



Curriculum vitae Prof. Mauro Botta

Verzuolo (CN, Italy), 07/07/1958

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Position: Full Professor of Inorganic Chemistry (SSD: CHIM03)

- Graduated in Chemistry at the University of Turin in 1985 (110 *cum laude*) with a thesis on "Activation of the M-M bond in the substitution reactions of CO in metal carbonyl clusters";
- Postdoc in the lab of Prof. Edward Rosenberg (CSUN, Los Angeles, 1987) working on the reactions of Ru carbonyl clusters with aliphatic amines;
- Postdoc in the lab of Prof. Silvio Aime (Faculty of Pharmacy, Turin) working on "*Paramagnetic metal complexes as contrast agents for MRI*" (1988-89);
- Assistant Professor at the Chemistry Department, University of Turin, 1990;
- Associate Professor of Inorganic Chemistry at the Faculty of Sciences of the University of Eastern Piedmont, Alessandria, 1998;
- Full Professor of General and Inorganic Chemistry at the University of Eastern Piedmont, Alessandria, 2004;
- The main research activity focuses on the development of metal complexes and nanosystems as diagnostic probes for MR imaging and on the investigation of paramagnetic compounds using fast field-cycling relaxometry. Currently (June 2023) is the author of 296 publications (Scopus: *h-index*: 65; *Citations* = 13915), four book chapters and four patents.

ACADEMIC RESPONSIBILITIES

2019-	Member of the Administration Council, University of Eastern Piedmont
2019-	Member of the Department Board
2018-2021	Member of the National Assessment Commission (habilitation in Inorganic Chemistry) of the Ministry of University and Research
2015-2018	Member of the Administration Council, University of Eastern Piedmont
2012-2015	Member of the Programming and Monitoring Committee for the Convention between the University of Eastern Piedmont and the " <i>Compagnia di San Paolo</i> "
2004-2006	Member of the Academic Spin-Off Committee
2003-2006	Board chairman of the degree courses in chemistry



SCIENTIFIC POSITIONS

2022-	Member of the International Advisory Board of " <i>Journal of Inorganic Biochemistry</i> "
2019-	Scientific director of the University research infrastructure "PRISMA" (NMR facility)
2016-2020	Italian representative in the Management Committee of the EU COST Action CA15209: " <i>European Network on NMR Relaxometry</i> " – Coordinator of the Working Group " <i>Biomedical applications</i> "
2012	Guest Editor of the thematic issue "Metal-Based MRI Probes" of the European Journal of Inorganic Chemistry (3 Communications; 11 Microreviews; 12 Full papers)
2009-2011	Coordinator of the Working Group " <i>MRI Contrast Agents</i> " of the EU COST Action D38: " <i>Metal-Based Systems for Molecular Imaging Applications</i> "
2007-2015	Member of the International Advisory Board of " <i>European Journal of Inorganic Chemistry</i> "
2003-2005	Project Coordinator of the NATO Collaborative Research Grants Programme: " <i>New Lanthanide Complexes as Diagnostic Probes of Enhanced Efficacy</i> ", with Charles University, Prague (Czech Republic), Tbilisi University (Georgia), Emory University, Atlanta, GA (USA)
2001-2006	Tutor of the Cluster C04 (" <i>Biomedicine</i> ") Projects N° 17-19-21 (Ministry of University and Research)
2000-2020	Co-organizer of the annual " <i>National School of Nuclear Magnetic Resonance</i> "
2000-2003	Member, Management Committee of the Interdivisional Group on Magnetic Resonances of the Italian Chemical Society (GIRM)
1998-2000	Project Coordinator of the NATO Collaborative Research Grants Programme: " <i>Solution and Solid State Characterization of Water Soluble Lanthanide(III) Complexes</i> ", in collaboration with Prof. K. Hardcastle, California State University Northridge, Los Angeles, CA (USA)
1995-2001	Member, Management Committee of the Italian Discussion Group on NMR (GIDRM)

MAIN FIELDS OF INTEREST

1. Metal-based MRI diagnostic probes
2. Coordination Chemistry of *f* elements and transition metal complexes
3. Fast field-cycling Relaxometry
4. Functionalized nanosystems for molecular imaging

AFFILIATIONS

1. Italian Chemical Society
2. European Rare Earth and Actinide Society
3. European Society of Molecular Imaging
4. Italian Discussion Group on NMR (GIDRM)



AWARDS

1. EurJIC & Italian Chemical Society Lectureship at CNR, Rome, 2019
2. Gold Medal of the NMR Italian Discussion Group (GIDRM), 2009
3. Gold Medal "Raffaello Nasini" of the Division of Inorganic Chemistry of the Italian Chemical Society, 1998

CURRENT RESEARCH PROJECTS

1. Development and multinuclear NMR characterization in solution of paramagnetic metal complex as diagnostic probes

Molecular probes in MRI have potential for early diagnosis, assessment of disease progression and prediction/evaluation of the effectiveness of therapy. NMR relaxometry (^1H and ^{17}O), has proven to be a fundamental technique to determine the molecular parameters responsible for the relaxation enhancement caused by the contrast agents (CA). The goal is the understanding of the chemical properties of metal-based MRI CA's (Gd^{III} , Mn^{II} , Fe^{III} chelates) and the dependence of their effectiveness (relaxivity) from the molecular parameters. These include: i) the factors that control the rate of exchange of bound water molecules; ii) the nature and role of different isomers in aqueous solution, and the occurrence of hydration equilibria; iii) the dominant role of the rotational dynamics to relaxivity, hence the different strategies to slow down and fine tune the molecular motion; iv) the role of the second sphere of hydration.

2. Synthesis and characterization of multi-functional inorganic nanoparticles

The challenge of further sensitivity improvement of CA has been addressed by developing nanosystems in which paramagnetic complexes are conjugated to platforms of various nature, size and complexity. These nanoprobe make it possible to deliver to the site of interest a large number of paramagnetic ions, thus increasing the sensitivity of the MRI modality. The systems include protein-bound chelates, polymers, dendrimers, micelles, liposomes, viral capsids, metal oxides, zeolites, mesoporous silicas. Desired properties are high imaging contrast and chemical stability, target specificity, and/or multimodality.

3. Development of multimeric systems as high-field MRI probes

The increasing availability of high-field MRI systems ($> 1.5 \text{ T}$) requires a different strategy for relaxivity enhancement of metal-based probes. We pursue: a) chemical control of the value of the rotational correlation time (ca. 0.2-0.5 ns), corresponding to that associated with small multimeric systems; b) high degree of motional coupling between local and global rotation; c) sufficiently fast rate of water exchange ($k_{\text{ex}} > 1 \times 10^7 \text{ s}^{-1}$); d) large contribution to relaxivity from water molecules in the second coordination sphere; e) additional contribution from the prototropic exchange of labile protons of the ligand.

4. Study of the structural and dynamic properties of metal complexes and macromolecules containing paramagnetic ions with NMR fast field-cycling relaxometric techniques

Relaxometry is the measurement of the frequency dependence of magnetic relaxation rates of solvent nuclei in aqueous systems to extract structural and dynamic information on the nature of



the solutes. We apply the technique to the study of detailed physico-chemical properties of complexes of transition metals and lanthanides in order to obtain information about the changes that take place across the series, on the nature of the relaxation processes and their dependence on pH and temperature, on self-recognition mechanisms, on the reversible formation of macromolecular adducts.

RECENT FUNDED PROJECTS

2021-23	Research contract with Bracco Imaging SpA: <i>“Low molecular weight and high-spin Fe^{III}-complexes as an alternative to Gd^{III}-based MRI contrast agents (≥1.5 T)”</i>
2019-21	Research projects of national interest: <i>“Rationally designed nanogels embedding paramagnetic ions as MRI probes”</i>
2018-20	P.O.R. FESR. Support for crucial regional research infrastructures. <u>Magnetic Resonance Platform – UPO</u>
2016-2020	EU COST Action CA15209. <u>European Network on NMR Relaxometry.</u> http://www.cost.eu/COST_Actions/ca/CA15209?
2017-18	UPO Research Grant: <i>“New Nanomaterials Functionalized with High Performance Paramagnetic Probes for MRI Applications”</i>
2013-15	PRIN 2012SK7ASN – <i>“Innovative chemical methodologies for advanced molecular strategies in biomedicine”</i>
2012-15	S. Paolo Bank Foundation. NANOPROGLY – <i>“Nanoparticles Loaded with MRI Probes with Enhanced Efficacy and Glycolipids for Increased Stealth Properties”</i>
2011-2014	Executive Programme of Scientific and Technological Co-operation between Italy and Hungary. PI of the Joint project: <i>“Synthesis and characterization of imaging probes for dual MRI–PET modality”</i>

SELECTED CONFERENCES (since 2015 - Invited Speaker)

1. *9th Conference on Fast Field-Cycling NMR Relaxometry*, Aberdeen, UK (July 2015)
2. *The 9th International Conference on f-Elements 2015*, Oxford, UK (September 2015; Plenary lecture)
3. *Chemical Opportunities in Molecular Imaging & Catalysis*, Hong Kong (November 2016; Keynote Lecture)
4. *ISMEC 2017 - International Symposium on Metal Complexes*, Dijon, France (June 2017; Plenary lecture)
5. *The 28th rare earth research conference*, Ames (Iowa), USA (June 2017; Spedding Award Symposium).
6. *Inorganic Chemistry Lab Seminars*, Oxford, UK (October 2017; invited seminar);
7. *Past, Present and Future of Inorganic Chemistry in Italy: A Path Defined by the Winners of the Nasini Prize*, Roma (February 2019).
8. *Challenges With Rare Earth Elements: The Periodic Table At Work For New Science & Technology*, Accademia Nazionale Dei Lincei e Fondazione «Guido Donegani» International Conference, Roma (November 2019)



9. 12th Conference on Fast Field Cycling NMR Relaxometry. Cambridge, UK (Keynote speaker; July 2022)
10. 11th International Conference on *f* Elements. Strasbourg, France (Keynote speaker; August 2023)
11. French-Italian Coordination Chemistry days. Strasbourg, France (Keynote speaker; January 2024).

MAIN COLLABORATIONS

1. Prof. David Parker, Department of Chemistry, University of Durham, U.K
2. Prof. Enzo Terreno, Department of Molecular Biotechnology, Università di Torino
3. Prof. Giacomo Parigi, CERM, University of Florence
4. Dr. Zsolt Baranyai, Bracco Imaging SpA, Trieste Research Centre
5. Prof. Carlos Platas-Iglesias, Department of Chemistry, Universidade da Coruña, Spain
6. Prof. Mark Woods, Department of Chemistry, University of Oregon, Portland, USA
7. Prof. Matthew Allen, Department of Chemistry, Wayne State University, Detroit, Michigan, USA
8. Prof. Valerie Pierre, Department of Chemistry, University of Minnesota, Minneapolis Minnesota, USA

FURTHER INFORMATION

External member of PhD juries at the Universities of Turin, Lausanne, Prague, Orléans, Coimbra, Debrecen, Durham, Delft.

SELECTED PUBLICATIONS (LAST 5 YEARS)

1. F. Carniato, M. Ricci, L. Tei, F. Garelo, E. Terreno, E. Ravera, G. Parigi, C. Luchinat, M. Botta
High Relaxivity with No Coordinated Waters: A Seemingly Paradoxical Behavior of [Gd(DOTP)]⁵⁻
Embedded in Nanogels
Inorg. Chem., **2022**, *61*, 5380-5387
2. Z. Baranyai, F. Carniato, A. Nucera, D. Horváth, L. Tei, C. Platas-Iglesias, M. Botta
Defining the conditions for the development of the emerging class of Fe^{III}-based MRI contrast
agents
Chem. Sci., **2021**, *12*, 11138–11145
3. S. Anbu, S. H. L. Hoffmann, F. Carniato, L. Kenning, T. W. Price, T. J. Prior, M. Botta, A. F. Martins,
G. J. Stasiuk
A single pot template reaction towards a manganese based *T*₁ contrast agent
Angew. Chem. Int. Ed. **2021**, *60*, 10736-10744
4. Z. Baranyai, D. Delli Castelli, C. Platas-Iglesias, D. Esteban-Gomez, A. Bényei, L. Tei, M. Botta
Combined NMR, DFT and X-ray studies highlight structural and hydration changes of
[Ln(AAZTA)]⁻ complexes across the series



Inorg. Chem. Front., **2020**, 7, 795 – 803

5. C. Charpentier, J. Salaam, A. Nonat, F. Carniato, O. Jeannin, I. Brandariz, D. Esteban-Gomez, C. Platas-Iglesias, L. J. Charbonnière, and M. Botta
pH dependent hydration change in a Gd based contrast agent with a phosphonated ligand
Chem. Eur. J., **2020**, 26, 5407 - 5418
6. M. Botta, F. Carniato, D. Esteban-Gómez, C. Platas-Iglesias, L. Tei,
Mn(II) compounds as an alternative to Gd-based MRI Probes
Fut. Med. Chem., **2019**, 11, 1461–1483
7. R. Pujales-Paradela, T. Savić, D. Esteban-Gómez, G. Angelovski, F. Carniato, M. Botta, C. Platas-Iglesias
Gadolinium(III)-based Dual $^1\text{H}/^{19}\text{F}$ MRI Probes
Chem. Eur. J., **2019**, 25, 4782-4792
8. D. Delli Castelli, L. Tei, F. Carniato, S. Aime, M. Botta
[Yb(AAZTA)(H₂O)]⁻: an unconventional ParaCEST MRI probe
Chem. Commun., **2018**, 54, 2004
9. Z. Wang, F. Carniato, Y. Huang, Y. Xie, Y. Li, S. He, N. Zang, J. D. Rinehart, M. Botta, N. C. Gianneschi
High Relaxivity Gadolinium-Polydopamine Nanoparticles
Small, **2017**, 13, 1701830
10. Y. Li, Y. Xie, Z. Wang, N. Zang, F. Carniato, Y. Huang, C. M. Andolina, L. R. Parent, T. B. Ditri, E. D. Walter, M. Botta, J. D. Rinehart, N. C. Gianneschi
Characterizing Synthetic Melanin
ACS Nano, **2016**, 10, 10186–10194