POLITECNICO DI MILANO

PhD in MODELLI E METODI MATEMATICI PER L'INGEGNERIA / MATHEMATICAL MODELS AND METHODS IN ENGINEERING - 38th cycle

PNRR_351_DOTT_RICERCA Research Field: ADVANCED NUMERICAL METHODS AND HPC TECHNIQUES FOR MOLECULAR ELECTROSTATICS

Monthly net income of PhDscholarship (max 36 months)
€ 1325.0 In case of a change of the welfare rates during the three-year period, the amount could be modified.

Context of the research activity	
Motivation and objectives of the research in this field	Electrostatics and solvation are among the main determining factors of biomolecular recognition and binding, influencing both selectivity and affinity. Therefore, providing faster and more accurate simulation tools for their computation can have a key role in modern structure-based drug design and in drug repurposing studies. Advanced versions of techniques such as MM / PBSA [2, 3, 4] would allow compound prioritization within large sets of molecular candidates. Interestingly, these tools could also be applied to molecular targets of unprecedented size such as those that are being discovered with the most recent experimental techniques, such as Cryo-Em and which at present pose significant challenges to many computational approaches. This compels the development of advanced and highly parallel numerical approaches able to leverage this incredible amount of knowledge. The proposed research activity is expected to bring significant knowledge advancement with respect to digitalization and innovation for farmaceutical industry and the healthcare system (Missione M1, componente C2 e Missione M6, componente C2 del PNRR). The Proposed Project is intended to expand the ongoing interdisciplinary collaboration between the MOX lab of the Department of Mathematics at PoliMI and the CONCEPT lab of IIT in the field of Numerical Methods

	and HPC Techniques for Molecular Electrostatics. In particular we intend to extend the easy_pbe scalable solver for the Poisson Boltzmann Equation recently developed in collaboration between PoliMI and IIT as a more flexible and efficient replacement for DelPHI [5]. [1] A. Khataniar, P. Upasana, S. Rajkhowa, and A. N. Jha. 2022. *"A Comprehensive Review of Drug Repurposing Strategies against Known Drug Targets of COVID-19",* COVID 2, no. 2: 148-167. https://doi.org/10.3390/covid2020011 [2] Behera, S.K., Vhora, N., Contractor, D. et al. *¿Computational drug repurposing study elucidating simultaneous inhibition of entry and replication of novel corona virus by Grazoprevir¿.* Sci Rep 11, 7307 (2021). https://doi.org/10.1038/s41598-021-86712-2 [3] D. Spiliotopoulos, P.L. Kastritis, A.S.J. Melquiond, A.M.J.J. Bonvin, G. Musco, W. Rocchia, A. Spitaleri, *¿dMM-PBSA: A New HADDOCK Scoring Function for Protein-Peptide Docking¿*, Front. Mol. Biosci. 3 (2016) https://doi.org/10.3389/fmolb.2016.00046 [4] M. Lazniewski, D. Dermawan, S. Hidayat, M. Muchtaridi, W.K. Dawson, D. Plewczynski,*"Drug repurposing for identification of potential spike inhibitors for SARS-CoV-2 using molecular docking and molecular dynamics simulations",* Methods, 203, 2022, https://doi.org/10.1016/j.ymeth.2022.02.004 . [5] W. Rocchia, E. Alexov and B. Honig, ¿Extending the applicability of the nonlinear Poisson-Boltzmann equation: Multiple dielectric constants and multivalent ions¿, J. Phys. Chem. B Vol. 105, n. 28, pp.6507-6514 https://doi.org/10.1021/jp010454y
Methods and techniques that will be developed and used to carry out the research	The research involves algorithmic reengineering and parallelization of existing state-of-the-art Poisson Boltzmann equation solving techiques. This will involve biophysical modelling, numerical analysis and HPC-oriented computer science. In particular, special consideration will be given to the analysis and implementation of regularization an singularity removal techniques [6] and to more advanced nonlinear continuum solvent models [7]. [5] A. Lee, W. Geng, and S. Zhao, Regularization methods for the poisson-boltzmann

	equation: Comparison and accuracy recovery, Journal of Computational Physics, 426 (2021), p. 109958 [7] Jan Forsman, A Simple Correlation-Corrected Poisson-Boltzmann Theory, J. Phys. Chem. B2004,108,9236-9245
Educational objectives	Acquire knowledge in basic electrostatic modelling of biomolecular interactions. Principles and applications of Poisson-Bolzmann equation. Software development of parallel solvers for partial differential equations.
Job opportunities	HPC-coding is of present and strategic interest for both research institutions and industry. Electrostatic calculations can be of interest for applications in material sciences and life sciences, e.g. drug discovery and repurposing.
Composition of the research group	5 Full Professors 6 Associated Professors 4 Assistant Professors 15 PhD Students
Name of the research directors	Carlo De Falco, Walter Rocchia

Contacts
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Additional support - Financial aid per PhD student per year (gross amount)			
Housing - Foreign Students	**1st year**	**2nd year**	**3rd year**
	1500.0 € per student	0.0 € per student	0.0 € per student
	max number of financial aid available: 3, given in order of merit ..		
Housing - Out-of-town residents (more than 80Km out of Milano)	--		

Scholarship Increase for a period abroad	
Amount monthly	662.5 €
By number of months	6

National Operational Program for Research and Innovation	
Company where the candidate will attend the stage (name and brief description)	
By number of months at the company	0
Institution or company where the candidate will spend the period abroad	

(name and brief description)	
By number of months abroad	6

Additional information: educational activity, teaching assistantship, computer availability, desk availability, any other information
Educational activities (purchase of study books and material, funding for participation to courses, summer schools, workshops and conferences): financial aid per PhD student per year 1st year: max 1.800,47 euros 2nd year: max 1.800,47 euros 3rd year: max 1.800,47 euros The PhD students are encouraged to take part in activities related to teaching, within the limits allowed by the regulations.1 individual PC per student + several shared PC. Access to one cluster with 32 processors and 384 GB RAM, and to several multi-processor servers and 1 individual desk per student are granted.