

## Beatrice Vallone – Curriculum Vitae

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E-mail	beatrice.vallone@uniroma1.it	
Nationality	Italian	
Date of birth	28/04/1963	
Gender	f	
<b>Occupational field</b>	BIO10 (Italian Ministry Discipline Group: Biochemistry and Biophysics).	
<b>Work experience</b>		
Dates	01/2016-30/2016 Alexander Bodini Research Fellow at the Italian Academy for Advanced Studies in America – Columbia University (USA) 07/2014 - 06/2015 Research Scholar at Columbia University (New York USA) 2009-present Full Professor (Professore Ordinario) 2000-2007 Assistant Professor (Professore Associato) 1991-1999: Research Associate (Ricercatore)	
Occupation or position held	Full Professor, Biochemistry	
Main activities and responsibilities	Head of research unit in structural biology, teaching chair Member of the Biological Macromolecules Commission of the International Union of Crystallography Chair of the committee "Biological Macromolecules" for the Italian Elettra Synchrotron Member of the Executive Committee of the Italian Society for Synchrotron Light (SILS) (2013-2017) Head of the CNR Biocrystal Facility ( <a href="http://www.biocrystalfacility.it">www.biocrystalfacility.it</a> ) Coordinator of the First Semester of the Medical School of the Sapienza University of Rome Member of the "Spin-off Committee" of the Medical School of the Sapienza University of Rome Teaching panel of the Doctorate School in Biochemistry (from 2013) Teaching panel of the Doctorate School in Biophysics (2007-2013) Member of the ESRF User Organization Committee 2010-2014 Member of the "Accademia Medica Romana" Editorial Board "AIMS Biophysics" Review Editor Frontiers in Molecular Biosciences – Structural Biology	
Name and address of employer	Università di Roma "La Sapienza", P.le A. Moro, 5. 00185, Rome, Italy.	
Sector	Academic, research.	
<b>Education and training</b>		
Dates	1991, PhD in Biochemistry 1987, Degree in Biology	
Title of qualification awarded	PhD in Biochemistry Degree in Biochemistry	
Name and type of organisation providing education and training	University of Rome "La Sapienza", Academic	

### Additional Information.

**Honors:** Schaefer Research Scholar at Columbia Medical Center (2014).

Alexander Bodini Research Fellow at the Italian Academy for Advanced Studies at Columbia (2016)

### **Fellowships.**

1988 Geneva University (CH) sponsored by EMBO- Dept. of Biochemistry (Prof.S.J. Edelstein)

1990 LMB-MRC, Cambridge (UK) sponsored by EMBO (Dr. K. Nagai)

1991 LMB-MRC, Cambridge (UK) sponsored by FEBS (Dr. G. Fermi).

1997 York University, Dept. of Biochemistry (UK) sponsored by FEBS (Prof. J. Tame)

2004 Cambridge University, Dept. of Biochemistry, (UK) sponsored by EMBO (Prof. B. Luisi)

### **Research Subject: structural biology and biochemistry.**

The mechanism of action of protein is investigated by using protein crystallography, single-particle cryo-EM and biochemical characterization. This includes the structure-function relationship of enzymes and structural proteins as well as their role within signalling networks that involves protein-protein recognition and complex formation.

The knowledge of the molecular mechanism exploited by proteins to carry out their function and involved in pathological processes is the starting point to design novel, targeted therapeutic strategies.

In this context, the main endeavour has been carrying out and coordinating the determination of protein structures by protein crystallography and their biochemical characterization using a wide array of methods (kinetics, protein engineering, spectroscopy). In collaboration with the Italian Association of Crystallography and Pavia University the first Italian Course on "Bridging the gap between *cryo-EM* and crystallography" was organized in September 2017.

### **Present Research projects.**

1. Steroid-5-alpha dihydrogenase, structural insights of an integral membrane enzyme playing a pivotal role in pharmacology of prostatic cancer and target for novel neuropsychiatric therapies (in collaboration with Columbia University) by Cryo-EM and Crystallography.

2. Ferritin and ferritin-receptor complex by Cryo-EM.

1. Crystal structure and functional characterization of HIPK2 (homeodomain protein kinase 2), a switch in tumour suppression.

2. Structural dynamics of heme proteins, by a combination of biophysical methodologies: time resolved X-ray crystallography and wide angle scattering, high pressure crystallography, XAS. The systems under analysis are neuroglobin, the EryK p450 cytochrome and hemoglobin.

3. Engineering and structural analysis of p450 cytochromes involved in antibiotics biosynthesis.

### **Results of ongoing and past research projects.**

1. The methodology of single-particle Cryo-EM has been successfully applied to engineered ferritins and to the ferritin-CD71 receptor (paper in preparation). We are currently investigating the structure of a family of membrane enzymes crucial for testosterone metabolism (SRD5A) by single particle cryo-EM. The projects are in collaboration with Columbia University, CUNY and the New York Structural Biology Center.

2. The determination of the structure of murine neuroglobin in different ligation states where a novel mechanism for ligand affinity regulation (heme sliding) has been described and the characterization of its reactivity towards nitric oxide, the presence of redox activity and capability of photoreduction and photodissociation by X-rays was shown and, recently, the presence of internal hydrophobic docking sites capable of hosting gaseous ligands was shown.

Break-through results have been obtained such as the crystal structure of neuroglobin, that protects neurons from hypoxic injury, and a leading role in the field has been acknowledged by the publication of reviews on this protein and by the invitations to present plenary lectures to International Conferences (XVth International Conference on Oxygen Binding and Sensing Proteins August, 2008 Aarhus, Denmark and XIII European Conference on the Spectroscopy of Biological Molecules 28 August-2 September 2009 Palermo, Italy).

3. The determination of the structure of a novel endoribonuclease essential small nucleolar RNA maturation, homologous to a SARS essential enzyme, with implications in the development of drugs targeted to a specific enzymatic activity of corona virus.

4. The study by time-resolved crystallography and molecular dynamics of myoglobin structural dynamics, that contributed to the description by direct detection of the pathway of ligands within the protein matrix and to the unveiling of a complex subnanosecond structural dynamics triggered by ligand dissociation.

5. The structural and functional analysis of three enzymes involved in antibiotic biosynthesis, that led to the determination of the structure of a new type of monooxygenase involved in the biosynthesis of aromatic polyketids and of a cytochrome P450 involved in the biosynthesis of a macrolide polyketide, Erythromycin.

## Grants.

As Grant Coordinator.

-Functional Genomics (CNR) 2003.

-VII Framework Program (2008)– EU – "CryoEm structure of gamma secretase: a key component in Alzheimer neurodegenerative disease"- Scientist in Charge.

-FIRC, Italian Cancer Research Foundation (2012) "The crystal structure of HIPK2: understanding at the molecular level a switch in tumour suppression".

-CNR, Life Sciences Dept. "Biocrystal Facility of the CNR".

-University of Rome "La Sapienza" (2012) "Espansione multidisciplinare della biologia strutturale verso una dimensione di facility: sistema di imaging per screening di cristallizzazione di proteine."

-Fondazione Cenci-Bolognetti/Pasteur Institute Grant (2013) "Bacterial P450 Cytochromes as tools for designing novel antimicrobial agents".

As Unit Member:

EuroBlood - European Framework Program VI in Blood Substitutes

PRIN 2007 Proteine redox in azione: dinamica strutturale, meccanismi e fisiopatologia

FIRB 2003 Biologia Strutturale PostGenomica, sviluppo di infrastrutture per la cristallografia di proteine.

EU H2020 (2014) Innovative Training Network "X-Probe" on frontier methods in protein structural dynamics (Coordinator)

EU H2020 (2018) Marie Skłodowska-Curie Research And Innovation Staff Exchange (RISE) as Coordinator, title: "ProMeTeus - Membrane protein integrated technologies development for drug design".

## Beatrice Vallone - Full list of publications (H-index=30 citations=2875).

1. Colloc'h N, Sacquin-Mora S, Avella G, Dhaussy AC, Prangè T, Vallone B, Girard E. Determinants of neuroglobin plasticity highlighted by joint coarse-grained simulations and high pressure crystallography. *Sci Rep.* 2017 Vol. 7 pp. 1858.
2. Scaglione A, Celeste Montemiglio L, Parisi G, Asteriti IA, Bruni R, Cerutti G, Testi C, Savino C, Mancia F, Lavia P and Vallone B. *Biochimie Open* (2017) Subcellular localization of the five members of the human steroid 5 $\alpha$ -reductase family. Vol. 4 pp. 99-106.
3. de Turris V, Cardoso Trabuco M, Peruzzi G, Boffi A, Testi C, Vallone B, Celeste Montemiglio L, Georges AD, Calisti L, Benni I, Bonamore A, Baiocco P. *Nanoscale.* (2017) Humanized archaeal ferritin as a tool for cell targeted delivery. Vol. 9 pp.647-655.
4. Montemiglio LC, Parisi G, Scaglione A, Sciara G, Savino C, Vallone B (2016) Functional analysis and crystallographic structure of clotrimazole bound OleP, a cytochrome P450 epoxidase from *Streptomyces antibioticus* involved in oleandomycin biosynthesis. *Biochim Biophys Acta.* Vol. 1860 pp.465-75.
5. Abbraini JH, Marassio G, David HN, Vallone B, Prangé T, Colloc'h N (2014) Crystallographic studies with xenon and nitrous oxide provide evidence for protein-dependent processes in the mechanisms of general anesthesia. *Anesthesiology.* Vol. 121 pp.1018-27
6. Avella G, Ardiccioni C, Scaglione A, Moschetti T, Rondinelli C, Montemiglio LC, Savino C, Giuffrè A, Brunori M, Vallone B. Engineering the internal cavity of neuroglobin demonstrates the role of the haem-sliding mechanism. (2014) *Acta Crystallogr D Biol Crystallogr.* Vol. 70 pp 1640-8.
7. Yang Y, Allemand F, Guca E, Vallone B, Delbecq S, Roumestand C. 1H, 15N and 13C Backbone resonance assignments of murine met-neuroglobin, free and in complex with cyanide. (2014) May 16. [Epub ahead of print].
8. Guca E, Roumestand C, Vallone B, Royer CA, Dellarole M. Low-cost equilibrium unfolding of heme proteins using 2  $\mu$ l samples. (2013) *Anal Biochem.* Vol 443 pp.13-5.
9. Montemiglio LC, Macone A, Ardiccioni C, Avella G, Vallone B, Savino C. Redirecting P450 EryK Specificity by Rational Site-Directed Mutagenesis. *Biochemistry.* (2013) Vol 52, pp 3678–3687
10. van der Linden P, Vitoux H, Steinmann R, Vallone B, Ardiccioni C. (2013) An open flow helium cryostat for synchrotron X-ray diffraction experiments. *Journal of Physics: Conference Series,* Vol. 425, p. 12015-12018.
11. Vallone B. (2013) Time-resolved crystallography for protein structure: the case of heme proteins. *Rend. Lincei* Vol. 24; p. 101-107.
12. Levantino M, Spilotros A, Cammarata M, Schiro G, Ardiccioni C, Vallone B, Brunori M, Cupane A. (2012) The Monod-Wyman-Changeux allosteric model accounts for the quaternary transition dynamics in wild type and a recombinant mutant human hemoglobin. *Proc Natl Acad Sci U S A* Vol. 109; p. 14894-14899.
13. Palladino P, Scaglione GL, Arcovito A, Maria Vitale R, Amodeo P, Vallone B, Brunori M, Benedetti E, Rossi F. (2011) Neuroglobin-prion protein interaction: what's the function? *J. Pept Sci.* 10.1002/psc.1333.

14. Montemiglio LC, Gianni S, Vallone B, Savino. Azole Drugs Trap Cytochrome P450 EryK in Alternative Conformational States. (2010) *Biochemistry*, Vol. 49; p.9199-206.
15. Arcovito A, Ardiccioni C, Cianci M, D'Angelo P, Vallone B., Della Longa S (2010). Polarized X-ray absorption near-edge structure spectroscopy of neuroglobin and myoglobin single crystals. *J. Phys. Chem. B*, vol. 114; p. 36415-36423.
16. Moschetti T, Giuffrè A, Ardiccioni C, Vallone B., Modjtahedi N, Kroemer G, Brunori M (2009). Failure of apoptosis-inducing factor to act as neuroglobin reductase. *Biochem. Biophys. Res. Commun.*, vol. 390; p. 121-124.
17. Moschetti T, Mueller U, Schultze J, Brunori M, Vallone B. (2009). The structure of neuroglobin at high Xe and Kr pressure reveals partial conservation of globin internal cavities. *Biophys. J.*, vol. 97; p. 1700-1708.
18. Pedotti M, Rosini E, Molla G, Moschetti T, Savino C, Vallone B., Pollegioni L (2009). Glyphosate resistance by engineering the flavoenzyme glycine oxidase. *J. Biol. Chem.*, vol. 284; p. 15-23.
19. Savino C, Miele A.E, Draghi F, Johnson K.A, Sciarra G, Brunori M, Vallone B. (2009). Pattern of cavities in globins: The case of human hemoglobin. *Biopolymers*, vol. 91; p. 1097-1107.
20. Savino C, Montemiglio LC, Sciarra G, Miele AE, Kendrew SG, Jemth P, Gianni S, Vallone B. (2009). Investigating the structural plasticity of a cytochrome P450: three-dimensional structures of P450 EryK and binding to its physiological substrate. *J. Biol. Chem.*, vol. 284; p. 29170-9-29179.
21. Anselmi M, Brunori M, Vallone B., Di Nola A (2008). Molecular dynamics simulation of the neuroglobin crystal: comparison with the simulation in solution. *Biophys. J.*, vol. 95; p. 4157-4162.
22. Arcovito A, Moschetti T, D'Angelo P, Mancini G, Vallone B., Brunori M, Della Longa S (2008). An X-ray diffraction and X-ray absorption spectroscopy joint study of neuroglobin. *Arch. of Biochem. Biophys.*, vol. 475; p. 7-13.
23. Brunori M, Bourgeois D, Vallone B. (2008). Structural dynamics of myoglobin. *Methods Enzymol.*, vol. 437; p. 397-416.
24. Giuffrè A, Moschetti T, Vallone B., Brunori M (2008). Is neuroglobin a signal transducer?. *IUBMB Life*, vol. 60; p. 410-413.
25. Giuffrè A, Moschetti T, Vallone B., Brunori M (2008). Neuroglobin: enzymatic reduction and oxygen affinity. *Biochem. Biophys. Res. Commun.*, vol. 367; p. 893-898.
26. Savino C, Sciarra G, Miele AE, Kendrew SG, Vallone B. (2008). Cloning, expression, purification, crystallization and preliminary X-ray crystallographic analysis of C-12 hydroxylase EryK from *Saccharopolyspora erythraea*. *Protein Peptide Lett.*, vol. 15; p. 1138-1141.
27. Anselmi M, Brunori M, Vallone B., Di Nola A (2007). Molecular dynamics simulation of deoxy and carboxy murine neuroglobin in water. *Biophys. J.*, vol. 93; p. 434-441.
28. Arcovito A, Benfatto M, Cianci M, Hasnain SS, Nienhaus K, Nienhaus GU, Savino C, Strange RW, Vallone B., Della Longa S (2007). X-ray structure analysis of a metalloprotein with enhanced active-site resolution using in situ x-ray absorption near edge structure spectroscopy. *Prof. Natl. Acad. Sci. USA*, vol. 104; p. 6211-6216.
29. Bourgeois D, Schotte F, Brunori M, Vallone B. (2007). Time-resolved methods in biophysics. 6. Time-resolved Laue crystallography as a tool to investigate photo-activated protein dynamics. *Photochem. Photobiol Sci.*, vol. 6; p. 1047-1056.
30. Brunori M, Vallone B. (2007). Neuroglobin, seven years after. *Cell. Mol. Life Sci.*, vol. 64; p. 1259-1268.
31. Bellelli A, Brunori M, Miele AE, Panetta G, Vallone B. (2006). The allosteric properties of hemoglobin: insights from natural and site directed mutants. *Curr. Prot. Peptide Sci.*, vol. 7; p. 17-45.
32. Bourgeois D, Vallone B., Arcovito A, Sciarra G, Schotte F., Anfinrud PA, Brunori M (2006). Extended subnanosecond structural dynamics of myoglobin revealed by Laue crystallography. *Prof. Natl. Acad. Sci. USA*, vol. 103; p. 4924-4929.
33. Nienhaus G.U, Nienhaus K, Holzle A, Ivanchenko S, Renzi F, Oswald F, Wolff M, Schmitt F, Rocker C, Vallone B., Weidenmann W, Heilker R, NAR H, Wiedenmann J (2006). Photoconvertible fluorescent protein EosFP: biophysical properties and cell biology applications. *Photochem. Photobiol. Sci.*, vol. 82; p. 351-358.
34. Nienhaus K, Renzi F, Vallone B., Wiedenmann J, Nienhaus G.U (2006). Chromophore-protein interactions in the anthozoan green fluorescent protein asFP499. *Biophys. J.*, vol. 91; p. 4210-4220.
35. Nienhaus K, Renzi F, Vallone B., Wiedenmann J, Nienhaus G.U (2006). Exploring Chromophore-Protein Interactions in Fluorescent Protein cmFP512 from *Cerianthus membranaceus*: X-ray Structure Analysis and Optical Spectroscopy. *Biochemistry*, vol. 45; p. 12942-12953.
36. Renzi F, Caffarelli E, Laneve P, Bozzoni I, Brunori M, Vallone B. (2006). The structure of the endoribonuclease XendoU: From small nucleolar RNA processing to severe acute respiratory syndrome coronavirus replication. *Prof. Natl. Acad. Sci. USA*, vol. 103; p. 12365-12370.

37. Renzi F, Panetta G, Vallone B., Brunori M, Arceci M, Bozzoni I, Laneve P, Caffarelli E (2006). Large-scale purification and crystallization of the endoribonuclease XendoU: troubleshooting with His-tagged proteins. *Acta Crystallogr Sect F Struct Biol Cryst Commun.*, vol. 62; p. 298-301.
38. Vallone B., Brunori, M (2006). A globin for the brain. *FASEB J.*, vol. 20; p. 2192-2197.
39. Bossa C, Amadei A, Daidone I, Anselmi M, Vallone B., Brunori M, Di Nola A. (2005). Molecular dynamics simulation of sperm whale myoglobin: effects of mutations and trapped CO on the structure and dynamics of cavities. *Biophys. J.*, vol. 89; p. 465-474.
40. Brunori M, Giuffrè A, Nienhaus K, Nienhaus GU, Scandurra FM, Vallone B. (2005). Neuroglobin, nitric oxide, and oxygen: functional pathways and conformational changes. *Prof. Natl. Acad. Sci. USA*, vol. 102; p. 8483-8488.
41. Wiedenmann J, Vallone B., Renzi F, Nienhaus K, Ivanchenko S, Rocker C, Nienhaus GU (2005). Red fluorescent protein eqFP611 and its genetically engineered dimeric variants. *J. Biomed. Opt.*, vol. 10; p. 14003.
42. Bossa C, Anselmi M, Roccatano D, Amadei A, Vallone B., Brunori M, Di Nola A. (2004). Extended molecular dynamics simulation of the carbon monoxide migration in sperm whale myoglobin. *Biophys. J.*, vol. 86; p. 3855-3862.
43. Brunori M, Bourgeois D, Vallone B. (2004). The structural dynamics of myoglobin. *J. of Struct. Biol.*, vol. 147; p. 223-234.
44. Savino C, Federici L, Johnson KL, Vallone B., Nastopoulos V, Rossi M, Pisani FM, Tsernoglou D Insights into DNA replication: the crystal structure of DNA polymerase B1 from the archaeon *Sulfolobus solfataricus*. *Structure*, vol. 12; p. 2001-2008.
45. Vallone B., Brunori M (2004). Roles for holes: are cavities in proteins mere packing defects?. *Ital. J. Biochemistry*, vol. 53; p. 46-52.
46. Vallone B., Nienhaus E, Brunori M, Nienhaus GU (2004). The structure of murine neuroglobin: novel pathways for ligand migration and binding. *Proteins*, vol. 56; p. 85-92.
47. Vallone B., Nienhaus K, Matthes A, Brunori M, Nienhaus GU. (2004). The structure of carbonmonoxy neuroglobin reveals a heme-sliding mechanism for control of ligand affinity. *Prof. Natl. Acad. Sci. USA*, vol. 101; p. 17351-17356.
48. Bourgeois D, Vallone B., Schotte F, Arcovito A, Miele AE, Sciara G, Wulff M, Anfinrud P, Brunori M. (2003). Complex landscape of protein structural dynamics unveiled by nanosecond Laue crystallography. *Prof. Natl. Acad. Sci. USA*, vol. 100; p. 8615-8617.
49. Miele AE, Federici L, Sciara G, Draghi F, Brunori M, Vallone B. (2003). Analysis of the effect of microgravity on protein crystal quality: the case of a myoglobin triple mutant. *Acta Cryst. D, Biol. Crystallogr.*, vol. 59; p. 982-988.
50. Nienhaus K, Vallone B., Renzi F, Wiedenmann J, Nienhaus GU. (2003). Crystallization and preliminary X-ray diffraction analysis of the red fluorescent protein eqFP611. *Acta Cryst. D, Biol. Crystallogr.*, vol. 59; p. 1253-1255.
51. Sciara G., Kendrew S.G., Miele A.E., Marsh N.G, Federici L., Malatesta F., Schimperna G., Savino L., Vallone B. (2003). The structure of ActVA-Orf6, a novel type of monooxygenase involved in actinorhodin biosynthesis. *EMBO J.*, vol. 22. p. 205-215.
52. Draghi F, Miele AE, Travaglini-Allocatelli C, Vallone B., Brunori M, Gibson QH, Olson JS. (2002). Controlling ligand binding in myoglobin by mutagenesis. *J. Biol. Chem.*, vol. 277; p. 7509-7519.
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54. Brunori M., Vallone B., Cutruzzolà F., Travaglini-Allocatelli C., Berendzen J., Chu K., Sweet R.M., Schlichting I (2000). The role of cavities in protein dynamics: crystal structure of a photolytic intermediate of a mutant myoglobin. *Prof. Natl. Acad. Sci. USA*, vol. 97; p. 2058-2063.
55. Kendrew S.G., Federici L., Savino C., Miele A.E., Marsh E.N.G., Vallone B. (2000). Crystallization and preliminary diffraction studies of a monooxygenase from *S. coelicolor* A3(2) involved in the biosynthesis of the polyketide actinorhodin. *Acta Cryst. D, Biol. Crystallogr.*, vol. D56; p. 481-483.
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57. Della Longa S., Arcovito A, Vallone B., Congiu-Castellano A., Kahn R., Vicat J., Soldo Y., Hazmann J.L. (1999) Polarized x-ray absorption spectroscopy of the low-temperature photoproduct of carbonmonoxy-myoglobin. *J. Synchrotron Rad.* 6, 1138-1147.
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76. Malatesta F, Antonini G, P. Sarti, Vallone B., Brunori M (1990). Structure and function of cytochrome c oxidase. *Gazzatta Chimica Italiana*, vol. 120; p. 475-484.
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