ROMA TRE
UNIVERSITÀ DEGLI STUDI

Prof. Maurizio Brunori

Laurea Honoris Causa in Biologia per la ricerca molecolare, cellulare e fisiopatologica

G. Antonini, Università Roma Tre, 17 Maggio 2017

Carriera Accademica

2016- Vice Presidente della Accademia Nazionale dei Lincei, Presidente della Classe di Scienze MFN
2014-2016 Accademico Amministratore, Accademia Nazionale dei Lincei
2011 - Emeritus Professor, Sapienza - University of Rome
2010- President of EMAN (Euro Mediterranean Academic Network)
2003-2007 President, Istituto Pasteur-Fondazione Cenci Bolognetti, Rome
2001 -2007 Director, Centro Linceo Interdisciplinare "Beniamino Segre", Accademia Nazionale dei Lincei
1998-2003 Director, Dept. of Biochemical Sciences "A. Rossi Fanelli", University of Rome "La Sapienza"
1997-2002 President, "Progetto Finalizzato Biotecnologie" of the National Research Council
1994-2001 Scientific Director, Istituto Pasteur-Fondazione Cenci Bolognetti, Rome
1994-1998 Member of the National Research Council Committee for Biology and Medicine
1990-1993 President of IUPAB (International Union of Pure and Applied Biophysics)
1986/88/90 International Fogarty Scholar in Residence, NIH, Bethesda, MD, USA
1974-2010 Full Professor of Chemistry and Biochemistry, University of Rome "La Sapienza"
1972-1974 Full Professor of Molecular Biology, University of Camerino
1968 Post-Doctoral Fellow, Urbana, IL, USA
1966 Post-Doctoral Fellow, Goettingen, D
1965 Docent in Biochemistry
1961 University degree in Medicine at the University of Rome

Riconoscimenti

- Member of the Italian Society of Biochemistry and Molecular Biology (SIB)
- Member of the Italian Society of Biophysics and Molecular Biology (SIBBM)
- Honorary Member of the American Society for Biochemistry and Molecular Biology, USA
- Fellow of the American Biophysical Society, USA
- Member of EMBO, and of the Scientific Advisory Committee of EMBL (European Molecular Biology Laboratory)
- Member of the Accademia Nazionale dei Lincei (1987)
- Premio Nazionale del Presidente della Repubblica (1985)
- FEBS Lecturer (1989)
- Member of the Accademia Europea (1998)
- Officier de l'Ordre National du Mérite du Président de la République Française (2002)
- Foreign Honorary Member of the American Academy of Arts and Sciences (2006).
- Member of the editorial board of Protein Science (2011)

Alcune tra le collaborazioni più significative

A. Alfsen, CNRS, Faculté de Medicine, Paris (FR)
A. Ascenzi, Istituto di Anatomia Patologica, Università "La Sapienza", Roma (IT).
P.A. Benedetti, Istituto di Biofisica del C.N.R., Pisa (IT).
M. Bolognesi, Dipartimento di Biochimica, Università di Milano (IT).
J. Bonaventura, Duke University Marine Laboratory, Beaufort, North Carolina (USA).
P. Brezinski, Department of Biochemistry, University of Stockholm (SW).
C. Cambillau, Centre du CNRS sur les Macromolécules Biologiques, Marseille (FR).
C.W. Canters, Department of Chemistry, University of Leiden, Leiden (NL).
P. Douzou, Institute de Biologie Physico-Chemique, Paris (FR).
W.A. Eaton, National Institutes of Health, Bethesda, MD (USA).
J. Engel, Department of Biophysical Chemistry, Biozentrum der Universität, Basel (CH).
G.M. Giacometti, Dipartimento di Biologia, Università di Padova (IT).
Q.H. Gibson, Department of Biochemistry, Cornell University, Ithaca, NY (USA).
S.J. Gill, Department of Chemistry, University of Colorado, Boulder, CO (USA).
C. Greenwood, Division of Biological Sciences, University of East Anglia, Norwich (UK)
G: La Mar, Department of Molecular Biology, University of California, Davis, CA (USA).
B.G. Malmstrom, Department of Biochemistry, Chalmers University, Goteborg (SW).
M.F. Perutz, L.M.B., Medical Research Council, Cambridge (UK).
M. Pocchiari, Istituto Superiore della Sanità, Roma (IT).
J.F. Taylor, Faculty of Medicine, University of Louisville, Louisville, KY (USA).
T. Traylor, Department of Chemistry, University of Southern California, San Diego, CA (USA).
F. Trottein, Institut Pasteur, Lille (FR).
G. Weber, Department of Biochemistry and Biophysics, University of Illinois, Urbana, IL (USA).
M.T. Wilson, Department of Chemistry and Biochemistry, University of Essex, Colchester (UK).
K.H. Winterhalter, Laboratorium für Biochemie, ETH, Zürich (CH).
K. Wütrich, Department of Molecular Biology, ETH, Zürich (CH).
J. Wyman, Istituto Regina Elena, Roma (IT).
T. Yonetani, Department of Biophysics, University of Pennsylvania, Philadelphia, PE (USA).

Le collaborazioni più frequenti (fonte: Scopus, Aprile 2017)

Antonini,Eraldo	154	Zolla,Lello	19
Sarti,Paolo	71	Condò,SaverioGiovanni	18
Bellelli,Andrea	71	Chiancone,Emilia	18
Wyman,Jeffries	64	Santucci,Roberto	18
Giardina,Bruno	62	Kuiper,HarryA.	17
Cutruzzola,Francesca	57	Greenwood,ColinT.	17
Vallone,Beatrice	51	Bolognesi,Martino	17
Malatesta,Francesco	44	Forte,Elena	17
Antonini,Giovanni	44	Angelucci,Francesco	16
Travaglini-Allocatelli,Carlo	43	Rotilio,Giuseppe	16
Giuffrè,Alessandro	43	Benedetti,PierAlberto	16
Gianni,Stefano	41	Bonaventura,CeliaJ.	15
Colosimo,Alfredo	39	Bossa,F.	15
Ascenzi,Paolo	36	Lendaro,Eugenio	15
Coletta,Massimo	32	Arese,Marzia	14
Ascoli,Franca	30	Ippoliti,Rodolfo	14
Amiconi,Gino	29	Arcovito,Alessandro	14
Falcioni.,GiancarloC.	29	D'itri,Emilio	14
Silvestrini,MariaChiara	28	Barra,Donatella	14
Bonaventura,Joseph	26	Rinaldo,Serena	13
Miele,AdrianaErica	24	Rossi-Fanelli,Alessandro	12
Giacometti,GiorgioMaria	20		

Prof. Alessandro Rossi Fanelli, prof. Eraldo Antonini, prof. Maurizio Brunori

Pubblicazioni (fonte: Scopus, 9 Maggio 2017)

Numero di pubblicazioni : 673(+2)
Citazioni: 13'982
H-index: 61

(H-Index: Of the 673 documents considered for the h-index, 61 have been cited at least 61 times.)

Scopus is in progress of updating pre-1996 cited references going back to 1970. The h-index might increase over time.

Pubblicazioni *

* Scopus database contains references going back to 1970.

Citazioni *

* Scopus is in progress of updating pre-1996 cited references going back to 1970.

Interessi scientifici

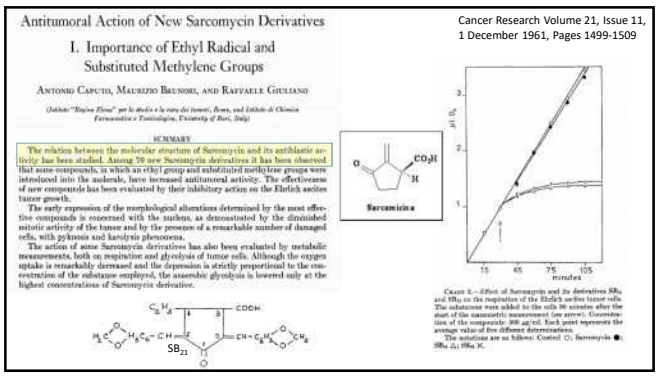
Il professore Brunori ha svolto ricerche fondamentali di rilevanza mondiale relative alla struttura, alla funzione e all'evoluzione delle proteine, con particolare riguardo alle metalloproteine coinvolte nel trasporto e nell'attivazione dell'ossigeno molecolare, nel trasferimento di elettroni e nella trasduzione dell'energia.

Inoltre, ha rappresentato un riconosciuto riferimento internazionale per lo studio della dinamica strutturale di proteine.

Particolarmente rilevante è stato anche il suo contributo al chiarimento delle basi molecolari della patogenesi delle malattie neurodegenerative.

Infine, di particolare pregio è stato anche il suo apporto nello sviluppo delle metodologie di cinetica rapida e di spettroscopia delle macromolecole.

Breve panoramica di alcune pubblicazioni fra le più significative della produzione scientifica del prof. Maurizio Brunori



Antitumoral Action of New Sarcomycin Derivatives

I. Importance of Ethyl Radical and Substituted Methylene Groups

Antonio Caputo, Maurizio Brunori, and Raffaele Giuliano

Cancer Research Volume 21, Issue 11, 1 December 1961, Pages 1499-1509

Eraldo Antonini, Maurizio Brunori
Hemoglobin and Myoglobin in their Reactions with Ligands, North-Holland, 1971

The present book has been written over the past five years and has been completed long after the initially expected time, due, at least in part, to the need of taking into consideration the advances in the knowledge of the subject which have recently occurred.... The aim of the volume is to give a comprehensive account of the present knowledge on the reactions of hemoglobin and myoglobin with ligands, and of their interpretation in terms of molecular structure. Although the subject has been under investigation for almost a century, it still represents one of the most active fields in science and occupies a central position in modern molecular biology. The main reason for this is that hemoglobin and myoglobin can be taken as prototypes of protein systems showing a specific reactivity of direct biological significance...
(dalla Prefazione)

1. Preparation and some general properties of hemoglobin and myoglobin
2. The derivatives of ferrous hemoglobin and myoglobin
3. The derivatives of ferric hemoglobin and myoglobin
4. Structure of hemoglobin and myoglobin
5. Solution properties of myoglobin and hemoglobin
6. Ligand-dependent conformational changes
7. The equilibrium of hemoglobin and myoglobin with ligands
8. Kinetics of the reactions of hemoglobin and myoglobin with ligands
9. Specific aspects of the reaction of myoglobin with ligands
10. Specific aspects of the reaction of hemoglobin with ligands
11. Functional properties of modified hemoglobins and normal hemoglobin under special conditions
12. Oxidation-reduction equilibria
13. Structure-function relationships in hemoglobin and myoglobin
14. Models and theories of ligand binding in hemoglobin

Eraldo Antonini, Maurizio Brunori
Hemoglobin and Myoglobin in their Reactions with Ligands, North-Holland, 1971

The present book has been written over the past five years and has been completed long after [illegible] experiments, due in part, to the need of taking into consideration the advances in the knowledge of the subject which have recently occurred.....The aim of the volume is to give a mechanistic account of the present knowledge on the reactions of hemoglobin and myoglobin with ligands and of their interpretation in terms of molecular structure. Although the subject has been under investigation for almost a century, it still [illegible] one of the most attractive in science and occupies a central position in modern molecular biology. The main reason for this is that hemoglobin and myoglobin can be taken as prototypes of protein systems showing a specific reactivity of direct biological significance...
(dalla Prefazione)

1. Preparation and some general properties of hemoglobin and myoglobin
2. The derivatives of ferrous hemoglobin and myoglobin
3. The derivatives of ferric hemoglobin and myoglobin
4. Structure of [illegible] and globin
5. Solution properties of [illegible] and [illegible]
6. Ligand-dependent [illegible]
7. The equilibrium [illegible]
8. Kinetics of [illegible]
9. Specific aspects of the reaction of myoglobin with ligands
10. Specific aspects of the reaction of hemoglobin with ligands
11. Functional properties of modified hemoglobins and normal hemoglobin under special conditions
12. Oxidation-reduction equilibria
13. Structure-function relationships in hemoglobin and myoglobin
14. Models and theories of ligand binding in hemoglobin

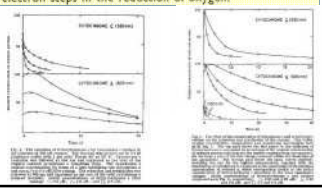
3’333 citazioni

936 NATURE VOL. 228 DECEMBER 5 1970

Catalytic Mechanism of Cytochrome Oxidase

by
ERALDO ANTONINI
MAURIZIO BRUNORI
Centro di Biologia Molecolare del CNR and Istituto di Chimica Biologica, Università di Roma, I-00185 Roma
COLIN GREENWOOD
School of Biological Sciences, University of East Anglia, Norwich NOR 88C, Norfolk
BO G. MALMSTRÖM
Department of Biochemistry, University of Göteborg and Chalmers Institute of Technology, Fack, S-402 20 Goteborg 5

Kinetic experiments in a stopped-flow apparatus provide evidence for multi-electron steps in the reduction of oxygen.



ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS 142, 276-280 (1971)

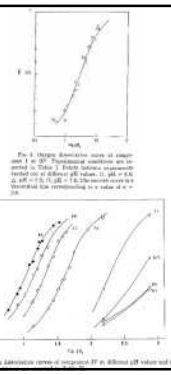
Studies on the Functional Properties of Fish Hemoglobins

II. The Oxygen Equilibrium of the Isolated Hemoglobin Components from Trout Blood.

I. BINOTTI, S. GIOVENCO, B. GIARDINA, E. ANTONINI, M. BRUNORI, AND J. WYMAN
Institutes of Biological Chemistry of the Universities of Rome and Camerino, C.N.R. Center for Molecular Biology, Rome, and Regina Elena Institute for Cancer Research, Rome, Italy

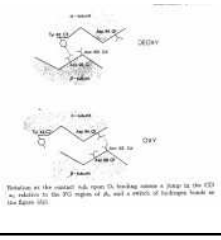
Received August 17, 1970; accepted October 16, 1970

Homogeneous components of trout hemoglobin (*Salmo iridens*) have been isolated by column chromatography.
The oxygen equilibrium of the two main components has been investigated. The oxygen affinity and the shape of the ligand equilibrium curve is independent of pH for component I. On the other hand, component IV is characterized by a very large Bohr effect, to which a considerable change in the shape of the oxygen equilibrium curve with pH is associated.
The different oxygen-binding behavior of the isolated components can explain data obtained with the whole blood and in particular the contribution of the various proteins to the Root effect.
The dependence on pH of the apparent ΔH for oxygenation has been measured for both components. Component I is characterized by a fairly low ($\Delta H \sim -3$ kcal/mole) and pH independent value of the enthalpy change, while for component IV the apparent ΔH decreases from ~ -14 kcal/mole at pH near 9 to ~ -7 kcal/mole at pH 7.



Molecular Adaptation to Physiological Requirem
The Hemoglobin System of Trout

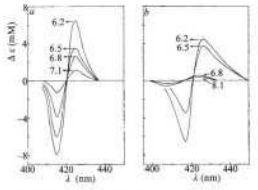
Curr Top Cell Regul. 1975;9:1-39. MAURIZIO BRUNORI*

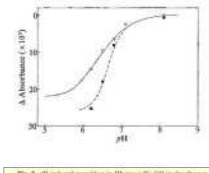


Spectral changes and allosteric transition in trout haemoglobin

BRUNO GIARDINA
FRANCA ASCOLI
MAURIZIO BRUNORI

Nature Vol. 256 August 28 1975 **761**





THE *ALPHA HELIX* EXPEDITION TO THE AMAZON FOR THE STUDY OF FISH BLOODS AND HEMOGLOBINS

Comp. Biochem. Physiol., Vol. 62A, pp. 1 to 7
© Pergamon Press Ltd 1979. Printed in Great Britain

THE R.V. Alpha Helix is a laboratory research ship designed primarily for physiological studies and designated as a National Oceanographic Facility under the University-National Oceanographic System (UNOLS). The ship is administered by the Scripps Institution of Oceanography. University of California, San Diego, and funding has been provided by the National Science Foundation.

J. Bonaventura, M. Brunori, M. Wilson.

J. Bonaventura, J. Wyman, M Reichlin, M. Brunori

…The present collection of papers are the results of the efforts in November and December, 1976. of an international group of 22 scientists from six countries to understand the properties and adaptations of the bloods and hemoglobins of fishes of the Amazon…

…Approximately 80% of the work of our expedition was done on board the ship; some blood samples were brought back to the participants' laboratories for the completion of the experiments. The variety and depth of work done on the ship gives some idea of the versatility of the Alpha Helix. Almost any physiological or biochemical experiment can—with proper planning—be done on board…

…But much more important in many ways is the theoretical framework developed by Jeffries Wyman for dealing with linked-function phenomena and cooperative processes in macromolecules…

AUSTEN RIGGS (Introduction)

Proc. Natl. Acad. Sci. USA
Vol. 74, No. 8, pp. 3128–3132, August 1977
Biochemistry

Oxygen "pulsed" cytochrome *c* oxidase: Functional properties and catalytic relevance

(electron transfer/oxidase intermediate/O_2 utilization)

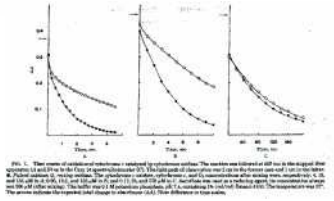
ERALDO ANTONINI*, MAURIZIO BRUNORI*†, ALFREDO COLOSIMO*, COLIN GREENWOOD‡, AND MICHAEL T. WILSON§

* Institutes of Chemistry and Biological Chemistry, Faculty of Medicine, University of Rome, C.N.R. Center for Molecular Biology, Rome, Italy; ‡ School of Biological Sciences, University of East Anglia, Norwich NOR 88 C, England; and § Department of Chemistry, University of Essex, Colchester CO4 3SQ, Essex, England

Communicated by Jeffries Wyman, March 17, 1976

ABSTRACT The kinetics of the reaction of cytochrome *c* with solubilized mammalian cytochrome *c* oxidase (ferrocytochrome *c*:oxygen oxidoreductase, EC 1.9.3.1) has been studied by a stopped-flow technique under two different experimental situations: (*i*) the completely oxidized enzyme (*resting oxidase* as obtained from the preparation) was mixed with reduced cytochrome *c*, and (*ii*) the completely reduced enzyme in the presence of reduced cytochrome *c* was exposed to a "pulse" of O_2 (*pulsed oxidase*). Both sets of experiments were performed with either "limiting" or "excess" O_2 (relative to oxidase), in the presence or absence of CO. Both the pre-steady-state events and the *steady-state* kinetics of cytochrome oxidase are found to be different in the two cases. This shows that the product of the reaction of fully reduced oxidase with O_2 (*pulsed oxidase*) is functionally different from the oxidase as prepared (*resting oxidase*). These differences are interpreted with the assumption of a different rate of intramolecular electron transfer in the *pulsed* and *resting* oxidases.

Implications of these experimental findings are discussed in the general framework of a tentative model for the catalytic cycle of the oxidase.



Nature Vol. 299 30 September 1982 421

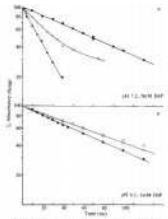
Stereochemistry of cooperative effects in fish and amphibian haemoglobins

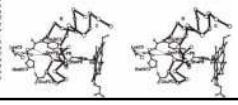
M. F. Perutz
MRC Laboratory of Molecular Biology, Hills Road, Cambridge CB2 2QH, UK

M. Brunori
Institute of Chemistry, Medicine, I University, and Department of Biochemistry, Medicine, II University, Rome, Italy

The low oxygen affinity of many fish haemoglobins at low pH is suggested to be due to the replacement by serine of the reactive cysteine F9β found in mammalian haemoglobins. Model building shows that hydrogen bonds between this serine and the C-terminal histidine stabilize the quaternary deoxy(T) structure. A stereochemical model for the binding of the allosteric effectors ATP or GTP is also advanced.

LACTIC ACID, secreted into the blood by a gland attached to the swim bladder, causes teleost fish haemoglobins to discharge oxygen into the bladder, and thus to raise the buoyancy of the fish[1]. This acid-activated discharge is known as the Root effect, but in fact it represents no more than an enhanced version of the alkaline Bohr effect exhibited by mammalian haemoglobins.





Mini-myoglobin: Preparation and Reaction with Oxygen and Carbon Monoxide

J. Mol. Biol. (1986) **188**, 73–76

Giampiero De Sanctis[1], Giancarlo Falcioni[1], Bruno Giardina[2]
Franca Ascoli[1] and Maurizio Brunori[3]

A domain of 108 amino acid residues (32 to 139), obtained by digestion of horse hea apomyoglobin with clostripain, was found to bind protoheme in a 1 to 1 molar ratio. Th domain is 33 amino acid residues larger than the protein segment encoded by the centr exon in seal myoglobin.

Flash photolysis experiments have shown that reconstituted "mini-myoglobin" is ve similar to myoglobin in the combination reaction with carbon monoxide and with oxyge and in the oxygen replacement reaction by carbon monoxide.

These experiments provide for the first time direct evidence for the presence of structural and functional domain, closely corresponding to the segment encoded by th central exon of the myoglobin gene, which contains the information for binding the natur heme and for maintaining the native folding typical of a respiratory protein.

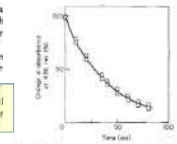
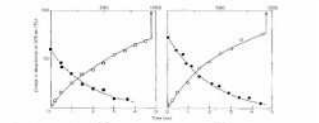


Figure 2. Time-course of the CO combination with horse heart mini-myoglobin (□), and myoglobin (○) followed by flash photolysis. The experiments were carried out at 2 μM-protein in 0·1 M-bis-Tris-HCl (pH 7·0). At this wavelength (436 nm), the observed total absorbance changes were 0·12 for mini-myoglobin and 0·15 for myoglobin; optical path, 1 cm. CO concentration was 50 μM. Temperature, 20°C.



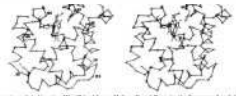
Aplysia limacina Myoglobin

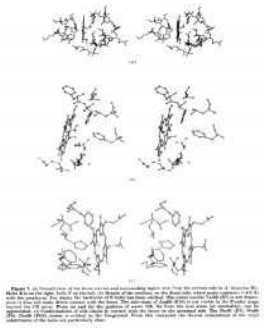
J. Mol. Biol. (1989) **205**, 529–544

Crystallographic Analysis at 1·6 Å Resolution

Martino Bolognesi†, Silvia Onesti‡, Giuseppina Gatti, Alessandro Coda
Paolo Ascenzi and Maurizio Brunori

The crystal structure of the ferric form of myoglobin from the mollusc *Aplysia limacina* has been refined at 1·6 Å resolution, by restrained crystallographic refinement methods. The crystallographic *R*-factor is 0·19. The tertiary structure of the molecule conforms to the common globin fold, consisting of eight α helices. The N-terminal helix A and helix G deviate significantly from linearity. The distal residue is recognized as Val63 (E7), which, however, does not contact the heme directly. Moreover the sixth (distal) co-ordination position of heme iron is not occupied by a water molecule at neutrality, i.e. below the acid–alkaline transition point of *A. limacina* myoglobin. The heme group sits in its crevice in the conventional orientation and no signs of heme isomerism are evident. The iron atom is 0·26 Å out of the porphyrin plane, with a mean Fe–N (porphyrin) distance of 2·01 Å. The co-ordination bond to the proximal histidine has a length of 2·05 Å, and forms an angle of 4° with the heme normal. A plane containing the imidazole ring of the proximal His intersects the heme at an angle of 29° with the (porphyrin) 4N–2N direction. Inspection of the structure of pH 9·0 reliefcates that a hydroxyl ion is bound to the Fe sixth co-ordination position.





Transient Spectroscopy of the Reaction of Cyanide with Ferrous Myoglobin EFFECT OF DISTAL SIDE RESIDUES

THE JOURNAL OF BIOLOGICAL CHEMISTRY
Vol. 265, No. 31, Issue of November 5, pp. 18886-18901, 1990

Andrea Bellelli, Giovanni Antonini, and Maurizio Brunori‡
Barry A. Springer and Stephen G. Sligar

The reaction of cyanide metmyoglobin with dithionite conforms to a two-step sequential mechanism with formation of an unstable intermediate, identified as cyanide bound ferrous myoglobin. This reaction was investigated by stopped-flow time resolved spectroscopy using different myoglobins, *i.e.* those from horse heart, *Aplysia limacina* buccal muscle, and three recombinant derivatives of sperm whale skeletal muscle myoglobin (Mb) (the wild type and two mutants). The myoglobins from horse and sperm whale (wild type) have in the distal position (E7) a histidyl residue, which is missing in *A. limacina* Mb as well as the two sperm whale mutants (E7 His → Gly and E7 His → Val).

All these proteins in the reduced form display an extremely low affinity for cyanide at pH < 10. The differences in spectroscopy and kinetics of the ferrous cyanide complex of these myoglobins indicate a role of the distal pocket on the properties of the complex. The two mutants of sperm whale Mb are characterized by a rate constant for the decay of the unstable intermediate much faster than that of the wild type, at all pH values explored. Therefore, we envisage a specific role of the distal His (E7) in controlling the rate of cyanide dissociation and also find that this effect depends on the protonation of a single ionizable group, with $pK \approx 7.2$, attributed to the E7 imidazole ring.

The results on *A. limacina* Mb, which displays the slowest rate of cyanide dissociation, suggests that a considerable stabilizing effect can be exerted by Arg E10 which, according to Bolognesi *et al.* (Bolognesi, M., Coda, A., Frigerio, F., Gatti, G., Ascenzi, P., and Brunori, M. (1990) *J. Mol. Biol.* 213, 621–625), interacts inside the pocket with fluoride bound to the ferric heme iron.

A mechanism of control for the rate of dissociation of cyanide from ferrous myoglobin, involving protonation of the bound anion, is discussed.

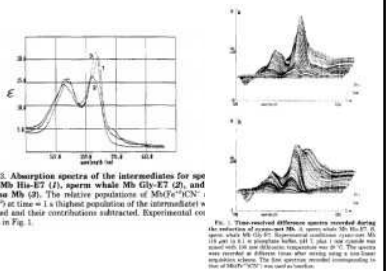


FIG. 3. Absorption spectra of the intermediates for spe whale Mb His-E7 (*1*), sperm whale Mb Gly-E7 (*2*), and *limacina* Mb (*3*). The relative populations of $Mb(Fe^{II})CN^-$: $Mb(Fe^{II})$ at time = 1 s (highest population of the intermediate) calculated and their contributions subtracted. Experimental co tions as in Fig. 1.

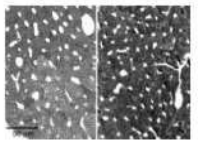
FIG. 1. Time-resolved difference spectra recorded during the reduction of cyano-met Mb. A, sperm whale Mb His-E7 (*1*, sperm whale Mb Gly-E7. Experimental conditions: cyano-met Mb 116 μM in 0.1 M phosphate buffer, pH 7, plus 1 mM cyanide was mixed with 116 mM dithionite; temperature was 20 °C. The spectra were recorded at different times after mixing using a tem-linear acquisition scheme. The first spectrum recorded corresponding to that of $Mb(Fe^{III})CN^-$) was used as baseline.

Nitric oxide, cytochrome-*c* oxidase and myoglobin

Opinion
TRENDS in Biochemical Sciences Vol.26 No.1 January 2001

Maurizio Brunori

Myoglobin, the monomeric haemoprotein expressed in red muscle, is reported in biochemistry and physiology textbooks to function as an intracellular oxygen carrier and oxygen reservoir. Here, Maurizio Brunori argues that myoglobin can also play the role of intracellular scavenger of nitric oxide, an inhibitor of mitochondrial cytochrome-*c* oxidase, thereby protecting respiration in the skeletal muscle and the heart.



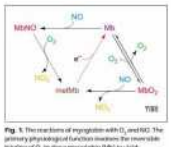
the NO scavenging function of MbO_2 should be taken into consideration when describing the physiology of skeletal muscle and heart at the molecular level, and its role in protecting respiration might be of significance in several pathophysiological states involving an increased NO flux.

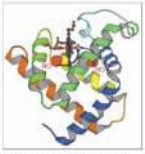
Nitric oxide moves myoglobin centre stage

Maurizio Brunori

Research Update TRENDS in Biochemical Sciences Vol.26 No.4 April 2001

It has been proposed that myoglobin (Mb), besides being an oxygen carrier, plays the role of a nitric oxide (NO) scavenger in heart and skeletal muscle. A paper reporting data obtained using perfused hearts isolated from either wild-type or Mb-knockout mice provides the first experimental evidence for this novel function of Mb. The biochemical basis underlying the effects of NO on cardiac function is outlined in this article, beginning with the idea that this gas is an inhibitor of cytochrome-c oxidase. Some of the consequences of this new role of Mb and a molecular mechanism to account for the high reactivity of oxymyoglobin with NO are also briefly discussed.





Cavities and packing defects in the structural dynamics of myoglobin

EMBO reports vol. 2 | no. 8 | pp 674–679 | 2001

Maurizio Brunori* & Quentin H. Gibson‡

Small globular proteins contain internal cavities and packing defects that reduce thermodynamic stability but seem to play a role in controlling function by defining pathways for the diffusion of the ligand/substrate to the active site. In the case of myoglobin (Mb), a prototype for structure-function relationship studies, the photosensitivity of the adduct of the reduced protein with CO, O_2 and NO allows events related to the migration of the ligand through the matrix to be followed. The crystal structures of intermediate states of wild-type (wt) and mutant Mbs show the photolysed CO to be located either in the distal heme pocket (primary docking site) or in one of two alternative cavities (secondary docking sites) corresponding to packing defects accessible to an atom of xenon. These results convey the general picture that pre-existing internal cavities are involved in controlling the dynamics and reactivity of the reactions of Mb with O_2 and other ligands, including NO.

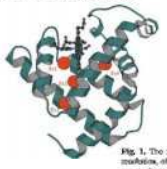


Fig. 1. The xenon binding sites of myoglobin. Crystal structure, at 1.9 Å resolution, of sperm whale met-Mb under Xe gas at 7 atm, pressure. The first seven atoms bound are shown as red spheres, and the protein backbone as a ribbon: the heme is seen edge-on, with the proximal His93 (H8) on the left. Xe^1 and Xe^2 are relatively close to each other on the proximal side of the heme; Xe^1 resides in a cavity near the surface, far (13.5 Å) from the iron; Xe^2 is on the distal side of the heme, ~5 Å from the iron (modified from Tilton *et al.*, 1984).

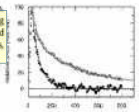


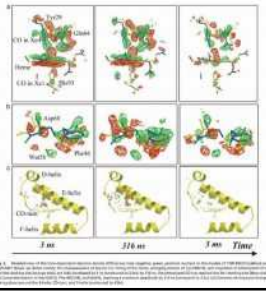
Fig. 3. Geminate rebinding of NO to myoglobin. The figure depicts the time-course of geminate rebinding of NO to the Mb mutant Mb-YQR (L29Y, H64Q, T67R; modified from Brunori *et al.*, 1999b). The upward deflection at shorter times indicates the laser-induced photodissociation obtained with a 9 ns laser pulse of green light. The geminate recombination of dissociated NO yields a biphasic time-course in the absence of xenon (open circles); however, under xenon at high pressure (filled circles), the geminate recombination becomes faster and more homogeneous because the slow kinetic component essentially disappears (and the total amplitude of the excursion decreases to one half, not shown in this representation). This result is consistent with the hypothesis that the slower component of the geminate rebinding reflects the ligand trapped in secondary docking sites, which in the presence of xenon are not available to host the ligand.

Complex landscape of protein structural dynamics unveiled by nanosecond Laue crystallography

PNAS | July 22, 2003 | vol. 100 | no. 15 8704–8709

Dominique Bourgeois[†‡¶], Beatrice Vallone[§], Friedrich Schotte[††], Alessandro Arcovito[‡], Adriana E. Miele[‡], Giuliano Sciara[‡], Michael Wulff[¶], Philip Anfinrud[††], and Maurizio Brunori[§]

Although conformational changes are essential for the function of proteins, little is known about their structural dynamics at atomic level resolution. Myoglobin (Mb) is the paradigm to investigate conformational dynamics because it is a simple globular heme protein displaying a photosensitivity of the iron–ligand bond. Upon laser photodissociation of carboxymyoglobin Mb a nonequilibrium population of protein structures is generated that relaxes over a broad time range extending from picoseconds to milliseconds. This process is associated with migration of the ligand to cavities in the matrix and with a reduction in the geminate rebinding rate by several orders of magnitude. Here we report nanosecond time-resolved Laue diffraction data to 1.55-Å resolution on a Mb mutant, which depicts the sequence of structural events associated with this extended relaxation. Motions of the distal E-helix, including the mutated residue Gln-64(E7), and of the CD-turn are found to lag significantly (100–300 ns) behind local rearrangements around the heme such as heme tilting, iron motion out of the heme plane, and swinging of the mutated residue Tyr-29(B10), all of which occur promptly (≤3 ns). Over the same delayed time range, CO is observed to migrate from a cavity distal to the heme known to bind xenon (called Xe4) to another such cavity proximal to the heme (Xe1). We propose that the extended relaxation of the globin moiety reflects reequilibration among conformational substates known to play an essential role in controlling protein function.



The structure of carbonmonoxy neuroglobin reveals a heme-sliding mechanism for control of ligand affinity

PNAS | December 14, 2004 | vol. 101 | no. 50 17351–17356

Beatrice Vallone*†, Karin Nienhaus*†, Annemarie Matthes‡, Maurizio Brunori*, and G. Ulrich Nienhaus*§¶

Neuroglobin (Ngb), a globular heme protein expressed in the brain of vertebrates, binds oxygen reversibly, with an affinity comparable to myoglobin (Mb). Despite low sequence identity, the overall 3D fold of Ngb and Mb is very similar. Unlike in Mb, in Ngb the sixth coordination position of the heme iron is occupied by the distal histidine, in the absence of an exogenous ligand. Endogenous ligation has been proposed as a unique mechanism for affinity regulation and ligand discrimination in heme proteins. This peculiarity might be related to the still-unknown physiological function of Ngb. Here, we present the x-ray structure of CO-bound ferrous murine Ngb at 1.7 Å and a comparison with the 1.5-Å structure of ferric bis-histidine Ngb. We have also used Fourier transform IR spectroscopy of WT and mutant CO-ligated Ngb to examine structural heterogeneity in the active site. Upon CO binding, the distal histidine retains (by and large) its position, whereas the heme group slides deeper into a preformed crevice, thereby reshaping the large cavity (~290 Å³) connecting the distal and proximal heme sides with the bulk. The heme relocation is accompanied by a significant decrease of structural disorder, especially of the EF loop, which may be the signal whereby Ngb communicates hypoxic conditions. This unexpected structural change unveils a heme-sliding mechanism of affinity control that may be of significance to understanding Ngb's role in the pathophysiology of the brain.

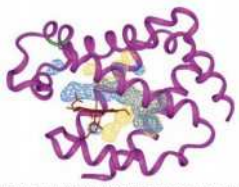


Fig. 3. Cavities in NgbCO (blue) and unliganted metNgb (yellow) as determined by using xenon (46). The position of Ser-55 is highlighted in green.

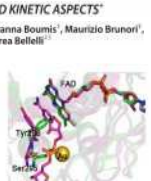
Inhibition of *Schistosoma mansoni* Thioredoxin-glutathione Reductase by Auranofin

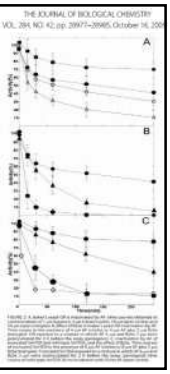
THE JOURNAL OF BIOLOGICAL CHEMISTRY VOL. 284, NO. 42, pp. 28977–28985, October 16, 2009

STRUCTURAL AND KINETIC ASPECTS

Francesco Angelucci[‡1], Ahmed A. Sayed[§1,2], David L. Williams[§¶], Giovanna Boumis[‡], Maurizio Brunori[‡], Daniela Dimastrogiovanni[‡], Adriana E. Miele[‡], Frida Paulyᵀ, and Andrea Bellelli[‡3]

Schistosomiasis is a parasitic disease affecting over 200 million people currently treated with one drug, praziquantel. A possible drug target is the seleno-protein thioredoxin-glutathione reductase (TGR), a key enzyme in the pathway of the parasite for detoxification of reactive oxygen species. The enzyme is a unique fusion of a glutaredoxin domain with a thioredoxin reductase domain, which contains a selenocysteine (Sec) as the penultimate amino acid. Auranofin (AF), a gold-containing compound already in clinical use as an anti-arthritic drug, has been shown to inhibit TGR and to substantially reduce worm burden in mice. Using x-ray crystallography we solved (at 2.5 Å resolution) the structure of wild type TGR incubated with AF. The electron density maps show that the actual inhibitor is gold, released from AF. Gold is bound at three different sites not directly involving the C-terminal Sec residue; however, because the C terminus in the electron density maps is disordered, we cannot exclude the possibility that gold may also bind to Sec. To investigate the possible role of Sec in the inactivation kinetics, we tested the effect of AF on a model enzyme of the same superfamily, *i.e.* the naturally Sec-lacking glutathione reductase, and on truncated TGR. We demonstrate that the role of selenium in the onset of inhibition by AF is catalytic and can be mimicked by an external source of selenium (benzeneselenol). Therefore, we propose that Sec mediates the transfer of gold from its ligands in AF to the redox-active Cys couples of TGR.





The Folding Pathway of the KIX Domain

DOI: 10.1021/acschembio.7b00289 ACS Chem. Biol. XXXX, XXX, XXX−XXX

Francesca Troilo,[†‡] Daniela Bonetti,[†] Angelo Toto,[†] Lorenzo Visconti,[†] Maurizio Brunori,[†] Sonia Longhi,[†] and Stefano Gianni*[†§]

ABSTRACT: The KIX domain is an 89-residues globular domain with an important role in mediating protein−protein interactions. The presence of two distinct binding sites in such a small domain makes KIX a suitable candidate to investigate the effect of the potentially divergent demands between folding and function. Here, we report an extensive mutational analysis of the folding pathway of the KIX domain, based on 30 site-directed mutants, which allow us to assess the structures of both the transition and denatured states. Data reveal that, while the transition state presents mostly native-like interactions, the denatured state is somewhat misfolded. We mapped some of the non-native contacts in the denatured state using a second round of mutagenesis, based on double mutant cycles on 15 double mutants. Interestingly, such a misfolding arises from non-native interactions involving the residues critical for the function of the protein. The results described in this work appear to highlight the diverging demands between folding and function that may lead to misfolding, which may be observed in the early stages of folding.

The Folding Pathway of the KIX Domain

DOI: 10.1021/acschembio.7b00289
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ABSTRACT: The KIX domain is an 89-residues globular domain with an important role in mediating protein−protein

Published: May 1, 2017

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CONCLUSIONI:

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EDITORIAL NOTE

Ten Qualities of a Good Researcher

Luis H. Toledo-Pereyra

Editor-in-Chief

ABSTRACT

Writing about the 10 Qualities of a Good Researcher represents a great responsibility since it is not simple to assemble in a concise manner all the important qualities of a good researcher. Knowing the difficulties lying ahead, I would like to suggest the following qualities: interest, motivation, inquisitiveness, commitment, sacrifice, excelling, knowledge, recognition, scholarly approach, and integration. The characterization and understanding of these qualities would be extremely helpful to those who are beginning the exciting field of research.
To be a good researcher first requires the intention to be involved in research and immediately thereafter to show a dedicated interest to do the best research possible. From there we must accumulate the knowledge needed to advance the current ideas already existent in the research world. The intention of this writing is to introduce 10 qualities that I consider essential for a good researcher to succeed.

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EDITORIAL NOTE

Ten Qualities of a Good Researcher

Luis H. Toledo-Pereyra

Rigore scientifico

ABSTRACT

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…INFINE, non si può tacere di un altro interesse del prof. Maurizio Brunori in cui egli eccelle ed anch'esso facente parte della tradizione di una parte consistente della Scuola Romana di Biochimica:

Da Alessandro Rossi Fanelli,
A Eraldo Antonini,
A Maurizio Brunori
e infine anche a diversi allievi…

LA VELA !

S/Y **MADIFRA II** del Prof. Maurizio Brunori

One tonner disegnato da Dick Carter e costruito in lamellare incrociato da Gallinari; varato nel 1974 ad Anzio

Ultima vittoria trovata sul web:
1° nella Classe Crociera Veloce
Argentario Sailing Week 16/06/2016

Fonti principali:

ME STESSO per aver avuto la fortuna di avere il Professor Maurizio Brunori come Maestro

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Ringraziamenti