

Structure-activity landscapes: a new way to study a structure-activity relationship

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When first confronted with a new SAR (structure-activity relationship), it is a challenge to identify the salient aspects of that SAR. We present a new method¹, Structure-Activity Landscapes, that facilitates the identification of those salient features, by studying the SAR pairwise, and ranking all pairs by a simple index

$$\text{SALI} = \Delta A_{ij} / (1 - S_{ij})$$

which highlights those pairs of molecules most similar, with the largest change in activity. The similarity of a pair of molecules is denoted S_{ij} ; their activity differences is denoted ΔA_{ij} .

In addition to simply looking at a list of pairs sorted by the SALI, one can use the SALI to convert an SAR into a graph representation, which further facilitates obtaining an overall perspective on the SAR.

Finally, the SALI index leads to a novel metric for assessing the performance of a computational model of that SAR, and can even be used as a metric for discovering novel models.

Examples of each of these applications will be highlighted using literature SAR.

1. Guha, R.; van Drie, J.H., The Structure-Activity Landscape Index: Identifying and Quantifying Activity Cliffs. *J. Chem. Inf. Model.* **2008**, accepted for publication.