

## Poster I-75

### A set of approaches for analysis of functional relationship in proteins.



#### Authors:

Joanna M. Sasin (*International Institute of Molecular and Cell Biology*)

Janusz M. Bujnicki (*International Institute of Molecular and Cell Biology*)

**Short Abstract:** We would like to present a set of methods for analysis of functional relationships in protein families that focus on comparisons of protein surfaces and structures.

#### Long Abstract:

With an increasing number of experimentally determined protein sequences and structures, prediction of protein function is a topic of interest. The most commonly used methods for functional predictions rely on sequence similarity between the functionally uncharacterized protein of interest and other proteins, for which the function is known. Although these methods can provide functional clues, the accuracy of predictions based on overall sequence similarity is limited by the paucity of tools for quantitative comparison of diverging residues responsible for the functional divergence in different subfamilies.

We would like to present a set of methods for analysis of functional relationships in protein families that focus on comparisons of protein surfaces and structures.

'SURF'S\_UP!' is a web server for analysis of functional relationships in protein families, as inferred from protein surface maps comparison according to the algorithm developed by Pawlowski & Godzik [1]. It assigns a numerical score to similarity between patterns of physicochemical (charge, hydrophobicity) features distribution on surfaces of pairs or groups of proteins. This allows recognizing groups of proteins within a broad homologous family that have similar surfaces, hence presumably similar functions. The server takes as an input a set of protein coordinates and returns files with 'spherical coordinates' of proteins in a PDB format and their graphical presentation, a matrix with values of mutual similarities between the surfaces, and the resulting unrooted tree calculated by the neighbor-joining method. SURF'S\_UP facilitates the comparative analysis of physicochemical features of the surface, which are the key determinants of the protein function. By concentrating on coarse surface features, SURF'S\_UP can work with models obtained from comparative modeling. Other valuable characteristic of our method is the lack of initial assumptions about the functional features that are to be compared.

'STRUCLA' is a metaserver for inference of evolutionary distances based on structural comparisons. It calculates evolutionary distances between the query proteins based on comparisons of their structures, using several measures developed by various researchers [2]. Methods based on structures allow inferring trees for proteins, whose sequences are too divergent to yield trees which the traditional sequence-based methods. The server is continuously updated with new methods. The newest method is based on the concept of "structural alphabet", that is a limited number of recurrent structural elements of proteins ("structural letters") [3]. The new method compares protein structures discretized to the strings of "structural letters" and uses a 'substitution matrix' to calculate the putative evolutionary distances, and to infer the phylogenetic tree.

All the methods are freely available for academic researchers at the website <http://asia.genesilico.pl/>

#### References:

- [1] K. Pawlowski, A. Godzik (2001), Surface Map Comparison: Studying Function Diversity of Homologous Proteins, *Journal of Molecular Biology* , 309: 793-800
- [2] Sasin JM, Kurowski MA, Bujnicki JM: STRUCLA: a WWW meta-server for protein structure comparison and evolutionary classification. *Bioinformatics* 2003, 19 Suppl 1:i252-254.
- [3] Camproux AC, Gautier R, Tuffery P: A hidden markov model derived structural alphabet for proteins. *J Mol Biol* 2004, 339(3):591-605.