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MOLECULAR DOCKING OF NANOSIZED TITANIUM DIOXIDE MATERIAL TO THE EXTRACELLULAR PART OF GABA_B-RECEPTOR

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A spatial model of nanosized titanium dioxide material was created using Discovery Studio Visualizer software, versions 2.0 and 2.5. A search for and analysis of possible sites of its docking to the extracellular part of GABA_{B1a} receptor subunit were performed using the algorithm for molecular docking PatchDock. The dimensions of the obtained TiO₂ nanoparticle surface were (18.925 × 3.785 × 19.028) Å. Four potentially possible sites of TiO₂ docking to the extracellular part of GABA_{B1a} receptor subunit of GABA_B were identified. The TiO₂ nanoparticle demonstrated high affinity of docking to one of the receptor sites with the geometric shape complementarity score of 12562, taking the following values in other sites: 10746; 10370; 10204. The approximate interface area of complex of the extracellular part of GABA_{B1a} receptor subunit of GABA_B with TiO₂ for the site with the highest geometric shape complementarity score was 1949.80 Å, and for others – 1273.20 Å, 1261.10 Å and 1170.30 Å, respectively. The evaluation of atomic contact energy demonstrated the following values for the sites of TiO₂ nanoparticle docking: 362.92; 173.93; 340.63 and 224.61. The nature of connections, stabilizing the sites of TiO₂ docking to the extracellular part of GABA_{B1a} receptor subunit of GABA_B, was analyzed in accordance to their amino acid composition.

Keywords: TiO₂ nanoparticles, GABA_B receptor, molecular docking, PatchDock.

INTRODUCTION

It is known that in the form of nanoparticles, many substances acquire fundamentally new physical and chemical properties and are quite active in that state regarding the biological objects, whose macromolecules are also at the level of the nanometer dimensions, revealing their function via the formation of supermolecular complexes. These materials include titanium dioxide (TiO₂), whose use in the form of nanoparticles has considerably extended in modern highly technological production processes in different sectors of economy, in particular, in food production and pharmacology [21]. According

to literature data [3, 4, 5, 14, 27], TiO_2 is a polar adsorbent, whose most active centers are superficial hydroxyl groups, capable of dissociating and forming positively and (or) negatively charged adsorption centers. It was shown [18] that TiO_2 particles are capable of adsorbing on its surface aminoacids, in particular, histidine (Fig. 1).

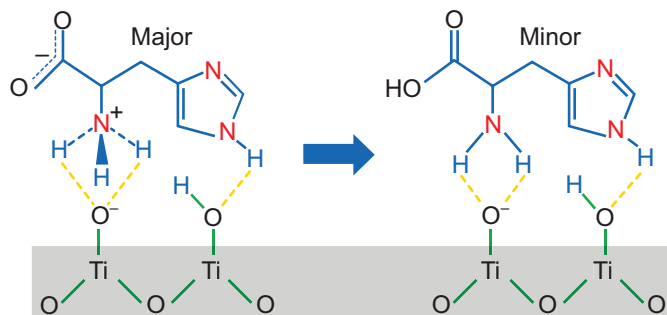


Fig. 1. Histidine adsorption on the surface of TiO_2 nanoparticles [18]. Amino acids are bound to the surface of TiO_2 , which creates conditions for intramolecular transfer of a proton onto the carboxyl group of adsorbed histidine. In addition, the imidazole ring may interact via π -orbitals with titanium atoms, located on the surface, and the amino acid may form H-bonds with superficial atoms of oxygen [4]

Рис. 1. Адсорбція гістидину на поверхні наночастинок діоксиду титану [18]. Аміногрупи зв'язуються з поверхнею TiO_2 , що створює умови для внутрішньомолекулярного перенесення протона на карбоксильну групу адсорбованого гістидину. Крім того, імідазольне кільце може взаємодіяти з атомами титану, що містяться на поверхні, через π -орбіталі, а аміногрупа може формувати Н-зв'язки з поверхневими атомами кисню [4]

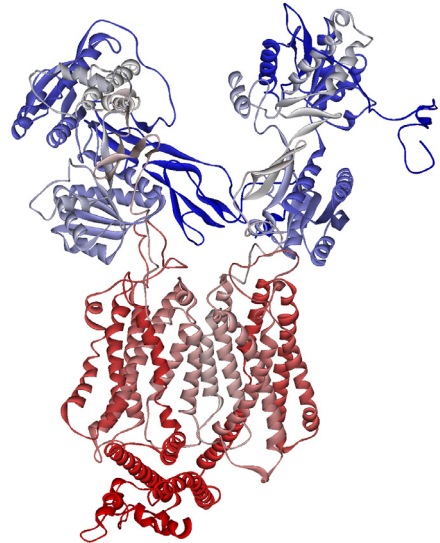
Taking that into consideration, it was interesting to investigate molecular mechanisms of interaction between TiO_2 nanoparticles and molecules of proteins-receptors, in particular, metabotropic GABA_B receptor [2, 11] whose the mediator is a known transmitter of the central nervous system, γ -aminobutyric acid, that participates in control over blood circulation, implemented by neurons of dorsomedial and ventrolateral divisions of medulla oblongata [23, 24, 26]. To solve this issue by the molecular docking method, the search for binding sites of TiO_2 particles and the extracellular part of GABA_B receptor was performed. The aim of our work was also to construct the spatial structure of TiO_2 particle, using Discovery Studio Visualizer software 2.0 and 2.5 of versions. The construction of the spatial structure of full-size GABA_B receptor (Fig. 2), the investigation of its molecular dynamics and estimation of the energy of nonvalent interactions in the model of the complex of GABA_B receptor with lipid bilayer membrane was performed in our previous work [19].

MATERIALS AND METHODS

In order to construct a spatial structure of TiO_2 nanoparticle, its crystal modification, anatase, was used [10]. A remarkable specificity of the modification of this nanoparticle material is a system of channels, oriented parallel to the plane of the crystallographic face. The channels in the cross section form a square with the side of 3.35 Å. The anatase structure has a form of three-dimensional chains made of TiO_6 octahedra. Each octahedron contains a central ion Ti^{+4} surrounded by six anions O^{-2} . Four anions are located in the equatorial plane, and two – in the axial points. The equatorial connections

Fig. 2. Spatial structure of GABA_B receptor. This is a heterodimer consisting of two subunits (GABA_{B1a} and GABA_{B2}) [22]. In its turn, each subunit consists of the extracellular part (β -elements successively interchanging α -helices forming unique “claws”); the transmembrane part (containing seven successively connected α -helices); the intracellular part (containing the part, that serves for the formation of the superhelical structure) [8, 9, 22]

Рис. 2. Просторова структура ГАМК_B-рецептора. Це гетеродимер, що складається з двох субодиниць (ГАМК_{B1a} та ГАМК_{B2}) [22]. У свою чергу, кожна субодиниця складається з зовнішньоклітинної частини (β -елементи, які послідовно чергуються з α -спіралями, утворюючи своєрідні “клешні”); трансмембранної частини (містить сім послідовно з'єднаних α -спіралей); внутрішньоклітинної частини (містить ділянку, що слугує для утворення надспіралізованої структури) [8, 9, 22]



in the anatase are 1.980 Å, axial ones – 1.985 Å [7]. In our work, according to [16] the spatial structure of titanium dioxide nanoparticle was constructed using Discovery Studio Visualizer software 2.0 and 2.5 of versions (Accelrys Software Inc. – <http://accelrys.com/>). PatchDock, a geometry-based molecular docking algorithm, was used in a search for interaction sites of the extracellular part of GABA_B receptor and the TiO₂ nanoparticle [6, 25]. This algorithm consists of three main stages: Molecular Shape Representation, Surface Patch Matching and Filtering and Scoring. PatchDock computes the three-dimensional transformations of one of two molecules with respect to the other with the goal of maximizing surface shape complementarity while minimizing the number of steric clashes. Docking programs adapted to native conditions, consequently these programs are used at physiological pH. The service is available at <http://bioinfo3d.cs.tau.ac.il/PatchDock/>. The visualization and analysis of the contact surfaces were performed using Discovery Studio Visualizer software 2.0 and 2.5 of versions.

RESULTS AND DISCUSSION

According to the catalog, the receptor subunit of gamma-aminobutyric acid, type B, was indicated in the work as GABA_{B1a} [1], where *a* relates to the subunit isoform, and 1 indicates its number. The spatial structure of the extracellular part of GABA_{B1a} subunit (15–592 amino acid residues) was obtained via the molecular simulation of the full-size GABA_B receptor, that was conducted in our previous studies (Fig. 3, A) [19]. The three-dimensional structure of the TiO₂ particle (Fig. 3, B) was simulated using Discovery Studio Visualizer software 2.0 and 2.5 of versions. Taking into consideration the data about the crystallography of anatase, the following parameters of the elementary cluster of TiO₂ were used in our work: A = B = 3.785 Å; C = 9.514 Å, where A, B, C – lengths of the crystalline grid. $a = b = \gamma = 90^\circ$, where a, b, γ – dimensions of crystal angles. The spatial symmetry group (the combination of symmetry transformations, remarkable for atomic structure of crystals) of titanium dioxide, is I4(1)/amd [7, 12]. The dimensions of the surface of TiO₂ nanoparticle obtained after the simulation of the spatial structure, were as follows: (18.925 × 3.785 × 19.028) Å.

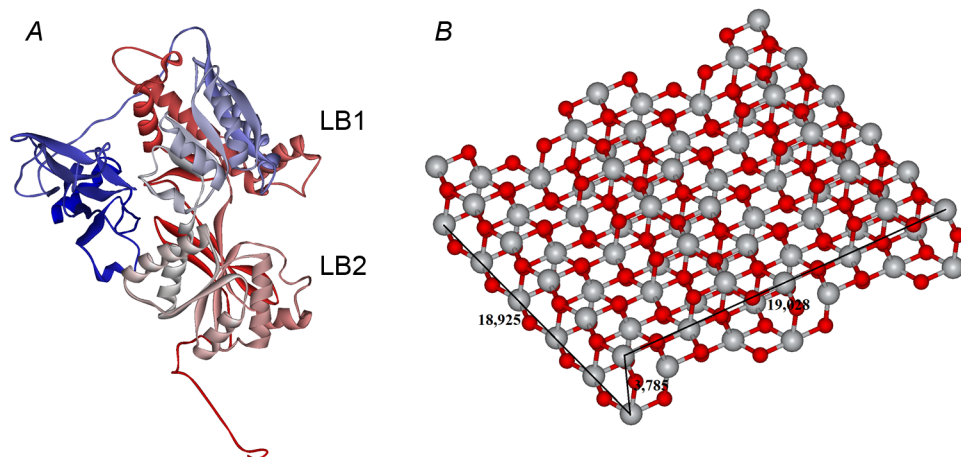


Fig. 3. A – Spatial structure of the extracellular part of GABA_{B1a} receptor subunit of GABA_B; B – spatial structure of the nanoparticle of TiO₂ anatase

Рис. 3. А – Просторова структура зовнішньоклітинної частини субодиноці ГАМК_{B1a} рецептора ГАМК_B; В – просторова структура наночастинки анатазу діоксиду титану

A search for and analysis of the interaction sites of TiO₂ and the extracellular part of the GABA_{B1a} of GABA_B receptor subunit was performed using PatchDock web-service. The input parameters for the docking were the PDB coordinate file for the extracellular part of the GABA_{B1a} receptor subunit and the TiO₂ nanoparticle. Clustering of RMSD (Root-mean-square deviation) was chosen as 4.0 Å. Clustering of RMSD is a positive number that specifies the radius of the RMSD clustering in angstroms. This value is used in the final clustering stage of the algorithm. It ensures that the distance between any of two output solutions will be at least the specified clustering of RMSD value. The default value for this parameter is 4 Å [25]. Complex Type was chosen as protein–small ligand. In the case of protein–small ligand docking, the algorithm uses a parameter set optimized for small-size molecules. Potential binding sites of the receptor and the ligand, respectively, were not chosen. A web page that presents the solutions is automatically generated. The output of PatchDock is a list of candidate complexes between extracellular part of GABA_{B1a} receptor subunit and TiO₂. The geometric score (Score), the atomic contact energy (ACE) [28], the size of interface area (Area) and the actual rigid transformation of the solution for the four binding sites are shown in Table 1. The atomic contact energy is used to estimate the contribution of the desolvation energy to the scoring function. The ACE score of a pair of protein atoms is defined as the free energy difference between two protein-atoms and water contacts and the sum of a protein-atom to protein-atom contact and a water to water contact. Presented transformations are 3D transformations that include 3 rotational angles and 3 translational parameters. These transformations are applied on the TiO₂ nanoparticle.

The results of the molecular docking of the TiO₂ nanoparticle demonstrate that the latter induces four potential sites of different affinity for its binding to the extracellular part of GABA_{B1a} of GABA_B receptor subunit. According to data of the estimations of PatchDock web-service, TiO₂ possessed high affinity of binding to one of receptor sites with the geometric shape complementarity score of 12562, and in other sites – 10746;

10370; 10204. The approximate interface area of the complex of the extracellular part of subunit GABA_{B1a} of GABA_B receptor and TiO₂ for one of sites is 1949.80 Å, and for others – 1273.20 Å, 1261.10 Å and 1170.30 Å, respectively. This value is in distinct correlation with the geometric shape complementarity score. It was determined that the level of affinity as a result of strong intramolecular interaction in the site of the protein-receptor binding TiO₂, the distribution within the site of amino acids forming long-term electrostatic hydrogen bonds, hydrophobic interactions are determined by their location on the receptor molecule, namely, the first one – on the side, opposite the slit between the lobes 1 (LB1) and 2 (LB2) closer to N-terminal part, the second one – in the slit between LB1 and LB2, the third one – on the surface of the receptor macromolecule near the slit between LB1 and LB2 and the fourth one – on the side, opposite the slit between LB1 and LB2 closer to the zone of their binding. The sites were numbered according to the reduction in their affinity degree.

Table 1. Docking analysis of the extracellular part of GABAB1a subunit and TiO₂ complex
Таблиця 1. Аналіз докінгу комплексу зовнішньоклітинної частини субодиноці ГАМК_{B1a} з діоксидом титану

| No sites | Score | Area | ACE | Transformation | | | | | |
|----------|-------|---------|--------|----------------|-------|-------|-------|-------|-------|
| 1 | 12562 | 1949,80 | 362,92 | 0.17 | 0.54 | 0.68 | 36.67 | -5.22 | 64.30 |
| 2 | 10746 | 1273,20 | 173,93 | -2.34 | -0.06 | -0.04 | 14.29 | 21.48 | 64.11 |
| 3 | 10370 | 1261,10 | 340,63 | -1.41 | -0.93 | 2.29 | 35.09 | 31.20 | 90.90 |
| 4 | 10204 | 1170,30 | 224,61 | 0.23 | 0.03 | -0.05 | 14.30 | -9.71 | 41.04 |

It was established (Fig. 4) that the amino acid composition and environment of the first binding site include the following amino acids: Trp37, Glu38, Val74, Thr92, Arg95, Cys96, Arg98, Gly116, Gly117, Asp118, Leu119, Pro120, Leu122, Pro153, Lys154, Pro155, His156, Arg258, Arg277, Gln278, Pro281, Gln503, Thr504, Asp507, Gln508, Tyr510, Arg511, Asn514, Asp528, Ala529, Ser530. The evaluation of the atomic contact energy demonstrated its value for this site of TiO₂ nanoparticle binding to be 362.92.

The analysis of the amino acid composition of the site with the highest affinity of binding TiO₂ (the first site) demonstrated that the variety of its composition includes all currently known amino acids with polar charged radicals capable of forming long-term electrostatic charges (the charge of the amino acid radical is indicated in brackets): Glu38 (-), Arg95 (+), Arg98 (+), Asp118 (-), Lys154 (+), His156 (+), Arg258 (+), Arg277 (+), Asp507 (-), Arg511 (+), Asp528 (-) with prevailing amino acids, whose radicals have a positive charge. Among these amino acids, arginine and lysine are amino acids with high occurrence degree and the least conformational entropy of the side chain (as the estimation of the amino acid ability of forming the helix), for which Gibbs free energy (ΔG) is (-0.68) kJ/mol and (-0.65) kJ/mol, respectively (calculated via changes in the temperature of the helix-coil transition while injecting a specific amino acid into the standard amino acid sequence of peptide), according to literature data [20]. As for glutamic and asparagine acids which are in this site composition, at the expense of the carboxylic group of side chains they are well-adsorbed on the surface of anatase [15]. The stabilization of the position of TiO₂ particle in this site of binding to the protein-receptor

GABA_B, in addition to the electrostatic interactions, is affected by the hydrogen bonds, whose formation, as seen from the model, is facilitated by the following polar uncharged amino acids: Thr92, Cys96, Gln278, Gln503, Thr504, Gln508, Tyr510, Asn514 and Ser530. ΔG of these amino acids is in the range of (-0.07) – (-0.35) kJ/mol. Noteworthy it is the presence of cysteine in the list of the mentioned amino acids, as high polarization capacity of the electronic envelope of its sulfur atom makes it an active center of interacting with reagents and, as may be assumed, – with TiO₂ in particular. The amino acid composition of this binding site also contains the hydrophobic amino acids, including four residues of proline. It is known [13, 20] that proline ($\Delta G = +3$ kJ/mol) is the only cyclic amino acid whose amino group is not free and is a part of heterocycle, so this amino acid does not participate in the formation of the hydrogen bond. Proline binds to the polypeptide chain via covalent bonds and forms its clear link with the open access of peptide bonds. According to literature data [18] regarding the capability of TiO₂ to form bonds both with amino groups of amino acid residues in protein and to its peptide bonds, they may become an additional place of interacting with nanoparticles. As stated above, the affinity of the first binding site acquires the value exceeding the value of this parameter for all three following sites. The results of estimating the approximate interface area of complex for each binding site of TiO₂ allowed revealing similar regularities (Table 1).

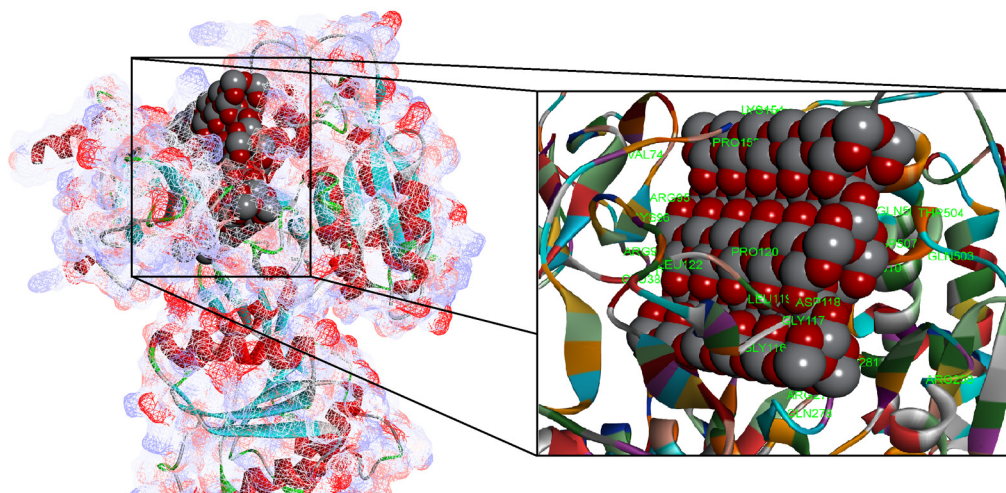


Fig. 4. The first site of TiO₂ binding to the extracellular part of GABA_{B1a} of GABA_B receptor subunit (Score – 12562, Area – 1949.80, ACE – 362.92)

Рис. 4. Перший сайт зв'язування діоксиду титану із зовнішньоклітинною частиною субодиниці ГАМК_{B1a} ГАМК_B рецептора (Score – 12562, Area – 1949,80, ACE – 362,92)

The following binding site (Fig. 5) for TiO₂ particle and its environment includes such amino acids: Gly181, Trp182, Cys246, Ser247, Ser248, Ser270, Ser271, Gln314, Thr316, Val318, Ser345, Tyr367, Glu368, Thr369, Arg372, Lys373, Trp395, Ala397, Ile403, Tyr404, Asp405, Pro406, Ser407, Glu459, Gly462, Gly463, Phe464, Gln465, Glu466. The estimations of ACE for this site performed using PatchDock web-server, demonstrated that it acquires the value of 173.93.

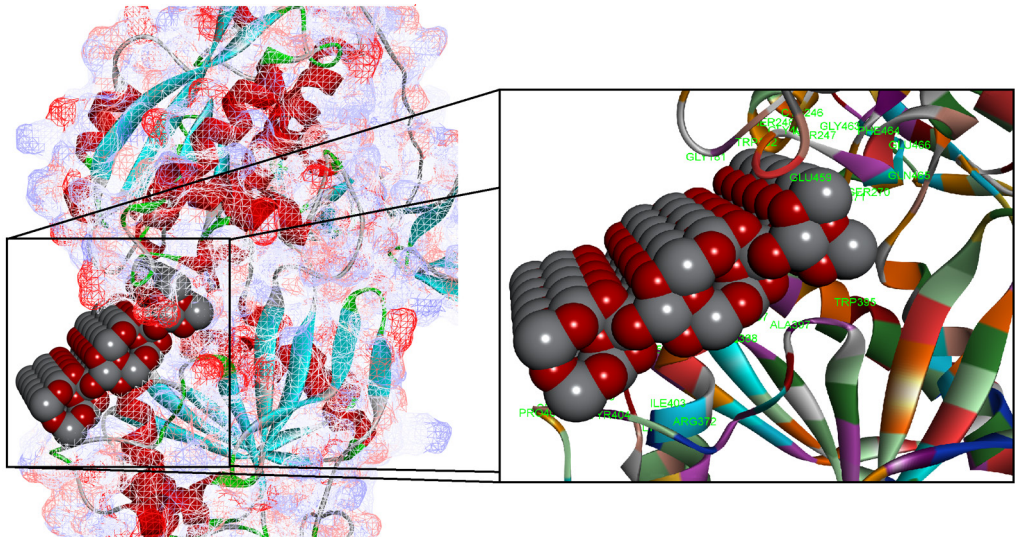


Fig. 5. The second site of TiO₂ binding to the extracellular part of GABA_{B1a} of GABA_B receptor subunit (Score – 10746, Area – 1273.20, ACE – 173.93)

Рис. 5. Другий сайт зв'язування діоксиду титану із зовнішньоклітинною частиною субодиниці ГАМК_{B1a} ГАМК_B рецептора (Score – 10746, Area – 1273,20, ACE – 173,93)

Fixing of the TiO₂ nanoparticle in the second binding site located in the slit between LB1 and LB2 of the extracellular part of the receptor, also occurs with the participation of the electrostatic interactions, ensured by polar radicals of amino acids, whose number is almost twice smaller than in the first site located opposite the slit between LB1 and LB2 close to N-terminal part (Glu368 (-), Arg372 (+), Lys373 (+), Asp405 (-), Glu459 (-), Glu466 (-)), which may be related to a low, compared to aqueous environment, value of the dielectric constant of the environment in the “claws” of receptor macromolecule. This site has fewer amino acids with a small value of conformational entropy: only one amino acid, arginine, and one amino acid, lysine, whose Gibbs free energy, as stated above, is (-0.68 and 0.65 kJ/mol). ΔG for other polar charged amino acids of this binding site takes the values from (-0.15) to (-0.27) kJ/mol. The analysis of obtained results demonstrated that a considerable number of bonds with TiO₂, formed at the second binding site, are hydrogen bonds, whose formation is promoted by the radicals of polar uncharged amino acids (Cys246, Ser247, Ser248, Ser270, Ser271, Gln314, Thr316, Ser345, Tyr367, Thr369, Tyr404, Ser407, Gln465), among which the prevalence in amount is attributed to the capping amino acid serine which is known to be the most reactive amino acid due to its functionally active hydroxyl group [17]. As stated above, cysteine is another amino acid among polar uncharged ones whose reactive capability is ensured by the sulfur atom with high polarization capacity of its electronic envelope. ΔG for the abovementioned amino acids is in the range of (-0.17) to (-0.35) kJ/mol. On contrary to the first binding site of TiO₂, a group of the hydrophobic amino acids in its composition contains one amino acid proline instead of four. In terms of quantity, the number of the hydrophobic and non-polar amino acids in both sites is practically the same.

The composition and environment of the third site (Fig. 6) of binding TiO_2 particle includes the following amino acids: Tyr171, Met178, Gln189, Pro190, Glu193, Asn200, Glu210, Leu211, Lys212, Leu213, Ile214, His215, His216, Asp217, Lys219, Lys227, Tyr228, Glu231, Asn235, Pro237, Arg453, Leu454, Arg456. The ACE value for this site is 340.63.

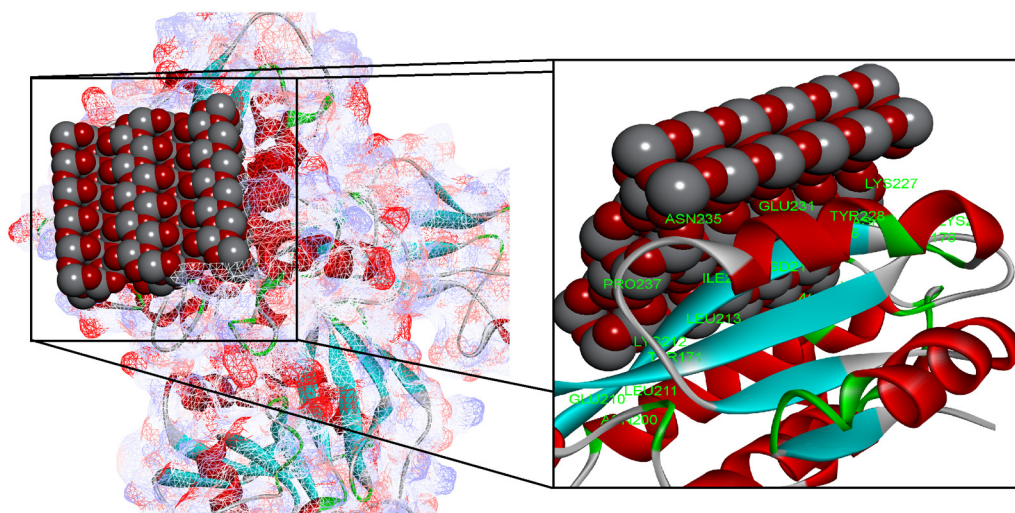


Fig. 6. The third site of TiO_2 binding to the extracellular part of $\text{GABA}_{\text{B}1\text{a}}$ of GABA_{B} receptor subunit (Score – 10370, Area – 1261.10, ACE – 340.63)

Рис. 6. Третій сайт зв'язування діоксиду титану із екстрацелюлярною (зовнішньоклітинною) частиною субодиниці $\text{GAMK}_{\text{B}1\text{a}}$ GAMK_{B} рецептора (Score – 10370, Area – 1261,10, ACE – 340,63)

The forces ensuring the binding of TiO_2 particle in the third site located at the surface of the receptor macromolecule near the slit between LB1 and LB2, are mostly presented with the electrostatic interactions at the expense of radicals of the following amino acids: Glu193 (-), Glu210 (-), Lys212 (+), His215 (+), His216 (+), Asp217 (-), Lys219 (+), Lys227 (+), Glu231 (-), Arg453 (+), Arg456 (+). The content of uncharged and hydrophobic amino acids at this site are of the same order as the ones at the site with high affinity, but, on contrary to all other binding sites, non-polar amino acids are completely absent.

It was determined (Fig. 7) that the amino acid composition of the fourth site of binding TiO_2 nanoparticle and the environment is as follows: Ile32, His34, Pro35, Gly39, Gly40, Ile41, Tyr43, Ala53, Asn55, Arg68, Lys299, Glu302, Lys303, Trp304, Gly305, Lys307, Glu332, Ala333, Gly334, Lys557, Asp558, Asp559, Trp562. The ACE value for this site is 224.61.

The comparison of the binding site with the lowest affinity (the fourth binding site), located opposite the slit between LB1 and LB2 closer to the zone of their connection. The binding site with the highest affinity demonstrates that on contrary to a second one, the content of polar uncharged amino acids, whose radicals participate in the formation of hydrogen bonds, is presented by two amino acids only: tyrosine and asparagine with the highest conformational entropy of the side chain (ΔG takes the values of (-0.17 and -0.11) kJ/mol). As for polar uncharged amino acids, whose radicals form electrostatic interactions, when compared against the site of high affinity of binding TiO_2 , its composition

also includes such amino acids as arginine and lysine, that have the least conformational freedom and a high value of Gibbs free energy. The composition of the fourth site is as following: His34 (+), Arg68 (+), Lys299 (+), Glu302 (-), Lys303 (+), Lys307 (+), Glu332 (-), Lys557 (+), Asp558 (-), Asp559 (-). The binding site under consideration also has non-polar amino acids, whose number regarding the site of comparison increases more than twofold: Gly39, Gly40, Ala53, Gly305, Ala333, Gly334. Glycine with the value of $\Delta G = 0$ kJ/mol, similar to proline ($\Delta G = +3$ kJ/mol), causes destabilizing impact on the polypeptide chain, whereas the amino acid alanine does not have any conformational freedom ($\Delta G = -0.77$ kJ/mol). As for hydrophobic amino acids, their number does not differ from their content at other binding sites for TiO₂. Fig. 8 shows the ratio of content of polar charged amino acids to polar uncharged amino acids in the sites of TiO₂ binding to the extracellular part of GABA_{B1a} subunit.

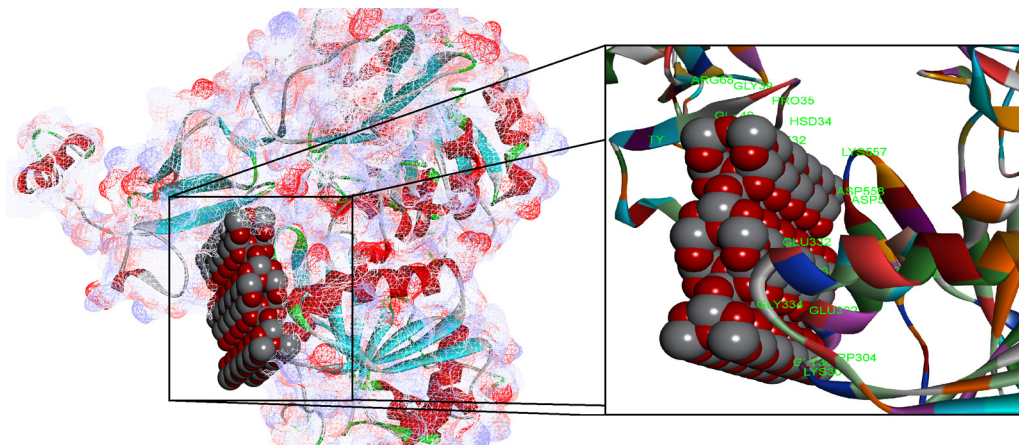
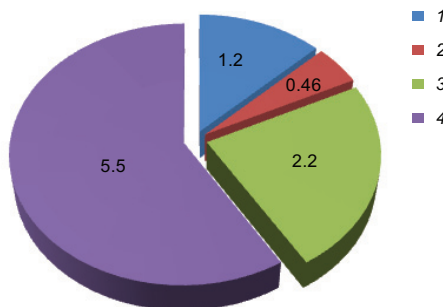


Fig. 7. The fourth site of TiO₂ binding to the extracellular part of GABA_{B1a} of GABA_B receptor subunit (Score – 10204, Area – 1170.30, ACE – 224.61)

Рис. 7. Четвертий сайт зв'язування діоксиду титану із зовнішньоклітинною частиною субоддиниці ГАМК_{B1a} ГАМК_B рецептора (Score – 10204, Area – 1170,30, ACE – 224,61)

Fig. 8. The ratio of content of polar charged amino acids to polar uncharged amino acids (vertical axis) in sites of the nanosized TiO₂ material binding to the extracellular part of GABA_{B1a} subunit. 1, 2, 3, 4 are numbers of binding sites

Рис.8. Відношення вмісту полярних заряджених до полярних незаряджених амінокислот (вісь ординат) у сайтах зв'язування нанорозмірного матеріалу діоксиду титану із зовнішньоклітинною частиною субоддиниці ГАМК_{B1a} рецептора ГАМК_B. 1, 2, 3, 4 – номери сайтів зв'язування



Thus, the molecular docking of TiO₂ nanoparticle to the extracellular part of GABA_{B1a} of GABA_B receptor subunit was performed using PatchDock web-service. The results of these studies demonstrated that TiO₂ in the form of nanosized material is capable of forming a supermolecular structure via interaction with the extracellular part of GABA_{B1a} of GABA_B receptor subunit, and it may be assumed that this will be accompanied by modulations in its spatial organization.

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МОЛЕКУЛЯРНИЙ ДОКІНГ НАНОРОЗМІРНОГО МАТЕРІАЛУ ДІОКСИДУ ТИТАНУ ІЗ ЗОВНІШНЬОКЛІТИННОЮ ЧАСТИНОЮ ГАМК_B-РЕЦЕПТОРА

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Сконструйовано просторову модель нанорозмірного матеріалу діоксиду титану за допомогою програми Discovery Studio Visualizer версій 2.0, 2.5, проведено пошук і аналіз можливих сайтів його зв'язування із зовнішньоклітинною частиною субодиниці ГАМК_{B1a} рецептора ГАМК_B за допомогою алгоритму для молекулярного докінгу PatchDock. Розміри поверхні одержаної наночастинки TiO₂ становили (18,925 × 3,785 × 19,028) Å. Встановлено чотири потенційно можливі сайти зв'язування TiO₂ із зовнішньоклітинною частиною субодиниці ГАМК_{B1a} рецептора ГАМК_B. Наночастинці TiO₂ була притаманна висока афінність зв'язування з одним із сайтів рецептора зі значенням параметра оцінки комплементарності геометричної форми 12562, в інших сайтах приймаючи значення: 10746; 10370; 10204. Орієнтовна площа інтерфейсу комплексу зовнішньоклітинної частини субодиниці ГАМК_{B1a} рецептора ГАМК_B з діоксидом титану для сайту з найбільшим значенням параметра оцінки комплементарності геометричної форми становила 1949,80 Å, а для інших – 1273,20 Å, 1261,10 Å та 1170,30 Å, відповідно. Розрахунки енергій атомного контакту підтвердили, що для сайтів зв'язування наночастинки TiO₂ ця енергія набуває таких значень: 362,92; 173,93; 340,63 та 224,61. Проаналізовано характер зв'язків, які стабілізують сайти зв'язування TiO₂ із зовнішньоклітинною частиною субодиниці ГАМК_{B1a} рецептора ГАМК_B відповідно до їхнього амінокислотного складу.

Ключові слова: наночастинки TiO₂, ГАМК_B рецептор, молекулярний докінг, PatchDock.

МОЛЕКУЛЯРНЫЙ ДОКИНГ НАНОРАЗМЕРНОГО МАТЕРИАЛА ДИОКСИДА ТИТАНА С ВНЕКЛЕТОЧНОЙ ЧАСТЬЮ ГАМК_B-РЕЦЕПТОРА

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Была сконструирована пространственная модель наноразмерного материала диоксида титана с помощью программы Discovery Studio Visualizer версий 2.0, 2.5, проведены поиск и анализ возможных сайтов его связывания с экстрацеллюлярной частью субъединицы ГАМК_{B1a} рецептора ГАМК_B с помощью алгоритма для молекулярного докинга PatchDock. Размеры поверхности полученной наночастицы TiO₂ составили (18,925 × 3,785 × 19,028) Å. Установлены четыре потенциально возможных сайта связывания TiO₂ с экстрацеллюлярной частью субъединицы ГАМК_{B1a} рецептора ГАМК_B. Наночастица TiO₂ показала высокую аффинность связывания с одним из сайтов рецептора со значением параметра оценки комплементарности геометрической формы 12562, в других сайтах принимая значения: 10746; 10370; 10204. Ориентировочная площадь интерфейса комплекса экстрацеллюлярной части субъединицы ГАМК_{B1a} рецептора ГАМК_B с диоксидом титана для сайта с наибольшим значением параметра оценки комплементарности геометрической формы составила 1949,80 Å, а для других – 1273,20 Å, 1261,10 Å и 1170,30 Å, соответственно. Расчеты энергий атомного контакта показали, что для сайтов связывания наночастицы TiO₂ она приобретает следующие значения: 362,92; 173,93; 340,63 и 224,61. Проанализирован характер связей, которые стабилизируют сайты связывания TiO₂ с экстрацеллюлярной частью субъединицы ГАМК_{B1a} рецептора ГАМК_B в соответствии с их аминокислотным составом.

Ключевые слова: наночастицы TiO₂, ГАМК_B рецептор, молекулярный докинг, PatchDock.

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