Bonding Principles in Bioinorganic Chemistry and Metals in Medicine

Compact Course held by Prof. Ulrich Abram (FU Berlin)
at UFSM Santa Maria
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Lesson 1
Which metals are biologically important and why?

Lesson 2
Typical biological bonding sites for metals – important ligands in biology

Lesson 3
Sodium and Potassium
Iron – uptake, transport, storage, biological functions

Lesson 4
Copper, zinc and vanadium bonding sites

Lesson 5
Metals in medicine

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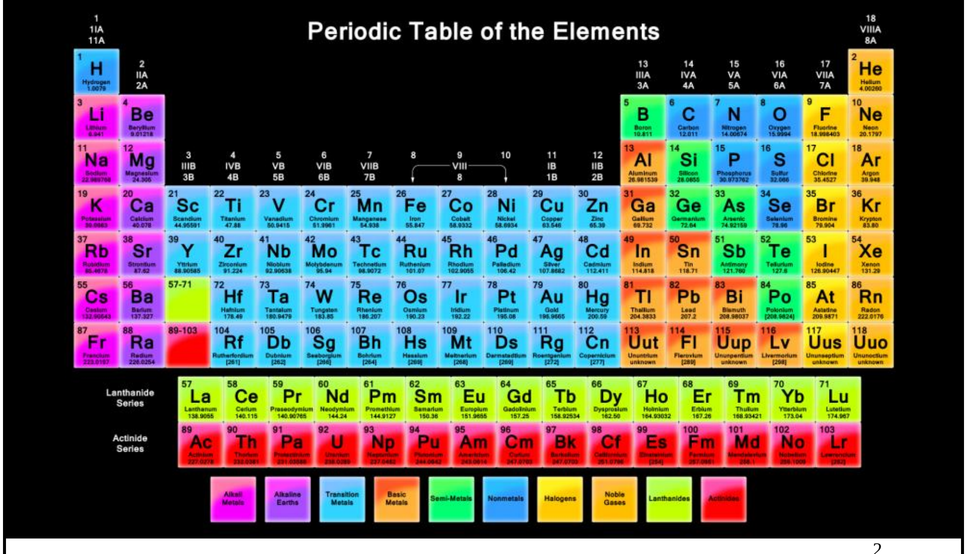
1) The importance of trace elements for life (1)

The distribution of elements in different compartments



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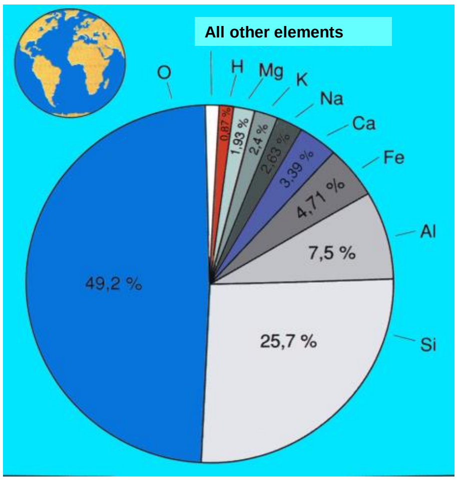
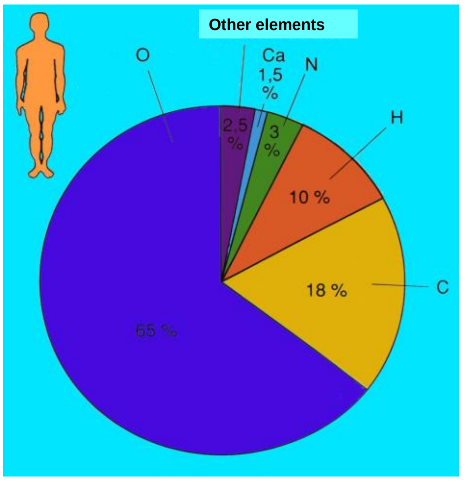
1) The importance of trace elements for life (2)

The distribution of elements in different compartments

Earth's crust



Human body



1) The importance of trace elements for life (3)

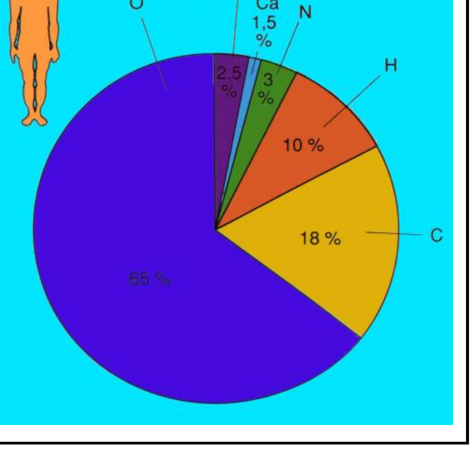
The distribution of elements in different compartments

The 'standard human'

Age	20-30 years
Life time	70 years (25,500 days)
Body weight	70 kg
Body surface	1.8 m^2
Body height	1.70 m

Human body

Other elements !!!



1) The importance of trace elements for life (4)

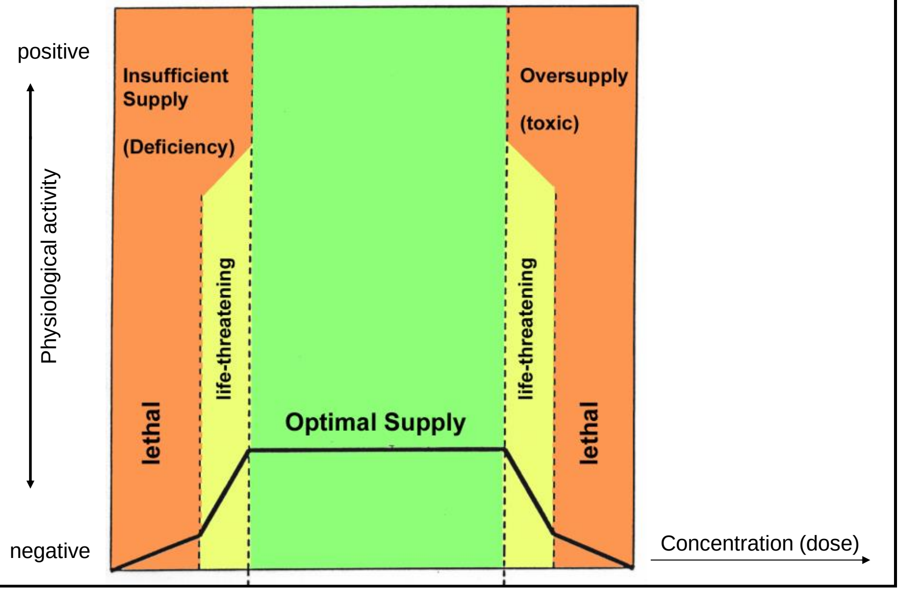
The elemental composition of a human

Element	Symbol	Mass (g)	Known to be essential since
Oxygen	O	45500	
Carbon	C	12600	
Hydrogen	H	7000	
Nitrogen	N	2100	
Calcium	Ca	1050	
Phosphorus	P	700	
Sulphur	S	175	
Potassium	K	140	
Chlorine	Cl	105	
Sodium	Na	105	
Magnesium	Mg	35	
Iron	Fe	4.2	17. Jh.
Zinc	Zn	2.3	1896
Silicon	Si	1.4	1972
Rubidium[a]	Rb	1.1	
Fluorine	F	0.8	1972
Zirconium[a]	Zr	0.3	
Bromine[b]	Br	0.2	

Element	Symbol	Mass (g)	Known to be essential since
Strontium[a]	Sr	0.14	
Copper	Cu	0.11	1925
Aluminium[a]	Al	0.10	
Lead	Pb	0.08	1977
Antimony[a]	Sb	0.07	
Cadmium[b]	Cd	0.03	1977
TIn	Sn	0.03	1970
Iodine	I	0.03	1820
Manganese	Mn	0.02	1931
Vanadium	V	0.02	1971
Selenium	Se	0.02	1957
Barium[a]	Ba	0.02	
Arsenium[b]	As	0.01	1975
Boron	B	0.01	
Nickel	Ni	0.01	1971
Chromium	Cr	0.005	1959
Cobalt	Co	0.003	1935
Molybdenum	Mo	<0.005	1953
Lithium[b]	Li	0.002	

1) The importance of trace elements for life (5)

Relationship between uptake and activity of trace elements



1) The importance of trace elements for life (6)

Relationship between uptake and activity of trace elements

Element	Undersupply (Deficiency)	Oversupply (Toxicity)
Cu	Disturbance of growth Cardiovascular deseases	Wilson's desease (Cu storage in tissues)[a)]
Co	Anemia	Cardiac insufficiency
Fe	Anemia	Hemochromatose (Fe storage in vaious organs)
Cr	Diabetes (malfunctioning glucose degradation))	Nephritis (kidney inflammation)
Mg	Deformation of skeleton	Ataxie (uncoordinated motion)
Mn	Deformation of skeleton, sterility	Mental deseases
Se	Myocardial deformations (Keshan desease))	General toxicity (damage of organs)
Hg		Minamata desease (damage of the central nervous system)
Cd		Itai-Itai desease (osteomalacia: weakening of the skeleton)
I	Thyroid disfunction (iodide struma)	Iodismus (skin irritations, mucous membrane irritations)
F	Caries, Osteoporosis	Fluorosis (ankylosis)

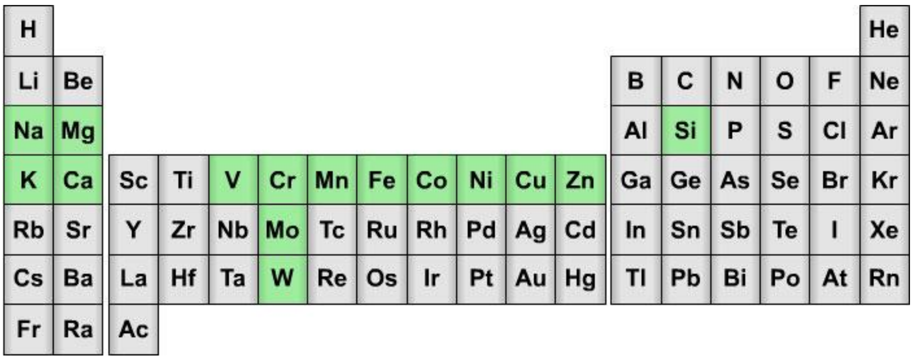
1) The importance of trace elements for life (7)

Nutrient recommendations to cover the daily element supply

Component	Recommended daily uptake (in mg)	
	Adults	Babies
K	2000 – 5500	530
Na	1100 – 3300	260
Ca	800 – 1200	420
Mg	350 – 400	60
Zn	60	

1) The importance of trace elements for life (8)

The inorganic building blocks of life



Remaining questions:

Why are especially these metals used?
What are the functions, for which particular metal can be used?
How do the reaction centers look like?
What are the mechanisms of the corresponding reactions?

1) The evolution of our biosphere (1)

The biosphere of the earth

Biosphere → Water (Hydrosphere), Ground (soil) (Pedosphere), Atmosphere

1) The evolution of our biosphere (2)

The biosphere of the earth

Biosphere: Partition of our planet, where all life processes take place

Hydrosphere	Pedosphere	Atmosphere
10 km	10 km (Pedosphere + Atmosphere)	

20 km	**Biosphere**
6400 km	**Earth radius**

Ratio:

2 : 640 !!!

1) The evolution of our biosphere (3)

The earth in its early stages

About 4.6 billion years go:

- Formation of the four solid protoplanets mercury, venus, earth, mars
- Heating by impact of solid matter and radioactive decay (melting)
- Slow cooling and separation into earth's core and earth's crust
- Subsequent cooling and condensation of solid matter from space

Genesis of the first atmosphere by degasing of the earth's crust

- Volcanism (release of H_2O – about 97%)
- other gases: H_2, CO_2, (N_2, NH_3, H_2S), **no O_2 !!**

Duration about 4.5 billion years !!!

Result:
Ancient Atmosphere which was completely different from our present one

1) The evolution of our biosphere (4)

The earth in its early stages

	Venus	Earth	Mars
Surface Temperature / ° C	462	15	-50
Surface pressure / bar	95	1	0.007
Mass /t	5.3×10^{17}	$5\ 3 \times 10^{15}$	$2{,}4 \times 10^{13}$
Percentage / %			
CO_2	95 – 97	0.03	95
N_2	3.5 – 4.5	78.09	3,0
O_2	0.003	20.95	0.13
Ar	0.003	0.93	1.5

Conclusion: ● Main differences are in the CO_2 content and the pressure

However: ● When all the earths carbon would be transferred into CO_2, the conditions would be similar to those on venus

Question: ● What makes earth so unique?

1) The evolution of our biosphere (5)

The earth in its early stages

Distance to sun: ● Warmer than mars, cooler than venus

Temperature: ● Between 0 and 100° C

Liquid water ● Allows condensation of water and, thus, further cooling by removal of this green-house gas from atmosphere

Binding of CO_2: ● The green-house gas CO_2 is partially dissolved in water

Secondary effect ● Dissolution of Ca^{2+} from rocks

● Chemical binding of huge amounts of CO_2 by precipitation of $CaCO_3$ and $MgCO_3$ (**Result**: ca. 80% of CO_2 is fixed in sediments)

$$CO_2 + 3\,H_2O \longrightarrow 2\,H_3O^+ + CO_3^{2-}$$

$$2\,H_3O^+ + CaO \bullet (Al_2O_3)_x \bullet (SiO_2)_y \longrightarrow Ca^{2+} + 3\,H_2O + (Al_2O_3)_x \bullet (SiO_2)_y$$

$$Ca^{2+} + CO_3^{2-} \longrightarrow CaCO_3$$

$$CO_2 + CaO \bullet (Al_2O_3)_x \bullet (SiO_2)_y \longrightarrow CaCO_3\downarrow + (Al_2O_3)_x \bullet (SiO_2)_y$$

1) The evolution of our biosphere (6)

The development of the present atmosphere (Where does the dioxygen, O_2, come from?)

Possible ‘Inorganic solutions”

Photolysis of CO_2 by hard UV radiation

$2\ CO_2 \xrightarrow{hv} 2\ CO + O_2$

• Should form carbon monoxide, but where is it??

Photolysis of H_2O by hard UV radiation

$2\ H_2O \xrightarrow{hv} 2\ H_2O + O_2$

• Calculation show, that only ca. 0.1% of the present O_2 could be formed via photolytic processes

•With increasing O_2 content, preferably O_2 is destroyed in favor to H_2O (Urey effect, positive chemical feedback

Thesis: All origin of dioxygen on earth is life!!!

Questions: Where does life come from? Where do the molecules of life come from?

1) The evolution of our biosphere (7)

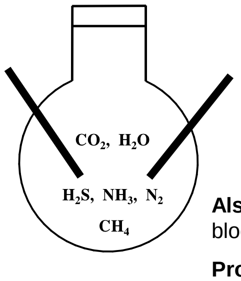
Where do the molecules of life come from?

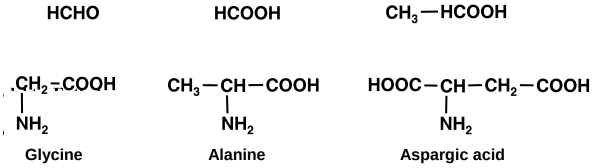
Theory 1:

- Molecules of life come from space with cosmic particles
- Problem: This simply shifts the synthesis of such molecules to another place

Theory 2:

- The Miller/Urey experiment: formation of a remarkable number of important molecules from simple inorganic molecules and electric discharges and/or UV light





Glycine Alanine Aspargic acid

Also: sugars, purine, porphyrine, adenine and other essential building blocks of life

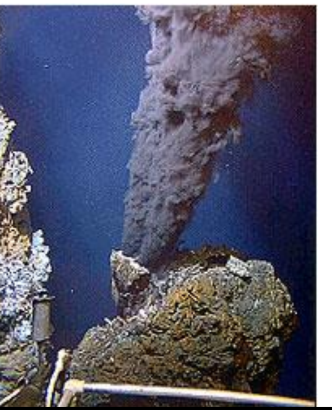
Problems: amino acids are formed as racemate, some products have not been used by evolution, time scale etc.

1) The evolution of our biosphere (8)

Where do the molecules of life come from?

Theory 3:

- Black smokers as place were prebiotic chemistry happened
- extreme conditions (300 atm, 350° C), release of H_2S
- good catalysts (porous structures with suitable metal ions: Cu_2S, FeS, ZnS, FeS_2)



1) The evolution of our biosphere (9)

Where do the molecules of life come from?

Theory 3:

- Black smokers as place were prebiotic chemistry happened
- extreme conditions (300 atm, 350° C), release of H_2S
- good catalysts (porous structures with suitable metal ions: Cu_2S, FeS, ZnS, FeS_2)

Possible reactions:

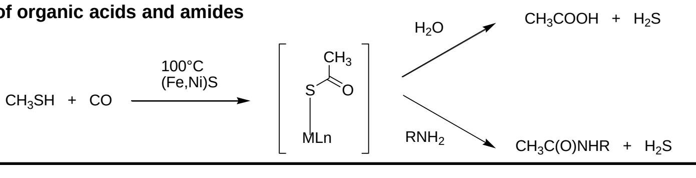
Formation of ammonia:

$FeS\ (s) + H_2S\ (aq) \rightarrow FeS_2\ (s) + H_2\ (g)$ $\Delta G = -38{,}4$ kJ/mol

$7\ FeS + 7\ H_2S + 4\ CO_2 \rightarrow$
$CH_2(COOH)_2\ (aq) + 7\ FeS_2\ (s) + 4\ H_2O\ (aq)$ $\Delta G = -420$ kJ/mol

$N_2\ (g) + 3\ FeS_2\ (s) + 3\ H_2S\ (aq) \rightarrow 3\ FeS_2\ (s) + 2\ NH_3\ (g)$ $\Delta G < 0$

Formation of organic acids and amides



1) The evolution of our biosphere (10)

Where do the molecules of life come from?

Theory 4 - ….:

Other hydrothermal reaction at mineral surfaces

- Classical Fischer-Trosch Synthesis on metal centers

$$CO_2 + H_2 \longrightarrow CH_4 + c_2H_6 + C_3H_8 + C_nH_{n+2} + ... \quad H_2O$$

$$2\ (FeO)_{rock} + H_2O \longrightarrow (Fe_2O_3)rock + H_2$$

- Carbon-fixation at magnetite (Fe_3O_4)

$$CO_2 + H_2O \xrightarrow[- Fe_2O_3]{350°C,\ 10\ bar,\ Fe_3O_4} CH_3CH_2OH + CH_3CHO + CH_3COOH + ...$$

- Catalysis at sulphur-containing minerals

$$FeS + H_2S \longrightarrow FeS_2 + H_2$$

$$3\ FeS + 3\ H_2S + CO \longrightarrow 3\ FeS_2 + CH_4 + H_2O$$

$$CH_3SH + CO + H_2O \longrightarrow CH_3COOH + H_2S$$

1) The evolution of our biosphere (11)

Where do the molecules of life come from?

Conclusions

- There exist several chemical reaction pathways, which provide ‘inorganic access’ to organic molecules and even ‘biomolecules’

- Most of such reactions require drastic conditions, but they are readily provided by hydrothermal spots
- Metal compounds act as catalyst (highly activated and large surface)
- Common metal ions such as Fe^{2+}, Zn^{2+}, Cu^{2+} are present at the reactive spots

Primitive, self-replicating systems (living organisms) can be formed under such conditions

Note! Reaction conditions are reductive (Fe^{2+} - no Fe^{3+}) !!!

1) The evolution of our biosphere (12)

The evolution of the oxygen-containing atmosphere

Atmospheral dioxygen is the result of life !!!

General process: Photosynthesis

$$6\ CO_2 + 6\ H_2O \longrightarrow C_6H_{12}O_6 + 6\ O_2$$

Products: - reduced carbon atoms (carbon hydrates, carbon containing sediments))

- Dioxygen (oxydation)

- The concentration of elemental oxygen in the atmosphere increased very slowly and huge amounts were trapped by chemical reactions
- Oxidation of dissolved Fe^{2+} and S^{2-} ions (formation of iron sediments)

  $4\ Fe^{2+} + 12\ H_2O + O_2 \longrightarrow 2\ Fe_2O_3 + 8\ H_3O^+$

  $S^{2-} + 2\ O_2 \longrightarrow SO_4^{2}$
- Dissolution of O_2 in sea water

Evolution of dioxygen may have been the first ecological desaster in the history of earth

1) The evolution of our biosphere (13)

The evolution of the oxygen-containing atmosphere

Atmospheral dioxygen is the result of life !!!

Evolution of dioxygen may have been the first ecological desaster in the history of earth

- Slow increase of O_2 concentrations allows the evolutionary development of protecting systems and mechanisms
- 1.5 billion years ago: development of first organisms, which can use reduced carbon for metabolism
- Respiration means enormous evolutionary advantage (14 x more energy)
- Coupling of CO_2 use and O_2 formation to one cycle
- Re-formation of inorganic carbon sediments is slower than the formation of biomass (formation of coal, oil and gas)
- 500 – 700 Mio years ago: O_2 concentration in atmosphere exceeds 10%
- New quality (allows O_3 formation and absorption of UV light): life out of the sea
- Since 300 Mio years: quasistationary O_2 concentration (21%)

1) The evolution of our biosphere (14)

The evolution of the oxygen-containing atmosphere

Other important biological processes which contribute to the composition of the atmosphere

Nitrification	NO_3^-, NO_2^-	→	N_2O, N_2, O_2
Sulphur bakteria	$2\ H_2S + O_2$	→	$2\ H_2O + 2\ S$
Nitrogen fixation	N_2, H_2O	→	NH_3

General conclusions:

- Life is thermodynamically a highly improbable process
  - decrease of entropy
  - is maintained by a permanent energy flux from sun
  - efficient metabolic processe (fermentation, respiration) are required
- Assumed that the life would finish on earth, all atmospheric oxygen would be bonded to sediments after 300 Mio. Years
- Life is a permanently fluxing equilibrium. Small changes of parameters may have dramatic consequences