Pharmacophore Refinement in the Chemical Structure Space

Satoshi FUJISHIMA, Yoshimasa TAKAHASHI and Takashi OKADA

Studies on the structure-activity relationship of drugs essentially require a relational learning scheme in order to extract meaningful chemical subgraphs; however, most relational learning systems suffer from a vast search space. On the other hand, some propositional logic mining methods use the presence or absence of chemical fragments as features, but rules so obtained give only crude knowledge about part of the pharmacophore structure. This paper proposes a knowledge refinement method in the chemical structure space for the latter approach. A simple hill-climbing approach was shown to be very useful if the seed fragment contains the essential characteristic of the pharmacophore. An application to the analysis of dopamine D1 agonists is discussed as an illustrative example.

Keywords: Knowledge refinement, Chemical structure space, Structure activity relationship, Pharmacophore