Statistical properties of activity landscapes

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Activity landscapes provide a comprehensive global description of structure-activity relationships (SARs). In three dimensions, activity landscapes are analogous to geographical landscapes. Their topographies are characterized by low-lying relatively flat regions that contain inactive compounds and by regions of gently rolling hills, peaks, ridges, cliffs, etc. that contain both active and inactive compounds. SAR methods work best in regions with topographies that typically resemble gently rolling hills, where small changes in structure are associated with small changes in activity as implied by the well-known “Similarity Principle.” However, such regions tend to be less informative than more irregular ones containing features such as activity cliffs, where small changes in structure are associated with large changes in activity. It will also be shown that scaffold hops, in which two active compounds that possess very different structures, can be characterized in a similar fashion. The talk will present an assessment of these features of activity landscapes based on their statistical properties and information content (“surprisal”) as described in Shannon’s information theory.

Biography

Gerry Maggiora has spent more than forty years in scientific research. He received his Ph.D in Biophysics from the University of California – Davis, in 1968 and did post-doctoral work in theoretical chemistry at the University of Kansas. In 1970 he joined the faculty there and rose to the position of full professor in the Departments of Chemistry and Biochemistry. His interests have spanned many areas of computational research from molecular quantum mechanics, organic reaction mechanisms, potential energy functions, and protein structure and function. In 1985 he joined the Upjohn Company as Director of Computer-Aided Drug Discovery. His interests then turned towards drug design and chemical informatics with special interest in the development and applications of molecular similarity and chemical space. In 2003 he retired from industry and joined the College of Pharmacy at the University of Arizona, where he continued his research until his retirement in 2007. In 2008 he received the Hermann Skolnik Award in Chemical Informatics from the Division of Chemical Information of the American Chemical Society. Currently, he is continuing his research on molecular similarity, chemical space, and activity landscapes, the latter being the subject of his presentation at CADD-2012.

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