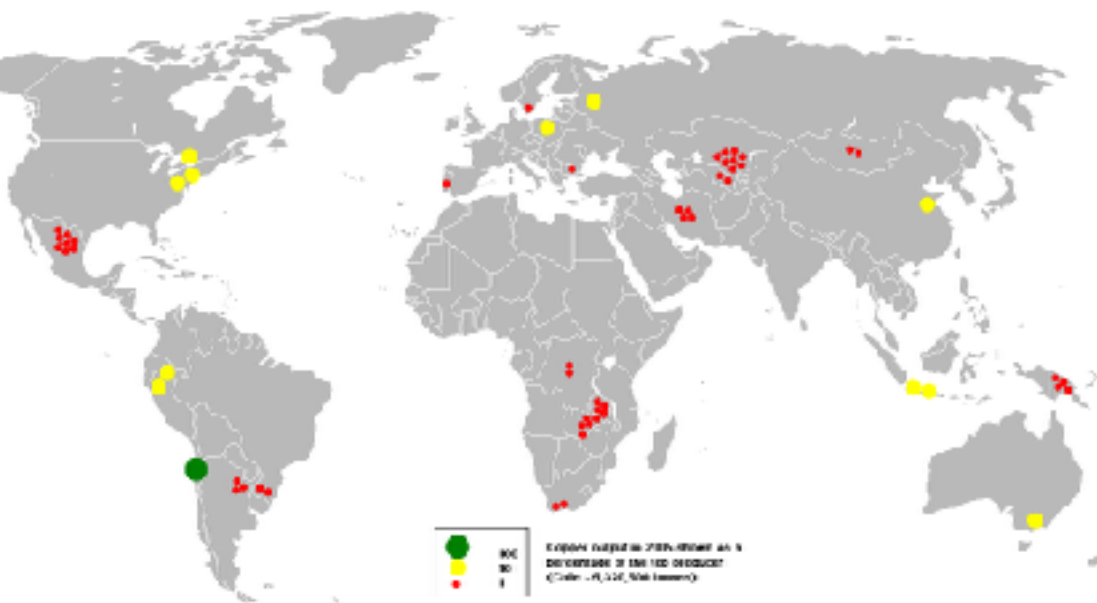


Química Bioinorgánica De Cobre

Curso de Introducción a la Química Bioinorgánica.
Dr. Manuel I. Azócar
Universidad de Santiago de Chile

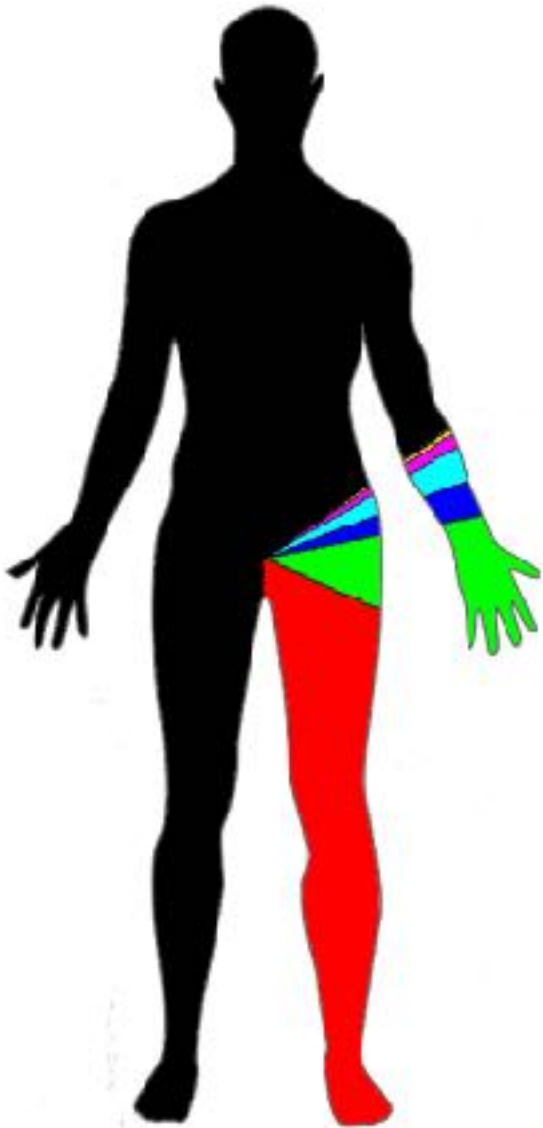
Generalidades del Cobre



Numero atómico	29
Valencia	1,2
Estado de oxidación	+1, +2
Conf. Electrónica	[Ar]3d ¹⁰ 4s ¹
Masa atómica (g/mol)	63,54

Abundancia %	Elemento
46.71	O
27.69	Si
8.07	Al
5.05	Fe
3.65	Ca
2.75	Na
2.58	K
2.08	Mg
0.12~	Cu

Generalidades del Cobre: *Composición elemental en un humano de 70 Kgs.*



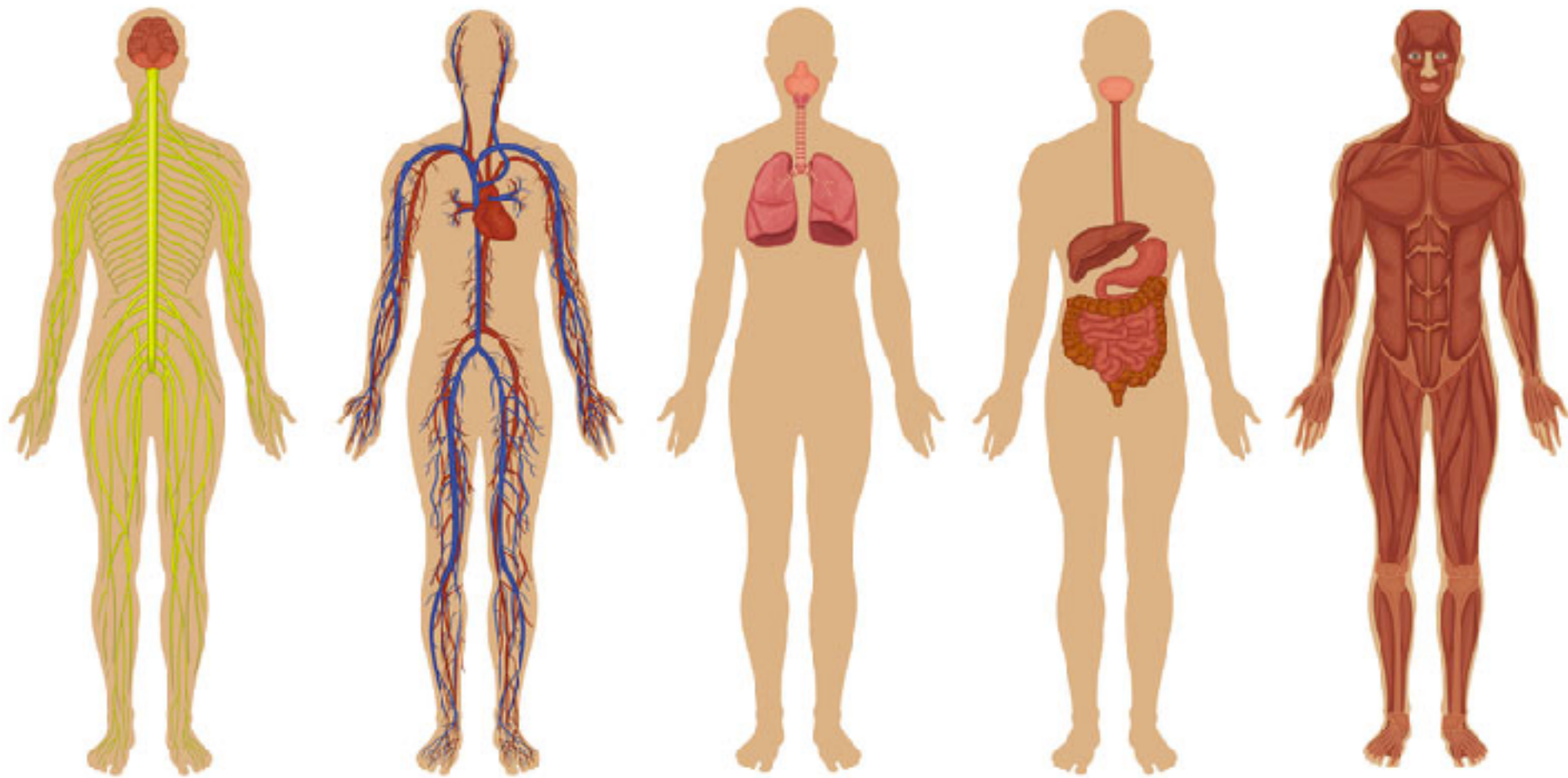
Masa de elementos e iones minerales

Oxígeno	44 Kg	Fosforo	0,68 Kg
Carbono	12.6 Kg	Potasio	0,250 Kg
Hidrógeno	6.6 Kg	Cloro	0,115 Kg
Nitrógeno	1.8 Kg	Azufre	0,100 Kg
Calcio	1.7 Kg	Sodio	0,070 Kg
		Magnesio	0,042 Kg

Generalidades del Cu: *Composición elemental en un humano de 70 Kgs.*



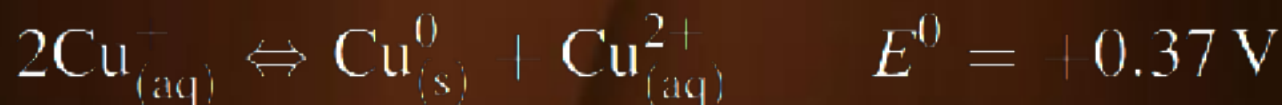
Elementos traza y ultra traza			
Fe	5 g	Pb	0,035 g
Zn	2,3 g	Ba	0,021 g
Si	1,4 g	Mo	0,014 g
Cu	0,11 g	B	0,014 g
F	0,8 g	As	0,003 g
Br	0,14 g	Co	0.003 g
Sn	0,14 g	Cr	0.003 g
Mn	0,070 g	Ni	0.003 g
I	0.070 g	Se	0.002 g
Al	0.035 g	Li / V	0.002 g



9 mg en cerebro - 6 mg en la sangre -
3 mg en riñones - 1,5 mg en corazón

10 mg en Hígado - 26 mg en músculos
46 mg en huesos

Generalidades del Cobre:



$$\Delta G^0 = -nFE \quad \Delta G^0 = -RT \ln K$$

$$K = \frac{[\text{Cu}^{2+}][\text{Cu}]}{[\text{Cu}^{+}]^2} = 10^6$$

Con ligandos biológicos:

$\text{Cu(II)} / \text{Cu(I)} = +200\text{mV}$ hasta $+800\text{mV}$

Generalidades del Cobre: Geometrías posibles

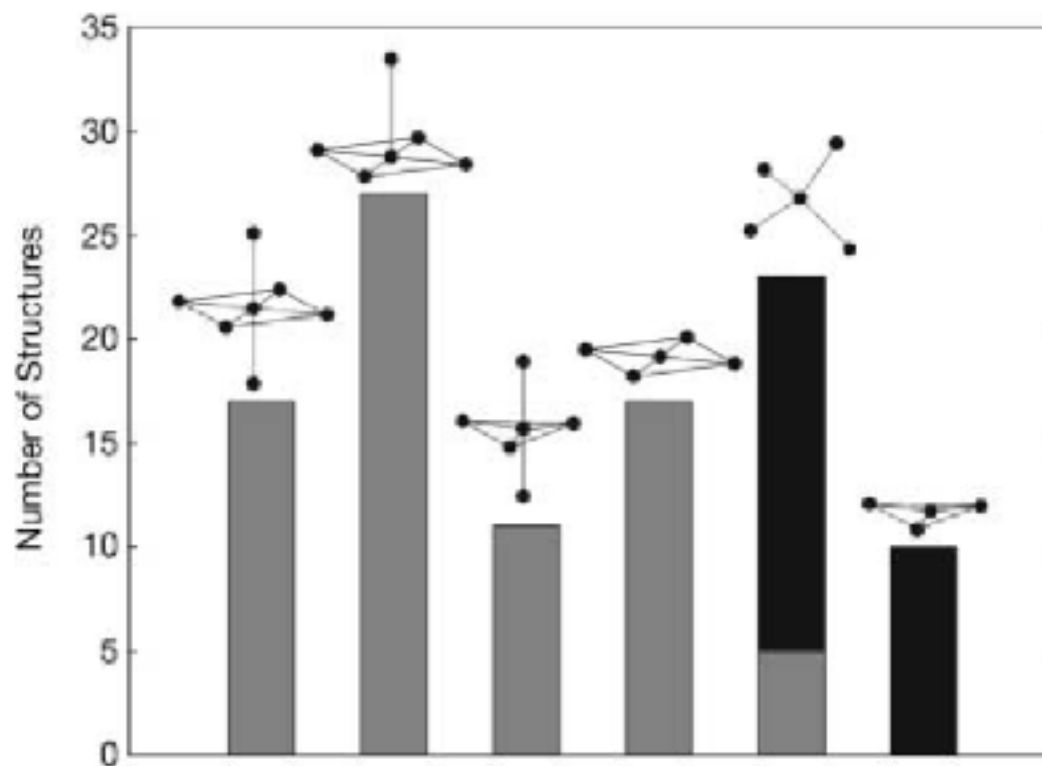
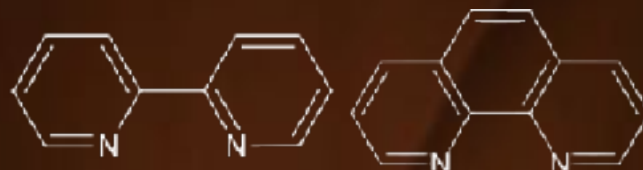


Fig. 1 Coordination geometries of the inorganic copper compounds examined by W.P. Schaefer: Cu(II), *gray*; Cu(I), *black*

Generalidades del Cobre: Geometrías posibles

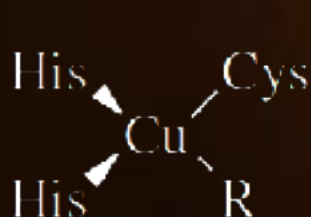
Cu (I) : -SR,



Cu(I) : Lineal y di-coordinada

Cu(II): tetraedro distorsionada, octahedrica (Jahn–Teller)

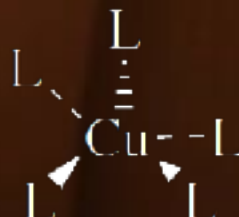
Cu(III): plano cuadrado



Tipo I

R = metil, N, o O: Tranf Electr.

Enzimas azules: 600-620 nm
(Cys) S → Cu⁺²

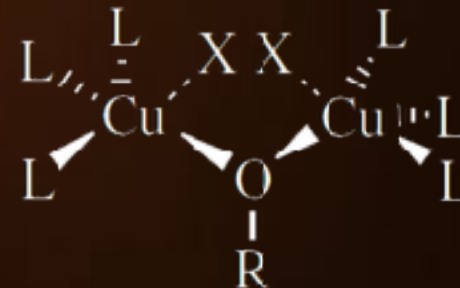


Tipo II

L = N, O ligands.

Oxidaciones catalíticas.

Combinadas con tipo I y III.



Tipo III

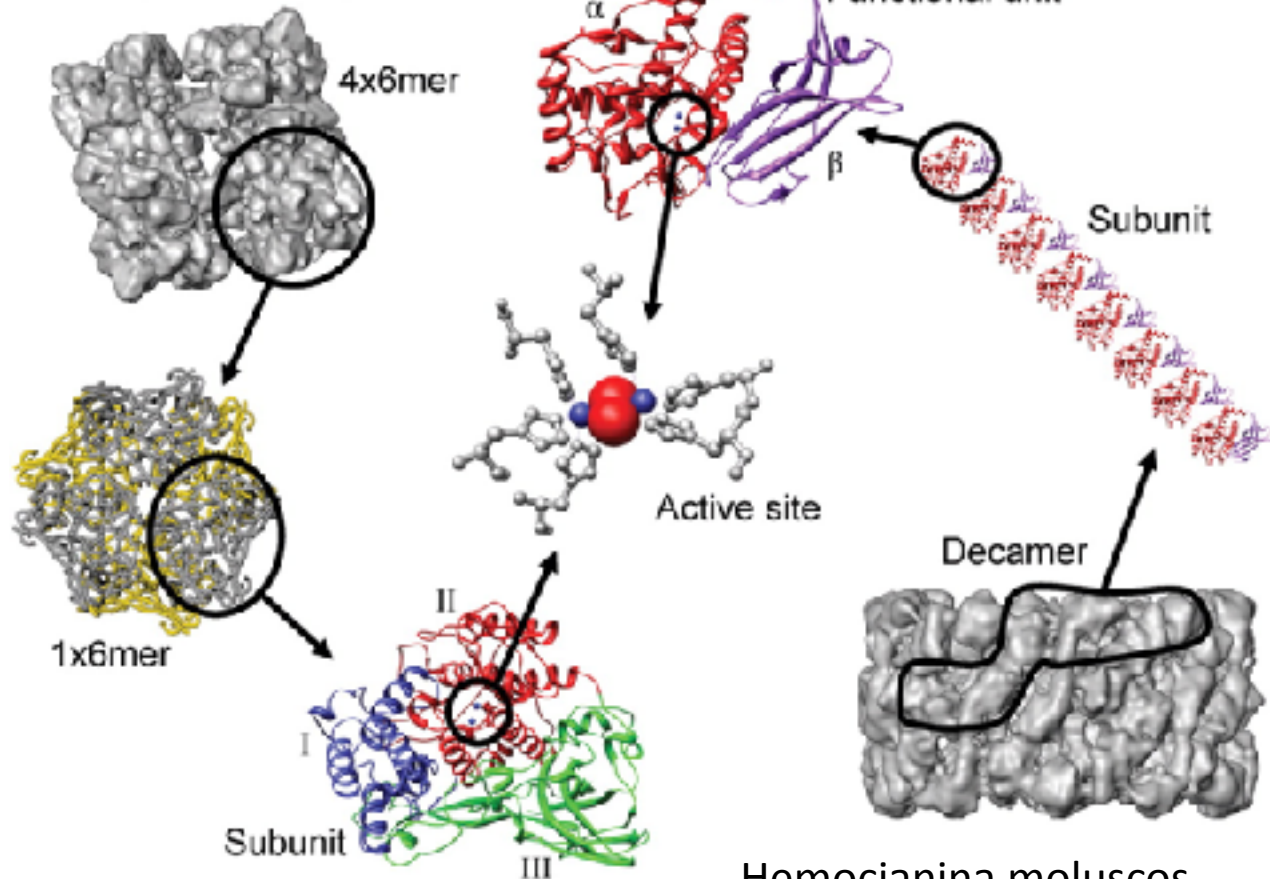
L = N ligandos, R = H, alquil o aromático, X = otros ligandos o O₂^{x-}

Cu(II): O₂ → peroxo y superóxido.

Hemocianinas: Composición del transportador de oxígeno



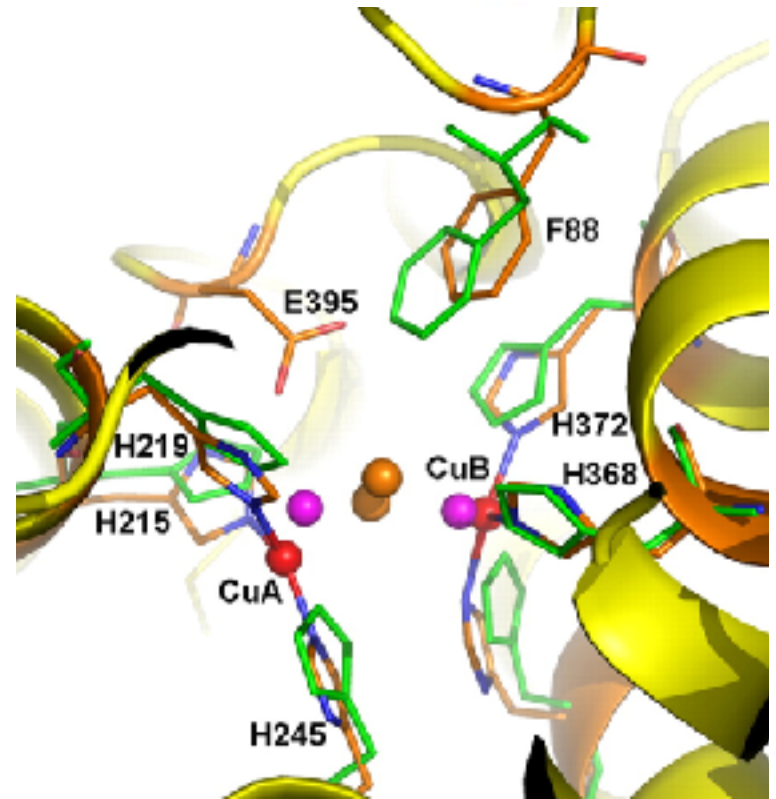
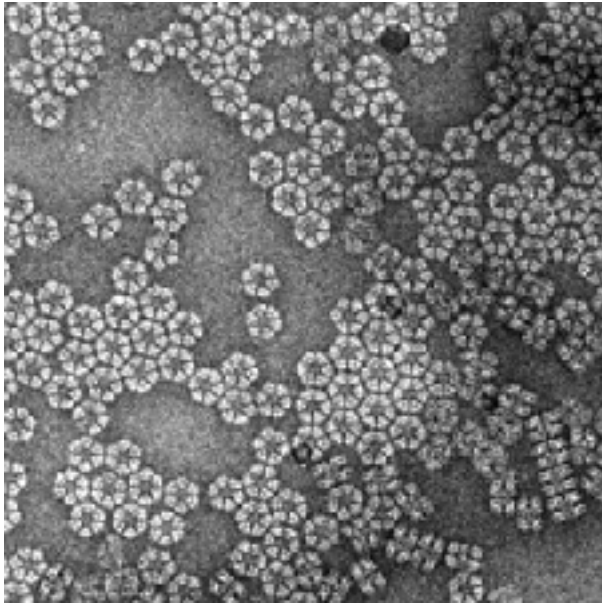
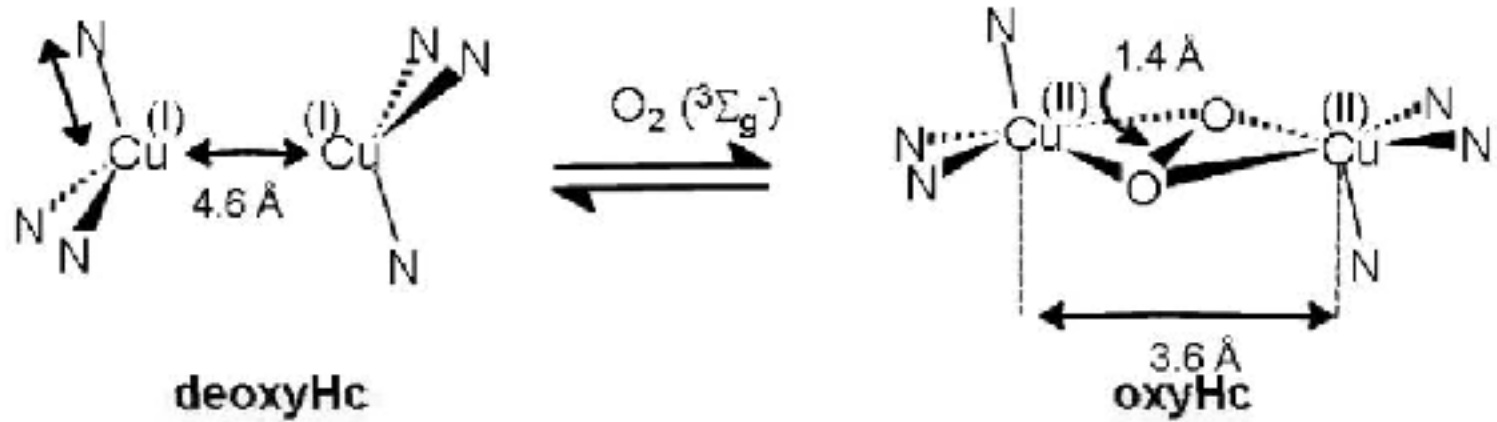
Hemocianina Crustaceo



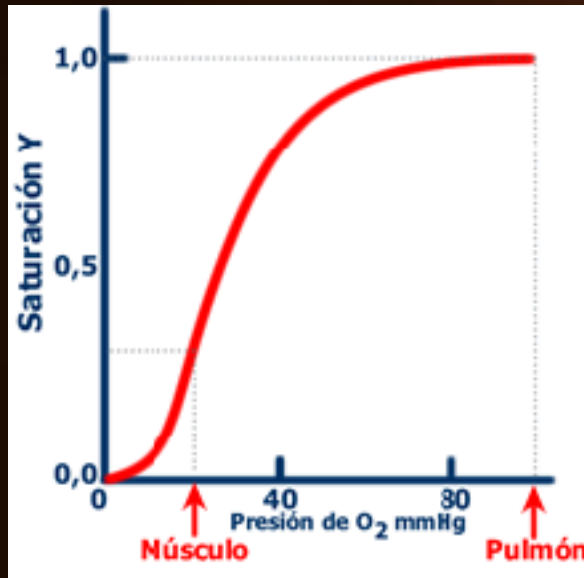
Hemocianina moluscos

PM: 7 a 8 x10⁶

Hemocianinas: *Composición del transportador de oxígeno*



Generalidades del Cobre:



Hemocinanas: $P_{1/2}$ (torr)

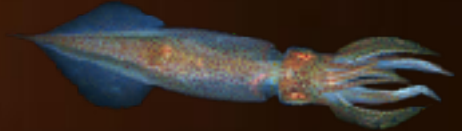
Sepia officinalis: 12



Loligo vulgaris: 14



Loligo paeleji: 42



Octopus vulgaris: 3



Busycon canaliculatum: 12



Limulus polyphemus: 11



Homarus americanus: 22



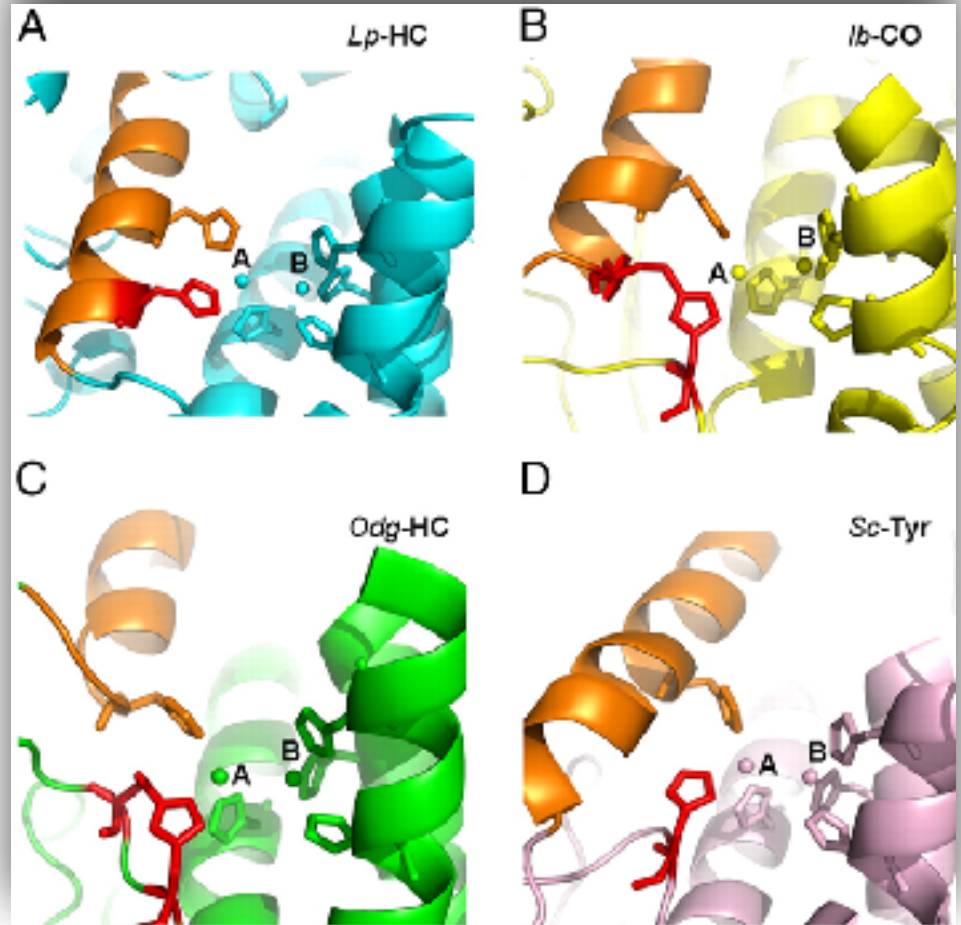
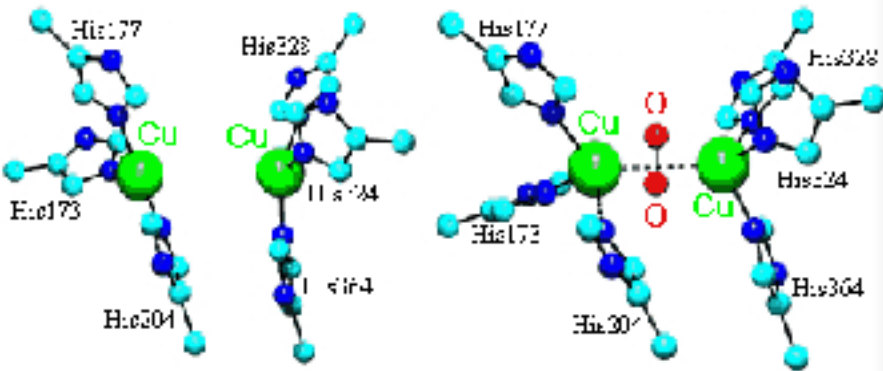
Panulirus interruptus: 6.5



Cancer irroratus: 12



Hemocianinas: Composición del transportador de oxígeno



Limulus polyphemus : hemocyanin (A) : Cl^- y Ca^{+2} reduce la afinidad por O_2 pero H^+ aumenta afinidad

batatas catechol oxidase (B)

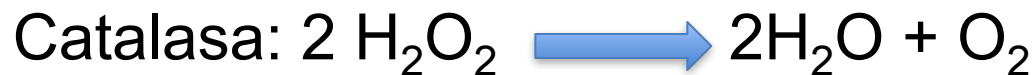
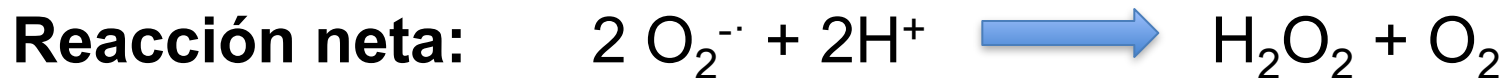
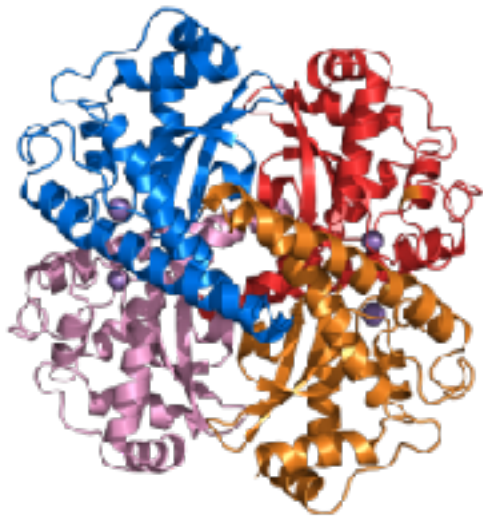
Octopus dofleini : hemocyanin (C)

Streptomyces castaneoglobisporus: tyrosinase (D).

Superoxido dismutasa: Catálisis de formación de peróxido

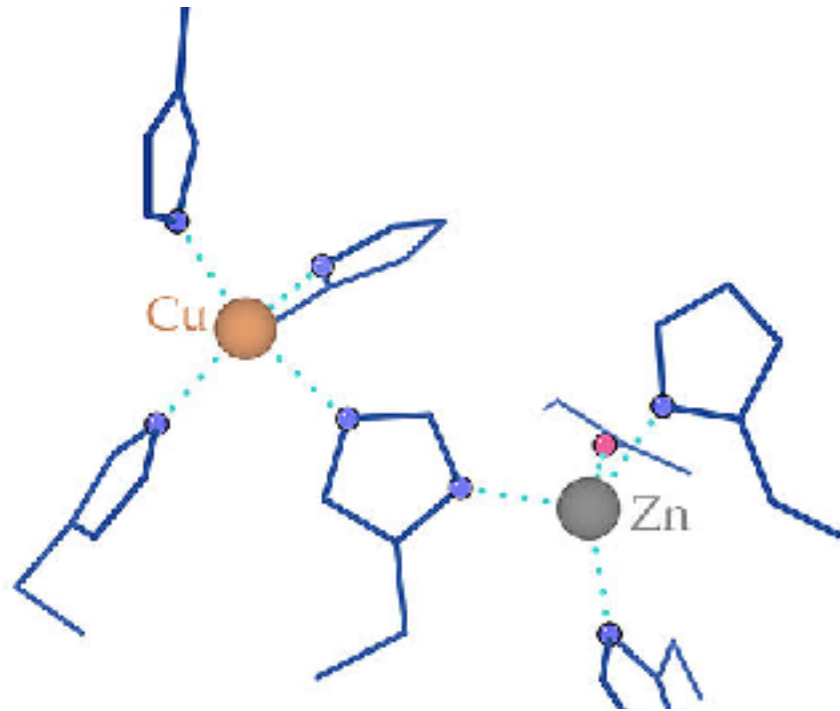
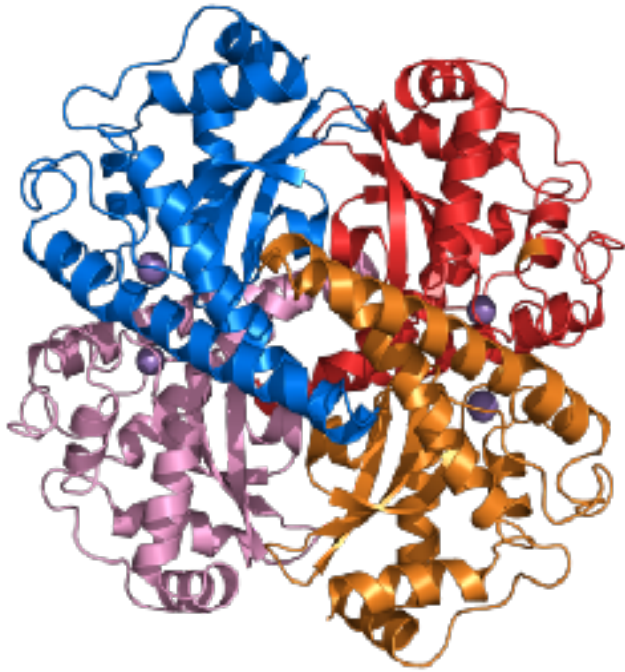
Antioxidante Natural: retrasa el envejecimiento celular

Globulos rojos de la sangre, citoplasma celular (SOD1), (SOD2) y liquido extracelular (SOD3)



$$2.4 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$$

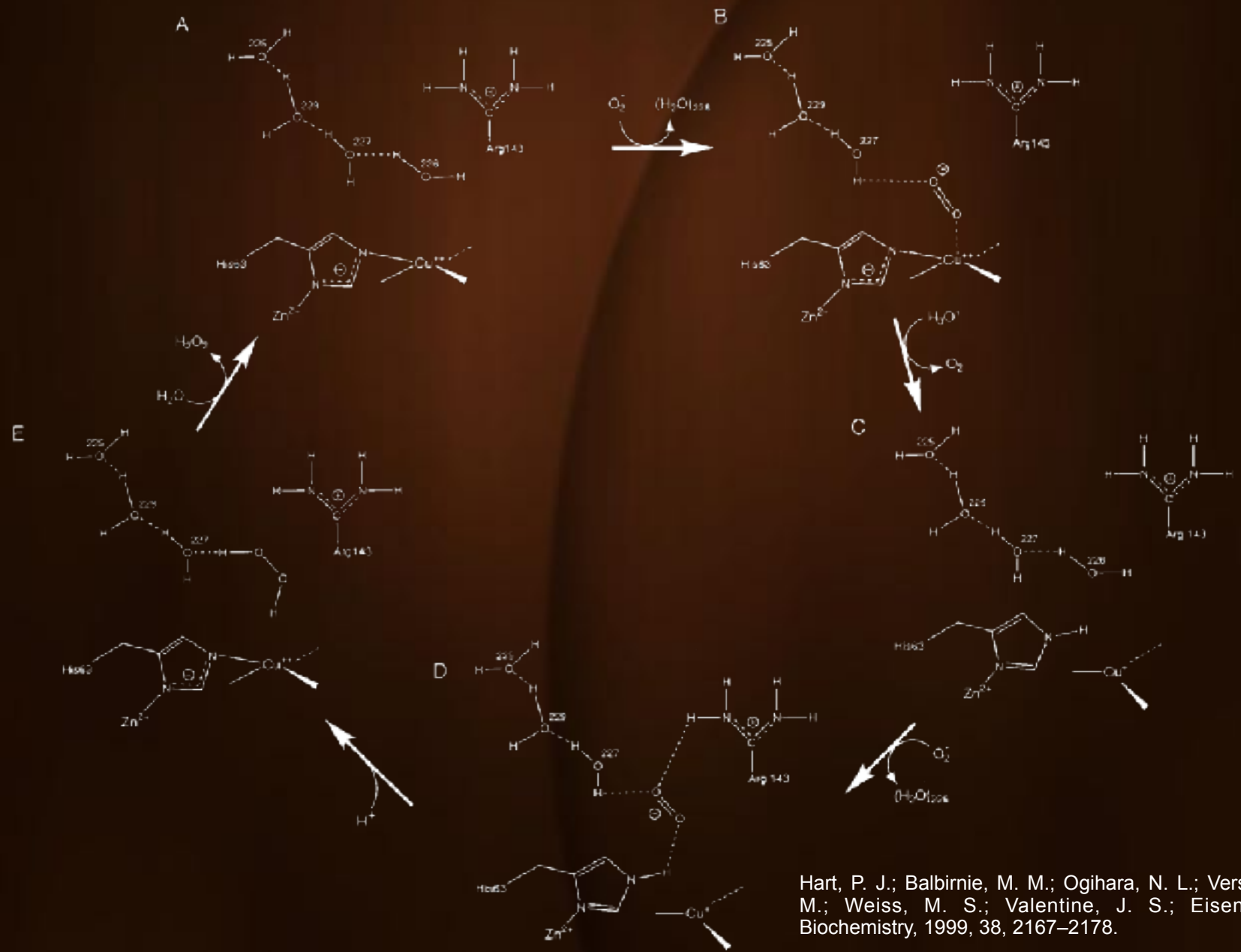
Superoxido dismutasa: Catálisis de formación de peróxido



Sin Zn: misma actividad

Mayor estabilidad?... Cu,Zn-SOD: Muy estable al calor (75°)

Superoxido dismutasa: Catálisis de formación de peroxido



Hart, P. J.; Balbirnie, M. M.; Ogiyara, N. L.; Versissian, A. M.; Weiss, M. S.; Valentine, J. S.; Eisenberg, D. *Biochemistry*, 1999, 38, 2167–2178.

Superoxido dismutasa: Catálisis de formación de peroxido

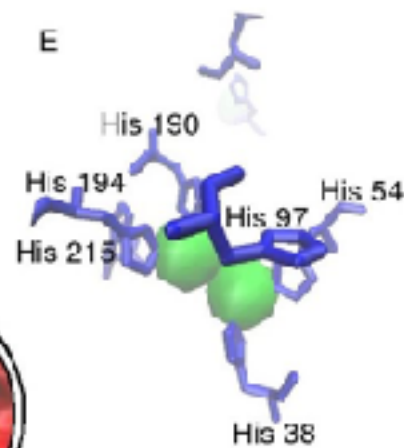
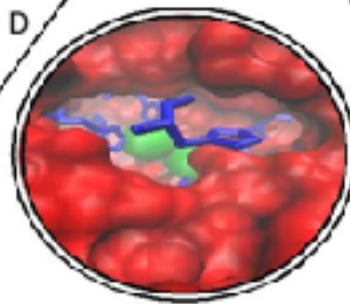
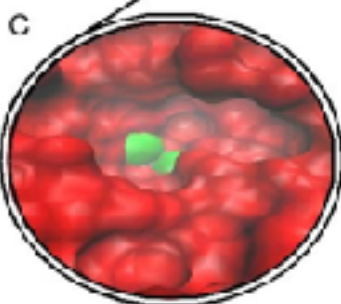
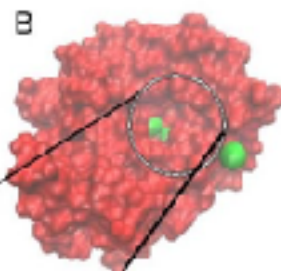
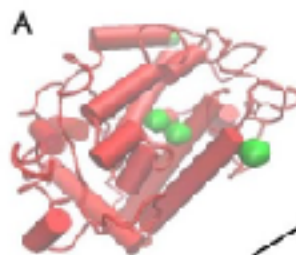
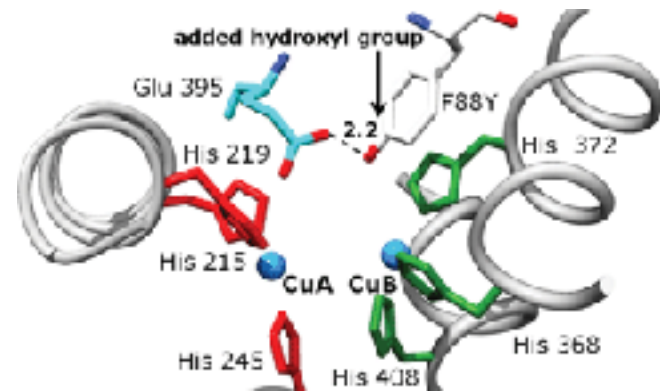
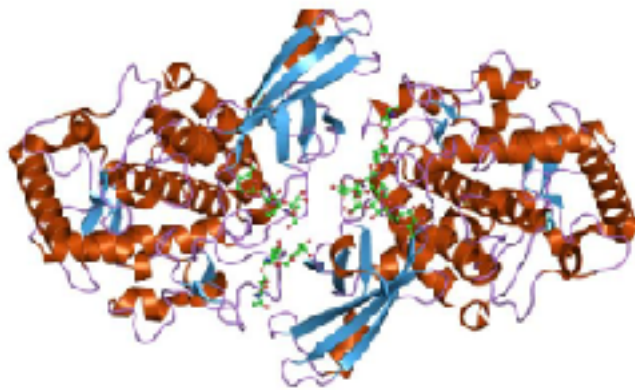
2168 *Biochemistry, Vol. 38, No. 7, 1999*

Hart et al.

Table 1: States of Eucaryotic CuZnSOD Observed by X-ray Crystallography

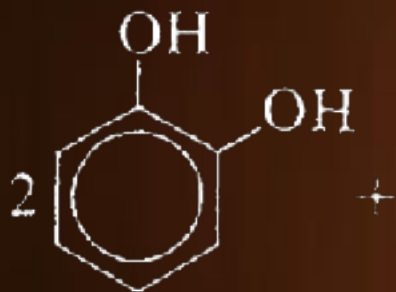
species	ligands	Cu bridge	Cu geometry	PDB code	AU	ref
bovine	4 His, 1 H ₂ O	intact	square planar	2SOD	2 dimers	8
bovine Cu(II)/Co	4 His, 1 H ₂ O	intact	square planar	1COB	1 dimer	53
bovine Cu(I)/Co	4 His, 1 H ₂ O	intact	square planar	2SXC	1 dimer	29
bovine ⁻ N ₃ -bound	4 His, 1 ⁻ N ₃	intact	square pyramidal	1SXZ	1 dimer	49, 56
bovine thiocyanate	4 His, 1 ⁻ SCN	intact	square planar	1SXS	1 dimer	56
bovine C6A	4 His, 1 H ₂ O	intact	square planar	3SOD	2 dimers	65
<i>Xenopus</i>	4 His, 1 H ₂ O	intact	square planar	1XSO	1 dimer	48
<i>Xenopus</i> CN-bound	4 His, 1 CN	intact	square planar	1XSO	1 dimer	21
spinach	4 His, 1 H ₂ O	intact	square planar	1SRD	2 dimers	18
human	4 His	intact	square planar	1SPD	1 dimer	64
human	4 His	intact	square planar	1SOS	5 dimers	20
human FALS mutant	4 His, 1 subunit	intact	square planar	1AZV	1 dimer	50
G37R	3 His, 1 subunit	broken	trigonal planar			
yeast	4 His, 1 H ₂ O	intact	square planar	1SDY	2 dimers	19
yeast Cu(I)	3 His	broken	trigonal planar	1JCW	1 monomer	26
yeast, 15 atm of oxygen	3 His	broken	trigonal planar	1b4l	1 monomer	this study
yeast ⁻ N ₃ -bound	4 His, 1 ⁻ N ₃	intact	square pyramidal	1yaz	1 monomer	this study
yeast H48C	3 His, 1 Cl ⁻ , 1 H ₂ O	intact	square pyramidal	1b4t	1 monomer	this study

Tirosinasa: *catálisis de catecolasa y cresolasa*

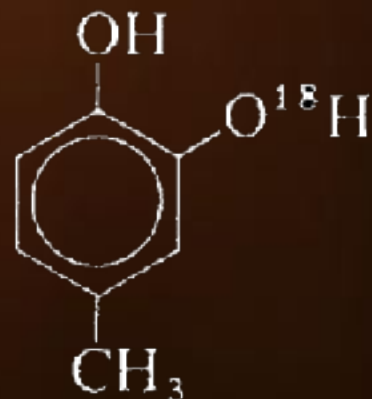
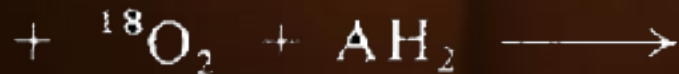
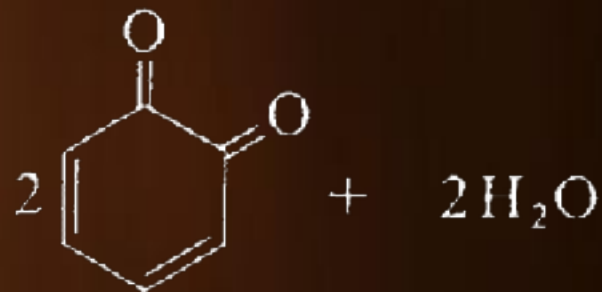


Tirosinasa: *catalisis de catecolasa y cresolasa*

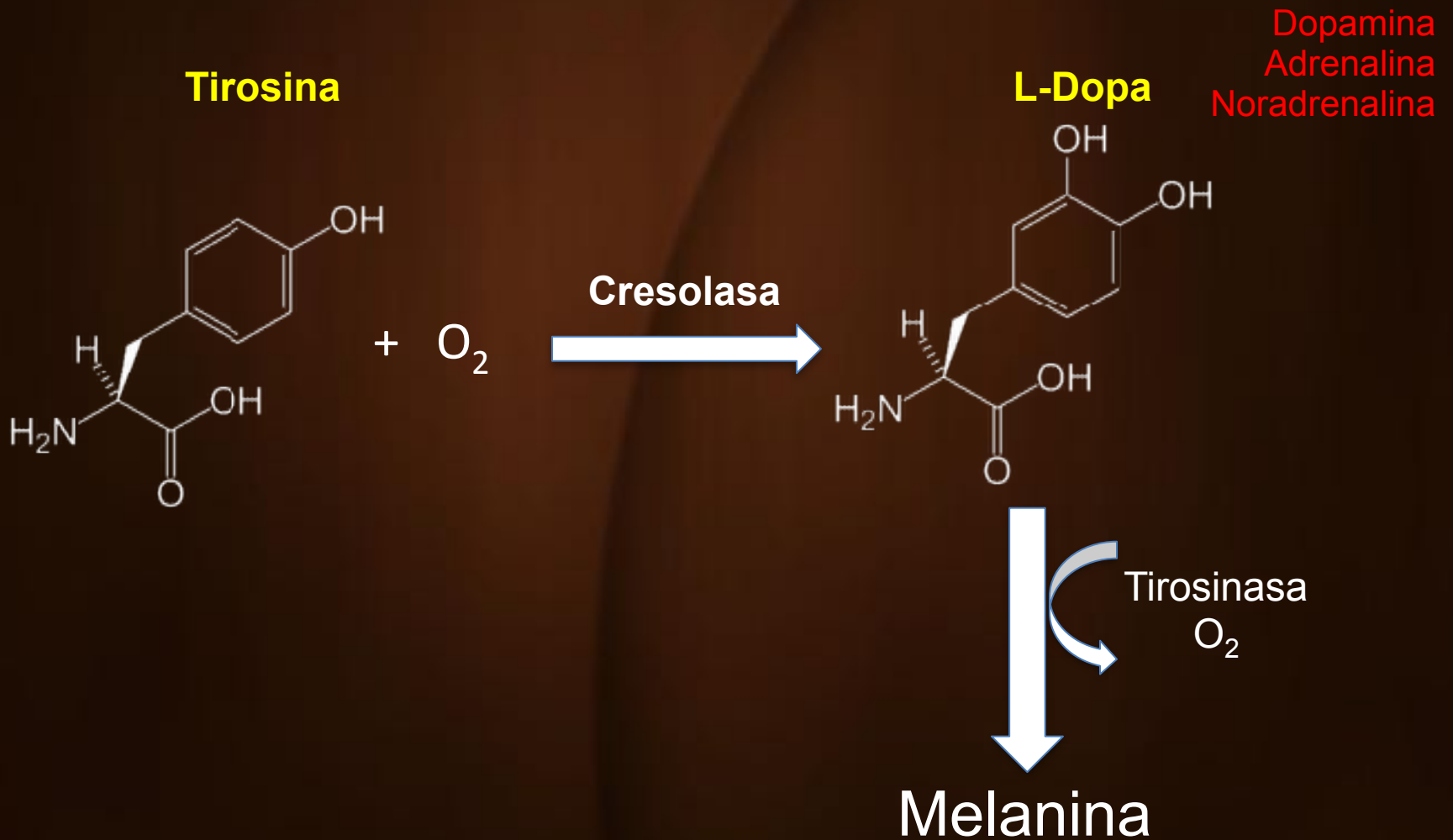
Catecol



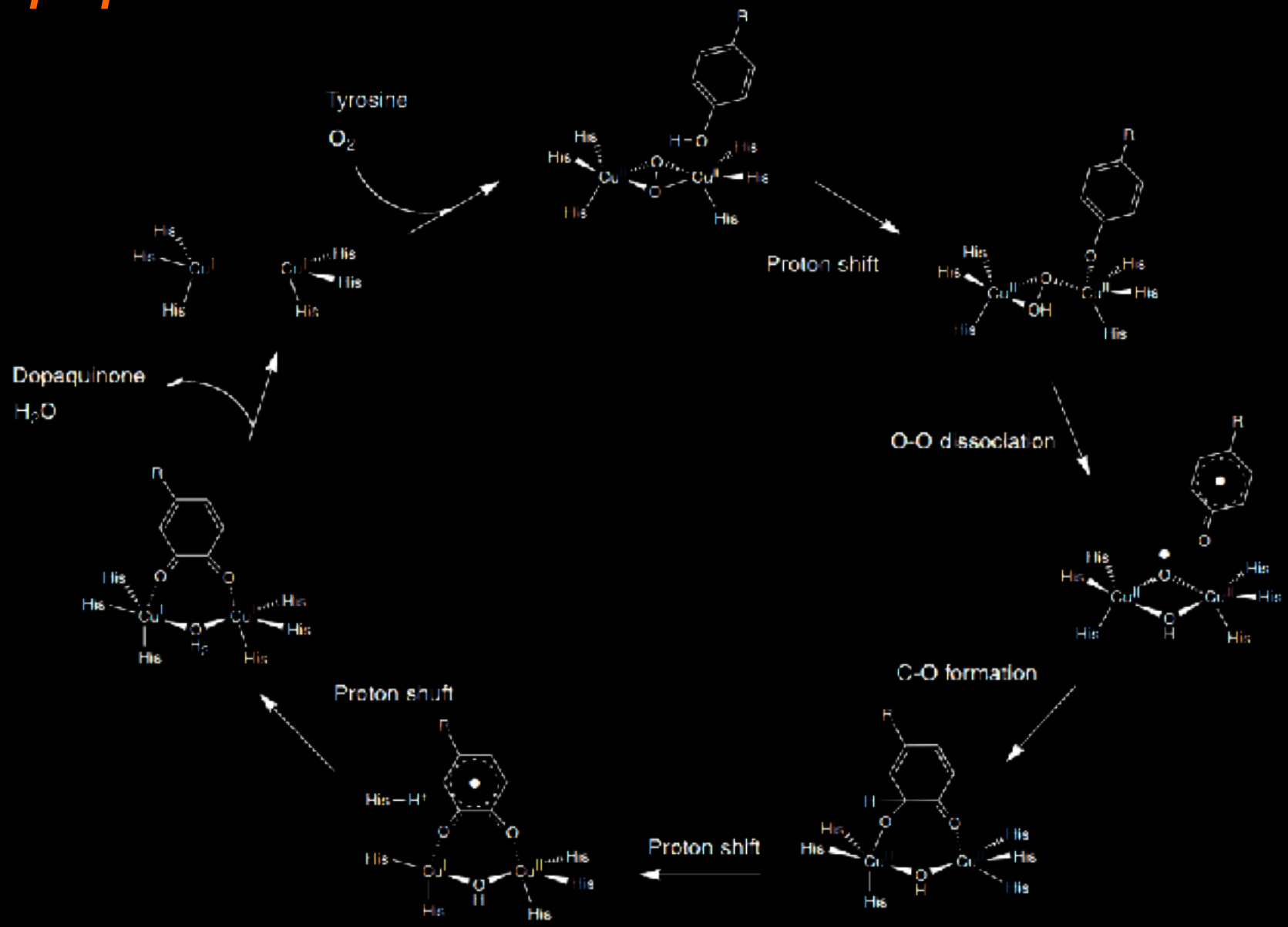
Benzoquinona



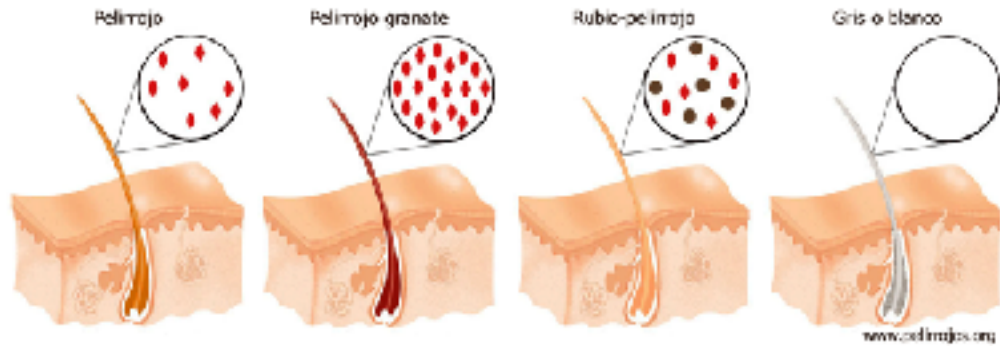
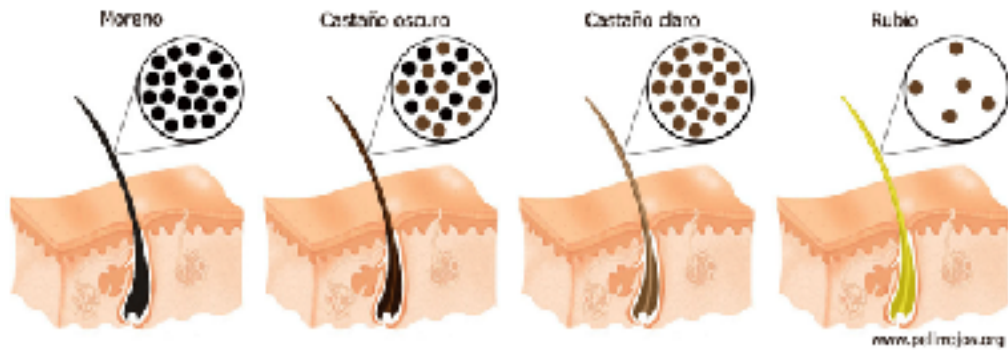
Tirosinasa: Formación de melanina



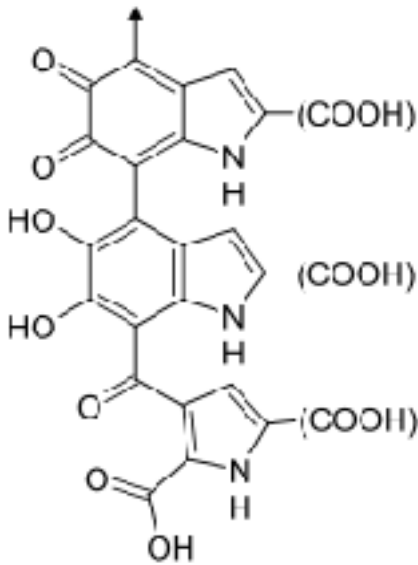
Tirosinasa: mecanismo catalítico de conversión de tirosina a dopaquinona



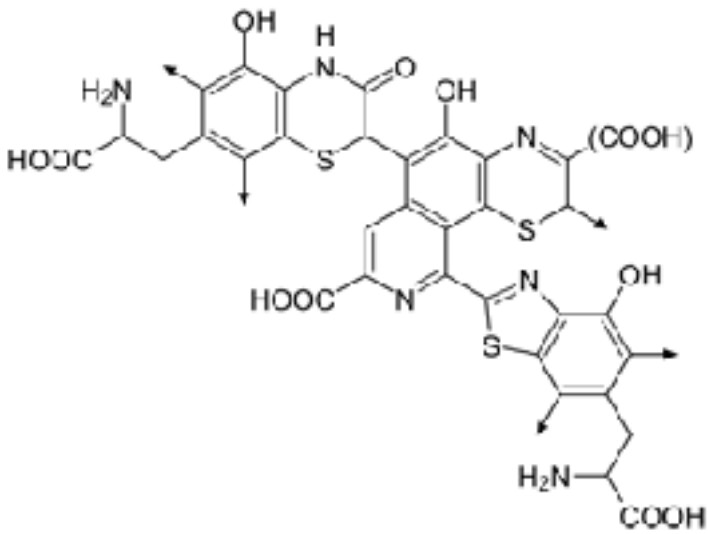
Tirosinasa: *Formación de melanina*



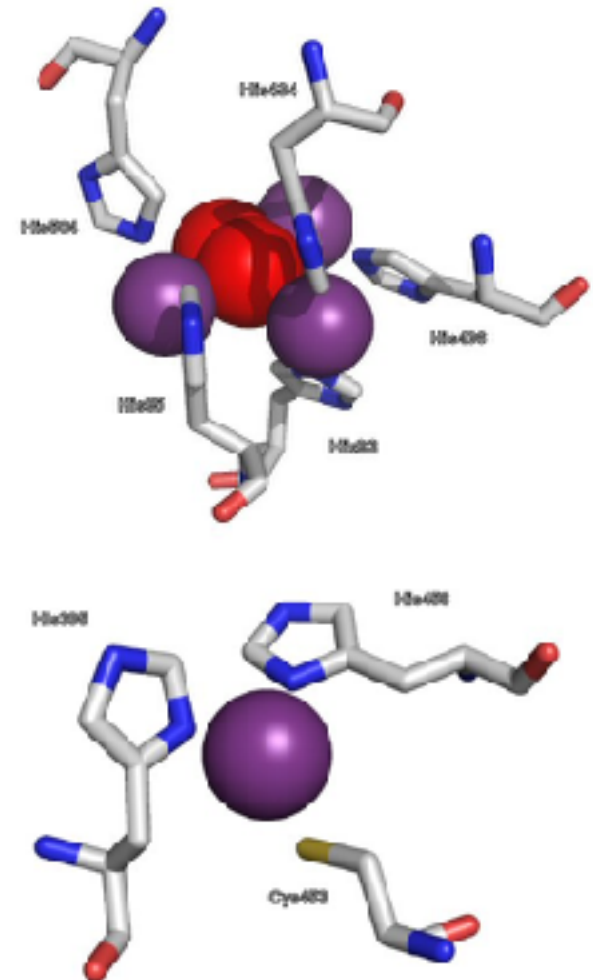
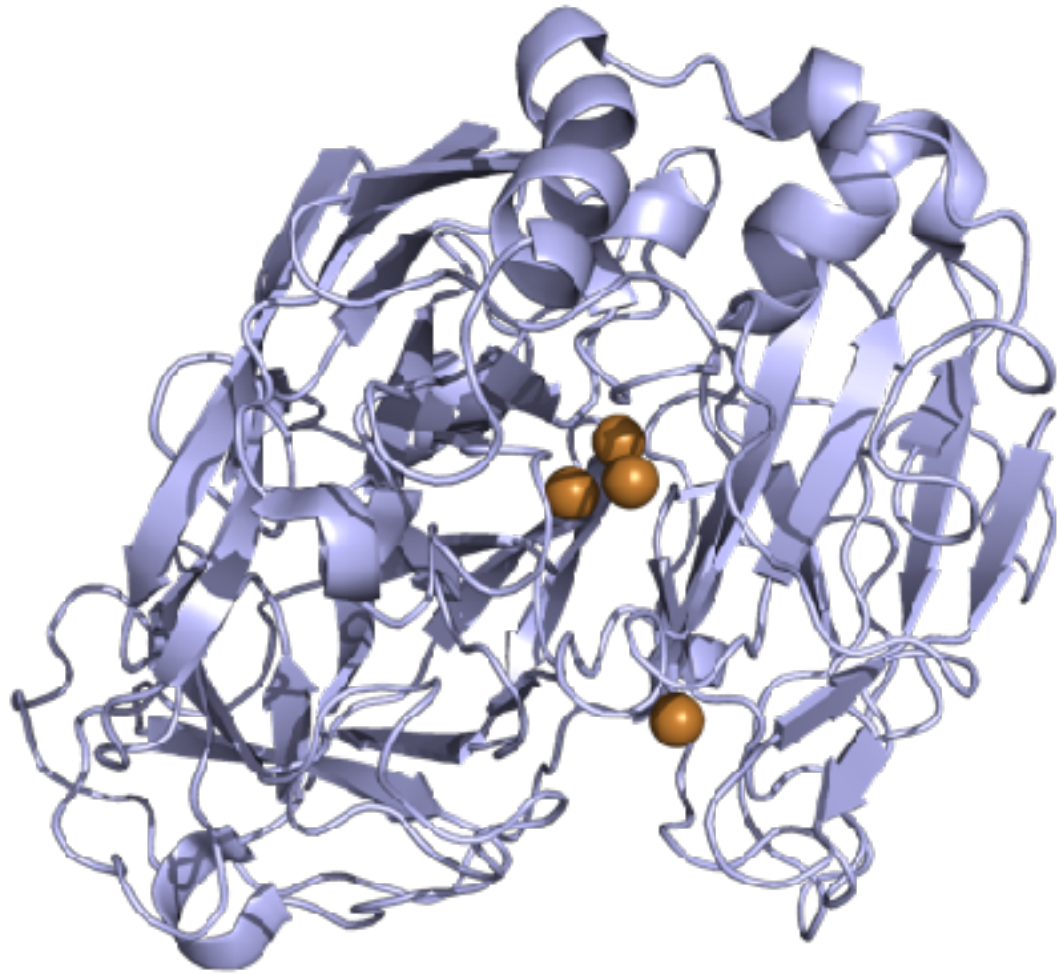
Eumelanina



Feomelanina



Lacasa: catálisis de oxidación de fenoles



Lacasa: aplicaciones sintéticas

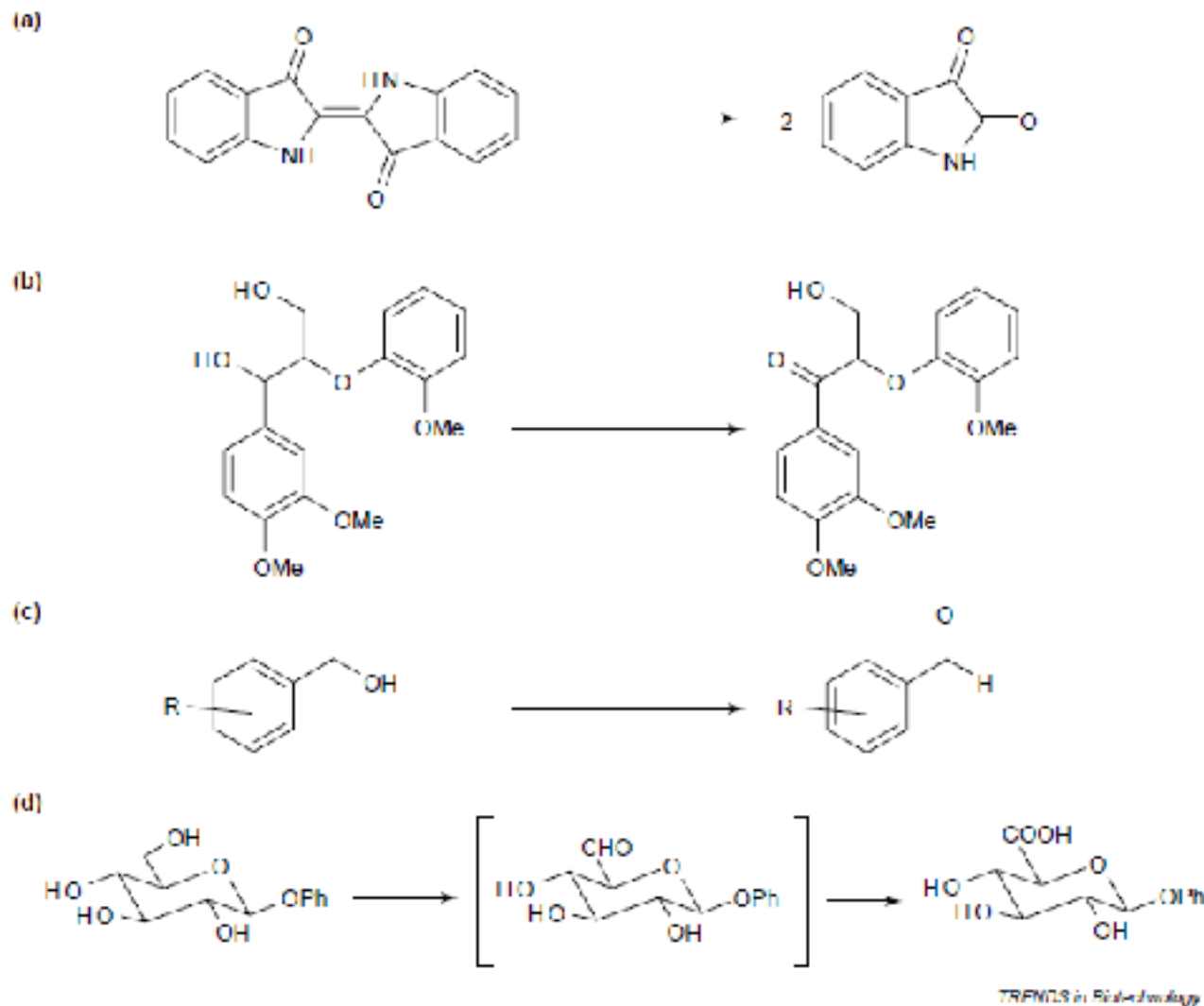
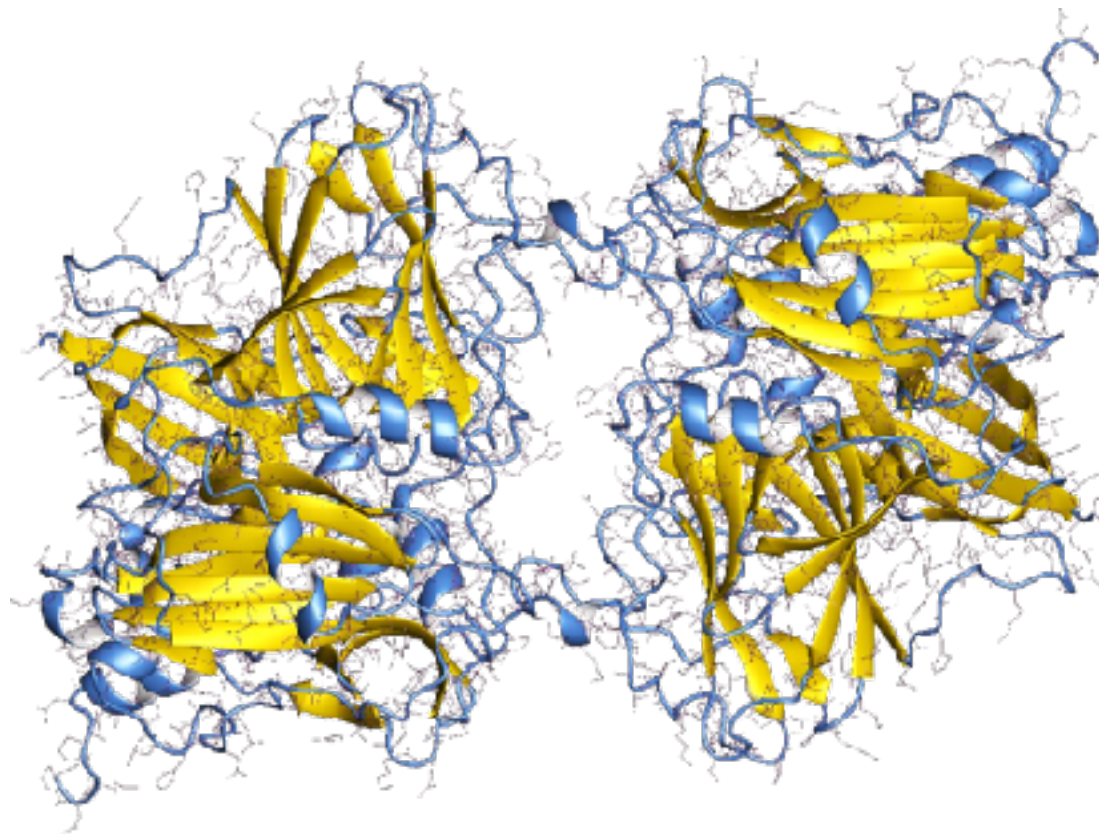
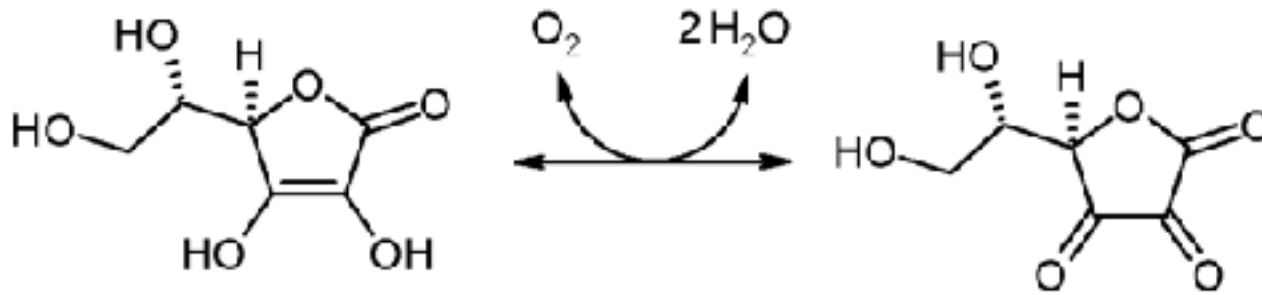


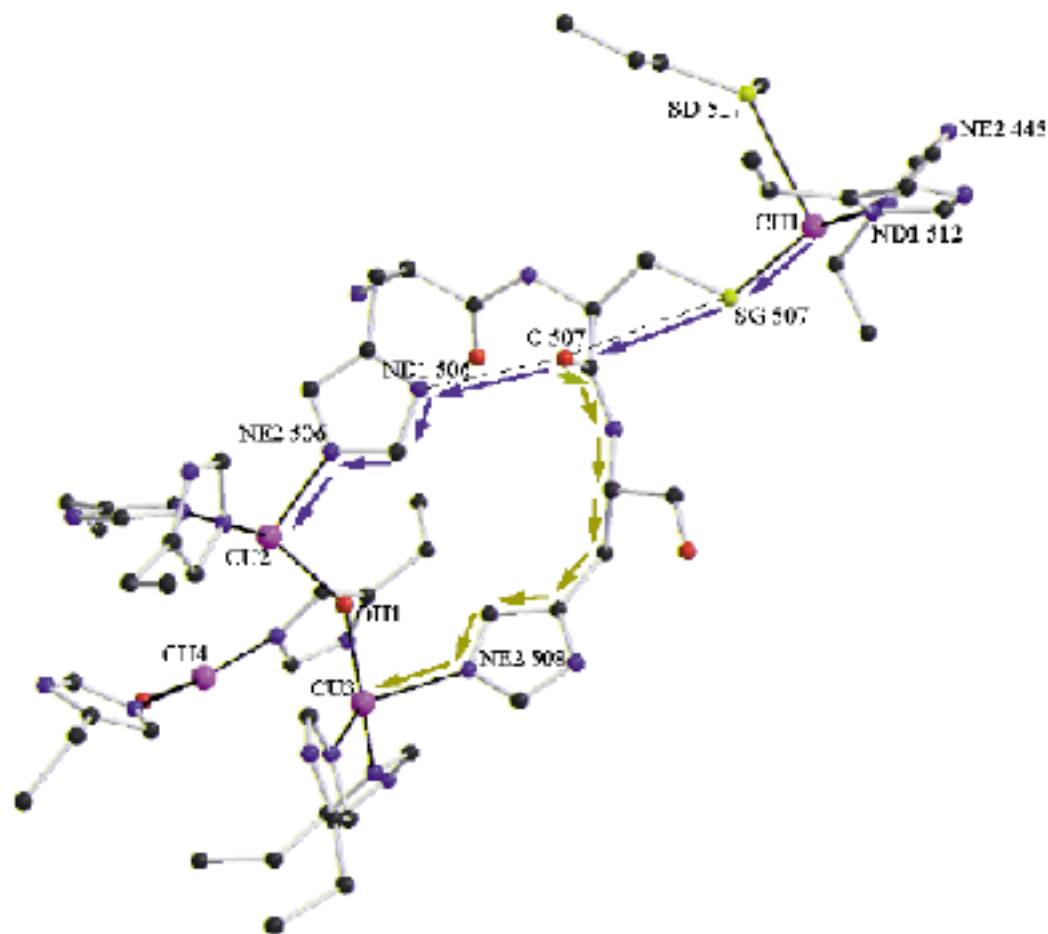
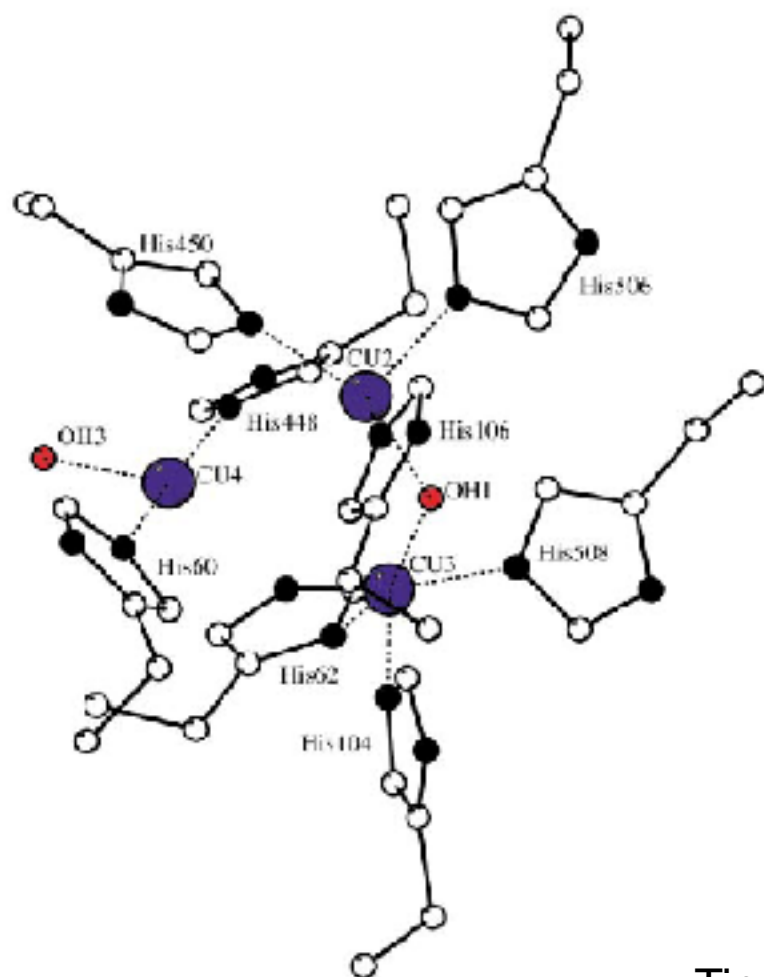
Figure 4. Examples of synthetic applications of the so-called lacase-mediator system (LMS). (a) The oxidation of indigo to isatin [24]. (b) The oxidation of allyl to alpha,beta-unsaturated ketone [20]. (c) The oxidation of benzyl alcohols to the corresponding aldehydes [25–26]. (d) The oxidation of alkyl β -glucosides to their corresponding glucuronides [32].

Ascorbato oxidasa: catálisis de oxidación de ácido ascórbico



8Cu
2 subunidades:
65.000
Cu(II) reducido
por el sustrato

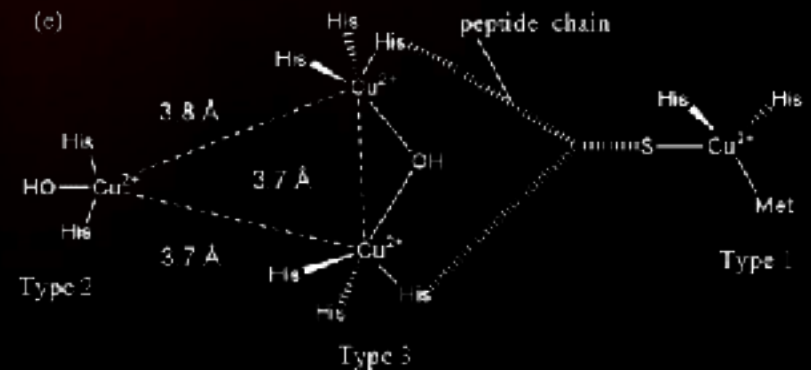
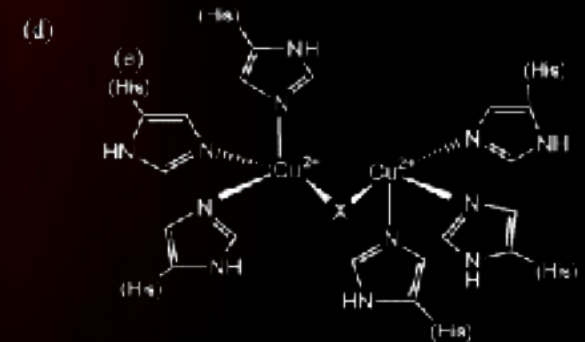
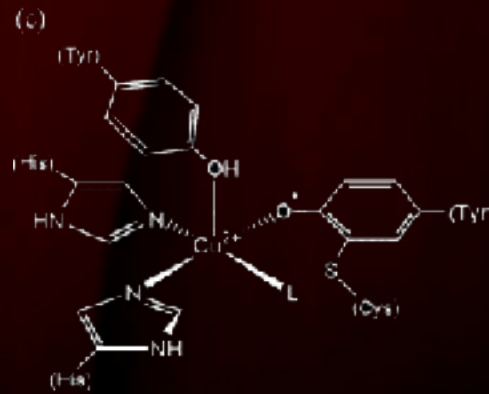
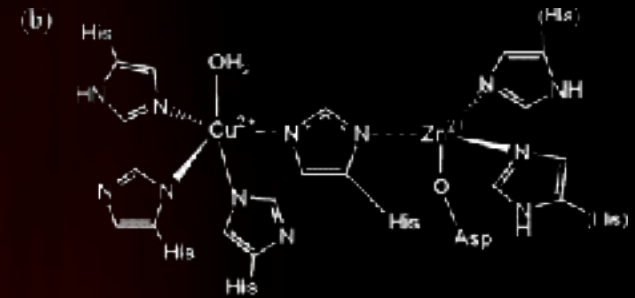
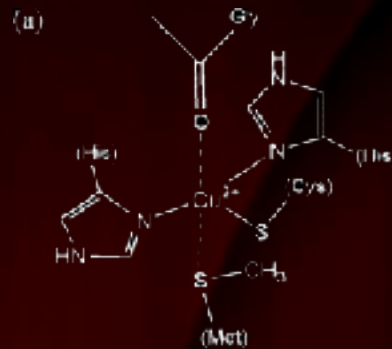
Ascorbato oxidasa: catálisis de oxidación de ácido ascórbico



Tipo III + Tipo II

Otras Oxidasas:

- (a) azurina (tipo 1),
- (b) superoxido dismutase (type 2),
- (c) galactose oxidase (type 2),
- (d) X = OH or OH₂: catechol oxidasa y tirosinasa (type 3),
- (e) ascorbato oxidasa (tipo 4 o multicobre oxidasa)



Urato oxidasa: cataliza la oxidación del ácido úrico a 5-hydroxyisourate



Insoluble

soluble

Plasma Amine Oxidase



Primary amine

Aldehyde

Proteínas azules

Bajo peso molecular
No se oxidan fácilmente

Estelacianina

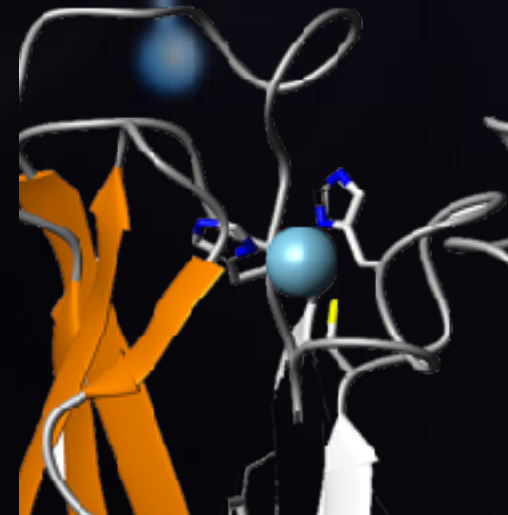
P.M. 16800 Da, 1xCu(tipo 1) + 2xN(his)
+1xS(cis) + 1xN(amida)

Plastocianina

En cloroplastos de plantas y en algas.
P.M. 21000 Da, 2xCu(tipo 1),
transportador de electrones en la
fotosíntesis.
2xN(His) + 1xS(Cis) + 1XS(Met): trigonal
plana o tetraédrica deformada .

Azurina

Aislada de bacterias (*Pseudomonas fluorescens*, y otras), P.M. 14.600-17.000 Da, 1xCu (tipo 1), componente del sistema de transporte de electrones que actúa en las bacterias entre la citocromo oxidasa y el citocromo C.



Proteínas azules

Potencial: +183 mV hasta +680 mV.

Table 1 Reduction potentials (mV vs. NHE) of blue copper proteins and their electron donors and acceptors

Protein	Potential (pH)	Donor	Potential (pH 7)	Acceptor	Potential (pH 7)
<i>P. nigrum</i> plastocyanin	370 (7.5)	cyt <i>f</i>	340	P700 ^a	490
<i>Thiobacillus ferrooxidans</i> rusticyanin ^a	680 (1–3)	sulfatiron(II) (pH 2.0)	≤650	cyt <i>a</i> (O ₂)	(820)
human ceruloplasmin	490, 580 (5.5)	iron(II) complexes	<300 ^b	type 3 Cu (O ₂)	(820)
<i>Rhus vernicifera</i> laccase	394 (7.5)	phenols	<300 ^c	type 3 Cu (O ₂)	434 (820)
<i>Polyporus versicolor</i> laccase	785 (5.5)	phenols	<300 ^c	type 3 Cu (O ₂)	782 (820)
<i>C. pepo medullosa</i> ascorbate oxidase	344 (7.0)	ascorbate	295 ^d	type 3 Cu (O ₂)	344 (820)

^aSee [54]

^bLigation-dependent potentials

^cWide range of potentials

^d E° for $\text{Asc} + \text{H}^+ + 2\text{e}^- \rightarrow \text{HAsc}^-$

Estelacianina

Plastocianina

Azurina

Proteínas azules Azurina

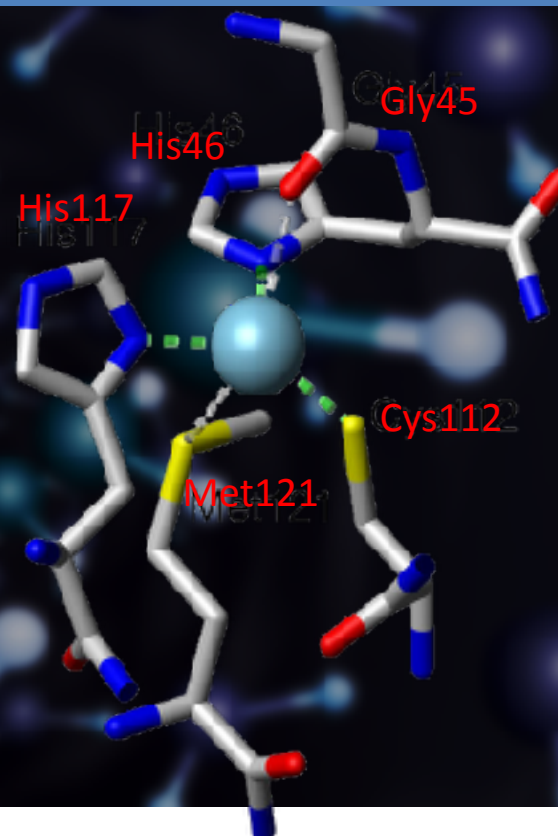


Table 3 Metal-ligand bond distances (Å)

<i>P. aeruginosa</i> azurin	M-N ^{δ1} (His46)	M-S ^γ (Cys112)	M-N ^{δ1} (His117)	M-S ^δ (Met121)	M-O (Gly45)
Cu(II) (pH 5.5) ^a	2.08	2.24	2.01	3.15	2.97
Cu(I) (pH 5.5) ^a	2.14	2.25	2.04	2.97	3.15
Cu(II) (pH 9.0) ^a	2.06	2.26	2.03	3.13	2.93
Cu(I) (pH 9.0) ^a	2.14	2.27	2.15	3.10	3.17
Co(II) ^a	2.32	2.20	2.25	3.49	2.15
Ni(II) ^a	2.23	2.39	2.22	3.30	2.46
Zn(II) ^{a,c}	2.01	2.30	2.07	3.4	2.32

Cobre en Chile: *Mayor productor de cobre en el mundo*



Fin clase
2016