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DEVELOPMENT AND SOME ASPECTS OF THE PRESENT SITUATION OF MACROMOLECULE-METAL COMPLEXES

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Abstract: Macromolecule metal complexes (MMCs) — the combination between a macromolecule, a metal chelate/complex/ion or cluster — are dominating factors for different functions in living systems, and are becoming more and more important in different sciences and applications as artifical synthesized systems.

WHERE DO THEY COME FROM......

After appearance of the earth some 4.5 billion years ago first hints for simple living systems are dated around 3.2 billion years ago (Ref. 1a). Before earth has possessed a highly oxidizing atmosphere which could not have been possible without biological help, it is generally agreed that the early atmosphere was a reducing one. Such a mixture as shown in Eq. 1 generated some of the simple organic molecules being basic building blocks for life. As shown by various laboratory experiments (Refs. 1b, c) it is likely that electrical discharge, UV light and also geological eruptions played an important part in promoting chemical reactions in the prebiotic evolution. As schematically shown in Eq. (1) HCN and aldehydes and then the whole range of amino acids (as precursors for proteins) were produced.

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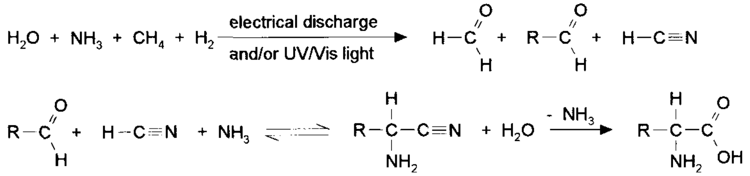
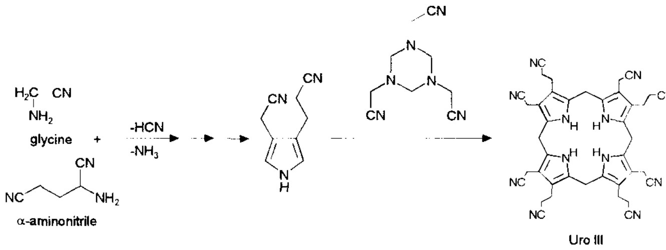


(1)

Also the formation of very small amounts of pyrroles and tiny amounts of porphyrins from a gaseous mixture of CH_4, NH_3 and H_2O were estimated. More efficient synthesis of porphyrins (in the absence of O_2 and H_2O) from α-aminonitriles (HCN present in the prebiotic environment) were carried out by adding the clay montmorillonite at 180°C (Ref. 2). Via a pyrrole called dinitrile version of porphobilinogen dinitrile in a yield of ~40 % the uroporphyrinogen III (thermodynamically stable isomer of the four different uroporphyrinogens) was obtained (Eq. 2). This is a biosynthetic precursor of the metal complexes heme, chlorophyll a, cobyrinic amide (for vitamin B_{12}), coenzyme F430 etc. (metal ions Fe(II), Mg(II), Co(II), Ni(II) present in the prebiotic soup).



(2)

Beside porphyrins being active parts in e.g. hemoglobin, photosystem I/II and cytochromes, metal clusters play an important part as catalysts or in electron transporting chains. The photosynthetic apparatus driven by the energy of solar light (formation of 1200 billion tons of CO_2, producing 700 billions tons biomass and 1000 billion tons O_2 per year) contains in photosystem 2 Mn_4 clusters responsible for 4 electron transfer from water to the chlorophyll P680^{+} (equation of PS2 see Eq. 3).

$$h\nu(\text{solar energy}) + 2H_2O + 2PQ \longrightarrow O_2 + 2\,PQH_2 \qquad (3)$$

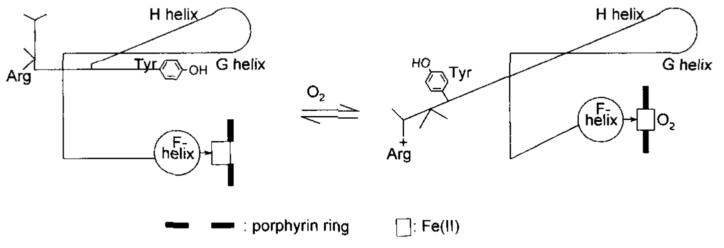
In the respiratory chain of mitochrondria containing beside cytochromes also $(FeS)_x$ clusters and Cu(II) now electrons flow down hill to reduce O_2 efficiently to H_2O and producing thereby ATP (from ADP) (Eq. 4). Hydrolysis of ATP is the energy source for human life (human needs 3000 kcal per day equal to the energy of 200.000 g ATP/ADP hydrolysis; in respiratory chains are only 50 g ATP/ADP, thus cycles run >5000 times per a day).

$$0.5\ O_2 + NADH + H^+\ (+\ ADP) \;\text{——}\; H_2O + NAD^+\ (+\ ATP) \qquad (4)$$

Now nature has had enough time to fish from the sea of different compounds (amino acids for proteins, metal ions for metal complexes and clusters etc.) those being profitable for precellular and then biological evolution, and determining our life up till today.

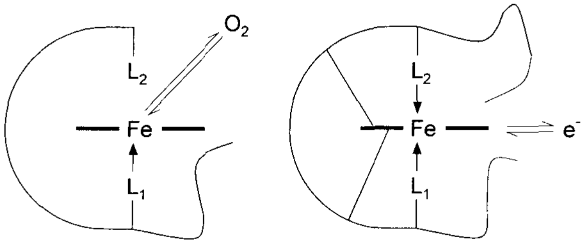
HOW MMCs WORK IN BIOLOGICAL SYSTEMS......

In addition to the photosynthetic apparatus and the respiratory chain few other examples of efficient functions are mentioned. In hemoglobin (Hb) cooperative effects between the more or less four myoglobin units demonstrate the reversible flexibility of a biological system. Hb shows sigmoid curve of four molecules O_2 uptake which means that the affinity of Hb for O_2 increases as O_2 is taken up. This is explained as follows. In deoxyHb all high spin Fe(II) are too big to fit into the core of the porphyrin (Eq. 5). In contrast, the low spin Fe(II) in oxyHb shrinks in volume of ~13 %, fit snuggly in the core of the porphyrin and move therefore 0,5 - 1 Å. This pulls down the proximal histidine, moves then the F helix closer to the H helix so that the tyrosine-containing pocket becomes too small, squeezes out and influences the O_2 uptake of the other Fe(II)-globin units (adult humans have to carry around 1 kg of Hb!).



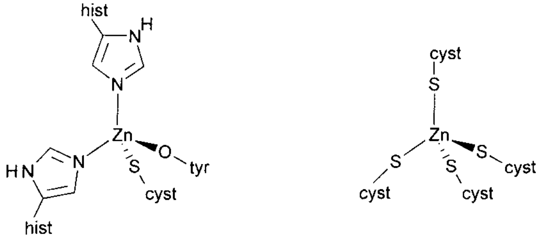
(5)

The chemical properties of metal complexes such as Fe porphyrins are significantly altered by the kind of macromolecular protein environment. In Hb the hemes are incorporated in a hydrophobic pocket by coordinative binding to an imidazole N of a histidine residue. O_2 can achieve now only the free axial position at Fe(II) for reversible binding. The high oxidation potential of Fe(II)/Fe(III) with $E^\circ = 0.82$ V reduces the possibility of irreversible Fe(III)-OH formation. In cytochrome *c* vinyl groups of heme have been converted to thioethers by covalent linkage to cysteins of the protein chain, and both axial positions are occupied by coordination. Cytochrome *c* has now $E° = 0,25$ V allowing easy Fe oxidation/reduction in electron transfer proteins via an accessible periphal porphyrin site.



heme in Hb cytochrome c

The range of metal ions in biological systems are very large reaching from alkaline metal ions to transition metal ions (J. Reedijk in Ref. 3). Some are relatively non-toxic (Na^+, K^+, Ca^{2+}, Mg^{2+} etc.). Some are essential benificial nutrients at low, but metabolic poisons at high concentrations (Mn^{2+}, Ni^{2+}, Cu^{2+} etc.), and the so-called dentrimental metal ions impair regular course of life functions at all concentrations (Pb^{2+}, Cd^{2+}, Hg^{2+} etc.). One example is mentioned. Pb^{2+} binds to functional sulfhydryl groups of proteins and inactivates enzymes. For example Pb^{2+} inhibits the formation of the pyrrole porphobilinogen (biochemical precursor of uroporphyrinogen III) from two molecules 5-aminolevulinic acid by the zinc enzyme porphobilinogen synthase (Ref. 4). This enzyme contains four Zn(II) in active Zn_A sites and four Zn(II) in the Zn_B sites. Pb^{2+} substitute Zn^{2+} in the Zn_B sites. This again shows cooperative effects to the active Zn_A sites.



Proposed structure of:
four Zn_A sites four Zn_B sites

WHAT KIND OF ARTIFICIAL MMCs CAN BE SYNTHESIZED......

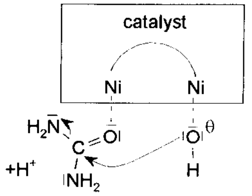
Nature shows us different kind of MMCs and for their understanding the necessity of detailed structural analysis. For synthetic MMCs now, beside detailed structural analysis, thermodynamics of formation, formation constants, cooperative effects had to be studied in detail (Ref. 3) to understand functions. Possible combinations of macromolecules with metals and their derivatives are (for a detailed review see Ref. 3):

- Typ I: Binding of a metal ion/complex/chelate at a macromolecular chain, network or surface (see also Ref. 5a)
- Typ II: Metal complex/chelate as part of a polymer via metal or the ligand (see also Refs. 5b, c).
- Type III: Physical interaction of metal complexes/chelates/clusters with organic and inorganic macromolecules.

Beside organic polymers as carriers, inorganic macromolecules (e.g. SiO_2, TiO_2, zeolites) often exhibit advantages: better chemical and mechanical stability, no shrinkage.

WHICH PROPERTIES ARE COMING OUT AND WHICH APPLICATIONS CAN BE ENVISAGED......

Artificial systems are synthesized with the aim of mimic natural functions and opening of new materials for different promising functions. Some examples, how to learn from biological systems are O_2 carriers, artificial photosynthesis (see Tsuchida et al., Kaneko et al. in Ref. 3), electron transfer chains, cytochromes. In the asymmetric two-center-catalysis (TCC) by the enzyme urease two Ni(II) are arranged in a distance of 3.5 Å. The hydrolysis of urea is enhanced by a factor of 10^{14} in TCC compared to normal HO^--catalysis (Ref. 6). Urea is bound via the O of C=O as nucleophile to one Ni(II) center, HO^- as nucleophil to the other Ni(II) center. HO^- now easily attacks the C of C=O under formation of NH_3 and CO_2. Based on this concept, artificial TCC were tested now successful e.g. for amide hydrolysis (Ref. 6). The combination of TCC with macromolecules were not realized up to now.



Tab. 1 exemplarily compares the activity of MMCs in various catalytic and photocatalytic functions. It is seen that compared to low molecular catalysts and photocatalysts corresponding MMCs exhibit improved properties (for details see the list of Refs.).

Tab. 1 Comparison of turnover numbers (TON: converted molecules per mol catalyst in one hour) of different catalytic and photocatalytic processes

Reaction	Equation	TON	Ref.
Cat. thiol oxidation[a]	$4RS^- + O_2 + 2H_2O$ $\rightarrow 2RSSR + 4HO^-$	low mol. cat. $8 \cdot 10^4$ cat. at polystyrene $< 2 \cdot 10^4$ cat. at silica $< 1.5 \cdot 10^5$	7a
Photocat. thiol oxidation[a]	$2RS^- + 3O_2$ $\rightarrow 2R\text{-}SO_3^-$	low mol. photocat. $< 10^4$ photocat. at silica $< 10^4$	7b
Electrocat. CO_2 reduction[a]	$CO_2 + 2H^+ + 2e^-$ $\rightarrow CO + H_2O$	low mol. electrocat. 10^4 electrocat. in polymers $5 \cdot 10^4$	7c
Cat. H_2O oxidation[b]	$2H_2O \rightarrow$ $O_2 + 4H^+ + 4e^-$	low mol. cat. $5 \cdot 10^2$ (deactivation $5 \cdot 10^2$ L mol^{-1} s^{-1} cat. in polymers $5 \cdot 10^2$ (deactivation 5 L mol^{-1} cm^{-1})	7d
Photoelectrocat. O_2 reduction[a]	$O_2 + 4H^+ + 4e^-$ $\rightarrow 2H_2O$	low mol. photocat. 50 photocat. in polymers $3 \cdot 10^2$	7e

[a] With metal phthalocyanines. [b] With Ruthenium Red.

In Tab. 2 now, various properties of MMCs and their potential applications are summarized (see subsequent contributions in this issue and Ref. 3). Applications realized and under consideration are underlined. Only one point is mentioned in addition. In chemotherapy the investigation of the interaction of antitumor drugs like cis-Pt compounds on the molecular level with DNA results in the development of new more active cytotoxic agents [8a]. Also phototherapy can successful contribute for cancer problems [8b].

Tab. 2. Properties characteristically observed for MMCs (possible applications underlined)

Properties	Potential applications
• Selectivity	⇒ Gas transport/separation, sensor, luminescence
• Electron interaction in solution	⇒ Electron transfer, catalysis
• Photoelectron interactions in solution	⇒ Photoelectron transfer, photocatalysis
• Electron interaction in solids	⇒ Conduction, electrocatalysis, electroluminesc.
• Photoelectron interaction in solids	⇒ Photoconduct., -catalysis, -energy conversion
• Photon interaction in solids	⇒ Molecular devices, information storage
• Ionic conduction	⇒ Batteries, ECD devices
• Non-linear optical effect	⇒ Integrated optics, modulator
• Therapeutic effect	⇒ Drugs, photodrugs
• Preceramics	⇒ Thermally stable comp., quantum devices

MMCs will — bearing also the function of biological systems in mind — contribute increasingly to several severe problems in the world during the next century.

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