

DNA-Dendrimer Nano-Cluster Electrostatics Prediction with the Nonlinear Poisson-Boltzmann Equation

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A DNA-dendronized polymer nano-cluster (or inclusion aggregate) is generally formed by wrapping the DNA around a dendronized polymer which has a cylindrical shape. The electrostatic free energy in terms of different contributions of fixed and mobile charges and the entropic free energy of mixing of mobile species and solvent have been determined by solving the nonlinear Poisson-Boltzmann equation. The electrostatic potential generated around the nano-cluster, which plays a central role in biological systems, is determined by a finite-difference method. Thermodynamics of fixed ions, mobile ions, solvent and total system is considered for several conformations in different ionic strengths. It is shown that in a series of conformations at constant temperature and constant ionic strength, the electrostatic and entropic free energies primarily decrease sharply and then smoothly increase with increment of the wrapped DNA pitches. This indicates that the average concentrations of positive and negative mobile ions have been increased and decreased, respectively in these conformations.

Keywords: Clustering, Dendrimer, Dendronized Polymer, DNA, dsDNA, Electrostatic Energies, Electrostatic Free Energy, Entropic Free Energy, Nano-Cluster, Nano-Cylinder, PAMAM, Poisson-Boltzmann Equation, Gene Therapy.

1. INTRODUCTION

There is a great deal of interest in DNA-dendronized polymer nano-cluster (or inclusion aggregate) formation for DNA delivery to cells in the human body. For example, DNA/PAMAM (Polyamidoamine) dendrimer complex is used for DNA delivery to cell nucleus due to its high transfection efficiency and very low toxicity.

Dendrimers are unique macromolecules that have applications in developing strategies for globular shapes with small cores. Dendronized polymers are cylindrical macromolecules that are composed of a linear polymeric backbone and dendritic side chains (Fig. 1). The thickness of the polymers is in the range of several nanometers. These nano objects have gained interest because of their cylindrical structure, which provides new unique properties that could be applied within the emerging field of nanotechnology.^{1,2} In the present report we have

developed an analytic computational scheme for calculation of thermodynamic behavior of dendronized polymer and DNA interaction for a nano-cluster formation. The DNA-dendronized polymer nano-cluster is formed by wrapping the DNA around the dendrimer. Electron microscopy photographs of dendronized polymer have revealed³ a cylindrical shape with its core made of polystyrene chain and its branches are PG2 (a polystyrene which substituted with the branch cells of the type G2 of PAMAM). High positive-charged-density due to the presence of protonized primary amine group (NH_3^+) on the surface of poly-amidoamine dendrimers (PAMAMs), provide a suitable condition for it to form a nano-cluster with DNA. These nano-clusters are candidates for DNA delivery to living cell systems.⁴⁻⁷

The charged polymers exhibit a variety of unique behaviors such as phase transition,⁸ specific adsorption,⁹ and aggregation.¹⁰ These behaviors are related to the electrostatic interactions between the charged polymer (particles) and their environment. The mathematical models, which are based on the electrostatic potential, can be applied to predict the behavior of these systems.¹¹⁻¹³ For example,

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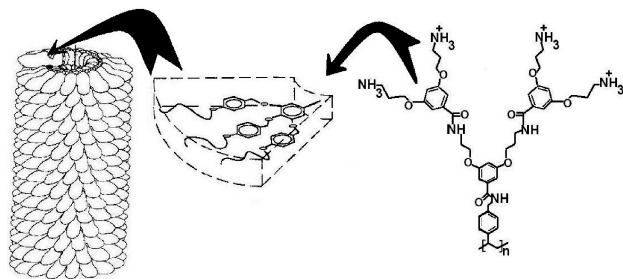


Fig. 1. Chemical structure and formation of PG2-PMAMA dendronized polymer nano-cylinder.

the Poisson-Boltzmann equation (PBE) has been used to simulate such systems. The simulation results have revealed there are various unusual phenomena related to a strong electrostatic field, existing around a polymer chain.¹¹

It is a well-known fact that the double stranded DNA (dsDNA) is an important biopolymer, which has a helix conformation. It has been considered to form a flexible-rod shape, which has nontrivial elastic properties, and under the influence of different forces forms various shapes.¹²

Gene therapy is a new process, which plays an important role in genetic science and engineering. In this process DNA must be delivered into the cell and, simultaneously, it must be protected from enzymatic degradation. For this purpose, DNA-dendronized polymer nano-clusters are suggested. Such nano-clusters are formed between DNA and a number of synthetic vectors or carrier systems, including polylysins, cationic liposomes and cationic polymers¹⁴ by which their positive electrostatic field condenses and aggregates the DNA. Dendronized polymers are a new class of synthetic cationic polymeric agents, which have the ability to have similar applications to the vector systems in DNA delivery.¹⁵ Dendronized polymers are made of three major architectural segments including; a core, an interior (branch cells), and a set of terminal groups. The unique shape of a Dendronized polymer and its size depend on its core and its interior repeated units of branch cells, while its terminal groups determine its reactivity.^{3, 16}

Park et al.¹⁷ proposed a theoretical approach, based on the linearized PBE, to describe the spontaneous overcharging of a negatively charged flexible chain wrapped around a positively charged cylinder of infinite length. They could predict capacitive charging energy of the resulting nano-cluster near its isoelectric point. They also found the entropic effects of electrostatic charges, which have an important role in the formation and conformation of a nano-cluster. Kunze et al.¹⁸ studied clusteration between a stiff charged cylinder and an oppositely charged semi flexible polymer by considering the bending, attraction, and repulsion energies between the two in their model. They investigated the helix and straight conformations and reported phase diagrams for these two conformations. Since they used the linear Debye-Hückel theory, their results were valid only for large enough salt concentrations in the environment of the nano-cluster or weakly charged polymers.

Generally, the electrostatic potential of the environment of a DNA-dendronized polymer nano-cluster should play a central role in formation of this system. The aim of the present work is to determine the role of this factor and its related thermodynamic impact, which has not been previously investigated.

2. THEORY

We have theoretically designed a model of DNA-dendronized polymer nano-cluster, which consists of the following parts as shown in Figure 2:

1. A polystyrene chain as a core, G2-type cells as the branch cells and NH_3^+ as terminal groups. These three segments form a cylindrical shape with a finite length.
2. A DNA chain with defined length, which forms a semi-flexible polyelectrolyte chain with negatively charged phosphates that wraps around the cylindrical shape of part 1.
3. A solvent (medium) with variable ionic strengths.

A finite-difference numerical computational method is used to solve the nonlinear PBE in a 3-D space. Thermodynamic properties, including the entropic free energy of mixing of solvent ΔG^{solv} , and of mobile species ΔG^{mob} , the electrostatic free energy for fixed ions ΔG^{ef} , mobile ions ΔG^{em} , and total system ΔG^{el} are calculated for several conformations of nano-clusters immersed in different ionic strengths media and the stability of conformations are investigated.

The Poisson-Boltzmann equation (PBE) has been derived from Poisson equation.¹⁹

$$\nabla \cdot \epsilon(\vec{r}) \nabla \psi(\vec{r}) = -\rho(\vec{r}) \quad (1)$$

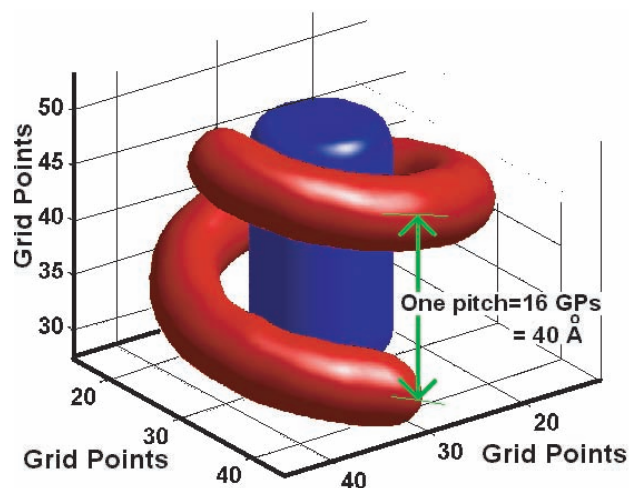


Fig. 2. Format of DNA wraps around the dendronized polymer resulting in 40 Å pitch (single helix characterized by the height per turn). Numbers on every axis represent the number of grid points chosen for finite difference calculation. Dimension of each grid point is 2.5 Å. On each axis number of grid points multiplied by 2.5 gives the dimension in Angstroms.

where $\varepsilon = (\varepsilon_r, \varepsilon_0 = 78 \times 8.85419 \times 10^{-12} \text{ C}^2\text{N}^{-1}\text{m}^{-2})$ is the permittivity of medium (water), $\varepsilon_r = 78$ is the relative permittivity or dielectric constant of water, $\varepsilon_0 = 8.85419 \times 10^{-12} \text{ C}^2\text{N}^{-1}\text{m}^{-2}$ is the vacuum permittivity, ψ [volt] is the electrostatic potential in any point of the system, ρ [$\text{C} \cdot \text{m}^{-3}$] is the charge density and $\vec{r}[m]$ is the position vector.

In solution with only mobile ions we can assume $\rho(\vec{r}) = \rho^m$. The Debye-Hückel theory can then be applied to this solution. However, in biological systems in addition to mobile ions there are different kinds of macromolecules, which have different properties such as flexibility, size and charge.

In this work a DNA-dendronized polymer nano-cluster system with the above-mentioned structure in aqueous solution of a 1:1 electrolyte salt such as sodium chloride is studied. This system contains three types of particles: (1) Small mobile ions surrounding the nano-cluster. (2) A cylindrical dendrimer which is rigid with fixed location in the solution and has positive surface charges. (3) A DNA which is like a flexible rod which is assumed to have negative surface charges and when it is located near the dendrimer with positive charge, will wrap around it to produce an inclusion aggregate known as a DNA-dendronized polymer nano-cluster. It is understood that the resulting conformation (nano-cluster) is surrounded by small mobile ions and is also stable at constant temperature and concentration of mobile ions. Thermal motions determine the distribution of small ions. The charge density in the system composed of the nano-cluster and mobile ions at any point is given as:¹⁹

$$\rho(\vec{r}) = \rho^{f+}(r) + \rho^{f-}(r) + \rho^m(r) \quad (2)$$

where ρ^{f+} and ρ^{f-} are the charge density of dendrimer and DNA, respectively, and ρ^m is the charge density related to the mobile ions. The sum of ρ^{f+} plus ρ^{f-} can be defined by the Kronecker Delta,²⁰

$$\rho^{f+}(r) + \rho^{f-}(r) = \sum_{j=1}^m q_j^+ \delta(r - r_j) + \sum_{i=1}^n q_i^- \delta(r - r_i) \quad (3)$$

where q_j^+ and q_i^- are positive and negative fixed charges, respectively. The last term in the right hand side of Eq. (2), ρ^m , illustrates the local density of mobile ions defined by the following summation over all the ions,

$$\rho^m = \sum e z_i c_i \quad (4)$$

Also, by application of the electroneutrality condition we have the following equation:

$$\sum z_i c_i = 0 \quad (5)$$

Considering the above equations the PBE will assume the following form known as the general, non-linear, Poisson-Boltzmann equation

$$\nabla \cdot \varepsilon(r) \nabla \phi(r) = \frac{-e}{kT} \left\{ \sum_{j=1}^m q_j^+ \delta(r - r_j) + \sum_{i=1}^n q_i^- \delta(r - r_i) \right\} + \kappa^2 \sinh \phi(\vec{r}) \quad (6)$$

In this equation

$$\phi = \psi \frac{e}{kT} \quad (7)$$

is the dimensionless electrostatic potential and κ is the modified Debye-Hückel parameter.

Analytical solution of Eq. (6) is available for very simple and symmetric systems.²¹ For the general solution of Eq. (6), which is of interest in this work, application of numerical methods seems to be inevitable. The three-dimensional version of the finite-difference method seems to provide an effective way of solving this equation for any desired system.

Applying the three-dimensional finite difference operator to the general, nonlinear, Poisson-Boltzmann differential Eq. (6) will result in the following finite-difference Equation²²

$$\phi_0 = \frac{\sum_i \varepsilon_i \phi_i + q_0/h \times e/kT}{\sum_i \varepsilon_i + \kappa^2 h^2 \left[1 + \frac{\phi_0^2}{3!} + \frac{\phi_0^4}{5!} + \dots + \frac{\phi_0^{2n}}{2n+1} \right]} \quad (8)$$

Where ϕ_0 is the dimensionless electrostatic potential at a particular grid point, ϕ_i is the dimensionless electrostatic potential at six neighboring grid points ($\phi_i, i = 1, \dots, 6$), ε_i is the dielectric constant at the center of each grid line joining the point to its neighbors,²³ q_0 is the charge in the block and $h (= 2.5 \text{ \AA})$ is the length of the block.

With the availability of the electrostatic potential one can calculate²¹ the electrostatic free energy (ΔG^{el}). Fogolari et al.²¹ have derived the following expression to calculate the electrostatic free energy.

$$\Delta G^{el} = \int_v \left(kT \sum_i C_i^b \left[1 - \exp\left(\frac{-Z_i e \psi}{kT}\right) \right] + \rho^f \psi + \frac{\varepsilon(\nabla \psi)^2}{8\pi} \right) dv \quad (9)$$

In this equation C_i^b is the local concentration of electrolyte and the summation is over all ions. The electrostatic free energy in terms of different contributions of fixed (ΔG^{ef}) and mobile (ΔG^{em}) charges and the entropic free energy of mixing of mobile species (ΔG^{mob}) and solvent (ΔG^{solv}) are given as the following:²¹

$$\Delta G^{el} = \Delta G^{ef} + \Delta G^{em} + \Delta G^{mob} + \Delta G^{solv} \quad (10)$$

According to Fogolari et al.²¹ the different terms in Eq. (10) are defined as follows:

$$\Delta G^{ef} = \int_v \frac{\rho^f \psi}{2} dv \quad (11)$$

$$\Delta G^{em} = \int_v \frac{\sum_i C_i Z_i e \psi}{2} dv \quad (12)$$

$$\Delta G^{mob} = kT \int_v \sum_i C_i \ln \frac{C_i}{C_i^b} dv \quad (13)$$

$$\Delta G^{solv} = kT \int_v \sum_i C_i^b \left[1 - \exp\left(\frac{-Z_i e \psi}{kT}\right) \right] dv \quad (14)$$

where,

$$c_i = c_i^b e^{(-e z_i \psi)/kT} \quad (15)$$

In what follows we describe the finite-difference computational procedure we have developed to calculate the electrostatic potential, electrostatic free energy and the four components of electrostatic free energy (free energy contributions of fixed and mobile charges and the entropic free energy of mixing of mobile species and solvent).

3. COMPUTATIONAL PROCEDURE

A cylinder (a part of dendronized polymer relevant to the applied grid) with the height 50 Å and 80(= 4 × 50/2.5, 4 positive charges per 2.5 Å) positive charges and a DNA with the length of 435 Å (the maximum length of DNA that can be wrapped around dendronized polymer¹⁶ and 255(= 2 × 435/3.4, 2) negative charges per 3.4 Å) negative charges were considered in this computational study. It is known that³ there are 4 positive charges on dendrimer per 2.5 Å and 2 negative charges on DNA per 3.4 Å. To calculate the electrostatic potential and electrostatic free energies a MATLAB 7.0 computer program including the following steps was developed:

1. The spatial points and the location of surface charge densities in the nano-cluster were defined to draw the shape of the complex (Fig. 2).
2. A cubical lattice including 61 × 61 × 61 grid points (this being the most suitable grid in which our finite difference computational model could be accommodated to) with the mesh size of 2.5 Å was designed and it was then assumed to be placed in the positive directions of X, Y and Z axes. Based on the finite difference method of calculation²³ and CPU of our computational facility these numbers were found to give us accurate results.
3. The charge and the location of each grid point were determined by comparing them with the points of nano-cluster with the same spatial coordinates. Then, dielectric constants of 2 (for inside the complex where there is no charge or it is electrically inert) and 78 (of water surrounding the complex surface and in the solution) were assigned.
4. The values of the electrostatic potential of the grid points on the boundary were calculated analytically using the Debye-Hückel equation.²³
5. For each lattice point, a finite difference equation was constructed that related the potential at that point to the potential at its six neighboring points, which resulted in 61³ simultaneous equations of the form of Eq. (8) and the electrostatic potential for inner grid points were then calculated.
6. The Thermodynamic quantities were then calculated through Eqs. (10–14) by using the three-dimensional finite-difference integral.

7. The program was then run for eleven different conformations of DNA-dendronized polymer nano-clusters. These conformations differed by the wrapping DNA pitches which were chosen to be 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, and 70 Å. The thermodynamics of all these conformations were studied through numerical solution of the PBE in different aqueous solutions of various ionic strength (1, 2.5, 5, 7.5, 10, 12.5 mM) of 1.1 electrolyte salt at 298.16 K.

The DNA chain was considered to be a flexible rod and the length, diameter and radius of its wrapping were assumed to be 435, 20, and 27 Å, respectively. We assumed two negative charges on DNA per 3.4 Å length and four positive charges on dendrimer per 2.5 Å.

4. RESULT AND DISCUSSION

Figure 2 represents the format of the nano-cluster and Figure 3 shows the related electrostatic potentials in the space for a slice of crossing through the middle of the nano-cluster, horizontally. The positive potential (red regions, Fig. 3) and the negative potential (blue regions, Fig. 3) correspond to dendronized polymer and DNA, respectively. Furthermore, it was found that the conformation with smaller pitch exhibits a higher negative electrostatic potential. Figure 4 indicates the contour plots of the local concentration of the positive mobile ions. This was also found (from different conformations) that the concentration of positive charges around the nano-cluster in conformation with smaller pitch is more than the concentration of positive charges in conformation with bigger pitch, which is in agreement with the electrostatic potentials. Figure 5 represents the concentration of cations on the axis which is vertical to surface of the cylinder and passes

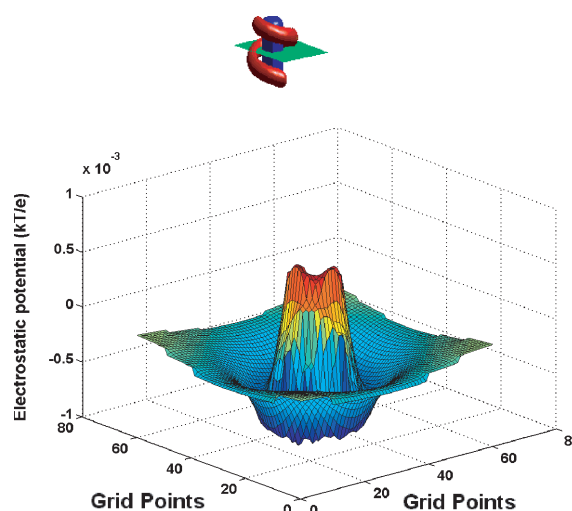


Fig. 3. Electrostatic potentials in a plane orthogonal to the DNA-dendronized polymer nano-cluster going through the center of the 40-pitch system. Numbers on every axis represent the number of 2.5 Å grid points chosen for finite difference calculation.

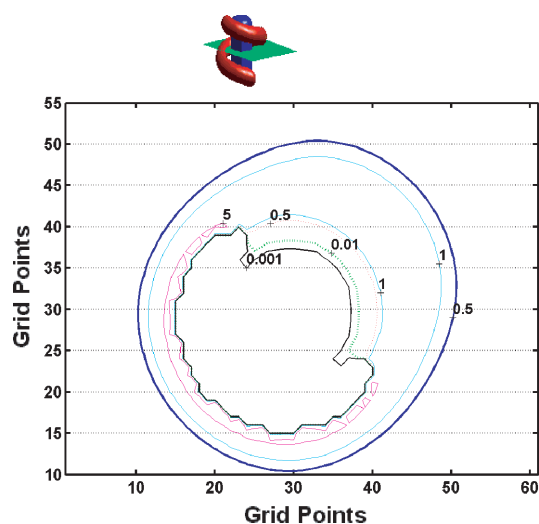


Fig. 4. Two dimensional map of the isoconcentration of positive ion contours in a plane orthogonal to the DNA-dendronized polymer going through the center of the 40-pitch system (like in Fig. 2).

thought the center of cylinder i.e., continuation of radius of cylinder. This axis also passes through the middle of the pitch. The cylinder has positive fixed charges on the surface then the concentration of cations near it must be minimum but DNA have negative fixed charges on the surface and attracts cations, then the concentration of cations near DNA must be maximum. According to Figure 5 the concentration of cations between the helix is larger than in the bulk solution, but near the cylinder the concentration of cations is effectively decreased. The concentration of ions in each point is determined by the Boltzmann expression, $c_i = c_i^b e^{(-eZ_i\psi)/kT}$. For cations ($Z_i > 0$), when the pitch decreases the electrostatic potential around the nano-cluster will decrease [$\psi < 0$]. Therefore, concentration of cations will increase, which is in agreement with the values of electrostatic potential.

A DNA and a cylinder PG2-PMAMA with constant lengths were also considered in order to investigate the free

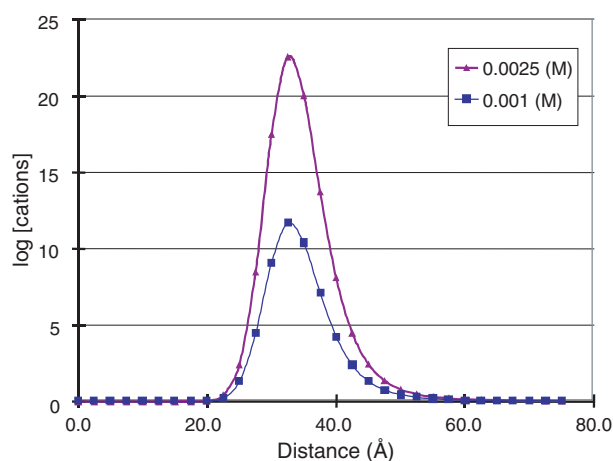


Fig. 5. The distribution of cation's concentration. The origin of the coordinates is placed on the center of nano-cluster.

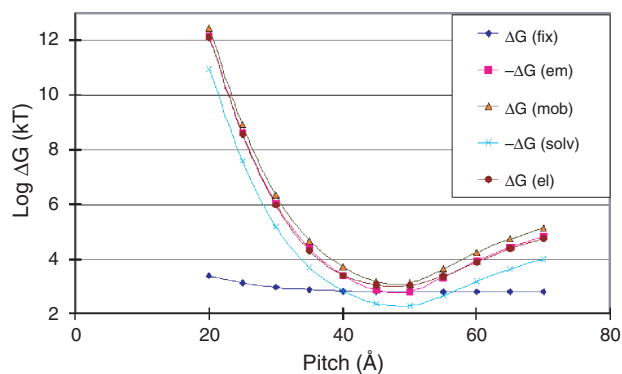


Fig. 6. Different contributions to the electrostatic (el) Gibbs free energy of DNA-dendronized polymer complexes in the solution versus pitch size in Angstroms. Note that the entropic free energy of solvent (shown by cross) and free energy of mobile charges (shown by solid square) are negative, while the entropic free energies of mobile charges (shown by solid triangle) and free energy of fixed charges (shown by solid lozenge) are positive.

energies of various conformations. For this it was assumed that the DNA, after clustering with dendronized polymer, will consist of two parts: (1) Wrapped part, the one which has been wrapped around the dendronized polymer and (2) Unwrapped part, which include the rest of DNA which is free and floating in the environment. The total electrostatic Gibbs free energy (Fig. 6, green) is then a summation of the Gibbs free energies of these two parts.

Figure 6 represents different contributions to the electrostatic (el) Gibbs free energy of DNA-dendronized polymer complexes in the solution versus pitch size in Angstroms. Note that the entropic free energy of solvent (shown by cross) and free energy of mobile charges (shown by solid square) are negative, while the entropic free energies of mobile charges (shown by solid triangle) and free energy of fixed charges (shown by solid lozenge) are positive. According to this figure the entropic free energies of mobile charges, ΔG^{mob} , is larger than all the other terms. Therefore this entropic term is the main conformational determinant.

The left arm of all curves (the part with negative slope) indicate that the potential is strongly affected by the size of the DNA pitch, i.e., the small change in the size of pitch will produce a big change in the electrostatic potential. The electrostatic free energy is directly proportional to any kind of charge density (ρ^{m+} and ρ^{m-}). According to Figure 4 the concentration of cations around the complex is higher than their concentration in the bulk solution. This reveals that the DNA's negative charges on the surface area dominant which produce an electrostatic potential. When the DNA pitch is increased the free part of the DNA will be increased which causes the density of the negative charges on the surface area to be decreased and the concentration of cations around the nano-cluster will be finally decreased. This process will continue down to the minimum point of the plots presented in Figure 6. Then the positive charge density on the surface area of the

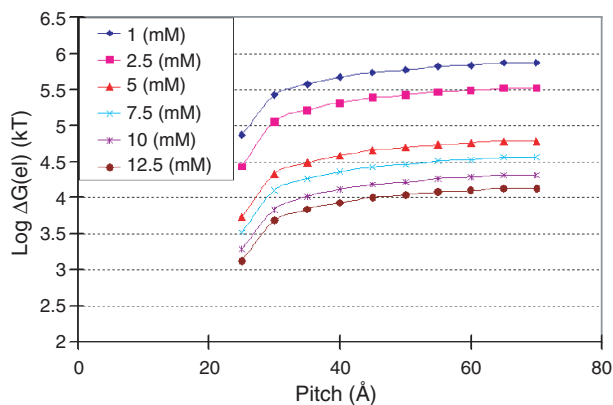


Fig. 7. Log of electrostatic free energy of free part of DNA vs DNA's pitch (in Angstroms) for different conformations of nano-cluster and at six different salt concentrations.

nano-cluster will be increased which causes the concentration of the anions to be increased around the nano-cluster which causes the electrostatic free energy to be increased (Fig. 6, the part with positive slope). Figures 7, 8, and 9 display the effect of the ionic strength on the electrostatic free energy of the systems which contain only DNA, nano-cluster and free DNA + nano-cluster, respectively. It should be noted that the length of the free DNA is directly related to the size of the DNA pitch. It should be also understood that the ionic strength has a general effect on the electrostatic potentials and electrostatic free energy, i.e., the electrostatic free energy will decrease with increasing the ionic strength.

A comparison between different conformations of the nano-cluster (Fig. 8) shows how the electrostatic free energy is sensitive to the ionic strength of the solution. This reveals that when density of mobile ions increases, the permeability of electrostatic field of macro-ion (nano-cluster) into the solution will decrease and the macro-ion neutralizes in a small space.

It should be mentioned that DNA-dendronized polymer nano-cluster is not electrically neutral and has local charged areas on its surface as a result of which it

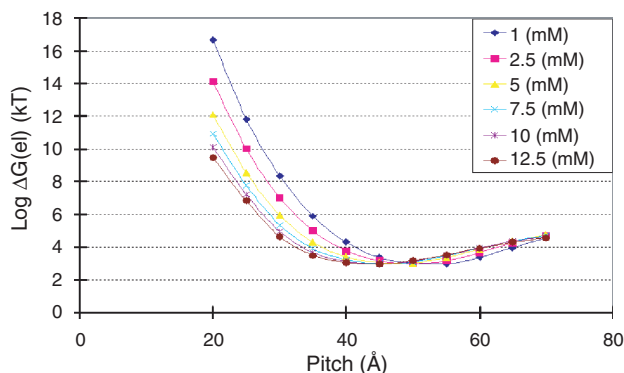


Fig. 8. Log of electrostatic free energy of wrapped DNA vs DNA's pitch (in Angstroms) for different conformations of nano-cluster and at six different salt concentrations.

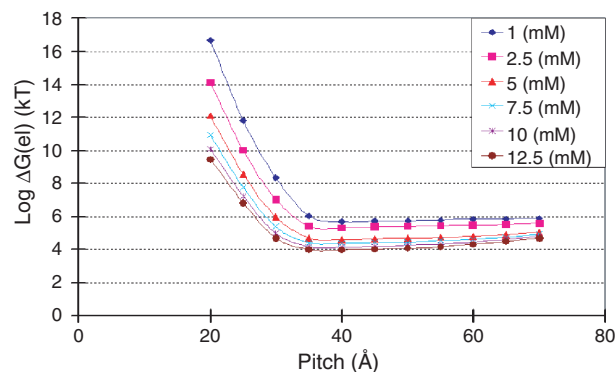


Fig. 9. Log of total electrostatic free energy of wrapped DNA vs DNA pitch size (in Angstroms) for different conformations of nano-cluster and at six different salt concentrations.

may be called a macro-ion. These charges will exert an electrostatic field on the surrounding which attract or repulse the mobile ions and causes the formation of a layer of opposite charges near the charged areas which shield the effect of electrostatic field on the farther ions to be reduced. Therefore increasing ionic strength will increase the concentration and the order of mobile ions near the macro-ion and the stochastic motion in the system will be reduced, consequently. This will decrease the entropic free energy, which is determinate factor.

Figure 8 also indicates that the most stable conformation is with the DNA pitch of 55 Å. At higher ionic strength values the most stable conformation point (minimum of curves in Fig. 8) moves to a lower pitch. Although this Figure 8 shows a large decrease in pitch accompanied with increase of the ionic strength, the determining factor for the system is the total free energy reported in Figure 9. According to Figure 9 there is a displacement for the stable conformation, but this is less pronounced than the ionic strength values reported in Figure 8.

5. CONCLUSIONS

By application of the finite difference numerical method the Poisson-Boltzmann equation, electrostatic potential and then electrostatic free energies, entropic free energies and distribution of counter ions are determined for a series of DNA-dendronized polymer nano-clusters with different DNA pitches. It is concluded that in a series of conformations at constant ionic strength, the electrostatic free energies and entropic free energies primarily decrease sharply and then smoothly increase with the increase in DNA pitch size. This is possibly due to increasing the charge density of the positive mobile ions and decreasing charge density of the negative mobile ions around DNA-dendronized polymer nano-cluster. It is also concluded that with the decrease in the ionic strength, electrostatic free energies and entropic free energies will decrease and the conformation with the least electrostatic free energy corresponds to the smallest DNA pitch.

The computations reported here are performed at the normal conditions of 298.16 K as it is usually needed for applications of such results. Of course, one can also study the effect of temperature on the results by using the temperature-dependent modified Debye-Hückel parameter,²⁴

$$\kappa^2 = \frac{2e^2 I}{kT} \quad (16)$$

where κ is the Boltzmann constant and I is the ionic strength of the bulk solution. However, it should be pointed out that small variations (of the order of ~ 5 – 10 °C) should not have an appreciable effect on result of computations. This is the case for all the condensed matter electrostatics, which are insensitive to small changes in temperature.

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Symbols and Abbreviations

c_i^b	Salt concentration in bulk solution
C	Coulomb
e	Charge of electron
G	Helmholtz free energy
h	Length of block
I	Ionic strength of the bulk solution
k	Boltzmann constant
m	meter
mM	Milli molar
N	Newton
PBE	Poisson-Boltzmann equation
q_0	Total charge in the block
q_n^{f+}	Positive fixed charge
q_n^{f-}	Negative fixed charge
$\vec{r}[m]$	Position vector
T	Absolute temperature
z_i	Number of charge

Greek Letters

ε	Dielectric constant ($= \varepsilon_r \varepsilon_0 = 78 \times 8.854 \times 10^{-12} \text{ Cm}^{-1} \text{ N}^{-1}$ in water)
ε_0	vacuum permittivity
ε_r	relative permittivity
ψ	Electrostatic potential [volt]
$\rho(\vec{r})$	Charge density

ρ^{f+}	Positive charge density
ρ^{f-}	Negative charge density
ρ^m	Charge density of mobile ions
$\phi = \psi(e/kT)$	Dimensionless electrostatic potential
ϕ_0	Electrostatic potential at considered grid point
κ	Modified Debye-Hückel parameter
$\sigma(r - r_i)$	Kronecker Delta
λ	Debye length
ΔG^{el}	Electrostatic free energy
ΔG^{ef}	Electrostatic free energy of fixed ions
ΔG^{em}	Electrostatic free energy of mobile ions
ΔG^{solv}	Entropic free energy of mixing of solvent
ΔG^{mob}	Entropic free energy of mixing of mobile species and solvent

References

1. A. Zhang, B. Zhang, E. Wächtersbach, M. Schmidt, and A. D. Schlüter, *Chem. Eur. J.* 9, 6083 (2003).
2. G. A. Mansoori, *Principles of Nanotechnology—Molecular-Based Study of Condensed Matter in Small Systems*, World Scientific Pub. Co., New York (2005).
3. I. Gaossel, L. Shu, A. D. Schlater, and J. P. Rabe, *J. Am. Chem. Soc.* 124, 6860 (2002).
4. A. U. Bielinska, C. Chen, J. Johnson, and J. R. Baker, *Bioconjugate Chem.* 10, 843 (1999).
5. A. U. Bielinska, J. F. Kukowska-Latallo, and J. R. Baker, Jr., *Biochim. Biophys. Acta* 1353, 180 (1997).
6. W. Chen, N. J. Turro, and D. A. Tomalia, *Langmuir* 16, 15 (2000).
7. C. L. Gebhart and A. V. Kabanov, *J. Controlled Release* 73, 401 (2001).
8. T. Tanaka, I. Nishio, S. T. Sun, and S. V. Nishio, *Science* 218, 467 (1973).
9. H. Okuzaki and Y. Osada, *Macromolecules* 27, 502 (1994).
10. V. A. Bloomfield, *Biopolymers* 31, 1471 (1991).
11. J. P. Gang and Y. Osada, *Electrochimica Acta.* 40, 13 (1995).
12. Z. Haijun, Z. Yang, and O. Y. Z. Can, *Phys. Rev. Lett.* 82, 22 (1999).
13. P. M. Biesheuvel, *J. Colloid Interface Sci.* 275, 97 (2004).
14. E. Wagner, M. Cotton, R. Foisner, and M. L. Birnstiel, *Proc. Natl. Acad. Sci. USA* 88, 4255 (1991).
15. G. R. Newkome, C. N. Moorefield, and F. Vogtle, *Dendrimers and Dendrons*, John Wiley and Sons, New York (2001).
16. K. Inoue, *Prog. Polym. Sci.* 25, 453 (2000).
17. S. Y. Park, R. F. Bruinsma, and W. M. Gelebart, *Europhys. Lett.* 46, 454 (1999).
18. K. K. Kunze and R. R. Netz, *Europhys. Lett.* 58, 299 (2002).
19. K. A. Sharp and B. Honig, *J. Phys. Chem.* 94, 7684 (1990).
20. D. B. Boyed, in *Reviews in Computational Chemistry*, John Wiley and Sons, New York (2003), p. 19, 1st ed.
21. F. Fogolari, P. Zuccato, G. Esposito, and P. Viglino, *Biophysical J.* 76, 1 (1999).
22. B. Jayaram, K. A. Sharp, and B. Honig, *Biopolymers* 28, 975 (1989).
23. I. Klapper, R. Hagstrom, R. Fine, K. Sharp, and B. Honig, *Proteins* 1, 47 (1986).
24. R. J. Hunter, *Foundation of Colloid Science*, Oxford University Press, New York (2001).

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