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2017 J. Phys.: Conf. Ser. 869 012055

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# DNA compaction by poly (amido amine) dendrimers of ammonia cored and ethylene diamine cored

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**Abstract.** The complexes build-up of DNA and soft particles poly amidoamine (PAMAM) dendrimers of ammonia cored of generations (G1-G6) and ethylenediamine cored of generations (G1-G10) have been studied, using a new theoretical model developed by Qamhieh and coworkers. The model describes the interaction between linear polyelectrolyte (LPE) chain and ion-penetrable spheres. Many factors affecting LPE/dendrimer complex have been investigated such as dendrimer generation, the Bjerrum length, salt concentration, and rigidity of the LPE chain represented by the persistence length. It is found that the wrapping chain length around dendrimer increases by increasing dendrimer's generation, Bjerrum length, and salt concentration, while decreases by increasing the persistence length of the LPE chain. Also we can conclude that the wrapping length of LPE chain around ethylenediamine cored dendrimers is larger than its length around ammonia cored dendrimers.

## 1. Introduction

Gene therapy derives its name from the idea that genetic materials can be used to supplement or alter gene expression within a specific cell. The challenge here is to transport the DNA through the cell walls, which can be achieved by condensing DNA with a cationic particles, such as poly (amido amine) (PAMAM) dendrimers. Dendrimers are branched polymeric molecules, which have a specific size and shape, affording a narrow weight distribution. With its unique molecular architecture and related properties, dendrimers have a great potential as delivery vectors for gene transfection. Transfection efficiency and functionality of DNA complexed with dendrimers depend on the structure, size, and the charge density of these polymers. The properties of the complexes were studied by various experimental and theoretical modeling [1-5]. The objective of our work is to study the complexation of DNA with dendrimers of different generations for ammonia cored dendrimers and for ethylenediamine cored dendrimers. Through our study different factors have been investigated, like salt concentration of the solution, persistence length ( $l_p$ ) represents the flexibility of LPE chain, dendrimer generation, and the strength of electrostatic interaction on the complexation represented by Bjerrum length ( $l_B$ ).

## 2. Analytical model

A theoretical model for the complexation of one sphere with one LPE chain, developed by Qamhieh et al. was adopted [5]. The complex was considered to be formed between soft (ion penetrable) sphere of radius  $R$  and charge  $Ze$  represents the dendrimer, where  $Z$  is the valency and  $e$  is the elementary charge, and the DNA as a LPE chain of  $l_p$  persistence length, radius  $r = 1$  nm, length  $L \gg R$  and the charge density of  $\lambda = -e/b$ , where  $b$  is the axial spacing between negative charges on the chain. The sphere and the LPE chain are



placed in 1:1 salt solution in a system characterized by Bjerrum length  $l_B = e^2/\epsilon k_B T$ , where  $\epsilon$  is the dielectric constant of the medium,  $k_B$  is Boltzmann constant,  $T$  is the thermal energy, and Debye screening length  $\kappa^{-1} = (\delta c_s \pi l_B)^{-1/2}$  where  $c_s$  is the salt concentration of the solution. The total free energy of a system consisting of one dendrimer and one LPE chain is given as the following:

$$F(l) = F_{compl}(l) + F_{chain}(L-l) + F_{compl-chain}(l) + F_{elastic}(l) \quad (1)$$

where  $l$  is the length of the LPE chain wrapped around the sphere, and the remaining chain is of length  $(L-l)$ . The first term is the electrostatic charging free energy of a spherical complex of charge  $Z(l)e$  given by:

$$F_{compl}(l) \cong \frac{3Z^2(l)l_B k_B T}{8\pi(\kappa R)^2} \left[ \cosh(\kappa R) - \frac{\sinh(\kappa R)}{\kappa R} \right] \frac{e^{-\kappa R}}{R} \quad (2)$$

$Z(l) = (Z - l/b)$  represents the charge of the complex consists of the sphere and the corresponding wrapped chain. The second term is the total entropic electrostatic free energy of the remaining chain  $(L-l)$  given by:

$$F_{chain}(L-l) \cong \frac{k_B T}{b} \cdot \Omega(a) \cdot (L-l) \cdot (1 - \xi^{-1}) \quad (3)$$

Where  $\Omega(a)$ , is the entropic cost describing the condensed DNA counterion,  $\xi = l_B/b$  is the so-called Manning parameter [6]. The third term is the electrostatic free energy of the interaction between the complex and the rest of the chain and is given by

$$F_{compl-chain}(l) \cong \frac{3Z(l)l_B k_B T}{4\pi(\kappa R)^2} \left[ \cosh(\kappa R) - \frac{\sinh(\kappa R)}{\kappa R} \right] \times \left[ \ln(r) - \sum_{n=0}^{\infty} \frac{(-1)^n}{(n+1)! \cdot (n+1)} \cdot (\kappa r)^{n+1} \right] \Big|_R^{L-l} \quad (4)$$

The final term in the free energy is the elastic (bending) free energy required to bend  $l$  of the chain around a sphere of radius  $R$  and is given by

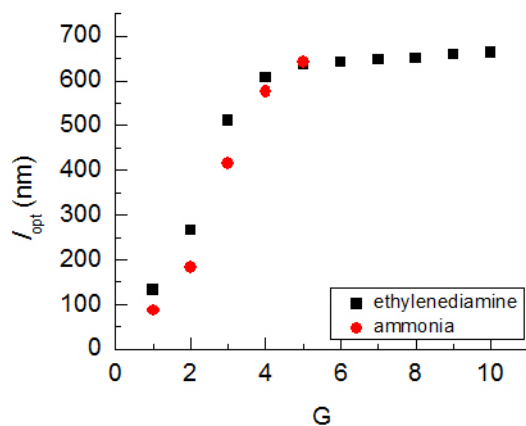
$$F_{elastic}(l) \cong \frac{k_B T l_p}{2R^2} l \quad (5)$$

### 3. Results and discussion

In order to estimate the optimal wrapping length  $l_{opt}$  of the LPE chain around the dendrimer, equation 1 should be solved. The model is applied to obtain a mechanistic understanding of how the complexation of 2000 bp DNA of  $L = 680$  nm, and  $b = 0.17$  nm, is affected when it is combined with one dendrimer of ammonia cored (G1-G6), or methylenediamine cored (G1-G10), in aqueous solutions, at room temperature. The  $l_{opt}$  is found to be larger with ethylenediamine cored dendrimers than it is with ammonia cored dendrimers as shown in figures 1-4. The difference is clearer with small generations.

### 3.1 Effect of dendrimer generation on optimal chain length condensed on PAMAM dendrimer

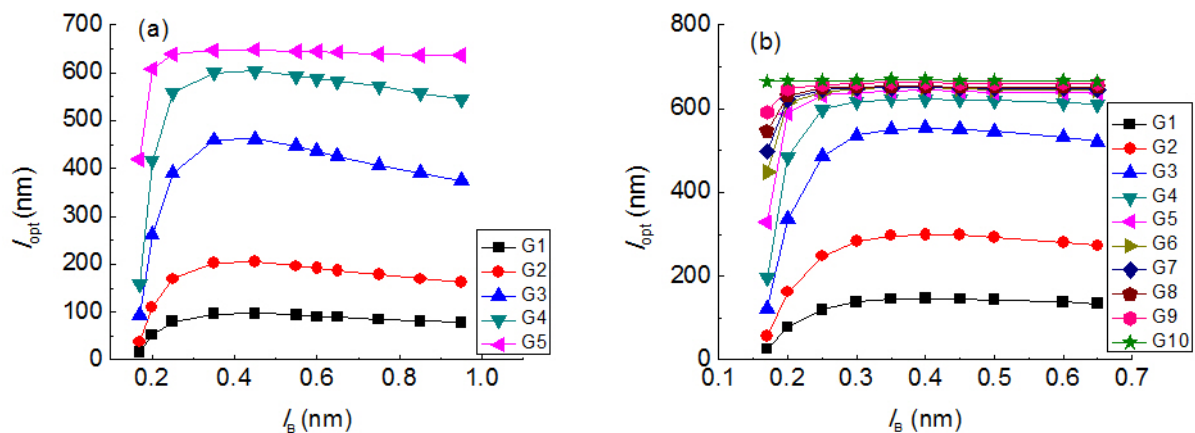
The complexation of one LPE chain represents the DNA of Bjerum length  $l_B = 0.71$  nm, and a persistence length  $l_p = 3$  nm, with one dendrimer at 1:1 salt concentration corresponding to Debye screening length of 6 nm, have been studied. Figure 1 shows that the optimal length is increased by increasing the generation (size) of the dendrimer, as the higher generation dendrimers have lower curvature and higher surface charge density, as a result they cost less free energy for bending than lower generations.



**Figure 1.** Optimal LPE chain condensed on (a) ammonia cored dendrimer, (b) ethylenediamine cored as a function of dendrimer generation. The persistence length  $l_p = 3$  nm, the Bjerum length  $l_B = 0.71$  nm, and the chain length  $L = 680$  nm, at 1:1 salt concentration corresponding to Debye screening length of 6 nm.

### 3.2 Effect of Bjerum length on optimal chain length condensed on PAMAM dendrimer

The  $l_{opt}$  for complexation of flexible LPE chain of persistence length  $l_p = 3$  nm, with dendrimers is shown as a function of  $l_B$  in Figure 2. From the figure we can conclude that the  $l_{opt}$  increases as the  $l_B$  increases, as long as  $l_B$  is less than  $b$ , when  $l_B$  exceeds the value of  $b$  the dendrimer is saturated and the  $l_{opt}$  is fixed by increasing  $l_B$ . With large generations larger than G5, the whole LPE chain is almost condensed around the dendrimer. At low  $l_B$  and less than  $b$  the complexation is very sensitive, a small change in  $l_B$  gives a large change in optimal length.



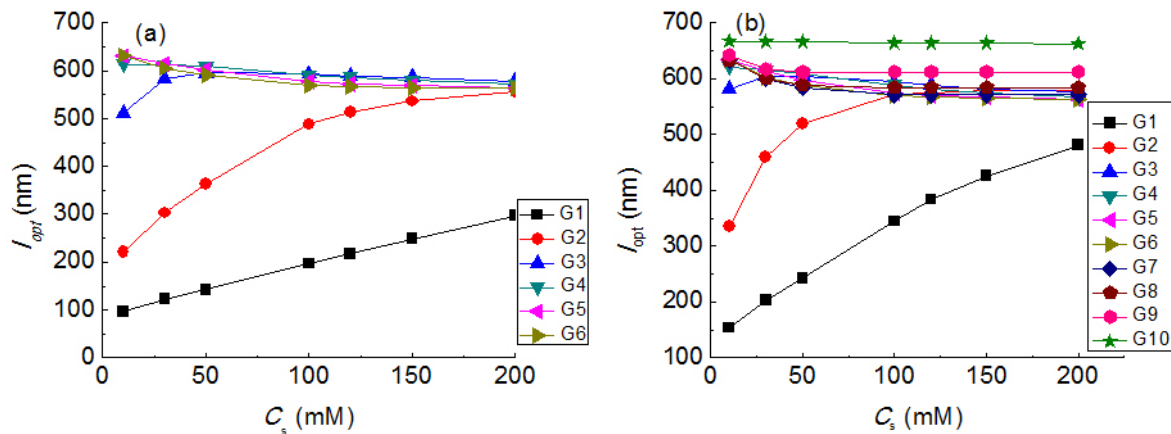
**Figure 2.** Optimal LPE chain condensed on (a) ammonia cored dendrimers, (b) ethylenediamine cored dendrimers as a function of  $l_B$ . The persistence length  $l_p = 3$  nm.

### 3.3 Effect of salt concentration on optimal chain length condensed on PAMAM dendrimer

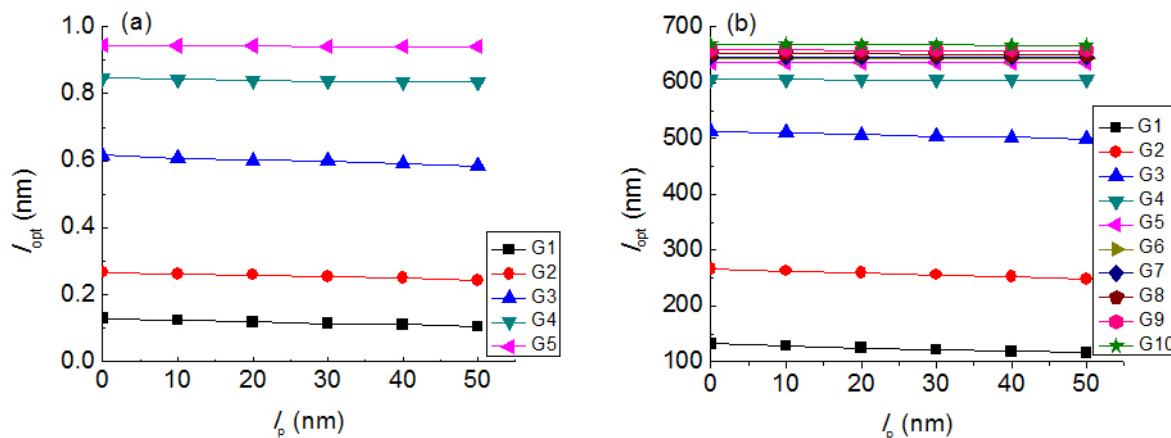
Figure 3 shows the  $l_{opt}$  as a function of 1:1 salt concentration for the complexation of flexible LPE chain and  $l_B = 0.71$  nm, with PAMAM dendrimers. The figure shows that the  $l_{opt}$  is increased by increasing the salt concentration with small generations of dendrimers, while with large generations the effect is less and the  $l_{opt}$  will not be affected by increasing the salt concentration.

### 3.4 Effect of Persistence length on optimal chain length condensed on PAMAM dendrimer

Figure 4 shows the optimal chain length as a function of the persistence length for the complexation of LPE chain of Bjerum length  $l_B = 0.71$  nm, and at 1:1 salt concentration corresponding to Debye screening length of 6 nm, with PAMAM dendrimers of different generations. From which we can conclude that the optimal chain length is decreased slightly by increasing the persistence length as the bending energy is decreased by increasing stiffness of the chain.



**Figure 3.** Optimal LPE chain condensed on (a) ammonia cored dendrimers, and (b) ethylenediamine cored dendrimers as a function of 1:1 salt concentration, and  $l_B = 0.71$  nm.



**Figure 4.** Optimal LPE chain condensed on (a) ammonia cored dendrimers, and (b) ethylenediamine cored dendrimers as a function of persistence length  $l_p$ , the Bjerum length  $l_B = 0.71$  nm.

#### 4. Conclusions

From the study we can conclude that the complexation of DNA with PAMAM dendrimers can be affected by different factors, by which we can control the compaction of the DNA with dendrimers. The effect is larger on the complexation with ethylenediamine cored dendrimers than with ammonia cored dendrimers.

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