A Method for Predicting the Active Sites of Protein Tyrosine Phosphotases Based on Protein Surface Patches

黃裕翔,劉志俊,張慧玫
Computer Science & Information Engineering
Computer Science and Informatics
ccliu@chu.edu.tw

Abstract

Proteins are main macro-mo lecules to operate the physical activities and catalytic functions in organisms. Proteins interacting with other proteins regulate the flows and various responses of biological signal transduction pathways. To ensure timing-switch of p rotein activities in signaling, the phosphorylation and de-phosphorylation reactions of the proteins involved are the most common and critical regulation.

The main focus of the present study is to predict the active site of protein family such as protein tyrosine phosphotases. We start off the training set using a PTP subclass-DSPs. DSPs are named after their ab ility to regulate the substrate activity by simu ltaneously removing the phosphate group from phosphate-modified tyrosine and serine/threonine residues in the substrate proteins. We first collected the conserved ” CXXXXXR” (X as arb itrary amino acid) active site sequences, and recorded the spatial coordinates of the cysteine (C) and arginine (R) fro m the active sites plus the aspartate (D) fro m catalytic sites of structure-solved DSPs, and those of the phosphates (P) fro m substrates. The distances between enzy matic C, R, and D are estimated as active site parameters to predict the possible presence of DSP active site cavity fro m unknown p roteins. To prevent some possible skew coordinates obtained from DSPs structure without their substrates, the distances from enzy matic C, R, and D to substrate P are estimated as interaction parameters.

The α-ball protein surface modeling was applied to screen unknown proteins for the possible presence of
active site topology before entering DSP-parameter co mparison. We were ab le to predict the active sites of 16
structure-solved DSPs as well as 23 PTPs with unknown structure.

Keyword：protein tyrosine phosphatases, dual-specificity phosphatases, active site, α-ball protein surface