

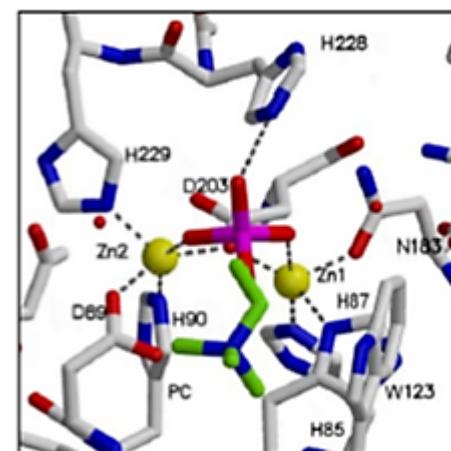
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Bioinorganic Chemistry

“The inorganic chemistry of the biological systems”

“Coordination chemistry applied to life”



Zn at the active site of esterase
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Bioinorganic Chemistry

Bioinorganic chemistry: what does it study?

Partially *inorganic* natural products:

- **Metalloenzymes**, especially:
 - oxidoreductases (**Fe, Cu, Mn, Mo, Ni, V**),
 - hydrolases (e.g. peptidases, phosphatases: **Zn, Mg; Ca, Fe**)
- **Non-enzymatic metalloproteins** (e.g. hemoglobin: **Fe**)
- **Low-molecular-weight natural products** (e.g. chlorophyll: **Mg**) and ATP-**Mg** complex
- **Coenzymes, vitamins** (e.g. vitamin B₁₂: **Co**)
- **Nucleic acids**: (e.g. ADN-M⁺ⁿ, M = **Mg**)
- **Hormones** (e.g. thyroxine, triiodothyronine: **I**)
- **Antibiotics** (e.g. ionophores: valinomycin-**K**)
- **Bio-minerals** (i.e. bones, teeth, shells, coral, pearls: **Ca, Si, . . .**).

The field of bioinorganic chemistry aims to understand the role of elements, specially metallic ones fulfilling specialized functions.

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5. Catalytic processes
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Chapter 1 - Introduction

- ➔ ■ 1.1 Elements essential for life
- 1.2 Terminology and Bio-ligands

1.1 Essential elements

The elements in biology:

- Around 25 are known to be essential for life:
 - *Major* elements: C, N, O, P, S, H; Na, K, Mg, Ca, Cl
 - *Trace* elements: some *d*-block elements such as Fe, Zn, Cu,...
- Toxic elements: Hg, Pb,...
- Medicinal elements (radio diagnostics, image signaling, chemotherapy...): Tc, Gd, Ba, Li, Pt, Au,...

Selection of the elements by the organisms

Elements have been selected by their:

➤ Intrinsic chemical properties

- e.g. **Zn**: acid-base catalysis, zinc fingers
- e.g. **Ca**: cellular signaling properties, solid-state structural function

➤ Availability:

- e.g. **Zn** *versus* **Co**
- e.g. **Fe** *versus* **Cu**

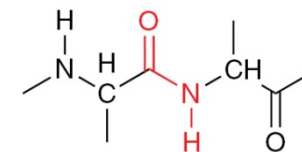
Biological roles of inorganic elements

1. **Solid-state structural functions** (endo- o exo-skeletons): **Ca, Mg and Zn** (as di-cations); **P, O, C, S, Si** and **F** (as parts of anions).
2. **Charge carriers** for fast information transfer (ion channels, ion pumps): **Na⁺, K⁺ and Ca²⁺**.
3. **Lewis acid/Lewis base catalysis** for organic products metabolism: **Zn²⁺ and Mg²⁺**.
4. **Transfer of electrons** for short-term energy conversion; mainly dependent of **redox-active metal centers**:
 1. **FeI/FeII/FeIII/FeIV**
 2. **CuI/CuII**
 3. **MnII/MnIII/MnIV**
 4. **MoIV/MoV/MoVI**
 5. **CoI/CoII/CoIII**
 6. **NiI/NiII/NiIII**.
5. **Multi-electron transfer** for redox activation of small, highly symmetrical molecules:
 1. Conversion of **H⁺** into **H₂** (hydrogenases): **Fe, Ni, Se**;
 2. Uptake, transport, storage and conversion (**Fe, Cu**) and, the opposite, generation (**Mn**), of **³O₂**;
 3. Cycle of nitrogen, including molecular fixation of **N₂** and its conversion into ammonia (**Fe, Mo, V**);
 4. Reduction of **CO₂** with hydrogen to give methane ("chemistry C1": **Ni, Fe**).
6. **Typical organometallic reactivity** by cobalamine coenzymes (σ bond between **Co** and alkyl groups).

Chapter 1 - Introduction

- 1.1 Elements essential for life
- ➔ ■ 1.2 Terminology and Bio-ligands

1.2 Terminology (a)



- peptide, peptide bond, polypeptide, protein
- metalloprotein: proteins which contain one or more metallic ions
- apoprotein: protein without its cofactor (i.e. M^{+n})
- cofactor
- metalloenzyme
- apoenzyme

apoprotein + Cofactor = Heteroprotein (ex. Metalloprotein)
(inactive protein) (no peptide) (active protein)

apoenzyme + Coenzyme = Holoenzyme (ex.: Metalloenzyme)

Cofactors.:

- inorganic: Mg^{2+} , Cu^+ , Mn^{2+} , Fe-S centers,...
- organic: -**coenzymes**: NAD^+ , $NADP^+$, FAD, ...
-**prosthetic groups**: Hemo,...

Terminology (b)

➤ **All metalloproteins are NOT metalloenzymes**

- Functions of metalloproteins:
 - a) Transport (**Hemoglobin, Hemocyanin, Hemerythrin,...**)
 - b) Initiation and regulation (**Calmodulin**)
 - c) Catalysis = enzymes

➤ **Enzyme: CATALYST in Biochemistry**

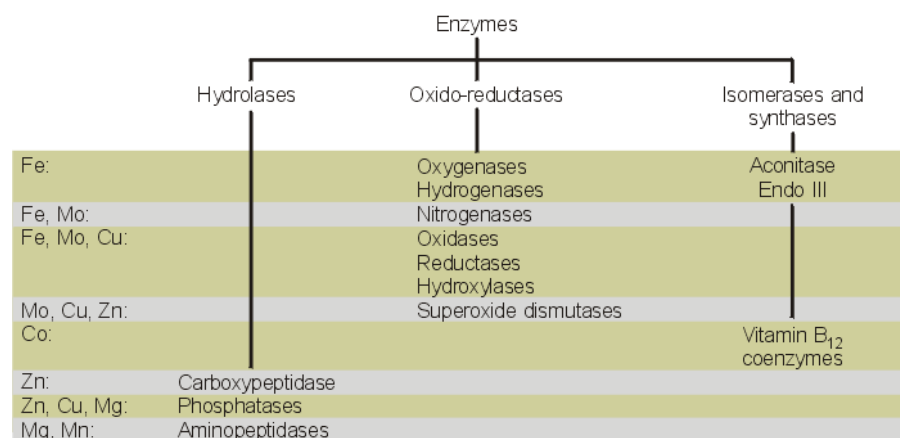
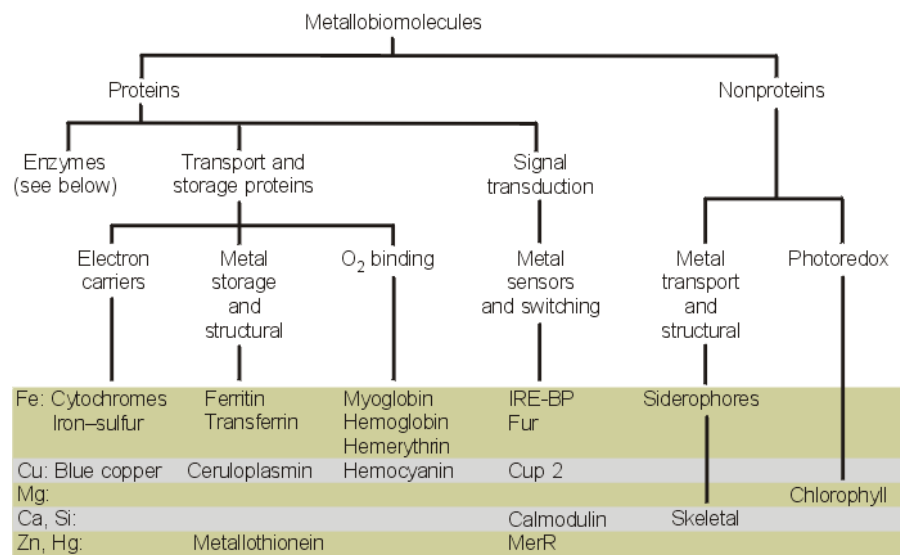
- The enzymes are designated from its function:
 - a) Acid-base hydrolysis: **hydrolases**
 - b) Redox reactions: **oxidases**
 - c) Processes involved in C-C bond changes: **synthases and isomerases**

Metal coordinating amino acids:
preferred aa: $\rightarrow M^{+n}$ combinations

- **Histidine** (N) = Zn(II), Cu(II,I), Fe(II)
- **Methionine** (S, thioether) = Fe(II, III), Cu(I,II)
- **Cysteine** (S^- , thiolate) = Zn(II), Cu(II,I), Fe(III,II)
- **Tyrosine** (O^- , phenolate) = Fe(III)
- **Aspartic and glutamic acid** (OO^- , carboxylate) = Fe(III,II), Zn(II), Mg(II), Ca(II)
- **Glycine** (as carbamate) = Mg(II) (in a photosynthesis enzyme)

Biomolecules containing metal ions

Table 19.2 The classification of some biomolecules containing metal ions

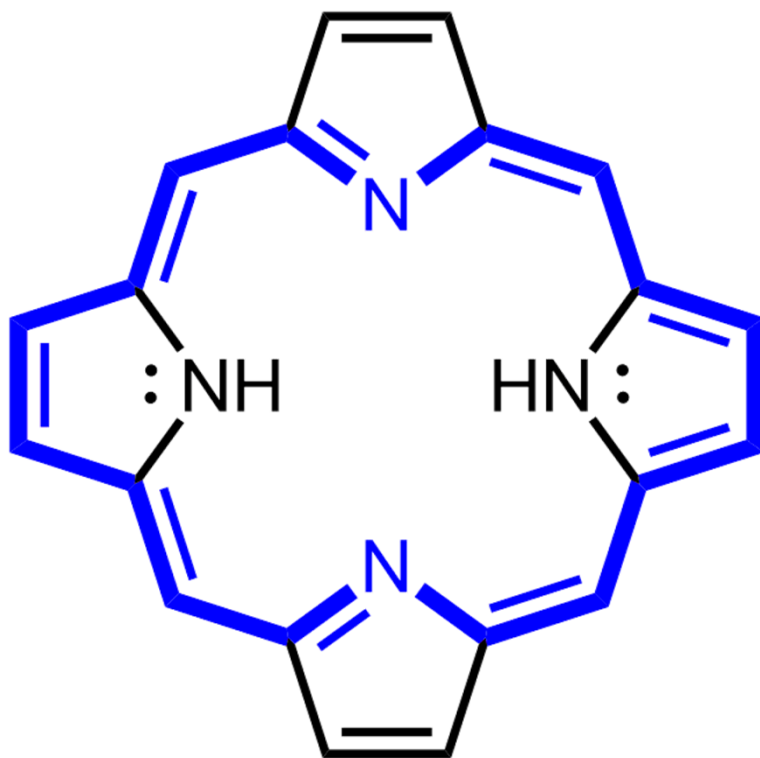


Augmented version of J.A. Ibers and R.H. Holm, *Science* **209**, 223 (1980)

Bioinorganic Chemistry

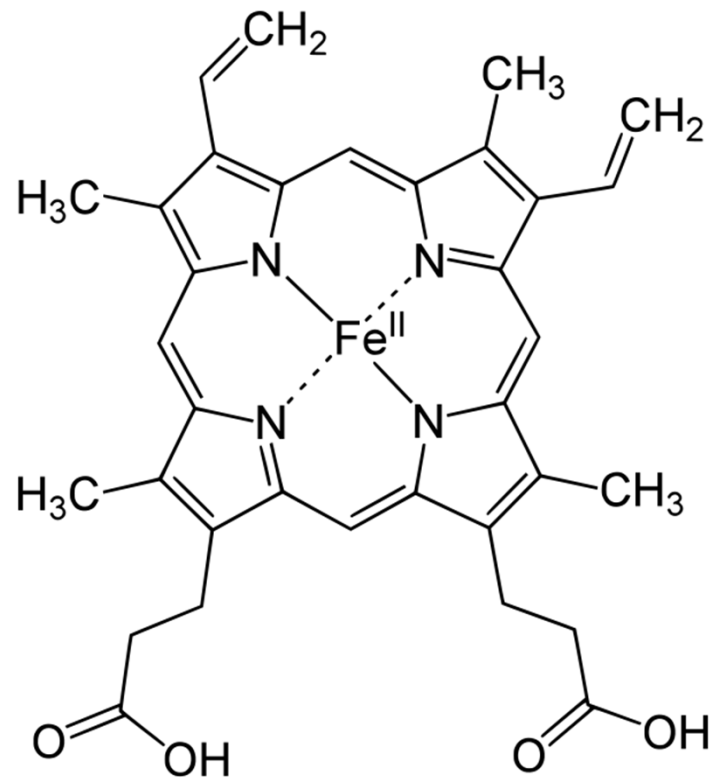
Table included in: *Inorganic Chemistry, Shriver and Atkins*, 3rd Ed., 1999, Oxford.

Special Bioligands: Porphyrins



The 18-electron cycle of porphin, the parent structure of porphyrin, highlighted. (Several other choices of atoms, through the pyrrole nitrogens, for example, also give 18-electron cycles.)

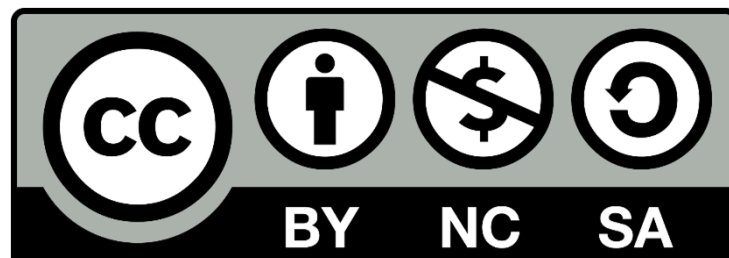
Metalloporphyrins



Heme b group

Este material docente ha sido elaborado en el marco de una convocatoria de ayudas para el desarrollo de proyectos de innovación educativa y mejora de la calidad docente (convocado por el Vicerectorat de Polítiques de Formació i Qualitat Educativa de la Universitat de València, en el curso 2017-2018)

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