

Università degli Studi di Salerno  
Facoltà di Scienze Matematiche Fisiche e Naturali



# **IN SILICO STUDY OF PROTEIN-PROTEIN INTERACTIONS**

*Philosophiae Doctor Thesis*  
in

*Scienza e Tecnologie dell'Industria Chimica,  
Alimentare e Farmaceutica – Indirizzo Chimico  
Ciclo XI*

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2009-2012

## ABSTRACT

Protein-protein interactions are at the basis of many of the most important molecular processes in the cell, which explains the constantly growing interest within the scientific community for the structural characterization of protein complexes.<sup>1</sup> However, experimental knowledge of the 3D structure of the great majority of such complexes is missing, and this spurred their accurate prediction through molecular docking simulations, one of the major challenges in the field of structural computational biology and bioinformatics.<sup>2,3</sup>

My PhD work aims to contribute to the field, by providing novel computational instruments and giving useful insight on specific case studies in the field. In particular, in the first part of my PhD thesis, I present novel methods I developed: i) for analysing and comparing the 3D structure of protein complexes, to immediately extract useful information on the interaction based on a contact map visualization (COCOMAPS<sup>4</sup> web tool, Chapter 2), and ii) for analysing a set of multiple docking solutions, to single out the key inter-residue contacts and to distinguish native-like solutions from the incorrect ones (CONS-COCOMAPS<sup>5</sup> web tool and CONS-RANK program, Chapter 3 and 4, respectively).

In the second part of the thesis, these methods have been applied, in combination with classical state-of-art computational biology techniques, to predict and analyse the binding mode in real biological systems, related to particular diseases. This part of the work has been afforded in collaboration with experimental groups, to take advantage of specific biological information on the systems under study. In particular, the interaction between proteins involved in the autoimmune response in celiac disease<sup>6,7</sup> (Chapters 5 and 6) has been studied in collaboration with the group directed by Prof. Sblattero, University of Piemonte Orientale (Italy) and the group directed by Prof. Esposito, University of Salerno (Italy). In addition, recognition properties of

the FXa enzymatic system<sup>8</sup> has been studied through dynamic characterization of a FXa pathogenic mutant that causes problems in the blood coagulation cascade (Chapter 7). This study has been performed in collaboration with the group directed by Prof. De Cristofaro, Catholic University School of Medicine, Rome (Italy) and the group directed by Prof. Peyvandi, Ospedale Maggiore Policlinico and Università degli Studi di Milano (Italy).

Finally, during my PhD I spent seven months in the groups of Prof. Charlotte Deane, Department of Statistics, University of Oxford (UK). During this period I studied the geometrical features of the proteins' regions most recurrent in the protein-protein interaction, the loops, clarifying some structural aspects of them in one of the most important and huge class of proteins: the membrane proteins (Appendix 1).

### **Web tools and programs:**

COCOMAPS<sup>4</sup> web tool freely available at:  
<https://www.molnac.unisa.it/BioTools/cocomaps/>

CONS-COCOMAPS<sup>5</sup> web tool freely available at:  
<https://www.molnac.unisa.it/BioTools/conscomaps/>

CONS-RANK program available upon request from the authors.

## REFERENCES

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