High-throughput exploration of functional residues in protein structures

Ausiello G.(1), Zanzoni A.(1), Peluso D.(1), Via A.(1), Helmer-Citterich M.(1)

(1) Department of Biology, University of Tor Vergata, Rome

Motivation

The detection of local similarities between protein structures may give insights for the identification of a common function. Different tools exist which try to elucidate the mechanisms connecting the similarity of local subsets of residues with the biological activity of whole proteins: i) databases of functionally annotated structures and ii) structural comparison algorithms. Both types of tools suffer from two major problems. The first is the low degree of integration among databases containing functional information. The second is the low or absent integration between existing methods for structural comparison and functional annotation resources.

Methods

We developed a method that tries to integrate for the first time all the major existing databases for 3D functional annotation together with a fast structural comparison algorithm. Ten datasources have been interconnected ranging from solvent exposure to ligand binding ability, location in a protein cavity, secondary structure, functional pattern, protein domain and catalytic activity. All this functional information is bound to the single residue and not to the structure as a whole, permitting to perform detailed queries on the features of single residue sets. All the structural and functional data are stored locally and managed by a fast and powerfull database management system that is also able to perform fast and high-throughput local structural comparison

Results

We made this integrated tool available through pdbFun (http://pdbfun.uniroma2.it/), a web server for the structural and functional analysis of proteins at the residue level. pdbFun gives fast access to the whole PDB Protein Data Bank organized as a database of annotated residues. Users can select any residue subset (even including any number of PDB structures) by combining the available functional annotations. Selections can be used as probe and target in multiple structure comparison searches. For example a search can involve, as a query, all solvent-exposed, hydrophylic residues that are not in alpha-helices and are involved in nucleotide binding. Possible examples of targets are represented by another selection, a single structure or a dataset composed of many structures. The output is a list of aligned structural matches offered in tabular and also graphical format. This instrument has allowed us to identify cases of convergent evolution in protein structures. Different examples of local structural similarity were highlighted where residues perfectly superposed in 3D are not colinear in the corresponding sequences. In one of these cases the residue order in the sequences is inverted

Contact email: gabriele@cbm.bio.uniroma2.it
URL: http://pdbfun.uniroma2.it/