Molecular dynamics studies on the interaction and encapsulation processes of the nucleotide and peptide chains inside of a carbon nanotube matrix with inclusion of gold nanoparticles

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Abstract. Studying of molecular systems as single nucleotides, nucleotide and peptide chains, RNA and DNA interacting with metallic nanoparticles within a carbon nanotube matrix represents a great interest in modern research. In this respect it is worth mentioning the development of the electronics diagnostic apparatus, the biochemical and biotechnological application tools (nanorobotic design, facilities of drug delivery in a living cell), so on. In the present work using molecular dynamics (MD) simulation method the interaction process of small nucleotide chains (NCs) and elongated peptide chains with different sets of metallic nanoparticles (NPs) on a matrix from carbon nanotube (CNT) were simulated to study their mechanisms of encapsulation and folding processes. We have performed a series of the MD calculations with different NC,peptides-NP-CNT models that were aimed on the investigation of the peculiarities of NC,peptide-NP interactions, the formation of bonds and structures in the system, as well as the dynamical behavior in an environment confined by the CNT matrix.

1. Introduction
The fundamental understanding of the chemical interactions and dynamics of the nucleotides, RNA and DNA molecules at the dry-wet interface has become a key scientific issue in nanoscience due to a great number of potential applications (in electronics, biochip design, diagnostic tools, future computer architectures with massive memories, so on). For example, immobilization of DNA onto various surfaces, the conformations and the dynamics of DNA molecule adsorbed onto a metal and/or

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semiconductors, or more complicated effects, the influence of energetic ions on DNA/surface interfaces are the hot topics of today research. The interaction of DNA or its fragments as single nucleotides with the carbon nanotubes (CNT), metallic and/or semiconductor matrices are the immense targets in modern research and applied sciences [1-3]. The immobilization of a biomolecule onto a desired surface is a crucial step for its application as it rapidly loses its biological activity in an external environment. In literature, there are several studies exists for developing patterned surface for successful functionalization of biological molecules, preferably through self-assembly techniques [4,5]. Most of the studies are performed on gold surfaces with thiol modified DNA molecules [6]. In this regard, the effect of low energy exchange (VdW interactions) as well as the molecular level orientation of the NC, peptides, RNA or DNA molecules adsorbed onto an CNT matrix or oxide surfaces have a great interest to understand the adsorption phenomena on the surface more clearly.

The CNTs as drug delivery vehicles have shown a potential interest due to a targeting of specific cancer cells with a lower dosage rather than conventional drugs have. With regard to the different aspects of the DNA-CNT application in the DNA nanotechnology there have been a great discussions from the point of view of molecular recognition processes, as a candidate material in cell drug delivery, as nucleic acid selection method (DNA aptamer) in SELEX (Systematic Evolution of Ligands by Exponential enrichment), so on. The conformational transition of aptamers (single chain DNA or RNA molecules that possess specific spatial structure) around CNT may cause some modification of the charge distribution on the CNT surface. It is worth noting that CNT surface has extremely sensitive to even a small change of the electrical charge of its environment. The replacement of even a single nucleotide for the DNA or RNA structure can modify, on the other hand, the charge environment around CNT. As a result, the CNT charge conductivity will be changed as well. So far, the DNA or RNA interactions with CNT could result to an essential modification for the charge distribution and consequent charge transfer through by the CNT surface. In the physical measurement the DNA-CNT charge distribution can be estimated trivially. This simple scheme from the point of view of application and diagnostic purposes has considered being one of the promising technologies in the DNA-CNT interaction processes with target proteins (say, of blood cells in human body). The DNA or RNA interaction mechanism with metallic nanoparticles and carbon nanotube is an important target of a great interest in modern nano- and bio-tehnologies, electronics industry and medicine. For example, one has to mention the design and development of the electronic mobile diagnostic facilities for the express blood analysis, the chemical or drug delivery inside living cell, and so on, where the NC-NP-CNT system are in use. The molecular structures like as nucleotide chain (NC) - gold nanoparticles (NPs) - carbon nanotube (CNT) is an important stage in the understanding of interaction mechanism of a whole DNA or RNA molecule with NP and CNT [7-18].

Metallic nanoparticle of gold, silver, etc. are of great research interest in modern biomedical applications [19-37]. In recent experiments [29], for example, such nanoparticles have been used, which consisted of porous gold discs with a diameter of 400 nanometers. By using the phenomenon of plasmon resonance (oscillation special electronic nanoparticles on the surface resulting from the irradiation with light at a particular angle) on can achieve on the surface of the nanoparticles an efficient radiation absorption and release of large amounts of heat. Further, on the disks of gold nanoparticles were placed three types of bacteria: *E.coli* (Escherichia coli) and heat-resistant *Bacillus subtilis* and *Exiguobacterium*, after which the nanoparticles are irradiated with infrared light. As the results show, the nanoparticles were heated up to 200 °C - and it is a temperature that exceeds the heat resistant bacteria. At the same time, *E.coli* colony completely die within five seconds, and *Bacillus subtilis* and *Exiguobacterium* 25 seconds. In another study designed nanoparticles generators - porous silicon disks, which penetrate the cancerous tumors and releasing the drug molecule. This method is extended half life of mice with breast cancer. Thus, the study of metal nanoparticles is increased interest primarily in terms of their interaction with biological materials. Applications include diagnostic purposes electronic tools for analyzing the composition of biochemical reagent, drug delivery inside the living cell, etc., where the carbon nanotubes are active implementation as a carrier for the biomaterials [19-25]. Therefore, the study of the interaction of biomolecules (nucleic acids,
nucleotide chains of DNA, proteins) with metal bass is very important to determine the extent of their links, which are in demand in the design and development of drug transport or analysis of biochemical reactions (DNA - NP) (Figures 1 and 2).

Fig. 1. A schematic view of the molecular dynamics models regarding on the interactions of metallic nanoparticles with single nucleotides, nucleotide or peptide chains, RNA, DNA and proteins.

Fig. 2. A schematic view of the molecular dynamics models on the interactions of metallic nanoparticles with single nucleotides, nucleotide and peptide chains, RNA and DNA molecules.

Increased computing power with molecular calculations every year can effectively investigate the above-mentioned objects at the atomic level and receive important information about the structure, dynamics and functional properties. But the important aspect of the application and that is of great practical interest in the above mentioned systems and facilities, primarily with a view to their use in biomedical applications [38-50]. For example, of great interest to the study of structures and aquatic toxicity cluster solutions C60 is connected with the possibility of their use for controlled drug delivery, diagnosis and treatment of cancer. Fullerene endohedral complexes with rare earth metals and a number of other metals (and endo-metall-fullerenes, fullerenols-soluble forms), Gd @ C82 (OH) X40, can be used in biomedical applications as an effective and non-toxic agents (Fig. 3).
Fig. 3. A fullerenol model with atoms of rare earth elements [38-49].

As tests shown, by animal studies, they can also provide a therapeutic effect thereby inhibiting the development of tumor - in mouse brain glioma. It should be noted that the CNTs, fullerenes, endofullerene, fullerenols with various biological molecules, also intensively studied by neutron scattering at the Laboratory of Neutron Physics IM Frank, JINR (Joint Institute for Nuclear Research), Dubna, Moscow Region, and the National Research Centre "Kurchatov Institute" PNPI "Petersburg Nuclear Physics Institute. BP KONSTANTINOVA" in Gatchina, St. Petersburg [38-50].

Recent experimental and simulation studies involve the DNA interaction with highly localized proton beams or metallic NPs (such as Ag, Au, etc.), aimed on targeted cancer therapy through the injection of metal micro- or nanoparticles into the tumor tissue with consequent local microwave or laser heating. Along with DNA-NP also the DNA-CNT system represents a great interest in today biomedicine applications due to diagnostic and treatment of oncology diseases. Cancer, in which cells grow and divide abnormally, is one of the primary diseases with regards to how it responds to CNT drug delivery. Representing a revolutionarily potential for the biochemistry and medicine the use of CNTs in drug delivery has based on the enhancing of sufficient solubility and allowing of efficient tumor targeting. These aspects prevent CNTs from being cytotoxic and altering the function of immune cells. For today, cancer therapy involves surgery, radiation therapy, and chemotherapy. The experimental and simulation studies involve the interaction of DNA with highly localized high power beams and various nanoparticles (Ag, Au, etc.). These studies are aimed on targeted cancer therapy through the injection of metal micro- or nanoparticles into the tumor tissue with consequent local microwave or laser heating. Due to their good heat conductivities of NPs (Ag, Au, and so on) the experiments reveal that the only tumor cells to destroy, remaining normal cells undamaged. Nevertheless, such kind treatment methods are usually painful and kill normal cells in addition to producing adverse side effects [7-18].

So far, the understanding of the nucleotides and peptides – nanoparticles – carbon nanotubes dynamics and binding, as an important stage of the DNA interaction mechanism with metallic nanoparticles and metallic surfaces embedded by the CNT environment, represents a potential target of modern research. In this work, the molecular dynamics (MD) simulations were performed on a small nucleotide chains (purines and pyrimidines) and peptides to investigate the interaction and binding processes with gold nanoparticles that happen within a carbon nanotube matrix. The behavior of a small NC, peptides models interacting with the NP-CNT system have to possess a lot of similarities with a full DNA or RNA molecule interacting in the NP and CNT environment.

2. Models and simulation method
A primary DNA or RNA structure consists of a linear sequence of nucleotides that are linked together by phosphodiester bonds. Nucleotides consist of 3 components: 1). Nitrogenous base - A (Adenine), G (Guanine), C(Cytosine), T (Thymine, present in DNA only) and U (Uracil, present in RNA only); 2). 5-carbon sugar which is called deoxyribose (found in DNA) and ribose (found in RNA); 3). One or more phosphate groups.
Fig. 4. (Left) A nucleotide chain (NC), consisting of a pyrimidine (C, cytosine) and a purine (G, guanine). (Right) A linear chain sequence of nucleotides that make up the primary structure of DNA or RNA.

We have simulated a three component molecular system consisting of a two nucleotide chain (NC), gold nanoparticles (NPs) and a carbon nanotube (CNT) under different temperature conditions ($T=100$, $200$ and $300$ K). Two nucleotides (one pyrimidine and one purine) as in the primary structure of DNA were relaxed in the vicinity of gold particles. In Fig. 5 (top) a schematic view of the simulation system consisting of a two nucleotide chain (NC), gold nanoparticles (NPs) and a carbon nanotube (CNT) is shown. In Fig. 5 (bottom) a two nucleotides chain, consisting of one pyrimidine (C, cytosine) and one purine (G, guanine) as in the primary structure of DNA is separately presented.

Fig. 5. (top) A schematic view of the simulation system consisting of a two nucleotide chain (NC), gold nanoparticles (NPs) and a carbon nanotube (CNT). (bottom) A two nucleotides chain, consisting of one pyrimidine (C, cytosine) and one purine (G, guanine) as in the primary structure of DNA is shown. A primary DNA or RNA structure consists of a linear sequence of nucleotides that are linked together by phosphodiester bonds. Nucleotides consist of 3 components: (1) Nitrogenous base - A (Adenine), G (Guanine), C(Cytosine), T (Thymine, present in DNA only) and U (Uracil, present in RNA only); (2) 5-carbon sugar which is called deoxyribose (found in DNA) and ribose (found in RNA); (3) One or more phosphate groups.
The nucleotide chain was located from gold atoms at distances [5-10] Å, i.e. within a range of Van der Waals (VdW) forces (Figs. 6). During the MD simulations, first, we have generated three positional slightly different gold particles enable to interact with the NC as NC-1Au, a one gold particle and a nucleotide chain NC, NC-2Au, a two gold particle and a nucleotide chain, and NC-3Au, a three (or more) gold particle and a nucleotide chain. Thus, we have made several small gold clusters and simulated the NC-NPs system as NC-2,3,...Au. Next, we extended the MD simulations for the elongated peptide chains interacting with metallic nanoparticles inside of a carbon nanotube matrix. So far, we have investigated for the single nucleotides, nucleotide and peptide chains interacting with NPs-CNT system multiple model configurations under the same simulation and temperature conditions (Figs. 6 and 7):

1. **Model 1**, NC-1Au,
2. **Model 2**, NC-2Au,
3. **Model 3**, NC-3Au.

![Models 1 (NC-1NP), Models 2 (NC-2NP), and Model 3 (NC-3NP) with Purine (G – Guanine) and Pyrimidine (C – Citosine).](image)

**Fig. 6.** The models of the nucleotide chain (NC) interacting with 1, 2 and 3 gold nanoparticles (NPs). The positions of one of two phosphorus (P) atoms of the NC and gold NPs are shown respectively by the dark brown and yellow spheres.
Fig. 7. The hierarchy of MD models for the single nucleotides, nucleotide chains and long peptides, interacting with metallic nanoparticles inside of a carbon nanotube matrix.

A classical molecular dynamics study was performed using the DL_POLY_2.20 [51-52] general-purpose code. The NVT ensemble with a Berendsen thermostat and a Verlet leapfrog scheme were employed. The integration time step of the dynamical equations of motion was 1 fs. The entire system (the nucleotide (N), nucleotide chain (NC) and peptides, gold atoms and carbon nanotube) were allowed to interact with each other via the VdW potential only. For describing of VdW interactions we used Lennard-Jones (LJ or 12-6) potential, which is commonly in use for simulation of liquids and condensed phases. The LJ and 12-6 potential look like:

$$ V(r) = 4\varepsilon \left[ \left( \frac{\sigma}{r} \right)^{12} - \left( \frac{\sigma}{r} \right)^{6} \right], \quad U = \frac{A}{r^{12}} - \frac{B}{r^{6}} $$

where $\varepsilon$, $\sigma$ are LJ interaction parameters and the cross-section interaction parameters were defined using the Lorentz-Berthelot mixing rule: $\varepsilon_{ij} = \left( \varepsilon_{ii} \varepsilon_{jj} \right)^{1/2}$ and $\sigma_{ij} = \frac{1}{2} (\sigma_{ii} + \sigma_{jj})$.

For the LJ interaction parameters we have used the data from the literature as reported, for example: $\varepsilon$(Au-Au)=0.039 kcal/mol, $\sigma$(Au-Au)=2.9 Å by Q. Pu et al. [53]; $\varepsilon$(C-Au)=0.29256 kcal/mol, $\sigma$(C-Au)=2.99 Å by Song Hai Yang and Zha Xin Wei [54]; $\varepsilon$(C-C)=0.1055 kcal/mol, $\sigma$(C-Au)=3.851 Å, $\varepsilon$(O-O)=0.156 kcal/mol, $\sigma$(O-O)=3.166 Å, by J.H. Walthier et al. [55]; $\varepsilon$(N-N)=0.072 kcal/mol, $\sigma$(C-Au)=3.31 Å by P. Kowalczyk [56]; $\varepsilon$(P-P)=0.40 kcal/mol, $\sigma$(P-P)=3.33 Å by P. Ballone, R.O. Jones [57], so on. Some potentials and parameters are also shown in Appendix (Tables 1-2), where C, O, N and P stands for carbon, oxygen, nitrogen and sulphur atoms of the nucleotides and DNA and C denotes the carbon atom of CNT. The force field parameters for the NC (nucleotide chain) and CNT (carbon nanotube) molecules were choosen from the DL_FIELD database [51]. The intramolecular interactions for the NC chain were described using the LJ, combined with angular and dihedral bonding potentials. The LJ, cross-interaction and bond parameters for the NC, peptide-NP-CNT system were the same as in our papers [18, 58-66].

For the describing CNT we have employed the quantum chemistry Tersoff potential, so far a co-called hybrid approach (the combination of quantum chemistry potential and classical trajectory calculations) has been realized to investigate the NC interaction with CNT. In CNTs we have chemical bonding is hybridization sp² (as graphite), which is stronger than sp³ bond (of diamond). The nature of chemical bonding in CNTs is described by quantum chemistry, through the process of orbital hybridization. The Tersoff potential in hybrid MD simulations correctly describes the nature of
covalent bonding in carbon nanotube; it allows the breaking and formation of chemical bonds, that it is associated with hybridization process. Tersoff potential is pair wise potential, but coefficient in attractive term depends on local environment, thus, Tersoff potential possesses a many body nature (see, [18, 51-52] and references therein).

3. Results and discussion

The MD simulations results for the single nucleotides (N), nucleotide chains (NC), peptides – metallic nanoparticles (NP) – carbon nanotube (CNT) models are shown below in three parts. During the MD statistics analysis we have focus on a comparative behaviour of two main physical characteristics:

(A) The N, NC – NP distance distributions,
(B) The N, NC – NP bond energy distributions.

The calculation results below illustrate the dependence of the total potential energy, the N,NC-NP interaction distances, the N,NC angular and torsion (dihedral) bond energies along with the configuration snapshots at the temperatures T=100 (thin lines), 200 (dotted lines) and T=300 K (thick lines).

At first, in Fig. 8 the total potential energy vs simulation time are presented for the NC-NP-CN system. The total potential energy are presented for all models (1-3: NC-1Au, NC-2Au and NC-3Au), respectively. Fig. 8 demonstrates the change on the interaction potential energies with adding another gold atom to the system at different system temperatures.
3.1. Single nucleotides (N) - metallic nanoparticles (NP) - carbon nanotube (CNT) system

In Figs. 9-11 the MD simulation results are shown for the single nucleotide (N) – NP interaction distances (top), the nucleotide’ angular (middle) and torsion (dihedral) (bottom) bond energies vs time for all models (1: Nucleotide–1NP–CNT, 2: Nucleotide–2NP–CNT and 3: Nucleotide–3NP–CNT). Black lines indicate Purine (G – Guanine), light lines Pyrimidine (C – Citosine). The N–NP interaction and binding processes that happen within a CNT matrix estimated from the MD data thereby built the distance distributions, the angular and dihedral (torsional) bond energy graphs versus simulation time at different temperatures. The MD simulation results show that with the temperature increase (from T=100 up to 300 K) many peculiarities of the Nucleotide–NP dynamics remain, though the Nucleotides exhibit larger oscillation that effect the Nucleotide–NP close bond formation for all Nucleotide–NP–CNT models.

Fig. 8. The NC-NP-CNT total potential energy for the models 1-3: NC-1Au, NC-2Au and NC-3Au at the temperatures T=100, 200 and 300 K.
The $N$ – NP distance distributions

Model 1 (Nucleotide–1NP–CNT)

In Fig. 9 (top) the Nucleotide–NP interaction distances vs time are presented for Purine (G – Guanine) (black line) and Pyrimidine (C – Cytosine) (light line) (T=100 K). It should be stressed out that the Nucleotide–NP distance, as shown in Fig. 9 (top), represents a larger distance between the nucleotide’ phosphorus (P) and gold (Au) atoms. All other Nucleotide–NP interatomic distances lie within $d$ [Nucleotide(P)–NP(Au)] values and are smaller than $d$ [Nucleotide(P)–NP(Au)]. From Figs. 9 (top) for the model 1 we observe that Pyrimidine (C – Cytosine) forms a strong bond with the gold NP, while for the Purine (G – Guanine) the disruption of the bond is clear. That is, even at low temperature (T=100 K) for the nucleic acid (Purine) the intramolecular vibrations dominate over the weak VdW non-bonding forces between the Nucleotide–NP.

Model 2 (Nucleotide–2NP–CNT)

Next, we simulated three different combinations of two gold atoms and a nucleotide. In Fig. 10 (top) the Nucleotide–2NP interaction distances are shown for Purine (G – Guanine) (black line) and Pyrimidine (C – Cytosine) (light line), respectively. As like as previous section, for the model 2 we can observe the Pyrimidine (C – Cytosine) –NP strong bond formation, while the bond disruption for the Purine (G – Guanine) to exist.

Model 3 (Nucleotide–3NP–CNT)

The three gold particle system (Nucleotide–3Au–CNT) for the next analyzing step could be associated with a small atomic cluster that possesses its own oscillation modes as a collective motion between the gold atoms. Even for such a small cluster one can assume the existing of more intense VdW interactions with the Nucleotides within of a CNT matrix. In Fig. 11 (top) the Nucleotide–NP interaction distances are shown for Purine (G – Guanine) (black line) and Pyrimidine (C – Cytosine) (light line), respectively. The distance distribution diagrams of Fig. 11 (top) have shown that the Nucleotide–3Au close contact has kept for both, Purine (G – Guanine) (black line) and Pyrimidine (C – Cytosine).

The $N$ – NP bond energy distributions

In Figs. 9-11 the Nucleotide’ angular (middle) and torsion (dihedral) (bottom) bond energies vs time are presented for the Nucleotide–1Au–CNT (model 1), Nucleotide–2Au–CNT (model 2) and Nucleotide–3Au–CNT (model 2), respectively (T=100 K). As it can be observed, the curves of the angular and torsion bond energies for the Pyrimidine (C – Cytosine) (light line) lies below than that of Purine (G – Guanine) (black line) ones. That is the comparison of the curves in Figs. 10-12 indicates that Purine (G – Guanine) possesses higher intramolecular bond oscillation modes than that of the Pyrimidine (C – Cytosine). That is a characteristics feature related the Nucleotide–NP bond formation or disruption. As the Nucleotide’ internal vibrations dominate over weak VdW nonbonding forces with the gold NP, it makes a strong bond formation with the gold atom difficult. Comparing Figs. 11 (Nucleotide–3NP–CNT) with Figs. 9-10 (Nucleotide–1NP–CNT and Nucleotide–2NP–CNT), one can conclude that the behavior of the Nucleotide’ angular and torsion bond energies at early stages of the dynamics define the systems final states. Thus, the initial interaction stages between nucleotides and gold nanoparticles could be a triggering point for the type of the bond formation within a CNT. This is another characteristics feature of the Nucleotide–NP dynamics in an environment, confined by a CNT matrix. From Figs. 9-11 on the Nucleotide’ angular and torsion (dihedral) bond energy distribution one can see that for the Pyrimidine (C – Cytosine) making its strong bond with the 1Au, 2Au and 3Au NP seem are always preferable, while for the Purine (G – Guanine), having more higher internal vibration modes, the only larger gold cluster can keep it on a close distant as long-lived contact. With the temperature increase (from T=100 up to 300 K) many peculiarities of the Nucleotide–NP dynamics, as described above, remain, though the Nucleotide’ angular and torsion (dihedral) bond energies exhibit larger oscillation that distort the Nucleotide–NP binding for all Nucleotide–NP–CNT models.
Fig. 9. The single nucleotide (N) – NP interaction distances (top), the nucleotide’ angular (middle) and torsion (dihedral) (bottom) bond energies vs time for the Model 1 (Nucleotide–1NP–CNT). Black line: Purine (G – Guanine), Light lines: Pyrimidine (C – Cytosine) (T=100K).
Fig. 10. The single nucleotide (N) – NP interaction distances (top), the nucleotide’ angular (middle) and torsion (dihedral) (bottom) bond energies vs time for the Model 2 (Nucleotide–2NP–CNT). Black line: Purine (G – Guanine), Light lines: Pyrimidine (C – Citosine) (T=100K).
Fig. 11. The single nucleotide (N) – NP interaction distances (top), the nucleotide’ angular (middle) and torsion (dihedral) (bottom) bond energies vs time for the Model 3 (Nucleotide–3NP–CNT). Black line: Purine (G – Guanine), Light lines: Pyrimidine (C – Citosine) (T=100K).
3.2. Nucleotide chains (NC) - metallic nanoparticles (NP) - carbon nanotube (CNT) system

The NC – NP distance and bond energy distributions

Model 1 (NC-1NP-CNT)

In Figs. 12 for the model 1 the NC-NP interaction distances, the NC angular and torsion (dihedral) bond energies vs time are presented for the temperatures T=100, 200 and 300 K. It should be stressed out that the NC-NP distance, as shown in Fig. 12 (top), represents a larger distance between the NC phosphorus (P) and gold (Au) atoms. (All other NC-NP interatomic distances lie within r[NC(P)-NP(Au)] values and are smaller than r[NC(P)-NP(Au)]). From Fig. 12 (top) for the model 1 we observe at high temperature T=300 K the disruption of the NC-NP bonds. That is, with the temperature growth the NC intramolecular vibrations begun to dominate over the weak NC-NP non-bonding VdW forces.

In Figs. 12 (middle and bottom) the NC angular and torsion (dihedral) bond energies vs time are presented for the temperatures T=100, 200 and 300 K. At low temperatures (T=100 and 200 K) the curves of the angular and torsion energies lie significantly below than that at T=300 K ones. One can also observe that, for NC-1Au the angular and torsion energy curves correlate with the distance distributions shown above. That is for the model 1 we observe a very close contact between the NC-1Au only at low temperatures; formation of a preferably strong NC-1NP bond is possible at T<200 K, which disrupts with the temperature increasing. The behavior of the angular and dihedral bond energies, Figs. 12 (middle and bottom), with the distance distribution characteristics as presented in Fig. 12 (top), typically show a weak nature of VdW interactions owe for one metallic particle system.

Models 2 (NC-2NP-CNT)

As described above, the NC interaction with gold NP inside a CNT matrix can produce preferably the weak NC-1NP bonds. Next, we simulated the two gold atom and a nucleotide chain as NC-2Au. In Fig. 13 (top) the NC-2NP-CNT interaction distances are shown for model 2, NC-2Au at the temperatures T=100, 200 and 300 K. From Fig. 13 (top) one can see that for NC-2NP-CNT system at low temperatures the formation of a strong bonds between the NC-2Au are mostly possible.

Figs. 13 (middle and bottom) demonstrate the NC angular and torsion (dihedral) bond energies vs time for the NC-2NP-CNT system. Now for the two gold atomic systems the weak VdW forces make an additional contribution to the NC angular and torsion bond energy profiles, thereby influencing the final NC-2NP binding states. Comparing Figs. 13 (NC-2NP model) and Figs. 12 (NC-1NP model), one can conclude that the behavior of the NC angular and torsion bond energies at early stages of the dynamics define the systems final states. Thus, the initial interaction stages between nucleotides and gold nanoparticles could be a triggering point for the type of the bond formation within a CNT. This is a characteristics feature of the NC-NP dynamics in an environment, confined by a CNT matrix.

Model 3 (NC-3NP-CNT)

The three gold particle system, for the next analyzing step, could be associated with a small atomic cluster that possesses the own oscillation modes as a collective motion. Even for such a small cluster one assumes the existing of more intense VdW interactions with the NC and CNT matrix. In Fig. 14 (top) the interaction distances, the NC angular (middle) and dihedral (bottom) bond energies are presented for the NC-3Au system at the temperatures T=100, 200 and 300 K, respectively. The distance distribution diagrams in Fig. 14 (top) show that the NC-3Au close contact has kept even at high temperatures. The comparison of the angular and torsion (dihedral) bond energy curves with the NC-1NP-CNT and NC-2NP-CNT models are straightforward.
Fig. 12. The NC-1NP-CNT interaction distances (top), the NC angular (middle) and dihedral (bottom) bond energies vs time at the temperatures T=100, 200 and 300 K.
Fig. 13. The NC-2NP-CNT interaction distances (top), the NC dihedral (middle) and angular (bottom) bond energies vs time at the temperatures T=100, 200 and 300 K.
Model 3 (NC-3NP-CNT)

Fig. 14. The NC-3NP-CNT interaction distances (top), the NC dihedral (middle) and angular (bottom) bond energies vs time at the temperatures T=100, 200 and 300 K.
The configuration snapshots in Figs. 15 demonstrate the NC-1Au (left) and NC-3Au (right) positional changes at the initial (t=0), intermediate (t=50 ps) and final (t=100 ps) simulation states. Obviously, for the three gold particle system the NC-3NP strong bond formation inside a CNT matrix is a comparably most probable event.

**Model 1 (NC-1NP-CNT)**

**Model 3 (NC-3NP-CNT)**

**Fig. 15.** Snapshots of the interaction process for the models 1 (NC-1Au; left) and 3 (NC-3Au; right) inside a CNT matrix at the t=0 (top), t=50 ps (middle) and t=100 ps (bottom) states (T=100 K).

### 3.3. Peptide chains (PC) - metallic nanoparticles (NP) - carbon nanotube (CNT) system

Below the results of MD simulations are presented for the extended molecular structures (single-filament peptide chains) and the mechanisms of their encapsulation and folding within the CNT. The peptide molecule (a chain with many bound nucleotides) in CNT environment modeled with different sets and positional variations gold NP. Initially, the system was investigated peptide-CNT without the presence of any metal particles (Fig. 16).

The study of the molecular mechanisms of the interaction and folding of peptide chains, and a variety of biomolecular compounds (fragments of chemical molecules, drugs) with metal nanoparticles (NPs) in a matrix of carbon nanotubes (CNT) and the spherical bodies (fullerenes) in today's nano-biotechnology and medical applications is a task of great importance [1-40]. Undoubtedly, the process of folding (encapsulation, folding) biomolecules inside CNTs can rank as the most exciting scientific spectacle (see Figs. 16-18 below). Especially when in the process of folding of biomolecules (peptides, proteins), taking place in a CNT matrix, make their own adjustments with metallic NP (Figs. 17-18), where gold nanoparticles contribute to the full encapsulation of the peptide chain within the CNT. This phenomenon is similar to the process of folding (dense packing) viruses within the foreign cells (the capsid) [1-40].

The results of Fig. 16 show the process of spontaneous packing peptide molecule from a linear to a globular-like structures as a result of intramolecular vibrations, studied in the previous sections for the individual nucleotides and small nucleotide chains.

However, the inclusion of a small cluster of gold NP for consideration in the peptide-CNT system as seen from Figs. 17-18, also did not significantly alter the final result of their interaction (compare Figs. 17-18 with Fig. 16 above).

So far, the results of MD simulations and graphical visualization demonstrate various scenarios of the effect of metal nanoparticles in the final conformation (twisting or folding) of the peptides within the CNT matrix. In some cases, the effect of a weak VdW forces acting between the peptide chain and metallic NP leads to the full package (encapsulation) of the peptide chain within the
CNT. In other cases, the metal nanoparticles (in this case gold NP) may hinder the process of encapsulation of the peptide inside the CNT matrix.

(a)

(b)

(c)

(d)

Fig. 16 (a-d, from top to bottom). The sequential configurations (snapshots), illustrating the folding process (encapsulation) peptide molecule (a chain of several nucleotides) inside carbon nanotubes.
Fig. 17 (a-d, from top to bottom). The sequential configurations (snapshots), illustrating the folding process (encapsulation) peptide molecule (a chain of several nucleotides) inside the carbon nanotube in interactions with nanochastitsvmi gold ((a-d), from top to bottom). Here gold nanoparticles contribute to the full encapsulation of the peptide chain within the CNT.
Fig. 18 (a-d, from top to bottom). The sequential configurations (snapshots), illustrating the folding process (encapsulation) peptide molecule (a chain of several nucleotides) inside the carbon nanotube in interactions with nanochastitsuvmi gold ((a-d), from top to bottom). Here gold nanoparticles contribute to the full encapsulation of the peptide chain within the CNT.
4. Conclusion

The multiple molecular dynamics (MD) simulations have been performed for the single nucleotides (N), nucleotide (NC) and peptide chains (PC), interacting with gold nanoparticles (NP) inside of a carbon nanotube (CNT) with periodic boundaries. We have been aimed to investigate the peculiarities of Van der Waals (VdW) interactions, a nature of the N,NC,peptide-NP bonding in a confined environment by the CNT matrix. The small nucleotide chain is an important stage in the understanding of interaction mechanism of a whole DNA or RNA molecule with the NPs and CNT. It is well known that a primary DNA or RNA structure consists of a linear sequence of nucleotides that are linked together by phosphodiester bonds. With regard to application aspects of the DNA-NP-CNT system one has to mention the development of the DNA-CNT mobile electronic devices for the purposes of diagnostic applications, for the chemical or drug delivery inside the living cells and related nanorobotic design. The NC intermolecular motions were estimated from MD data thereby building the distance distributions, the angular and dihedral (torsional) bond energy graphs versus simulation time at different temperatures from T=100 K up to 300 K. The MD simulation results have shown that depending on the relative NC-NP position a different scenario of bonding between the N,NC-NP within a CNT matrix is possible. We have observed the possibilities of formation of weak, strong and intermediate bonds between the N,NP-NC, which are overestimated by a presence of CNT matrix as a confining environment. The NC chain can form with a particular gold atom a close contact, while with another under the same positional and temperature conditions the weak resultant bonding formation might be possible. At high temperatures, as the NC intramolecular oscillations have grown, the picture of the NC-NPs bonding inside a CNT matrix has essentially modifies. We observe more fluctuations in the NP-NC bonding processes, not only for a single gold atomic case (model 1, N,NC-1NP-CNT) but also for the two (model 2, N,NC-2NP-CNT) and three (model 3, N,NC-3NP-CNT) gold particle ones. Thus, we observe a concurrent effect between the NC intramolecular vibrations and a weak VdW interaction between the N,NC and gold NP, thereby defining their final binding in CNT matrix. In conclusion, the peculiarities of the N,NC-NP-CNT structural and dynamical behaviour, investigated in the present study, could be important stage for the understanding of binding mechanism of a full DNA molecule with NP and CNT.

The behavior of the peptide chain or the DNA inside the nanotube is an important link in understanding the folding mechanism (encapsulation) of biological macromolecules in a living cell. In all cases, the competition show a concurrent effect of the intra-molecular vibrations with weak VdW forces. The effect of the cross-correlation of the two main types of atomic and molecular interactions determine the formation or destruction of relationships gold nanoparticles with the peptide or nucleotide chains. It is well known, for example, a common feature - the encapsulation of virus process in the restricted area (capsids, nano-objects and micro-sized) in guest cells, leading eventually to various diseases (as the parent cell will not recognize a foreign gene and allow its penetration, incubation and further reproduction). In this respect, a variety of mechanisms to encapsulate a single-chain-peptide chain, freely fit within the CNT indicates the implementation and design of the new micro-nano-devices for transportation of biomaterials and drug delivery inside the living cell and the blood of those or other diagnostic purposes of analysis.
## Appendix

### Table 1. The 12-6 potential parameters of the NC chain.

| Pair   | \( A_{12} \) kcal/mol | \( B_{12} \) kcal/mol | Pair   | \( A_{12} \) kcal/mol | \( B_{12} \) kcal/mol |
|--------|------------------------|------------------------|--------|------------------------|------------------------|
| C-C    | 1171340                | 567.5                  | P-P    | 8350780                | 3369.4                 |
| C-P    | 3145970                | 1481.6                 | P-O    | 1476420                | 1016.6                 |
| C-O    | 535958                 | 452.2                  | P-N    | 1985180                | 1117.9                 |
| C-N    | 730530                 | 500.7                  | N-N    | 450301                 | 373.4                  |
| O-O    | 232116                 | 198.1                  | N-O    | 325886                 | 334.9                  |

### Table 2. The intermolecular potential parameters of the NC chain.

| Bonds | \( k \) kcal/mol | \( r_0 \) Å | | Bonds | \( k \) kcal/mol | \( \theta_0 \)° |
|-------|------------------|--------------|----------|-------|------------------|-----------------------|
| O-H   | 300              | 1.724        |          | O-P-O | 100.33           | 93.300                |
| C-N-C | 109.00           | 106.70       | C-N-H   | 109.00           | 106.700              |
| C-O-C | 106.70           | 104.510      | O-C-H   | 112.50           | 109.471              |
| N-C-N | 133.33           | 120.000      | H-C-H   | 112.50           | 109.471              |
| N-C-C | 133.33           | 120.000      | O-C-C   | 112.50           | 109.471              |
| C-N-C | 133.33           | 120.000      | C-C-C   | 112.50           | 109.471              |

| Bonds | \( A \) | \( \delta \) | \( m \) | Bonds | \( A \) | \( \delta \) | \( m \) |
|-------|--------|---------|------|-------|--------|---------|------|
| P-O-C-H | 0.3333 | 0       | 3    | P-O-C-C | 0.3333 | 0       | 3    |
| C-O-C-H | 0.3333 | 0       | 3    | C-O-C-N | 0.3333 | 0       | 3    |
| C-O-C-C | 0.3333 | 0       | 3    | C-O-P-O | 0.5000 | 0       | 3    |
| C-N-P-C | 2.5000 | 180     | 2    | N-C-C-O | 2.5000 | 180     | 2    |
| N-C-C-N | 2.5000 | 180     | 2    | C-C-O-O | 2.5000 | 180     | 2    |
| C-C-C-N | 2.5000 | 180     | 2    | C-N-C-N | 2.5000 | 180     | 2    |
| H-C-N-C | 11.250 | 180     | 2    | N-C-N-C | 11.250 | 180     | 2    |
| N-C-C-H | 5.6250 | 180     | 2    | N-C-C-C | 5.6250 | 180     | 2    |
| H-C-C-H | 5.6250 | 180     | 2    | H-C-C-C | 5.6250 | 180     | 2    |

Harmonic bonds: \( U(r) = k(r - r_0)^2/2 \)

Valence angles: \( U(\theta) = k(\theta - \theta_0)^2/2 \)

Dihedral angles: \( U(\phi) = A[1 + \cos(m\phi - \delta)] \)
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