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FMO-based cluster analysis for drug design by multi-dimensional scaling

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Recently, *in silico* drug design has attracted a great deal of general attention. On the basis of the fragment molecular orbital (FMO) method, a clustering method called VISCANA to analyze the pattern of interactions between receptor protein and ligand molecule was proposed [1], in which conventional, hierarchical clusterings for the inter-fragment interaction energies (IFIEs) were performed. Although this method is useful to understand the similarity of the interaction pattern, it does not tell us how and why the patterns are different between two clusters. In addition, while it can sort out the existing ligands and explain their experimental results, it cannot predict or design a novel ligand with favorable affinity and other appropriate properties. Here, we study how to cope with these difficulties by a multi-dimensional scaling (MDS) method for drug design. The MDS method, which is somewhat related to the self-organizing map (SOM) [2], is a method to construct a low-dimensional map from the knowledge of the distance between elements [3]. This method can help us understand why the difference takes place between the clusters of ligands, and can predict the binding characteristics of unknown ligands. We estimated the usefulness of this method for some examples.

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