Title	Provide a title for the research project
PI	MORO Stefano
Research Group	Molecular Modeling Section (MMS) – DSF
Curriculum	Scienze Farmaceutiche
Contact	**web:** mms.dsfarm.unipd.it
	email: stefano.moro@unipd.it

Project description:

Title: New computational methodologies in inspecting ligand-receptor recognition pathways: a valuable strategy to speed up the identification of drug candidates.

State of art: One of the most challenging issues for the future of drug discovery is the capability to understand the receptor-ligand recognition pathway with the aim to facilitate the development of drug candidates with more favorable phamacodynamic profiles. Unfortunately, the recognition process between a ligand and its receptor is a very rare event to describe at the molecular level, and even with the recent GPU-based computing resources, it is necessary to carry out classical molecular dynamics (MD) experiments in a long microsecond time scale. In order to overcome this limiting factor, we have implemented an alternative MD approach, named supervised molecular dynamics (SuMD), that enables us to follow receptor-ligand approaching process within a time scale reduced up to 3 orders of magnitude compared to classical MD. SuMD enables the investigation of ligand-receptor binding events independently from the starting position, chemical structure of the ligand, and also from its receptor binding affinity.

Objectives: Theme A – Application of SuMD technology in different hot therapeutic area such as oncology, inflammation and immunology. Theme B – Extending and improving the development of SuMD methods, in particular implanting novel approach to predict the free energy of binding and the corresponding binding kinetic parameters.

Skills of the candidate: Theme A – Background in Chemistry, Medicinal Chemistry, Pharmacy and Biotechnologies with a basic knowledge in informatics. Theme B – Background in Chemistry or Medicinal Chemistry with a good knowledge in informatics (linux environments) and solid skills in programming.

Publications:

Salmaso V, Sturlese M, Cuzzolin A, Moro S. "Exploring Protein-Peptide Recognition Pathways Using a Supervised Molecular Dynamics Approach." Structure 25, 655-662 (2017)

Cuzzolin A, Sturlese M, Deganutti G, Salmaso V, Sabbadin D, Ciancetta A, Moro S. "Deciphering the Complexity of Ligand-protein Recognition Pathways using Supervised Molecular Dynamics (SuMD) Simulations." J Chem Inf Model 56, 687-705 (2016)

Ciancetta A, Sabbadin D, Federico S, Spalluto G, Moro S. "Advances in Computational Techniques to Study GPCR-Ligand Recognition." Trends Pharmacol Sci. 36, 878-890 (2015)

Collaborations/Network:

Dr. Kenneth A. Jacobson, National Institutes of Health (NIH), Bethesda – USA
Dr. Jon Manson, Heptares Therapeutics, Hertfordshire – UK
Prof. Ajith A. Welihinda, Molecular Medicine Research Institute, Sunnyvale – USA

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