

===== MATHEMATICAL MODELING =====

Nanoscale Electric Potential and Electron Work Function of the Hydroxyapatite Surface

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Abstract. The article presents the results of a study of the electrostatic potential and the work function of the hydroxyapatite (HAP) surface. To study the electrostatic potential and the electron work function of the HAP surface, modeling of the HAP structures and calculation of their properties using density functional theory (DFT) methods were used. To perform these simulations and calculations, a HAP supercell model was used, extended to a structure that includes a region of vacuum space near the HAP surface. The electron work function was calculated using the Quantum ESPRESSO program. To construct the model, a surface with the (001) orientation was taken, the thickness of the entire model is $L \sim 26.5$ Å, the thickness of the HAP substrate is ~ 12.5 Å, and the vacuum layer is ~ 14 Å. The equilibrium state of the entire model is achieved by relaxation of its surface HAP layers, leaving the internal layers at $z < z_0 = 5.2$ Å with fixed atoms positions. After optimizing the initial HAP structure, surface layer modifications (substitution of Ca for Mg, Mn, Sr, and Se; removal/addition of Ca) were simulated, and the change in the work function and potential profile were calculated. The analysis of the obtained results with known data yields a good agreement.

Key words: *hydroxyapatite, density functional theory, surface, work function, electrostatic potential, substitutions, cations, defects*

INTRODUCTION

Modern studies have shown that the formation of bone tissue on the implant surface is determined by the quality of biocompatibility of the implant surface coating material with bone tissue cells [1–6]. Only cells attached to such an implant surface are involved in tissue regeneration when the implant serves as a scaffold. In this case, the influence of the physicochemical properties, morphology and surface roughness of the implant coating on the attachment of bone cells is very important [7]. The attachment of any specific protein molecule, which is part of a cell, to such a surface is based on the features of particle adhesion based on the theory of aggregation stability of lyophobic dispersed systems [8]. This theory takes into account the dispersion and electrostatic interactions between the particle and the substrate (or support). An important role here is played by the electrostatic potential, which has a strong influence on the capture of the electrically charged part of the cell when it is near the surface of the substrate covering the surface of the implant. This electrostatic interaction can be enhanced by changing the electric charge of the surface of this substrate (implant coating). This approach is applicable to a number of dielectric biomaterials, such as calcium

phosphates [3, 4], including Hydroxyapatite (HAP) [4, 5], one of the most widely used materials in medicine [9]. HAP is a mineral component of human bones and teeth [3, 4, 9] and it has a natural biocompatibility with the bone tissues of the human body. Therefore, the field of application of HAP is orthopedics, bone and dental surgery, and its use as a filler and coating for bone implants [1–6].

The electric charge of the HAP surface layer can be changed by irradiation [10], polarization [11], doping and surface reconstruction, atomic-molecular interactions [5, 9, 12, 13], etc. The surface charge of HAP nanoparticles used to create implant coatings depends on both the radius of these particles [9, 12] and their composition. In this regard, the surface roughness of the coating made of such HAP material, which has peaks and valleys (or troughs) characterized by different radii and compositions of structural elements (HAP can be different from the stoichiometric composition, and with different cationic substitutions, vacancies and inclusions), will affect the surface charge of the HAP coating. Depending on the emerging structure of the surface layer of the HAP coating, both the value of the electron work function from the HAP surface and the corresponding distribution of the electrostatic potential change, which determines the entire surface charge of the HAP coating, which affects the cells of growing bone tissue attached there. At the same time, the coatings applied to the implant material must adhere well to its surface. Titanium and titanium-based alloys are currently widely used for the manufacture of implant bases [14]. They are biocompatible and corrosion-resistant due to the oxide layer formed on their surface [15].

In general, such biocoatings must be both biocompatible with body tissues and corrosion-resistant in a biological environment, as well as have high adhesion and bond strength to the implant base material. This problem is currently being addressed by using various methods for forming coatings on the surface of medical implants [4, 16, 17]. The surface morphology of HAP is usually modified, and there are a number of methods exist for forming HAP coatings, such as sol-gel [18], plasma spraying [19], magnetron sputtering [20], and others [21]. However, all of these methods have their drawbacks and limitations.

Among the many existing methods, microarc oxidation (MAO) is considered to be one of the most suitable for forming a textured and rough (porous) HAP surface. It is a complex multi-stage plasma-chemical and electrochemical process. However, this MAO method is more convenient and effective for producing HAP coatings on complex-shaped implants, and it provides them with good physicochemical properties [22, 23]. The application of such HAP coatings in a microarc discharge involves high-temperature chemical processes in the zone of localized microplasma and microarc discharges under the influence of an external high-voltage source [22–25]. The coating is formed due to the oxidation of the base material and the transfer of an ultradispersed phase present in the electrolyte into the coating. The coatings obtained by the MAO method have a complex polyphase composition and exhibit good physicochemical properties (high corrosion resistance, hardness, and chemical stability in aggressive environments).

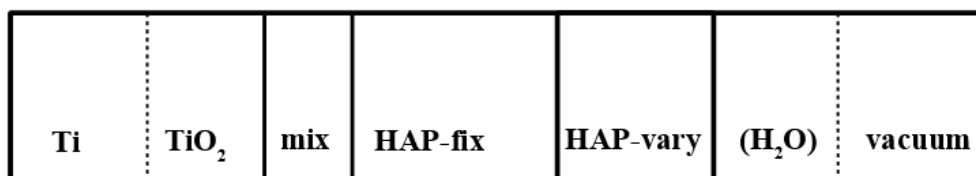


Fig. 1. Schematic representation of the layered structure model "Ti-TiO₂-HAP-medium-vacuum": the scheme of layers, where in the central region HAP-fix is the crystalline structure of HAP with atoms that occupy fixed positions in the depth of the HAP volume, the HAP-variable layer is a transition layer on the surface of HAP, in which the positions of the atoms relax to the optimal minimum energy of the entire system, taking into account the vacuum layer (and water molecules, if they are included in the model); the other side includes an internal transition layer mix between titanium oxide TiO₂ and the HAP-fix layer

In this case, HAP interacts with the implant surface (titanium and, primarily, titanium oxide – rutile) and a transition layer is formed between HAP and TiO_2 . Also, the outer surface of the HAP is formed with the surrounding medium (this is usually an aqueous medium or electrolyte; in the simplest model, a vacuum). An approximate layer diagram of the "Ti- TiO_2 -HAP-medium-vacuum" structure is shown in Figure 1.

In this paper, we will consider the structure of the HAP layers and the transition layer between HAP and the vacuum region. Water molecules at the HAP surface will not be considered for now. We will also not examine the TiO_2 -HAP interface here, as this is a separate task.

The main goal of this paper is to investigate the transition region between HAP and vacuum and evaluate how changes in the structure of this surface layer during modification (introduction/removal of calcium atoms, substitution of various calcium ions with other ions—Mg, Mn, Sr, Se, etc.) will affect changes in the electron work function and the corresponding electrostatic potential at the HAP surface. It is important to evaluate these effects in order to understand their influence on the adhesion of bone cells (osteoblasts and others) and their activation for bone tissue growth.

To investigate these issues, this paper uses modeling of HAP structures and calculations of their properties using density functional theory (DFT) methods, developed and applied by us earlier in [13, 26–31]. To perform these modeling and calculations, we use the HAP supercell model extended to a structure that includes a region of vacuum space near the HAP surface (see Fig. 1 – the "HAP-fix + HAP-vary + vacuum" region, but without the inclusion of water molecules). In such a model of lamellar geometry ("slab-plate: HAP-substrate/vacuum" or "slab-vacuum" model), the electron work function (WF) can be calculated "from first principles" by DFT methods, using the Quantum ESPRESSO (QE) program [32]. The electrostatic potential inside the model of such a slab plate, calculated using the QE program, is saturated to a constant value in the vacuum region and we can determine its average value.

It is important to take into account that the WF varies depending on both the surface orientation and its composition (morphology). In a material such as HAP, the surface composition can vary greatly with different surface orientations and at different cleavage points [9, 33, 34]. This also changes the electric charge of such a surface and the electrostatic potential, as shown both experimentally [9, 35] and by various theoretical methods [36–39]. Consequently, the WF can vary even by several eV [39]. In this study, we took a HAP surface with the (001) orientation, which is closer to a number of experimental studies and known data.

After optimization of the initial stoichiometric structure of HAP, we studied modifications of the surface layers (removal/addition of Ca; substitution of Ca with Mg, Mn, Sr, Se, etc.), and calculated changes in the work function and potential profiles. Good agreement between the results and the experimental data in [12] was obtained.

BASIC APPROACHES, MODELS AND METHODS

Basic computational details and parameters of the DFT calculations

In this work, we applied the computational approach we had developed earlier, which allows us to obtain highly accurate results by performing the DFT calculations in two stages. This approach was successfully applied in [13, 26–31] for various DFT calculations, both for the original HAP structures and for HAP with defects and various cation substitutions [40], on the HAP model of a single unit cell and a supercell (Fig. 2).

It is based primarily on the Perdew, Burke, Ernzerhof (PBE) functional in the generalized gradient approximation (GGA) [41] in the 1st main step of the calculations and in combination with the Heyd, Scuseria, Ernzerhof (HSE06) hybrid exchange-correlation functional [42, 43] in the 2nd step. The ground state electronic structure was calculated using

the QUANTUM ESPRESSO package (version 7.5) [32] within the DFT approach with the functionals mentioned above. The electron ground states are described using the optimized norm-conserved (ONCV) DFT pseudopotentials [44, 45]. The kinetic energy thresholds were set at 60 and 240 Ry (1 Ry = ~ 13.6057 eV) for the Kohn–Sham wave functions and the semilocal potential. The exchange operator value was calculated with an energy cutoff of 120 Ry. The forces acting on the atoms were estimated based on the calculated electronic structure of the ground state. The search for a stable atomic configuration was performed using the Broyden–Fletcher–Goldfarb–Shanno algorithm [46, 47] for numerical optimization of the total energy, which continued until any component of the force on any atom was greater than 0.01 eV/Å and the energy difference was 10–4 eV. In this paper, we perform the main TFP calculations in HAP with a vacuum layer using the PBE functional.

Main models of calculated HAP structures

In this paper, we consider the substitution of calcium ions by different ions. For numerical studies, we use a $2 \times 2 \times 2$ HAP supercell consisting of 8 unit HAP cells containing 352 atoms. For clarity, the supercell model is presented in such a way that two OH channels are in its center (Fig. 2). For the pure HAP model, the following HAP cell parameters were used (for the supercell per unit cell) [13, 26–31]: $a = b = 18.962$ Å / 2 = 9.481 Å and $c = 13.717$ Å / 2 = 6.8585 Å.

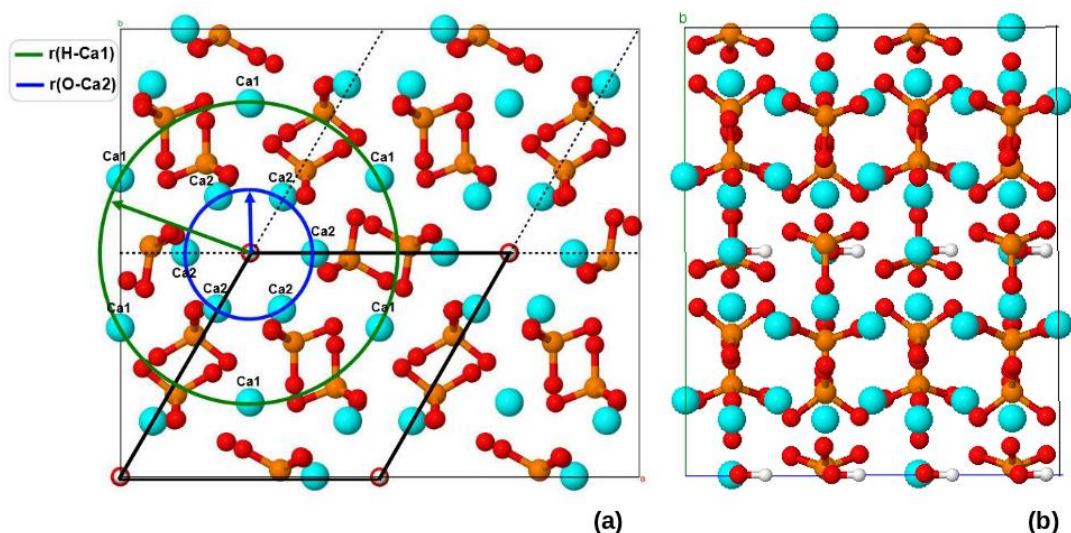


Fig. 2. The HAP supercell model (352 atoms) and its relation to the hexagonal unit cell model containing 44 atoms (marked by thick black lines), in projection along the z-axis (a); side view along the z-axis (b). Ca1 (green circle) and Ca2 (blue circle) are shown around the OH channel axis. Atom designations: blue – Ca, red – O, brown – P, white – H (image (a) is taken from [27])

Figure 3 shows the initial model structure of the "HAP-vacuum" constructed based on the supercell model (Fig. 2) projected along the z axis. In this work, we took the HAP surface with orientation along the (001) direction and assumed the thickness of the entire model equal to $L = 50$ Bohr ~ 26.5 Å (1 Bohr = 0.529 Å), the thickness of the HAP substrate is ~ 12.5 Å, followed by a vacuum with a thickness of ~ 14 Å. To obtain the equilibrium state of the entire model structure, we first relax the atoms in the surface layers, leaving the internal deep HAP layers at $z < z_0 = 5.2$ Å with fixed atomic positions (other variants of the layer value z_0 are also possible). The resulting equilibrium model, with atoms in the surface layer relaxed into other positions under the influence of the vacuum layer, is now the initial (reference) model for studying changes in the potential profile and work function after substituting calcium atoms with various cations, as well as other changes in the surface layer. The main parameters and characteristics of this model are shown in Figure 4 and Table 1.

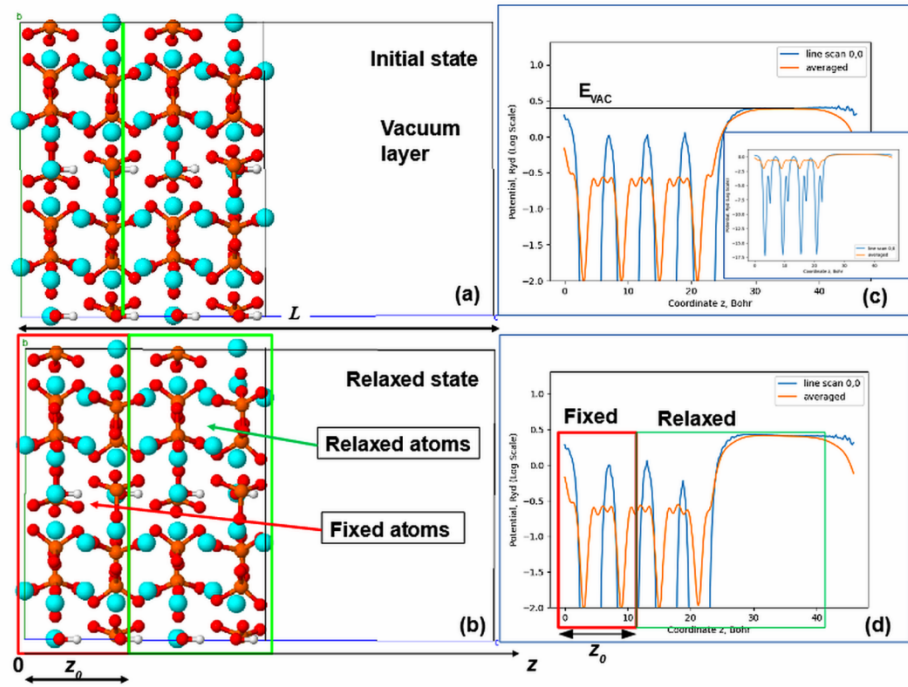


Fig. 3. Model of the “HAP-slab-vacuum” structure: (a) initial model structure; (b) relaxation of the model structure - the region $z < z_0$ with fixed positions of atoms, then the relaxation region, including the vacuum layer; (c) potential profile for the initial model structure cut off at -2 Ry for ease of monitoring the potential changes (inset - full profile shown).; (d) potential profile after relaxation of the surface layer

It should be noted here that all relaxation and optimization procedures performed in this work are carried out using the Broyden-Fletcher-Goldfarb-Shanno algorithm [46, 47] for numerical optimization of the total energy of the modeled structure, embedded into the Quantum ESPRESSO program [32]. It should also be noted that the proposed model with the inclusion of a vacuum layer is in some ways similar to the approaches in [36–39], but we use a more detailed and well-tested supercell model taking into account the transition surface layer of relaxing atoms and a high-precision DFT method.

Electron Work Function and Other Energy Characteristics

The main energy characteristics of our system can be represented as an energy level diagram, shown in Figure 4. In a dielectric crystal, which is essentially a HAP is, the energy band structure is determined primarily by the energy levels that electrons can occupy: the highest occupied energy level E_{HOMO} (or the top of the valence band E_{V}) and the lowest unoccupied energy level E_{LUMO} (the bottom of the conduction band E_{C}). The difference between these levels forms the energy gap: the band gap width $E_{\text{g}} = E_{\text{C}} - E_{\text{V}}$ (Fig. 4). The thermodynamic equilibrium state of filling all energy levels with electrons is determined by the Fermi level E_{F} .

For an electron to leave the crystal and enter a vacuum, it must be energized to at least the vacuum energy E_{VAC} . This can be accomplished either by photoexcitation by irradiating the sample with light with a photon energy of $\hbar\omega$

$$W = \hbar\omega = E_{\text{VAC}} - E_{\text{V}} = (E_{\text{VAC}} - E_{\text{C}}) + (E_{\text{C}} - E_{\text{V}}) = \chi + E_{\text{g}}, \quad (1)$$

or, thermodynamically, by exciting an electron into a vacuum from the Fermi level energy.

$$\Phi = E_{\text{VAC}} - E_{\text{F}}, \quad (2)$$

where $\chi = E_{\text{VAC}} - E_{\text{C}}$ - the electron affinity energy.

That is, the photoelectron work function W differs from the thermoelectron work function Φ of the electron by value $\varphi = \Phi - E_{\text{F}}$ - called the Schottky barrier height.

We obtain all these key characteristics by performing DFT calculations on the QE program. To do this, we first perform a relaxation of the studied HAP system and a full self-consistent calculation. Then we use a special QE subroutine (pp.x – post-processing program) to calculate the electrostatic potential with the plane-averaged potential and output this data to a special digital file and a plotted graph as a function of the z -coordinate (perpendicular to the x - y surface), selecting the desired format and scale. On the plotted graph, the potential should reach a plateau in the vacuum region, where it is constant – the value of this plateau is the vacuum level E_{VAC} . This is schematically shown in the graphs in Figure 3c and d. This level is determined using a special Python script subroutine.

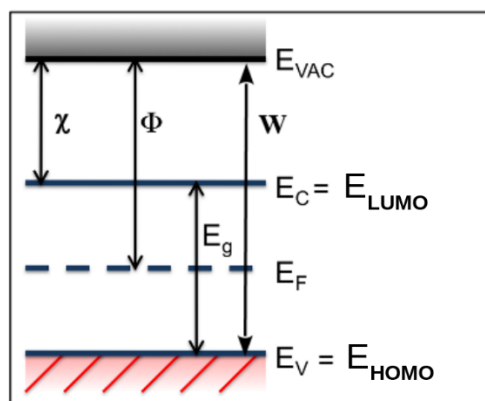


Fig. 4. Energy level diagram of a dielectric crystal at the boundary with a vacuum. Here, E_{VAC} is the vacuum level, W and Φ are the photoelectron and thermoelectron work functions of the electron, χ is the electron affinity energy, E_{F} is the Fermi level, $E_{\text{C}} = E_{\text{LUMO}}$ is the conduction band bottom, $E_{\text{V}} = E_{\text{HOMO}}$ is the valence band top, and $E_{\text{g}} = E_{\text{C}} - E_{\text{V}}$ is the band gap

MAIN RESULTS AND DISCUSSION

Analysis of the initial data for the HAP-slab-vacuum model

To perform these calculations, we used the «HAP-slab-vacuum» model (Fig. 3), in which the vacuum layer is thick enough to avoid interaction between the periodic layers of this slab. The parameters of our model are close to the data in [38, 39], where the thickness of the HAP substrate was ~ 15 Å, and the vacuum layer was ~ 10 Å. We used periodic boundary conditions in the directions parallel to the surface (x and y), and the vacuum layer in the direction (z) perpendicular to the surface $x - y$. The main calculated characteristics of the model structures are presented in Table 1.

For comparison, we present here the calculation results for a model of slabs of varying total thickness L at fixed positions of all atoms. We also provide the values of the fundamental energy levels for the original model of the HAP supercell in the crystal. We also monitored the change in the potential profile for all models and found that at $L = 50$ Bohr, the energy level in vacuum reaches a plateau (see Figure 3c), and this value of L can be taken as the fundamental vacuum layer in our model. The inset in Figure 3c also shows the full potential profile inside and outside the crystal (blue line) and its average potential level (orange line). This clearly shows the difference in potential energy in the depth of the crystal, on the surface, and in vacuum.

The main characteristics of the initial HAP model with a transition surface layer in the vacuum region, in which the positions of all atoms are in the optimal relaxed state, correspond to virtually pure (without impurities, defects, or substitutions) stoichiometric HAP and can be used as a basis for studying various inhomogeneities in the HAP surface layer. These characteristics are marked with asterisks) in the last column of Table 1. Comparing

these values with known experimental data and theoretical estimates (3.8–5.6 eV), we see that they correspond to these data [9–13, 35–39, 48–53].

Table 1. Main parameters and energy characteristics for the initial stoichiometric HAP supercell model and its slab-vacuum model with a size of $L = 50 \text{ \AA}$, Bohr $\approx 26.5 \text{ \AA}$, with a fixed atomic position region at $z < z_0 = 5.2 \text{ \AA}$, before and after relaxation of the surface layer atomic positions at the vacuum boundary. All DFT calculations are made on the PBE GGA (QE 7.5)

Simulated structures based on the supercell and slab-vacuum layers					
Main Parameters and Energies	Model of the original HAP crystal supercell without the vacuum layer	Slab model total thickness $L = 35 \text{ Bohr}$	Slab model total thickness $L = 40 \text{ Bohr}$	Slab model total thickness $L = 50 \text{ Bohr}$	Slab model total thickness $L = 50 \text{ Bohr}$, with a transition layer at $z > z_0 = 5.2 \text{ \AA}$
Calculation mode	Fixed calculation after full optimization	Fixed calculation for all atomic positions	Fixed calculation for all atomic positions	Fixed calculation for all atomic positions	Optimized calculation: atoms are fixed at $z < z_0 = 5.2 \text{ \AA}$
E_{tot} , Ry	–13235.4529	–13231.7924	–13231.6833	–13231.6576	–13232.2718
E_{VAC} , eV	–	6.7567	6.4241	5.3116	5.6816 ^{*)}
E_{C} , eV	11.1078	5.4501	4.2753	2.8570	2.7867
E_{F} , eV	7.2396	4.2210	3.0474	1.6489	1.6580
E_{V} , eV	5.7394	3.7057	2.7365	1.3635	1.1718
$\chi = E_{\text{VAC}} - E_{\text{C}}$, eV	–	1.3557	2.1488	2.4546	2.8949
$\Phi = E_{\text{VAC}} - E_{\text{F}}$, eV	–	2.5357	3.3767	3.6627	4.0236 ^{*)}
$E_{\text{g}} = E_{\text{C}} - E_{\text{V}}$, eV	5.3684	1.7444	1.5388	1.4935	1.6149
$W = E_{\text{g}} + \chi = E_{\text{VAC}} - E_{\text{V}}$, eV	–	3.1001	3.6876	3.9481	4.5098 ^{*)}

In particular, it should be noted that a spread of work function values is observed for different HAP surfaces [9, 39, 52]. But, for the (001) surface model with OH-terminated ends considered here, our data are consistent with the calculations in [38, 39], where they are $\sim 5.1 \text{ eV}$, which is also consistent with the experimentally obtained values, which vary from 4.7 eV to 5.1 eV [39, 48]. It is also important to note that all experimental work on measuring the photoelectron work function W from the HAP surface is usually carried out under vacuum conditions and at photon energies in the range of 3–6 eV [9, 12, 48]. And here there is a difference between the thermoelectron work function Φ of the electron and the photoelectron work function W (of the order of $\sim 0.5 \text{ eV}$). This difference $W > \Phi$, as can be seen from (1) and (2), is equal to the value of the Schottky barrier. In this regard, it is interesting to note the changes in the surface potential by a value of the order of $\sim (0.3\text{--}0.5) \text{ V}$ due to the possible shift of the Schottky barrier by electron charges introduced during irradiation of the modified HAP surface with low-energy electrons, which was established in [53] by measuring the wettability of HAP.

Assessment of the effect of water or aqueous electrolytes, taking into account their average permittivity $\epsilon \sim 80$, and that the vacuum layer medium in our model were filled with such a liquid, yields a value for the potential at the outer boundary of the vacuum layer $U =$

$E_{\text{VAC}} / (q_e \cdot \varepsilon) = \sim 5.6816 \text{ eV} / [(-1e) \cdot 80] = -0.07102 \sim -70 \text{ mV}$. Here the charge $q_e = -1e$ is the electron charge, and accordingly $E = 1 \text{ eV}$ yields a potential $U = -1 \text{ V}$.

This value fits well within the potential range (from -40 mV to -120 mV) measured experimentally on similar calcium phosphate coatings in studies of bone cell adhesion, depending on the type of coating heterogeneity (thickness and roughness, the size of the heterogeneity area – the presence of protrusions and recesses) [7]. Of course, for a rigorous assessment, we will also need to conduct modeling and DFT calculations explicitly incorporating water molecules into our layered HAP slab model, as well as solutions and electrolytes.

The effect of substitution of calcium ions for other cations in the surface layer of HAP

To conduct these studies, we need to select a suitable Ca ion. In this case, we selected atom #30 from the set of 80 Ca ions in our supercell. This atom belongs to the Ca1 ion type and is located further from the OH channel axis than Ca2 ions. Its coordinates in the original model are ($x = 9.4691 \text{ \AA}$, $y = 10.9512 \text{ \AA}$, $z = 10.2877 \text{ \AA}$). In this work, we replace this Ca ion with Mg, Mn, Sr, and Se cations. We then perform the corresponding optimization of the surface layer at the boundary with the vacuum layer, similar to the procedure described above. We then compare the obtained results with the data for the undoped HAP slab model (Table 1) and analyze the changes.

Effect of Mg/Ca substitutions on the HAP properties in the vacuum surface layer

The introduction of Mg/Ca substitution at the Ca1 position with the specified coordinates of the Ca # 30 atom and subsequent optimization of the entire HAP slab structure leads to the relaxation of atoms in the transition layer at the boundary with the vacuum and a change in the potential energy profile, as well as the vacuum energy level E_{VAC} , as the average energy level in the vacuum layer (Fig. 5).

An analysis of the dynamics of the transition layer optimization process to minimize the total energy of the entire system revealed that, in the initial stages, the magnesium ion has no direct chemical bonds with the nearest oxygen atoms of the PO_4 groups and shifts slightly toward the boundary with the vacuum region. However, chemical bonds then arise with the oxygen atoms of the surrounding PO_4 groups, and the magnesium ion in this bound state relaxes slightly in the opposite direction. During this process, the atoms in the entire interface layer gradually rearrange the PO_4 groups shift slightly, unfold and rotate. The results of the final structure are visible in Figures 5c and 5d; the change in the potential profile is shown in the inset of Figure 5d. The actual shifts of the Mg ion positions along the z coordinate axis are as follows: from the initial state with $z_{01} = 10.2877 \text{ \AA}$, movement to position $z_2 = 10.5599 \text{ \AA}$, when a direct chemical bond arises with 3 oxygen atoms of 3 PO_4 groups, and then relaxation in this bound form to position $z_3 = 10.5046 \text{ \AA}$.

In the initial state, the distance from the Mg ion to the oxygen ions of the PO_4 groups was $r(\text{Mg-O}) \sim 2.44 \text{ \AA}$, at which there was no chemical bond. In the final bound state, these distances became equal to $r(\text{Mg-O}) \sim 2.12 \text{ \AA}$ (Fig. 6). These results are in good agreement with the studies of the dynamics of changes in Mg/Ca substitutions at the Ca1 positions of HAP performed in [27], where it was noted that the critical distance for the formation of the Mg-O bond is $r_c(\text{Mg-O}) \sim (2.09 - 2.19) \text{ \AA}$. These data correspond to the ionic radii of oxygen $r(\text{O}^{2-}) = 1.30\text{--}1.32 \text{ \AA}$ [54]) and magnesium $r(\text{Mg}^{2+}) = 0.69\text{--}0.89 \text{ \AA}$ [54–56], which gives a total range of $r_c(\text{Mg-O}) \sim (1.99\text{--}2.21) \text{ \AA}$, when their stable chemical ionic bond is formed.

Figure 6 demonstrates the dynamics of changes in the state of the Mg ion in the surface layer with vacuum during relaxation of the entire HAP-slab-vacuum with cation-substituted Mg-HAP.

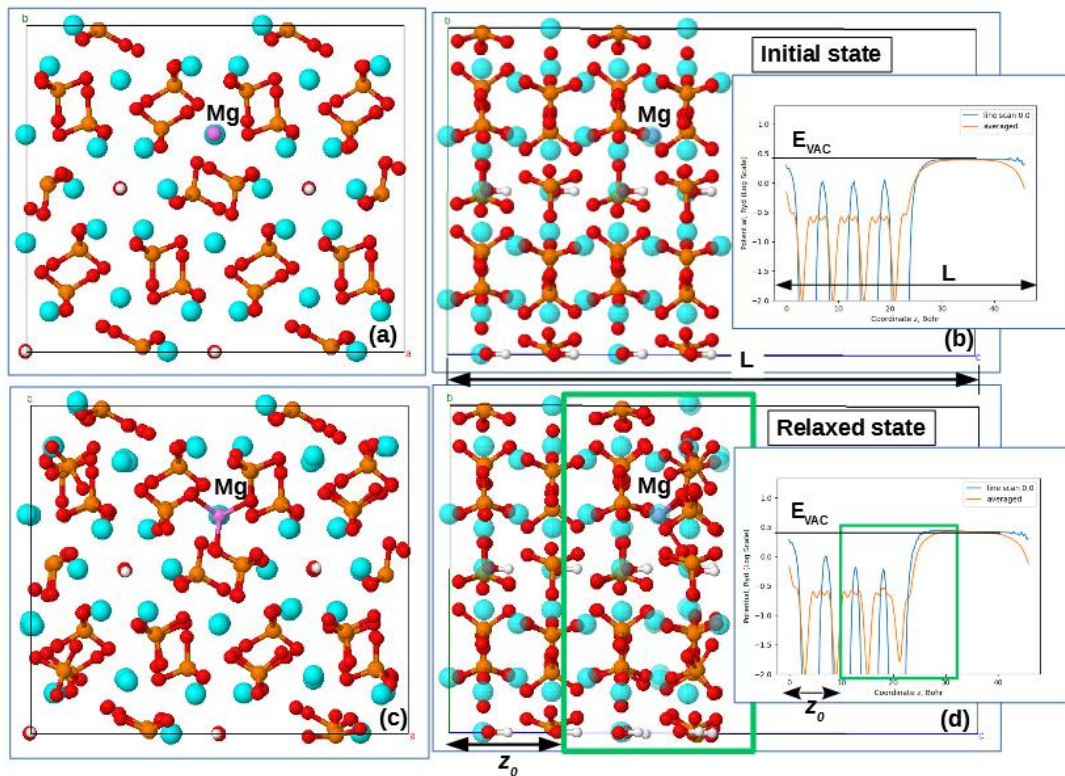


Fig. 5. Model of the "HAP-slab-vacuum" structure with the introduction of Mg/Ca substitution at the Ca1 atom site No. 30 of the HAP supercell: (a) and (b) the initial state in projection perpendicular to the (x, y) plane and along the c-axis (in the z-coordinate direction); (c) and (d) model structures in the same projections after optimization of the entire structure and relaxation of the transition layer with vacuum. The colors of the atoms are the same as in Figure 1, the color of the Mg atom is violet (purple). The potential profiles and their changes are shown in the corresponding insets, where the E_{VAC} vacuum level is also noted. The regions of relaxing transition layer atoms and potential changes are highlighted in green

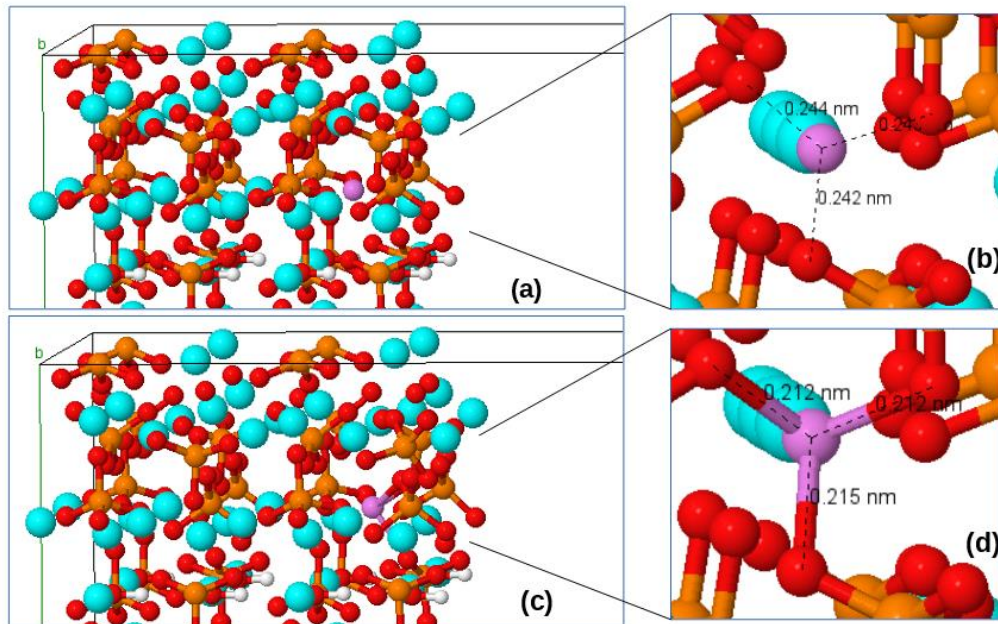


Fig. 6. Fragments of the HAP-slab-vacuum structures with cation-substituted Mg-HAP, demonstrating the emergence of Mg-O chemical bonds during optimization of the entire structure and relaxation of Mg ions in the transition surface layer at the boundary with vacuum: (a) and (b) initial states of the structure; (c) and (d) after optimization of the entire structure and the emergence of Mg-O chemical bonds with 3 oxygen atoms from PO_4 groups

Table 2 presents the calculated results for all characteristics of the Mg-HAP slab-vacuum structure after its optimization and relaxation of the Mg ion in the surface layer. It is clear that the vacuum energy E_{VAC} has increased slightly compared to the state of the cation-unsubstituted HAP slab-vacuum transition interface layer, and the photoelectron work function W has become slightly higher.

The main conclusion, however, is a significant decrease in the thermoelectronic work function Φ of the electron, almost to $\Delta\Phi \sim -0.7$ eV. This result is in qualitative agreement with experimental data on measuring the electron work function of HAP and its changes under the influence of magnesium introduced into HAP coatings on the implants, which affects the adhesion and anchoring of bone cells [12, 57]. It should be noted that Mg is an essential element for any living organism and is often used to improve the quality of HAP coatings, their biocompatibility with cells, and implant survival rate [27, 58, 59].

Effect of Sr/Ca substitutions on the properties of HAP in the surface layer with vacuum

Strontium is also a key element [58–63], affecting the quality of implant coatings and the active proliferation of living bone cells and bone tissue growth. Therefore, we have also conducted and presented a study of the effect of Sr/Ca substitutions (in the analogous Ca1 position and for atom #30 in our supercell model).

Figure 7 demonstrates a change in the HAP-slab-vacuum structure and potential profile upon the introduction of a Sr ion and optimization of the entire structure until the final relaxation of the simulated transition surface layer.

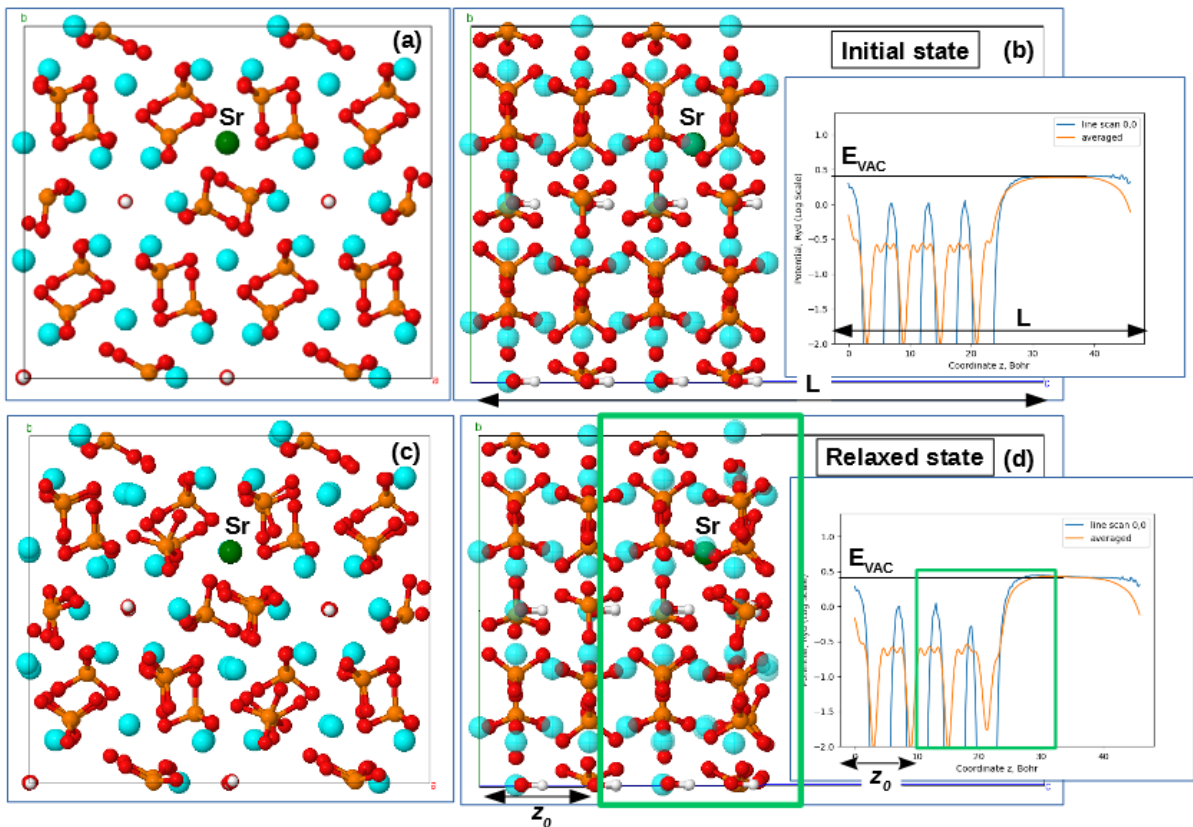


Fig. 7. Model of the HAP-slab-vacuum structure with the introduction of Sr/Ca substitution at the Ca1 position for atom site No. 30 of the HAP supercell: (a) and (b) the initial state in projection perpendicular to the (x, y) plane and along the c-axis (in the direction of the z-coordinate); (c) and (d) model structures in the same projections after optimization of the entire structure and relaxation of the transition layer with vacuum. The colors of the atoms are the same as in Figure 1, the color of the Sr atom is dark green. The potential profiles and its changes are shown in the corresponding insets, where the E_{VAC} vacuum level is also noted. The regions of relaxing transition layer atoms and potential changes are highlighted within the green area

Table 2. Key parameters, energy characteristics, and their changes for HAP structures upon introducing cationic substitutions (at the Ca1 position of the Ca#30 atom in the extended supercell model) compared to the initial stoichiometric HAP supercell model and slab-vacuum model ($L = 50$ Bohr = ~ 26.5 Å, with a fixed atomic positions at $z < z_0 = 5.2$ Å), after relaxation of all surface layer atomic positions at the vacuum boundary. The studied structures are Me-HAP, where the substitutions are Me/Ca (Me = Mg, Mn, Sr, Se). DFT calculations were performed on PBE GGA (QE version 7.5)

Simulated Me-HAP structures based on the supercell and slab-vacuum layers					
Main Parameters and Energies	Slab model of total thickness $L = 50$ Bohr, with a transition layer at $z > z_0 = 5.2$ Å	Slab model Mg-HAP total thickness $L = 50$ Bohr	Slab model Sr-HAP total thickness $L = 50$ Bohr	Slab model Mn-HAP total thickness $L = 50$ Bohr	Slab model Se-HAP total thickness $L = 50$ Bohr
Calculation mode	Optimized calculation of the layer near the surface, the remaining atoms are fixed at $z < z_0 = 5.2$ Å	Optimized calculation with Mg ion in the layer near the surface, the remaining atoms are fixed at $z < z_0 = 5.2$ Å	Optimized calculation with Sr ion in the layer near the surface, the remaining atoms are fixed at $z < z_0 = 5.2$ Å	Optimized calculation with Mn ion in the layer near the surface, the remaining atoms are fixed at $z < z_0 = 5.2$ Å	Optimized calculation with Se ion in the layer near the surface, the remaining atoms are fixed at $z < z_0 = 5.2$ Å
E_{tot} , Ry	-13232.2718	-13267.0685	-13220.8626	-13357.0333	-13176.8170
E_{vac} , eV	5.6816	5.7441	5.8288	5.7699	5.6275
E_c , eV	2.7867	2.7514	2.7639	3.1160	2.8038
E_f , eV	1.6580	2.4254	1.6746	3.0332	2.2391
E_v , eV	1.1718	1.1161	1.1224	3.0212	1.6979
$\chi = E_{\text{vac}} - E_c$, eV	2.8949	2.9927	3.0649	2.6534	2.8237
$\Phi = E_{\text{vac}} - E_f$, eV	4.0236	3.3187	4.1542	2.7368	3.3884
$\Delta\Phi$, eV	0	-0.705	+ 0.1306	-1.2868	-0.6345
$E_g = E_c - E_v$, eV	1.6151	1.6353	1.6415	1.8828	1.1059
$W = E_g + \chi = E_{\text{vac}} - E_v$, eV	4.510	4.628	4.706	4.53	3.9296
ΔW , eV	0	+0.118	+0.196	+0.027	-0.579

A characteristic difference between the Sr/Ca substitution case and the Mg/Ca substitution case is the absence of any chemical bonds with any surrounding atoms (oxygen or calcium) during the relaxation process. First, this is probably due to the differences in the radii of the Sr and Mg ions, as well as the different lengths of the possible chemical bonds of these cations with oxygen. Note that the Sr and Mg atoms are located next to each other in the same column of the periodic table and have atomic radii: $R(\text{Ca}) = 1.80$ Å, $R(\text{Sr}) = 2.00$ Å, $R(\text{Mg}) = 1.50$ Å. This immediately leads to such a significant difference in the change in the characteristics of HAP materials upon the introduction of Mg/Ca and Sr/Ca substitutions as the behavior of the unit cell parameters and their volumes: for Mg-HAP, a decrease in the cell parameters and its volume is observed [27], whereas for Sr-HAP, an increase in the cell parameters and its volume occurs [63]. At the same time, the radius of strontium ions is $r(\text{Sr}^{2+}) \sim 1.12\text{--}1.18$ Å [64], and considering that the radius of oxygen ions is

$r(\text{O}^{2-}) = 1.30\text{--}1.32 \text{ \AA}$ [54], we find that the distance $r(\text{Sr-O}) \sim 2.42\text{--}2.50 \text{ \AA}$ is required for the formation of a chemical bond here. There are also some differences in the formation of chemical bonds in different types of crystals. For example, in strontium oxide (SrO) with a cubic structure of the NaCl type, the bond length is usually even longer, about $r(\text{Sr-O}) \sim 2.55 \text{ \AA}$ [65].

In our case, the initial distances in the HAP supercell structure with the introduction of Sr/Ca substitution are the same as for the initial state with Mg: $r(\text{Sr-O}) \sim 2.44 \text{ \AA}$, which prevents the immediate formation of bonds between Sr and O. Upon optimization and gradual relaxation of the Sr-HAP structure in the surface layer, we obtain even larger distances in the final optimal state, ranging from $r(\text{Sr-O}) \sim 2.59$ to $2.68 \text{ \AA}$, which also prevents the formation of direct chemical bonds. This analysis clarifies the reasons for the absence of bonds.

At the same time, it is characteristic that, under the influence of the Sr ion, the surrounding PO_4 groups undergo shifts, rotations, and changes in their configurations, which is clearly visible in their final state in Figure 7c. The potential profile in Figure 7d (inset) also changes significantly. All calculated final energy characteristics are also presented in Table 2. We note here an important difference between the Sr/Ca and Mg/Ca substitutions: here, the change in the thermoelectron work function Φ of the electron, relative to the initial state, occurred in the opposite direction. Here, an increase in the electron work function $\Delta\Phi \sim + (0.13\text{--}0.15) \text{ eV}$ was obtained. This is a significant difference and it is also observed experimentally [12, 62]. At the same time, the vacuum level E_{VAC} and the photoelectron work function W increased.

The Effect of Mn/Ca Substitutions on the Properties of HAP in the Surface Layer with Vacuum

The case of Mn/Ca substitution is of a completely different nature: here, immediately upon the introduction of a Mn ion instead of Ca in the Ca1 position, a chemical bond with 6 oxygen atoms of the PO_4 groups is formed (Fig. 8), and all 6 bonds are formed at once according to the coordination number [54]. This situation is completely consistent with our earlier DFT calculations of the Mn-HAP structure, where the Mn-HAP structure is compressed (atomic radius $r(\text{Mn}) \sim 1.40 \text{ \AA} < r(\text{Ca}) \sim 1.80\text{--}2.00 \text{ \AA}$) [29]. The radius of the Mn^{2+} ion in this case is on average $r(\text{Mn}^{2+}) \sim 0.89 \text{ \AA}$ [29], while the radius of the Ca ion is of the order of $r(\text{Ca}^{2+}) \sim 1.00 \text{ \AA}$, therefore, both a noticeable compression of the unit cell volume and a decrease in all bonds and cell parameters occur here [29, 30]. Accordingly, since $r(\text{O}^{2-}) \sim 1.30\text{--}1.32 \text{ \AA}$ [54], the critical Mn–O bond length will be of the order of $r_c(\text{Mn-O}) \sim 2.19\text{--}2.21 \text{ \AA}$. Considering that the initial distances in our Mn-HAP structure are $r(\text{Mn-O}) \sim 2.44 \text{ \AA}$, all bonds here will be immediately activated upon compression of the Mn-HAP structure (Fig. 8). In general, optimization of the structure and its relaxation in the surface layer leads to a gradual compression of the distances between the Mn and O ions, as shown for the bulk of the crystal in [29, 30].

The behavior of the Mn ion during relaxation in the surface layer of the Mn-HAP-vacuum structure is interesting (Fig. 9). In the first stage, gradual compression and shortening of bond distances occurs, but the Mn ion itself shifts more toward the vacuum surface, and its bonds with oxygen ions located deeper from the surface are broken as the distances increase (Fig. 9b). Then, the reverse movement occurs, and the bonds are restored. Ultimately, the configuration of the Mn ion and six oxygen ions is restored, but with different bond lengths (Fig. 9d).

The main energy characteristics of the Mn-HAP structure are listed in Table 2, and their analysis is provided at the end of the article. Importantly, that a decrease in the thermoelectron work function Φ of the electron by almost $\Delta\Phi \sim - (1.2\text{--}1.3) \text{ eV}$ was observed.

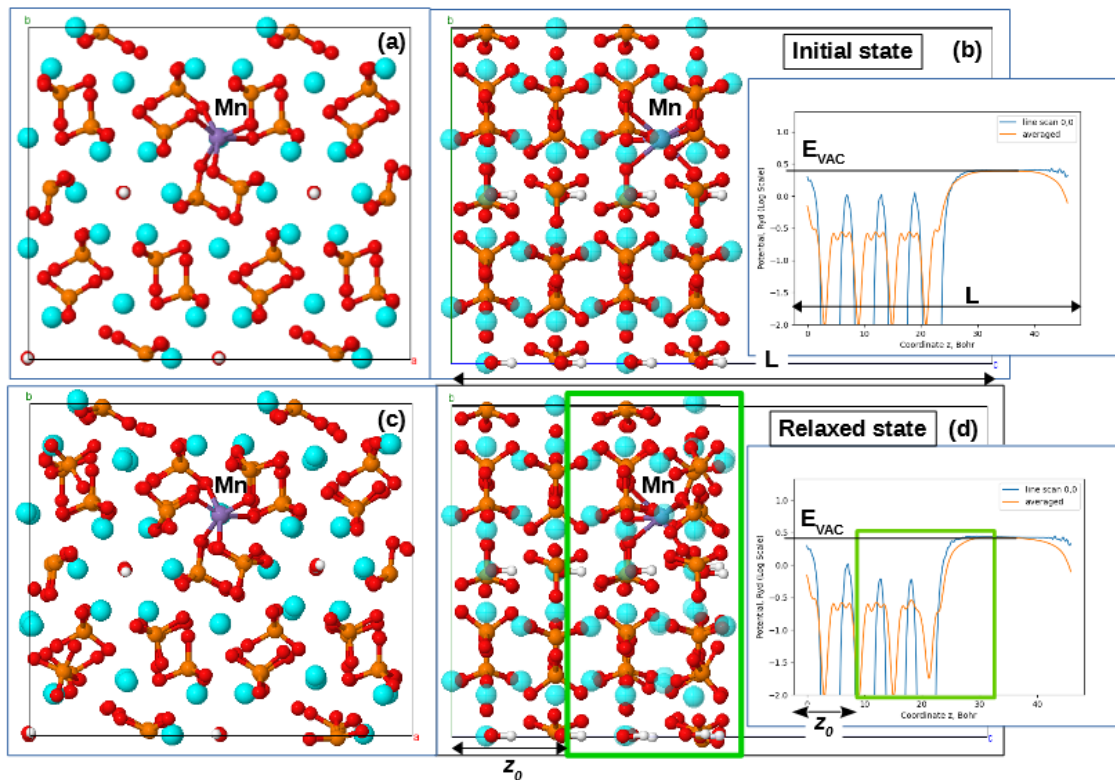


Fig. 8. Model of the HAP-slab-vacuum structure with the introduction of a Mn/Ca substitution at the Ca1 position for atom site No. 30 of the HAP supercell: (a) and (b) the initial state in projection perpendicular to the (x, y) plane and along the c-axis (in the z-coordinate direction); (c) and (d) model structures in the same projections after optimization of the entire structure and relaxation of the transition layer with vacuum. The colors of the atoms are the same as in Figure 1, the color of the Mn atom is purple. The potential profiles and its changes are shown in the corresponding insets, where the E_{VAC} vacuum level is also noted. The regions of relaxing transition layer atoms and potential changes are highlighted in green

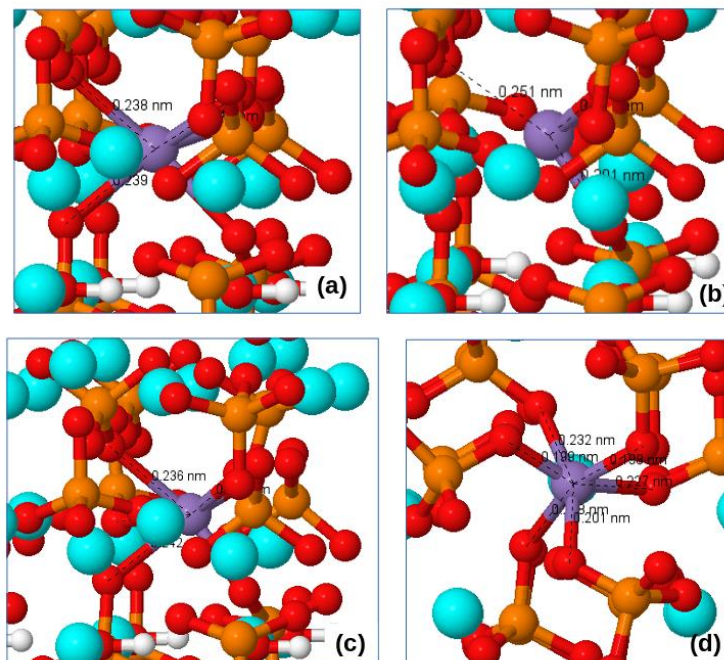


Fig. 9. Images of the dynamics of changes in the configuration of Mn ion bonds during relaxation in the surface layer of Mn-HAP at the boundaries with vacuum: (a) initial stages of bonds; (b) breaking of some bonds when approaching the surface; (c) return into the depth and restoration of bonds; (d) final state of the Mn ion in the surface layer

It should be noted that among the various ions affecting the properties of HAP, Mn ions have long attracted attention due to their positive therapeutic effects, and the incorporation of Mn into the crystal structure of HAP has been studied using various experimental and theoretical methods [29, 30, 66–68]. However, the study of the changes in work function under the influence of Mn has been little studied so far.

The effect of Se/Ca substitutions on the properties of HAP in the surface layer with vacuum

The interaction of Se ions in the hydroxyapatite crystal lattice remains poorly understood. However, there are some interesting experimental data [69, 70] and various theoretical estimates of the influence of Se/Ca substitutions in the hydroxyapatite structure, including the effect on the electron work function [12]. Selenium has a significant effect on hydroxyapatite, increasing its biocompatibility, bioactivity, and strength. Adding 0.30–0.50 % selenium to hydroxyapatite-based implants improves their compatibility, accelerates bone regeneration, and stimulates osteogenesis [71]. At the same time, selenium deficiency can cause osteoporosis [72].

The main changes in relaxation dynamics are shown for our Se-HAP-vacuum model structure below in Figure 10. As can be seen, there are specific features in the final configuration—symmetric bonds with oxygen from the surrounding PO_4 groups arise.

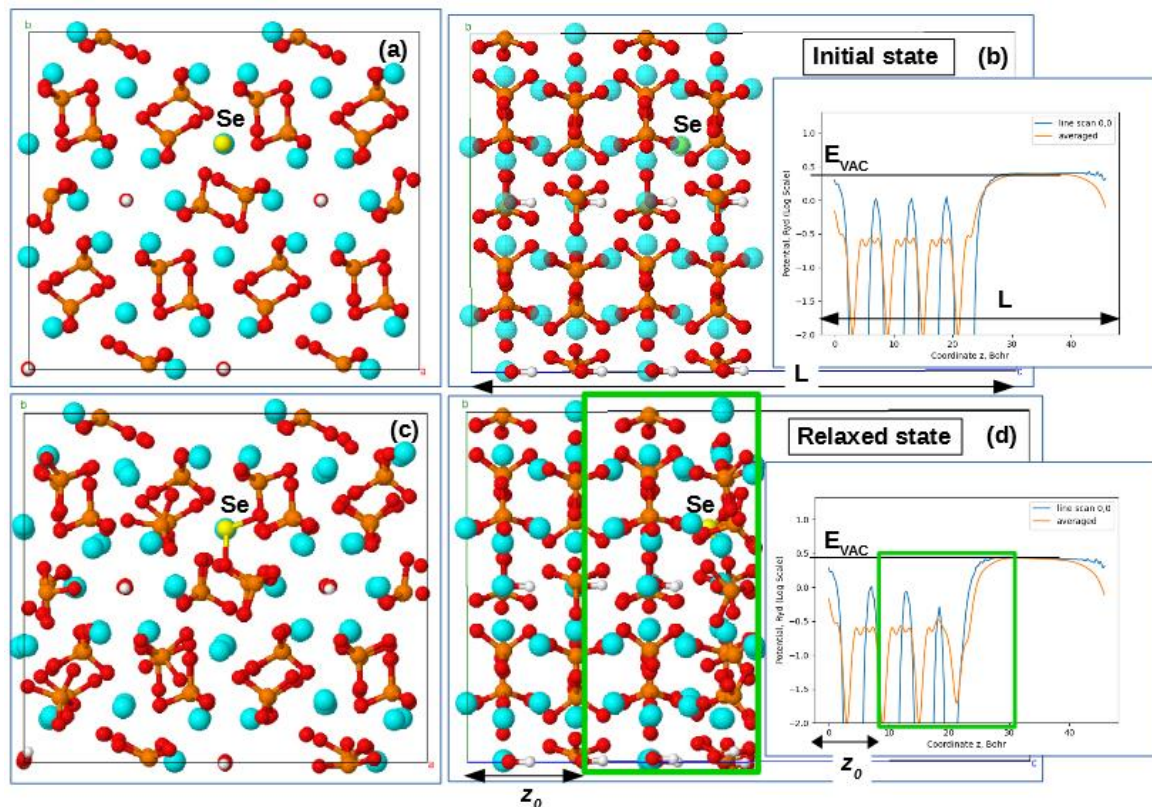


Fig. 10. Model of the "HAP-slab-vacuum" structure with the introduction of a Se/Ca substitution at the Ca1 position for atom No. 30 of the HAP supercell: (a) and (b) the initial state in projection perpendicular to the (x, y) plane and along the c-axis (in the z-coordinate direction); (c) and (d) model structures in the same projections after optimization of the entire structure and relaxation of the transition layer with vacuum. The colors of the atoms are the same as in Figure 1, the color of the Se atom is yellow. The potential profiles and its changes are shown in the corresponding insets, where the E_{VAC} vacuum level is also noted. The regions of relaxing transition layer atoms and potential changes are highlighted in green

The selenium ion radius is $r(\text{Se}) \sim (1.15\text{--}1.40) \text{ \AA} < r(\text{Ca}) \sim (1.8\text{--}2.0) \text{ \AA}$ [64], which in principle should lead to compression of the HAP crystal structure after introducing Se/Ca substitutions. However, the selenium ion radius significantly depends on its oxidation state.

And here there is a significant scatter in the data on the selenium ion radius. For example, $r(\text{Se}^{4+}) \sim 0.64 \text{ \AA}$, whereas with a negative charge the selenium ion radius reaches values of $r(\text{Se}^{2-}) \sim 1.84\text{--}1.98 \text{ \AA}$ [73]. The selenium anion (selenide) is formed upon acceptance of electrons, which is why its radius becomes larger than the atomic one. Some features of the influence of Se are shown in Figure 11.

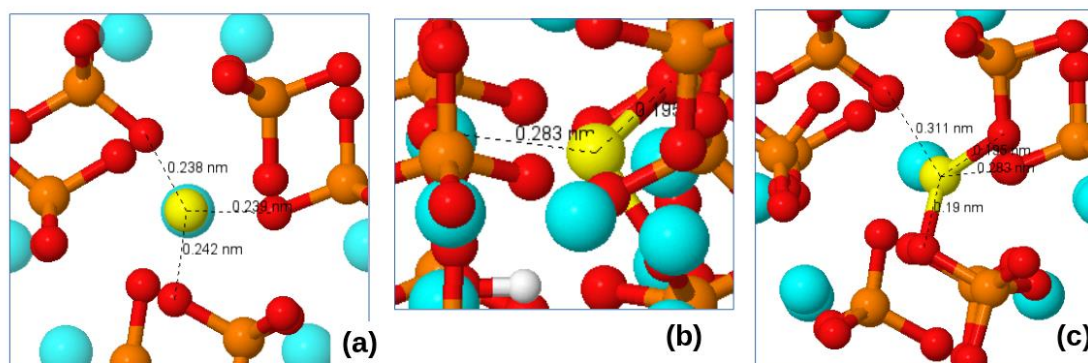


Fig. 11. Images of the dynamics of changes in the configuration of Se ion bonds during relaxation in the surface layer of Se-HAP at the boundaries with vacuum: (a) initial stages of bonds; (b) intermediate state – the emergence of bonds with oxygen ions of PO_4 groups lying closer to the HAP surface at the boundary with vacuum; (c) final state and bond lengths $r(\text{Se-O})$

The effects of Se substitutions are shown in Figure 11. Differences in the lengths of the forming bonds are clearly visible here. While in the initial state the bond lengths $r(\text{Se-O})$ are $\sim 2.38\text{--}2.42 \text{ \AA}$, and no bonds form here, in the intermediate state the Se ions shift toward the vacuum boundary and the distances change asymmetrically (lengthening to $\sim 2.83 \text{ \AA}$ on one side and shortening to $\sim 2.18\text{--}1.85 \text{ \AA}$ on the other side, when bonds are already formed). In the final state, the Se ion is shifted more toward the surface and is asymmetrically located in the center, so that the bond length $r(\text{Se-O})$ is $\sim 1.90 \text{ \AA}$, and the distance to the oxygen ions on the other side reaches values of $\sim 3.11 \text{ \AA}$, and here, of course, no bonds are formed.

The main characteristics are presented in Table 2. Note that a decrease in the thermoelectron work function of the electron about of $\Delta\Phi \sim -0.63 \text{ eV}$ was also observed. At the same time, a significant decrease in the photoelectron work function was also observed.

ANALYSIS OF RESULTS AND MAIN CONCLUSIONS

The main results obtained and all the characteristic changes in the structures of HAP with the introduced cationic substitutions Me/Ca (Me = Mg, Mn, Sr, Se) are summarized here in Table 2. The results are also presented in the graph of Figure 12, which shows changes in the work function in accordance with the difference in the atomic radii of the introduced cations, similar to what was done in [12]. The data on experimental measurements of the work function and a number of theoretical estimates, which were also presented and analyzed in [12], are also presented there.

The results of more accurate DFT calculations by using a new extended model of the HAP supercell, which includes a transition surface region with a vacuum layer, convincingly demonstrate characteristic changes in the $\Delta\Phi$ electron work function under the influence of the introduced cations, which alter the electrical potential of the HAP coating surface and thereby affect cell adhesion.

These new calculated data obtained here are qualitative in nature. The changes $\Delta\Phi$ obtained in the thermoelectron work function Φ of the electron demonstrate the fundamental influence of a number of ions introduced into the surface layers of HAP (when they replace calcium ions here) on the electron work function and the surface electric potential of the HAP

coating. Thus, the possibility of regulating and controlling the electron work function and the surface electric potential of the HAP using introduced cationic substitutions is clearly demonstrated. This is necessary to create the required level of electric potential and its distribution on the HAP surface for better adhesion of bone tissue cells (osteoblasts and others) to the HAP coating [7].

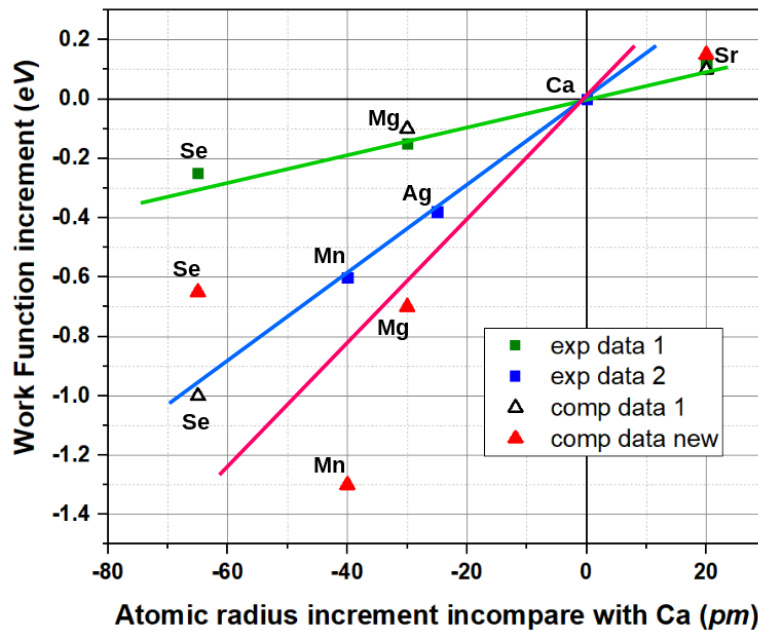


Fig. 12. Experimental and calculated data on the change in the electron work function for some cationic substitutions Me/Ca (Me = Mg, Mn, Sr, Se) in HAP samples compared with the change in the atomic radius relative to the Ca atom. Newly calculated data are indicated here by red triangles. For comparison, previously calculated data (comp data 1) from [12] are presented, as well as experimental data obtained for different cases of change in the electron work function (with a change only in the band gap width – exp data 1; with the appearance of additional energy levels within the band gap – exp data 2) [12]

Under experimental conditions, the created HAP and HAP-coating samples, of course, have many features that are difficult to theoretically account for, including various structural and compositional defects, deviations, impurities, etc. However, it is important that the fundamental qualitative nature of the change in the electron work function and electric potential on the surface of the HAP-coating can be modelled and calculated, thereby predicting the necessary direction for creating the desired changes. In our case, by introducing certain cation substitutions in the HAP. To match the proposed models to real samples, a more detailed study of the various model variants and calculations is required. For example, it is necessary to take into account the presence and influence of the hydroxyl OH vacancies and the appearance of additional energy levels E_i within the band gap E_g [12, 13]. It is also necessary to consider the dependence on the introduction of the different cation concentrations in the HAP layers near the surface with a vacuum, as was done in bulk HAP models [26–31]. It is also necessary to study the introduction of substitutions in different types of calcium positions: Ca1 and Ca2; as well as in different configurations of the positions of the replaced atoms as their concentration increases. And, and, of course, further it is necessary to consider in more detail the role and influence of water molecules, and in general water as a medium in the vacuum layer region, as well as other media, such as various electrolytes, which were used here in the experiment. For example, estimates made on the basis of the relative permittivity $\epsilon \sim 80$ (the vacuum medium is filled with water) give the following variations of values for the electric potential $U = E_{VAC}/(q_e \cdot \epsilon)$: $U(\text{Mg}) = \sim -71.8$ mV, $U(\text{Sr}) = \sim -72.86$ mV, $U(\text{Mn}) = \sim -72.12$ mV; $U(\text{Se}) = \sim -70.34$ mV compared to the native $U(\text{HAP}) = -71.02$ mV.

In general, the obtained values of the electron work function $\Phi(\text{Me})$ upon introduction of Me/Ca substitutions in HAP ($\Phi(\text{Mg}) = 3.319$ eV; $\Phi(\text{Sr}) = 4.154$ eV; $\Phi(\text{Mn}) = 2.737$ eV; $\Phi(\text{Se}) = 3.388$ eV) and for the initial unsubstituted HAP $\Phi(\text{HAP}) = 4.024$ eV, are in good agreement with data on the work function of HAP [12, 57, 62]. And their changes relative to unsubstituted HAP ($\Delta\Phi(\text{Mg}) = -0.705$ eV; $\Delta\Phi(\text{Sr}) = +0.131$ eV; $\Delta\Phi(\text{Mn}) = -1.287$ eV; $\Delta\Phi(\text{Se}) = -0.634$ eV) (Fig. 12) show noticeable local changes in the work function Φ for different cations and are in good agreement with a number of known data [12]. These changes can also be well registered experimentally by various methods, especially by measurements on an atomic force microscope using the Kelvin probe method [74, 75] or by using contact potential difference [76]. Surface potential can also be measured experimentally by other known methods [7]. The further development the modeling and calculation part of the proposed approach is necessary in order to adequately take into account the sizes of the experimental samples and areas of their surface inhomogeneities, the sizes of the changes in the surface relief and variations in composition.

This is especially important if we consider the changes that arise from the addition and removal of just one Ca atom in the surface layer (see data in Table 3), which immediately reveals noticeable shifts $\Delta\Phi$ in the Φ . Due to space limitations, we do not present detailed images of the atomistic models and potential profiles for this DFT calculation here; we provide only the most basic characteristics and their changes (in Table 3).

Table 3. Calculated changes in the energy parameters of the surface layer of HAP at the boundary with vacuum upon removal and addition of one Ca atom in a column with atom Ca # 30 along the z axis

Main computed parameters and energies	Simulated structures		
	Initial HAP model with a transition layer at $z > z_0 = 5.2$ Å	HAP model with a transition layer – when 1 of Ca-30 atom is removed	HAP model with a transition layer – when 1 atom of Ca-81 is added
Optimized calculation of the HAP layer near the surface with a vacuum	All atoms are fixed in the depth at $z < z_0 = 5.2$ Å	All atoms are fixed in the depth at $z < z_0 = 5.2$ Å	All atoms are fixed in the depth at $z < z_0 = 5.2$ Å
E_{vac} , eV	5.6816	5.8966	5.8415
$\Phi = E_{\text{vac}} - E_f$, eV	4.0236	4.4042	2.2970
$\Delta\Phi$, eV	0	+ 0.3806	– 1.7266
$W = E_{\text{vac}} - E_v$, eV	4.510	5.14637	4.28758
ΔW , eV	0	+ 0.6366	–0.2222
$U = E_{\text{vac}}/(\varepsilon \cdot q_e)$, mV ($\varepsilon = 80$)	–71.0203	–73.7072	–73.0185

Here, it is immediately evident that there are noticeable changes $\Delta\Phi$ in the work function of opposite signs: $= +0.38$ eV upon removal of 1 Ca atom, and $\Delta\Phi = -1.72$ eV upon addition of 1 Ca atom. There are also differences in the magnitude of the electrical potential U . This approach models the presence of "valleys" ("pits" or "sockets") and "protrusions" ("hills") on the surface of the HAP coating and, thus, demonstrates its surface roughness [7]. In this case, with a difference in the positions of Ca atoms along the z axis of about ~ 7 Å, the roughness parameter can be estimated as $R_a \sim 0.7$ nm. This is, of course, very small compared to known roughness values for known HAP coatings $R_a \sim 1\text{--}5$ μm [7]. However, this model is still at the atomic nanoscale; with an increase in the scale of the model, one can expect to obtain values of these parameters that are closer to the experiment.

It is important to note that already at this atomistic nanoscale level of modeling, we obtain results that are qualitatively consistent with the experimentally observed data on changes in

the electron work function and electrical potential of the HAP surface when the chemical composition and relief of the modified HAP coating on the implant change.

CONCLUSION

Calculations using DFT methods based on an extended HAP supercell model with a vacuum layer enabled us, for the first time, to accurately and directly calculate the electron work function from first principles and estimate the surface electric potential for such a layered HAP-coating-vacuum model. We also calculated the change in the electron work function upon introducing a series of Me/Ca cation substitutions (Me = Mg, Mn, Sr, Se) into the structure of a modified cation-substituted Me-HAP implant coating based on the developed Me-HAP-vacuum model. We also estimated the change in the work function and surface electric potential of HAP with changes in the surface topography. This makes it possible to estimate the change in surface electric potential, and opens the way for targeted modeling of such structures and the search for experimentally synthesized HAP-based coatings with various cation substitutions and topography changes that can more actively adhere to bone tissue cells. Thus, it becomes possible to regulate and control the magnitude of the electrical potential on the surface of HAP-coatings to improve bone cell adhesion and proliferation, thereby enhancing bone tissue growth on an implant coated with this modified HAP material. Further development of this approach requires more detailed and extensive modeling of the structural features of the surface layers of HAP coatings with different types of cationic substitutions and concentrations, as well as with various changes in their topography.

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СПИСОК ЛИТЕРАТУРЫ

1. Ratner B.D., Hoffman A.S., Schoen F.J., Lemons J.E. *Biomaterials Science*. Oxford: Academic Press, 2013.
2. *Comprehensive Biomaterials II*. Eds. Ducheyne P., Healy K., Hutmacher D.E., Grainger D.W., Kirkpatrick C.J. Amsterdam: Elsevier, 2017.
3. Barinov S.M., Komlev V.S. Biokeramika na osnove fosfatov kal'tsiya (Bioceramics based on calcium phosphates). Moscow: Nauka, 2005. 204 p. (In Russ.)
4. Dorozhkin S.V. Calcium orthophosphate deposits: Preparation, properties and biomedical applications. *Mater. Sci. Eng. C Mater. Biol. Appl.* 2015. V. 55. P. 272–326. doi: [10.1016/j.msec.2015.05.033](https://doi.org/10.1016/j.msec.2015.05.033)
5. Ratnayake J.T.B., Mucalo M., Dias G.J. Substituted hydroxyapatites for bone regeneration: A review of current trends. *J. Biomed. Mater. Res. B Appl. Biomater.* 2017. V. 105. P. 1285–1299. doi: [10.1002/jbm.b.33651](https://doi.org/10.1002/jbm.b.33651)
6. Leon B., Janson J.A. *Thin Calcium Phosphate Coatings for Medical Implants*. Berlin: Springer, 2009.
7. Khlusov I., Dekhtyar Y., Sharkeev Y., Pichugin V.F., Khlusova M.Y., Polyaka N., Tyulkin F., Vendinya V., Legostaeva E.V., Litvinova L.S., et al. Nanoscale Electrical Potential and Roughness of a Calcium Phosphate Surface Promotes the Osteogenic Phenotype of Stromal Cells. *Materials*. 2018. V. 11. No. 6. Article No. 978. doi: [10.3390/ma11060978](https://doi.org/10.3390/ma11060978)
8. Derjaguin B., Landau L. Theory of the stability of strongly charged lyophobic sols and of the adhesion of strongly charged particles in solutions of electrolytes. *Progress in Surface Science*. 1993. V. 43. P. 30–59. doi: [10.1016/0079-6816\(93\)90013-L](https://doi.org/10.1016/0079-6816(93)90013-L)
9. Bystrov V.S. Computational Studies of the Hydroxyapatite Nanostructures, Peculiarities and Properties. *Math. Biol. Bioinform.* 2017. V. 12. P. 14–54. doi: [10.17537/2017.12.14](https://doi.org/10.17537/2017.12.14)
10. Aronov D., Chaikina M., Haddad J., Karlov A., Mezinskis G., Oster L., Pavlovskaya I.,

- Rosenman G. Electronic states spectroscopy of Hydroxyapatite ceramics. *J. Mater. Sci: Mater. Med.* 2007. V. 18. P. 865–870. doi: [10.1007/s10856-006-0080-3](https://doi.org/10.1007/s10856-006-0080-3)
11. Horiuchi N., Nakaguki S., Wada N., Nozaki K., Nakamura M., Nagai A., Katayama K., Yamashita K. Polarization-induced surface charges in hydroxyapatite ceramics. *J. Appl. Phys.* 2014. V. 116. Article No. 01490. doi: [10.1063/1.4886235](https://doi.org/10.1063/1.4886235)
12. Bystrov V.S., Coutinho J., Bystrova A.V., Dekhtyar Y.D., Pullar R.C., Poronin A., Palcevskis E., Dindune A., Alkan B., Durucan C. Computational study of the hydroxyapatite structures, properties and defects. *J. Phys. D Appl. Phys.* 2015. V. 48. Article No. 195302. doi: [10.1088/0022-3727/48/19/195302](https://doi.org/10.1088/0022-3727/48/19/195302)
13. Bystrov V., Paramonova E., Avakyan L., Coutinho J., Bulina N. Simulation and Computer Study of Structures and Physical Properties of Hydroxyapatite with Various Defects. *Nanomaterials*. 2021. V. 11. Article No. 2752. doi: [10.3390/nano11102752](https://doi.org/10.3390/nano11102752)
14. Brunette D.M., Tengvall P., Textor M., Thomsen P. *Titanium in medicine*. Berlin: Springer, 2001.
15. Geetha M., Singh A.K., Asokamani R., Gogia A.K. Ti based biomaterials, the ultimate choice for orthopaedic implants – A review. *Prog. Mat. Sci.* 2009. V. 54. P. 397–425. doi: [10.1016/j.pmatsci.2008.06.004](https://doi.org/10.1016/j.pmatsci.2008.06.004)
16. Paital S.R., Dahotre N.B. Calcium phosphate coatings for bio-implant applications: Materials, performance factors, and methodologies. *Mat. Sci. Eng. R.* 2009. V. 66. P. 1–70. doi: [10.1016/j.mser.2009.05.001](https://doi.org/10.1016/j.mser.2009.05.001)
17. Narayanan R., Kim K.H., Rautray T.R. *Surface modification of titanium for biomaterial applications*. NY: Nova Science, Hauppauge, 2010. 352 p.
18. Ben-Nissan B., Choi A.H. Sol-gel production of bioactive nanocoatings for medical applications. Part 1: An introduction. *Nanomedicine*. 2006. V. 1. P. 311–319. doi: [10.2217/17435889.1.3.311](https://doi.org/10.2217/17435889.1.3.311)
19. Fauchais P. Understanding plasma spraying. Topical review. *J. Phy. D. Appl. Phys.* 2004. V. 37. P. R86–R108. doi: [10.1088/0022-3727/37/9/R02](https://doi.org/10.1088/0022-3727/37/9/R02)
20. Kelly P.J., Arnell R.D. Magnetron sputtering: a review of recent developments and applications. *Vacuum*. 2000. V. 56. P. 159–172. doi: [10.1016/S0042-207X\(99\)00189-X](https://doi.org/10.1016/S0042-207X(99)00189-X)
21. Surmenev R.A. A review of plasma-assisted methods for calcium phosphate-based coatings fabrication. *Surf. Coat. Tech.* 2012. V. 206. P. 2035–2056. doi: [10.1016/j.surfcoat.2011.11.002](https://doi.org/10.1016/j.surfcoat.2011.11.002)
22. Chen J.Z., Shi Y.L., Wang L., Yan F.Y., Zhang F.Q. Preparation and Properties of Hydroxyapatite-Containing Titania Coating by Micro-Arc Oxidation. *Mater. Lett.* 2006. V. 60 P. 2538–2543. doi: [10.1016/j.matlet.2006.01.035](https://doi.org/10.1016/j.matlet.2006.01.035)
23. Frauchiger V.M., Schlottig F., Gasser B., Textor M. Anodic plasma-chemical treatment of CP titanium surfaces for biomedical applications. *Biomaterials*. 2004. V. 25. P. 593–606. doi: [10.1016/S0142-9612\(03\)00560-X](https://doi.org/10.1016/S0142-9612(03)00560-X)
24. Wang Y., Yu H., Chen C., Zhao Z. Review of the biocompatibility of microarc oxidation coated titanium alloys. *Mat. Design*. 2015. V. 85. P. 640–652. doi: [10.1016/j.matdes.2015.07.086](https://doi.org/10.1016/j.matdes.2015.07.086)
25. Terleeva O.P., Sharkeev Yu.P., Slonova A.I., Mironov I.V., Legostaeva E.V., Khlusov I.A., Matykina E., Skeldon P., Thompson G.E. Effect of microplasma modes and electrolyte composition on micro-arc oxidation coatings on titanium for medical applications. *Surf. Coat. Tech.* 2010. V. 205. P. 1723–1729. doi: [10.1016/j.surfcoat.2010.10.019](https://doi.org/10.1016/j.surfcoat.2010.10.019)
26. Avakyan L.A., Paramonova E.V., Coutinho J., Öberg S., Bystrov V.S., Bugaev L.A. Optoelectronics and defect levels in hydroxyapatite by first-principles. *J. Chem. Phys.* 2018. V. 148. Article No. 154706. doi: [10.1063/1.5025329](https://doi.org/10.1063/1.5025329)
27. Bystrov V.S., Paramonova E.V., Avakyan L.A., Eremina N.V., Makarova S.V., Bulina N.V. Effect of Magnesium Substitution on Structural Features and Properties of Hydroxyapatite. *Materials*. 2023. V. 16. Article No. 5945. doi: [10.3390/ma16175945](https://doi.org/10.3390/ma16175945)

28. Bystrov V.S., Paramonova E.V., Filippov S.V., Avakyan L.A., Chaikina M.V., Eremina N.V., Makarova S.V., Bulina N.V. Zinc-Substituted Structures of Hydroxyapatite: Modeling and Experiment. *Mathematical Biology and Bioinformatics*. 2023. V. 18. P. 580–601. doi: [10.17537/2023.18.580](https://doi.org/10.17537/2023.18.580)
29. Bystrov V.S., Parmonova E.V., Avakyan L.A., Makarova S.V., Bulina N.V. Structure and properties of manganese-substituted hydroxyapatite. *Bulletin of the Russian Academy of Sciences: Physics*. 2024. V. 88. P. 745–751. doi: [10.1134/S1062873824706524](https://doi.org/10.1134/S1062873824706524)
30. Bystrov V.S., Paramonova E.V., Avakyan L.A., Makarova S.V., Bulina N.V. Study of manganese substitutions in hydroxyapatite using density functional theory methods: Optical and magnetic properties. *Next Materials*. 2025. V. 8. Article No. 100583. doi: [10.1016/j.nxmzte.2025.100583](https://doi.org/10.1016/j.nxmzte.2025.100583)
31. Bystrov V.S., Paramonova E.V., Avakyan L.A., Makarova S.V., Bulina N.V. Hydroxyapatite with substitution of calcium cations by magnetic iron ions. *Bulletin of the Russian Academy of Sciences: Physics*. 2025. V. 89. P. S375–S382. doi: [10.1134/S1062873825714679](https://doi.org/10.1134/S1062873825714679)
32. Quantum ESPRESSO. URL: <https://www.quantum-espresso.org/> (accessed 07.06.2026).
33. Terpstra R.A., Bennema P., Hartman P., Woensdregt C.F., Perdok W.G., Senechal M.L. F faces of apatite and its morphology: theory and observation. *J. Cryst. Growth*. 1986. V. 78. No. 3. P. 468–478. doi: [10.1016/0022-0248\(86\)90149-1](https://doi.org/10.1016/0022-0248(86)90149-1)
34. Kittel C. *Introduction to solid state physics*. New York: J. Wiley and Sons, Inc., 1978.
35. Vandiver J., Dean D., Patel N., Bonfield W., Ortiz C. Nanoscale variation in surface charge of synthetic hydroxyapatite detected by chemically and spatially specific high-resolution force spectroscopy. *Biomaterials*. 2005. V. 26. P. 271–283. doi: [10.1016/j.biomaterials.2004.02.053](https://doi.org/10.1016/j.biomaterials.2004.02.053)
36. Astala R., Stott M.J. First-principles study of hydroxyapatite surfaces and water adsorption. *Phys. Rev. B*. 2008. V. 78. Article No. 075427. doi: [10.1103/PhysRevB.78.075427](https://doi.org/10.1103/PhysRevB.78.075427)
37. Rulis P., Yao H., Ouyang L., Ching W.Y. Electronic structure, bonding, charge distribution, and x-ray absorption spectra of the (001) surfaces of fluorapatite and hydroxyapatite from first principles. *Phys. Rev. B*. 2007. V. 76. P. 245–410. doi: [10.1103/PhysRevB.76.245410](https://doi.org/10.1103/PhysRevB.76.245410)
38. Slepko A. *Theory of biomineral Hydroxyapatite*: Dissertation for Degree of PhD. The University of Texas at Austin. 2013. 160 p.
39. Slepko A., Demkov A.A. First-principles study of hydroxyapatite surface. *J. Chem. Phys.* 2013. V. 139. Article No. 044714. doi: [10.1063/1.4813828](https://doi.org/10.1063/1.4813828)
40. Bystrov V.S., Paramonova Ye.V., Avakyan L.A., Makarova S.V., Bulina N.V. Svoystva gidroksiapatita s kationnymi zameshcheniyami (Properties of hydroxyapatite with cationic substitutions}. In: *International Conference "Biomaterials: from research to practice": collection of materials*. Moscow: IMET RAS, 2025. P. 128–130. (In Russ.).
41. Perdew J.P., Burke K., Ernzerhof M. Generalized Gradient Approximation Made Simple. *Phys. Rev. Lett.* 1996. V. 77. P. 3865–3868. doi: [10.1103/PhysRevLett.77.3865](https://doi.org/10.1103/PhysRevLett.77.3865)
42. Heyd J., Scuseria G.E., Ernzerhof, M. Hybrid functionals based on a screened Coulomb potential. *J. Chem. Phys.* 2003. V. 118. P. 8207–8215. doi: [10.1063/1.1564060](https://doi.org/10.1063/1.1564060)
43. Krukau A.V., Vydrov O.A., Izmaylov A.F., Scuseria G.E. Influence of the exchange screening parameter on the performance of screened hybrid functionals. *J. Chem. Phys.* 2006. V. 125. Article No. 224106. doi: [10.1063/1.2404663](https://doi.org/10.1063/1.2404663)
44. Schlipf M., Gygi F. Optimization algorithm for the generation of ONCV pseudopotentials. *Computer Phys. Comm.* 2015. V. 196. P. 36–44. doi: [10.1016/j.cpc.2015.05.011](https://doi.org/10.1016/j.cpc.2015.05.011)
45. Hamann D.R. Optimized norm-conserving Vanderbilt pseudopotentials. *Phys. Rev.* 2013. V. B88. Article No. 085117. doi: [10.1103/PhysRevB.88.085117](https://doi.org/10.1103/PhysRevB.88.085117)

46. Nocedal J., Wright S.J. *Numerical Optimization*. New York: Springer, 2006.
47. Avriel M. *Nonlinear Programming: Analysis and Methods*. Dover Publishing, 2003.
48. Bystrov V.S., Paramonova E., Dekhtyar Y., Katashev A., Karlov A., Polyaka N., Bystrova A.V., Patmalnieks A., Kholkin A.L. Computational and experimental studies of size and shape related physical properties of hydroxyapatite nanoparticles. *J. Phys.: Cond. Matter*. 2011. V. 23. Article No. 065302. doi: [10.1088/0953-8984/23/6/065302](https://doi.org/10.1088/0953-8984/23/6/065302)
49. Tofail S A M, Haverty D, Stanton K T and McMonagle J B. Structural Order and Dielectric Behaviour of Hydroxyapatite. *Ferroelectrics*. 2005. V. 319. P. 117–123. doi: [10.1080/00150190590965523](https://doi.org/10.1080/00150190590965523)
50. Lang S.B., Tofail S.A.M., Kholkin A.L., Wojtaś M., Gregor M., Gandhi A.A., Wang Y., Bauer S., Krause M., Plecenik A. Ferroelectric Polarization in Nanocrystalline Hydroxyapatite Thin Films on Silicon. *Scientific Reports*. 2013. V. 3. Article No. 2215. doi: [10.1038/srep02215](https://doi.org/10.1038/srep02215)
51. Bystrov V.S., Coutinho J., Avakyan L.A., Bystrova A.V., Paramonova E.V. Piezoelectric, ferroelectric, and optoelectronic phenomena in hydroxyapatite with various defect levels. *Ferroelectrics*. 2020. V. 559. No. 1. P. 45–55. doi: [10.1080/00150193.2020.1722005](https://doi.org/10.1080/00150193.2020.1722005)
52. Sato K., Kogure T., Iwai H., Tanaka J. Atomic-Scale $\{101\bar{0}\}$ Interfacial Structure in Hydroxyapatite Determined by High-Resolution Transmission Electron Microscopy. *J. Am. Ceram. Soc.* 2002. V. 85. Article No. 3054. doi: [10.1111/j.1151-2916.2002.tb00578.x](https://doi.org/10.1111/j.1151-2916.2002.tb00578.x)
53. Aronov D., Rosen R., Ron E.Z. Electron-induced surface modification of hydroxyapatite-coated implant. *Surface and Coatings Technology*. 2008. V. 202. P. 2093–2102. doi: [10.1016/j.surfcoat.2007.08.060](https://doi.org/10.1016/j.surfcoat.2007.08.060)
54. Orekhov M. Coordination Numbers of Bivalent Ions in Organic Solvents. *Russian Journal of Physical Chemistry A*. 2021. V. 95. P. 2059–2064. doi: [10.1134/S0036024421100204](https://doi.org/10.1134/S0036024421100204)
55. Ren F., Leng Y., Xin R., Ge X. Synthesis, Characterization and Ab Initio Simulation of Magnesium-Substituted Hydroxyapatite. *Acta Biomater*. 2010. V. 6. P. 2787–2796. doi: [10.1016/j.actbio.2009.12.044](https://doi.org/10.1016/j.actbio.2009.12.044)
56. Stipnice L., Salma-Ancane K., Borodajenko N., Sokolov M., Jakovlevs D., Berzina-Cimdina L. Characterization of Mg-substituted hydroxyapatite synthesized by wet chemical method. *Cer. Int.* 2014. V. 40. P. 3261–3267. doi: [10.1016/j.ceramint.2013.09.110](https://doi.org/10.1016/j.ceramint.2013.09.110)
57. Palcevskis E., Dindune A., Dekhtyar Y., Polyaka N., Veljović D., Sammons R.L. The influence of surface treatment by hydrogenation on the biocompatibility of different hydroxyapatite materials. *IOP Conf. Ser. Mater. Sci. Eng.* 2011. V. 23. Article No. 012032. doi: [10.1088/1757-899X/23/1/012032](https://doi.org/10.1088/1757-899X/23/1/012032)
58. Šupova M. Substituted hydroxyapatites for biomedical applications: A review. *Ceram. Int.* 2015. V. 41. P. 9203–9231. doi: [10.1016/j.ceramint.2015.03.316](https://doi.org/10.1016/j.ceramint.2015.03.316)
59. Tite T., Popa A.-C., Balescu L.M., Bogdan I.M., Pasuk I., Ferreira J.M.F., Stan G.E. Cationic Substitutions in Hydroxyapatite: Current Status of the Derived Biofunctional Effects and Their In Vitro Interrogation Methods. *Materials*. 2018. V. 11. Article No. 2081. doi: [10.3390/ma11112081](https://doi.org/10.3390/ma11112081)
60. Capuccini C., Torricelli P., Boanini E., Gazzano M., Giardino R., Bigi A. Interaction of Sr-doped hydroxyapatite nanocrystals with osteoclast and osteoblast-like cells. *J. Biomed. Mater. Res. A*. 2009. V. 89. No. 3. Article No. 594. doi: [10.1002/jbm.a.31975](https://doi.org/10.1002/jbm.a.31975)
61. Bystrov V.S., Paramonova E.V., Bystrova A.V., Avakyan L.A., Bulina N.V. Structural and physical properties of hydroxyapatite modified by Sr/Ca substitutions. *Ferroelectrics*. 2023. V. 605. No. 1. P. 117–128. doi: [10.1080/00150193.2023.2169018](https://doi.org/10.1080/00150193.2023.2169018)
62. Dekhtyar Y., Bystrov V., Bystrova A., Dindune A., Katashev A., Khlusov I., Palcevskis E., Paramonova E., Polyaka N., Romanova M., Sammons R., Veljović D.

- Engineering of the hydroxyapatite cell adhesion capacity. *IFMBE Proc.* 2013. V. 38. P. 182–185. doi: [10.1007/978-3-642-34197-7_48](https://doi.org/10.1007/978-3-642-34197-7_48)
63. Bystrov V.S., Paramonova E.V., Bystrova A.V., Avakyan L.A., Bulina N.V. Structural and physical properties of Sr/Ca and Mg/Ca substituted hydroxyapatite: modeling and experiments. *Ferroelectrics*. 2022. V. 590. P. 41–48. doi: [10.1080/00150193.2022.2037937](https://doi.org/10.1080/00150193.2022.2037937)
 64. Greenwood N.N., Earnshaw A. *Chemistry of the Elements*. Oxford: Butterworth–Heinemann, 1997.
 65. Istomin S.Y., Morozov A.V., Kazakov S.M., Antipov E.V., Lyskov N.V. High-temperature properties of layered oxides (LA,TB,SR)₂CUO_{4±δ} with T*-structure. *Russian Journal of Inorganic Chemistry*. 2022. V. 67. No. 6. P. 754–760. doi: [10.1134/S0036023622060109](https://doi.org/10.1134/S0036023622060109)
 66. Silva L.M.D., Tavares D.D.S., Santos E.A.D. Isolating the Effects of Mg²⁺, Mn²⁺ and Sr²⁺ Ions on Osteoblast Behavior from those Caused by Hydroxyapatite Transformation. *Mater. Res.* 2020. V. 23. No. 2. Article. No. E20200083. doi: [10.1590/1980-5373-mr-2020-0083](https://doi.org/10.1590/1980-5373-mr-2020-0083)
 67. Rau J.V., Fadeeva I.V., Fomin A.S., Barbaro K., Galvano E., Ryzhov A.P., Murzakhanov F., Gafurov M., Orlinskii S., Antoniac I., Uskoković V. Sic Parvis Magna: Manganese-Substituted Tricalcium Phosphate and Its Biophysical Properties. *ACS Biomater. Sci. Eng.* 2019. V. 5. No. 12. P. 6632–6644. doi: [10.1021/acsbiomaterials.9b01528](https://doi.org/10.1021/acsbiomaterials.9b01528)
 68. Shurtakova D.V., Grishin P.O., Gafurov M.R., Mamin G.V. Using DFT to Calculate the Parameters of the Crystal Field in Mn²⁺ Doped Hydroxyapatite Crystals. *Crystals*. 2021. V. 11. Article No. 1050. doi: [10.3390/cryst11091050](https://doi.org/10.3390/cryst11091050)
 69. Monteil-Rivera F., Masset S., Dumonceau J., Fedoroff M., Jeanjean J. Sorption of selenite ions on hydroxyapatite. *Journal of Materials Science Letters*. 1999. V. 18. P. 1143–1145. doi: [10.1023/A:1006661419741](https://doi.org/10.1023/A:1006661419741)
 70. Duc M., Lefevre G., Fedoroff M., Jeanjean J., Rouchaud J.C., Monteil-Rivera F., Dumonceau J., Milonjic S. Sorption of Selenium Anionic Species on Apatites and Iron Oxides from Aqueous Solutions. *Journal of Environmental Radioactivity*. 2003. V. 70. P. 61–72. doi: [10.1016/S0265-931X\(03\)00125-5](https://doi.org/10.1016/S0265-931X(03)00125-5)
 71. Bjørklund G., Shanaida M., Lysiuk R., Antonyak H., Klishch I., Shanaida V., Peana M. Selenium: An Antioxidant with a Critical Role in Anti-Aging. *Molecules*. 2022. V. 27. No. 19. Article No. 6613. doi: [10.3390/molecules27196613](https://doi.org/10.3390/molecules27196613)
 72. Peng S., Zhang G., Wang D. Association of selenium intake with bone mineral density and osteoporosis: the national health and nutrition examination survey. *Frontiers in Endocrinology*. 2023. V. 14. doi: [0.3389/fendo.2023.1251838](https://doi.org/10.3389/fendo.2023.1251838)
 73. Bagnall K.W. *The Chemistry of Selenium, Tellurium, and Polonium*. Elsevier Publishing Company, 1966. (Topics in inorganic and general chemistry, Iss. 7). 200 p.
 74. Rossi S., Fedel M., Deflorian F., Vadillo M. Localized electrochemical techniques: Theory and practical examples in corrosion studies. *Comptes Rendus Chimie – C. R. CHIM.* 2008. V. 11. P. 984–994. doi: [10.1016/j.crci.2008.06.011](https://doi.org/10.1016/j.crci.2008.06.011)
 75. Zharin A.L. Macro- and micro Kelvin probe in tribological studies. In: *Fundamentals of tribology and bridge the gap between the macro-and micro/nanoscales*. Kluwer, Dordrecht, 2001. P. 451–463.
 76. Zharin A.L. Contact potential difference techniques as probing tools in tribology and surface mapping. In: *Scanning probe microscopy in nanoscience and nanotechnology*. Springer Berlin. 2010. P. 687–720.

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