==================== **MATHEMATICAL MODELING** =====================

Interaction of charged hydroxyapatite and living cells. I. Hydroxyapatite polarization properties

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Abstract. The most principal methods of studying hydroxyapatite (HAP) nanostructures and proton transfer peculiarities, its polarization properties are presented in this paper. HAP is one of the most widely used materials in medicine and biotechnology. The interaction between HAP biomaterials and living cells is improved, if the HAP surface is charged. The charge is inducible on HAP ceramics by the proton transport along the OH chains in columnar channels. These chains are formed by OH ions along c-axis and are surrounded by calcium triangles. The paper presents *ab initio* quantum-chemical calculations (with Gaussian98 code, HF, 6-31G(d)), which clarify the double-well asymmetric potential energy profile and were held to investigate the energy barriers for proton transport along the columnar channel. The calculated values of barriers can explain long storage of polarization charge, which is observed in experiments. The value of applied electric field could switch asymmetry of double-wall potential and made the proton transfer possible is of the order of 10^9 V/m, but proton tunneling is possible at 10^6 V/m. The estimated value of HAP surface polarization ~ 0.1 C/m^2 influences movement of living cells and leads to their adhesion on the charged HAP surface.

Key words: hydroxyapatite, proton transfer, electrical properties, surface properties.

INTRODUCTION

In recent years there is an increasing necessity of inserting implants into human beings. It is known that, as a minimum, biomaterials for implants should be non-toxic, relatively bio-inert, and mechanically appropriate. One of the first most suitable bone implant materials is hydroxyapatite (HAP) and some kinds of HAP-ceramics. From experimental data [1] follows that the charged surface of HAP ceramics enhances osteoconductivity and promotes bone reconstruction more than the nonpolarised HAP ceramic surface. It is known [2] that electrically polarized HAP enhances cell adhesion on its surface and bone formation. Also HAP can store large charge up to 0.1 C/m^2 within the time significant for biomedical purposes – more than 1.5 months [2].

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HYDROXYAPATITE MAIN STRUCTURAL AND COMPUTED PROPERTIES

In this paper we present molecular mechanics and *ab initio* quantum-chemical calculations (with HyperChem and Gaussian98 code, HF, 6-31G(d)), which were held to investigate the optimized HAP structure and energy barriers on possible proton transport ways to clarify HAP surface polarization mechanism. Also we have studied the influence of electric field on energy barriers, substitution of OH ion group by F ion. Calculated values of barriers can explain long storage of polarization charge, which is observed in experiments. The model and calculated data are available for explanation of HAP surface reconstruction under proton charge movement and interaction with living cells.

A significant property of the HAP is existence of OH− chains [3] along crystallographic c-axes in columns formed by Ca-triangles and phosphate groups, Fig.1. HAP can occur in two

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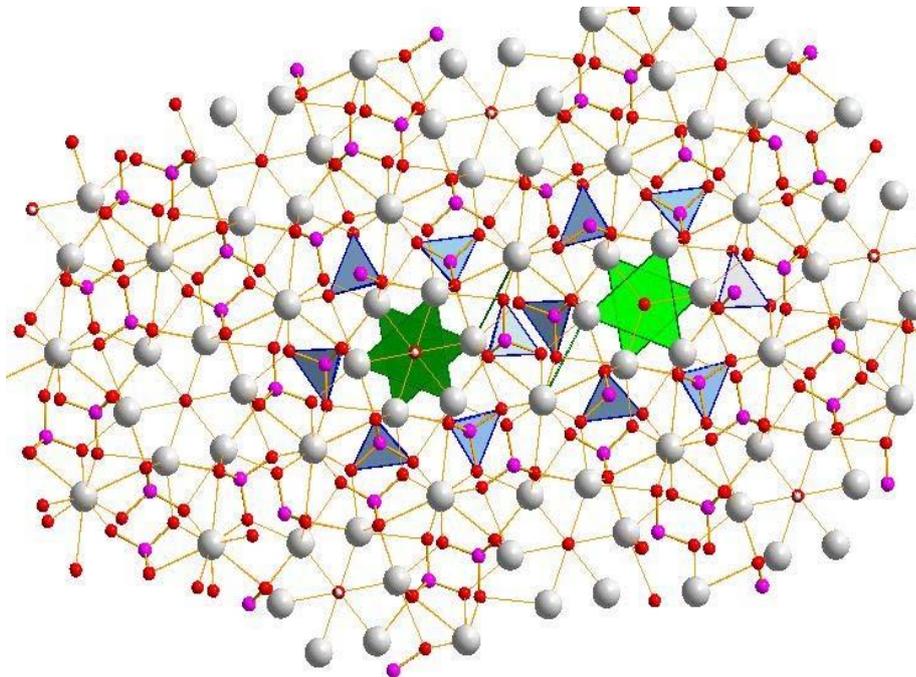
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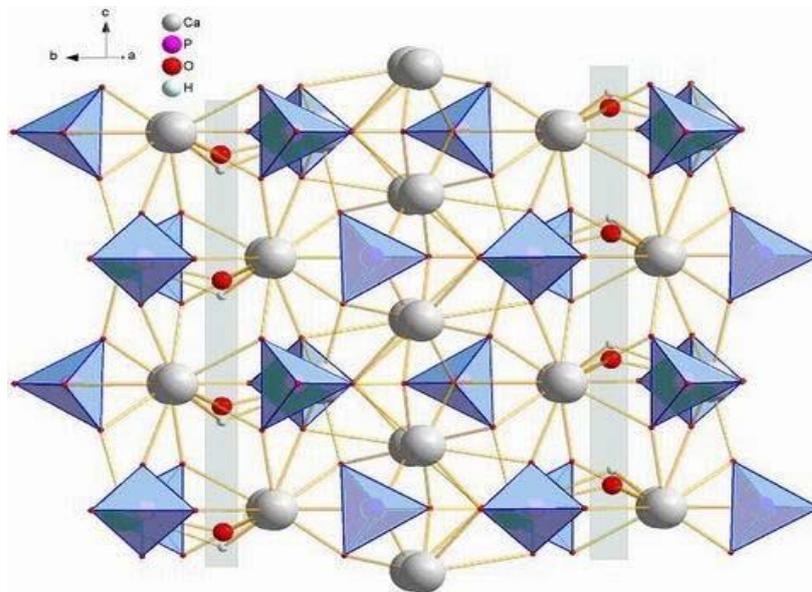
Fig. 1. HAP structure - formation of pseudo-one-dimensional OH channels (a) OH dipoles form chains along crystallographic c-axes, (b) view on the OH channels from the plane cross-section. PO4 group is shown as tetrahedra.

crystallographic space groups – monoclinic P2$_1$/b and hexagonal P6$_3$/m, with known cell parameters [4]. In hexagonal phase OH dipoles in the same columnar channel may be oriented differently (disordered column model) or they may be oriented the same way in the given column but the orientation is independent on the orientation in neighboring columns (ordered column model of the hexagonal phase).

The *ab initio* Hartree-Fock (HF) method realized in GAUSSIAN 98 code [5] was used to calculate energy barrier values on all possible ways of proton transport. The 6-31G(d) basis was used. It is assumed that proton transport along the columnar channel consists of two steps – the first one is rotation of a proton around the O^{2-}, and then the proton moves to the nearest proton vacancy. The PO$_4$ group influences the potential energy profile. It is also possible that a proton can transfer along a column through the oxygen from a PO$_4$ group.

RESULTS AND DISCUSSION

For all cases calculated energy curve profile clearly reveals double well asymmetric potentials. Calculated energy barrier values for different cases without applied external electric field are in Table 1.

Table 1. Calculated energy barrier values

		Along c-axes			Through oxygen from PO$_4$		
		ΔE_1, eV	ΔE_2, eV	ΔE_{12}, eV	ΔE_1, eV	ΔE_2, eV	ΔE_{12}, eV
OH	monoclinic	3.38	2,65	0.71	4.09	0.81	3.28
	hexagonal ordered	2.86	1.76	1.1	5.21	1.09	4.12
	hexagonal disordered	0.68	0.84	0.15	2.89	1.0	1.89
F,OH	monoclinic	2.96	0.05	2.92	3.72	0.81	2.92
	hexagonal	3.66	0.5	3.16	3.29	1.14	2.15

The large energy barrier values for both apatite phases allow making a conclusion that in normal conditions (room temperature, without external forces) the proton transfer is practically impossible and have a statistically distributed character. That is, the proton has not sufficient thermal energy for overcoming a potential barrier. That explains the long-time charge storage observed in experiment. For monoclinic phase (P2$_1$/b) the difference between energy barrier values is relatively small $\Delta E_{mon} = 0.71$ eV. That brings a conclusion that both variants of proton migration are possible, though the first way is preferable one. At the case of hexagonal disordered phase there are no large energy barriers ($\Delta E_1 = 0.68$ eV, $\Delta E_2 = 0.84$ eV) on the first direction.

For HAP with F substitution (F,OH-apatite) the calculated energy barrier values are: for monoclinic phase 1st direction $\Delta E_1 = 2.96$ eV it is less than ΔE_1 for pure OH-apatite ($\Delta E_1 = 3.38$ eV), and for the second direction -$\Delta E_2 = 3.72$ (4.09 eV for OH-apatite). That means that for F,OH-apatite the energy barriers are less than for the pure OH-apatite, but also they too large for the proton transfer due to the thermal energy only. In the cases of hexagonal ordered, monoclinic OH and F,OH-apatites the proton is localized in one part of the asymmetric double-well potential.

It is known that electric field influences the energy profiles. To estimate the influence of the electric field on proton transfer along the apatite channel we perform a series of

calculations under the different electric field values. We try to find the value of external electric field that switches the minima of the calculated asymmetric double-well potential. The field was applied along the c- axes (along the channel) in all cases (see on Fig. 2.). Comparison of energy barrier values under the electric field in monoclinic and hexagonal phases is given in Table 2. Switching phenomena was found only for monoclinic phase at $2.57 \cdot 10^9$ V/m. For hexagonal phase (ordered) it should be greater. The switching field is superimposed on a considerably larger field due to the asymmetry of the wells. Calculations were made for monoclinic and hexagonal phases under the large set of electric field values. In the Table 2 only two values of electric field are given for comparison between phases.

Such a huge field values are not unusual. Thus the sufficient electric field intensity value has the same order that has the electric field intensity caused by voltage in biological membranes. In work [6] fields with components of order 10^9 V/m were applied. Calculations have shown that fields of the order of 10^9 V/m can exist in protein. But, from the other hand, it was shown [6, 7] that at this conditions the "switching" of the proton position from one double-wall minima to another can occur only under additional shift of electric field on the order of 10^6 V/m. It would be explained by quantum tunneling effect of proton transfer in this case. It should be noticed that the experiments on HAP polarization are made at 400° C and electric field $\sim 10^6$ V/m, but our calculations were made at room temperature in vacuum [1,2], without temperature influences and quantum tunneling. The obtained values of HAP polarization is in the order of ~ 0.1 C/m^2, that is very close to the experimental data [3, 8]. The further problem is to make detailed computational exploration taking in account the effect of quantum tunneling of protons and temperature dependence.
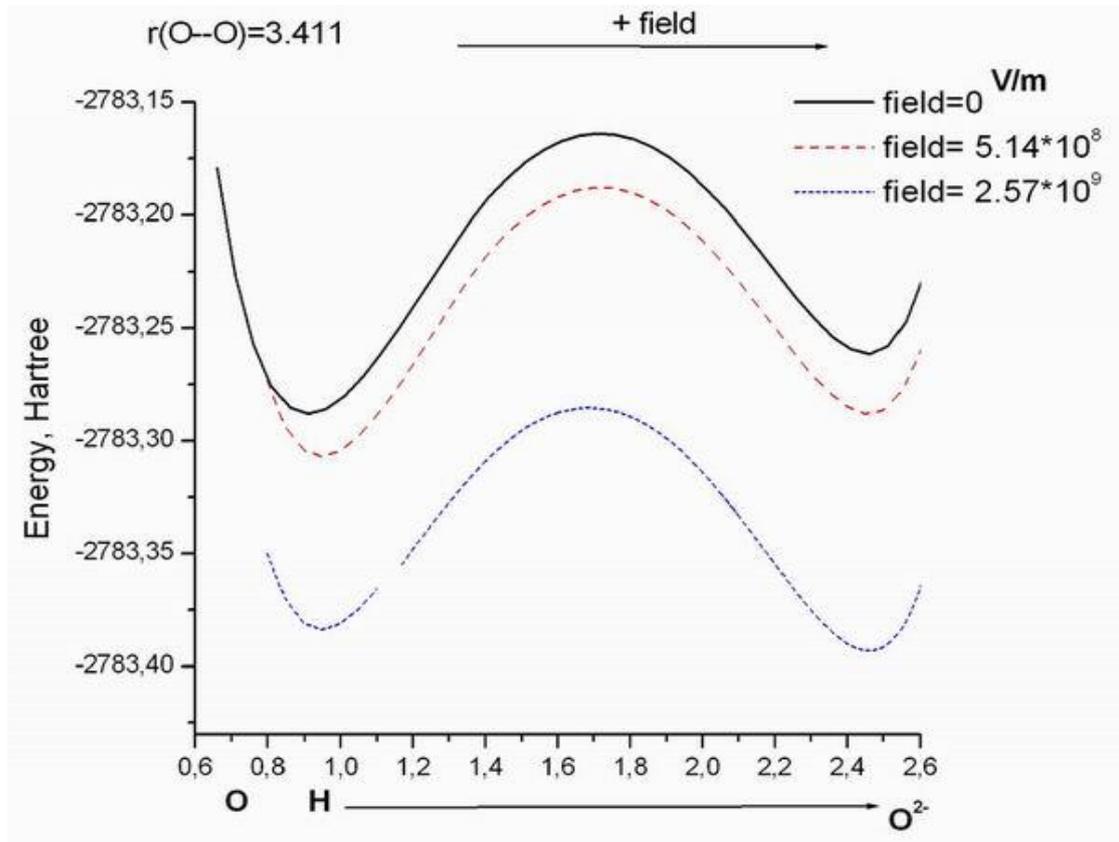

Fig. 2. Energy profile of HAP along c-axis and its changes under influence of applied electric field.

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Table 2. Energy barrier values for monoclinic and hexagonal ordered phases if external electric field is applied

Phase	Electric field, V/m	ΔE_1, eV	ΔE_2, eV	ΔE_{12}, eV
Monoclinic, $P2_1/b$	0	3.38	2.65	0.73
	$5.14*10^8$	3.24	2.72	0.52
	$2.57*10^9$	2.68	2.93	- 0.25
Hexagonal ordered, $P6_3/m$	0	2.86	1.76	1,1
	$5.14*10^8$	2.81	1.83	0.98
	$2.57*10^9$	2.43	1.94	0.49

CONCLUSIONS

All calculated energy curve profile clearly show double well asymmetric potentials. Calculate large energy barrier values for both apatite phases allow making a conclusion that in normal conditions (room temperature, without external forces) the proton transfer is practically impossible. The search of electric field switching the minima in double well potential gives us the value of the order of 10^9 V/m, but proton tunneling is possible at 10^6 V/m at theses conditions. The calculated value of polarization ~ 0.1 C/m^2 for HAP is consistent with the experimental data of the apatite that are usually obtained 400° C and electric field ~ 10^6 V/m, where our calculations were made at room temperature and in vacuum. The non-uniform electrical field arising on the polarized HAP surface attracts living cells to this charged HAP.

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