

A HYBRID SOM/FUZZY ARTMAP METHODOLOGY FOR THE PREDICTION OF ECOTOXICITY IN PHENOLS USING MOLECULAR DESCRIPTORS AND MODES OF TOXIC ACTION

R. Rallo^a, G. Espinosa^b, Francesc Giralt^b

Grup de Fenòmens de Transport

^aDepartament d'Enginyeria Informàtica i Matemàtiques

^bDepartament d'Enginyeria Química

Universitat Rovira i Virgili, Campus Sescelades

Av. Dels Països Catalans 26, 43007 Tarragona, Catalunya, Spain

Toxicity modelling is a challenging task, mainly due to the variability in experimental endpoints and the scarcity of public data. A variety of QSAR models have been reported in the literature, some of them based on the selection of structural analogues, which produce QSAR models that are dependent on the assumption that compounds of the same "chemical class" behave in a similar toxicological manner. However, the correct identification of a chemical class is not an easy task. An alternative approach is to develop QSAR models based on the concept of modes of toxic action (MOA) instead of using chemical classes.

The aim of this study is to derive a descriptor-based classification of 220 phenols grouped into four MOAs (153 polar narcotics, 18 respiratory uncouplers, 27 pro-electrophiles and 23 soft electrophiles). The MOA data set of Shüürmann et al.(2003)¹ is used. The goodness of the SOM model is assessed by comparing the resulting classifier with other well-known classification models from the literature.

The methodology developed proceeds in a two steps procedure. First, in a preprocessing stage, redundant descriptors are removed and the best set of descriptors to predict the toxicity is found. Second, in the modelling stage, all the compounds are classified according to their MOA and a Fuzzy ARTMAP based QSAR model is developed for each class.

The good performance of the proposed integrated SOM-fuzzy ARTMAP approach is assessed by comparing predicted and measured toxicity log 1/IGC₅₀ (mmol/L) data.

¹ Aynur O. Aptula, Tatiana I. Netzeva, Iva V. Valkova, Mark T. D. Cronin, Schultz, T. W. Ralph Kühne and Garrit Schüürman, Multivariate discrimination between modes of toxic action of phenols. Quant. Struct.-Act. Relat. 21, 12-22 (2002)