

Marco BISAGLIA

POSITION TITLE: Associate Professor of Physiology, Department of Biology, University of Padova

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Department of Chemistry, University of Versailles (France)	Erasmus internship	9-11/1997	Chemistry
Department of Chemistry, University of Padua (Italy)	Master's degree	7/1999	Chemistry
Ecole Polytechnique (France)	Ph.D.	11/2002	Structural Biology
National Institute on Aging (NIA/NIH) (USA)	Visiting scientist	10-12/2007	Cell Biology
Department of Biomedical Science, University of Sheffield (UK)	Visiting scientist	3-8/2013	Drosophila genetics

A. Personal Statement

I am a molecular physiologist affiliated with the Physiology, Genetics, and Behavior Unit at the Department of Biology, University of Padova, with expertise in Biochemistry, Cell Biology, and *Drosophila* genetics. For almost 20 years, I have been interested in the analysis of the pathogenesis of neurodegenerative disorders with particular emphasis on Parkinson's disease (PD) and amyotrophic lateral sclerosis (ALS). After a Ph.D. in Structural biology attained at the École Polytechnique of Paris-Palaiseau, France, I moved back to Italy, where my acquired skills were functional to investigate the structure/function relationship of α -synuclein, which was emerging as a key protein involved in both familial and sporadic forms of Parkinson's disease. In this frame, I contributed to the characterization of the membrane-bound structure of the protein, to the definition of a high-affinity mononuclear site in the copper(II)- α -synuclein complex, and to the assessment of the toxicity related to the dopamine-derived oxidation products towards α -synuclein.

To validate the results in a more physiologically relevant environment, thanks to an EMBO fellowship, I spent a few months in Dr. Mark Cookson's lab at the National Institute on Aging (NIA/NIH) of Bethesda, USA, where I learned the principal techniques of cellular biology, that were applied to further explore the potential involvement of the oxidation products of dopamine in PD pathogenesis. In 2013, I spent 6 months as a visiting scientist in the laboratory of Dr. Alex Whitworth (University of Sheffield, UK), one of the main experts on *Drosophila melanogaster* models of PD, who helped decipher the physiological functions of PINK1/parkin in the mitochondrial quality control process. That period represented a great chance to become aware of the high potential and usefulness of *Drosophila* models to explore, in synergy with cellular models, the complexity of neurodegenerative processes.

My current research activity is mainly focused on the interplay between protein aggregation, metal dyshomeostasis, autophagic impairment, mitochondrial dysfunction, and redox unbalance. A better understanding of the fine-tuning of physiological redox signaling and the cellular redox alterations associated with neurodegenerative disorders is essential for the definition of valuable diagnostic and therapeutic strategies. In this frame, my lab recently contributed to a better understanding of the physiological role of the "antioxidant" protein DJ-1, demonstrating, in *Drosophila melanogaster*, that the protein participates in the control of autophagy and mitochondrial homeostasis by regulating the intracellular levels of reactive oxygen species.

Since 2021, I have been a member of the Center for Study of Neurodegeneration (CESNE), coordinated by Prof. Angelo Antonini. The CESNE aims to bring together experts in neurology, anatomy, biology, neuropsychology, and gastroenterology to stimulate discussions and collaborations by sharing complementary expertise available at the University of Padua.

B. Positions, Scientific Appointments, and Honors

POSITIONS

2018 – present: Associate Professor of Physiology, Dept. of Biology, University of Padua, Italy
2008 – 2018: Assistant Professor of Physiology, Dept. of Biology, University of Padua, Italy
2006 – 2008: Senior Postdoctoral Fellow, Dept. of Biology, University of Padua, Italy
2003 – 2006: Junior Postdoctoral Fellow, Dept. of Chemistry, University of Padua, Italy

COMMISSIONS OF TRUST

2023: Evaluation Committee for the selection of PhD students to be enrolled in the Bioscience PhD Programme
2021: Evaluation Committee for the selection of China Scholarship Council PhD candidates to be enrolled in the Bioscience PhD Programme
2020: External referee for the Sir Henry Wellcome Postdoctoral Research Programme for the Wellcome Foundation – UK
2020: External referee for grant evaluation for the Knut and Alice Wallenberg Foundation – Sweden
2017 and 2018: External referee for grant evaluation for the Multiple Sclerosis Research Australia
2016: Evaluation Committee for the selection of PhD students to be enrolled in the Bioscience PhD Programme
2010 and 2015: External referee for grant evaluation for the Parkinson's UK Foundation

EDITORIAL ACTIVITIES

2025: Guest Editor of a thematic issue entitled “Redox Signaling in Brain Aging and Neurodegeneration” for Antioxidants
2023: Guest Editor of a thematic issue entitled “Mitochondrial Dysfunction and Oxidative Stress in the Pathogenesis of Neurodegenerative Diseases” for Antioxidants
2015: Guest Editor of a thematic issue entitled “Critical Analyses of Mechanism-Based Therapies Against Parkinson's Disease: Concepts and Perspectives” for Current Neuropharmacology
2011- 2018: Associate Editor to BMC Structural Biology

HONORS AND AWARDS

2022: R&D Advisory Board of the Maharishi Markandeshwar University – Mullana – India
2021: Invited Speaker – XXXIX Annual Meeting of the Indian Academy of Neurosciences – online
2020: Workshop co-organizer (with Prof. L Bubacco and E Greggio) – Molecular Mechanisms of Neurodegeneration – Padua – Italy
2019: Invited Speaker – 6th Neurocon International Conference – Mullana – India
2019: Session co-chair (with Prof. R. Cappai and Prof. G. Reiser) – 6th Neurocon International Conference – Mullana – India
2017: Invited Speaker – 5th Neurocon International Conference – Haldia – India
2017: Session co-chair (with Dr. LW Lee) – 5th Neurocon International Conference – Haldia – India
2007: European Molecular Biology Organization (EMBO) – Three-month short-term Fellowship
2006: Italian Group on Magnetic Resonance Discussions (GIDRM) Congress, 1st place in poster competition
2003 and 2004: Italian Group on Magnetic Resonance Discussions (GIDRM) Congress, 3rd place in poster competition
2002: Medical Research Foundation (France), One-year Fellowship

C. Contributions to Science

One of the first contributions I worked on was the study of the **structure/function relationship of alpha-synuclein**, whose aggregation into Lewy bodies represents a pathological hallmark of Parkinson's disease (PD). We therefore set out to investigate the influence exerted by the protein on the pathogenesis of PD, with particular interest in the role played by membranes and metals in the process that leads to the formation of fibrils and the degeneration of dopaminergic neurons. I was among the first authors worldwide who contributed to obtaining information on the topology of alpha-synuclein in membrane-mimetic environments (Bisaglia et al. 2005 Biochemistry; Bortolus et al. 2008 JACS), also hypothesizing a possible physiological role of the N-terminal region in selecting the lipid composition of the membranes with which the protein interacts (Bisaglia et al. 2006 Biopolymers). Then, the structural characterization of the central region of the protein considered the seeding site for fibril formation, allowed a better understanding of the aggregation process at the molecular level (Bisaglia et al. 2006 Prot Science). I also participated in the structural

characterization of the high-affinity copper-binding site of alpha-synuclein in solution (Bortolus et al. 2010, JACS) and in a membrane-like environment (Bacchella et al. 2023 Biomolecules) and in untangling the role of iron on alpha-synuclein-mediated toxicity, *in vivo*, in a *Drosophila* model of the disease (Agostini et al. 2023 Antioxidants).

Another topic I have been interested in since my postdoctoral studies concerns the **pathological role of dopamine and its oxidative metabolites** in inducing the preferential death of this neuronal population, which represents the second pathological hallmark of PD. In this frame, I contributed to the structural and chemical characterization of the first intermediates of the dopamine oxidation process, which ends in the formation of neuromelanin (Bisaglia et al. 2007 JBC) and I participated in the definition of the more reactive dopamine oxidative metabolite towards different protein directly and indirectly involved in PD, including alpha-synuclein (Bisaglia et al. 2007 JBC; Bisaglia et al. 2010 BBRC; Masato et al. 2023 NPJ Parkinsons Dis), DJ-1 (Giroto et al. 2012 JBC), and SOD2 (Belluzzi et al. 2012 PloS One). The renown reached in this field is certified by numerous reviews that I have written over the years on this topic.

In parallel to these *in vitro* studies, a further field of interest that started at the very beginning of my academic career and is still active in my lab is represented by the role of **mitochondrial dysfunction in neurodegeneration**. I started working on this topic by characterizing the effects of dopamine-derived quinones on mitochondrial functionality, demonstrating that the oxidative metabolites of dopamine induce the opening of the transition pore in isolated mitochondria, most likely by promoting the oxidation of the NADH pool (Bisaglia et al. 2010 BBA). These data were further confirmed in my lab in a cellular model where we also emphasized alterations in mitochondria morphology and functionality (Biosa et al. 2018 ACS Chem Neurosci).

My latest contributions, which coincide with the establishment in my lab of the facilities required to exploit *Drosophila* as a model for the study of neurodegenerative disorders, are related to proteins and molecules involved in the **antioxidant response**. The interest relies on the fact that they might represent potential therapeutic strategies. In this frame, my lab demonstrated the protective roles of SOD1, SOD2, and the SOD-mimetic compound M40403 in both sporadic and genetic *Drosophila* PD, as well as in cells (Filograna et al. 2016 JBC; Biosa et al. 2018 Hum Mol Res; Biosa et al. 2019 Neurotox Res). The protein DJ-1, involved in both PD and amyotrophic lateral sclerosis, is another topic thoroughly investigated in the lab. While the protein is clearly involved in the antioxidant response, the exact mechanism through which it exerts its protection is largely unknown. In this regard, I contributed to proposing a potential cooperative action of the antioxidant protein SOD1 and the protein DJ-1 in the same oxidative stress response pathway, based on a copper-mediated interaction between the two proteins (Giroto et al. 2014 JBC), although in my lab we then demonstrated that, in *Drosophila*, the proteins act independently in the protection against an anoxic insult (De Lazzari et al. 2022 Antioxidants). More recently, my lab contributed to a better understanding of the physiological role of DJ-1, demonstrating, in *Drosophila melanogaster*, that the protein participates in the control of autophagy and mitochondrial homeostasis by regulating the intracellular levels of reactive oxygen species (De Lazzari et al. 2023 Neurobiol Dis).

Research output (2025.06.10)

N° of publications: 62 peer-reviewed papers, 1 book chapter

N° of citations: 3023/4264 (Scopus/Google Scholar)

h-Index: 35/39 (Scopus/Google Scholar)

For a full list of publications, please refer to the following links:

https://scholar.google.com/citations?hl=en&user=Hljox6EAAAAJ&view_op=list_works&sortby=pubdate

<https://pubmed.ncbi.nlm.nih.gov/?term=bisaglia+marco&sort=date&page=1>