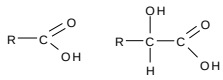
2) Important ligand systems of Bioinorganic Chemistry (1)

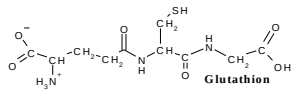
Overview

- Metals in biological systems are mostly bonded to ligand systems
- transport and storage of metals normally require ligand systems
- Stabilization of oxidation states is frequently ligand-controlled
- Reactivity of macromolecules is frequently metal-controlled
- Metal catalysis is main functionality of metalloproteins

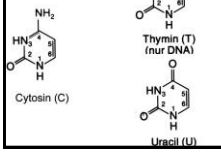
Carboxylates and Hydroxycarboxylates

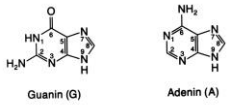


Amino acids, peptides, proteins

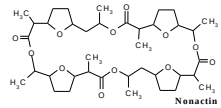


Nucleic acids





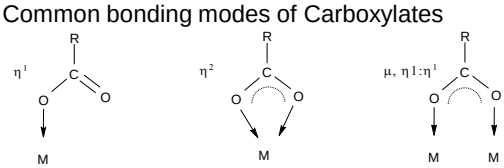
Ionophores



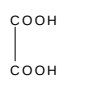
2) Important ligand systems of Bioinorganic Chemistry (2)

Carboxylates and Hydroxycarboxylates

- Common bonding modes of Carboxylates

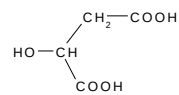


- Frequently occuring Hydroxycarboxylates

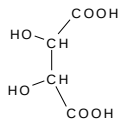


Oxalic acid

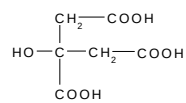
Malonic acid



Malic acid



Tartric acid



Citric acid

- Frequent ligand systems in plants (metal transport and storage)
- Complicated coordination chemistry due to the formation of various species, which show various pH-dependent equillibria
- Oligomeric structures are common
- rare ligand systems in animals (there amino acid coordination is preferred, but citrate represents an exception)

2) Important ligand systems of Bioinorganic Chemistry (3)

Carboxylates and Hydroxycarboxylates

Fulvic and humic acids

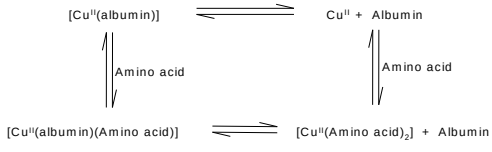
- Polymeric, organic acids in soils and ground water
- Bonded in pores of soil and important for the soil quality
- Control pH of soils and capabilities for metal storage and/or transport
- Affinity of metal ions to humic and fulvic acids control their bioavailability
- Outer-sphere coordination of metal ions (monodentate)

	Fulvic acid	Humic acid
Molar weight	about 5×10^6	smaller
Affinity	$Fe^{III}>Al^{III}>Cu^{II}>Mn^{II}>Zn^{II}$	$Fe^{III}>Cu^{II}>Zn^{II}>Mn^{II}>Ca^{II}>Mg^{II}$
Sum acidity	10.3	6.7
Carboxyl	8.2	3.6
Phenolic	3.0	3.9
Aliphatic OH	6.1	2.6
Ketonic, chinoid	2.7	2.9

2) Important ligand systems of Bioinorganic Chemistry (4)

Amino acids, Peptides, Proteins

- Exchange equillibrium between Cu^{2+} species in blood



- Frequent ligand systems in animals (metal transport and storage)
- Main functions:
  - decrease of the toxicity of metal ions
  - fine-tuning of metal concenttrtions
  - 'masking# of competitive ions
- Complicated equilibria are common (including H_2O and OH^- ligands)
- rare ligand systems in plants

- Typical equillibrium of non-proteinbonded metal ions in blood (computer simulation)

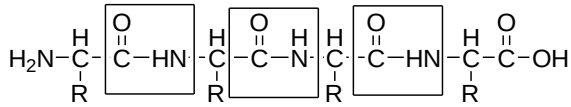
Mn^{II}		**Fe^{III}**		**Cu^{III}**		**Zn^{III}**	
$[Mn(HCO_3)]^+$	24	$[Fe(Cit)(OH)]^-$	99	$[Cu(HisO)(CystO)]^-$	21	$[Zn(CystO)]^{2-}$	40
$[Mn(Cit)]^+$	10	$[Fe(Cit)(Sal)]^{3-}$	<1	$[Cu(His)(CystO)]^0$	17	$[Zn(CystO)(HisO)]^-$	24
				$[Cu(HisO)_2]^0$	11	$[Zn(HisO)(L)]^+$	4

2) Important ligand systems of Bioinorganic Chemistry (5)

Amino acids as ligands

Typical reaction pattern:

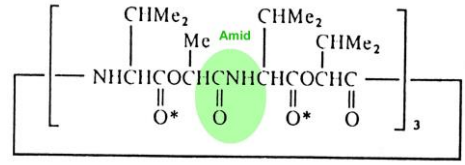
- Condensation under formation of peptide bonds: ….peptides …..proteins



Ability for N,O chelate formation gets lost

Carbonyl oxygen atoms are frequently used for coordination of ‘hard’ metal ions

e.g. valinomycine



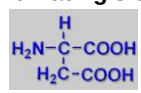
Valinomycin

2) Important ligand systems of Bioinorganic Chemistry (6)

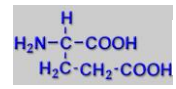
Amino acids as ligands, side chains

Amino acids with coordinating side chains:

Carboxylic groups

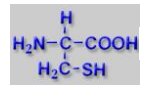


Aspartic acid



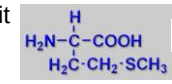
Glutamic acid

Mercapto group



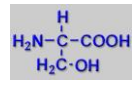
cystein

Thioether unit

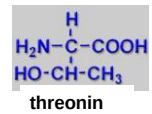


methionin

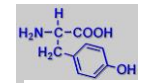
Hydroxyl groups



serin

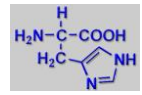


threonin

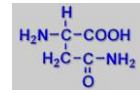


tyrosin

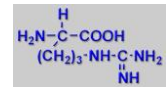
Amines



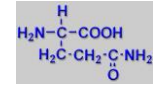
histidin



asparagin



arginin



glutamin

2) Important ligand systems of Bioinorganic Chemistry (7)

Amino acids, Peptides, Proteins

- **Metal complexes with peptides (oligopeptides) influence**
  - metal transport through membranes (ion pumps, ion channels)
  - detoxification (removal of toxic metal ions)
  - enzyme activity
  - redox processes (e.g. glutathione)

- Metal-binding to proteins is not always metal-specific (e.g. transport protein albumin, M=66000 Ca^{2+}, Mg^{2+}, Zn^{2+}, Ni^{2+}, Cu^{2+}

- Typical features of protein bonded metal ions:
  - strongly distorted geometry
  - coordinatively unsaturated

-Typical bonds:

Zn^{2+}	$His, Cys^-, Glut$	tetrahedral
Cu^{2+}	Cys^-, His	square
Cu^{2+}	Cys^-, His, Met	tetrahedral
Fe^{3+}	$Glu^-, Asp^-, Tyr^-, Cys^-$	octahedral

2) Important ligand systems of Bioinorganic Chemistry (8)

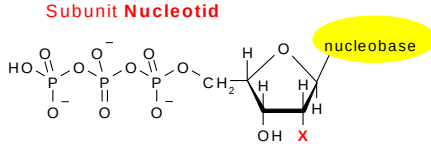
Nucleic acids

- **Composition:**

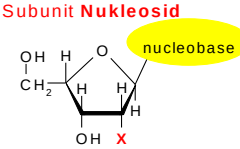
Nucleotide + Nucleobase

((Oligo)phosphate + sugar)

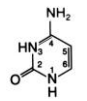
Subunit **Nucleotid**

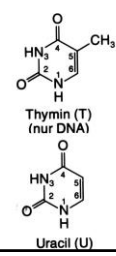


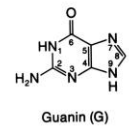
Subunit **Nukleosid**

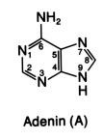


- **Nucleobase:**


Cytosin (C)




Guanin (G)


Adenin (A)

2) Important ligand systems of Bioinorganic Chemistry (9)

Nucleic acids

- Frequently coordinating metal ions: Mg^{2+}, Ca^{2+}, Zn^{2+}
- gen transscription
- DNA replication
- Coordination at phosphate and/or nucleobases possible

- Coordination of metal ions frequently influences complex formation properties of nucleic acids; e.g. pK values for metals at adenosinphosphates

Metal ion	AMP	ADP	ATP
Mg^{2+}	1.97	3.17	4.22
Ca^{2+}	1.85	2.86	3.97
Mn^{2+}	12.40	4.16	4.78
Co^{2+}	2.64	4.20	4.66
Ni^{2+}	2.84	4.50	5.02
Cu^{2+}	3.18	5.90	6.13
Zn^{2+}	2.72	4.28	4.85

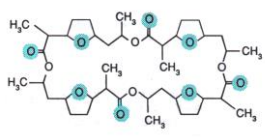
Note! The coordination of Pt^{2+} fragments at DNA is the chemical basis of the cancerostatic activity of the inorganic anticancer drug cis-Platinum

2) Important ligand systems of Bioinorganic Chemistry (10)

Ionophores

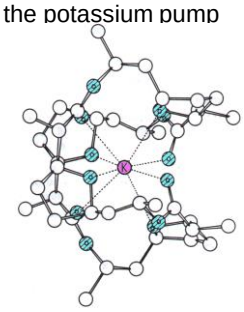
- Specially designed ligand systems, which are responsible for uptake and transport metal ions
- Membrane permeability

e.g.. Nonactin – ligand for K^+ (preferes K^+ over Na^+) part of the potassium pump



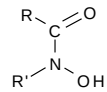
Ligand

complex

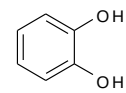


Siderophores: Special ligands for Fe^{3+} uptake

Hydroxamate

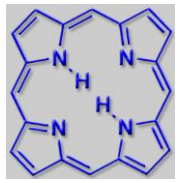


Catecholate

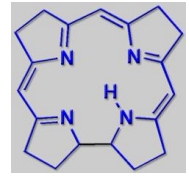


2) Important ligand systems of Bioinorganic Chemistry (11)

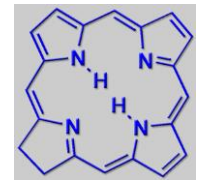
Porphyrines and related systems



Porphyrine



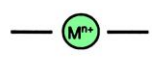
Corine



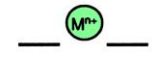
Chlorine

- Various biological functions and various bonding modes
- Ring size determines the bonding capabilities of the systems

Bonding modes::



in-plane



out-of- plane

2) Important ligand systems of Bioinorganic Chemistry (12)

Porphyrines and related tetrapyrrol systems

- Various biological functions and various bonding modes
- Ring size determines the bonding capabilities of the systems

Metal ion	Ion radius (pm)	Suitable for coordination with tetrapyrrols
Be^{2+}	45	too small
Mg^{2+}	72	fits (chlorophyll)
Ca^{2+}	100	too large
Al^{3+}	53	relatively small (no biological importance)
In^{3+}	80	relatively large (rare element, no role)
$O=V^{2+}$	ca. 60	frequently in oil, not in biology
Mn^{2+} (high spin)	83	too large (no biological role)
Fe^{2+} (high spin)	78	too large (out-of-plane coordination)
Fe^{2+} (low spin)	61	relatively small
Fe^{3+} (high spin)	65	fits
Fe^{3+} (low spin)	55	too small
Co^{2+} (low spin)	65	fits (cobalamines)
Ni^{2+}	69	fits (coenzym F430)
Cu^{2+}	73	relatively large, no biological role
Zn^{2+}	74	relatively large, no biological role