Identification of protein functional regions

Francesca Nerattini[1], Matteo Figliuzzi[2], Luca Tubiana[1], Chiara Cardelli[1], Valentino Bianco[3], and Ivan Coluzza*[4]

[1]University of Vienna – Austria
[2]Sorbonne Universites – Sorbonne Universités, UPMC, CNRS – France
[3]Complutense University of Madrid – Spain
[4]CIC biomaGUNE – Spain

Abstract

Functional regions of proteins have evolved to have specific patterns of amino acids tailored to the activity of the biomolecule. The identification of the functional residues of such protein families was obtained with large scale mutation experiments where the effect on the protein function was tested against each alteration [1]. The information obtained with such experiments can have important implications for the mapping of the proteome interactions, as well as for many pharmaceutical applications, e.g. by identifying ligand-binding regions for targeted pharmaceutical protein design. However, the experimental determination of the functional regions is generally time-consuming and require extensive resources; hence a computational approach could help towards the final goal.

In this work, we propose an approach to identify functional regions of proteins to distinguish between residues that have a strictly functional role from the one that is important for the protein structural stability. The methodology that we propose here is based on the hypothesis that an artificial evolution process based on protein design, in the absence of any functional constraints, would lead only to co-evolution events of the structural type. Using Direct Coupling Analysis (DCA) [2], we identify conserved and co-evolved residues both in natural and artificial evolution processes. Just by subtracting the list of structural residues from the natural correlated and conserved ones, we show that we identify the functional residues.

References

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*Speaker