

Biographical sketch			
<i>Name:</i> Gabriele	<i>Position title:</i> Associate Professor (tenure track) in Organic Chemistry at Department of Chemical Sciences of the University of Padua (Italy)		
<i>Surname:</i> Giachin			
Education			
<i>Institution and location</i>	<i>Degree</i>	<i>Completion date</i>	<i>Field of study</i>
University of Udine, Italy	B.S.	03/2005	Agricultural Science and Technology
University of Udine, Italy	M.S.	03/2007	Biotechnology
Scuola Internazionale Superiore di Studi Avanzati (SISSA), Italy	Ph.D.	03/2012	Neurobiology, structural biology

A. PERSONAL STATEMENT

Since the beginning of my scientific career, I have focused on studying macromolecular systems using interdisciplinary approaches, including biophysical methods, NMR, small-angle X-ray scattering (SAXS), X-ray diffraction, and cryo-EM. My primary research interests lie in understanding the structural and functional mechanisms underlying neurodegenerative diseases, such as prion disorders, and mitochondrial dysfunctions linked to neurodegeneration, particularly Complex I deficiencies. My Ph.D. research at SISSA provided key insights into prion biology, including the identification by NMR of a structural “hot spot” critical for prion conversion, and the development of an antibody fragment capable of halting prion formation (*JACS*, 2014). At the European Synchrotron Radiation Facility (ESRF), I specialized in synchrotron-based techniques, contributing to studies on metal ion coordination in prion proteins (*Biophysical Journal*, 2020) and regulatory mechanisms in mitochondrial ACAD9 (*Angewandte Chemie*, 2021). As a Marie Skłodowska-Curie Fellow at the University of Trento, and now as a principal investigator at the University of Padua, I lead research into mitochondrial Complex I assembly factors, combining methods such as cryo-EM, SAXS, NMR, and fluorescence spectroscopy. My integrative approach has yielded contributions to understanding mitochondrial bioenergetics, neurodegeneration, and enzyme regulation.

B. POSITIONS AND HONORS

Positions and Employment

2012 – 2013 Research associate. Prion Biology Laboratory, SISSA. Trieste, Italy.
 2013 – 2014 Visiting research associate. National Institute of Chemistry, Ljubljana, Slovenia.
 2014 – 2017 Research associate. Structural Biology Group (ESRF), Grenoble, France.
 2017 – 2019 Junior beamline scientist. Structural Biology Group (ESRF), Grenoble, France.
 2019 – 2020 Marie Skłodowska-Curie fellow. CIBIO Department, University of Trento, Italy.
 2020 – 2022 Research associate. Department of Chemical Sciences, University of Padua, Italy.
 2022 – 2025 Associate Professor tenure track position (RTD-b), Department of Chemical Sciences University of Padua, Italy.
 2025 – Associate Professor, Department of Chemical Sciences University of Padua, Italy.

Other experiences and professional memberships

2014 – 2018 Beamline local contact. X-ray diffraction and scattering (ESRF), Grenoble, France.
 2015 Editor for the book: Legname G, and Giachin G (2015) “The Prion Phenomena in Neurodegenerative Diseases - New Frontiers in Neuroscience”. Nova Science Publishers, Hauppauge NY, US. ISBN 978-1-63483-399-8.
 2017 – Member of Società di Chimica Italiana (SCI); American Chemical Society (ACS,); Associazione Italiana Cristallografia (AIC); SISSA-Alumni (Trieste, Italy).
 2018 Organizing conference. ESRF User Meeting 2018, Grenoble, France.
 2021 – Expert evaluator. Xjenza Malta, R&I National Funding.
 2022 – 2023 Guest editor. “Intrinsically Disordered Proteins Interactions with Their Molecular Environment at the Crossroad between Theory and Experiments” – Biology – MDPI.
 2023 – Expert evaluator. European Research Executive Agency, European Commission.

- 2023 – Expert evaluator. University of Florence, Italy, Competitive biennial projects for fixed-term researchers.
- 2024 Organizing conference. ECM34, Padova 26-30 August.

Honors

2009. Finalist at the business plan competition “Start Cup FVG” (Italy).
- 2014 Selected for the inclusion in the “ESRF HIGHLIGHTS 2014” for the paper Abskharon et al., JACS 2014.
- 2015 Selected for the inclusion in the “ESRF HIGHLIGHTS 2015” for the paper Giachin et al., Sci Report 2015.
- 2016 Cover art. Journal of Biological Chemistry, October 14, 2016; 291 (42).
- 2016 Awarded the “Performance Bonus” by the ESRF management in recognition of professional performance during the year.
- 2017 Marie Skłodowska-Curie Actions “Seal of Excellence”.
- 2019 Cover art. PLoS Pathog. 2019 Dec 9;15(12):e1008139.
- 2021 Featured in the “Spotlight on Early Career Investigators 2020” by the Biophysical Journal (Cell Press) as Early Career Investigator.
- 2021 Selected for the inclusion in the “ESRF HIGHLIGHTS 2021” for the paper Giachin et al., Angewandte chemie 2021.

C. SELECTED PEER-REVIEWED PUBLICATIONS

10 selected publications in the field of structural biology.

1. **Giachin G**, Mai PT, Tran TH, Salzano G, Benetti F, Migliorati V, Arcovito A, Della Longa S, Mancini G, D'Angelo P, Legname G. *The non-octarepeat copper binding site of the prion protein is a key regulator of prion conversion*. Sci Rep. **2015** Oct 20;5:15253.
2. **Giachin G**, Nepravishta R, Mandaliti W, Melino S, Margon A, Scaini D, Mazzei P, Piccolo A, Legname G, Paci M, Leita L. *The mechanisms of humic substances self-assembly with biological molecules: The case study of the prion protein*. PLoS One. **2017** Nov 21;12(11):e0188308.
3. Salzano G, Brennich M, Mancini G, Tran TH, Legname G, D'Angelo P, **Giachin G**. *Deciphering Copper Coordination in the Mammalian Prion Protein Amyloidogenic Domain*. Biophys J. **2020** Feb 4;118(3):676-687.
4. **Giachin G**, Jessop M, Bouverot R, Acajjaoui S, [...] Gutsche I, Soler-Lopez M. *Assembly of The Mitochondrial Complex I Assembly Complex Suggests a Regulatory Role for Deffluvination*. Angew Chem Int Ed Engl. **2021** Feb 23;60(9):4689-4697.
5. Fabbian S, **Giachin G**, Bellanda M, Borgo C, Ruzzene M, Spuri G, Campofelice A, Veneziano L, Bonchio M, Carraro M, Battistutta R. *Mechanism of CK2 Inhibition by a Ruthenium-Based Polyoxometalate*. Front Mol Biosci. **2022** Jun 2;9:906390.
6. Semrau MS, **Giachin G**, Covaceuszach S, Cassetta A, Demitri N, Storici P, Lolli G. *Molecular architecture of the glycogen- committed PP1/PTG holoenzyme*. Nat Commun. **2022** Oct 19;13(1):6199.
7. Mollica L, **Giachin G**. *Recognition Mechanisms between a Nanobody and Disordered Epitopes of the Human Prion Protein: An Integrative Molecular Dynamics Study*. J Chem Inf Model. **2023** Jan 23;63(2):531-545
8. Mantonico MV, De Leo F, Quilici G, [...] **Giachin G**, Ghitti M, Bianchi ME, Musco G. *The acidic intrinsically disordered region of the inflammatory mediator HMGB1 mediates fuzzy interactions with CXCL12*. Nat Commun. **2024** Feb 8;15(1):1201. doi: 10.1038/s41467-024-45505-7.
9. Malatesta M, Fornasier E, Di Salvo ML, Tramonti A, Zangelmi E, Peracchi A, Secchi A, Polverini E, **Giachin G**, Battistutta R, Contestabile R, Percudani R. *One substrate many*

enzymes virtual screening uncovers missing genes of carnitine biosynthesis in human and mouse. Nat Commun. **2024** Apr 13;15(1):3199

10. Fornasier E, Fabbian S, Shehi H, Enderle J, Gatto B, Volpin D, Biondi B, Bellanda M, **Giachin G**, Sosic A, Battistutta R. *Allostery in homodimeric SARS-CoV-2 main protease*. Commun Biol. **2024** Nov 4;7(1):1435.

Full-listed publications are available here:

<https://pubmed.ncbi.nlm.nih.gov/?term=giachin%20g&sort=date>

Bibliometric indexes: <https://www.scopus.com/authid/detail.uri?authorId=36607977700>

D. CONTRIBUTIONS TO SCIENCE

Throughout my career, I have employed interdisciplinary approaches to address fundamental questions in structural biology and molecular mechanisms of disease, with a particular focus on neurodegeneration, mitochondrial dysfunction, and the development of advanced biophysical methodologies.

1. **Structural Insights into mitochondrial Complex I and assembly factors.** My research has advanced the understanding of mitochondrial Complex I (CI), with a particular focus on its assembly factors, such as ACAD9. Using integrative approaches including cryo-EM, SAXS and mass spectrometry, I elucidated the molecular mechanisms underlying CI assembly and regulation. A key achievement was the discovery of a de flavination regulatory mechanism in ACAD9, published in *Angewandte Chemie* (2021). These findings provide critical insights into mitochondrial bioenergetics. **Selected Publications:**
 - i. Giachin et al, *Angew Chem Int Ed Engl*. 2021 Feb 23;60(9):4689-4697.
 - ii. Giachin et al, *Front Mol Biosci*. 2016 Aug 22;3:43.
2. **Contributions to prion biology and neurodegenerative disorders.** During my Ph.D. and postdoctoral studies, I focused on the structural mechanisms underlying prion diseases. I identified a critical structural “hot spot” in the human prion protein using NMR spectroscopy, which was instrumental in understanding prion conversion. This work led to the development of an antibody fragment capable of halting prion formation. I also investigated prion protein – metal interactions using biophysical methods, contributing to studies that elucidated their molecular interfaces with other cellular components. **Selected Publications:**
 - i. Abskharon R, Giachin G, et al. *JACS*. 2014;136(45):15985-15991.
 - ii. Giachin G, et al. *Sci Rep*. 2015;5:15253.
3. **Development of biophysical and synchrotron-based techniques.** At the European Synchrotron Radiation Facility, I specialized in SAXS, XRD, and X-ray absorption spectroscopy (XAS) to study macromolecular assemblies. My work revealed novel metal ion coordination mechanisms in prion proteins and developed innovative approaches for studying protein dynamics. These methods have broad applicability in structural biology. **Selected Publications:**
 - i. Salzano G, et al. *Biophys J*. 2020;118(3):676-687.
 - ii. Mantonico MV, et al. *Nat Commun*. 2024 Feb 8;15(1):1201.
 - iii. Mollica L, Giachin G, et al. *J Chem Inf Model*. 2023;63(2):531-545.
 - iv. Mota C, et al. *FEBS J*. 2024 Aug;291(15):3384-3402.
4. **Translational research and protein-targeted therapeutics.** My recent work includes elucidating mechanisms of enzyme inhibition and allosteric regulation, with applications in drug discovery. Highlights include studies on SARS-CoV-2 main protease and CK2 kinase inhibition. **Selected Publications:**
 - i. Fornasier E, et al. *Commun Biol*. 2024;7(1):1435.
 - ii. Fabbian S, et al. *Front Mol Biosci*. 2022;9:906390.

E. RESEARCH FUNDING

- 2009 Ministero degli Affari Esteri Italiano (MAE), Wallonie-Bruxelles International (W.B.I.), Fondo della Ricerca Scientifica (F.R.S. - F.N.R.S.), IX scientific collaboration program Italy - Belgium 2009-2010. Project title: Nanobody assisted crystallography on the prion protein. Grant covered the travel and accommodation expenses. [PI of the project]
- 2012 – 2014 European Union (Social European Funds) and Friuli Venezia Giulia autonomous Region, SHARM (Supporting Human Assets in Research and Mobility), funded through the Operational Program of the European Social Fund 2007/2013; Grant agreement n° FP1123744003. Project title: “Structural and functional studies on the prion protein in complex with the neuronal cell adhesion molecule.” Amount: €59,416. Grant covered salary. [PI of the project]
- 2016 European Union, INSTRUCT, project n° 1710. Project title: “Structural and molecular basis for ECSIT protein recognition and its implication in Alzheimer’s pathogenesis.” Grant covered the access costs to the facility: ESPRIT, Kbiosystems K3 robot for library screening (Institut de Biologie Structurale, Grenoble, France). [PI of the project]
- 2019 European Union, EU-OPENSREEN Small Molecule Screening Call, project n° 9260. Project title: “Dissecting the functional interaction between the cellular Prion Protein and G-protein coupled receptors.” Grant covered the access costs to the facilities: (a) Innopharma screening platform (BioFarma research group, University of Santiago de Compostela, Spain) and (b) MEDINA’s compound management platform (Parque Tecnológico Ciencias de la Salud, Granada, Spain). [Participant]
- 2019 – 2020 European Commission, Marie Skłodowska-Curie Actions – Individual Fellowship (MSCA-IF-2018), EU project n° 844194. Project title: “The Role of Complex I Assembly Factors during Prion Diseases: Insights into Mitochondrial Neurobiology.” Amount: €171,473.28. [PI of the project]
- 2020 – 2023 University of Padua (Italy), Supporting Talent in ReSearch (STARS 2019). Project title: “Role of Mitochondrial Complex I Assembly (MCIA) Complex during Neurodegeneration: an Integrative Structural Biology Project.” Amount: €180,000. [PI of the project]
- 2022 Central European Research Infrastructure Consortium (CERIC), project n° 20212004. Project title: “Cryo-EM structural determination of mitochondrial bovine Complex I bound to ACAD9: understanding the interplay between fatty acid beta oxidation and OXPHOS.” Grant covered the access costs to the facility: Cryo-Electron Microscopy at SOLARIS synchrotron, Krakow, Poland. [PI of the project]
- 2022 UniPD P-Disc SID 2022 research grant, “Characterization of ¹³C palmitoyl-CoA metabolism in mammalian mitochondria using real-time NMR metabolomics.” [Participant; PI of the project Prof. Elisabetta Schievano] Amount: €43,000.
- 2023 Central European Research Infrastructure Consortium (CERIC), project n° 20232154. Project title: “Cryo-EM structural determination of the mitochondrial bovine Complex I bound to a fatty acid beta oxidation enzyme.” Grant covers the access costs to the cryo-EM at SOLARIS synchrotron, Krakow, Poland. [PI of the project]
- 2024 UniPD P-Disc SID 2024 research grant, “Novel Inhibitors Targeting Kinase NEK6 - Combining Synthetic Approaches and Protein Co-crystallization Experiments.” [Participant; PI of the project Prof. Michele Maggini] Amount: €25,000.

F. TEACHING AND MENTORSHIP EXPERIENCE

Teaching Assignments

- 2023–2024 Course: “Chimica 2 (chimica organica e bio-organica)” (64 hours lectures + 16 hours exercises, 9 credits) for “Laurea Triennale in Biotecnologie,” University of Padua. Student evaluation: Overall satisfaction (mean 7.73, median 8); Didactic action (mean 7.72, median 8).
- 2022–2023 Course: “Chimica 2 (chimica organica e bio-organica)” (same as above). Student evaluation: Overall satisfaction (mean 7.63, median 8).
- 2021–2022 - Course: “Chimica 2 (chimica organica e bio-organica)” (same as above). Student evaluation: Overall satisfaction (mean 7.82); online organizational aspects (mean 8.45).
- Laboratory sessions for “Analysis of Biomolecules” (33 hours across two departments), University of Padua.
- 2018–2019 Course: “Laboratory of Biochemistry,” Master’s in Biotechnology, University of Milan-Bicocca.

Supervision of Students and Researchers

Postdoctoral researcher:

- Dr. Lorenza Iolanda Tsansizi (2021–2022) – Project on CI assembly factors, funded by STARS@UniPD grant. At University of Padua.
- Luca Ferrari (2022) - Project on CI assembly factors, funded by STARS@UniPD grant. At University of Padua.

Ph.D. students:

- Cristian Buratto (2024–present): PhD project on phospholipid synthesis and protein-lipid interactions with EPR and cryo-EM approaches. At University of Padua.

Master’s students:

- Beatrice Masciovecchio (2023–2024): Structural characterization of mitochondrial acyl-CoA dehydrogenases. At University of Padua.
- Gianmarco Paloscia (2023-2024): structural studies on HPDL protein. At University of Padua.
- Serena Pantalone (2016–2017): SAXS and ITC analysis on MCIA proteins. At ESRF (France)

Bachelor’s students:

- Beatrice Lion (2023–2024): Structural analysis of ACAD9 mutations affecting mitochondrial functionality. At University of Padua.
- Lisa Dao (2023–2024): Bioinformatic and structural studies on HPDL mutations linked to NEDSWMA disease. At University of Padua.

G. OUTREACH AND PUBLIC ENGAGEMENT

I have actively engaged in outreach and public science communication to promote awareness and understanding of research among diverse audiences. As part of the MSCA Marathon@Unipd training courses in 2023 and 2024, I delivered lectures titled “Behind the scenes of the evaluation process,” aimed at equipping postdoctoral researchers with insights into the Horizon Europe Marie Skłodowska-Curie Postdoctoral Fellowships evaluation process. In 2022, I contributed to MASTERCLASS@UNIPD with a lecture, “I criteri di valutazione, la prospettiva del valutatore,” sharing expertise on European research funding criteria. My engagement extends to public-facing platforms, including an interview with Il Bo Live, the official online newspaper of the University of Padua, discussing advancements in spider silk composition. Additionally, I participated in the Researchers’ Night initiatives (Venetonight 2021 and Science4All 2022), leading interactive sessions on the role of X-ray microscopy in protein structure determination and its biomedical applications. Earlier in my career, I contributed to the TV show Polifemo on MTV, discussing Italy’s brain drain in the episode “Italia senza Cervelli.”