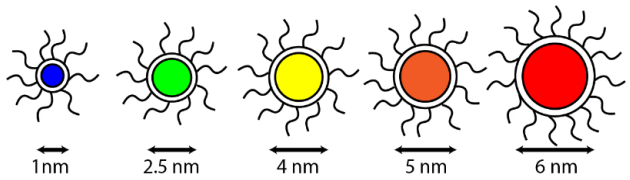


*Figure 1: Graphical representation of the UV emission wavelength change with the QD size.*

In this presentation, we analyse the contents of the database and present the development of a series of predictive models. The examples will serve to discuss the effect of different features, including calculated descriptors and experimental measurements. Furthermore, we explore the division of the dataset in two groups, primary cells and cell-lines. The objective is to have two different but complementary models to enrich the interpretation of the data and to explore their potential as antitumoral treatments.

## 4. Acknowledgements

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