Fabrizio Marinelli

E-mail: fabrizio.marinelli@nih.gov
https://www.linkedin.com/in/fabrizio-marinelli-7246b8158/

National Heart, Lung, & Blood Institute
Building 10, Room 5N319
10 Center Dr, Bethesda
MD, 20814, USA
Phone: +1 301 827 0825

PERSONAL STATEMENT

I am a Staff Scientist at the National Institutes of Health, where I perform independent research in membrane protein biophysics and on the development of quantitative computational methods.

The aim of my research is to characterize the molecular mechanisms of prominent biomolecules involved in membrane transport and/or cell signaling. The premise of my studies is that a deeper molecular understanding of such processes will help identifying more effective therapeutic agents for pathophysiological conditions.

My studies entail the use of computationally intensive molecular simulation techniques and are often performed in synergy with experimental collaborators such as structural biologists and biophysicists.

One central aspect of my research is the proposal and implementation of novel machine learning (ML) approaches for integrative structural biology, based on the combination of computational/theoretical models and experiments, such as measurements from double electron-electron resonance (DEER) and hydrogen-deuterium exchange coupled to mass spectrometry (HDX-MS). I am also interested in the development of enhanced sampling methods and novel approaches for the rational analysis of simulation/bioinformatics data.

POSITIONS

National Heart, Lung and Blood Institute, National Institutes of Health, Apr 2016-
Theoretical Molecular Biophysics Section, Bethesda, MD, USA
Staff Scientist

National Heart, Lung and Blood Institute, National Institutes of Health, Aug 2013-Apr 2016
Theoretical Molecular Biophysics Section, Bethesda, MD, USA
Visiting Fellow. Advisor: Dr. José Faraldo-Gómez

Max Planck Institute of Biophysics, Frankfurt am Main, Germany, Nov 2009 – Aug 2013
Theoretical Molecular Biophysics Department
Postdoctoral Researcher. Advisor: Dr. José Faraldo-Gómez

EDUCATION

PhD Statistical and Biological Physics, SISSA/ISAS, Trieste, Italy Nov 2005 – Oct 2009

Thesis: Insights on protein structure and dynamics from multiple biased molecular dynamics simulations [Link]

Advisor: Prof. Alessandro Laio

MS Chemistry, "La Sapienza" University, Rome, Italy Oct 1998 – Feb 2005

Thesis: Study of thermodynamic and spectroscopic properties of dilute solutions using quantum mechanics/molecular dynamics methods

Advisors: Alfredo Di Nola and Andrea Amadei

PROFESSIONAL MEMBERSHIP & ACTIVITIES

PROFESSIONAL ACTIVITIES

- Member of the Staff Scientists recruiting committee of NHLBI, NIH 2022

MEMBERSHIPS

- American Chemical Society 2013, 2018-2020
- Society of General Physiologists 2018-2020
- Biophysical Society 2009-

HONORS & AWARDS

- Italian associate professor habilitation in molecular biology 2023
- Italian associate professor habilitation in condensed matter physics, applied physics & biochemistry 2021
- NIH visiting fellowship 2013-2016
- SISSA Ph. D. fellowship 2005-2009
- *Magna cum laude* MS Chemistry 2005

EDITORIAL & ACADEMIC SERVICE

EDITORIAL BOARD MEMBER
(https://www.webofscience.com/wos/author/record/1375820)

- *Frontiers in Molecular Biosciences* (Associate Editor) 2023-
- *Scientific Reports* (Nature Portfolio) 2018-

REVIEWER (https://www.webofscience.com/wos/author/record/1375820)

- *Nature Communications* 2023-
- *ACS Central Science (ACS)* 2022-
- *eLife* 2018-
- *Journal of Medicinal Chemistry* 2023-
- *Communications Biology (Nature)* 2018-
- *National grants of the Czech Science Foundation* 2014-
- *Biophysical Journal (Cell Press)* 2010-
- *The Journal of General Physiology* 2018-
- *Journal of Chemical Theory and Computation (ACS)* 2012-
- *Proteins: Structure, Function, and Bioinformatics (Wiley)* 2018-
- *BBA Biomembranes (Elsevier)* 2017-

- *Scientific Reports (Nature)* 2015-
- *Journal of chemical information and modeling (ACS)* 2019-
- *The Journal of Physical Chemistry (ACS)* 2013-
- *Frontiers Molecular Biosciences* 2020-
- *European Biophysics Journal (Springer)* 2015-

SCIENTIFIC SOFTWARE DEVELOPMENT

- FCAM: software tools for free energy analysis based on mean forces (Python) [Link] 2021-
- HDXer: hydrogen deuterium exchange ensemble reweighting software (Python) [Link] 2020-
- Member of the PLUMED consortium [Link] 2019-
- Co-developer of the *Colvars* simulation software (C++) [Link] 2015-
- Co-developer of the METAGUI simulation analysis tool (Tcl/fortran) [Link] 2011-
- Co-developer of the PLUMED (version 1) simulation software (ANSI C) [Link] 200-2013

INVITED SEMINARS & CONFERENCE TALKS

POSTDOCTORAL

- **Macromolecular complexes: from ab initio and integrative modelling to functional dynamics.** CECAM, Lausanne, Switzerland (upcoming). 2023
- **Biophysics week event**, Biophysical Society, University of Maryland Baltimore. 2023
- **Ions, membrane and channels: Multiscale simulations from quantum to coarse-grain. A symposium in honor of Mike Klein's 80th birthday.** CECAM, Rome, Italy. 2022
- **NAMD Developers Workshop** at Urbana, IL, USA 2021
- **EPR Symposium, Rocky Mountain Conference**, Denver, CO, USA 2019
- **Snowmass Summer Biophysics Workshop**, Snowmass, CO, USA 2015
- **Gordon Research Conference**, *'Mechanisms of Membrane Transport'.* Lewiston, ME, USA. 2015
- **NIH Tenure-track investigator job interview.** National Institute on Drug Abuse, National Institutes of Health, Baltimore, MD, USA 2014
- **CNRS Research Scientist job interview.** Physical, Theoretical and Analytical Chemistry. Paris, France 2014
- **CNRS Research Scientist job interview.** Modeling and Analysis of Biological Data and Systems. Paris, France. 2014
- **CNRS Research Scientist job interview.** Chemistry for Living Systems and Medicinal Chemistry. Paris, France 2014
- **Gordon Research Conference**, *'Protons & Membrane reactions'.* Ventura, CA, USA. 2014
- **Membrane Protein Interest Group and Structural Biology Interest Group Postdoc Symposium**, NIH, Bethesda MD, USA 2014
- **Biophysical Society Annual Meeting**, San Francisco, CA, USA 2014
- **Assistant professor job interview at Universidad de la República**, Paysandú, Uruguay 2013

- **PLUMED developers and contributors meeting**, Trieste, Italy 2012
- **European Bioenergetics Conference (EBEC)**, Freiburg, Germany 2012
- **Universidad de la República**, Montevideo, Uruguay 2012
- **Pasteur Institute,** Montevideo, Uruguay
- **CECAM Workshop, '***Exploring Protein Interactions through Theory and Experiment's*, Lausanne, Switzerland 2012
- **Swiss Institute of Bioinformatics**, Laussane, Switzerland 2011
- **Biophysical Society Annual Meeting**, Baltimore MD, USA 2011
- **German Research School for Simulation Sciences**, Jülich, Germany 2010

PhD STUDENT

- **International Workshop (CECAM),** *'From Structure to Function: Influx and Efflux Systems'*, Cagliari, Italy. 2009
- **Mini symposium, Angelos Michaelides group, UCL university**, London, England. 2008
- **Marie Curie Training Course (CECAM),** *'Progress in simulating activated events'*, Casaprota, Italy. 2008

PROJECTS & GRANTS

- **ANTON 2**: *Mechanisms of ion conduction, selectivity and inhibition of the human lysosomal K+ channel TMEM175*. Wenchang Zhou, Fabrizio Marinelli, José D Faraldo-Gómez 2020
- **PRACE**: *Ab initio molecular dynamics simulations of proton transport in a biological ion channel*. Emiliano Ippoliti, Chao Zhang, Fabrizio Marinelli, Paolo Carloni 2010

TEACHING & MENTORING

LECTURE SERIES & WORKSHOPS

- Course on Enhanced sampling techniques in classical MD simulations, QUITEL 2016, Montevideo, Uruguay. 2016
- Invited lectures on membrane protein atomistic simulations at the membrane transporters seminar series, Max Planck Institute of Biophysics, Max Planck Institute of Biophysics, Frankfurt, Germany 2013
- Computer Lab of the IMPReS course on modeling & simulation, Max Planck Institute of Biophysics, Frankfurt, Germany 2010
- Computer Lab of Current Techniques in Membrane Proteomics (Module C1) summer school, Goethe University of Frankfurt, Germany 2010

MENTORING

- Co-supervisor of Dr. Esam Orabi in the Theoretical molecular biophysics section (NHLBI, NIH) 2021-
- Assisted Dr. Tugba ozturk in the Theoretical molecular biophysics section (NHLBI, NIH) and Washington University in St. Louis 2021-2022
- Co-supervised Dr. Wenchang Zhou in the Theoretical molecular biophysics section (NHLBI, NIH) 2016-2021
- Co-supervised Noah Schwartz (postbaccalaureate Fellow) in the Theoretical molecular biophysics section (NHLBI, NIH) 2020-2021

- Co-supervised Dr. Rahul Banerjee in the Theoretical molecular biophysics section (NHLBI, NIH) 2017-2019
- Co-supervised Dr. Richard Bradshaw in the Computational Structural Biology Section (NINDS, NIH) 2018-2020
- Co-supervised Irina Shlosman, post baccalaureate in the Theoretical molecular biophysics section (NHLBI, NIH) 2016-2018
- Co-supervised Corinne Nief, summer student in in the Theoretical molecular biophysics laboratory (NHLBI, NIH) 2015
- Co-supervised the Ph.D. research of Carles Corbi-Verge (Ph.D. obtained in late 2012) 2011-2013

CONFERENCE POSTERS

1. Marinelli F, Giacomo Fiorin, Faraldo-Gómez JD (2017). Molecular breakdown of DEER data from self-learning atomistic simulations. *Biophysical Society Thematic Meeting: Conformational Ensembles from Experimental Data and Computer Simulations*. Berlin, Germany.
2. Marinelli F, Faraldo-Gómez JD (2017). Molecular mechanism of ion exchange and binding-site occlusion in a sodium/calcium exchanger. *Gordon Research Conference, Mechanisms of Membrane Transport.* Colby-Sawyer College, New London, NH, USA.
3. Marinelli F (2015). Ion Occupancy Shapes Conformational Free-Energy Landscape of a Na^+/Ca^{2+} Exchanger and Allosterically Controls Its Alternating-Access Mechanism. *Gordon Research Conference, Mechanisms of Membrane Transport.* Bates College, Lewiston, ME, USA.
4. Marinelli F, Faraldo-Gómez JD (2014). Molecular basis for ion binding and conformational change in the Na^+/Ca^{2+} exchanger. *Gordon Research Conference, Protons & Membrane Reaction*. Ventura CA, USA.
5. Marinelli F, Faraldo-Gómez JD (2013). *Molecular basis for Na^+ vs Ca^{2+} binding to the Na^+/Ca^{2+} exchanger*. *Gordon Research Conference, Mechanisms of Membrane Transport.* Mount Holyoke College South Hadley, MA, USA.
6. Marinelli F, Kuhlmann SI, Grell E, Bienert R, Kunte H-J, Ziegler C, Faraldo-Gómez J.D (2011). Enhanced substrate release from a TRAP transporter binding protein by allosteric reduction of Its affinity. *Gordon Research Conference, Mechanisms of Membrane Transport*. University of New England, Biddeford, ME, USA.

LIST OF PUBLICATIONS

(●) denotes corresponding authorship

(**#**) denotes equal first author contribution.

Research articles and reviews

POSTDOCTORAL

Manuscripts published

1. Marinelli F●, Faraldo-Gómez JD (2023). The molecular mechanism of selective and active transport in a Na^+/Ca^{2+} exchanger. bioRxiv. doi: https://doi.org/10.1101/2023.01.20.524959 [Abstract]
2. Oh S, Marinelli F#, Zhou, Lee J, Choi HJ, Kim M, Faraldo-Gómez JD, Hite RK (2022). Differential ion dehydration energetics explains selectivity in the non-canonical lysosomal K+ channel TMEM175. *eLife*. 11: e75122. [Abstract]
3. Lee PS, Bradshaw R, Marinelli F, Kihn K, Smith A, Wintrode PL, Deredge DJ, Faraldo-Gómez JD, Forrest LR (2021). Interpreting Hydrogen-Deuterium Exchange Experiments with Molecular Simulations: Tutorials and Applications of the HDXer Ensemble Reweighting Software. *LiveCoMS, 3*(1), 1521. [Abstract]
4. Marinelli F●, Faraldo-Gómez JD (2021). Force correction analysis method for derivation of multidimensional free energy landscapes from adaptively-biased replica simulations. *J. Chem. Theory Comput.* 17: 6775–6788 [Abstract]
5. Bradshaw RT, Marinelli F#, Faraldo-Gómez JD, Forrest LR (2020). Interpretation of HDX Data by Maximum-Entropy Reweighting of Simulated Structural Ensembles. *Biophys. J.* 118: 1649-64 [Abstract]
6. Fiorin G, Marinelli F and Faraldo-Gómez JD (2019). Direct derivation of free energies of membrane deformation and other solvent density fluctuations from molecular dynamics simulations. *J Comput. Chem.* 9999: 1– 11. [Abstract]
7. Bonomi M, Bussi G, Camilloni C, Tribello G, ..., Marinelli F, et al. (2019) Promoting transparency and reproducibility in enhanced molecular simulations. *Nature Methods* 16: 670–673. [Abstract]
8. Li M, Wang Y, Banerjee R, Marinelli F, Silberberg S, Faraldo-Gómez JD, Hattori M, Swartz KJ. Molecular mechanisms of human P2X3 receptor channel activation and modulation by divalent cation bound ATP (2019). *eLife* 8:e47060. [Abstract]
9. Marinelli F●, G. Fiorin (2019). Structural characterization of biomolecules through atomistic simulations guided by DEER measurements. *Structure* 27:359-370. [Abstract].
10. Hustedt E, Marinelli F#, Stein R, Faraldo-Gómez JD, Mchaourab H (2018). Confidence Analysis of DEER Data and its Structural Interpretation with Ensemble-Biased Metadynamics. *Biophys. J.* 115: 1200-16. [Abstract]
11. Shlosman I, Marinelli F, Faraldo-Gómez JD, Mindell JA (2018). The prokaryotic Na+/Ca2+ exchanger NCX_Mj transports Na+ and Ca2+ in a 3:1 stoichiometry. *J Gen Physiol*. 150:51-65. [Abstract]
12. Zhou W, Marinelli F●, Nief C, Faraldo-Gómez JD (2017). Atomistic simulations indicate the c-subunit ring of the F1Fo ATP synthase is not the mitochondrial permeability transition pore. *eLife* 6: e23781. [Abstract]
13. Liao J, Marinelli F#, Lee C, Huang Y, Faraldo-Gómez JD, Jiang Y (2016). Mechanism of extracellular ion exchange and binding-site occlusion in the sodium-calcium exchanger. *Nat. Struct. Mol. Biol.* 23: 590–599. [Abstract]
14. Marinelli F●, Faraldo-Gómez JD (2015). Ensemble-Biased Metadynamics: A Molecular Simulation Method to Sample Experimental Distributions. *Biophys. J.* 108:2779-82. [Abstract]

15. Branduardi D, Marinelli F, Faraldo-Gómez JD (2015). Atomic-resolution dissection of the energetics and mechanism of isomerization of hydrated ATP-Mg^{2+} through the SOMA string method. *J. Comput. Chem.*, DOI: 10.1002/jcc.23991. [Abstract]

16. Marinelli F, Almagor L, Hiller R, Giladi M, Khananshvili D, Faraldo-Gómez JD (2014). Sodium recognition by the Na^{+}/Ca^{2+} exchanger in the outward-facing conformation. *Proc Natl Acad Sci USA* 111:E5354-62. [Abstract]

17. Corbi-Verge C, Marinelli F**#**, Zafra-Ruano A, Ruiz-Sanz J, Luque I, Faraldo-Gómez JD (2013). Two-state dynamics of the SH3-SH2 tandem of Abl kinase and the allosteric role of the N-cap. *Proc Natl Acad Sci USA* 110:E3372-80. [Abstract]

18. Marinelli F● (2013). Following easy slope paths on a free energy landscape: the case study of the Trp- Cage folding mechanism. *Biophys J* 105:1236-47. [Abstract]

19. Marinelli F●, Sorrenti A, Corvaglia V, Leone V, Mancini G (2012). Molecular description of the propagation of chirality from molecules to complex systems: different mechanisms controlled by hydrophobic interactions. *Chem Eur J* 18:14680–88. [Abstract]

20. Biarnés X, Pietrucci F, Marinelli F, Laio A (2012). METAGUI. A VMD interface for analyzing metadynamics and molecular dynamics simulations. *Comput Phys Commun* 183:203-11. [Abstract]

21. Marinelli F, Kuhlmann SI, Grell E, Kunte HJ, Ziegler C, Faraldo-Gómez JD (2011). Evidence for an allosteric mechanism of substrate release from membrane-transporter accessory binding proteins. *Proc Natl Acad Sci USA*, 108:E1285-92. [Abstract]

22. Leone V, Marinelli F, Carloni P, Parrinello M (2010). Targeting biomolecular flexibility with metadynamics. *Curr Opin Struct Biol*, 20:148-54. [Abstract]. REVIEW (refereed)

PhD STUDENT

23. Crespo Y, Marinelli F●, Pietrucci F, Laio A (2010). Metadynamics convergence law in a multidimensional system. *Phys Rev E* 81:055701. [Abstract]

24. Cossio P, Marinelli F, Laio A, Pietrucci F (2010). Optimizing the performance of Bias-Exchange Metadynamics: folding a 48-residue LysM domain using a coarse-grained model. *J Phys Chem B* 114:3259-65. [Abstract]

25. Marinelli F, Pietrucci F, Laio A, Piana S (2009). A kinetic model of Trp-cage folding from multiple biased molecular dynamics simulations. *PLoS Comput Biol* 5:e1000452 doi:10.1371/journal.pcbi.1000452. [Abstract]

26. Pietrucci F, Marinelli F, Carloni P, Laio A (2009). Substrate binding mechanism of HIV-1 protease from explicit solvent atomistic simulations. *J Am Chem Soc* 131:11811–18. [Abstract]

27. Bonomi M, Branduardi D, Bussi G, Camilloni C, Provasi D, Raiteri P, Donadio D, Marinelli F, Pietrucci F, Broglia RA, Parrinello M (2009). PLUMED: A portable plugin for free-energy calculations with molecular dynamics *Comput Phys Commun* 180:1961-72. [Abstract]

28. Todorova N, Marinelli F, Piana S, Yarovsky I (2009). Exploring the folding free energy landscape of insulin using bias exchange metadynamics. *J Phys Chem B* 113:3556-64. [Abstract]

29. Piana S, Laio A, Marinelli F, Van Troys M, Bourry D, Ampe C, Martins JC (2008). Predicting the effect of a point mutation on a protein fold: the villin and advillin headpieces and their Pro62Ala mutants. *J Mol Biol* 375:460-70. [Abstract]

MS STUDENT

30. D'Abramo M, Aschi M, Marinelli F, Di Nola A, Amadei A (2007). Theoretical prediction of thermodynamic equilibrium constants of chemical reactions in water. *J Mol Structure Theochem* 811:197–201. [Abstract]
31. Amadei A, Marinelli F, D'Abramo M, D'Alessandro M, Anselmi M, Di Nola A, Aschi M (2005). Theoretical modeling of vibroelectronic quantum states in complex molecular systems: Solvated carbon monoxide, a test case. *J Chem Phys* 122:124506. [Abstract]
32. D'Alessandro M, Marinelli F, D'Abramo M, Aschi M, Di Nola A, Amadei A (2005). Ground and excited electronic state thermodynamics of aqueous carbon monoxide: A theoretical study. *J Chem Phys* 122:124507. [Abstract]

Conference Abstracts

1. Marinelli F, Ficici E, Faraldo-Gómez J (2022). The alternating-access mechanism of transport of the Na^+/Ca^{2+} exchanger. *66th Biophysical Society Annual Meeting*. San Francisco, CA, USA.
2. Marinelli F, Ficici E, Faraldo-Gómez J (2019). Molecular Basis for Ion Recognition and Transport in a Na+/Ca2+ Exchanger. *63th Biophysical Society Annual Meeting*. Baltimore, MD, USA.
3. Marinelli F, Ficici E, Faraldo-Gómez J (2018). How the Substrate Occupancy of a Membrane Transporter Determines the Viability of its Alternating-Access Mechanism and thus its Functional Specificity. *62th Biophysical Society Annual Meeting*. San Francisco, CA, USA.
4. Shlosman I, Marinelli F, Mindell JA, Faraldo-Gómez JD (2018). Dissecting the Thermodynamics of Transport of a Sodium-Calcium Exchanger. *62th Biophysical Society Annual Meeting*. San Francisco, CA, USA.
5. Marinelli F, Faraldo-Gómez JD (2017). Molecular Breakdown of Double Electron-Electron Resonance Data with Atomistic Simulations. *61th Biophysical Society Annual Meeting*. New Orleans, LA, USA.
6. Marinelli F, Faraldo-Gómez JD (2016). Keeping Secondary Transporters under Control: Lessons from a Na^+/Ca^{2+} Exchanger. *60th Biophysical Society Annual Meeting*. Los Angeles, CA, USA.
7. Marinelli F, Faraldo-Gómez JD (2015). Minimally-biased Metadynamics method to sample conformational ensembles compatible with experimental measurements. *59th Biophysical Society Annual Meeting*. Baltimore MD, USA.
8. Marinelli F, Faraldo-Gómez JD (2014). Molecular basis for sodium versus calcium binding in the sodium-calcium exchanger. *58th Biophysical Society Annual Meeting*. San Francisco CA, USA.
9. Marinelli F, Faraldo-Gómez, JD (2012). Insights into the mechanism of the Na^+/Ca^{2+} exchanger from atomistic dynamics simulations *16th. European Bioenergetics Conference.* Freiburg, Germany.
10. Marinelli F, Kuhlmann S.I., Grell E, Bienert R, Kunte H-J, Ziegler C, Faraldo-Gómez J.D. (2011). Enhanced substrate release from a trap transporter binding protein by remote modulation of its intrinsic conformational dynamics. *55th Biophysical Society Annual Meeting.* Baltimore MD, USA.

11. Marinelli F, Piana S, Pietrucci F, Torodova N, Yarovsky I, Laio A (2009). Insights on protein structure and dynamics from multiple biased molecular dynamics simulations. *53rd Biophysical Society Annual Meeting.* Boston MA, USA.

12. Martins J, Laio A, Marinelli F, Van Troys M, Ampe C, Bourry D, Piano S (2007). Atomistic Prediction of the structure of the Advillin headpiece and its Pro62Ala mutant. *Programme and Book of Abstracts Euromar,* 158–158.

BIBLIOMETRICS (Source: Scopus, 08/21/2023)
~3700 citations, H-index = 23