NANO-QSAR MODELS ON THE TOXICITY OF NANOMATERIALS

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Developing new materials often prioritizes enhancing specific properties, but assessing the potential risks these materials pose to human health and the environment is equally important. Computational methods offer a valuable solution, helping minimize this assessment's economic, ecological, and ethical impacts. Among these, QSAR models (Quantitative Structure-Activity Relationships) stand out for their widespread use and acceptance in regulatory evaluations, particularly for discrete organic molecules. Recently, researchers have expanded these models to cover nanomaterials (NMs), a field known as nano-QSAR, to better predict and understand these complex substances' behavior. [1]

Unlike traditional molecules, where describing substances solely by their chemical structure is enough (such as the SMILES code), nanomaterials have unique structural features, like size and complex composition (Figure 1), that significantly influence their physicochemical and biological behavior. In our recent review, [2] we recognized the need for a new classification of numerical descriptors to represent nanomaterials. This classification (Figure 2) distinguishes between direct descriptors, which offer a direct representation of the nanomaterial's structure, and indirect descriptors, which incorporate additional experimental parameters.

Direct descriptors provide information about the chemical composition of the core (a), surface substituents (b), or the physical structure of the particles (c). Indirect descriptors, on the other hand, capture experimental features that either depend on the structure (d) or cause changes to the structure (e). Additionally, we include descriptors that don't directly describe the nanomaterial but relate to the conditions under which endpoint measurements are taken (f). However, using experimental data brings its own challenges, as inconsistencies in methods and characterization across the literature complicate the creation of reliable modeling databases for nano-QSAR.

ProtoNANO, a module of the *in silico* prediction server ProtoPRED® [3], is at the forefront of advancing nano-QSAR models for various inorganic NMs. ProtoNANO is instrumental in assessing the risks associated with nanomaterials and improving their characterization by focusing on human toxicity, ecotoxicity, and physicochemical properties. In this presentation, we will explore the obstacles faced in developing nano-QSAR projects and highlight some of the models in ProtoNANO as case studies. These examples demonstrate how different features, including calculated descriptors and experimental data, can influence model outcomes and risk predictions.

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References

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[2] Moncho, S.; Serrano-Candelas, E.; de Julián-Ortiz, J. V.; Gozalbes, R. Beilstein J. Nanotechnol. 15, (2024), 854–866.
[3] Moncho, S.; et al. ProtoNANO: A module of ProtoPRED® 2023 https://protopred.protoqsar.com/ProtoNANO_info

Figures

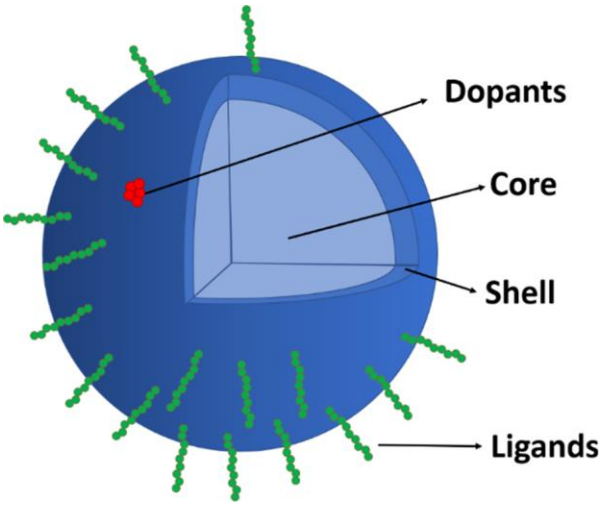

Figure 1. Schematic depiction of the parts of a complex nanoparticle.

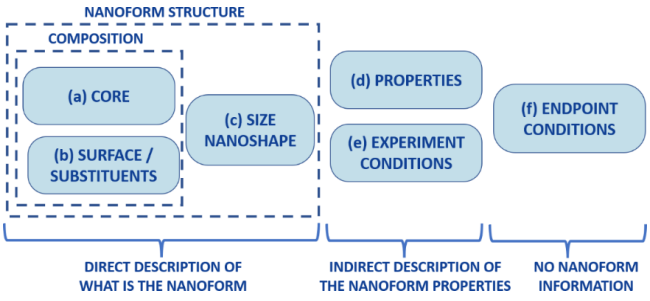

Figure 2. Classification of nanoQSAR descriptors