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Structural nucleic acid nanotechnology: liquid-crystalline approach

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1. Introduction

Bionanotechnology constitutes a branch of nanotechnology aimed at the creation of spatial nanoconstructions (nano-objects) possessing dimensional properties and made up of the molecules of biological origin as 'building blocks' [1]. Despite the diversity of biological molecules, real practical results have been obtained so far only in one direction of bionanotechnology, namely, in *nucleic acid nanotechnology*. The last technology is aimed at building the spatial objects (nanostructures and nanoconstructions) with controllable properties, which are made of nucleic acid (NA) molecules or their complexes. This area of bionanotechnology is also called *structural nucleic acid nanotechnology* [2].

In this paper, we consider the basic principles of the liquid-crystalline approach to creating spatial nanoobjects based on double-stranded DNA (deoxyribonucleic acid) molecules with different properties. The physical chemistry of polymers, including nucleic acids and their complexes, shows that a few scenarios of creating such nanoobjects are possible, taking into account the concept of the ordering of neighboring double-stranded NA molecules in particles of liquid-crystalline dispersions.[1]

2. 'Liquid' particles in liquid-crystalline dispersions based on double-stranded DNA molecules

It is known that the phase exclusion of rigid, linear, double-stranded NA molecules [3] with a molecular mass smaller than 1×10^6 Da from the aqueous salt solutions of some polymers, for example, poly(ethyleneglycol) (PEG), is accompanied by the formation of NA dispersions. The phase exclusion efficiency depends on a number of factors indicated in Fig. 1. Two factors, the molecular mass and solubility of double-stranded DNA molecules, are especially important. The higher the molecular mass of DNA, the lower the compatibility of this molecule with the PEG solution, and the higher the phase exclusion efficiency. The lower the solubility of DNA molecules, the higher their immiscibility with a PEG solution and the higher the phase exclusion efficiency [3].

Theoretical estimates based on the application of various methods (sedimentation analysis, scattering of UV radiation, dynamic light scattering, etc.) have shown that for double-stranded DNA molecules with the molecular mass $(0.6-0.8) \times 10^6$ Da, the mean diameter of dispersion particles is close to 500 nm. The molecular mass of one dispersion particle reaches $\sim 10^{10}$ Da, i.e., a particle contains approximately 10^4 DNA molecules [3].

Dispersion particles have several characteristic features. First, a polymer is not contained in dispersion particles. Second, neighboring DNA molecules are separated by a distance of 2.5–5.0 nm, i.e., particles have properties typical for crystals; in addition, neighboring DNA molecules are mobile, i.e., particles possess the property inherent in fluid. These facts allow one to describe such particles using the terms *liquid-crystalline dispersions* (LCDs) or even a DNA *liquid particle*. Third, the interaction between neighboring

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[1] Disperse systems comprise microheterogeneous systems with a strongly developed interface between phases, consisting of two or more phases, at least one of them (the disperse phase) being distributed in the surrounding continuous disperse medium — gas, liquid, or solid — in the form of small particles (crystal particles, drops, bubbles). Instead of the term 'disperse phase', simply the word 'dispersion' is often used. Also, expressions 'polymer dispersions' or 'liquid-crystalline dispersions' are commonly used in chemistry.

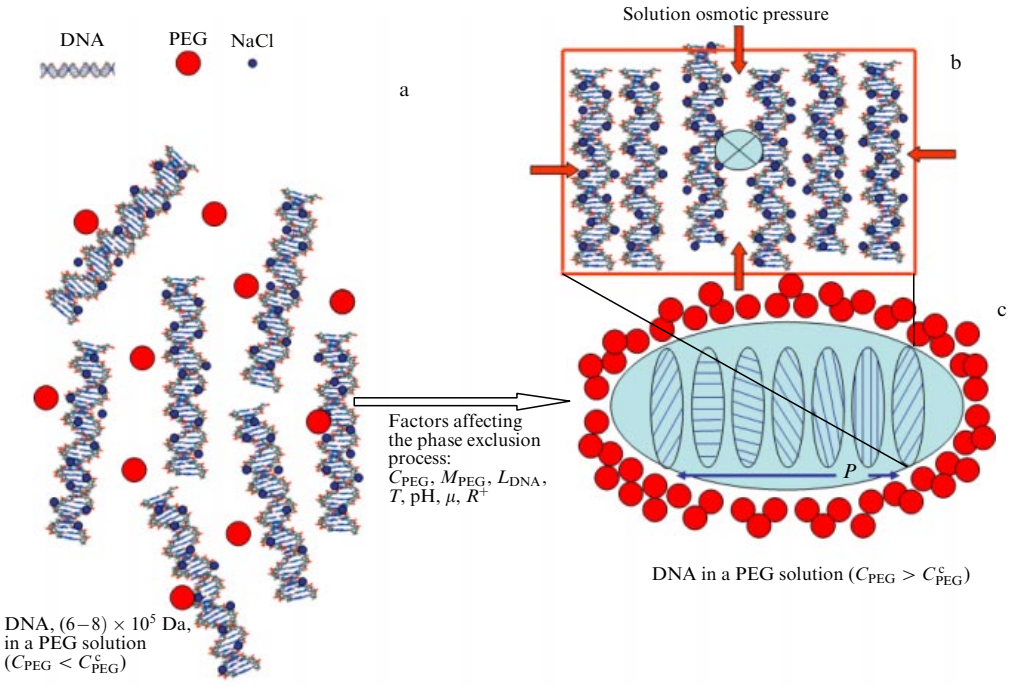

Figure 1. Schematics of the formation of DNA LCD particles by the phase exclusion of rigid double-stranded DNA molecules from an aqueous salt PEG-containing solution: C_{PEG} is the PEG concentration in solution, M_{PEG} is the molecular mass of PEG, L_{DNA} is the DNA molecule length, T is temperature (usual temperature range from 4 °C to ≈ 96 °C), μ is the ionic force of solution (dependent on the salt concentration required to neutralize the negative charges of DNA phosphate groups), and R^+ is the single-charged salt cation used to produce the ionic force of solution. (a) Double-stranded DNA molecules in the PEG-containing solution for C_{PEG} below the critical value of C^c_{PEG} (PEG molecules are shown by circles). (b) A quasinematic layer formed by double-stranded DNA molecules (the circle in the center denotes the rotation axis of the cholesteric structure). The rectangular frame and arrows correspond to the osmotic pressure of the PEG-containing solution. (c) A particle with the spatially twisted (cholesteric) structure having specific optical properties, prepared at a PEG concentration exceeding C^c_{PEG} (P is the step of the helical structure).

DNA molecules leads, due to their chirality, to the formation of the spatially twisted structure of dispersion particles.

All these properties of DNA LCDs, including their lamellar structure [4], were taken into account in the development of the phenomenological theory of circular dichroism (CD) of such particles [5, 6]. This theory described and predicted many features of the CD spectra of DNA LCD particles. Because DNA molecules contain chromophores (nitrogen bases) absorbing UV radiation, the theory predicts the appearance of a very intense (abnormal) band in the CD spectrum of DNA LCDs in the absorption region of nitrogen bases. The presence of this band recorded with a CD spectrometer gives a conclusive indication of the macroscopic (cholesteric) twisting of neighboring quasinematic layers formed by DNA molecules. To also emphasize this feature of such disperse systems, the terms *cholesteric liquid-crystalline dispersion* (CLCD) or DNA *cholesteric* are used [6, 7].

Thus, studies of the physicochemical properties of DNA CLCD particles have given fairly detailed information on the conditions of their formation and factors that can be used to control their properties. This information provides the basis for approaches to the transformation of 'liquid' DNA CLCD particles into 'rigid' bionanoobjects.

3. Formation of 'rigid' particles in liquid-crystalline DNA dispersions

3.1 Physicochemical approach

When estimating the properties of liquid DNA particles, taking into account the polymer chemistry, one would note that only two variants of the physicochemical approach exist for preparing rigid particles in DNA LCDs: (i) the cross-linking of neighboring DNA molecules inside DNA CLCD particles, and (ii) the salting out of DNA molecules inside DNA CLCD particles.

3.1.1 Cross-linking of neighboring DNA molecules inside CLCD particles. Figure 2a displays the hypothetical structure of a 'liquid' double-stranded DNA particle. Based on the general considerations of polymer physics [8], we can assume that the transition of a particle from the 'liquid' state to the 'rigid' state can occur due to the formation of 'bridges' between neighboring double-stranded DNA molecules (Fig. 2b, c). Taking into account the distance between molecules (2.5–5.0 nm, depending on the solution osmotic pressure), such bridges can be called *nanobridges*, the construction produced in this way a *double-stranded DNA-based nanoconstruction* or *bionanoobject*, and the approach itself a *DNA-based nanoconstructing*.

The basic idea of this method of producing rigid DNA particles can be formulated in the following way. *DNA molecules are resided in the 'soluble' state in quasinematic layers of CLCD particles and are separated by 'free' space. The molecules of chemically or biologically active compounds ('guests') entering the free space due to diffusion can 'cross link' neighboring DNA molecules. Such a cross-linking can result in an integrated structure containing all DNA molecules ordered in quasinematic layers of CLCD particles.*

The integrated structure having a very high molecular mass will be incompatible with a polymer-containing solution. This means that the cross-linking of neighboring DNA

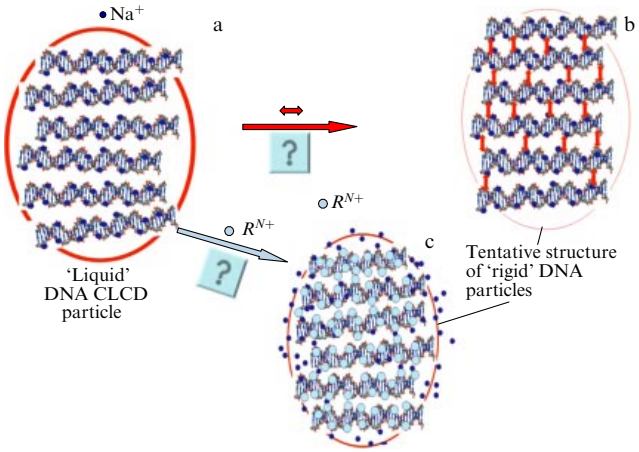

Figure 2. Hypothetical structure of a 'liquid' double-stranded DNA particle (a) and possible ways of transforming it into a 'rigid' particle: by cross linking neighboring DNA molecules or (b) by salting out DNA molecules in quasinematic layers, resulting in the local deformation of molecules in the layers (c). R^{N+} is a multiply charged salt cation used to neutralize the negative charges of DNA phosphate groups; the arrows in Fig. 2b show nanobridges cross linking DNA molecules in quasinematic layers.

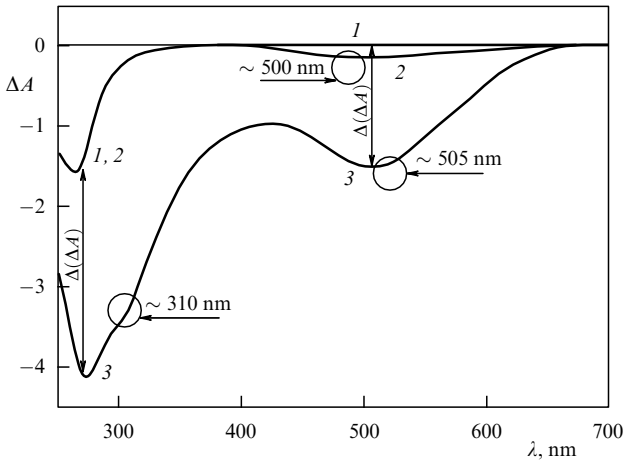

Figure 3. Circular dichroism spectra of DNA CLCD particle before and after its treatment: (*1*) CD spectrum of the initial DNA CLCD, (*2*) CD spectrum of the same DNA CLCD after its treatment by an antineoplastic anthracycline antibiotic (daunomycin), (*3*) CD spectrum of the DNA–daunomycin CLCD complex after its treatment by $CuCl_2$. $\Delta A = (A_L - A_R) \times 10^{-3}$ (in optical units) is the difference between the absorption of left (A_L) and right (A_R) circularly polarized light; the optical path is $l = 1$ cm. $\Delta(\Delta A)$ is the increment of bands due to formation of nanobridges.

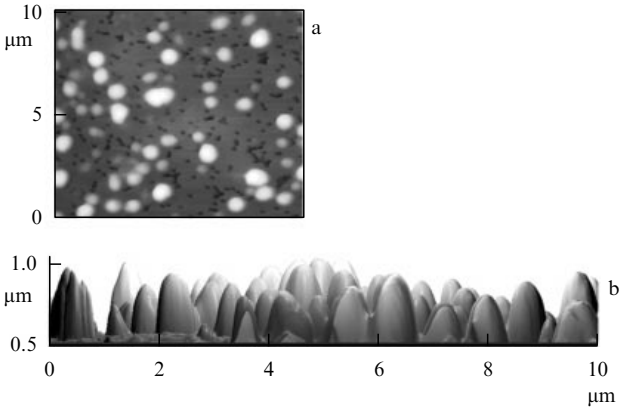

Figure 4. AFM images of rigid particles produced through the formation of artificial nanobridges between double-stranded DNA in quasinematic layers of CLCD particles and immobilized on a nuclear membrane filter: (a) top view, and (b) side view.

molecules will lead to the transition of CLCD particles from the liquid to the rigid state.

From the physicochemical point of view, this method is similar, in fact, to gelation due to the formation of chemical 'cross-links' between neighboring double-stranded DNA molecules (note that we should bear in mind that nanobridges between polymer molecules in classical gelation can have different lengths and can be arbitrarily positioned in space [8]). In the case under study, gelation should be realized in such a way that the fixed distance between neighboring double-stranded DNA molecules in quasinematic layers in one CLCD particle does not change, and the spatial helical structure of DNA CLCD particles is preserved. Therefore, we are dealing with a rather specific gelation process 'inside a particle' with nanometer-scale parameters.

This approach has been implemented experimentally [1]. It was shown that nanobridges consisting of alternating molecules of the anthracycline antibiotic daunomycin and bivalent copper ions link DNA molecules located both in one quasinematic layer and in the neighboring layers. Such a gelation method considerably changes the properties of liquid DNA CLCD particles, transforming them into rigid particles. The formation of rigid particles leads to a drastic increase in the amplitude of the abnormal 270-nm absorption band of DNA chromophores in the CD spectrum, and induce the emergence of an abnormal 510-nm absorption band of daunomycin chromophores contained in nanobridges (Fig. 3).

The stability of rigid DNA particles depends on the number and properties of nanobridges rather than on the solution osmotic pressure. In this case, the possibility arises of immobilizing rigid particles on the surface of a membrane filter and determining their shape and size (the liquid character of packing of DNA molecules in initial CLCD particles makes this impossible). AFM (atomic-force microscope) images of rigid particles are shown in Fig. 4. The shape of the particles is close to sphero-cylindrical and, although their size changes from about 100–200 nm to about 800–1000 nm, the average diameter of particles ranges 400–500 nm, i.e., coincides with the size of initial DNA CLCD particles estimated theoretically for solutions with a fixed osmotic pressure (see above).

The AMF results allow one to estimate several parameters of rigid DNA particles [2]. It was shown that one rigid DNA particle contains approximately 1.6×10^4 DNA molecules and the molecular mass of one rigid particle amounts to $\approx (1.0-1.2) \times 10^{10}$ Da, i.e., it is close enough to the molecular mass of initial DNA CLCD particles formed in the course of the phase exclusion (4.76×10^{10} Da). Finally, the packing density of nitrogen bases (chromophores) in DNA is about 1 chromophore per nm^3. This estimate is also important because it implies that theoretical requirements [6] for the appearance of the abnormal band in the CD spectrum are also preserved in the case of rigid DNA particles.

Thus, the first scenario allows one to prepare rigid DNA particles that can be suitable for manipulations.

3.1.2 Salting out DNA molecules inside CLCD particles. Figure 2 illustrates the results of the second approach to the formation of rigid DNA particles.

The idea of this approach can be formulated as follows. *Neighboring DNA molecules in quasinematic layers of CLCD particles are resided in the 'soluble' state. Multiply charged cations diffusing to dispersion particles can expel sodium ions and efficiently neutralize the negative charges of phosphate groups in DNA molecules, drastically lowering the solubility of these molecules* (*down to DNA precipitation, so-called DNA salting-out*) [3]. *The interaction even between individual parts of neighboring* (*double-stranded DNA–multiply charged cation*) *complexes can lead to the formation of an integrated* (*rigid*) *structure containing all DNA molecules ordered in quasinematic layers of the CLCD particle. The structure produced in this way will exist in the absence of the osmotic pressure of the polymer-containing solution.*

From the physicochemical point of view, this approach differs from that described in Section 3.1.1, because it is based not on the chemical cross-linking of double-stranded DNA molecules, but on the initiation of gelation by virtue of the physical cross-linking of DNA molecules. Such a gelation inside a CLCD particle occurs as a result of the decrease in the solubility of double-stranded DNA molecules (DNA salting-out).

For the case of DNA salting-out, cations of rare-earth elements are of special interest. First, rare-earth cations neutralize the negative charges of phosphate groups in DNA, complexes of these cations with the phosphate groups being virtually insoluble (for example, the solubility constant of gadolinium phosphate is about 10^{-12} M). Second, by interacting with the base pairs of linear double-stranded DNA, these cations cause local distortions of its secondary structure, similar to the known B $\rightarrow$ Z transition [9], i.e., the transformation of the right-handed helical DNA form (B-form) to the left-handed form (Z-form).

The second approach to producing 'rigid' DNA particles was developed utilizing gadolinium salts. It was shown in Refs [10, 11] that, at a certain concentration of gadolinium (Gd) cations in PEG-containing DNA CLCD solutions, the intensity of the negative abnormal absorption band in their CD spectrum increases. The inhomogeneous chemical nature of base pairs in DNA molecules shows its worth in such a way that the interaction of Gd cations with double-stranded DNAs incorporating CLCD particles leads to local distortions in the secondary DNA structure. These distortions cause a decrease in the amplitude (up to complete vanishing) of the characteristic peak in curves of small-angle X-ray scattering on phases formed from DNA CLCD particles treated by the Gd salt solution [12]. (Despite the disappearance of the ordered arrangement of neighboring double-stranded DNA molecules in quasinematic layers, chromophores do not come out from the planes of these layers.)

It should be noted that the CD band intensity increases at a high gadolinium concentration in the PEG-containing solution, at which sodium ions are replaced by gadolinium ions in the immediate environment of double-stranded DNA molecules, and DNA molecules themselves, whose phosphate groups form complexes with Gd ions, lose their solubility (DNA salting-out in CLCD particles occurs [10]). Under these conditions, the interaction between neighboring DNA molecules (their parts) in quasinematic layers enhances, resulting in the formation of the integrated structure of the CLCD particle. The high molecular mass of such a particle, in conjunction with the DNA salting-out, makes the integrated structure incompatible with the PEG-containing solution, and liquid DNA CLCD particles transform into rigid particles.

Such particles can exist in the absence of the osmotic pressure of the PEG-containing solution, which is confirmed by their immobilization on the surface of a nuclear membrane filter. One can see from Fig. 5 that particles exist as independent objects, which suggests that they carry an uncompensated surface charge preventing their aggregation. The average size of rigid particles, lying between 400–500 nm (coinciding with the size of initial DNA CLCD particles), suggests that the high packing density of base pairs (chromophores) in DNA molecules is preserved in 'rigid' particles formed by DNA–Gd complexes.

Thus, the second scenario allows one to produce rigid DNA particles, which can also be suitable for manipulations. Note that the scenarios considered above cover, in fact, all the approaches for producing rigid DNA particles that are possible in the physical chemistry of polymers.

3.2 Nanotechnological approach

The development of nanotechnologies opened up the possibility of another way to form rigid DNA particles.

In recent years, a number of reviews have been published [13–16] devoted to studies of the properties of liquid-crystalline low-molecular compounds in the presence of nanoparticles of different originations. It was shown in these reviews that nanoparticles of different origin not only are compatible with liquid-crystalline phases of low-molecular compounds but, under certain conditions, can change the structure of these phases. Such investigations are composing a new discipline in nanotechnology, which has no name so far, but opens up the possibility of directionally changing optical and electro-optical parameters of liquid crystals with the help of nanoparticles as 'controling' additions and developing new liquid-crystalline materials having novel properties.

The advent of this discipline (Fig. 6) allows us to formulate the idea of the nanotechnological approach to the preparation of rigid DNA particles in the following way. *Double-stranded DNA molecules in quasinematic layers of CLCD particles are resided in the 'soluble' state, and 'free' space exists between these molecules. Nanoparticles comparable in size to the distance between neighboring double-stranded DNA molecules can fill in the free space, playing the role of a homogeneous medium through which the interaction occurs between double-stranded DNA molecules in quasinematic layers. Under these conditions, an integrated structure can be formed, containing all DNA molecules ordered in quasinematic layers of the CLCD particle and incompatible with the aqueous polymer solution.*

From the point of view of nanotechnology, gold nanoparticles (nano-Au) attract the greatest interest. First, nano-Au have unique chemical and physical properties depending on their size, shape, structure, and dielectric environment [17]. Second, it is known that nano-Au can form ensembles (aggregates) near the surface of linear single-stranded DNA molecules. It has been shown that the formation of ensembles from nano-Au is accompanied by the formation of superstructures consisting of alternating double-stranded DNA molecules and nano-Au. These results suggest that DNA molecules after interacting with nano-Au can form planar structures despite the existing anisotropic properties of the initial DNA molecules. Third,

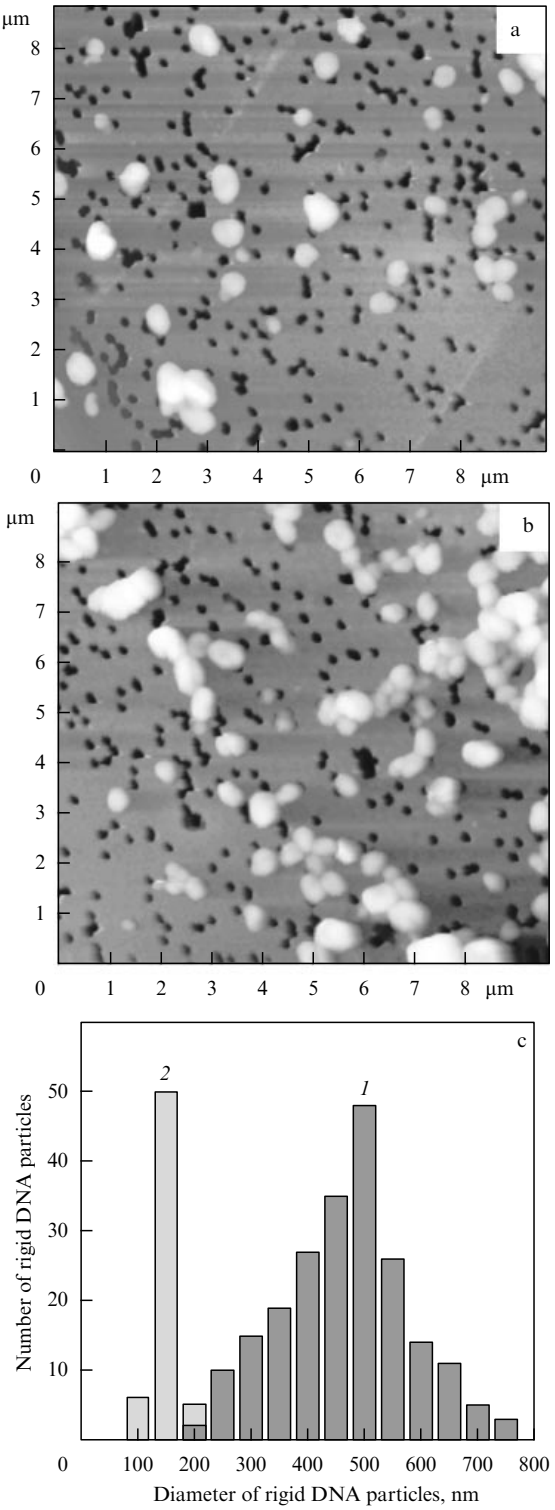

Figure 5. (a, b) Two-dimensional AFM images of rigid DNA particles (at different concentrations) prepared by treating DNA CLCD particles with Gd ions and immobilized on a nuclear membrane filter. Small dark regions are holes in the nuclear membrane filter made of polyethylene phthalate. (c) The size distribution of 'rigid' DNA particles (*1*) and pores in the nuclear membrane filter (*2*).

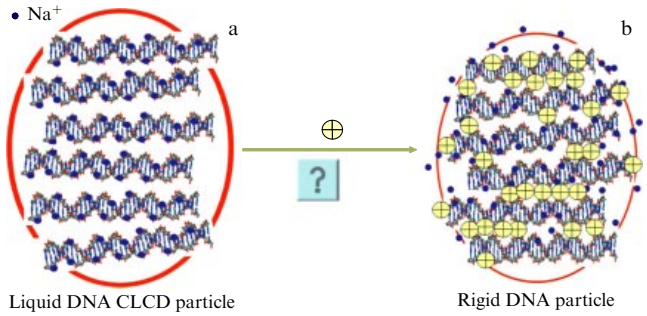

Figure 6. Nanoparticles (shown by crosshairs) comparable in size to the distance between neighboring double-stranded DNA molecules in a liquid DNA CLCD particle (a) can fill in 'free' space, playing the role of a homogeneous medium through which double-stranded DNA molecules interact with each other in quasinematic layers of CLCD particles (b).

the approach of neighboring nano-Au and the formation of aggregates from such nanoparticles near single-stranded DNA molecules lead to the enhancement of the so-called localized surface plasmon resonance (SPR) band in the visible region of the absorption spectrum and the interaction between neighboring 'plasmons' ('plasmon overlap'), accompanied by a red or blue shift of the SPR band, depending on a number of parameters (the distance between particles, the size and shape of the aggregates formed, the permittivity of the medium, the presence of interlayers between neighboring nano-Au, etc.) [17].

Notice additionally that the answer to the question about the reasons for the formation of aggregates from neighboring nano-Au near DNA molecules, especially small-sized nano-Au (5 nm and smaller) is lacking at present [13, 18]. Finally, studies on the action of nano-Au on the properties of liquid crystals or double-stranded DNA LCDs are at the initial stage [24], although the results of such studies would be of interest for both biology [25] and nanotechnology.

The CD spectra of cholesteric liquid-crystalline dispersions formed from two types of NAs and treated with nano-Au are displayed in Fig. 7. One can see that the amplitudes of abnormal bands drastically decreases upon increasing the nano-Au concentration in the polymer-containing solution [the zeta-potential (electrokinetic potential) of nano-Au fall in the range of (30–40) mV, i.e., nanoparticles carry a negative charge]. The amplitude of the abnormal band begins to decrease from the critical concentration of nano-Au, amounting to approximately 1000 nano-Au per DNA CLCD particle and depending on the nanoparticle size. According to the theory in Ref. [6], such a decrease in the optical activity points to the untwisting of the spatial helical structure of CLCD particles, i.e., the nematization of their structure, irrespective of the features of the secondary structure of nucleic acids. Thus, DNA CLCD particles treated with nano-Au, unlike rigid DNA CLCD particles of a different origin, do not have the abnormal optical activity.

This effect of the decrease in abnormal optical activity is unique, because none of the important chemical substances or biologically active compounds interacting with DNA molecules ordered in the structure of CLCD particles cause the nematization of the spatial structure of these particles at room temperature.

A structural analysis of phases formed by DNA CLCD particles and nano-Au was performed by the technique of small-angle X-ray scattering. This analysis showed that: (i) the X-ray diffraction ordering of neighboring double-stranded DNA molecules in such particles is not distorted and the distance between molecules can increase only weakly or not at

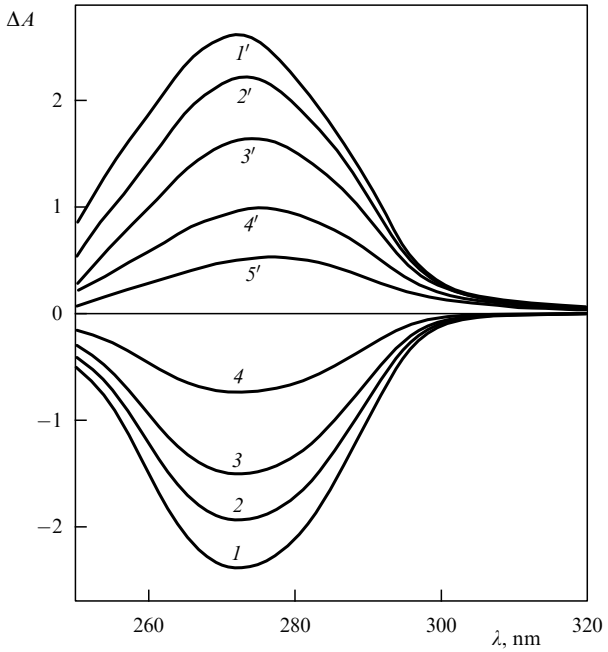

Figure 7. CD spectra of double-stranded DNA CLCD (curves *1–4*) and double-stranded polyribonucleotide (poly (I) × poly (C)) CLCD molecules (curves *1′–5′*) treated with Au nanoparticles (2 nm) at different concentrations; $C_{DNA} = C_{poly\,(I)\times poly\,(C)} = 9\ \mu g\,ml^{-1}$; $C_{PEG} = 150\ mg\,ml^{-1}$; $\Delta A = (A_L - A_R) \times 10^{-6}$ (in optical units), and $l = 1$ cm.

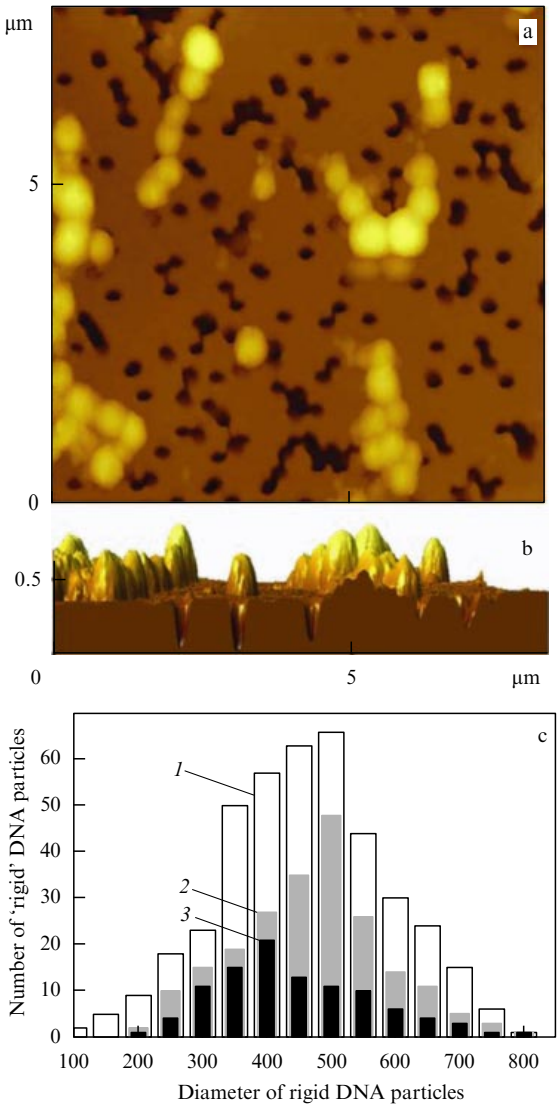

Figure 8. Free space between double-stranded DNA molecules ordered in quasinematic layers of CLCD particles contains gold clusters 40–50 nm in size. (a) Two-dimensional AFM image of rigid DNA particles produced by treating DNA CLCD particles with gold nanoparticles and immobilized on a nuclear membrane filter. (b) Side view of the same particles. (c) Size (diameter) distribution of rigid DNA particles produced by: (*1*) cross-linking DNA CLCD molecules with nanobridges, (*2*) treating DNA CLCD particles with gadolinium salts, and (*3*) treating DNA CLCD particles with gold nanoparticles.

all [12], and (ii) free space between double-stranded DNA molecules ordered in quasinematic layers of CLCD particles contains gold clusters reaching 40–50 nm in linear size [21].

First of all, the formation of gold clusters between DNA molecules can be accompanied by the distortion of the spatial arrangement of neighboring quasinematic layers. Under these conditions, the helical twisting of layers in DNA CLCD particles should change. Second, the fixation of single nano-Au between neighboring DNA molecules and the formation of extended gold clusters between them means that the action of nano-Au on DNA CLCD particles causes their 'metallization'. Third, the formation of gold clusters in free space between DNA molecules fixed in quasinematic layers of DNA CLCD particles leads to an enhancement of the interaction between these molecules, which is realized via single nanoparticles and especially through gold clusters. As a result, the physical cross-linking of neighboring DNA molecules occurs in quasinematic layers. Under these conditions, an integrated structure is formed which includes virtually all the DNA molecules of one particle. The solubility of this structure having a high molecular mass lowers, and it becomes incompatible with the PEG-containing solution. The stability of the integrated structure is determined not by the properties of the initial PEG solution but by the number and properties of single nano-Au and gold clusters contained in the structure. This means that DNA CLCD particles undergo transition from the liquid to solid state. The rigid (insoluble) structure can exist even in the absence of a high solution osmotic pressure (Fig. 8).

Unlike 'rigid particles' formed by virtue of gelation inside particles (Section 3.1), 'rigid' metallized particles of DNA–nano-Au complexes are weakly coupled with the surface of a nuclear membrane filter. As a result, metallized DNA CLCD particles move over the membrane filter surface during the approach of an AFM cantilever, and they can be fixed in certain places on the filter (Fig. 9). The displacement of metallized DNA CLCD particles can also be of interest for nanotechnology, opening up the possibility for manufacturing matrices with specific properties.

Thus, the nanotechnological scenario makes possible the creation of rigid DNA particles that can also be suitable for efficient manipulations.

4. Fields of applications of liquid and rigid nanoconstructions based on double-stranded nucleic acids and their complexes

At the present, we can already talk about the following applications of nanoconstructions built around double-stranded DNA (RNA) molecules:

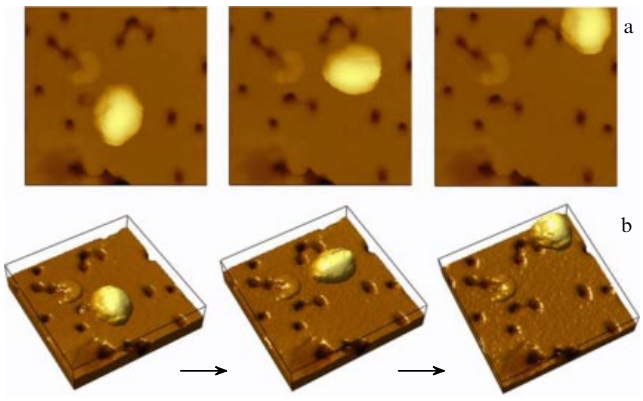

Figure 9. Metallized DNA CLCD particles move over the surface of a membrane filter during the approach of an AFM cantilever and can be fixed at certain places on the filter: (a) two-dimensional AFM image, and (b) three-dimensional AFM image.

(i) 'Liquid' nanoconstructions based on double-stranded DNA (RNA) molecules (or their complexes) are polyfunctional sensor elements (biosensors) for optical analytical systems permitting the detection of biologically active compounds (BACs): antibiotics, genotoxicants, nanoparticles, etc., in laboratory and physiological fluids in *medicine* (*diagnostics, pharmacokinetics*), *ecology, and biotechnology*.

(ii) Rigid nanoconstructions, in which the concentration of DNA (RNA) or 'guest' molecules (BACs) exceeds a few hundred milligrams per milliliter, can be used as carriers of BACs introduced into these structures in *medicine* (*therapy*) and *biotechnology*, for example, as gadolinium carriers in the neutron-capture therapy of new malignant growths.

(iii) Rigid nanoconstructions with controllable physicochemical properties incorporated into polymer films (hydrogels) can be utilized in technics (*optics and electronics*), in particular, as secondary optical activity standards or filters and molecular sieves, etc.

Other examples of practical applications of liquid and rigid DNA particles based on different liquid-crystalline approaches are presented in Refs [1–3].

5. Conclusions

The study of the properties of liquid-crystalline dispersions opens up the way for a new branch of the DNA structural nanotechnology. Considering different approaches to the formation of rigid double-stranded DNA CLCD particles from the point of view of structural nanotechnology, we emphasize once more a number of key points.

First, all the approaches were based on the assumptions of selecting double-stranded DNA molecules forming quasinematic layers in CLCD particles for nano-sized 'building' blocks, with DNA molecules being treated simply as chemical compounds having a specific spatial structure.

Second, in all cases, the process which occurs at nanometer distances between DNA molecules in quasinematic layers was used (this process can be conditionally called *gelation inside DNA CLCD particles*).

Third, all possible scenarios of the liquid-crystalline approach lead to the formation of an integrated DNA structure that is incompatible with the PEG-containing solution.

Finally, although the produced integrated DNA structures have constant spatial parameters, they differ not only in the content of chemically important substances or biologically active compounds, but also in their specific properties.

Thus, the liquid-crystalline approach to structural nanotechnology allows the preparation of rigid DNA CLCD particles (DNA nanoconstructions) with different properties [2], which can find various (sometimes unexpected) applications.

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