A similarity testing computational approach for grouping nanomaterials

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Overview

The use of non-testing strategies in the hazard assessment of nanoforms (NF) is deemed essential to perform the safety assessment of all NFs in due time and at lower costs. The identification of physicochemical properties affecting the hazard potential of NFs is crucial, as it could enable to predict impacts from similar NFs and outcomes of similar assays, reducing the need for experimental testing. To this end, a computational grouping approach for NFs are presented aiming at identifying classes of similar NFs depending on dose-response curves. An application to reactivity data is presented, however the method can be readily applied to any dose-response relationship data and extended to dose-response-time data. Our findings suggest that similarity assessment could be used to verify and strengthen grouping hypotheses as well as the link between NF properties and the biological effect considered.

Similarity testing strategy

Fig. 1 is presenting three dose-response curves. **Questions of interest are: Are data coming from the same distribution? If that is the case, are all distributional parameters the same?**
To answer the above questions, three possible scenarios (Hypotheses) are tested:
H_1: 'data curves are replicates'
H_2: 'data curves have the same growth rate'
H_3: 'all data curve parameters are different'

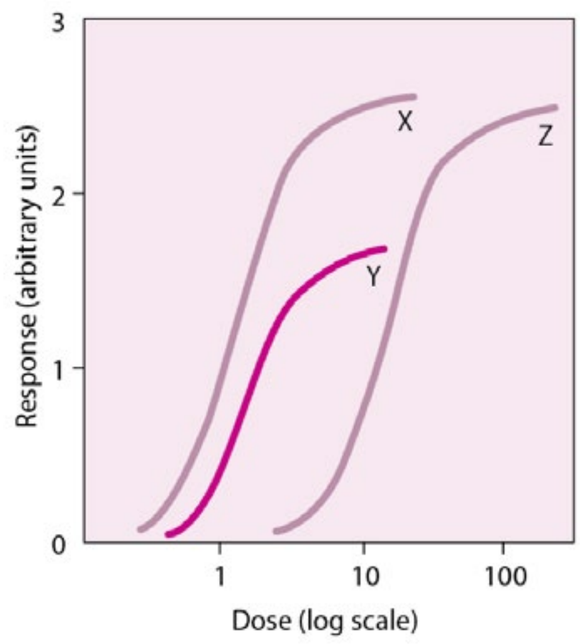

Figure 1:A schematic representation of possible dose-response curves. Simulated curves X, Z describe the same distribution with different sets of parameters which causes a shift of X to the right of the x-axis. Simulated curve Y is describing a different distribution from that of X, Z.

Methods

Data are assumed to follow a two-component mixture logistic regression model similarly to Hennessey et al.(2010). All possible NF pairwise comparisons are then considered given the three scenarios (H_1, H_2, H_3) presented above. Bayes Factor calculations are used to test whether pairs of curves are 'similar' or 'dissimilar', whilst uniform prior probabilities are imposed assigning equal weight to the possible NF pairs. Gaussian and Cauchy prior options are also considered.

An application to reactivity data

Reactivity data were downloaded from the GRACIOUS database which comprises data for three different assays, namely FRAS, EPR and DCFH. Fig. 2 shows Bayes Factor values to compare models H_1, H_3 for pairs of 12 different NFs in FRAS and EPR assays respectively. The model that bests describes the data can be used to compare pairs of curves from different NFs.

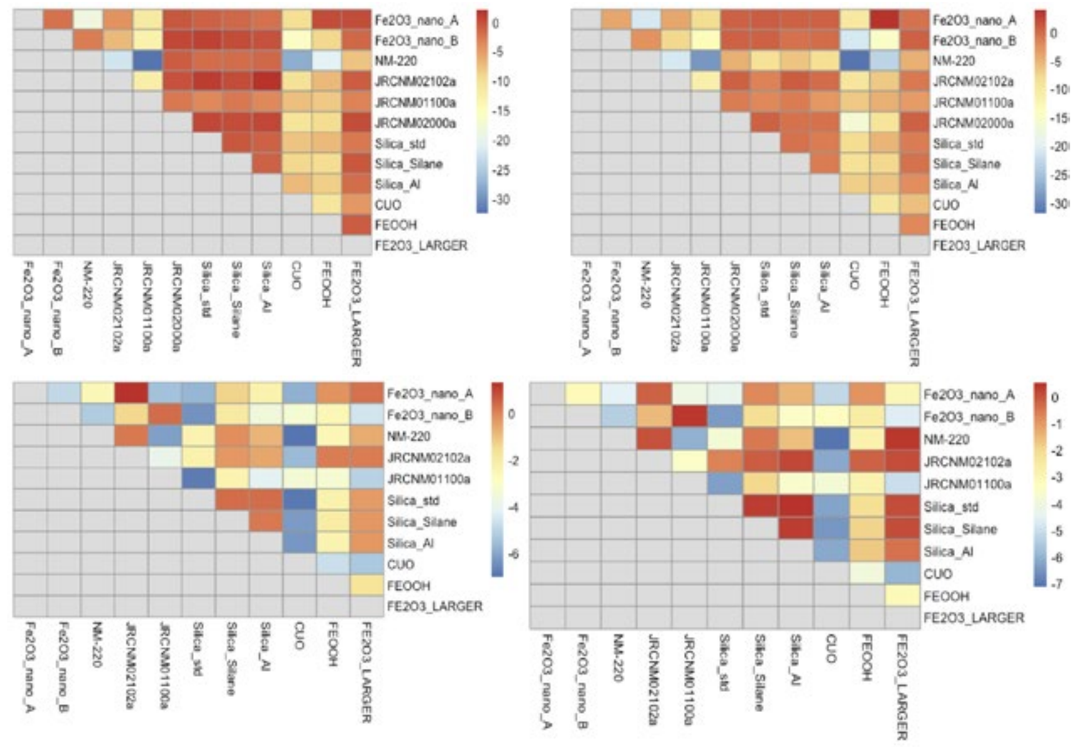

Figure 2:Bayes factor values for all possible pairs of NFs. Each value in the upper diagonal colour tables above shows how likely pairs of NFs are to have identical dose-response reactivity curves as opposed to quite different curves (orange colouring is supporting high similarity). NFs are then grouped based on colouring.

Conclusions

The Bayesian analysis approach considered accounts for similarity searches while retaining some flexibility on the identification of the groups by comprising user-specific prior information. Furthermore, similarity measurements serve as the basis for grouping NFs to different physicochemical specific categories. The method presented was found to be more accurate compared to traditional statistical testing methods, such as the F-test, however, further testing with extensive data sets should be performed for model validation as well as extensive comparisons to well-known dose-response models, i.e. linear and logistic regression models.

References

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