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Aluminum in dental implants: how to reduce a potential risk to patient´s health?

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INTRODUCTION

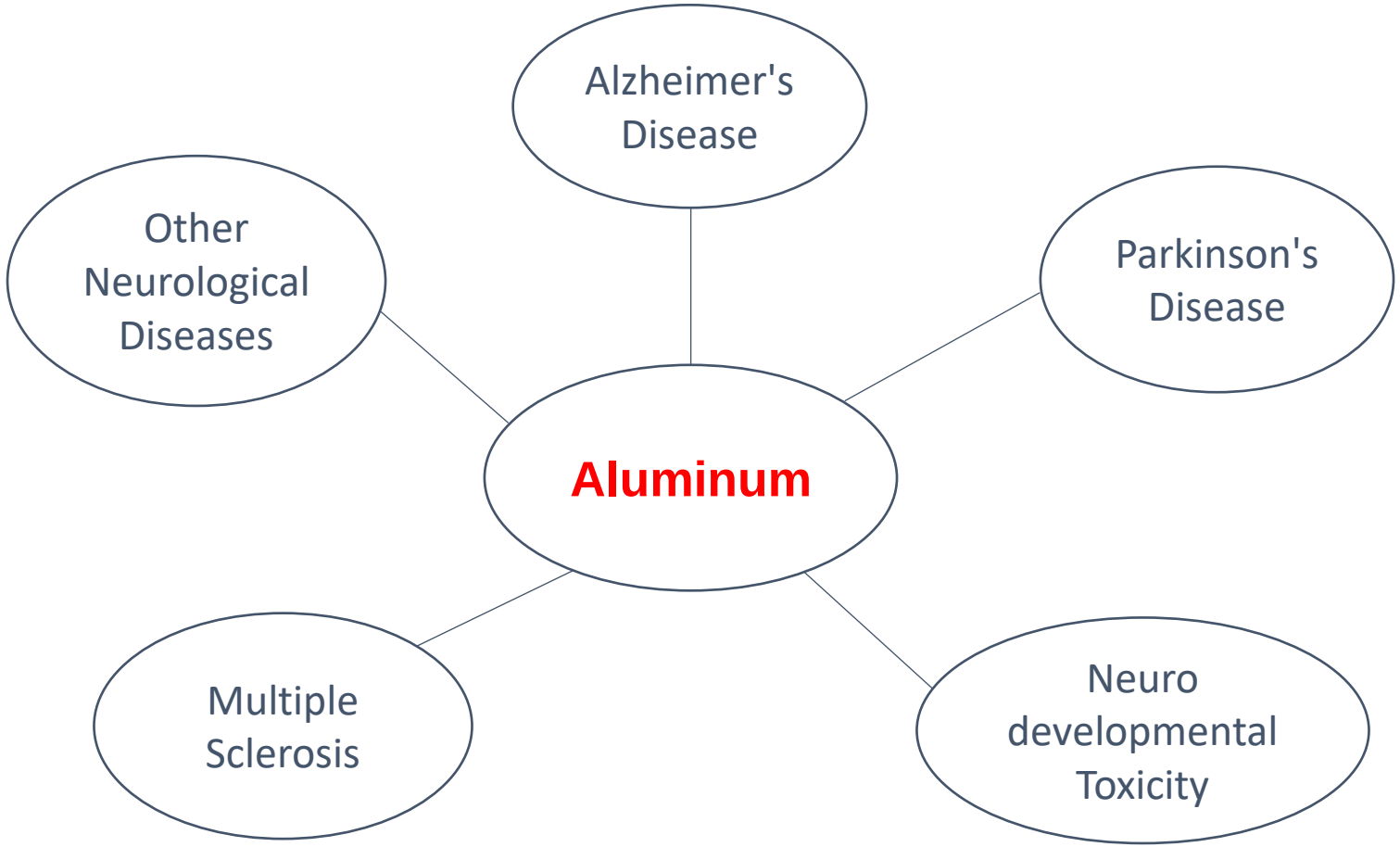
- A huge problem using dental implants is a chemical “contamination” of their surface.

- Different processes during the implant production are a source of contamination. For example, during sandblasting and acid etching, as the most commonly used treatment to achieve optimal implant surface roughness necessary for osseointegration (formation of a direct and functional connection between bone and implant), Al_2O_3 particles are used.

- These Al particles could be trapped on the implant surface and participate in a corrosion process allowing ions release in surrounding tissues and bloodstream!!

POTENTIAL RISK FOR HEALTH OF PATIENTS!!! **WHY???**

Aluminum NEUROTOXICITY – recognized as a neuro-toxin!!



Al is everywhere!!

AVOID Aluminum!!

-in cosmetics, deodorants, vaccines, frozen dinners, Al-foil, to-go containers…

- Therefore, it is very important to control surface characteristics and chemical composition of implants in order to minimize possible negative effects on patient's health.

- An approach is implant surface modification/functionalization by bio(organic) molecules.

The aim of the study:

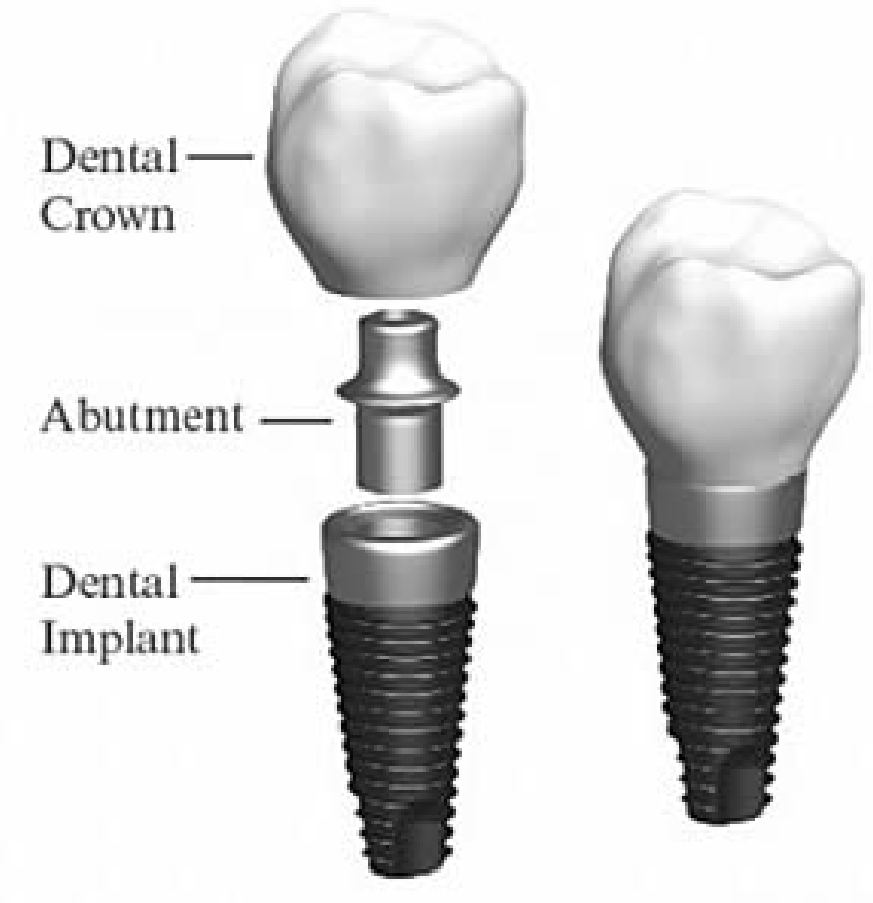
Surface functionalization of the commercial implant with detected Al was performed by alendronate sodium and hydrolyzed collagen, molecules with positive effect on the bone system, to enhance anti-corrosion protection as a basic prerequisite for implant's long-term life in the human body without possible negative biological effects.

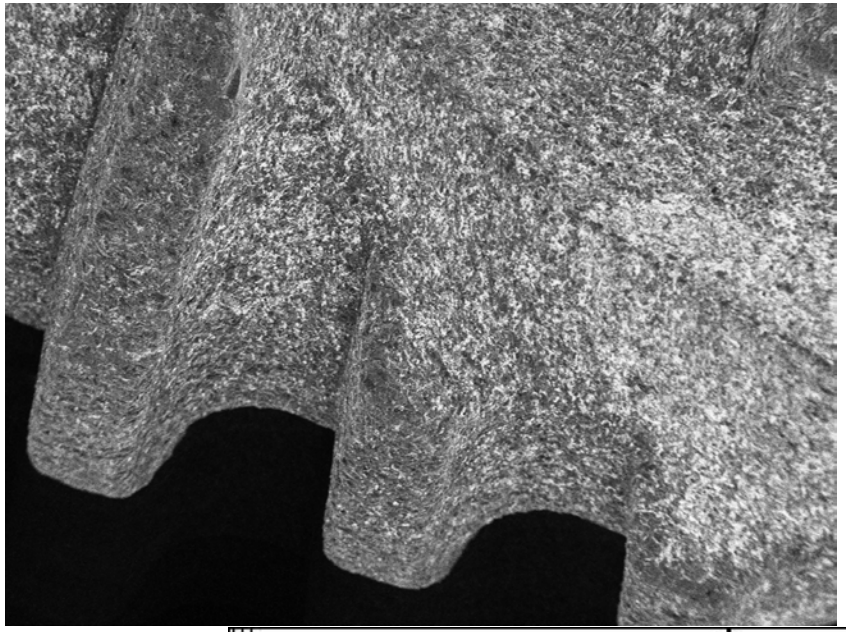
EXPERIMENTAL

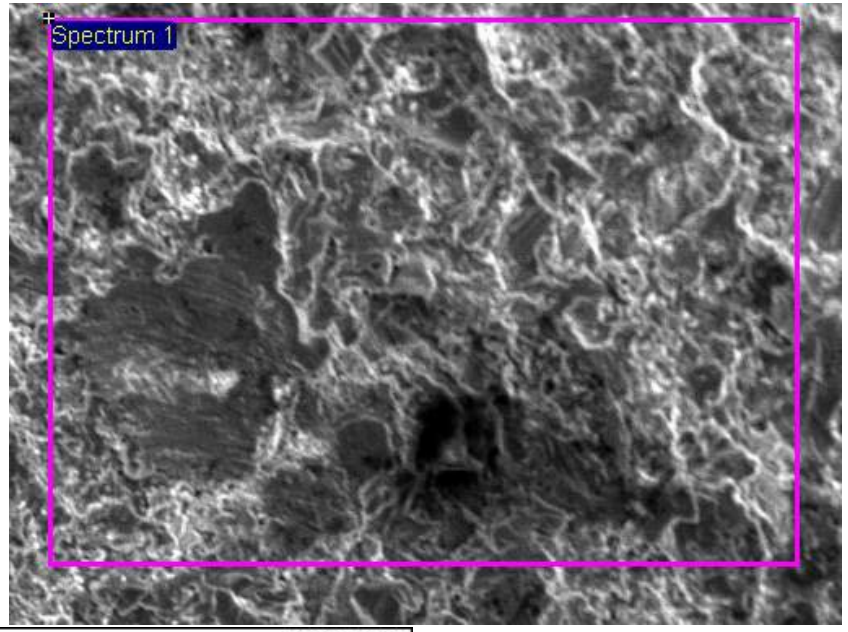
- Dental implant: C/X A11, Ankylos ® - made of titanium grade 2

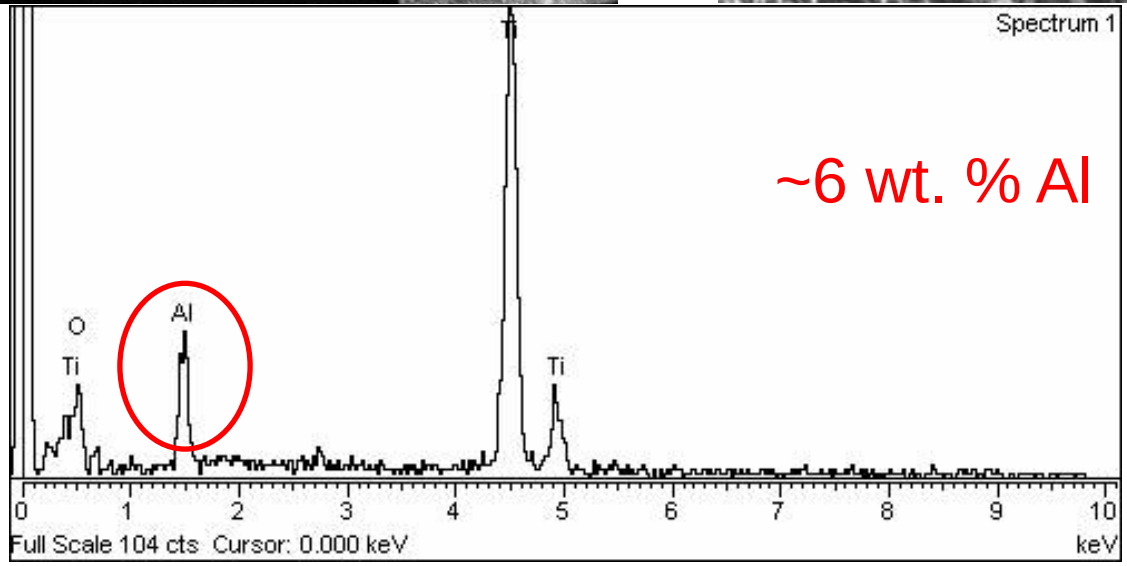
Element	N	C	O	Fe	H	Ti	Other
wt %	0.03	0.10	0.25	0.30	0.0155	Balance	0.4

A11 implant





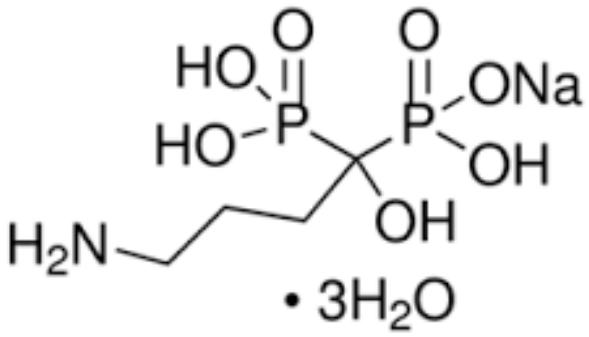


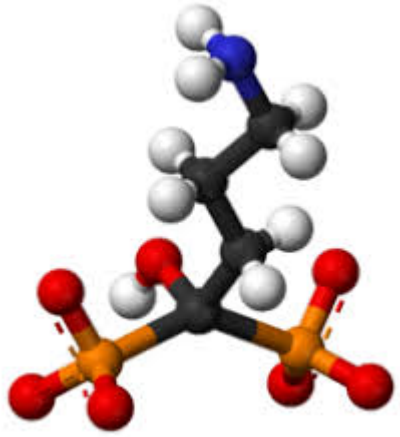


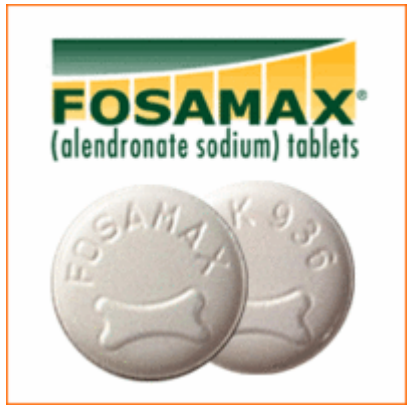
SEM revealed a microstructured surface layer, TiO_2 as confirmed by XPS measurements; EDS revealed the presence of aluminum.

- Molecules for functionalization of the implant surface:

A) SODIUM ALENDRONATE TRIHYDRATE - FOSAMAX ®



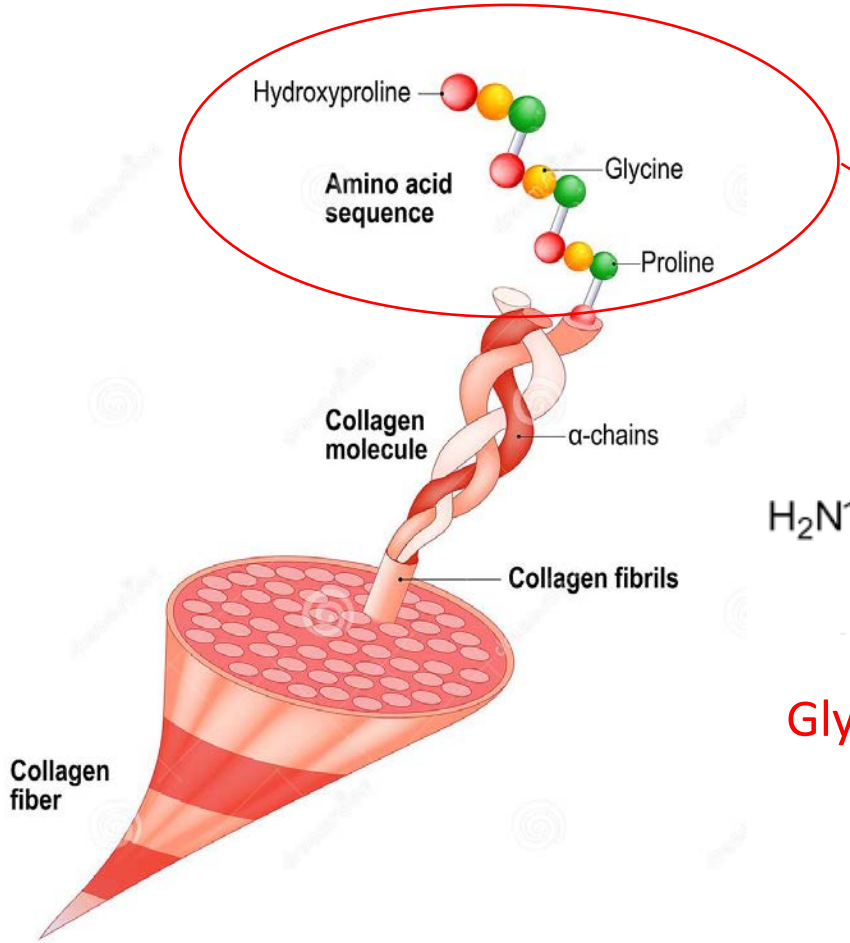


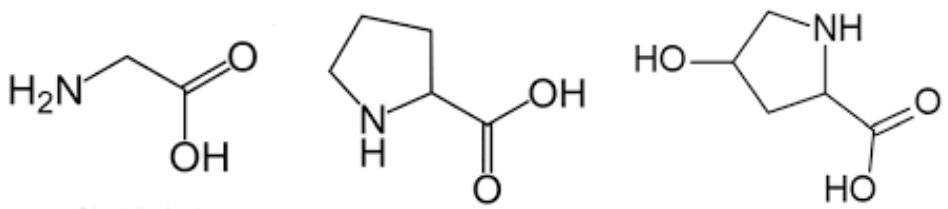


- commercially known as Fosamax®, a drug used for bone diseases: osteoporosis, osteopenia…
- molecule that possesses a strong affinity for binding to bone mineral phase and positively affects bone's density

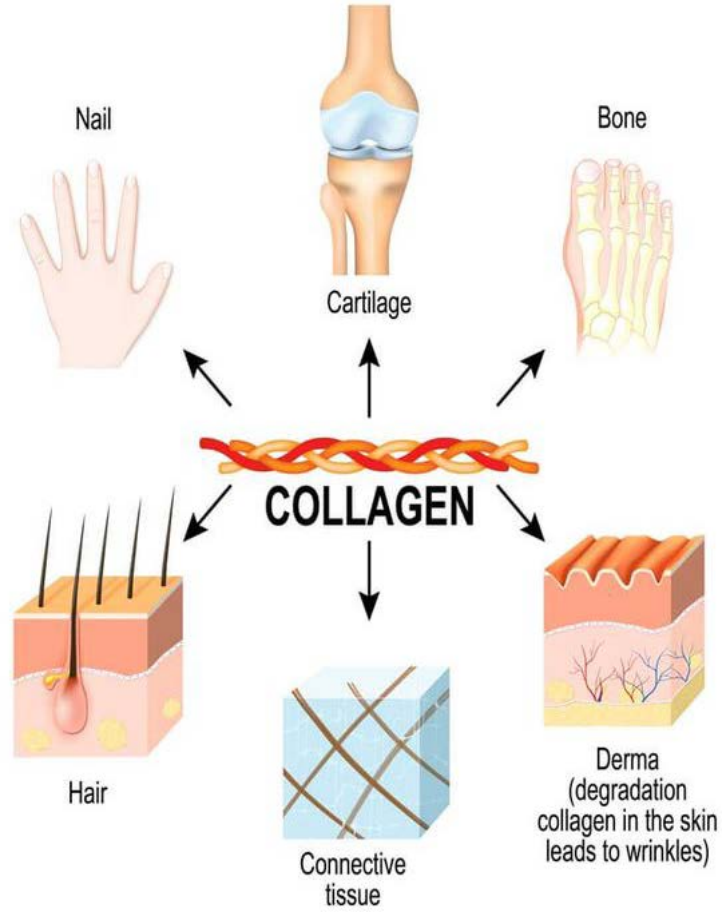
B) HYDROLIZED COLLAGEN

- extracted from different sources: bovine or porcine
- collagen is the most important protein mainly formed by glycine, proline and hydroxyproline in a triple helix formed by 3 α chains; molecular weight ~300 kDa
- hydrolyzed collagen: α chains are separated into small low-molecular-weight peptides,~ 3-6 kDa





Glycine – Proline - Hydroxyproline



EXPERIMENTAL CONDITIONS OF COATINGS PREPARATION

- 10 mmol dm^{-3} aqueous solutions of alendronate and hydrolyzed collagen
- method of coatings preparation : self-assembly at T = 22 ± 2 °C; 24 hours

- Implant/Alendronate coating
- Implant/Hydrolyzed collagen coating

- Characterization techniques:

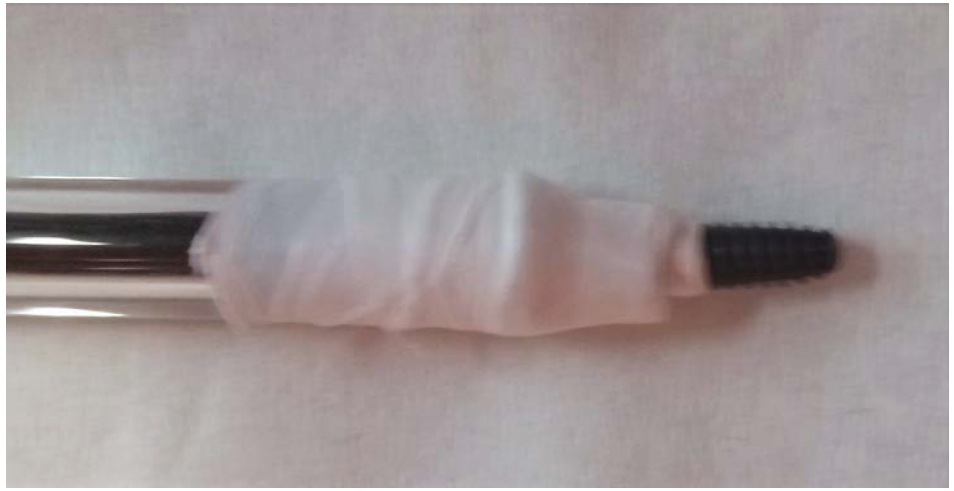
-SEM
-EDS
-EIS

- Computational study: DFT
implant surface was modelled with small $(TiO_2)_{10}$ nanocluster
for all possible molecular implant/organic molecule interaction predictions

RESULTS

Electrochemical impedance spectroscopy, EIS characterization:

- standard three-electrode cell:
- counter electrode: Pt sheet
- reference electrode: Ag|AgCl, 3.0 mol dm^{-3} KCl
- working electrode: unmodified and modified implant (A = 0.98 cm^2)

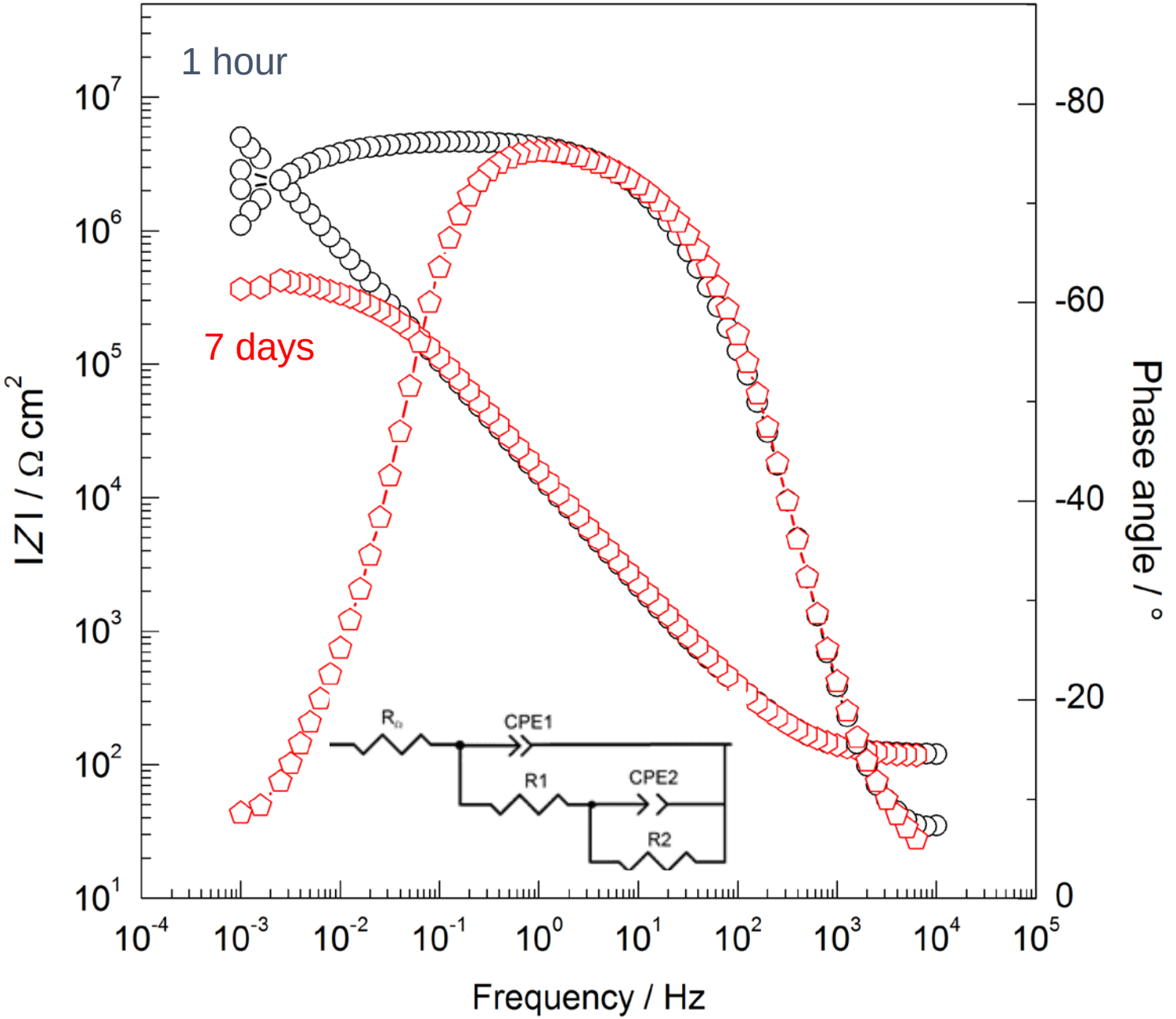


- electrolyte: Fusayama artificial saliva, *pH* = 6.8
- open circuit potential, E_{OP}
- T = 22 ± 2 °C
- stabilization period: 1 hour and 7 days in artificial saliva solution

Implant / Artificial saliva interface

Element	1 hour	7 days
R_1 / Ω cm^2	760	307
R_2 / MΩ cm^2	9.90	0.44

responsible for good barrier properties of the as-received implant; $R_2 >> R_1$



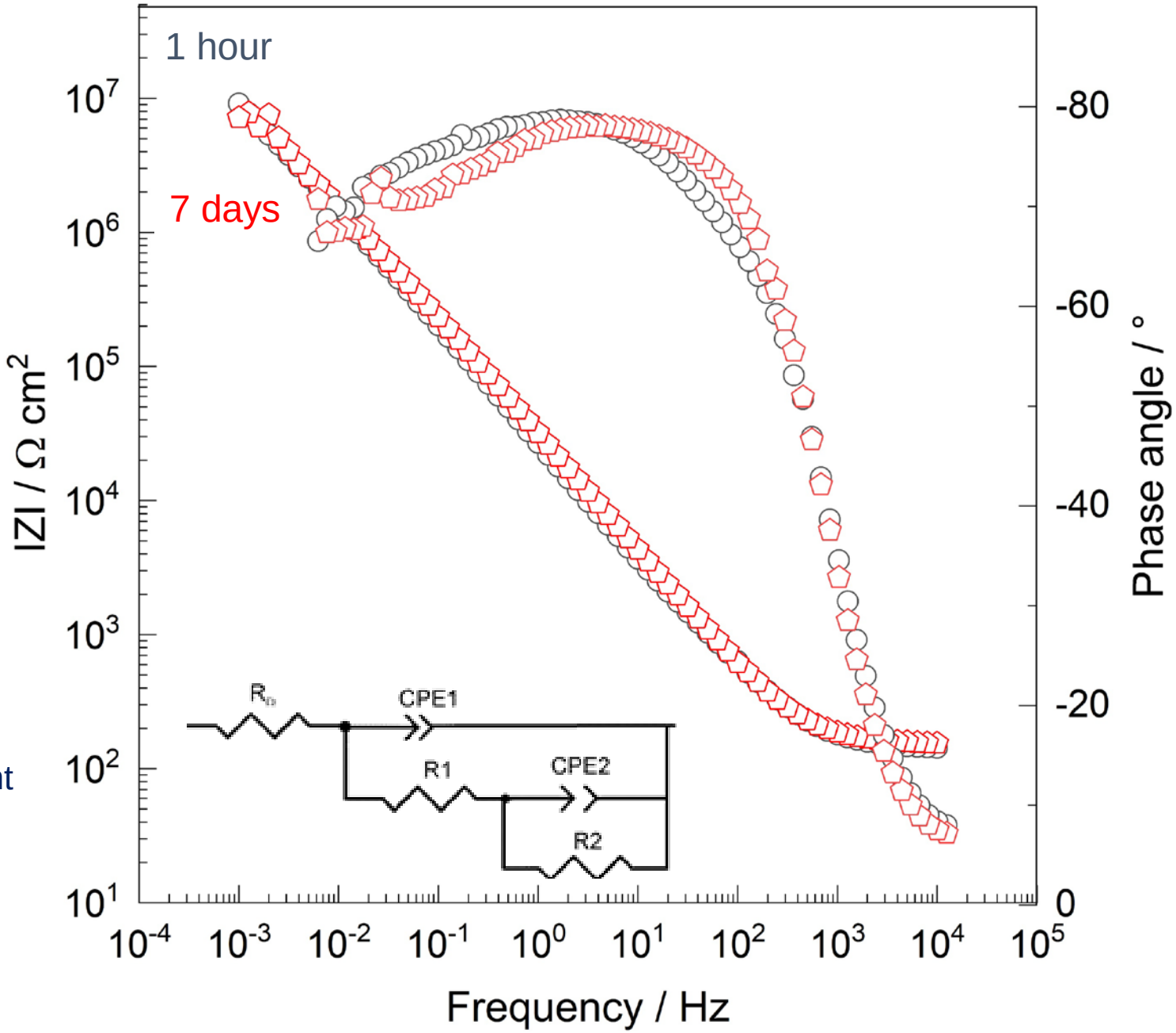
Two-time constant electrical equivalent circuit:

-(CPE_1R_1): outer part of the oxide layer present on the implant

-(CPE_2R_2): inner part of the oxide layer present on the implant

Implant / Alendronate / Artificial saliva interface

Element	1 hour	7 days
R_1 / Ω cm^2	307	302
R_2 / MΩ cm^2	39.0	5.88
Protection efficiency / %	74.6	92.5



Two-time constant electrical equivalent circuit:

-(CPE_1R_1): alendronate coating on the implant

-(CPE_2R_2): structural defects of the alendronate coating

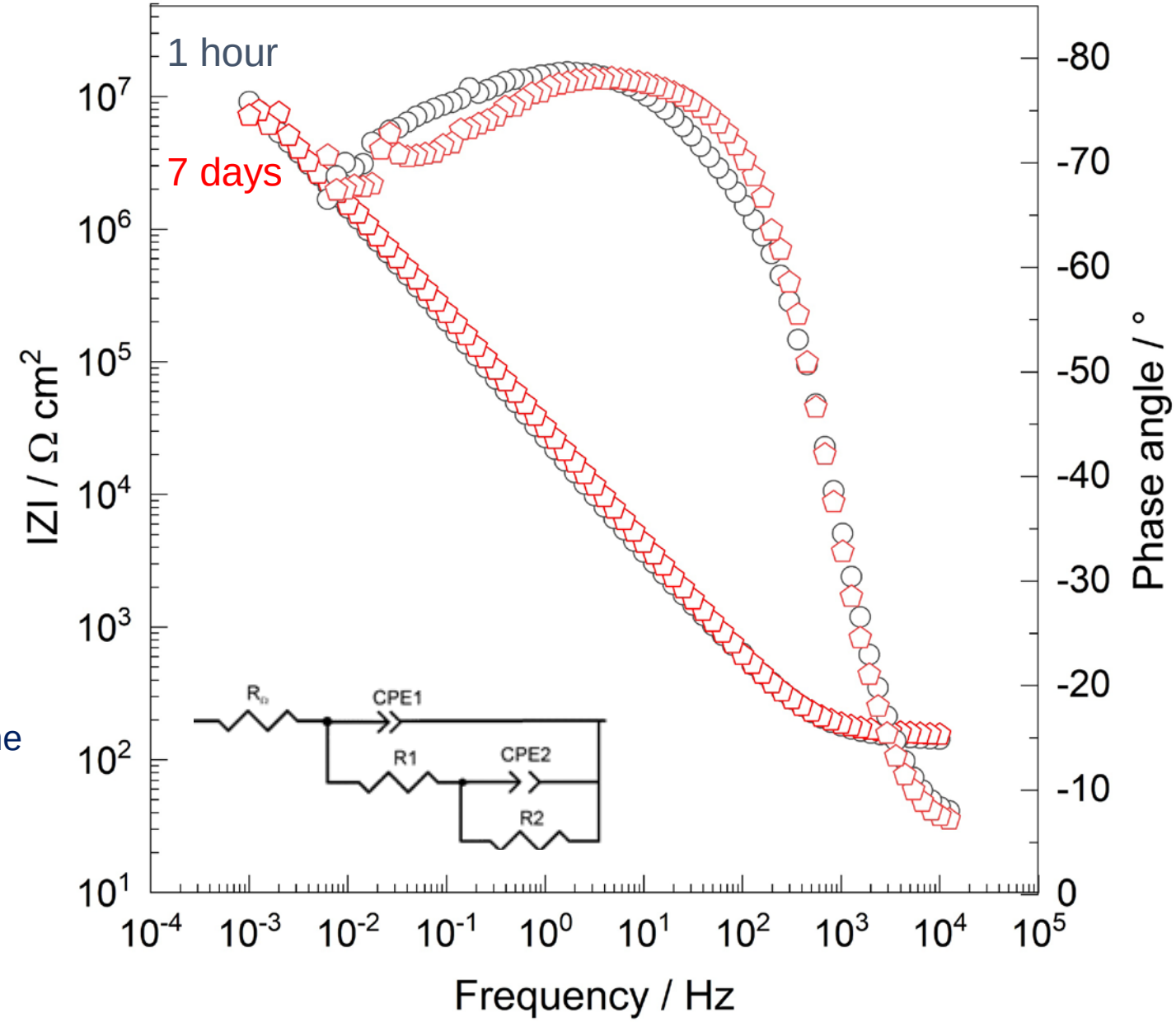
Implant / Hydrolyzed collagen / Artificial saliva interface

Element	1 hour	7 days
R_1 / kΩ cm^2	10.1	6·10^3
R_2 / MΩ cm^2	40.8	24.2
Protection efficiency / %	75.7	98.2

Two-time constant electrical equivalent circuit:

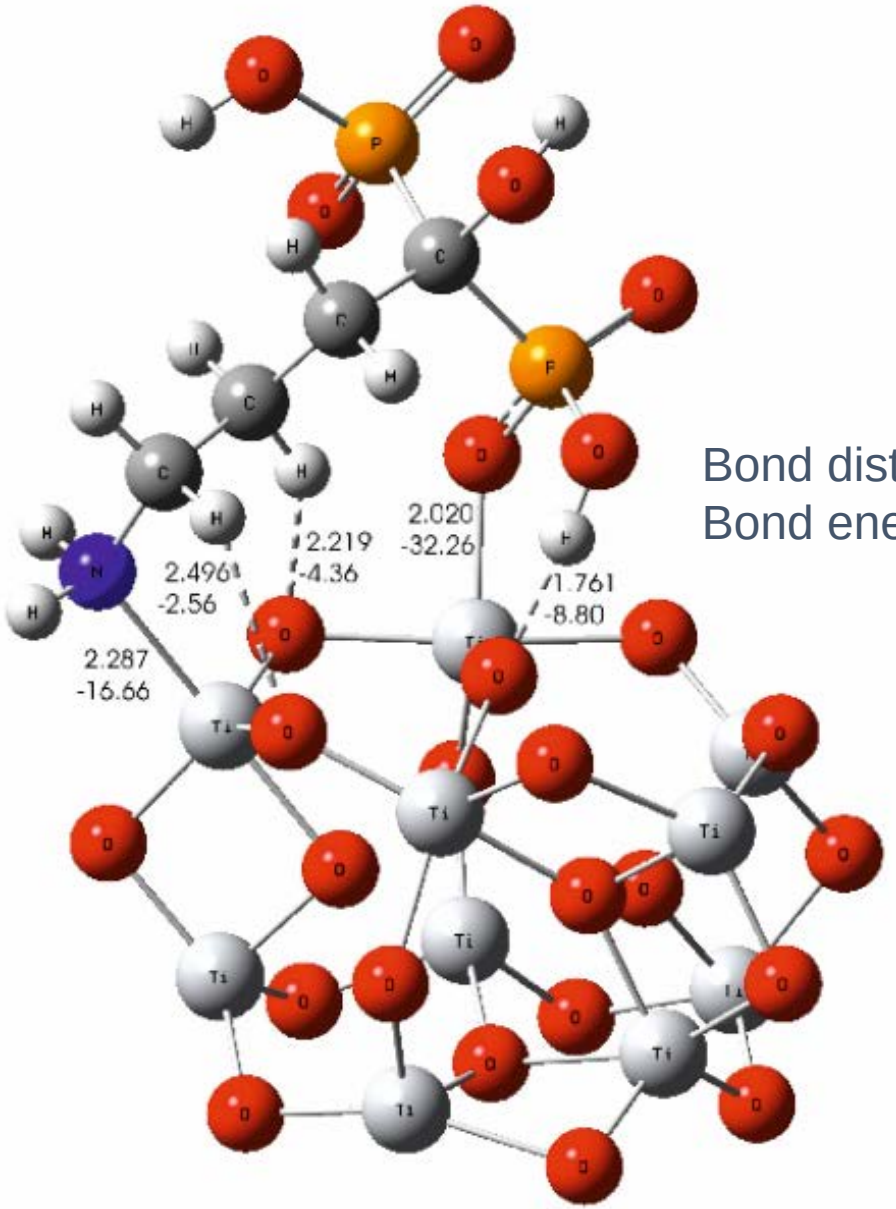
-(CPE_1R_1): hydrolyzed collagen coating on the implant

-(CPE_2R_2): structural defects of the hydrolyzed collagen coating



Coating formation mechanism on the implant: DFT study

The most favorable
$(TiO_2)_{10}$ / Alendronate interaction



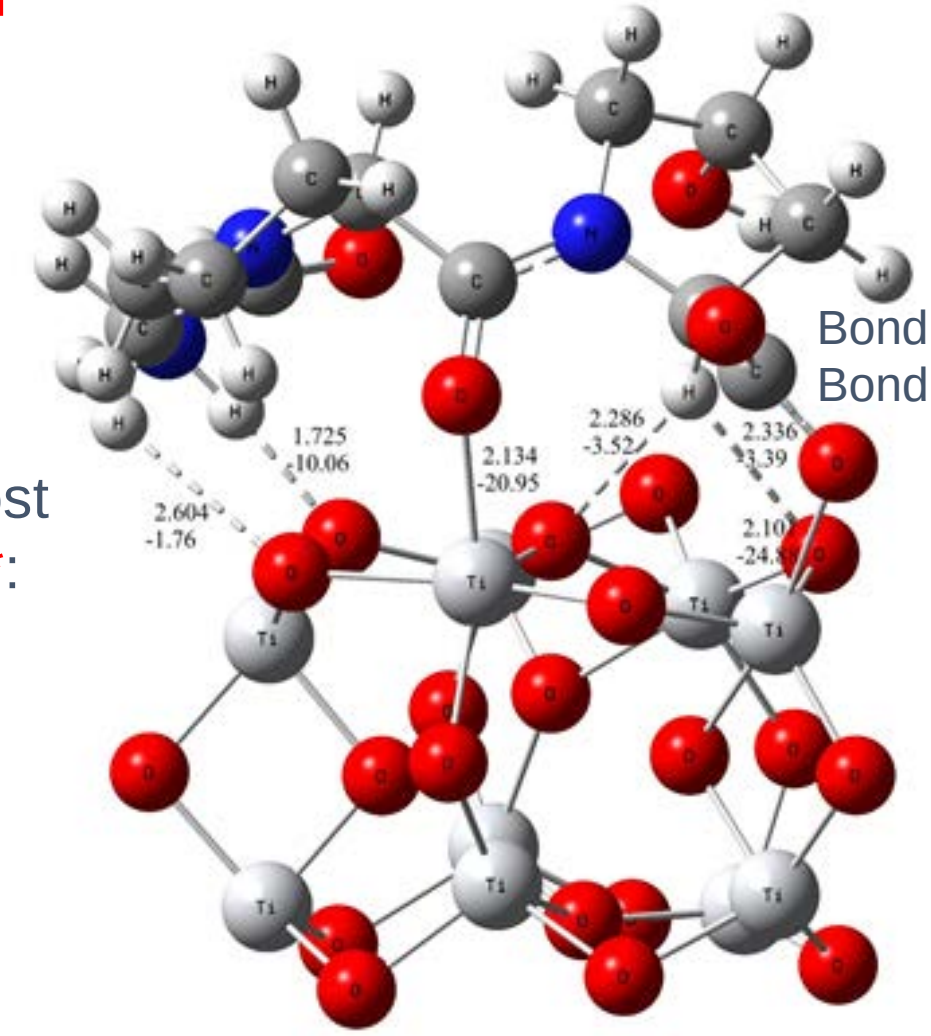
Bond distances: Å;
Bond energy: kcal mol^{-1}

Gibbs free energy of interactions of the most stable structure $(TiO_2)_{10}$ / alendronate:

ΔG^*_{INT} = -13.64 kcal mol^{-1}

The most favorable

$(TiO_2)_{10}$ / Hydrolyzed collagen* interaction



Bond distances: Å;
Bond energy: kcal mol^{-1}

Gibbs free energy of interaction of the most stable structure $(TiO_2)_{10}$ / hydrolyzed collagen*:

ΔG^*_{INT} = -6.45 kcal mol^{-1}

*Hydrolyzed collagen was modelled by the most frequent tripeptide unit, NH^{3+}-Gly-Pro-Hyp-COO^-

CONCLUSIONS

✓Stable alendronate and hydrolyzed collagen coatings on the titanium dental implant are prepared by a simple self-assembly for 24 hours.

✓According to the DFT findings, chosen molecules possess an affinity ($\Delta G^*_{INT} < 0$) to the implant surface. Alendronate coating formation occurs via two coordinate Ti–O and Ti–N bonds, while hydrolyzed collagen coating formation takes place via two coordinate Ti–O bonds. Both coating structures are additionally stabilized by hydrogen bonds, which obviously provide a good stability during 7-days exposure of modified implants to the saliva solution.

✓The notable difference in values of Gibbs free energies released for the $(TiO_2)_{10}$–alendronate (ΔG^*_{INT} = -13.64 kcal mol^{-1}) or $(TiO_2)_{10}$–hydrolyzed collagen (ΔG^*_{INT} = -6.45 kcal mol^{-1}) molecular interactions points to more favorable formation of alendronate coating on the titanium implant.

✓Both coatings enhance anti-corrosion protection of the implant and act as an additional barrier during exposure to the saliva:

η_{7days}(Implant/alendronate) = 92.5 % η_{7days}(Implant/hydrolyzed collagen) = 98.2 %

Therefore, prepared coatings, especially hydrolyzed collagen coating minimize a potential risk of releasing harmful ions (as Al) into surroundings.

✓Very good stability of the hydrolyzed collagen-modified implant during 7 days-immersion period can be correlated with closed structure of the collagen coating, which like „umbrella" protects the implant surface. In comparison, in the alendronate –modified implant, -PO_3H, -COH, and –NH_2 are free, unbounded functional groups, which can interact easily with water/ions present in the saliva what results in increasing coating defects size and density.

✓Results indicate that both modified implants are good candidates for *in vitro* investigations of osteoconductivity and bioactivity, which are crucial for a long-life cycle of dental implants without negative reactions.