Milan, 24 March 2021

Scientific and teaching curriculum vitae

After graduating in Industrial Chemistry (1999), at the University of Milan, Dr. Giuseppe Zampella (GZ) has attended the Department of Biotechnologies and Life Sciences as a contributor to research at the Laboratory of Molecular Modeling in the development and use of calculation codes for the analysis of structure-function of proteins and the reactivity of bioinorganic, transition-metal based systems.

-2000-2001: holder of two Scholarships of CMR (Milan Research Consortium) entitled:
a) "Computational research on new molecules molecules with potential pharmaceutical interest."
b) "Bioinformatics of compounds with pharmacological activity"

-2002: Master Degree in Bioinformatics at the University of Milano-Bicocca,

-29/12/2002: permanent position as Researcher (SC: 03/B1; SSD CHIM/03) at the Department of Biotechnologies and Life Sciences of the University of Milano-Bicocca.

-23/12/2013: Habilitation as Associate Professor (SC: 03/B1)

-October 2018: Associate Professor (SC: 03/B1; SSD CHIM/03) at the Department of Biotechnologies and Life Sciences of the University of Milano-Bicocca.

**Teaching activity**

since: 2003:
i) Laboratory of General and Inorganic Chemistry for Biotechnologies (LT)
ii) Laboratory of General Chemistry for Biological Sciences (LT) (this one up to 2013)
iii) Structure-Function Correlations (mod. B/C) for Bioinformatics. (LM, closed in 2011)

2008-2010:
i) Course of Design of Molecules as Substrates (Mod C) for Bioinformatics.
ii) Essentials of General Chemistry for Bioinformatics.

2010-2011: Course of Design and Theory of Molecular Systems (Mod C) for Bioinformatics.

2007 and since 2013: General and Inorganic Chemistry for Biotechnologies degree course (LT).

**Scientific Activity**

Field of research/ Key words:

Quantum mechanics based modelling of the activation of small molecules by organometallic complexes-Molecular Inorganic Chemistry-Bioinorganic Chemistry-Organometallic and Coordination Chemistry-bimetallic iron and molybdenum complexes as models of hydrogenase and formate dehydrogenase active site-DFT of vanadium compounds.

GZ research is mainly focused on the investigation of the stereoelectronic structure of inorganic and bioinorganic relatively small systems, performed by quantum mechanics techniques and ab initio approaches (such as DFT). He is coauthor of 70 publications, 67 of which on peer-reviewed international journals and books (vide infra).
Such systems include, for example, simple metal clusters of which has been determined accurately the molecular structure and the properties of both the ground state and the excited states (publ on J. Chem. Phys., 2002). Other systems treated at rigorous level are the equilibrium between species HNCNH ¿ H2NCN and their products of hydrolysis (publ on J. Phys. Chem., 2003) and Cu(II) complexes with small peptides and their models of enzyme catalysis (publ on Inorg. Chem. Commun 2003, Theoretical Chemistry Accounts 2012, J Phys Chem B 2012). Very recent is a DFT contribution (2015, Journal of Biological Inorganic Chemistry) on the generation of OH· radical species from H2O2 by Cu(I) amyloid beta peptide model complexes.

Concerning theoretical bioinorganic chemistry of vanadium compounds, it can be mentioned:

-the study of models of the metal cofactor of Vanadium Haloperoxidase (VHPO) by means of DFT; this work aims at elucidating some features of the vanadium (V) complex, so as it appears in the resting form of the enzyme (publ on Inorg. Chem., 2004). Studies have been carried out on reactivity of the catalytically active form of the cofactor and theoretical justification of the necessity of protonated it has been clarified. (presented to EUROBIC7, Garmisch, 2004 and pubbl. on JACS, 2005). In addition, the whole catalytic cycle turnovered by the enzyme cofactor VHPO has been DFT investigated (publ on Inorg. Chem., 2006). Also, the reactivity was investigated of complexes which are synthetic functional models of the enzyme, towards various oxidation reactions (publ on Eur. J. Inorg. Chem, 2007).

-Another vanadium based system investigated is amavadine, a small complex in which the central vanadium ion can switch through the IV and V states and that is able to catalyze a large number of different oxidative processes. Results on the thiol-to-disulfide oxidation and on the bromoperoxidation reaction are published on Dalton Transactions 2011 and Chemical Communications 2014, respectively.

Concerning hydrogenase based systems, some noteworthy contributions are:

-Study of models of the active site of Ni-Fe hydrogenase using different DFT functionals, aimed at contributing to the knowledge of the electronic structure of the Ni ion cofactor, and the definition of some structural parameters which are not clearly observable from crystallographic structure. (publ on J. Biol. Inorg. Chem., 2004).
-A work (published in JACS, 2005) aimed to study the reactivity of some hydrogenase functional models (based on Ni and Pd), which have been shown to be non-efficient catalysts (vs enzyme) of dihydrogen splitting.
-Investigation on the mechanism of cyanation of models which are functional analogues of FeFe hydrogenase site, (publ on Chem. Eur. J., 2005) and characterization of the mechanism of oxidation of H+ reduction (and H2 oxidation) on a theoretical model of the enzyme active site (published on Inorg. Chem., 2006).
-Electrocatalysis of the hydrogen production by a synthetic model of the cofactor has also been DFT investigated (publ on Inorg. Chem. 2007). Similarly, a contribution was provided to the study (publ on Chem. Eur. J., 2007) of protonation regiochemistry of a different synthetic model of FeFe-hydrogenase. More recently, the regiochemistry of protonation of synthetic analogues of the FeFe-hydrogenase cofactor has been investigated (publ on JACS 2009) and the mechanism with which the protonated kinetic isomer turns into the thermodynamic isomer has been elucidated (publ on Chem Commun 2011).

-As for the study of bioinspired synthetic mimics of the FeFe-hydrogenase, GZ and prof L. De Gioia (Milano-Bicocca University) have been collaborating since 2005 with the group of prof TB Rauchfuss (Department of Chemistry, University of Illinois at Urbana-Champaign) in order to provide rationalization theoretical justification of the experimental evidences, and also to help design novel syntetic catalysts for H2 production/oxidation.
Such collaboration has led to several joint publications (JACS 2005, Inorg. Chem. 2007, Chem. Commun. 2007, Organometallics 2008, JACS 2008, Inorg. Chem. 2008 and Angew. Chem. Int. Ed .2008, Chem Commun 2011, JACS 2012, Organometallics 2013). Also the reactivity of photoactivated hydrides of diiron dithiolates, able to catalyze H2 production has been investigated (JACS 2012, Inorg Chem 2013). Remarkably, in 2013 the structure has been solved by X-ray diffraction and its stereoelectronic properties characterized by DFT, of a Fe(I)Fe(I) dithiolate featuring a “rotated” conformation, exactly like that observed for a crystal structure of the bio-system. Such outcome had been sought for long by inorganic chemists operating in the field of synthetic models of FeFe-hydrogenases (see also below).

Also, results of a collaboration with Professor X. Liu (Department of Chemistry University of Nanchang, China) on similar topics were published in J Organomet Chem (2008 and 2010), Inorg Chem Commun 2010 and Dalton Transactions 2012

In parallel, a collaboration with the Chemistry Dept. of the Brest University (France) has led to unravel important issues related to the electrochemical behavior of some biomimetic diiron compounds, whose results are published on Inorg Chem 2010 and 2011, Organometallics 2012 and Chem Eur J. 2012 and 2013. The last publication shows for the first time a synthetic diiron dithiolate having the same structural feature observed in the crystallographic structure of the hydrogenase (in parallel with results obtained in collaboration with prof TB Rauchfuss). Electrochemical behavior of an oxidized state (FeIIFeII) of another synthetic analogue has been investigated to analyze similarity/differences with the HOX_CO state of the enzyme.

Concerning other metal based bio-systems, studied at DFT level:

Recently GZ, in collaboration with prof VL Pecoraro (JT Groove Collegiate Professor of Chemistry, Michigan University, Associate Editor of Inorganic Chemistry, ACS) has investigated the As(III) and Pb(II) binding mode to de novo designed peptide systems, with the aim of shedding new light on the toxicity of heavy metals, which is associated with the high affinity of the metals for thiolate rich proteins, well-known to constitute a problem worldwide. Results are published on Chem Eur J 2012.

Another system investigated is the molybdenum cofactor of the formate dehydrogenase, able to catalyze the carbon dioxide/formate interconversion and thus relevant for the anthropogenic global warming issue. Results, published on Inorg Chem 2012, allowed to propose a new mechanistic route of the rate determining step of catalysis, entailing a Mo hydride formation.

Some of abovementioned researches have led GZ to contribute to the publication on Coordination Chemistry Reviews (2005), Current Topics in Chemistry (2007), Theoretical Chemistry Accounts, (2007) and Vanadium: The Versatile Metal, Book of the ACS SYMPOSIUM SERIES, concerning the state of research on theoretical models of hydrogenases and other bio-systems.

A second aspect of GZ's research concerns the study of large bio-systems by Molecular Docking and Molecular Dynamics techniques. In this context, he has worked on the characterization of structural models of biological systems, such as the active sites of enzymes (and related chemical reactions), the receptor

binding pockets for biomolecules and ligands which are potentially relevant under a pharmacological perspective
Since June 2000 he has collaborated with the Chemistry Department of Dompè SpA in a research project aimed to identify new inhibitors of biological activity of IL-8 chemokine (whose inhibition is crucial in preventing damage from post-ischemic reperfusion, typical of organ post-transplant), highlighting some fundamental aspects of the mechanism of action at the molecular level of these potential drugs on CXCR1 and CXCR2 receptor, active in the signal transduction for the recruitment of polymorphonucleates and neutrophyls (chemotaxis) on transplanted tissue. One of the molecules under study (patent deposited as Repertaxin) is currently in advanced stages of clinical development.
Results are published on PNAS, 2004, and J Med Chem, 2005.
Moreover, it can be mentioned an investigation of mutants with increased ability to turn-over of the L-lactate dehydrogenase enzyme, in collaboration with the research group Prof. Danilo Porro, University of Milano-Bicocca (publ on Microbial Cell Factories, 2006). Docking procedures have also been used to investigate the binding mode of syalic acide derivatives to the humane sialidase Neu2 (publ on Proteins-Structure Function and Bioinformatics 2012).

Other activities:
-Referee for various scientific journals of the following Publishers:
American Chemical Society, Elsevier , Royal Society of Chemistry, Nature Communications and Wiley Pub. Ed.
-Member of the Ph.D School in Chemistry, Environmental and Geological Sciences, University of Milano-Bicocca.
-Co-founder of DELOS srl, a University of Milano-Bicocca spin-off operating in the field of molecular modelling.
-PRIN admitted to financing:
i) 2003. Study on the interaction of Prion Protein and ß-Amiloid to molecules with anti-fibrillogenic activity. Role: Participant Prot: 2003031424_006. Scientific Resp. prof. D. Pitea.
ii) 2006. Title: Molecular Biology of Sialidases: Investigation on Human Sialidase NEU2 by Site-Specific Mutagenesis and expression of membrane Sialidases NEU3 and NEU4. Role: Participant Prot: 2006058157_003. Scientific Resp.: dr Paola Fusi.

**Bibliographic indexes**

Scopus:

**92** Documents by author

**3212** Citations by ***2024*** documents

**32** *h*-index