タンパク質結晶構造解析

LDetector: a new module of LAFIRE for locating and fitting ligands

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With the technique progress in X-ray crystallography, the time consumption on obtaining the structure model of a protein or a protein-ligand complex in an atomic scale has become shorter and shorter. This reduction in time consumption made the structure based drug design (SBDD) a feasible method in the study of drug design. Compared with the classic methods of drug design, SBDD is advantageous in refining the ligand library on base of the analysis of the known protein structure so that the efficiency of discovering a drug can be dramatically improved. Even though, in the refined library, there are still hundreds or thousands ligands required to be screened for crystallization and structure analysis. This analysis is still a time-consuming process. Therefore, the request for automating this process becomes urgent.

Rooted on the software LAFIRE, which was developed for the purpose of automating the process of refining protein structure model, a new function module Ligand Detector (LDetector) aiming to automatically locate and fit ligands to the known protein structures with the reference of the electron-density map has been developed. In this module, the blobs suitable to an inputted ligand are picked out firstly. Then, the ligand will be automatically divided into several inflexible elemental parts and these elemental parts will be located among the blobs in a distributed manner. Finally, the distributed elemental parts will be recombined and evaluated to find a solution of the fitted complete ligand.

LDetector has been incorporated into LAFIRE and tested in sets of data from our laboratory and protein data bank. For most of them, the correct structures of the protein-ligand complexes have been achieved automatically. In this presentation, I will report some results and make a discussion on them.