Paulo Siani, Ph.D.

University of Milano-Bicocca, Milano, MI, Italy

Department of Materials Science

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CURRENT POSITION

University of Milano-Bicocca (UNIMIB), Milano, Italy

Senior Researcher (July 2023 - present)

University of Milano-Bicocca (UNIMIB), Milano, Italy

Postdoctoral Fellow (April 2019-June 2023)

EDUCATION

University of São Paulo (USP), Brazil & University of Southern Denmark (SDU), Denmark.

Ph.D. in Chemistry 2014-2018 (Sandwich Ph.D. program)

University of São Paulo (USP), Brazil.

M.Sc. in Chemistry 2011-2013

State University of Maringá (UEM), Brazil.

B.Sc. in Chemistry 2007-2010

RESEARCH EXPERIENCE

University of Milano-Bicocca (UNIMIB), Department of Materials Science, Milano, Italy

July 2023 – present

Senior Researcher and member of the NanoQlab group led by Prof. Cristiana Di Valentin

April 2019 – June 2023 (4-year research contract)

ERC Postdoctoral Fellow and member of the NanoQlab group led by Prof. Cristiana Di Valentin

Project: Development of smart bioinorganic hybrids for active targeting of tumor cells

- Conducted computational studies employing multi-scale modeling and simulations encompassing equilibrium and non-equilibrium molecular dynamics. Utilized quantum mechanics molecular mechanics and classical molecular mechanics approaches to explore the structural, dynamic, electrodynamics, and thermodynamic properties of functionalized metal oxide nanoparticles tailored for biomedical applications.
- Investigated the partitioning free energy and penetration mechanisms of anti-tumor drugs within bio-membranes of relevant lipid compositions. This exploration aimed at informing the rational formulation of lipid-based nanocarriers in collaboration with the experimental research group led by Prof. Francesca Re.
- Employed Metadynamics and Machine Learning analysis techniques, such as Self-Organizing Maps, to elucidate the loading/release mechanisms of drugs on organic-functionalized metal oxide nanoparticles. These insights were pivotal in designing optimal nano-carrier systems to advance targeted drug delivery strategies.
- Currently engaged in ongoing projects focused on the in-silico evaluation of key structural-functional parameters of tumor-targeting agents within ligand-activated nanodevices. Employing a synergistic blend of advanced MD techniques including Molecular Docking, Machine Learning, Metadynamics, Thermodynamic Integration, Adaptive Biasing Force, and Free Energy Perturbation methods.

University of Sao Paulo (USP), Department of Chemistry, Ribeirao Preto, Sao Paulo

April 2014 – May 2018 (3-year PhD scholarship)

PhD fellow and member of the research group led by Prof. Luis Gustavo Dias (advisor)

Project: Development of coarse-grained models for oxidized lipids and sterols.

- Parametrization of coarse-grained force field based on point-dipole electrostatics and extension of coarse-grained models for simulation of biomolecular assemblies composed of hydroperoxided lipids and cholesterol.

University of Southern Denmark (SDU), Department of Physics and Chemistry, Center for biomembrane physics (MEMPHYS), Odense, Denmark

October 2015 – September 2016 (1-year visiting PhD scholarship)

Visiting PhD fellow and member of the Khandelia group led by Prof. Himanshu Khandelia (co-advisor)

Project: Computer Simulation of the solubilization and permeation of photosensitizers in oxidized lipid bilayers.

- Study of initial steps of lipid oxidation of biological membranes induced by photoactivation under continuous illumination and its impact on photodynamic therapy.

University of Sao Paulo, Department of Chemistry, Ribeirao Preto, Sao Paulo

August 2011 – December 2013 (2-year MSc scholarship)

MSc fellow and member of the research group led by Prof. Luis Gustavo Dias (advisor)

Project: Molecular dynamics simulation of methylene blue and 1,9-dimethyl methylene blue in realistic bio-membrane models.

- Drug design and atomistic modeling and simulation of drug-membrane systems to improve the efficiency of photosensitizer drugs for photodynamic therapy.

PEER-REVIEWED PUBLICATIONS

1) Frigerio, G., Motta, S., **Siani, P.**, Donadoni, E., & Di Valentin, C. **(2025)**. Unveiling the drug delivery mechanism of graphene oxide dots at the atomic scale. *Journal of Controlled Release*, *379*, 344-362.
2) **Siani, P.**, Bianchetti, E., & Di Valentin, C. **(2025)**. Building up accurate atomistic models of biofunctionalized magnetite nanoparticles from first-principles calculations. *npj Computational Materials*, *11*(1), 20.
3) Soria, F. A., **Siani, P.**, & Di Valentin, C. **(2024)**. Nature of TiO_2–oligonucleotides interactions by atomistic molecular dynamics simulations. *Surfaces and Interfaces*, 52, 104889.
4) Donadoni, E., **Siani, P.**, Frigerio, G., Milani, C., Cui, Q., & Di Valentin, C. **(2024)**. Effect of polymer coating on nanoparticles interaction with lipid membranes by coarse-grained molecular dynamics simulations. *Nanoscale*, 16(18), 9108-9122
5) Frigerio, G., Donadoni, E., **Siani, P.**, Vertemara, J., Motta, S., Bonati, L., Gioia, L. D., & Di Valentin, C. **(2024)**. Mechanism of RGD-conjugated nanodevice binding to its target protein integrin $\alpha_V\beta_3$ by atomistic molecular dynamics and machine learning. *Nanoscale*, *16*(8), 4063–4081.
6) Donadoni, E., Frigerio, G., ***Siani, P.***, Motta, S., Vertemara, J., De Gioia, L., Bonati, L., & Di Valentin, C. **(2023)**. Molecular dynamics for the optimal design of functionalized nanodevices to target folate receptors on tumor cells. *ACS Biomaterials Science & Engineering*, *9*(11), 6123–6137.
7) **Siani, P.**, Frigerio, G., Donadoni, E., & Di Valentin, C. **(2023)**. Modeling zeta potential for nanoparticles in solution: water flexibility matters. *The Journal of Physical Chemistry. C, Nanomaterials and Interfaces*, *127*(19), 9236–9247.
8) Motta, S., **Siani, P.**, Donadoni, E., Frigerio, G., Bonati, L., & Di Valentin, C. **(2023)**. Metadynamics simulations for the investigation of drug loading on functionalized inorganic nanoparticles. *Nanoscale*, *15*(17), 7909–7919.

9) **Siani, P.**, & Di Valentin, C. **(2022)**. Effect of dopamine-functionalization, charge and pH on protein corona formation around TiO_2 nanoparticles. *Nanoscale*, *14*(13), 5121–5137.
10) **Siani, P.**, Donadoni, E., Ferraro, L., Re, F., & Di Valentin, C. **(2022)**. Molecular dynamics simulations of doxorubicin in sphingomyelin-based lipid membranes. *Biochimica et Biophysica Acta. Biomembranes*, *1864*(1), 183763.
11) **Siani, P.**, Frigerio, G., Donadoni, E., & Di Valentin, C. **(2022)**. Molecular dynamics simulations of cRGD-conjugated PEGylated TiO_2 nanoparticles for targeted photodynamic therapy. *Journal of Colloid and Interface Science*, *627*, 126–141.
12) Donadoni, E., **Siani, P.**, Frigerio, G., & Di Valentin, C. **(2022)**. Multi-scale modeling of folic acid-functionalized TiO_2 nanoparticles for active targeting of tumor cells. *Nanoscale*, *14*(33), 12099–12116.
13) Motta, S., **Siani, P.**, Levy, A., & Di Valentin, C. **(2021)**. Exploring the drug loading mechanism of photoactive inorganic nanocarriers through molecular dynamics simulations. *Nanoscale*, *13*(30), 13000–13013.
14) **Siani, P.**, Bianchetti, E., Liu, H., & Di Valentin, C. **(2021)**. Parametrization of the Fe-O_{water} cross-interaction for a more accurate Fe_3O_4/water interface model and its application to a spherical Fe_3O_4 nanoparticle of realistic size. *The Journal of Chemical Physics*, *154*(3), 034702.
15) Liu, H., **Siani, P.**, Bianchetti, E., Zhao, J., & Di Valentin, C. **(2021)**. Multiscale simulations of the hydration shells surrounding spherical Fe_3O_4 nanoparticles and effect on magnetic properties. *Nanoscale*, *13*(20), 9293–9302.
16) **Siani, P.**, Motta, S., Ferraro, L., Dohn, A. O., & Di Valentin, C. **(2020)**. Dopamine-Decorated TiO_2 Nanoparticles in Water: A QM/MM vs an MM Description. *Journal of Chemical Theory and Computation*, *16*(10), 6560–6574.
17) Liu, H., Bianchetti, E., **Siani, P.**, & Di Valentin, C. **(2020)**. Insight into the interface between Fe_3O_4 (001) surface and water overlayers through multiscale molecular dynamics simulations. *The Journal of Chemical Physics*, *152*(12), 124711.
18) Martins, W. K., Santos, N. F., Rocha, C. de S., Bacellar, I. O. L., Tsubone, T. M., Viotto, A. C., Matsukuma, A. Y., Abrantes, A. B. de P., **Siani, P.**, Dias, L. G., & Baptista, M. S. **(2019)**. Parallel damage in mitochondria and lysosomes is an efficient way to photoinduce cell death. *Autophagy*, *15*(2), 259–279.
19) **Siani, P.**, Khandelia, H., Orsi, M., & Dias, L. G. **(2018)**. Parameterization of a coarse-grained model of cholesterol with point-dipole electrostatics. *Journal of Computer-Aided Molecular Design*, *32*(11), 1259–1271.
20) de Souza, R. M., **Siani, P.**, Schmidt, T. F., Itri, R., & Dias, L. G. **(2017)**. Methylene blue location in (hydroperoxized) cardiolipin monolayer: implication in membrane photodegradation. *The Journal of Physical Chemistry. B*, *121*(36), 8512–8522.
21) **Siani, P.**, de Souza, R. M., Dias, L. G., Itri, R., & Khandelia, H. **(2016)**. An overview of molecular dynamics simulations of oxidized lipid systems, with a comparison of ELBA and MARTINI force fields for coarse grained lipid simulations. *Biochimica et Biophysica Acta*, *1858*(10), 2498–2511.

ORAL AND POSTER PRESENTATIONS

1. "Mechanistic insights from molecular dynamics simulations in nanomedicine". **Oral presentation** (in English) delivered at the "2024 Meeting of the

International Society of Quantum Biology and Pharmacology (ISQBP)" in the Academy of Athens on 19th May 2024, Athens, Greece.

2. "Mechanistic insights from molecular dynamics simulations in nanomedicine". **Oral presentation** (in English) delivered at the "NANOMIB CONFERENCE - Recent Advances in Nanomedicine: Opportunities and Challenges" in the University of Milano-Bicocca on 1st, 2024, Milano, Italy.
3. "Mechanistic insights from molecular dynamics simulations in nanomedicine research". **Oral presentation** (in English) delivered at the "Department of diagnostics and public health" in the University of Verona on 9th, 2023, Verona, Italy.
4. "A structural and thermodynamic study of doxorubicin in lipid membrane models". **Oral presentation** (in English) delivered at the "International School of Nanomedicine in the Ettore Majorana Foundation and Centre for Scientific Culture on July 23rd, 2022, Erice (Sicily), Italy.
5. "A structural and thermodynamic study of doxorubicin in lipid membrane models". **Oral presentation** (in English) delivered at the "NANOMIB congress 2022" in the Department of Biotechnology and Bioscience on April 7th, 2022, Milano, Italy.
6. "Molecular Dynamics Simulations: State of the Art". **Oral presentation** (in Portuguese) delivered online at the Oswaldo Cruz Foundation (FIOCRUZ) on October 20th, 2021, Rio de Janeiro, Brazil.
7. "Dopamine-Decorated TiO_2 Nanoparticles in Water: A QM/MM vs an MM Description". **Poster presentation** (in English) delivered online at the "Winter Workshop on Multiscale Modeling" at the Karlsruhe Institute of Technology on November 23rd, 2021, Eggenstein-Leopoldshafen, Germany.
8. "Molecular Dynamics of methylene blue and 1,9-dimethyl methylene blue drugs in POPC membrane model". **Poster presentation** (in English) delivered at the "XXXIX Annual meeting of the Federation of Society for Experimental Biology" on August 30th, 2014, Caxambu, Brazil.
9. "Interaction of methylene blue and 1,9-dimethyl methylene blue with POPC lipid bilayer: A study by molecular dynamics simulation". **Poster presentation** (in English) delivered at the "XXXVIII Congress of Theoretical Chemists of Latin Expression" on December 02nd, 2012, Natal, Brazil.

CONFERENCES and SCHOOLS

1. 2024 Meeting of the International Society of Quantum Biology and Pharmacology (ISQBP)" in the Academy of Athens on 19th–23rd May 2024, Athens, Greece.
2. Workshop NANO23@uniVR, June 8-9th, 2023, Verona, Italy.
3. International School of Nanomedicine, July 20-25th, 2022, Erice (Sicily), Italy.
4. School of Nanomedicine, June 8th-10th, 2022, Rome, Italy.

5. School of Nanomedicine, December 11th-13th, 2019, Trieste, Italy.
6. Quantum Mechanical Simulations Can Elevate the Design of Materials, October 9th, 2019, Turin, Italy.
7. School on Biological Soft Matter: from molecular interactions to engineered materials, ICTP-SAIFR, March 13th–24th, 2017, Sao Paulo, Brazil. (80 hrs.)
8. Minischool on Biophysics of proteins interactions, ICTP-SAIFR, March 9th-13th, 2015, Sao Paulo, Brazil. (40 hrs.)
9. Onuchic Minicourse on Energy Landscapes in Biophysics, ICTP-SAIFR, March 9th, 2015, Sao Paulo, Brazil. (4 hrs.)
10. VII Latin American Postgraduate Program of Biophysics, August 26th-27th, 2014, Caxambu, Brazil.
11. XXXIX Annual Meeting of the Federation of Society for Experimental Biology, August 27th-30th, 2014, Brazil.
12. XXXVIII Congress of Theoretical Chemists of Latin Expression, December 02nd ,2012, Natal, Brazil.
13. Plagiarism in Scientific Publications, June 1st, 2012, Ribeirao Preto, Brazil. (2 hrs.)

PARTICIPATION TO SCIENTIFIC PROJECTS

1. PNRR project "Heal Italia" (Project No. PE_00000019 – NextGenerationEU) as Scientific Researcher conducting research and teaching activities at the University of Milano-Bicocca from 2023 to 2026.
2. KNMFi Joint Project (Project No. 2023-029-031627) "Mechanism of Lipid Spreading on Graphene/Graphene Oxide" serving as co-PI. Project being conducted jointly at the University of Milano-Bicocca and the Karlsruhe Institute of Technology in 2024.
3. European Research Council (ERC) Consolidator Grant Horizon 2020 (Project No. 647020) "BIOINOHYB: Smart bioinorganic hybrids for nanomedicine" as Postdoctoral Fellow (2019-present).
4. Ateneo project (Fondo di Ateneo Quota Competitiva 2020) "Photodynamic Therapy for Brain Tumors by Multi-Functional Particles using *in situ* Cerenkov and Radioluminescence Light" at the University of Milano-Bicocca as postdoctoral fellow (2020-2022).
5. European project "Designing New Materials with Quantum Mechanics" as postdoctoral fellow (2019-2020).
6. FAPESP-Brazil project Grant n. 17/03204-7 "Development and application of coarse-grained force field in self-assembled systems" as PhD fellow (2017-2018).
7. FAPESP-Brazil project Grant n. 12/50680-5 "Photosensitization in life science" as MSc and PhD fellow (2013-2017).

TEACHING ACTIVITIES

- Supervision of undergraduate and bachelor students engaged in scientific projects:

PhD students:

1. Undergraduate PhD Thesis **supervisor**, University of Milano-Bicocca
   Title: "Computational study of peptide-activated PEGylated TiO_2 nanosystems and their interactions with over-expressed proteins in cancer cells"
   Student: Giulia Frigerio
   Course: Scienze e Tecnologie Chimiche, a.a. 2022-2024

2. Undergraduate PhD Thesis **supervisor**, University of Milano-Bicocca
   Title: "Computational investigation of folate functionalized PEGylated TiO_2 nanoparticles and their interactions with proteins and lipid membranes via atomistic and coarse-grained techniques"
   Student: Edoardo Donadoni
   Course: Scienze e Tecnologie Chimiche, a.a. 2021-2023

Master students:

1. Undergraduate Master Thesis **co-advisor**, University of Milano-Bicocca
   Title: "Studio Computazionale e Analisi Conformazionale del Rivestimento Polimerico (PEG) di Nanoparticelle di Biossido di Titanio per la Nanomedicina"
   Student: Carolina Milani
   Course: Scienze e Tecnologie Chimiche, a.a. 2020-2021

   Course: Scienze e Tecnologie Chimiche, a.a. 2021-2022
2. Undergraduate Master Thesis **co-advisor**, University of Milano-Bicocca
   Title: "Computational study of RGD-functionalized TiO_2 nanosystems for active targeting of cancer cells"
   Student: Giulia Frigerio
   Course: Scienze e Tecnologie Chimiche, a.a. 2020-2021

3. Undergraduate Master Thesis **co-advisor**, University of Milano-Bicocca
   Title: "Computational simulation of permeation through phospholipid membranes of different composition by the antitumor drug doxorubicin"
   Student: Edoardo Donadoni
   Course: Scienze e Tecnologie Chimiche, a.a. 2019-2020

4. Undergraduate Master Thesis **co-advisor**, University of Milano-Bicocca

Title: “Molecular dynamics study of the interaction between the anticancer drug doxorubicin and a functionalized TiO_2 nanocarrier”

Student: Andrea Levi

Course: Fisica, a.a. 2019-2020

Bachelor students:

1. Bachelor Thesis **co-advisor**, University of Milano-Bicocca
   Title: “Studio computazionale di modelli di nanodiamanti rivestiti con glicole polietilenico per applicazioni in nanomedicina.”
   Student: Simone Gambari
   Course: Scienze e Tecnologie Chimiche, a.a. 2023-2024

2. Bachelor Thesis **co-advisor**, University of Milano-Bicocca
   Title: “Computational Study of Gold Nanoparticles by Varying the Extent of PEG coating”
   Student: Marialaura D’Alessio
   Course: Scienze e Tecnologie Chimiche, a.a. 2023-2024

3. Bachelor Thesis **co-advisor**, University of Milano-Bicocca
   Title: “Studio computazionale dell’interazione tra glicani e la superficie di membrane fosfolipidiche”
   Student: Beatrice Quarta Castelbarco Albani
   Course: Scienze e Tecnologie Chimiche, a.a. 2022-2023

- Assistance Professor in teaching laboratory activities in General Chemistry at the University of Milano-Bicocca (UNIMIB), Milano, Italy, 2023-2024

- Assistance Professor in teaching laboratory activities in General Chemistry at the University of Milano-Bicocca (UNIMIB), Milano, Italy, 2024-2025

FELLOWSHIPS

Scientific Researcher Contract: 3-year fixed-term contract as Senior Researcher. Selection process involved evaluation of CV and oral interview. University of Milano-Bicocca, 2023-present.

ERC Postdoctoral Fellowship: 5-year research contract as Postdoctoral Fellow. Selection process entailed CV evaluation and oral interview. University of Milano-Bicocca, April 2019-2023.

CNPq-Brazil Doctoral Fellowship: 3-year contract (process n. 141896/2014-0) as PhD Fellow. Selection process based on CV evaluation and performance in a chemistry written exam (awarded to the candidate with the highest mark in the PhD admission written exam). University of Sao Paulo, 2014-2018.

CNPq-Brazil "Science without borders" Sandwich Doctoral Fellowship. 1-year contract (process n. 234433/2014-0) as visiting PhD Fellow abroad. Selection process based on the university's excellence level and candidate's merit. University of Southern Denmark, 2015-2016.

CAPES-Brazil Master Fellowship. 2-year contract (process n. 1045403) as MSc Fellow. Selection process based on CV evaluation and performance in a chemistry written exam. University of Sao Paulo, 2011-2013.

HARD-SKILLS

Computational Chemistry Methods:

- Expertise in Quantum-Mechanics Molecular-Mechanics Molecular Dynamics (**QMMM-MD**), specializing in the study of organic-functionalized metal oxide nanoparticles for nanomedical applications.
- Non-equilibrium Molecular Dynamics (**NEMD**). Prediction of electrokinetic properties experimentally relevant in nanoparticle characterization in solution.
- Extensive experience in All-Atom (**AA-MD**) and Coarse-Grained (**CG-MD**) molecular dynamics., particularly in computational studies of drug and lipid assemblies for precision-enhanced photodynamic therapies & calibration of **AA** and **CG** force fields for general applications in materials science and biophysics projects.

Free Energy Techniques:

- Skilled in advanced methods of free energy calculations, including Thermodynamic Integration (**TI**), Free Energy Perturbation (**FEP**), Metadynamics (**MetaD**) and Adaptive Biasing Force (**ABF**) methods.

Molecular Docking and Machine-Learning Analysis:

- Experience in molecular docking and machine learning analysis based on Self-Organizing Maps (**SOM**) with a focus on studying ligand-receptor interactions in proteins over-expressed in tumor cells.

Computational Chemistry Software:

- Utilized a range of computational chemistry software including DFTB+, GAUSSIAN, ASE, LAMMPS, NAMD, AMBER, GROMACS, MAESTRO, GLIDE, AUTODOCK, AVOGRADO, PACKMOL, MOLTEMPLATE, and VMD for various projects.

Data analysis:

- TCL/TK, CPPTRAJ, LOOS, VMD, GROMACS tools, on-the-fly analysis, and in-house scripting.

Programming skills:

- Intermediate coding level in Fortran and Python, TCL/TK, Shell scripting, with extensive experience working in High-Performance Computing (HPC) and Unix environments.

Language skills:

- Portuguese (Native), English (Fluent), Italian (Pre-intermediate)

PEER-REVIEW ACTIVITIES

Scientific Report
Journal of Computational Information and Modeling
Journal of Chemical Physics