Journal of Radiation and Nuclear Applications
An International Journal

http://dx.doi.org/10.18576/jrna/040304

Molecular Dynamic Studies of the DNA Radiation and Conformation Processes on a Zirconium Dioxide Surface

Mirzoaziz Khusenov[1,*] *Dilshod Nematov*[1], *Amondullo Burhonzoda*[1], *Kholmirzo Kholmurodov*[2,3,*] *Aleksandr Doroshkevych*[2], *Nelly Doroshkevych*[2], *Tatyana Zelenyak*[3] *and Subrata Majumder*[4]

[1]Tajik Technical University named after M.S. Osimi, 724000, Dushanbe, Republic of Tajikistan.
[2]Joint Institute for Nuclear Research,141980, Dubna, Moscow Region, Russian Federation.
[3]Dubna State University, 141980, Dubna, Moscow Region, Russian Federation.
[4]National Institute of Technology, N.I.T., Patna: 800 005, India.

Received: 3 Jul 2019, Revised: 22 Jul. 2019, Accepted: 3 Aug. 2019.
Published online: 1 Sep 2019.

Abstract: In this work a complex study of the DNA immobilization and conformation processes on the zirconium dioxide (ZrO_2) surface is performed. The DNA+ZrO_2 nanoparticles and nanosized films were investigated with the MD modeling, experimental spectral and integral methods, including nuclear physics. Using the MD hybrid classical and quantum chemistry potentials, for the DNA solvated with water the DNA+ZrO_2 surface interactions were simulated We have generated series MD models, thereby simulating a different scenario of the DNA with possible charge modifications. The DNA charge modification were introduced in the DNA central region via its two phosphorus atoms, P_a and P_b, and for several set of MD models for the relaxed DNA structures we have estimated the positional changes of the distance D[DNA(P_a,P_b) - ZrO_2(O)] between the phosphorus atoms (P_a,P_b) and selected oxygen atoms of the ZrO_2 surface. The work is aimed to the development of functional hetero-junctions such as a biological molecule - wide-gap dielectric. These hetero-junctions are intended for using in the field of molecular electronics, in particular, for the creation of biochips, memory arrays and computer architectures of the future.

Keywords: Immobilization of DNA molecules on the surface of dielectrics, molecular electronics, nanotechnologies, modular-dynamic modeling, DNA conformation in the electric field, genotoxic effects.

1 Introduction

Molecular simulation studies are performed within the research activities of Molecular Dynamics (MD) modeling groups of the Neutron Optics sector in the Department of Neutron Investigations of Condensed Matter, Frank Laboratory of Neutron Physics (FLNP), Joint Institute for Nuclear Research (JINR), Dubna, Russian Federation and Faculty of Energetic, Tajik Technical University named after M.S. Osimi, Dushanbe, Republic of Tajikistan, thereby outlining the international research collaborations closely performed with Japanese (Keio University, Waseda University, RIKEN, etc.) and Indian groups (National Institute of Technology, NIT.-Patna). The examples have to cover a general issue on “Computer Design for New Drugs and Materials”, which demonstrate the efficient use of computer MD in both classical (conventional) and quantum chemical methods implementations. Some aspects of our recent studies include computer modelling of non-equilibrium chemo-electronic conversion of water adsorption on the surface of yttria-stabilized zirconia. The tasks of the work include the simulation of radiation-induced conformations of a DNA chain on a zirconia dioxide (ZrO_2) surface by MD (molecular dynamics) method. Interdisciplinary research in the field of nanotechnology has a breakthrough potential and the main hopes of nanoscale technologies are associated with new effects at the intersection of the physics of chemistry and biology. The combination of biomolecules with solid nanoparticles generates a new class of materials, primarily for new electronic sensory and optical systems, the prospects for the development of molecular electronics, the creation of biochips, memory arrays and computer architectures of the future become real. DNA molecules have good electrical conductivity, are able to store and transmit by copying terabytes of information self-

*Corresponding author e-mail: kelany12@yahoo.com

reproducing and moving in the electric field, therefore, are extremely interesting as a functional element of bio-electronic devices. The purpose of this work is to obtain biologically modified structures by immobilizing of DNA molecules on the surface of biocompatible crystals, an experimental and theoretical study of the fundamental mechanisms of physical-chemical interaction and dynamics of the DNA molecule on interfaces with a solid bases under the influence of external electric fields and radiation fluxes [1-14].

2 Methodical Parts

For a triple system DNA + water + ZrO_2 surface, all the interatomic interactions are described with standard molecular mechanics potentials, as a sum of two-, three-, and four atom terms. All-atom interactions include harmonic bonds, angles, improper torsions, and dihedral angles The long-range interactions include Lennard-Jones van der Waals potentials and electrostatic potentials between atom-based partial charges:

$$U(r) = U_b + U_\theta + U_\varphi + U_\omega + U_{LJ} + U_{el} + U_{HB} + \ldots$$

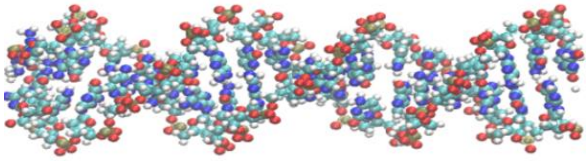
Here valence length potential, $U_b = \frac{1}{2}\sum_b K_b\,(r - b_0)^2$, the valence angle potential, $U_\theta = \frac{1}{2}\sum_\theta K_\theta\,(\theta - \theta_0)^2$,the torsion dihedral potential, $U_\varphi = \frac{1}{2}\sum_\varphi K_\varphi[\cos(n\varphi - \delta) + 1]$, the Van-der-Waals interaction and hydrogen bonding potentials are Lennard-Jones (LJ; 12-6) or (12-10) types, $U_{LJ} = \sum_{i,j}\left[\frac{A}{r_{ij}^{12}} - \frac{B}{r_{ij}^{6}}\right]$ and $U_{HB} = \sum_{i,j}\left[\frac{A'}{r_{ij}^{12}} - \frac{B'}{r_{ij}^{10}}\right]$, the electrostatics potential,$U_{el} = \sum_{i,j}\frac{q_i q_j}{\varepsilon r_{ij}}$, represents long-range interactions in the system. For the DNA solvated with water, based on the experimental data, *ab initio* and semiempirical electronic structure calculations, a number of self-consistent and well-tested sets of parameters are published and available (see, for example, all-atom sets in CHARMm22; Brooks et al., 1983). For ZrO_2 surface we have used Buckingham interaction potential,

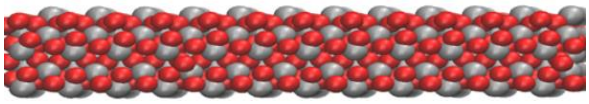
$$U(r) = A\exp\left(-\frac{r}{\rho}\right) - \frac{C}{r^6}$$

with the interaction parameters A, C and ρ.

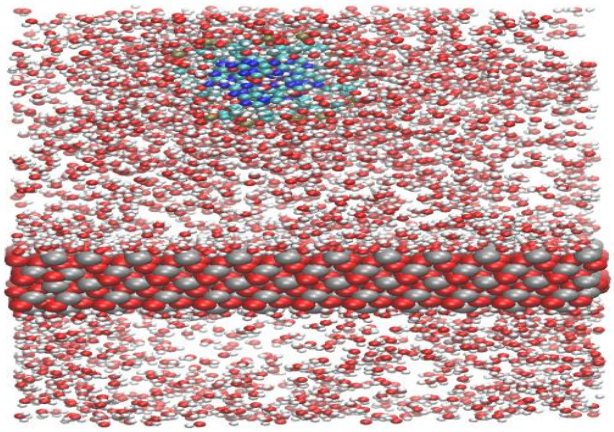
In Figs.1(a,b) the initial position of a DNA chain on ZrO_2 (zirconia dioxide) surface and the whole system solvated with water are shown, respectively. The DNA chain was located at a well-separated distance from the zirconia dioxide. After appropriate preparation of the DNA+ZrO_2 surface a water box was introduced. The MD trajectory calculations performed for multiple DNA+water+ZrO_2 models were next used to simulate the effect of the radiation introduced on a DNA side chain with consequent conformation changes [9-14].

(a)





(b)



Figs.1 (a,b): The initial position of DNA chain on ZrO_2 (zirconia dioxide) surface.

3 Results and Discussion

For the DNA molecule solvated with water and interacting with the ZrO_2 surface we have consider different model structures, thereby simulating different scenario of the DNA possible charge modification. From two opposite DNA directions we have arbitrarily chosen two P (phosphorus) atoms as possible damage sites. The DNA charge modification we have introduced in its central region through two set of MD models (set A: models 1-3 and B: models 4-6) for both phosphorus atoms P_a and P_b.

In Figs. 2-3 the MD simulation results are shown for the D[DNA(P_a,P_b) - ZrO_2(O)] dynamics for the models 1-3 (Q(P_a)=+1,1659|e|, Q(P_a)=0 and Q(P_a)=-1,1659|e|, native DNA and two damaged versions, respectively) and models 4-6 (Q(P_b)=+1,1659|e|, Q(P_b)=0 and Q(P_b)=-1,1659|e|), native DNA and two damaged versions, respectively).

The distance distribution D[DNA(P_a,P_b) - ZrO_2(O)] between the phosphorus (P_a,P_b) and selected oxygen (O) atoms of the zirconium dioxide surface are compared for the native DNA (Q(P_a,P_b)=+1,1659|e|) and two damaged versions (Q(P_a,P_b)=0 and Q(P_a,P_b)=-1,1659|e|). The charge state of the phosphorus (P_a,P_b) atoms mimics the effect of external radiation (UV or other) induced on the site of DNA, such that the value of Q(P_a,P_b) spontaneously vary in the interval [+1,1659;-1,1659]|e|. From the distance diagrams in Figs. 2-3 we can see both different D[DNA(P_a,P_b) - ZrO_2(O)] time dependent behavior and different DNA-surface close contact on a final state. So far, starting from the same relaxed state (but with different Q(P_a,P_b)) the DNA molecule while interacting with ZrO_2 surface will undergo a different conformational shape, thereby approaching the surface.

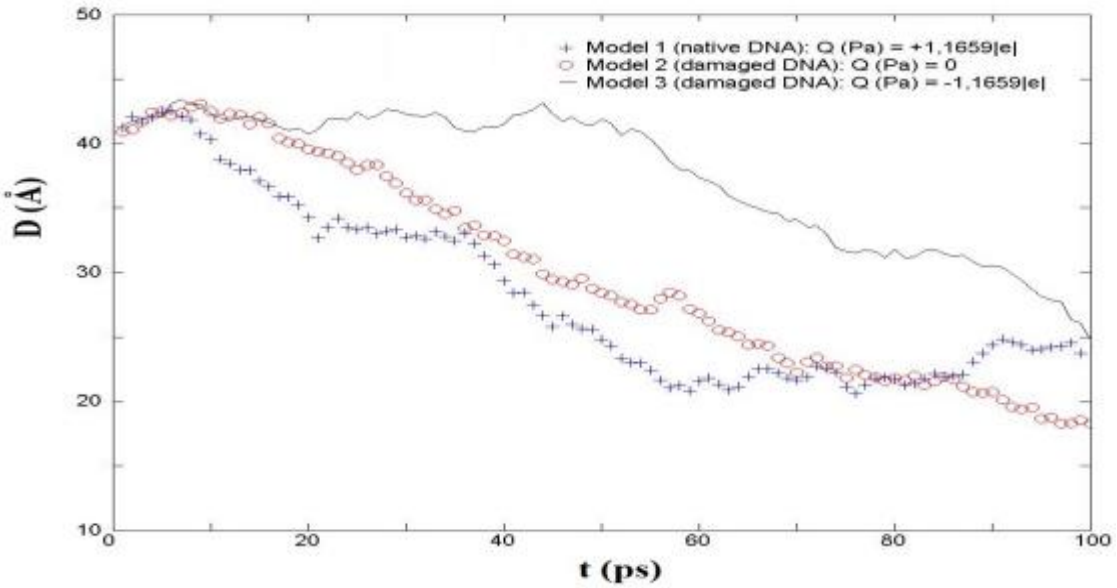


Fig. 2: The distance D[DNA(P_a) - ZrO_2(O)] between phosphorus (P_a) and selected oxygen (O) atoms of the zirconium dioxide surface for the MD models 1-2-3.

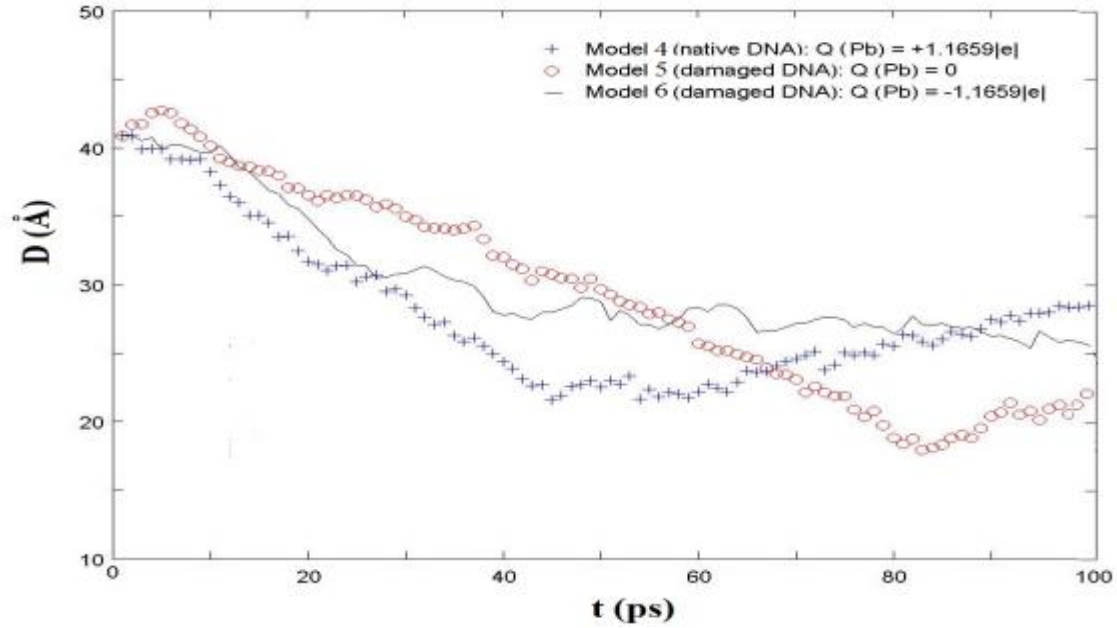


Fig. 3: The distance D[DNA(P_b) - ZrO_2(O)] between phosphorus (P_b) and selected oxygen (O) atoms of the zirconium dioxide surface for the MD models 4-5-6.

It is worth noting that the above choice of phosphates in theDNA charge modification introduced by Figs. 4-5, were due to the DNA - ZrO_2 surface interactions as in paper (J. Phys. Chem. B, 2015, 119 (11030-11040)), where the author have studied via molecular dynamics simulations several DNA phosphate and surface silanol groups hydrophobic bonding between DNA base and silica hydrophobic region. Also they have find two major binding mechanisms to be attractive interactions between DNA phosphate and surface silanol groups, hydrophobic bonding between DNA base and silica hydrophobic region.

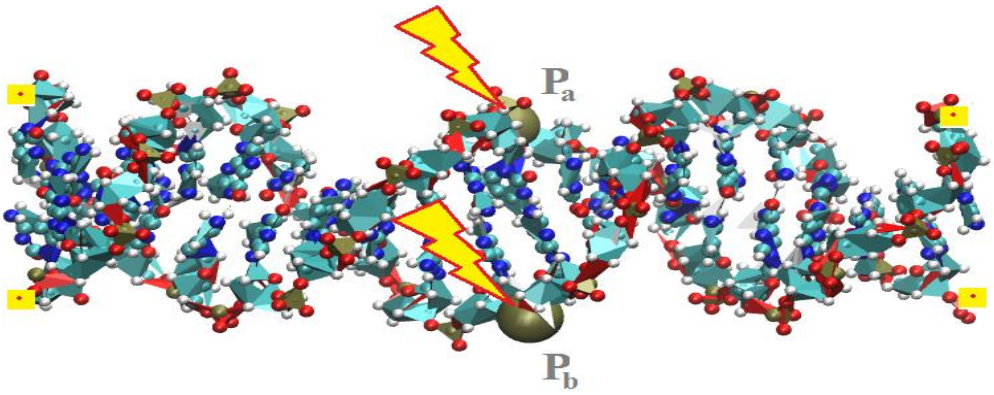


Fig. 4: The position of two P (phosphorus) atoms (P_a and P_b; grey color) of the DNA molecule are shown as possibly DNA damaged sites.

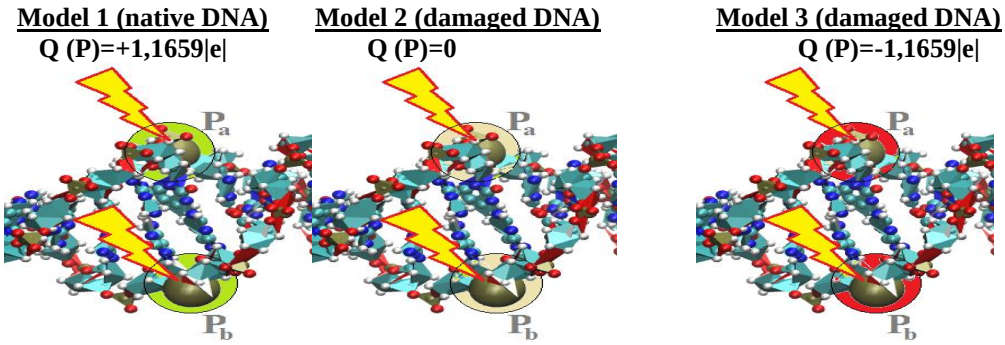
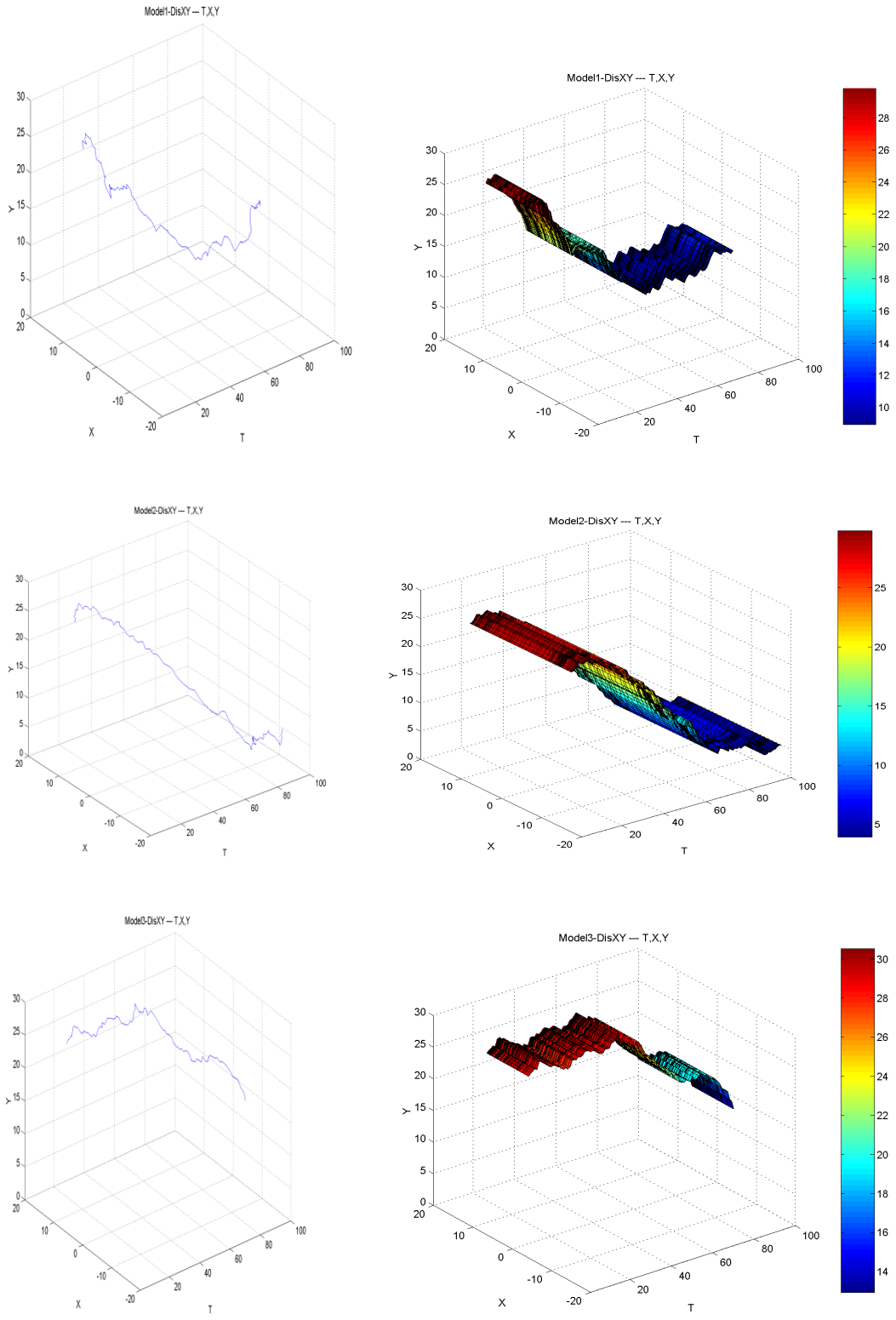


Fig. 5: The charge modification on two P (phosphorus) atoms of the DNA damaged sites.

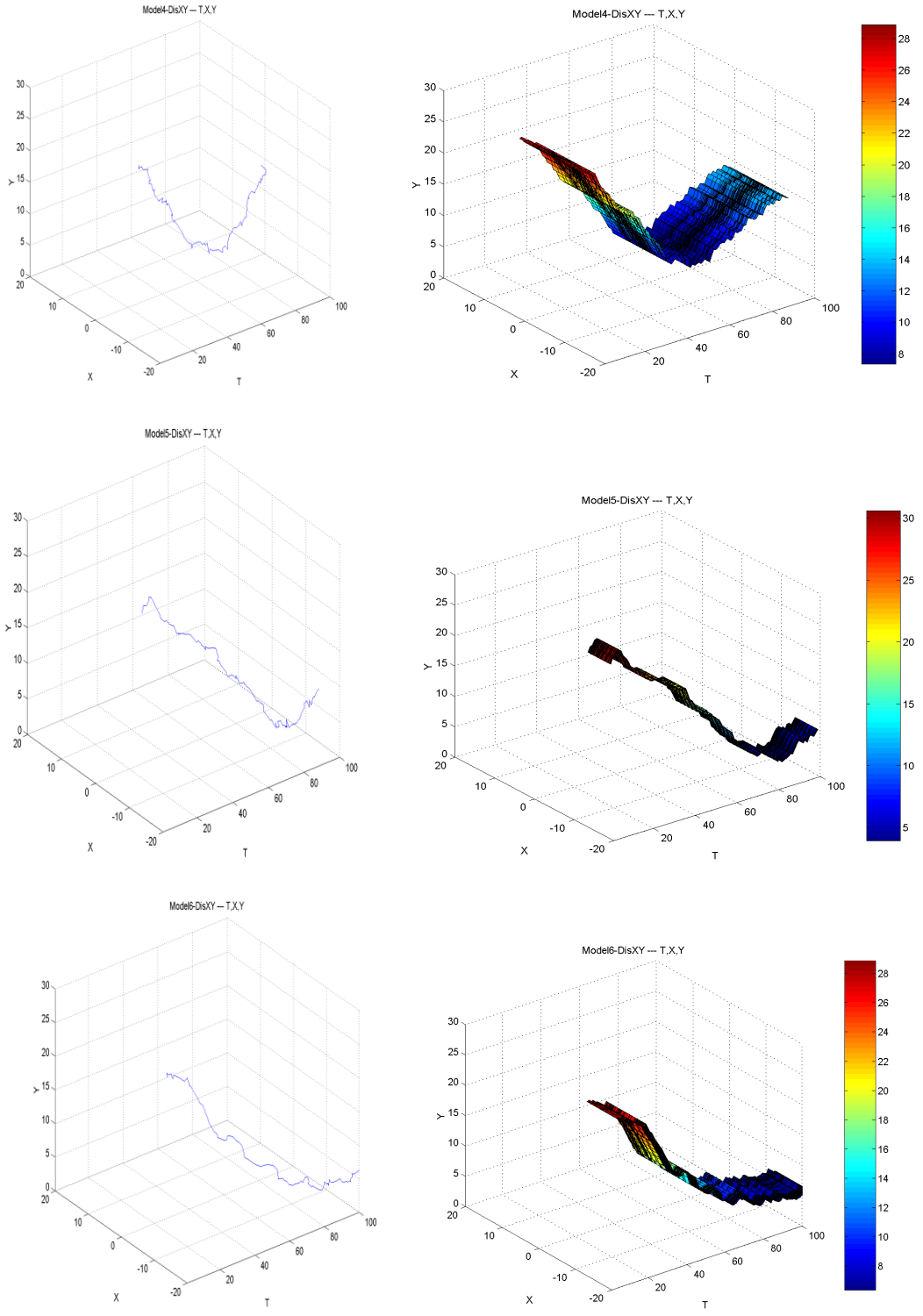
Next, the DNA conformational behavior has built through a graphical 3-D representation analysis. We have used MD trajectory calculations for the DNA chain to investigate the DNA interaction and immobilization processes on the ZrO_2 surface. In Figs. 6 the DNA orientation dynamics on ZrO_2 are presented for the models 1-2-3 (model 1: $Q(P_a)$=+1,1659|e|, model 2: $Q(P_a)$=0, and model 3: $Q(P_a)$=-1,1659|e|; native DNA and two damaged versions, respectively). The MD simulation results in Figs. 6 demonstrate the DNA/ZrO_2 dynamical changes and distance distributions D[DNA(P_a) - ZrO_2(O)] between the phosphorus (P_a) and selected oxygen (O) atoms of the zirconium dioxide surface. The Figs. 6 compare the MD results for the native DNA (model 1: $Q(P_a)$=+1,1659|e|) and two damaged versions (models 2: $Q(P_a)$=0 and 3: $Q(P_c)$=-1,1659|e|). In Figs. 7 the DNA orientation dynamics on ZrO_2 are presented for the models 4-5-6 (model 4: $Q(P_b)$=+1,1659|e|, model 5: $Q(P_b)$=0, and model 6: $Q(P_b)$=-1,1659|e|, native DNA and two damaged versions, respectively). The MD simulation results in Figs. 7 demonstrate the DNA/ZrO_2 dynamical changes and distance distributions D[DNA(P_b) - ZrO_2(O)] between the phosphorus (P_b) and selected oxygen (O) atoms of the zirconium dioxide surface. The Figs. 7 compare the MD results for the native DNA (model 4: $Q(P_b)$=+1,1659|e|) and two damaged versions (models 5: $Q(P_b)$=0 and 6: $Q(P_b)$=-1,1659|e|). The MD simulation results in Figs. 6-7 for the distance D[DNA(P_a,P_b) - ZrO_2(O)] diagrams demonstrate the interaction and conformation processes for the DNA/ZrO_2 system. For time dependent behavior D[DNA(P_a,P_b) - ZrO_2(O)] we have seen a different DNA-surface conformational changes. It is important that, starting from the same relaxed state (but with different $Q(P_a)$ and $Q(P_b)$) the DNA molecule while interacting with ZrO_2 surface will undergo a different conformational shape, thereby approaching the surface.

D[DNA(P_a)-ZrO_2(O)]-----XY~f(T)-----Models 1-2-3



Figs. 6: The distance D[DNA(P_a) - ZrO_2(O)] between phosphorus (P_a) and selected oxygen (O) atoms of the zirconium dioxide surface for the MD models 1-2-3.

D[DNA(P_b)-ZrO_2(O)]-----XY~f(T)-----Models 4-5-6



Figs. 7: The distance D[DNA(P_b)-ZrO_2(O)] between phosphorus (P_b) and selected oxygen (O) atoms of the zirconium dioxide surface for the MD models 4-5-6.

4 Conclusions

For a triple system DNA + water + ZrO 2 surface we built several set of MD models as setA (Model 1 (native DNA): $Q(P_a)$ = +1,1659|e|; Model 2 (damaged DNA): $Q(P_a)$ = 0; Model 3 (damaged DNA): $Q(P_a)$ = -1,1659|e|) and setB (Model 4 (native DNA): $Q(P_b)$ = +1,1659|e|; Model 5 (damaged DNA): $Q(P_b)$ = 0; Model 6 (damaged DNA): $Q(P_b)$ = -1,1659|e|), where e is electron charge, thereby simulating different scenario of the DNA possible charge modification. From two opposite DNA directions we have arbitrarily chosen two P (phosphorus) atoms as possible damage sites. The MD results compare the DNA conformational behavior at the initial and final states and the DNA orientation dynamics on ZrO_2 were presented for the native DNA ($Q(P_a,P_b)$ = +1,1659|e|) and two damaged versions ($Q(P_a,P_b)$=0 and $Q(P_a,P_b)$=-1,1659|e|), respectively. So far, starting from the same relaxed state (but with different $Q(P_a,P_b)$) the DNA molecule while interacting with ZrO_2 surface will undergo a different conformational shape, thereby approaching the surface. We have related the DNA molecular orientations due to the immobilization process or similar to the B-Z-transition happening on the zirconium dioxide (ZrO_2) surface. The DNA conformations arise when the relative orientation of individual parts of the molecule changes as a result of the rotation of atoms or groups of atoms around simple bonds, bending of bonds, etc. For example, the DNA B-Z-transition can be stimulated by an increase in the content of ions in solution (say, zirconium dioxide ZrO_2 surface) or by certain proteins that stabilize the Z-form of DNA. When a molecule transitions from B- to Z-form, the double helix of DNA unfolds, and then turns in the other direction, turning from right-wound into left-wound [1-18].

In conclusion, for today the DNA+ZrO_2 system emerges itself as a breakthrough potential material for developing new nano-bio-electronics tools as well as the interdisciplinary research target in the field of nanotechnology. Wherein, the questions of the DNA interaction and immobilization with the mentioned oxide material as ZrO_2 have not been studied yet. A novel data obtained above for the DNA conformational behavior through a graphical 3-D representation analysis provide the DNA/ZrO_2 interaction and immobilization processes on the atomic/molecular level. The zirconium dioxide (ZrO_2) has seen to be a promising material as DNA or RNA molecules absorber due to a good biocompatibility and a high dielectric constant (ε=25). For today the combination of bio-molecules with solid nano-particles generates a new class of materials, primarily for new electronic sensory and optical systems. The prospects cover the development of molecular electronics, the creation of biochips, memory arrays and future computer architectures as well. In this respect, the DNA and RNA molecules have good electrical conductivity, capable to store and transmit by copying terabytes of information with self-reproducing and moving in the electric field, therefore, are extremely interesting as a functional element of bio-electronic devices [15-16].

Acknowledgments: This work is performed within the framework of a collaborative research program under Indo-Russian Joint Research-2016 (DST-RFBR), grant No. 17-52-45062 “Studies of the molecular orientation and radiation damage of DNA adsorbed on Zirconia”. This work in part is supported by the IGSF (International Fund for Humanitarian Cooperation), based in JINR, Dubna, ISTC (International Innovative Nanotechnology Center) of the CIS. This work in part is supported by JINR=ASRT (ARE) grant "Molecular Modeling Analysis of the Effect of Nano-Metal Oxides on Biological Molecules".

References

[1] Subrata Majumder, I. Mishra, U. Subudhi, and Shikha Varma. "Enhanced biocompatibility for plasmid DNA on patterned TiO2 surfaces". Appl. Phys. Lett., **103**, 063103, 2013.

[2] H.B.Gray, J.R.Winkler, "Electron transfer in proteins", Annu. Rev. Biochem, (1996), v. 65, pp.537-561.

[3] J. Deisenhofer, J.R.Norris, (eds.), "The Photosynthetic Reaction Center", Academic Press, N.Y., II, **500**, 1993.

[4] Q.Gu, C.Cheng, R.Conela, et al., Nanotechnology, v. 17, R 14, 2006.

[5] Bernard R. Brooks Robert E. Bruccoleri Barry D. Olafson David J. States S. Swaminathan Martin Karplus, "CHARMM: A program for macromolecular energy, minimization, and dynamics calculations". Journal of Computational Chemistry, https://doi.org/10.1002/jcc.540040211, 1983.

[6] David A. Case, Thomas E. Cheatham, Tom Darden, Holger Gohlke, Ray Luo, Kenneth M. Merz, Alexey Onufriev, Carlos Simmerling, Bing Wang, and Robert J. Woods. "The Amber Biomolecular simulation programs". Journal of Computational Chemistry., **26(16)**, 1668-1688, 2005.

[7] Smith W., Forester T. R. DL_POLY_2.0: "A general-purpose parallel molecular dynamics simulation package". J. Mol. Graph., **14**, 136-141, 1996.

[8] Smith W., Forester T.R. and Todorov I.T., "THE DL POLY 2 USER MANUAL", STFC Daresbury Laboratory Daresbury, Warrington WA4 4AD Cheshire, UK, Version 2.19, April, 2008.

[9] Kholmirzo Kholmurodov (Ed.), "Molecular Simulation Studies in Material and Biological Sciences. International Workshop", Nova Science Publishers Ltd., 2007, 196p., ISBN: 1-59454-607-x

[10] Kholmirzo Kholmurodov (Ed.), "Molecular Simulation in Material and Biological Research", Nova Science Publishers Ltd.,ISBN: 978-1-60741-553-4., 155, 2009,

[11] Kholmirzo Kholmurodov (Ed.), "Molecular Dynamics of Nanobistructures", Nova Science Publishers Ltd., ISBN: 978-1-61324-320-6., 210, 2011.

[12] Kholmirzo Kholmurodov (Ed.), "Models in Bioscience and Materials Research: Molecular Dynamics and Related Techniques", Nova Science Publishers Ltd., ISBN: 978-1-62808-052-0., 219, 2013.

[13] Kholmirzo Kholmurodov (Ed.), "Computational

Materials and Biological Sceinces", Nova Science Publishers Ltd.ISBN: 978-1-63482-541-2., 208, 2015.
[14] Kholmirzo T. Kholmurodov (Ed). «Computer Design for New Drugs and Materials. Molecular Dynamics of Nanoscale Phenomena», (Leading Scientist, Frank Laboratory of Neutron Physics, Joint Institute of Nuclear Research, Dubna, Moscow Region, Russia), ISBN: 978-1-53612-082-0, Nova Science Publishers, New York., 231, 2017.
[15] Arivazhagan Rajendran, Masayuki Endo, Kumi Hidaka, and Hiroshi Sugiyama. Direct and Real-Time Observation of Rotary Movement of a DNA Nanomechanical Device // Journal of American Chemical Society., **135(3)**, 1117–1123., 2013.
[16] Chengde Mao, Weiqiong Sun, Zhiyong Shen & Nadrian C. Seeman. A nanomechanical device based on the B–Z transition of DNA // Nature., **397**, 144–146, 1999.
[17] Ibraheem, A.A., El-Taher, A., Alruwaili, M.H.M.. Assessment of natural radioactivity levels and radiation hazard indices for soil samples from Abha, Saudi Arabia // Results in Physics., **11**, 325-330, 2018.
[18] El-Taher, A., Najam, L.A., Hussian, I., Omer, M.A.A. Evaluation of natural radionuclide content in Nile river sediments and excess lifetime cancer risk associated with gamma radiation // Iranian Journal of Medical Physics., **16(1)**, 27-33, 2019.