New guided docking approaches for virtual screening and drug design

M. Bhattacharyya[1], J. Seco[1], F. J. Luque[1] & X. Barril[1,2]

[1] Dept. Fisicoquímica, Facultat de Farmàcia, Universitat de Barcelona, Av. Joan XXIII, s/n. 08028 Barcelona, Spain; [2] ICREA

Molecular docking is a computational tool widely applicable to the various stages of drug discovery, but it is particularly useful for high throughput screening of virtual chemical collections and examples of successful hit identification docking experiments abound in the scientific literature. For all its usefulness, docking still presents many important limitations which are difficult to overcome using a more rigorous theoretical framework. Guided docking techniques follow an alternative, more pragmatic, approach consisting in biasing the docking results with empirical information. Here we introduce new guided docking approaches to improve binding mode predictions as well as to get better outcome from virtual screening of chemical libraries.

Genome sequencing projects and structural genomics initiatives have generated a wealth of freely available information that is feeding the drug design efforts. In an attempt to further exploit this information, we have first used genomic information to bias the docking results, which yields better performance in virtual screening simulations. In a second study, we have analysed the interaction preferences of ligand chemical groups with protein target sites and introduced this information in the docking protocol. The ability of this approach to address some of the shortcomings of the scoring functions is discussed.