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MOLECULAR DESCRIPTION OF DIOXYGEN BINDING AND REDOX CONTROL IN HEMOGLOBIN - A REVIEW

Priya Arjun Sharma
T.Y.B.Sc. (Chemistry)
Priyasharma151204@gmail.com

ABSTRACT

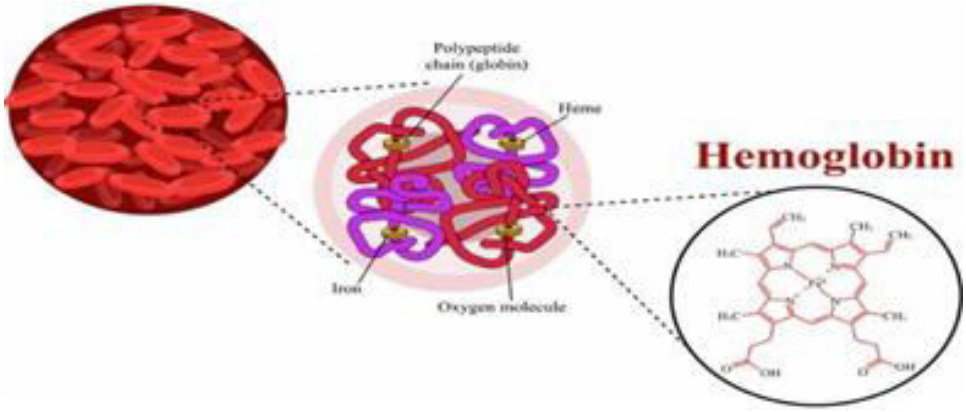
Hemoglobin (Hb) and myoglobin (Mb) are essential oxygen-binding metalloproteins whose function depend on precise control of iron spin states, coordination geometry, and protein environment. This review integrate modern biochemical perspective on oxygenation, redox reaction, and allosteric regulation. Emphasis is placed on iron–porphyrin geometry, dioxygen bonding models, cooperativity, and the distinction between thermodynamic and kinetic control of oxidation. Comparative analysis highlight how theoretical electronic-structure model align with physiological behavior and experimental observations.

Keywords: *Dioxygen binding, hemoglobin, myoglobin, heme proteins, iron–porphyrin, spin state, bio-inorganic chemistry.*

INTRODUCTION

The reversible binding of molecular oxygen by hemoglobin enable aerobic life. Despite the strong thermodynamic tendency of oxygen to oxidize ferrous iron (Fe^{2+} Fe^{3+}), hemoglobin achieve controlled oxygenation without rapid oxidation. Understanding this balance require integration of electronic structure theory, spin-state chemistry, and protein allostery.

Early quantum chemical calculation provided a molecular-level explanation for oxygen binding, challenging long-standing assumptions about low-spin iron state in oxyhemoglobin. Later biochemical studies expanded this understanding to include redox regulation, oxidative stress, and evolutionary adaptation.



Structure of the Heme Active Site

https://share.google/sXSwV5g2KXM0SFN5A

The heme group consist of an iron atom coordinated to four nitrogen atoms of a porphyrin ring. A proximal histidine from the globin protein serves as the fifth ligand, while the sixth coordination site is available for dioxygen binding.

Structure of the Heme Group in Hemoglobin (Schematic)

IRON SPIN STATES AND COORDINATION GEOMETRY

Four-Coordinate Fe–Porphyrin Complexes Quantum chemical calculations demonstrates that both high-spin (S = 2) and intermediate-spin (S = 1) ferrous iron state are energetically accessible in four-coordinate Fe–porphyrin systems. Importantly, iron remain in the porphyrin plane for both states, disproving the long-held belief that high-spin Fe^{2+} is inherently too large to fit within the porphyrin cavity.

Five-Coordinate Deoxyhemoglobin

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In deoxyhemoglobin, iron is five-coordinate and displaced approximately 0.s–0.4 Å out of the porphyrin plane.

displacement arises primarily from nonbonded repulsive interaction between the axial ligand and porphyrin nitrogen orbitals, rather than from steric size effect of high-spin iron alone.

MODELS OF DIOXYGEN BINDING OZONE (PAULING) MODEL

Pauling

http3://3hare.google/NbMBfkkOfOK2O6uZJ

Thi3 model predict3 limited charge tran3fer (~0.1 electron) and 3succe33fully explain3 the ob3erved 3tructural and magnetic propertie3 of oxyhemoglobin.

REJECTION OF THE WEI33 MODEL

The Wei33 model propo3e3 a full electron tran3fer re3ulting in Fe^{3+}–O_2^- character. However, computational re3ult3 3how in3ufficient charge tran3fer to 3upport thi3 de3cription, favoring the ozone model in3tead.

SIX-COORDINATE OXYHEMOGLOBIN

Upon oxygen binding, hemoglobin become3 3ix-coordinate and the iron atom move3 into the porphyrin plane. Although the oxyhemoglobin complex i3 diamagnetic, calculation3 reveal that thi3 doe3 not ari3e from a cla33ical low-3pin Fe^{2+} 3tate. In3tead, 3pin coupling between iron and dioxygen orbital3 produce3 an overall 3inglet 3tate.

COOPERATIVITY AND ALLO3TERIC EFFECT3

Oxygen binding induce3 a tran3ition from the low-affinity T-3tate to the high-affinity R-3tate of hemoglobin. The a33ociated iron movement toward the porphyrin plane i3 relatively 3mall (~0.04 Å), indicating that cooperativity i3 governed mainly by protein conformational change3 rather than large metal di3placement3.

T-3tate (deoxy) Fe out of plane Low O2 affinity R-3tate (oxy) Fe in plane High O2 affinity Redox Behavior of Hemoglobin Hemoglobin oxygenation mu3t be di3tingui3hed from oxidation. While oxygenation i3 rever3ible, oxidation produce3 methemoglobin (Fe^{3+}), which cannot bind oxygen. HbFe2+ + O2 HbFe2+–O2 HbFe2+ +O2 HbFes+ +O2

Only a 3mall fraction (1–s%) of hemoglobin undergoe3 oxidation daily under phy3iological condition3, highlighting the efficiency of intrin3ic protective mechani3m3.

THERMODYNAMIC V3 KINETIC CONTROL

Redox potential determine3 whether oxidation i3 thermodynamically favorable, whilea3 reaction kinetic3 determine how rapidly oxidation occur3.

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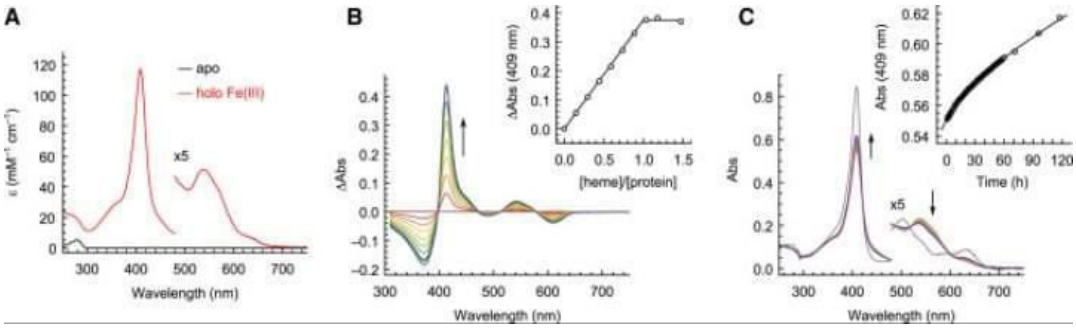

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Hemoglobin resists oxidation primarily through kinetic barriers imposed by the protein environment.

PHYSIOLOGICAL AND BIOMEDICAL IMPLICATIONS

A molecular understanding of hemoglobin oxygenation and redox control is essential for interpreting oxidative stress, hemoglobinopathies, and the design of hemoglobin-based blood substitutes. Theoretical insights into iron–oxygen bonding provide guidance for minimizing oxidative toxicity in biomedical applications.

Comparative Summary Chart

Table: Comparison of Hemoglobin States

Feature	Deoxy Hb	Oxy Hb	Met Hb
Iron state	Fe^{2+}	Fe^{2+}	Fe^{3+}
Spin	High	Coupled (S = 0)	High
Coodrination number	5	6	6
Fe position	Out of plane	In plane	In plane
Magnetism	Paramagnetic	Diamagnetic	Paramagnetic
Function	O_2 release	O_2 transport	Inactive

CONCLUSION

Hemoglobin function arises from subtle electronic and structural effects rather than drastic changes in iron oxidation or spin state. Ab initio calculations reveal that dioxygen binding is best described by an ozone-like model and that cooperativity and redox stability are primarily controlled by protein-mediated kinetics. These findings remain fundamental to modern bioinorganic chemistry and hemoglobin research.

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