PERSONAL INFORMATION

Emiliano De Santis

Via dei campi di Annibale 50, Rocca di Papa (Rm), Italy

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Sex Male | Date of birth 25/05/1988 | Nationality Italian

CURRENT POSITION
(UNTILL OCTOBER 2018)

3nd year PhD student in Physics
University of Rome “Tor Vergata”

October 2012 - May 2015

University of Rome “Tor Vergata”
MSc in Physics, 110/110 magna cum laude
Dissertation Title: "*Cu(II)–Zn(II) cross-modulation in amyloid-beta peptide binding. An X-ray Absorption Spectroscopy study* ".
Advisors:
Prof. Silvia Morante, University of Rome “Tor Vergata
Dr. Francesco Stellato, INFN”

CV studiorum: Biophysics, Medical Physics, Measurement and analysis of biosignals, Experimental and simulative biophysical techniques, Theory of many body systems, Out of equilibrium thermodynamics

October 2006 - May 2012

University of Rome “Tor Vergata”
BSc in Physics
Dissertation Title: "*Protein misfolding and the Amyotrophic Lateral Sclerosis* ".
Advisor:
Prof. Silvia Morante, University of Rome “Tor Vergata”

CV studiorum: Mathematical analysis, Linear algebra, Chemistry, Classical Physics (Mechanics, Thermodynamics, Electromagnetism, Optics), Physics laboratories, Modern Physics (Quantum and Statistical Mechanics, Condensed Matter Physics, Fundamentals of Nuclear Physics and Astrophysics), Mathematical Methods for Physics.

September 2001 - July 2006

High school “Bruno Touschek” of Grottaferrata (Rm)
High school graduation, 100/100

Research interests

The problem of protein misfolding is of the utmost biological and medical interest, since it is at the basis of a class of pathologies known as protein conformational disorders or amyloidosis. These diseases are characterised by the mis-folding of proteins that, becoming insoluble, accumulate in aggregates of fibrillar shape. It is interesting to notice that, despite the fact that the proteins involved in the different diseases of this class are not related among themselves and do not present homologies neither in the sequence nor in the structure, all amyloid fibrils have remarkably similar histochemical properties and ultrastructure morphologies.

All known neuro-degenerative diseases belong to the class of amyloidosis pathologies. Among them, I focused my research activity in on the study on the Alzheimer Disease (AD) [1]. The brain of AD patients is known to display accumulation of Amyloid β peptides (Aβ) in the amyloid plaques. The process that leads to the misfolding, aggregation and amyloid plaques formation is not yet fully elucidated. It seems, however, that the “starting point" of the process is an abnormal switch of the peptide secondary structure that leads to β-sheet formation, a peculiar structure able to promote the formation of “stackable" sheets with intermolecular bonding.

Unfortunately, nowadays, an effective treatment for AD is still missing. The most attractive therapeutic strategies for AD consist in blocking the early steps of the misfolding and aggregation of soluble Aβ peptides. Several effectors have been studied in order to interfere with the Aβ aggregation process. An important role seems to be played by metal ions [2, 3, 4] that have been observed to be abundant in fibril aggregates. Recently, the observation that short synthetic peptides, called β-sheet breaker (BSB's), are able to directly interact with soluble oligomers or amyloid aggregates precluding amyloid polymerisation [5, 6], was at the origin of a significant scientific effort aimed at trying to modulate and prevent Aβ aggregation and fibrillation processes. In addition, it should be said that, in preclinical and early clinical trials, it was also shown that active and passive Aβ immunotherapies can become a potentially useful strategy against AD.

In this general framework and admittedly with the ultimate ambitious goal of providing structural information for the possible development of a really effective pharmaceutical strategy, it appears of the utmost bio-medical importance to clearly understand the way Aβ peptides interact with such compounds.

During my master thesis I analyzed at a structural level the mechanism by which Cu(II) and Zn(II) ions compete for binding to the Aβ peptides. I’ve collected X-ray Absorption Spectroscopy data at the ESRF light source facility of Grenoble on samples containing Aβ peptides with Cu and Zn at different concentration ratios. Our results show that the metal-peptide coordination mode depends not only, as already pointed out in literature, on the relative metal ions concentrations, but also on the order in which the two metal ions are added to the Aβ solution. This work was published on the Journal of Physical Chemestry B [2].

During my PhD, my research activity is focused on the use of classical Molecular Dynamics (either All Atoms MD or Coarse Grained MD) simulations for the study of Aβ peptides. In this context, two are the main project I am carrying on.

Firstly, I am performing extensive AA-MD simulations aimed at unraveling at a molecular level the details of the interatomic interaction between anti-Alzheimer antibodies and the Aβ peptide. In particular, my attention is focused on the Aducanumab, a recent developed antibody that can slow down AD progression entering the blood brain barrier and significantly reducing the number of the Aβ plaques in patients with clinical diagnosis of prodromal or mild AD [7].

Our idea is to use MD simulations to evaluate the binding affinity of Aducanumab antibody to an Aβ monomer and to compare it with the one of other antibodies, in particular of Gantenerumab (Gante). The binding energy (ΔGbind) is computed from the knowledge of the potential of mean force, in turn extracted from a series of umbrella sampling simulations.

My second PhD project is a multiscale MD simulations study on the aggregation of Aβ peptides in the presence or in the absence of the BSB's peptides. The main idea driving these investigations is that fibril formation could be strongly suppressed if the residues belonging to the hydrophobic central region of the $A\beta_{1\text{-}40}$ sequence could interact with these short peptides [8]. I am simulating, in the Coarse Grained representation, systems with dozens of Aβ peptides in interaction with hundreds of BSB’s. The simulations are performed using the recently developed Go-Martini Model [9]. We plan to back-map portions of the aggregates from the Coarse Grained to the All-Atoms representation and then follow the evolutions of the smaller system to appreciate the atomistic details of its evolution.

In addition to the projects above described, I am also in collaboration with Prof. Chapman’s group in CFEL-DESY Hamburg, to model the protein motion within the crystals by the use of MD simulations. The idea is to model such collective motions so as to be able to correctly predict (and interpret) the spectral features that emerge from protein diffuse scattering. In order to follow the correlated motion of atoms sitting in different unit cells, we are studying a crystal supercell made by tenths of unit cells in presence of explicit water. Considering the huge number of degree of freedom of such large systems, we decided to tackle the problem by using a Coarse Grained MD approach [10, 11]. As a starting systems, in order to build a robust simulation and analysis protocol, we decided to study the orthorhombic lysozyme and staphylococcal nuclease. I am now simulating more complicated and more interesting systems, like aquaporine crystals.

References

[1] R. A. Stelzmann, et al, Clin anat, vol. 8, no. 6, pp. 429–431, 1995.
[2] S. Morante and G. Rossi, Advanc Alz Res, vol. 2, pp. 100–147, 2014.
[3] E. De Santis, et al, J Physic Chem B, vol. 119, no. 52, pp. 15813–15820, 2015.
[4] E. De Santis, et al, J Phys: Conf Series, vol. 689, pp. 012028, IOP Publishing, 2016.
[5] V. Minicozzi, et al, J Biol Chem, vol. 289, no. 16, pp. 11242–11252, 2014.
[6] F. Stellato, et al, J Biophys Chem, 2017.
[7] J. Sevigny, et al, Nature, vol. 537, no. 7618, pp. 50–56, 2016.
[8] C. Hilbich, et al, J Mol Biol vol 228, pp. 460-473, 1992.
[9] A.B. Poma, et al, J Comp Theo and Comp, vol 13, pp. 1366–1374, 2017.
[10] S. J. Marrink, et al, J Phiys Chem B, vol. 111, no. 27, pp. 7812–7824, 2007.
[11] L. Monticelli, et al, J Chem Theo and Comp, vol. 4, no. 5, pp. 819–834, 2008.

Scientific skills

- Good experience with classical molecular dynamics on High Parallel Computing resources. Experience with both all atom and coarse-grained simulation approaches. Simulations are performed on solvated protein systems (mainly amyloid peptides in interaction with other bio-compounds), via Gromacs and Lammps packages. Post processing analysis are made using available tools (Gromacs' tools, VMD and Vega software) as well as ad hoc written python scripts
- Good experience with Extended X-ray Absorption Fine Structure (EXAFS) data acquisition, reduction and analysis (Athena and Excurve packages). Beamtime experiences at the ESRF synchrotron light source
- Basic experience with ab initio molecular dynamics on High Parallel Computing resources (Quantum Espresso suite)

Formative Experiences (Conferences, Seminars, Projects, etc.)

- 8th – 10th November 2017, CINECA, Rome (Ita), Introduction to Scientific and Technical Computing in C++ (**training course**)
- 3rd July – 2nd October 2017, Deutsches Elektronen-Synchrotron, Hamburg (DE), Coarse Grained Molecular Dynamics modeling for diffuse scattering in protein crystals (**visiting student project**)
- 15th March – 14th June 2017, Leiden Institute of Chemistry (NL), Abeta peptides, metal ions and beta sheet breackers. A multiscale simulation approach (**visiting student project**)
- 5th – 7th December 2016, CINECA, Casalecchio di Reno (Ita), Material Science codes on innovative HPC architectures: targeting the exascale (**training course**)
- 25th - 27th October 2016, CINEA, Rome (Ita), Python for Computational Science (**training course**)
- 11th - 22th July 2016, CINECA, Rome (Ita), 25th Summer School on Parallel Computing (**summer school**)
- 27th June 2016, CINECA, Rome (Ita), Introduction to Marconi supercomputer (**training course**)
- 7th - 9th June 2016, CINECA, Rome (Ita), Introduction to Parallel Computing with MPI and OpenMP (**training course**)
- 8th - 11th March 2016, CINECA, Rome (Ita), Introduction to Modern Fortran (**training course**)
- 3rd - 5th February 2016, CINECA, Rome (Ita), Introduction to Scientific and Technical Computing in C (**training course**)
- 22th - 24th September 2015, CINECA, Rome (Ita), High Performance Molecular Dynamics (**training course**)
- 12th - 18th November 2014, ESRF, Grenoble (Fr), XAS spectra acquisition (**data acquisition**)
- 22th - 23th May 2014, CNR, Rome (Ita), Biophysics@Rome2014 (**auditor**)
- 22th April 2014, CNR, Rome (Ita), 'Luci di Sincrotrone' meeting (**auditor**)
- January 2006, CERN, Geneva (CH), EEE (Extreme Energy Events) (**project**)
  June 2005, LFN Frascati (Rm, Ita) (**Summer Stage**)

Teaching Experiences

- November 2017**,** University of Rome Tor Vergata, cycle of theoretical and practical lectures on protein and nucleic acids sequence alignments for the Biophysics course under the responsibility of Prof Silvia Morante
- March-May 2016, University of Rome Tor Vergata, stage for bachelor's degree (6 cfu): "Classical Molecular Dynamics: examples of full atomistic and coarse grained approaches", course under the responsibility of Prof Silvia Morante
- 4th May 2016, University of Rome Tor Vergata, Practical lesson: "X-ray Absorption Spectroscopy: Data Reduction and Analysis" for the 'Laboratory of Biological Physics' course under the responsibility of Dr. Velia Minicozzi

Oral Presentations

- 4th April 2018, University of Rome Tor Vergata, Roma (Ita), Seminario interdisciplinare sulla biologia
- 13th – 15th December 2017, UniBa, Bari (Ita), SM&FT 2017 High Performance Computing in Theoretical Physics
- 18th - 21st September 2016, SIBPA, Cortona (Ita), XXIII Congresso Nazionale SIBPA
- 4th - 9th September 2016, EPS, Groningen (NL), Condensed Matter in Groningen (CMD26)
- 12th - 14th October 2015, GSSI, L'Aquila (Ita), 6th Young Researcher Meeting 2015
- 9th -11th September 2015, SIBPA, Florence (Ita), Biophys 2015 - From physics to biology and beyond

Publications

- E De Santis, V Minicozzi, S Morante, G C Rossi and F Stellato, "The role of metals in protein conformational disorders - The case of prion protein and Aβ-peptide", *J. Phys. Conf. Ser.,* **2016**, 689(012028), DOI:10.1088/1742-6596/689/1/012028

- E De Santis, V Minicozzi, O Proux, G C Rossi, K I Silva, M J Lawless, F Stellato, S Saxena, and S Morante, "Cu(II)-Zn(II) Cross-Modulation in Amyloid-Beta Peptide Binding: An X-Ray Absorption Spectroscopy Study", *J. Phys. Chem. B*, **2015**, 119(53), PP 15813-15820, DOI:10.1021/acs.jpcb.5b10264

Memberships

SIBPA – Italian Society for Pure and Applied Biophysics
INFN – Istituto Nazionale Fisica Nucleare, Sezione di Roma Tor Vergata

Mother tongue(s) Italian

Other language(s)

	UNDERSTANDING		SPEAKING		WRITING
	Listening	Reading	Spoken interaction	Spoken production	
English	C1	C1	B2	B2	C1

Common European Framework (CEFR) Levels C1.

Communication skills

- Capability of collaborating in multicultural environment
- Capability of communicating efficiently
- Good team-leading skills

Computer skills

- Good command of:
  - Microsoft Windows operating system
  - Unix operating system
  - Os operating system
  - Microsoft Office tools
  - Latex language
- Good knowledge of:
  - Python programming language
  - C programming language
  - Fortran programming language
- Basic knowledge of:
  - MPI paradigm
  - OpenMP paradigm
  - C++ programming language

Other skills and interests

- Gardening, sport (cycling, canoeing, trekking, swimming, water polo), bricolage, dogs training

Driving licence

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