Inversion of DNA charge by a positive polymer via fractionalization of the polymer charge

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Charge inversion of a DNA double helix by an oppositely charged flexible polyelectrolyte (PE) is widely used for gene delivery. The positive charge of DNA-PE complex facilitates DNA contact with a typically negative cell membrane making penetration into the cell hundreds times more likely. Charge inversion of DNA-PE complexes was confirmed recently by electrophoresis. If, at a given concentration of long DNA helices, the concentration of shorter PE molecules increases, at some critical point the electrophoretic mobility of a DNA-PE complex changes sign from negative to positive. Intuitively, one can think that when a PE completely neutralizes a DNA double helix new molecules of PE stop adsorbing on DNA. Indeed, the Poisson-Boltzmann approximation for description of screening of a DNA helix by any counterions including PE does not lead to charge inversion. The counterintuitive phenomenon of charge inversion of a macroion by oppositely charged PE has attracted significant attention recently. Such PE “matching”. We also assume that minimal distance that the PE bond length is exactly equal to the distance \( a \) between negative charges of a spiral. It can be explained if one takes into account that the surface potential of an already neutralized DNA is locally affected by a new approaching PE molecule, or in other words, taking into account correlations between PE molecules. Due to repulsive interaction between PE molecules a new PE molecule pushes aside PE molecules which are already adsorbed on DNA surface and creates on the surface an oppositely charged image of itself. The image attracts the new PE molecule leading to charge inversion. This phenomenon is similar to attraction of a charge to a neutral metal.

For quantitative consideration, charges of DNA are often assumed to be smeared and to form uniformly charged cylinder. This approach seems to be justified when density of charge of PE is larger than density of charge at the DNA surface so that most of DNA surface is empty. However, it is clearly far from satisfactory when these densities are almost equal and PE charges strongly compete for charges of DNA (see figures below). Approximation of uniform charge also ignores interference between chemical structure of DNA surface and of PE. Therefore, generally speaking, it is not even clear whether charge inversion exists in the case of discrete charges or it is just an artifact of the assumption of uniformly smeared charge. In this paper, we consider effects of discreteness of charges of DNA. We show that in this case charge inversion exists as well. It can be explained as a result of the “fractionalization” of charge of PE molecules. Such explanation turns out to be even simpler and more visual than for the model of smeared charges of DNA.

Negative elementary charges of DNA phosphates are situated along the two spirals at the exterior of both helices. When unfolded, each spiral is an one-dimensional lattice of such charges, with the lattice constant \( a=6.7\,\text{Å} \). Let us consider a toy model of a PE as a freely jointed chain of \( Z \) small \( +e \) monomers. To maximize the role of discreteness of DNA charge we begin from the assumption that the PE bond length \( b \) is exactly equal to the distance \( a \) between negative charges of a spiral. We call such PE “matching”. We also assume that minimal distance, \( d \), between a PE charge and a charge of DNA is smaller than \( a \). Then PE molecules can attach to a DNA charge spiral in such a way that every charge of the spiral is locally compensated by a PE charge and, therefore, DNA is completely neutralized.

The case of a very short polymer (oligomer) with \( Z = 3 \) is shown in Fig. 1a, as a simplest illustration. The neutralization by a matching PE is so perfect that it is difficult to imagine how another PE molecule can be attached to DNA. Thus, it seems to be impossible to overcharge DNA. In this paper, we show that even in this worst possible for charge inversion scenario, there is a mechanism...
which brings an additional PE to the neutralized DNA and leads to charge inversion. We call this mechanism fractionalization and Fig. 1 shows how this mechanism works for the case of $Z = 3$ When a new PE comes to the DNA double helix which is already neutralized by PE, it creates a place for itself or, in other words, the oppositely charged image in the following way.

In each of $Z$ already-adsorbed PE molecules one PE monomer detaches from DNA surface. This leads to formation of positive defects (tails and arches) and $Z$ negative vacancies on DNA. All $Z$ vacancies can join together and form a large vacancy of a length $Z$ by shifting of adsorbed PE molecules along DNA. A new PE molecule is accommodated in this vacancy. As a result of consumption of this molecule $Z$ defects with charge $+e$ each appear on top of the completely neutralized spiral (see Fig. 1b).

This effectively looks as cutting of the new PE molecule into $Z$ individual monomers and spreading them out along the spiral. In other words, charge inversion of DNA happens by fractionalization of the PE molecule charge. Of course, none of the chemical bonds is really cut, and this phenomenon is solely due to the correlated distribution of PE molecules, which avoid each other at the DNA spiral. In this sense, fractionalization we are talking about is similar to what happens in fractional quantum Hall effect or in the polyacetylene, where many-electron correlations result in the fractionalization of the electron charge.

Fractionalization is driven by elimination of the self-energy of free PE molecules. By the self-energy we mean the energy of repulsive interactions of $Z$ positive charges of the PE molecule in extended conformation which it has in the solution. In the fractionalized state, charges of monomers are very far from each other and practically do not interact, so that the positive PE self-energy is eliminated and, therefore, gained.

In the next section we calculate fractionalization induced charge inversion by a matching flexible PE. In Sec. III we discuss what happens when PE does not match the DNA spiral of charges so that linear densities of charge are different. In Sec. IV we generalize these ideas to adsorption on two-dimensional lattices of discrete macrion charge. We show that in the case of matching flexible PE fractionalization works perfectly even in two-dimensions. This is interesting because many other physical examples of charge fractionalization do not work beyond one dimension. Furthermore, this is the first classical example of real two-dimensional fractionalization. In Sec. V we generalize our theory to flexible polymers, which do not have linear structure. We concentrate there on charge inversion of DNA by dendrimers and show that in this case fractionalization ideas lead to charge inversion, too. In Sec VI, we discuss additional mechanism of charge inversion related to the fact that DNA charges can be accessible from two opposite sides. We conclude in Sec. VII. A short version of this paper is published elsewhere.

II. FRACTIONALIZATION INDUCED CHARGE INVERSION: A MATCHING POLYELECTROLYTE

Let us now calculate the linear density of the net charge of DNA, $\eta^*$, using the fractionalization mechanism. The chemical potential of the PE absorbed at the spiral is

$$\mu_s = Z k_B T \ln (\eta^*/\eta_0) + Z e \psi(0).$$

The first term in the right hand side of Eq. (1) is the chemical potential of the one-dimensional gas of defects ($-\eta_0 \approx 0.6e/\AA$ is the bare charge density of DNA). We used expression for the chemical potential of an ideal gas because the Coulomb interaction energy between defects at the a distance of a few $a$ is much smaller than $k_B T$ ($a \approx l_B$, where $l_B = e^2/D k_B T \approx 7\AA$ is the Bjerrum length.)

The second term in the right hand side of Eq. (1) is the repulsion energy of the new PE from the inverted charge of the DNA. In this term, $\psi(0)$ is the averaged surface potential of the DNA helix. We assume in this paper that the net charge of DNA is screened by a monovalent salt at the screening length $r_s$, which is much larger than $a$. Then $\psi(0)$ can be calculated as the surface potential of a cylinder with radius of DNA helix $R$ and linear density of charge $\eta^*$

$$\psi(0) \approx \frac{2\eta^*}{D} \ln \frac{r_s + R}{R}.$$  

To find $\eta^*$ in the equilibrium state, one has to equate the chemical potential of adsorbed PE molecules with that of a free PE in the solution. The later one can be calculated as following. Due to the repulsive Coulomb interaction between monomers, a free PE in the solution has an extended shape to minimize its energy. Therefore, the chemical potential of a free PE in solution can be written as the self-energy of a rigid rod with the length $Z a$ and
the linear charge density \( e/a \) plus the standard ideal gas contribution \( k_B T \ln(Nv_0) \) \((N\) is the number concentration of free PE in solution and \( v_0\) is the volume of a PE molecule):

\[
\mu_0 = (Ze^2/Da) \ln(L/a) + k_B T \ln(Nv_0) ,
\]
where \( L = \min(r_s, Za) \) and \( D \) is the dielectric constant of water.

Equating the chemical potentials of Eqs. (3) and (4), one has

\[
\psi(0) = \frac{e}{Da} \ln \frac{L}{a} + \frac{k_B T}{e} \ln \frac{\eta_0}{\eta^*} + \frac{k_B T}{Ze} \ln(Nv_0) .
\]

In Eq. (4) one can interpret the right hand side as a “correlation” voltage that (over)charges the DNA to the potential \( \psi(0) \). Complete analysis of Eq. (4) is given in the Appendix. It shows that with growing \( N \) the net charge of DNA \( \eta^* \) experiences a first order transition from negative to positive values. Here we concentrate only at large enough \( N \), where \( \eta^* \) is positive.

Let us make two simplifying approximations. Firstly, we assume that the concentration \( N \) of PE in the solution is large enough so that PE translational entropy term (the last term in Eq. (4)) can be neglected. In other words, we calculate the maximum possible charge inversion. This limit is reached when \( N \gg N_0 \), where

\[
N_0 = v_0^{-1} \exp(-Zl_B \ln(L/a)/a) \quad (5)
\]
is an exponentially small characteristic concentration. For a long PE \( N_0 \) is so small that one does not need large \( N \) to get to this limit.

Secondly, as a good approximation, one can now neglect second term of the right side of Eq. (4), which is responsible for the entropy of defects on DNA. This easily leads to a solution for the net charge density

\[
\eta^* \simeq \frac{e}{2a} \frac{\ln(L/a)}{\ln[(r_s + R)/R]} .
\]

Now one can check that this solution is consistent with the assumption that the entropic term can be neglected by substituting it back into Eq. (4).

Equation (4) shows that \( \eta^* \) is positive indicating that the bare DNA charge is inverted. Knowing \( \eta^* \) and using \(|\eta| = 0.6e/\AA \simeq 3.9e/a \) the charge inversion ratio can be calculated

\[
\left| \frac{\eta^*}{\eta_0} \right| = 0.13 \frac{\ln(L/a)}{\ln[(r_s + R)/R]} .
\]

For DNA \( R = 10 \AA \) and \( a = 6.7 \AA \), so that \( r_s \geq 10 \AA \) the ratio of logarithms can be only slightly larger than unity. Thus, the charge inversion ratio created by fractionalization is limited by 20%. Up to such point we indeed can neglect Coulomb interactions between defects in the chemical potential of the gas of defects (the first term in the right hand side of Eq. (4)).

Remarkably, the extremely crude bead-and-stick model of PE discussed above can give reliable and universal predictions. The calculation described above is not sensitive to many microscopic details and chemically-specific effects on atomic scale. One could worry about behavior of dielectric constant of water at small distances, destruction of water solvation shells, other interactions (van der Waals, hydrogen bonds, etc.) All of them are not important because they all modify energy of interaction of PE with DNA which does not enter in the above calculation. This energy is identical for configurations on Fig. 1a and Fig. 1b. The only difference between these configurations is the self-energy of a free PE molecule, which does not depend on any details of the PE-DNA interaction. Only this self-energy drives charge inversion.

One could also ask about the role of the finite flexibility of PE for the tails. As we all know, freely jointed chain model of polycation is useful on length scales of several nanometers, but is not literally valid even on length scales of 6-7 \( \AA \). We want to emphasize that we do not need ideal flexibility of tails, which lets them to be perpendicular to DNA cylinder surface. The only requirements for flexibility of tails assumed in our calculation is that the tail can be raised in such a way that its end monomer avoids the end monomer the neighboring PE molecule. This requirement is fulfilled in many cases, for example, for the spermine \((Z = 4)\). (One should take into account that the neighboring PE charged monomers are usually connected by a chain of several neutral monomers).

Small arches shown on Fig. 1b, however, are more sensitive to flexibility than tails. If the persistent length of PE, \( l \) is larger than the distance between charges, \( a \), loops (arches) have a typical length \( l \). In a long PE where arches dominate this leads to replacement of \( \ln(L/a) \) by \( \ln(L/l) \) in Eq. (4) and therefore to a somewhat weaker charge inversion.

In the mostly theoretical case of a short and extremely rigid PE when even tails can not bend at all, so that a PE charge of a neutralized DNA is totally incompressible, both fractionalization and charge inversion disappear. This is similar to what happens when Z-ions are hard spheres and one layer of them exactly compensates the uniformly charged background. Charge inversion disappears in these cases, because there are no internal degrees of freedom of molecules to make the system compressible.

Until now we talked about one-dimensional periodic chain of negative charges. If we recall that in DNA this chain actually is a spiral we face another requirement for the flexibility of a long PE. A PE molecule should be flexible enough to follow DNA spiral. Most of PE can do that, for example spermine does\([3]\). On the other hand, extremely rigid long PE can not follow a spiral of charge and, therefore, screens DNA as an uniformly charged cylinder, namely PE rods in this case arrange themselves at its surface collinearly with the cylinder axis and each other.
Absolutely rigid a new PE molecule creates with vacant places (see Fig. 2a). Even if the PE is an analog of Wigner crystal where PE molecules alternate. In this case, PE molecules due to Coulomb repulsion form grain boundaries (domain walls), where one vacancy is missing. Charge of each grain boundary is +\(e\). Wigner-crystal-like ground state of a periodic chain of negative charges neutralized by PE molecules with \(Z = 3\) and \(b = a/2\) (their charges are shown by black spheres). A new PE molecule is approaching DNA. b) The new PE molecule is "digested" by DNA. Its charge is split in +\(e\) charges of \(Z\) grain boundaries.

Concluding this section, we would like to say that the discreteness of charges does not prevent charge inversion even in the worst case of perfect matching.

III. Polyelectrolyte with Non-Matching Density of Charge

How does fractionalization work when distance between charges of PE, \(b\) is not equal to the distance between charges of an unfolded DNA spiral, \(a\)? Consider, for example, commensurate PE with \(b = a/2\), which has linear density of charge twice larger than a DNA spiral. In this case, PE molecules due to Coulomb repulsion form an analog of Wigner crystal where PE molecules alternate with vacant places (see Fig. 2a). Even if the PE is absolutely rigid a new PE molecule creates \(Z\) distant grain boundaries (domain walls), where one vacancy is missing (see Fig. 2b). The charge of each grain boundary is +\(e\), so that charge of the new PE molecule is fractionalized, and a part of the self-energy of PE is eliminated in the way similar to what happens in the case of matching PE.

Fractionalization continues to work when the linear charge density of multivalent counterion (Z-ion) is even larger. We can imagine such limit, when replacing PE with a metallic multivalent ion (for example, \(La^{+3}\)), which touches only one negative charge of DNA. Then we arrive at a ground state of neutralized DNA which resembles Wigner crystal even closer (see Fig. 3a). Fractionalization of a new charge into \(Z\) monovalent charges of grain boundaries (see Fig. 3b) decreases self-energy and drives charge inversion. In contrary to obvious elimination of interaction between monomers in the case of Fig. 1, it is more difficult to see how self-energy is eliminated in Figs. 2 and 3. For example, to get an idea how this happens in the case of Fig. 3 it helps to draw a sphere with radius a bit larger than \(a\) both around the new free Z-ion on Fig. 3a and around the center of each of \(Z\) domain walls on Fig. 3b. They are shown by broken circles. Let us consider now what happened to the energy of the electric field of the new Z-ion concentrated in the external space of these spheres. Due to fractionalization of Z-ion the energy of the charge \(Z\) is clearly replaced by the smaller sum of \(Z\) energies of monovalent ions. This illustrates what we mean talking about elimination of the self-energy in this case.

In Fig. 3 we already arrived at a model of charge density wave and fractionalization in polyacetylene and a very crude picture for the fractional Hall effect at filling factor 1/3. In the latter case, empty circles mean discrete Landau states and an electron charge −\(e\) is split in 3 charges −\(e/3\).

Fig. 3 also resembles what happens in the case of adsorption of Z-ions on the line of surface with uniform distribution of background charge. In that case, the charge of a new Z-ion is smeared along the background due to small elastic deformations of Wigner-crystal-like strongly correlated liquid. In other words, Z-ion is fractionalized into infinitesimally small portions. One can visualize the transition to the case of uniform surface charge imagining that both elementary charge of our lattice and lattice constant \(a\) vanish, while charge density of DNA and charge of Z-ion are kept constant.

Let us return to adsorption of PE with a finite linear charge density on DNA and discuss more complicated situations, when \(b < a\), but \(b\) and \(a\) are incommensurable. Even in this case ground state of a neutralized DNA is a crystal. If an additional PE molecule is adsorbed it is still fractionalized to \(Z\) grain boundaries with charge +\(e\). The only difference from commensurate case shown on Fig. 2 is that grain boundary can include several PE molecules.

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FIG. 2: The origin of charge fractionalization for a PE with linear charge density twice larger than for a DNA spiral. a) A Wigner-crystal-like ground state of a periodic chain of negative charges neutralized by PE molecules with \(Z = 3\) and \(b = a/2\) (their charges are shown by black spheres). A new PE molecule is approaching DNA. b) The new PE molecule is "digested" by DNA. Its charge is split in +\(e\) charges of \(Z\) grain boundaries.

FIG. 3: The origin of charge fractionalization for multivalent counterions. a) A Wigner-crystal-like ground state of a periodic chain of negative charges (white spheres) neutralized by PE molecules with \(Z = 3\) (larger black spheres). The new Z-ion is "digested" by DNA. Its charge is split in +\(e\) charges of \(Z\) grain boundaries. Broken circles are explained in the text.
IV. FRACTIONALIZATION OF POLYELECTROLYTE CHARGE IN TWO-DIMENSIONS

It is well known that fractionalization of charge of Z-ions into free (to move to infinity) grain boundaries shown for example in Fig. 3 can not be generalized to a two-dimensional case. Let us imagine a two-dimensional analog of the problem of Fig. 3 using a square lattice of monovalent negative charges which is neutralized by Z-ions with charge $Z = 4$ forming a square lattice with period $2a$. If we bring another Z-ion and try to split it into two point like grain boundaries with charge $+2e$ along the main axes of the square lattice, we realize that the lattice of Z-ions loses energy everywhere between them because of the shear deformation created (See Fig. 4). This is equivalent to a string between charges $+2e$ with energy proportional to length. Thus, charges $+2e$ of the defects are not permitted to move very far away from each other. In other words, they are confined in a finite domain.

Nevertheless, in the first approximation, charge inversion can be still calculated as if products of the Z-ion fractionalization were free to move to infinity. Indeed, one can estimate the defect confinement size and find that it is much larger than $a\sqrt{Z}$ (the average distance between Z-ions on the surface), because the energy of abovementioned strings is proportional to the shear modulus of the Coulomb lattice of Z-ions on the negative background lattice which is known to be numerically small. Therefore, most of the self-energy of Z-ion concentrated in the electric field at radius larger than $a\sqrt{Z}$ is eliminated in spite of defects confinement.

Remarkably, for a reasonably flexible matching PE fractionalization into free tails and arches is not a strictly one-dimensional phenomenon. It is easy to see that the same mechanism applies equally well to a two-dimensional square lattice of discrete negative charges with the lattice constant, $a$, equal to the PE bond length $b$. Indeed, one can see in Fig. 5 that all previous arguments about the role of tails and arches can be carried over to this case. There are no strings between tails and arches in this case. This is a remarkable consequence of the involvement of additional degrees of freedom related to the third dimension. We do not know any other classical example of charge fractionalization in a really two-dimensional system.

There are, however, small modifications of the analytic formulae for charge inversion. Defects with $+e$ charges form now a two-dimensional gas with concentration $\sigma^*/e$, where $\sigma^*$ is the net positive surface charge density playing the roles of $\eta^*$. The chemical potential of this gas is $k_BT\ln(\sigma^*/e)$. The surface potential is $\psi(0) = 2\pi\sigma^*r_s/D$. The balance of the chemical potential of PE molecules adsorbed at the surface with that of a free PE in the solution reads

$$\frac{2\pi\sigma^*r_s}{D} = \frac{e}{Da} \ln \frac{L}{a} + \frac{k_BT}{e} \ln \frac{e}{a^2\sigma^*} + \frac{k_BT}{Ze} \ln(Nv_0).$$ (8)

Again, assuming that the PE concentration $N$ is large (or calculating the maximum possible charge inversion) the solution to Eq. (8), for $a \approx l_B$, within a numerical factor, is

$$\sigma^* \approx \left( e/\pi r_s \right) / \ln(r_s/a).$$ (9)

One can see that, for $a \approx l_B$, in the free energy gained by fractionalization of the PE molecule charge, the entropy contribution is comparable to the self-energy, in contrary with the one-dimensional case, where the entropic term can be neglected. This is due to a higher number of degrees of freedom which a two-dimensional surface provides to the gas of defects. If $r_s \gg a$, the charge inversion ratio for the two-dimensional case is smaller than for DNA:

$$\frac{\sigma^*}{e/a^2} = \frac{a}{r_s} \ln \frac{r_s}{a}. $$ (10)
An important role of elimination of the self-energy for adsorption of a flexible PE on an oppositely uniformly charged surface can be traced in Refs. 4, 6, 13.

V. CHARGE INVERSION OF DNA BY DENDRIMERS AND FRACTIONALIZATION

Until now we considered adsorption of linear charged molecules (PE) both on one- and two-dimensional lattices of the background charge. It is interesting to note that the fractionalization mechanism works for molecules of other shapes, too. Let us, for example, consider dendrimers (star-like branching molecules with a large number of monovalent positive charges on their periphery), which were also shown to invert the charge of DNA[5]. Dendrimers with charges \(Z = 4\), 8 can easily compensate a compact group of nearest \(Z\) charges of both DNA helices. If a DNA double helix is totally covered and neutralized by such dendrimers (see the schematic Fig. 6a for \(Z = 4\)) an additional dendrimer can still be adsorbed on DNA. This happens because two charges +\(e\) of two distant already adsorbed dendrimers can be raised above the DNA surface when a new dendrimer molecule is adsorbed on DNA (see Fig. 6b). As in the case of linear molecules, this fractionalization of the dendrimer with charge +4e into two charges +2e leads to the gain of its self-energy and to charge inversion.

Again we see that all these phenomena became possible only due to the additional of freedom of PE molecules, which in this case is rotational. (Fractionalization into charges +\(e\) in this case can leads to a larger energy because all adsorbed dendrimers between two dendrimers raising one tail should be deformed leading to a string with energy proportional to the length between them.)

If we deal with higher generations of dendrimers which have very large charges such as 32e or 64e, we arrive at a different Wigner-crystal-like picture (see Fig. 6). Because of the three-dimensional structure of their chemical bonds these molecules cannot expand enough so that each charge of them reaches an opposite charge of DNA and compensates it. In other words, when projected to a DNA double helix, these high generation dendrimers have much larger linear density of charge than the double helix itself. Thus, large segments of the helix between adsorbed dendrimers remain negatively charged, and form a Wigner-Seitz cells around each dendrimer. This is how with growing charge of dendrimers the fractionalization mechanism is replaced by the mechanism of Wigner-crystal-like correlations. Qualitative difference between DNA complexes with dendrimers of low and high generations has been clearly demonstrated experimentally[6]. Because large fraction of DNA charges is not neutralized by dendrimers the high generation complexes are more sensitive to the salt concentration.

VI. SHARING OF DNA CHARGES AS A MECHANISM OF CHARGE INVERSION

Let us return to complexation of a DNA double helix with PE molecules with the matching bond length, \(b = a\), and discuss another possible mechanism of charge inversion, which is also related to the discreteness of DNA charge and further increases the positive charge of DNA-PE complex. Let us consider a monomer tail of PE on Fig. 6, and explore whether some energy can be gained if the positive charge of this monomer moves down to the plane of DNA charges, approaches already neutralized negative charge of the DNA and shares it with the end monomer of the neighboring PE molecule in a way shown in Fig. 6. If these two end monomers may sit on exactly opposite sides of the negative charge of DNA, the additional energy \(e^2/2d\) can be gained, where \(d\) is the distance of the closest approach of a PE monomer and a DNA charge. At a sufficiently small \(d\) this energy can be even larger than the gain per tail from elimination of the self-energy. In a DNA double helix, all the negative charges indeed are on the ridge above neighboring neutral atoms. Two sufficiently small monomers may fit into the large and small groves on both sides of the ridge. On the other hand, if because of sterical limitations they can not be in the perfect opposition the energy gain is smaller. If both end monomers PE have the same size as the negative charge of DNA the additional energy of...
a) DNA double helix (gray) neutralized by a Wigner-crystal-like liquid of a high generation dendrimers (dark spheres). A new dendrimer molecule is approaching DNA. b) The new dendrimer molecule is integrated into Wigner-crystal-like liquid while neighboring already adsorbed dendrimers slide away from it and smear its charge over the helix.

FIG. 8: A view from the top on an unfolded spiral of negative charges of DNA (white spheres) and two PE molecules (black). Two positive end monomers share a negative charge of DNA in the perfect opposition. Sharing vanishes when all three spheres touch each other forming equilateral triangle. This still leaves room for sharing effect, while say one monomer perfectly fits in large grove but the second one only partially fits in the small grove.

VII. CONCLUSION

The main result of this paper is that discreteness of surface charges of a macroion, for example, double helix DNA does not prevent its overcharging by oppositely charged PE and other Z-ions. For a flexible PE even in the worst scenario of matching PE and DNA geometries, when in the neutral state all charges of DNA are perfectly neutralized by PE, charge inversion happens due to fractionalization of PE charge into +e charges of defects. This is extremely transparent mechanism as illustrated on Fig. 1. It is clearly related to internal degrees of freedom of a flexible PE. In the non-matching cases, the mechanism of charge inversion for discrete surface charges looks more similar to the one previously discussed in a model of uniformly charged macroion surface, but still is accompanied by fractionalization.

In conclusion, we emphasize that in any case charge inversion happens due to the fact that a new PE molecule rearranges already adsorbed PE in such away that its image or correlation hole strongly attracts this new PE molecule. This physics can not be described by the Poisson-Boltzmann theory because this theory uses the mean-field potential which does not depend on the position of a new PE molecule.

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APPENDIX A: CHARGE OF DNA AS A FUNCTION OF POLYELECTROLYTE CONCENTRATION

In Sec. 1, we assumed the bulk PE concentration, \( N \), is very large so that the translation entropy cost of condensing them on DNA can be neglected. Equation (6), thus, gives the upper limit for the DNA net inverted charge. On the other hand, at very small \( N \), the entropy cost cannot be neglected and leads to the undercharging of DNA. In this appendix, we would like to calculate \( \eta^*(N) \) explicitly and show that in the matching case DNA molecules change their sign with increasing \( N \) by a first order phase transition.

When DNA is undercharged, \( \eta^* < 0 \), instead of a gas of raised monomers (tails and arches) on the DNA surface, one has a gas of vacancies. These are the DNA charges which are not covered by any PE monomers. At low concentration (small undercharging), these vacancies practically do not interact and their chemical potential can be approximated by that of an ideal gas at the same concentration \( k_B T \ln(\eta_0/|\eta^*|) \). Thus, Eq. (4) needs only a small modification to properly describe both the over- and under-charged DNA:

\[
\frac{2\eta^*}{e/I_B} \ln \frac{r_s + R}{R} - \ln \frac{\eta_0}{|\eta^*|} = \frac{1}{Z} \ln \frac{N}{N_0} \quad (A1)
\]

where the second term is the chemical potential of raised monomers in the overcharging case and it is the chemical potential of vacancies in the undercharging case. In Eq. (A1), we have also combined two terms of Eq. (4) using the characteristic concentration \( N_0 \) given by Eq. (6).

It should be noted that, the apparent divergence of the left side of Eq. (A1) at small \( \eta^* \) is related to the fact that we neglected a small concentration of intrinsic defects (raised monomers and vacancies). This concentration is
of the order $a^{-1}\exp(-e^2/2\hbar B T)$. It exists even at $\eta^* = 0$ and truncates the divergence of $\ln(\eta_0/|\eta^*|)$ at small $\eta^*$. However, when $|\eta^*| \gg e a^{-1}\exp(-e^2/2\hbar B T)$ one type of defects dominates over the other and one can neglect the contribution from the minority ones. This is what we did in Eq. (A1).

To understand how $\eta^*$ varies with $N$, it is very instructive to solve Eq. (A1) graphically. One can see the following behavior:

When $N$ is large such that $N > N_1$, where

$$\ln(N_1/N_0)/Z = -1 - \ln(2\eta_c\ln(r_s + R)/\epsilon/|e|B),$$

Eq. (A1) has only one solution for $\eta^*$. This solution is positive, indicating that the DNA helix is overcharged.

When $N$ decreases a little bit below $N_1$, there are three solutions $\eta_1^* > 0 > \eta_2^* > \eta_3^*$ of Eq. (A1) (Fig. 9a). The solution $\eta_1^*$ corresponds to the stable overcharged state. The solution $\eta_3^*$ corresponds to the metastable undercharged state. The solution $\eta_2^*$ is unstable (it corresponds to a local maximum in the grand potential of the system located between two local minimums at $\eta_1^*$ and $\eta_3^*$.)

When $N$ decreases below $N_0$, where $N_0$ is defined as the PE concentration at which the two shaded areas in Fig. 9 equal each other (Maxwell rule), a first order phase transition happens. (Note that at $\exp(-e^2/2\hbar B T) \ll 1$ a calculation of $N_c$ can be done with help of Eq. (A1) because the truncation due to intrinsic defects produces only a small correction to one of areas.) The overcharged solution $\eta_1^*$ becomes metastable while the undercharged solution $\eta_3^*$ becomes stable. Thus, the function $\eta^*(N)$ has a finite jump at $N = N_c$. This function is plotted by the solid line in Fig. 9b. The metastable branches of $\eta^*(N)$ are plotted as the dashed line.

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