An introduction to molecular dynamics simulation and docking studies for applications in biomedical sciences

Acronym

MolSimBioMed

Course language

English

Course provided by

Dr. hab. Adolfo Poma Bernaola, Assistant professor, IPPT PAN
Dr. Luis Fernando Cofas-Vargas, Assistant professor, IPPT PAN

Course type

Online lectures and tutorials will be prepared with implementation of inputs for molecular modelling and simulations. If all participants agree, there is a possibility to conduct the lecture in-class.

Number of hours

15 × 2h, 4 ECTS

Course description

A one-semester course introducing the basis of molecular modelling and simulations with direct applications to biomedical sciences. This course will aim at delivering theoretical lectures and also hangs-on sessions aiming at executing molecular simulations by the students. Molecular dynamics (MD) simulation of biomolecules plays a crucial role nowadays advancing biomedical sciences by providing insights into the behaviour, structure, and function of biological macromolecules. This powerful computational technique bridges the gap between theoretical models and experimental observations, offering valuable contributions to various aspects of biomedical research. The course is built on the expertise of the tutors within a multidisciplinary approach from physics, chemistry and biophysics into the field of biomedical sciences. Also, we will include new tools for molecular visualisation and analysis for a broad level of PhD students with engineering and molecular interest. In addition, students with a more practical orientation will find in the course the tools needed to understand computational modelling and engage in collaboration within computational projects.

Special emphasis will be put on state-of-art topics such as coarse-grained techniques of biomolecular systems that are designed for large-scale applications, drug binding, protein mutations, stability of large biomolecules (e.g. proteins) and direct assessment of single-molecule force spectroscopy by simulations.

Course contents.

15 lectures distributed among 10 theoretical, 4 practical courses and 1 project according to the following plan:

Part I (**Dr. Luis Fernando Cofas-Vargas**)

1. Introduction to molecular visualization of proteins
2. Preparation of structures for molecular dynamics (modelling, equilibration, production)
3. Molecular dynamics (MD) simulations of ligand-protein complexes (Classical force fields)
4. Mixed-solvents MD simulations and hotspots identification
5. Molecular docking for medical applications
6. Hands-on exercise III (based on topics 2-3)
7. Hands-on exercise IV (based on topics 4-5)

Part II (**Dr. hab. Adolfo Poma**)

8. Practical concepts in MD simulation: Configurational space, equilibrium ensembles and MD engines and file preparation
9. Accurate and computational expensive MD simulations: all-atom MD approach
10. Computational efficient coarse-grained MD simulations: coarse-grained MD approaches
11. Introduction of VOTCA Software for coarse-graining biomolecular systems
12. Advanced simulation of rare biological event: Transition Path Sampling and Temperature Accelerated MD simulation
13. Hands-on exercise I (based on topics 9-10)
14. Hands-on exerciseII (based on topics 11-12)
15. Final project Q&A

Learning outcomes

PhD students will be acquainted with commonly used computational protocols and open software packages for MD simulation of biomolecular systems such as GROMACS v2020.x, NAMD 3 and AMBER as well as the structure and topology files required to conduct MD simulation for system with a larger number of particles (>1M atoms) and docking studies for biomedical applications. This course will provide sufficient background in molecular modelling and simulations to grasp the state-of-the-art for undertaking large-scale applications, enhance the skills of biomedical/engineering students to deploy their own MD simulations for conducting advanced research and prepare them for a multidisciplinary profile in biomedical sciences. By the end of course the student will be able to run moderated MD simulation, prepare files for execution and analysis tools for molecular trajectories.

Prerequisites

None.

Literature

1. Frenkel, Daan, and Berend Smit. *Understanding molecular simulation: from algorithms to applications*. Elsevier, 2023.
2. Allen, Michael P., and Dominic J. Tildesley. *Computer simulation of liquids*. Oxford university press, 2017.
3. Tuckerman, Mark E. *Statistical mechanics: theory and molecular simulation*. Oxford university press, 2023.
4. VOTCA software framework for systematic coarse-graining (https://github.com/votca)
5. Ruhle, Victor, Christoph Junghans, Alexander Lukyanov, Kurt Kremer, and Denis Andrienko. "Versatile object-oriented toolkit for coarse-graining applications." *Journal of chemical theory and computation* 5, no. 12 (2009): 3211-3223.
6. Pettersen, Eric F., Thomas D. Goddard, Conrad C. Huang, Elaine C. Meng, Gregory S. Couch, Tristan I. Croll, John H. Morris, and Thomas E. Ferrin. "UCSF ChimeraX: Structure visualization for researchers, educators, and developers." *Protein Science* 30, no. 1 (2021): 70-82.
7. Trott, Oleg, and Arthur J. Olson. "AutoDock Vina: improving the speed and accuracy of docking with a new scoring function, efficient optimization, and multithreading." *Journal of computational chemistry* 31, no. 2 (2010): 455-461.
8. Ruiz-Carmona, S., Alvarez-Garcia, D., Foloppe, N., Garmendia-Doval A. B., Juhos, S., Schmidtke, P. , Barril, X., Hubbard, R. E., and Morley, S. D. “rDock: A Fast, Versatile and Open Source Program for Docking Ligands to Proteins and Nucleic Acids”. PLoS Comput Biol 10(4) (2014): e1003571. doi:10.1371/journal.pcbi.1003571.
9. Alvarez-Garcia, D., and Barril, X. “Molecular Simulations with Solvent Competition Quantify Water Displaceability and Provide Accurate Interaction Maps of Protein Binding Sites”. J. Med. Chem. 2014, 57, 20, 8530–8539
10. Webb, B., Sali, A. “Comparative Protein Structure Modeling Using Modeller”. Current Protocols in Bioinformatics 54, John Wiley & Sons, Inc., 5.6.1-5.6.37, 2016.
11. O'Boyle, N. M., Banck, M., James, C. A , Morley, C., Vandermeersch, T., and R Hutchison, G. “Open Babel: An open chemical toolbox”. Journal of Cheminformatics volume 3, Article number: 33 (2011)

Examination

Yes.

Contact

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Course webpage

TBA under the link http://pomalab.ippt.pan.pl/web/ → /course