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*Hetero- and low-dimensional structures*

# Nanophysics in modern medicine

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**Abstract.** Nanophysics is rapidly developing for the recent couple of decades. Unique physical properties of materials at the nanoscale are the reason for this rapid development. Ideas, materials and structures of nanophysics have found their wide application in related fields of modern science, including biology and medicine. This short review is devoted to the application of nanophysics in modern medicine. The main focus was on application of ideas and physical phenomena of nanophysics in oncology and antiviral therapy. We have focused on the use of nanosystems both for tumor imaging and for the struggle against some types of tumors. The use of nanoparticles as nanocontainers for targeted drug delivery was briefly discussed. We also demonstrated how the effects of nanophysics can be used to develop new non-traditional methods of antiviral therapy. The focus of these methods was the idea of physical (field) action of nanoparticles on the viruses, which is based on the local-field enhancement effect that is the reason of ponderomotive forces acting on the viruses up to destruction of viral envelopes.

**Keywords:** nanophysics, nanoparticles, oncology, antiviral therapy, ponderomotive forces.

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## 1. Introduction

Nanophysics is rapidly developed for the recent couple of decades [1–3]. Unique physical properties of the materials at the nanoscale are the reason for this rapid development. These properties of nanomaterials at the nanoscale are caused by two main factors:

– First, nanoobjects have a relatively larger surface area as compared to the bulk material of the same mass. This can make materials more chemically reactive (in some cases materials that are inert in their bulk form are reactive when being produced in their nanoscale form), and affect their electrical and optical properties;

– Second, quantum effects can begin to dominate behavior of matter at the nanoscale – particularly at the lower end – affecting the optical, electrical and magnetic behavior of materials. These features of the nanomaterial properties are, of course, determined by the shape and dimension of nano-objects.

Attractivity of nanophysics in the natural sciences has its origin not only in the unique properties of nanomaterials but from the nontrivial viewpoint of the physical processes demonstrated in nanophysics. The ideas of nanophysics are the base of different branches of natural sciences including biology and medicine. Moreover, a new branch of medicine – nanomedicine – is rapidly developing nowadays [4].

Different nano-objects and nanostructures can be used in nanomedicine. In this paper, we have mainly touched upon application of nanoparticles (NPs). The nanomaterials (usually in the form of NPs) are widely used in nanomedicine, particularly, in diagnostics and therapy.

The advantages of NPs used in these branches of nanomedicine are well known. One of the directions of diagnostics is visualization of organs and tissues of the living organism. The most important use of NPs in diagnostics is the use of different NPs in visualization of tumor tissues. Since nanoparticles for both diagnosis and treatment must enter the tumor, it is possible to consider what features of the structure of blood vessels in tumors can contribute to localization of nanoparticles in the tumor. On the other hand, NPs are used in antiviral therapy. Both of these aspects of using the nanostructures will be considered in this work.

The latter aims at introduction of physicists studying solid state, particularly, semiconductor physics, to new aspects of nanophysics widely used in nanomedicine.

## 2. Visualization of a tumor with nanoparticles

The tumor cells and blood vessels are mainly structurally abnormal. These differ from the blood vessels found in normal tissues. The differences between blood vessels in tumors and normal tissues play an essential role in using the nanoparticles for visualization and treatment of the cancer tissues. Tumor vessels have excessive branching. Tumor blood vessels contain small gaps (fenestrations) from 200 up to 1200 nm [5]. These small gaps allow the excess fluid and blood components to flow into a tumor's interior by pressurizing it like a water balloon. On the other hand, this effect leads to accumulation of NPs in the tumor. The intercell spaces in a tumor are usually larger than those in normal tissues. Thus, the branched blood vessels system in the tumor and the specific structure of the blood vessel walls lead to the fact that after intravenous injection of NPs, the latter after some time gather in the tumor area (Fig. 1). These properties of blood vessels in the tumor are the base for diagnostics of cancer by visualization, and an effective non-chemical method of antitumor therapy – plasmon photothermal therapy of tumor (PPTT) – can be applied.

The problem of diagnostics of tumor tissues is a part of the antitumor struggle. Nowadays a rather small number of patients in oncostatus are diagnosed at early stages, which is caused by non-effective conventional diagnostic techniques. Thus, the diagnostic techniques should be improved. Visualization of tumor cells is one branch of such advanced diagnostics. Due to the well-known and predicted optical properties of NPs, they are the most widely studied objects for preclinical optical imaging of tumors at early stages. As compared with organic fluorophores, NPs possess many useful properties for biological imaging. They are characterized by a strong resistance to photobleaching and chemical degradation, high quantum yields, and continuous absorption spectra within a wide range of wavelengths – from the ultraviolet to near-infrared ones. The interest is related to the problem of developing targeted systems consisting of photoluminescent NPs and targeting modules that ensure their delivery to the tumor cells. Some specific features of tumor tissues allow accumulation of NPs inside the tumor tissue.

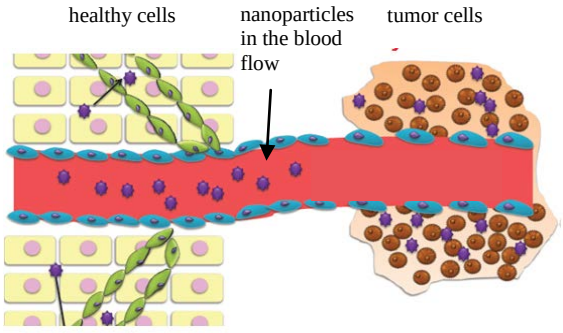



**Fig. 1.** Accumulation of nanoparticles near the tumor due to the specific structure of blood vessels in this tumor (scheme).

The excessive branching of blood vessels inside the tumor tissue and the abnormal basement membrane of a blood vessel, which allows penetration of NPs through the membrane, are the factors facilitating NPs accumulation inside the tumor. Moreover, the structure of tumor tissue is characterized by a rather large volume of intercellular liquid. These nanosystems that accumulate in tumor cells can enhance the contrast of these cells against the background of healthy tissues due to photoluminescent response to excitation with light of a certain wavelength. The use of photoluminescent systems capable of targeted binding to an appropriate cell tumor marker provides the most sensitive and non-invasive early diagnostic method for cancer. In [6], the problem of developing targeted composites based on photo-luminescent NPs that have targeting modules, which ensure their delivery to the target cells, is discussed. The method for direct visualization of metastatic breast cancer with luminescent NP coated by circulating tumor cells under dark field illumination was demonstrated in [7]. Namely, the scientists transduced the cells of the metastatic breast cancer line (4T1) with a non-native target protein (Thy1.1). Gold nanoparticles with the core diameter and shell thickness 80 and 15 nm, respectively, were synthesized and characterized. Positive 4T1-Thy1.1 cells were incubated with antibody-coated metallic nanoshells. These complex NPs were used for visualization of breast cancer cells inside other organs. NPs appeared overly bright at low magnification. Thus, the quick screening of samples and easy visual detection of even single isolated circulating tumor cells was demonstrated. A murine metastatic tumor model with the 4T1-Thy1.1 cell line was also implemented in the work. Murine blood was drawn over one month, and circulating tumor cells were successfully detected in all positive subjects. The work demonstrated the successful applying the metallic nanoshells as labels for direct visualization of circulating tumor cells.

The imaging technologies described above, reflect mostly anatomical changes that enable one to see the pathological tissue faster than analyze the biological processes responsible for the disease. Molecular imaging is a biomedical research method that enables to visually represent and characterize the biological processes in the living cell at the molecular level [8]. Several molecular imaging modes are currently used. There are fluorescence and bioluminescence imaging, molecular magnetic resonance imaging, magnetic resonance spectroscopy, *etc*.

The main idea of NPs usage in molecular imaging consists in exploiting the nanoplatforms for carrying molecules or molecular complexes for visualization of molecular processes in the living cells. These NPs come in a wide variety of sizes, shapes, and structures; they are fabricated from a variety of materials. Modified NPs can recognize, bind to and internalize into tumor cells *via* receptor-mediated endocytosis when modified with tumor-targeting molecules, such as antibodies, nucleic acids, proteins, or other ligands. Molecular imaging with NPs can provide not only structural images using

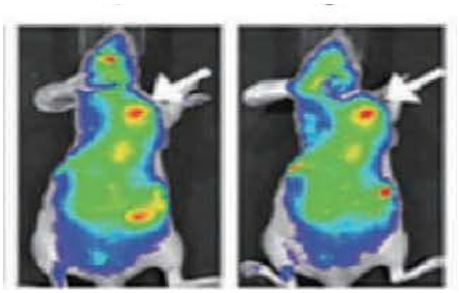


**Fig. 2.** Luminescent images of SKOV3 tumor-bearing mice [8].

traditional imaging techniques but also functional and molecular information by using many newly emerging imaging techniques. The use of NPs multimodality for this purpose can lead to a precise assessment of tumor biology and the tumor microenvironment. For example, as it was pointed out in the brief review [8], fluorescence imaging can be provided in the range from visible to infrared light with rather high spatial resolution (fluorescence reflectance imaging). In part, the dorsal images of SKOV3 tumor-bearing (arrows) mice injected with NPs QD710-Dendron-RGD2 conjugate were visualized *in vivo* near-infrared fluorescence imaging (Fig. 2) – 4 hours after injection of the NPs preparation – left panel, and 5 hours after injection of the NPs preparation – right panel.

In conclusion, it should be noted that the specific optical properties of NPs of different types are used to diagnose cancer in the early stages, which allows for developing an effective strategy for their treatment. In particular, such types of diagnostics include fluorescent and other methods for imaging the small tumors.

## 3. Nanoparticles in the struggle against cancer

The fight against cancer is a challenge for modern medicine and the development of new non-traditional methods of anticancer therapy is an important task of our time. For a few recent decades, the use of methods of nanoscience is the main trend in solving the problem. In this chapter, we point out one of the branches of developing the nontraditional methods of antitumor therapy, namely, the use of NPs for antitumor nanomedicine.

### 3.1. Drug delivery to tumor cells by using the nanoparticles

Nanoparticles have various advantages over the other conventional chemotherapeutic drug delivery, namely, NPs can be considered as a new alternative therapeutic drug delivery option to treat a wide range of diseases. The methods for using NPs can provide efficient drug delivery to the targeted tissue or the affected cell, which can minimize the risk of side effects. Size and surface characteristics of NPs play a crucial role in modulating nanocarrier efficiency and biodistribution of chemical drugs inside the body [9].

The main aim of targeting the tumors with chemotherapeutic drugs is to maximize the killing effect and minimize the side effects on the organism [9]. Targeted drug delivery directly to the tumor is a response to the challenges posed by the main aim pointed out above. One should note the passive and active targeting of drug delivery to cancer cells [9, 10]. Passive targeting mainly depends on the tumor physiological properties, which promotes accumulation of NPs by delivery systems in the tumor. NPs used for passive targeting drug delivery are similar to micellar systems, liposomes, polymeric-drug conjugates, and polymeric NPs.

Passive targeting is mainly dependent on the NP size as passive diffusion is achieved by diffusion-mediated transport [9].

Tumor tissues require more nutrients than normal cells, leading to secretion of vascular endothelial growth factors and other growth factors that promote angiogenesis in tumors. Thus, modification of NPs by growth factor molecules (*e.g.*, folic acid) can effectively increase accumulation of NPs inside the tumor. These modified NPs can be used as nanocontainers to deliver drugs to the tumor. Thus, such NPs are the base of the active regime for drug delivery. Active cancer-targeting is performed with NPs modified by attaching targeted moieties for better delivery of NP systems to the tumor site. For this aim, NPs were modified by ligands from proteins (antibodies), nucleic acids, peptides, or carbohydrates. These ligands can be easily attached to the receptors expressed in cancer cells. Then NPs can be attached and accumulated inside the tumor site *via* receptor-mediated endocytosis.

The example of using the drug delivery with NPs has been already demonstrated in [11]. The targeted nanodrug delivery when treating breast cancer is to target the molecular recognition markers by using nanocarriers (Fig. 3). This method improves the target specificity of drugs only toward cancer cells and is less toxic to the healthy cells. Action of the different anticancer drugs, which was described in [11] (for example, doxorubicin – DOX), is schematically shown in Fig. 3.

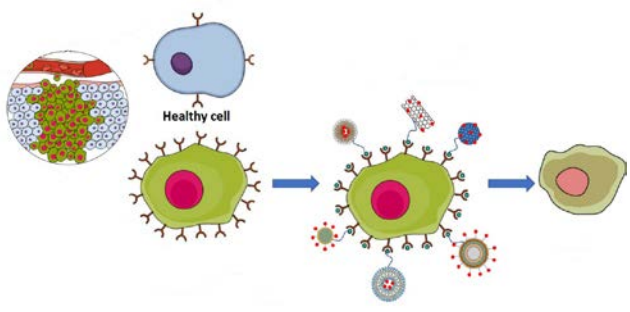



**Fig. 3.** The targeting of drug delivery to the tumor tissue with nanoparticles [11].

### 3.2. Plasmon photothermal therapy of tumor

Nanoparticles are widely used not only for drug delivery but also directly for the therapy of cancer. One of the methods for direct application of nanoparticles in antitumor therapy is plasmon photothermal therapy of tumors. PPTT refers to minimally invasive interventionism, in which the energy of external electromagnetic radiation is converted into heat to kill the tumor [11–13]. The main idea of PPTT consists of at least two reasons. One of them touches upon the properties of tumor tissues and another – upon the specific optical properties of NPs. In detail: the tumor tissues grow very rapidly, therefore, the tissue needs to obtain the nutrients and energy in higher amounts. Then the branched system of blood vessels permeates cancerous tissue. It means that the probability to find out NP in the blood vessels of cancerous tissue is very high. Moreover, the walls of the blood vessels of the tumor tissue are pierced by pores of a fairly large size, which enables accumulation of NPs inside the intercell medium of the tumor tissue. *I.e*., the majority of injected into the blood NPs gather in the tumor tissue. Because of the anomalously large absorption cross-section of light by NPs, the absolute majority of incident photons are absorbed by NPs. The photon energy is converted to the heat inside NPs. As a result, the tumor tissue, in which NPs are accumulated, is heated. The cancer cells are very sensitive to the increased temperature. Then, increasing the temperature up to 45 °C leads to thermal destruction of the cancer cells. Note, the choice of NPs of the desired shape and size to provide their resonant frequency falls in the range of transparency of living tissues. This greatly enhances the efficiency of light absorption by NPs, which implies enhancing the efficiency of this method.

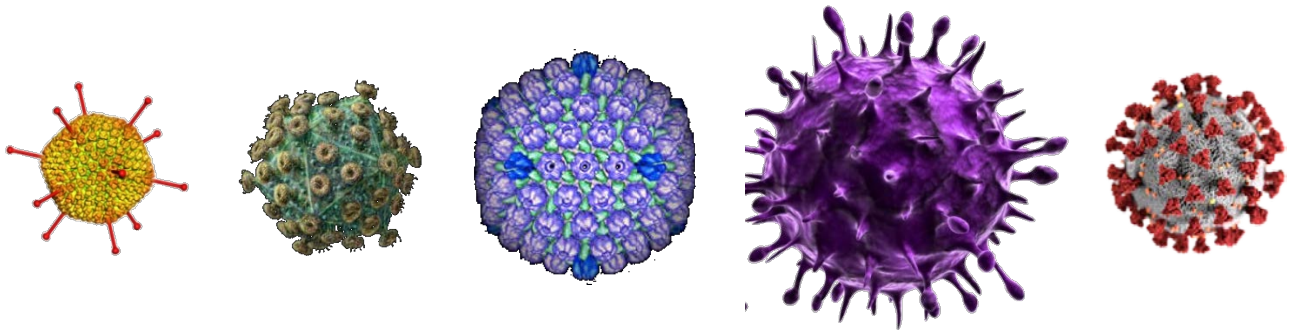
To use NPs for PPTT, one takes into account that the resonant wavelength of NPs should be in the transparency window of alive tissues, and the efficiency of transformation of radiation energy into heat must be high to use the low-intense radiation.

Gold nanorods are known to be efficient converters of photon energy into heat, which results in hyperthermia and suppression of tumor growth. On the other hand, by choosing the desired geometric parameters, it can be achieved that the resonant wavelengths fall into the window of transparency for living tissues (approximately 800…1200 nm). As it was reported in [12], Au nanorods are very promising for plasmon photothermal therapy of different cancer types. From the viewpoint of cancer therapy, low laser powers are essential ($\leq$1 W·cm$^{-2}$) to ensure minimal side effects such as skin burning. The authors of [12] investigated the polyethylene glycol functionalized with reduced graphene oxide (rGO-PEG) enrobed Au nanorods for the photothermal destruction of human glioblastoma astrocytoma (U87MG) cells in mice. It was shown that Au nanorods functionalized with rGO-PEG are effective multifunctional theranostic nano-structures that can exert efficient photothermal destruction of tumors in mice upon low doses of NIR light excitation and can act as fluorescent cellular markers due to the NIR dye integrated into the rGO shell. Due to specific interaction between Tat protein modified with Au nanorods-GO-PEG nanostructures and the human glioblastoma astrocytoma (U87MG) cells, selective targeting of the tumor was achieved. *In vivo* experiments in mice show that upon irradiation of the tumor implanted in mice at 800 nm under low fluxes (0.7 W·cm$^{-2}$), U87MG tumor growth gets suppressed.

## 4. Antiviral and antimicrobial properties of nanoparticles

Viral and bacterial diseases pose a great danger to humanity. In particular, one should mention the plague pandemic in the Middle Ages or the flu pandemic (H1H1 – Spanish) in the early 20th century. Nowadays, the COVID-19 pandemic is changing the modern world beyond recognition. Thus, the fight against these diseases together with the fight against cancer is a serious challenge for modern civilization. The search for antiviral and antimicrobial drugs consists of both traditional methods of pharmacology and non-traditional methods that use the achievements of modern nanoscience. Traditional chemicals based on chemical interaction have a significant disadvantage – viruses and microbes are successfully protected from such drugs through mutagenesis. On the other hand, the physical (field) effect on pathogens is universal and cannot be overcome by simple mutagenesis [14–16]. Consequently, despite the finding of new effective antiviral/antibacterial preparations the looking for new preparations does not finish. In this section, we will consider methods for antiviral and antimicrobial therapy based on the physical interaction between viruses and microbes on the one hand, and NPs on the other.

The search for new antiviral preparations or non-traditional methods for antiviral therapy is a consistent and relevant task. When solving this task, one should take into account the new achievements of modern science and technology, as they can propose to us some interesting and unexpected solutions. One of such solutions can be found in nanoscience. It is well known that various types of NPs occupied an important place in nanomedicine including antiviral therapy. Firstly, NPs were used as nanocarriers for drug delivery. In this case, NPs were functionalized with medicines, which act as antiviral ones [*e.g*., 17–19]. But functionalized NPs act on the viruses or microbes *via* chemical actions of medicines, from which viruses and microbes have the effective defense due to mutagenesis. On the other hand, it is known that non-functionalized (pure) NPs also demonstrate antiviral [*e.g.*, 20–25] and antimicrobial activity [*e.g*., 26–30]. The bright feature of antiviral and antimicrobe action of NPs is its universality, namely, different NPs – metallic, oxides, polymers – demonstrate the effects against various viruses and microbes. But there is no integrated theory for the mechanism of NPs interaction with microbes and viruses, which could explain their antimicrobial and antiviral activity. However, knowledge about this mechanism is required to develop antiviral or antimicrobial drugs and techniques.



*a* *b* *c* *d* *e*

**Fig. 4.** Dimensions of different viruses: *a* – adenovirus ~ 70…90 nm; *b* – human immunodeficiency virus (HIV) ~ 100 nm; *c* – herpes simplex virus I ~ 170 nm; *d* – influenza virus ≤ 200 nm; *e* – coronavirus SARS COV-2 ~ 100 nm.

There are some reasons, which allow supposing that there is some common mechanism for all of the observed effects. In the work [31], we showed that all the mentioned experimental results can be easily explained in the framework of the proposed in [22, 24, 32, 33] idea of the physical mechanism for this action. It indicates that the model of near-field interaction [31] between the nanoparticle and the virus explains all the experimental results.

It is well known that the virus does not demonstrate properties of a living object until entering the cell. It means that there are no biochemical interactions between NP and the virus outside the cell. Furthermore, from the physical viewpoint, viruses can be considered as nanoobjects (Fig. 4). The microscopic investigations performed in [21, 34, 35] showed that NPs are adsorbed on the surface of the virus envelope, which leads to local surface transformations, such as agglutination of glycoproteins [34, 35], preventing penetration of the virus into the cell. Thereby, we consider interaction between the virus and NP outside the cell (NPs act mainly as virucidals or inhibitors of viral entry). Taking into account the mentioned above, one can consider that interaction between virus and NP leading to inhibition of viral infectivity consists of at least three stages: (*i*) adsorption of NP on the virus; (*ii*) formation of local-field inhomogeneous distribution at the virus envelope due to local field enhancement; and (*iii*) appearance of the ponderomotive forces causing the damage of viral molecules up to destruction of viral envelope. It is supposed that the NP adsorption on the virus is caused by physical interaction (similar to van-der-Waals forces). This mechanism is well known and described in detail, *e.g.*, in [36, 37]. This interaction is caused by redistribution of the charges on NP and the virus. In this case, the equilibrium distance of adsorption is about the size of the smallest particle [38], so it is higher than 1 nm. Here, we follow the approach to calculating the energy of interaction between NPs based on finding the ground state of the system by minimizing the free energy of the system similar to that developed in [38–40]. Let us consider two NPs '*a*' and '*b*', situated at a distance *d* one to another (see, *e.g.*, [39]). To obtain the ground state of the system, we shall use the general approach based on minimization of the free energy inherent to the system consisting of two particles. As a result, one can obtain the dependence of the ground state on the distance between the particles. Then, the free energy of the system consisting of two NPs can be written in the form

$$
\begin{aligned}
F = {} & \frac{1}{2}\frac{1}{\varepsilon_0}\int\limits_{\Omega_a} \lambda_{ij}^{a} P_i^{a}(\mathbf{R}) P_j^{a}(\mathbf{R}) d\mathbf{R} - \\
& - \int\limits_{\Omega_a} P_j^{a}(\mathbf{R}) E_j^{a}\left(P_i^{a}, P_i^{b}, \mathbf{R}\right) d\mathbf{R} + \\
& + \frac{1}{2}\frac{1}{\varepsilon_0}\int\limits_{\Omega_b} \lambda_{ij}^{b} P_i^{b}(\mathbf{R}) P_j^{b}(\mathbf{R}) d\mathbf{R} - \\
& - \int\limits_{\Omega_b} P_j^{b}(\mathbf{R}) E_j^{b}\left(P_i^{a}, P_i^{b}, \mathbf{R}\right) d\mathbf{R} + \\
& + \int\limits_{\Re^3} d\mathbf{R}\, \varepsilon\varepsilon_0 \frac{E_i^{2}\left(P_i^{a}, P_i^{b}, \mathbf{R}\right)}{2},
\end{aligned}
\tag{1}
$$

where $P_i^{\alpha}(\mathbf{R}_\alpha)$, $\alpha = a,b$ is the dipole moment of this two-particle system, $\lambda_{ij}^{\alpha}$, $\alpha = a,b$ is the parameter defining the polarizability of the particles, $E_j^{\alpha}\left(P_i^{a,b}, P_i^{b,a}, \mathbf{R}_\alpha\right)$, $\alpha = a,b$ is the self-consistent field at the particles '*a*' and '*b*'. The local field in (1) satisfies the equation [41]

$$
\begin{aligned}
E_j^{\alpha}(\mathbf{R}_\alpha) = {} & E_j^{ex}(\mathbf{R}_\alpha) - k_0^2 \int\limits_{\Omega_a} d\mathbf{R}'_a\, G_{ji}(\mathbf{R}_\alpha, \mathbf{R}'_a)\, P_i^{a}(\mathbf{R}_a) - \\
& - k_0^2 \int\limits_{\Omega_b} d\mathbf{R}'_b\, G_{ji}(\mathbf{R}_\alpha, \mathbf{R}'_b)\, P_i^{b}(\mathbf{R}_b), \quad (\alpha = a,b)
\end{aligned}
\tag{2}
$$

with the external field acting on the system $E_j^{ex}(\mathbf{R}_\alpha)$, $k_0 = \omega/c$, and electrodynamic Green function of the medium into which the particles are embedded $G_{ji}\left(\mathbf{R}_\alpha, \mathbf{R}'_{a,b}\right)$. Here, we use the quasi-point-like particle model, in which we suppose that the particles are polarized as the objects characterized by any dimensions and shapes but interact as point-like dipoles [42].

Thereby, the ground state can be obtained from equations as in [38]

$$\delta F/\delta P_i(\mathbf{R}_\alpha)=0,\ \alpha='a'\text{ or }'b'. \quad (3)$$

Knowing the local polarizations and local fields at NPs, one can calculate the interaction potential between NPs. Interaction potential between NPs can be calculated according to [35]

$$U(R)=-\frac{1}{2}P_i^a E_i^a-\frac{1}{2}P_i^b E_i^b-U(R=\infty). \quad (4)$$

Let us suppose that fluctuations of the vacuum field are the origin of interparticle interaction. As a result, one can write the interaction potential between two different-sized NPs (one is at least 4 times larger than another one) as a function of the distance between the centers of NPs, which may be rewritten as

$$U(R)=\frac{\sigma_1}{R^{12}}-\frac{\sigma_2}{R^6}. \quad (5)$$

Expressions for coefficients $\sigma_1$ and $\sigma_2$ have a bulky look and are presented in [39].

Let us consider the spherical Au NP located near the, say, HSV-I virion. The virion has glycoprotein spikes on its surface [29], which means that its uneven surface should be taken into account. The virion has an icosahedral shape and a much larger size as compared to NPs. All the mentioned above allow simulating the studied system as the spherical homogeneous NP located close to the nanostructured surface. To understand how NP adsorbs on the virus surface, we consider the different locations of NP and calculate the adsorption potential between NP and the surface.

Results of calculations of the adsorption potential of the systems with different NP locations show that the NP adsorption to the virus spike is the most energy-efficient state. It means that NP does not mainly penetrate between the spikes and does not get closer to the virus envelope. Hence, based on the results of calculations, it can be hypothesized that NPs are adsorbed on the virus surface uniformly to its spikes.

This may disturb the virus attachment to the cellular receptors and prevent entry to the cell or fusion with its membrane. The process of the NP adsorption to the HSV-I virion was studied by Cryo-TEM (Fig. 5). It can be seen that NPs likely adsorb to the virus spikes as it was described previously, which indicated that this process is likely caused by the dispersion interaction between NP and the virus.

We have noted above that due to interaction between the virus and NP a stable structure can be formed. The sizes of the objects are much less as compared to the wave-length of the visible light. Then, we can apply the near-field approximation for such systems. It means that the electromagnetic field distribution in such systems is quasi-static and may be described from this point of view [33].

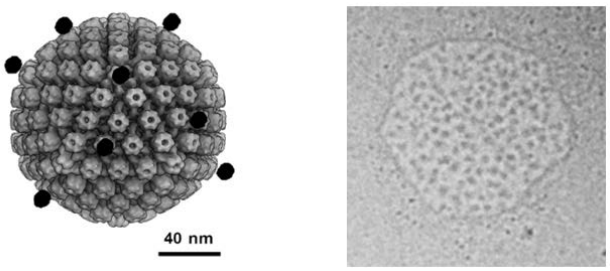



**Fig. 5.** Cryo-TM of the process of the nanoparticle adsorption to the HSV-I virion. Left: hypothetical interaction of Au nanoparticles and HSV-1 virion (The HSV-1 model adapted from [32]). Right: Cryo-TEM of HSV-1/AuNPs 10 nm (1 h incubation time).

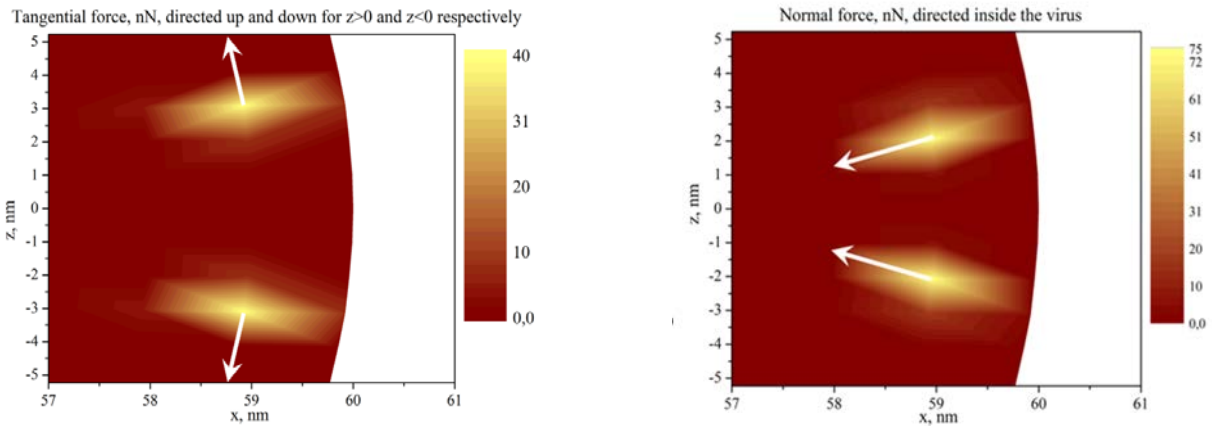



**Fig. 6.** Ponderomotive forces acting on the virus shell (model). The distribution of tangential (left) and normal (right) forces at the shell surface of the nanoparticle of radii 60 nm with the shell of 10-nm thickness (the nanoparticle core dielectric constant $\varepsilon_{core}$ = 2, $\varepsilon_{shell}$ = 4), which is located near the gold nanoparticle of the radius 2.5 nm.

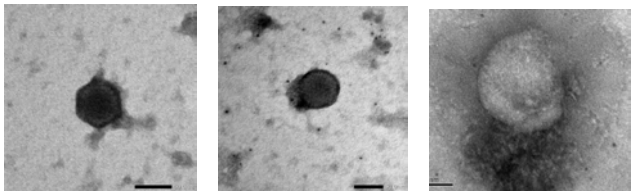


**Fig. 7.** TEM of adenovirus (left) with adsorbed nanoparticles at the virus surface 1 hour after incubation (middle) and after 5 hours of incubation (right).

If knowing the local self-consistent field distribution at the virus shell, one can write the force acting on the virus shell

$$F_i(\mathbf{R}) = \left( P_j(\mathbf{R}) \cdot \frac{\partial}{\partial x_j} \right) E_i(\mathbf{R}). \qquad (6)$$

The distribution of the ponderomotive forces acting on the virus shell is shown in Fig. 6. The system of two NPs – shelling big one and small NP localized at the surface of large NP – is a good model for describing the interaction between the virus and NP at the virus surface. This interaction is the reason of antiviral activity inherent to NPs, which is the base of antiviral properties of preparations of NPs fabricated from various materials. This interaction leads to not only antiviral activity but to the direct destruction of the virus envelope, which is shown, as an example, in Fig. 7. One can see that in both cases the virion envelope was destroyed for 5 hours after incubation.

These results suggest the main principles of the field model of interaction between the virus and NPs.

### 5. Problem of nanoparticles toxicity and solving it

As it was mentioned above, NPs are being employed as a novel drug delivery system, active elements of plasmon photothermal therapy of tumor and systems of tumor visualization. In the recent decade, NPs in antiviral and antimicrobial therapy are widely discussed. NPs are more toxic to health as compared to large-sized particles of the same chemical substance, and it is usually suggested that toxicities are inversely proportional to the size of NPs. Then, the task of extracting NPs from the organism and destruction of NPs located inside the living organs is the most important problem in nanomedicine. The small size of NPs allows them to find their way easily to enter the human body and cross the various biological barriers and may reach different organs. It is considered a well-established fact that NPs of small size (less than 10 nm) can enter human tissues easily and may disrupt the cell normal biochemical environment [44]. There are different ways for NPs to penetrate into living organisms. These methods can be subcutaneous and intramuscular injections, injections into the bloodstream, inhalations, oral penetration, and through mucous membranes. Studies on animals and humans have shown that after inhalation and oral exposure, NPs spread to the liver, heart, spleen, and brain in addition to the lungs and gastrointestinal tract [44, 45]. These organs receive a massive attack of NPs and other methods of penetration of NPs into the body. NPs are hostile agents for living organisms. As a result, the immune system is activated to neutralize the possible pathological effects of these agents on the body. One of the ways for this activity is the removal of NPs from the internal organs and mucous membranes. It is known that the estimated half-life of NP in human lungs is about 700 days; due to the metabolism, NPs can accumulate in the liver tissue for a fairly long period [46, 47]. The way to reduce toxicity related to NPs preparations is obviously to use NPs that either dissolve or break down and are excreted from the body. The first step in this way was made in the work [24], where the complex NPs, namely, Au core with $SiO_2$ shell or the large $SiO_2$ NPs, at the surface of which the small Au NPs were located (see Fig. 8). As the toxicology study has shown, these complex NPs were excreted from the rat body rather quickly. Unfortunately, only preliminary studies have been performed, and the results still need further verification. But the direction of research is already clear – it is necessary to synthesize $SiO_2$-containing nanoparticles, which living organisms either dissolve or excrete from the body.

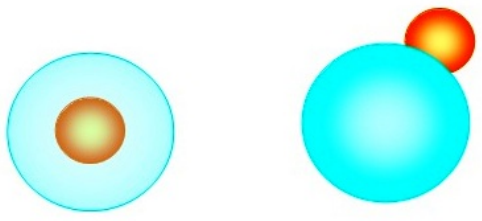


**Fig. 8.** The complex Au-$SiO_2$ nanoparticles are excreted from the rat organism (scheme).

### 6. Nanostructured surfaces and surface plasmon resonance as a base of antiviral therapy

Interaction between the virus and NPs enables to propose the other approach to develop antiviral methods based on the nanostructured surface. Indeed, looking at the microscopic images of the gold surface used in surface plasmon resonance (Fig. 9), one can see that an object near such a surface is able to interact with the protruding part of the nanoparticles located on a perfectly flat gold surface.

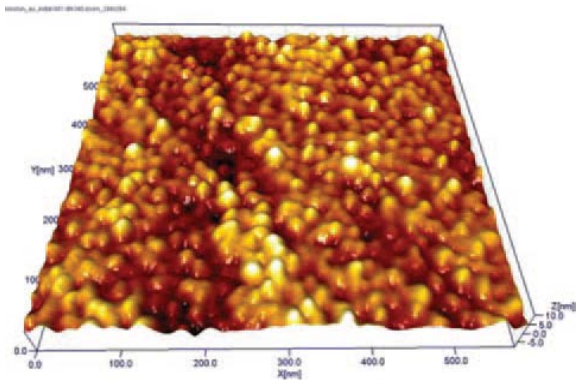


**Fig. 9.** STM scan of the gold film surface along which the surface wave is propagating.

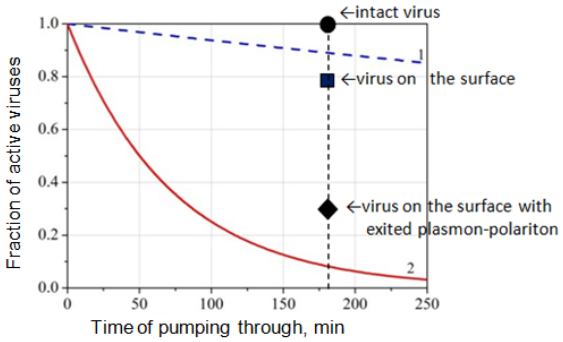



**Fig. 10.** Decreased infection activity of the viruses after pumping. In this plot: *1* – without the influence of surface plasmon-polariton; *2* – under the action of the surface plasmon-polariton. The points in the figure are the average values according to the results of experiments after 180 min of pumping.

And this interaction, as we have seen, leads to the loss by the virus of its infectious properties. When surface plasmon-polariton is excited, its evanescent field can be enhanced due to the acute shape of the roughness unit. As a result, a rather strong local field can be formed at the surface of the viral envelope. This local field can damage the active centers of the viral surface up to destroying the viral envelope. In this case, the viral infectious activity is inhibited by the strong local field acting on the virus receptors located on its envelope. Because of this interaction between the virus and the gold surface, the virus loses its infective activity, and the approach of the virus to the surface leads to inhibition of virus activity. Then, when the active center at the surface of the virus capsid finds itself in the strong local field, this field can destroy/modify it, and the virus becomes unable to penetrate inside the living cell with this activity center. It means that each virus that approaches the surface rather close loses its infectious activity with a probability ~0.2 (approximately 20% of viral capsid surface is under action of the local field in this case).

Then we may calculate the part of viruses that will be still active after a certain number of circulations through the cuvette $N$ and compare them with experimental results. The total time of the preparation circulation, as well as the presence of the surface plasmon-polariton, clearly affects the result of the experiment [48] (Fig. 10).

## 7. Conclusions

Nanoparticles and nanostructured surfaces are widely used in modern medicine for both diagnostics and treatment. The numerous methods of therapeutic effect are being widely developed and laboratory (in some cases – clinically) used for the treatment of oncology and infection deceases. The brightest feature of using the nanoparticles in modern medicine and biology is the wonderful optical properties of nano-objects. The nanoparticles of different nature and with various processing are used as agents for visualization of tumors. The plasmon resonance properties of metal nanoparticles lie at the base of the method for plasmon photothermal therapy of tumors (PPTT). PPTT is used for the treatment of cancer tissues both under lab and clinical conditions. The study of antiviral activity of nanoparticles of different nature, dimensions and shapes is widely applied. The small nanoparticles prepared from different materials demonstrated antiviral activity against different viruses both of DNA and RNA types, namely: the influenza virus, simple herpes virus, adenovirus, *etc*. This fact suggests that action of nanoparticles on these viruses has a general character, which is not related to chemical interactions only. The physical aspects of the antiviral action of nanoparticles are discussed in this work, and most of the known features inherent to the antiviral activity of nanoparticles have been described in the frame of the physical model discussed in this work.

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**Нанофізика у сучасній медицині**

**В.З. Лозовський, В.С. Лисенко, Н.М. Русінчук**

**Анотація.** Нанофізика швидко розвивається останніми роками. Унікальні фізичні властивості матеріалів на нанометровому масштабі є причиною такого швидкого розвитку. Ідеї, матеріали та структури нанофізики знайшли свій широкий розвиток і у суміжних областях сучасної науки, зокрема у біології та медицині. Цей невеликий огляд присвячено питанню про застосування нанофізики у сучасній медицині. Основну увагу зосереджено на застосуванні ідей та фізичних явищ нанофізики в онкології та антивірусній терапії. Ми звернули увагу на використання наносистем як для візуалізації пухлин, так і для боротьби з деякими видами злоякісних пухлин. Коротко розповіли про використання наночастинок як наноконтейнерів для цільової доставки ліків. А також продемонстрували, як ефекти нанофізики можуть бути використаними для розвитку нових нетрадиційних методів антивірусної терапії. У центрі уваги цих методів розглянуто ідею фізичної (польової) дії наночастинок на віруси, яка базується на ефекті посилення локального поля, що є причиною виникнення пондеромоторних сил, що діють на віруси аж до руйнування вірусних оболонок.

**Ключові слова:** нанофізика, наночастинки, онкологія, антивірусна терапія, пондеромоторні сили.