UNIVERSITY OF BIRMINGHAM

A strategy for grouping of nanomaterials based on key physico-chemical descriptors as a basis for safer-by-design NMs

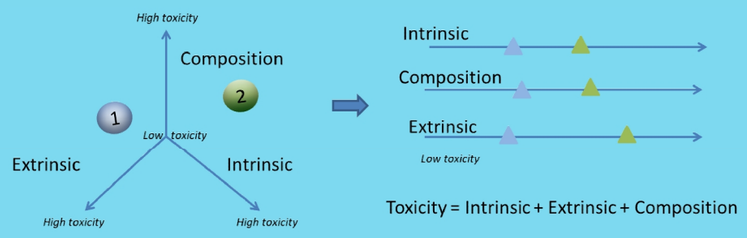
Iseult Lynch,[1] Carsten Weiss[2] and Eugenia Valsami-Jones[1, 3]

[1] Department of Geography, Earth and Environmental Sciences, University of Birmingham, Edgbaston, Birmingham, B15 2TT, United Kingdom; [2] Karlsruhe Institute of Technology, Campus North, Hermann-von-Helmholtz-Platz 1, 76344 Eggenstein-Leopoldshafen, 76021 Karlsruhe, Germany; [3] Earth Sciences, Natural History Museum, Cromwell Road, London, SW7 5BD, UK

***Classification* (noun):** the act or process of putting things into groups based on ways that they are alike, or, a systematic arrangement in groups or categories according to established criteria; specifically: taxonomy.

Identification of critical Nanomaterial (NM) properties (physicochemical descriptors) that confer the ability to induce harm in biological systems is crucial to facilitate safe & responsible implementation of nanotechnologies, enabling both prediction of impacts from related NMs (via quantitative nanostructure-activity relationships (QNARs) and read-across approaches) and development of strategies to ensure these features are avoided or minimised in NM production in the future ("safety by design").

A novel approach to identify interlinked physicochemical descriptors, and on this basis identify overarching descriptors (axes or principle components) which can be used to correlate with toxicity is proposed. An example of the approach is provided, using three principle components which we suggest can be utilised to fully describe each NM, these being the *intrinsic* (inherent) properties of the NM, *composition* (which we propose as a separate parameter) and *extrinsic* properties (interaction with media, molecular coronas etc.).



Schematic of the proposed 3 dimensions (principle components) of toxicity, and the application of this to compositionally (and architecturally) diverse NMs.

Position of a specific NM along these axes will determine / predict its toxicity. Thus, particle 1 (in blue) has less structural strain, lower interactions and less dissolution than particle 2 (in green) and thus has lower toxicity.

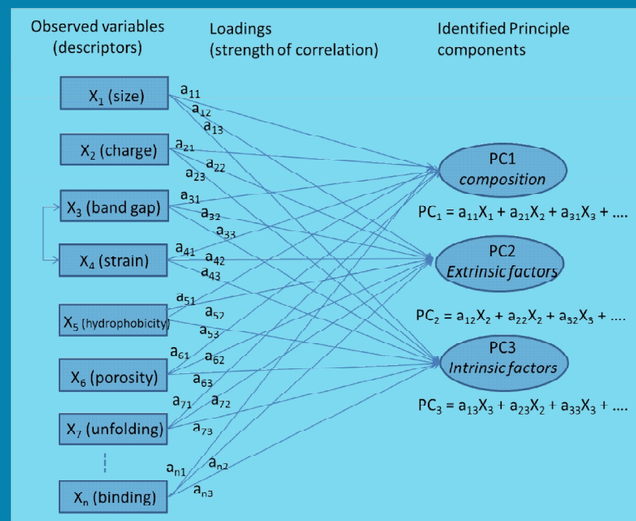
Three principle components:

***Intrinsic* properties** (e.g. structure and structural strain) with NM properties including shape, porosity, structural configuration and bandgap mapping to this..

Extrinsic properties (e.g. surface interactions and transformations as a result of binding) including resultant biomolecule conformational effects (e.g. unfolding, receptor activation, membrane damage, fibrillation etc.)

Composition, including inherent molecular toxicity, charge, hydrophobicity and coating (although also linked to both intrinsic / extrinsic axes)

Our concept allows the development of a scale describing their relative contributions to each axis.



Schematic illustration of use of PCA as applied to determination of primary descriptors of NM toxicity.

Initially, each variable (measured end-point) is considered equal. Using latent variable analysis determines the principle components and how much of the total variance in the starting dataset is described by each component.

Interdependence of descriptors, or principle components, can also be accounted for, represented by double-headed arrows between the interrelated entities, and the degree of inter-dependence is also calculated (e.g. arrow between band-gap and strain for example).

NanoMILE (coordinated by UoB) is a €10M FP7 flagship project assessing the mechanisms of nanomaterials interactions with living systems. The overarching objective of NanoMILE is to develop a framework for the classification of nanomaterial safety and to facilitate the implementation of "safety by design" principles.