Scientific activity description

The scientific activity of our group is focused on the application and development of computational methods to determine the structure and the dynamics of biologically relevant molecules. To this end, we employ different molecular dynamics approaches, ranging from coarse-grained simulations to ab initio calculations by means of HPC resources.
The computational strategy is also applied to analyse experimental results we get through XAS absorption X-ray diffraction using Large Scale facilities.

The main research lines are:

a) Protein aggregation
Classical MD is used to study systems composed by hundred thousand atoms on the microsecond time-scale. We are interested in the proteins aggregation phenomenon and in particular in the influence the presence of small molecules can have in its progression.
Systems we studied are: insulin in the presence of epigallocathechin [Carbonaro 2016; Carbonaro 2018]; amiloyd β (Aβ) peptides involved in the Alzheimer's disease) in the presence of beta sheet breakers [Minicozzi 2014; Morante 2014; De Santis 2015; Stellato 2017].

b) Anti-cancer peptides
Peptides bound to radioactive elements are a promising theranostic tools in oncology. We designed a functionalized peptide capable of binding to tumour negatively charged membranes [Capozzi 2018].

c) X-ray Absorption Spectroscopy(XAS) & X-ray diffraction
First-principle computations of the low energy part of the XAS spectrum is applied to simulate the XAS spectrum of Cu(II) [La Penna 2015] and Zn(II) [Stellato 2018] ions in water to be compared with the experimental recorded spectra.
Coarse grained molecular dynamics is used to detect collective motions of protein crystals responsible of the so called "diffuse scattering".

d) Competition between copper and zinc in the modulation of chemical and physical properties of amyloid peptides.
We performed, by using computational resources provided within the INFN-Cineca agreement, simulations of amyloid-beta (Abeta) fragments 1-16 and 1-28. The study of structure and function of d-block metal ions (specifically Cu, Zn and Fe) both in the protein aggregates (hallmarks of irreversible cognitive impairment) and in early soluble oligomers (targets of early-stage therapies) is the frontier in the field of neurodegeneration.
Computational models are compared with experimental data of X-ray absorption spectroscopy (XAS), obtained within the same research group. We are concluding the work about the comparison between simulations of Zn in water with XAS data. This will serve as the basis of further works concerning Zn-Abeta(1-16) and Zn-Abeta(1-28).

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S.Morante and G.C.Rossi, “From the Scientific Optimism of the Age of Enlightenment to the Problems of Modern research Conceptualization” (2017) *Giornale di Fisica*, **58:1**

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La Penna, G, “When water plays an active role in electronic structure: Insights from first-principles molecular dynamics simulations of biological systems”, in “Computational methods to study the structure and dynamics of biomolecules and biomolecular processes. From bioinformatics to molecular quantum mechanics”, A. Liwo ed., Springer series in bio/neuroinformatics,

Organized Workshop

INFN workshop “From experiments to theory & models A computational challenge for Biophysics”, physics department of the University of Roma-Tor Vergata, 5/12/2017

Given Talks

1. Giovanni La Penna talk at Dublin workshop (14-15/12/2017)
2. Giovanni La Penna talk at the INFN workshop “From experiments to theory & models A computational challenge for Biophysics”, physics department of the University of Roma-Tor Vergata, 5/12/2017
3. E. De Santis Contributed talk at the XVII SM&FT workshop – Bari, December 2017
“Abeta peptides and beta-sheet breakers. A coarse grained molecular dynamics approach"
4. E. De Santis Colloquio interdisciplinare sulla biologia – Roma “Tor Vergata”, April 2018
“Coarse Grained Molecular Dynamic Simulations in support of crystallography experiments"
5. F. Stellato
Colloquio interdisciplinare sulla biologia – Roma “Tor Vergata”, May 2017
Supercomputers e large scale facilities per lo studio dei sistemi biologici
6. F. Stellato
Contributed talk at the Biophysics@Rome meeting – Rome, May 2017
First principle calculation of X-ray absorption spectra
7. F. Stellato
Contributed talk at the Società Italiana di Cristallografia Conference – Perugia, June 2017
Protein serial crystallography at Free Electron Laser and Synchrotrons
8. Stellato
Contributed talk at the Società Italiana di Fisica Conference – Povo, Trento, September 2017
Designing effective anticancer-radiopeptide carriers: a Molecular Dynamics study of their interaction with tumor and healthy cell membranes
9. Stellato
Contributed talk at the XVII workshop on Statistical Mechanics and non Perturbative Field Theory – Bari, December 2017
Multi-scale molecular dynamics & first-principle calculations of X-ray absorption spectra: an application to the study of metal cations coordination in water
10. V. Minicozzi Contributed talk at the XVII SM&FT workshop “Designing effective anticancer-radiopeptide carriers A Molecular Dynamics study of their interaction with model tumor and healthy cell membranes”
11. S. Morante Invited talk to SM&FT 2017 – Bari – “A summary of the BioPhys IS scien5fic activity.”

Published papers

1. Carbonaro, M., Di Venere, A., Filabozzi, A., Maselli, P., Minicozzi, V., Morante, S., ... & Stellato, F. (2016). Role of dietary antioxidant (−)-epicatechin in the development of β-lactoglobulin fibrils. Biochimica et Biophysica Acta (BBA)-Proteins and Proteomics, 1864(7), 766-772.
2. Stellato, F., Fusco, Z., Chiaraluce, R., Consalvi, V., Dinarelli, S., Placidi, E., ... & Morante, S. (2017). The effect of β-sheet breaker peptides on metal associated Amyloid-β peptide aggregation process. *Biophysical chemistry*, 229, 110-114.
3. Gati, C., Oberthuer, D., Yefanov, O., Bunker, R. D., Stellato, F., Chiu, E., ... & Beyerlein, K. R. (2017). Atomic structure of granulin determined from native nanocrystalline granulovirus using an X-ray free-electron laser. *Proceedings of the National Academy of Sciences*, *114*(9), 2247-2252.
4. Popp, D., Loh, N. D., Zorgati, H., Ghoshdastider, U., Liow, L. T., Ivanova, M. I., ... & Gati, C. (2017). Flow-aligned, single-shot fiber diffraction using a femtosecond X-ray free-electron laser. *Cytoskeleton*.
5. S.Morante and G.C.Rossi, “From the Scientific Optimism of the Age of Enlightenment to the Problems of Modern research Conceptualization” (2017) *Giornale di Fisica*, **58:1**
6. S.Morante and G.C. Rossi, “A novel proof of the DFT formula for the interatomic force field of Molecular Dynamics” (2017) *Annals of Physics Annals* **37:** 71–76
7. La Penna, Giovanni; Mai Suan, Li, “Towards a high-throughput modelling of copper reactivity induced by structural disorder in amyloid peptides” Chem. Eur. J., 24, 5259-5270 (2018), 10.1002/chem.201704654
8. Ferrario, M. et al. (2018). EuPRAXIA@ SPARC_LAB Design study towards a compact FEL facility at LNF. *Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment,* in press.
9. La Penna, Giovanni; Chelli, Riccardo, “Structural Insights into the Osteopontin-Aptamer Complex by Molecular Dynamics Simulations”, Frontiers in Chemistry, 6, 2 (2018), 10.3389/fchem.2018.00002
10. Villa, F. et al. (2018). Design study of a photon beamline for a soft X-ray FEL driven by high gradient acceleration at EuPRAXIA@ SPARC_LAB. *Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment* in press.