Stepwise Disproportionation in Polyelectrolyte Complexes

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Abstract: Structural properties and the topology of polyelectrolyte complexes (PECs) formed in solution have been investigated under different conditions by Monte Carlo simulations using a coarse-grained model. The extension of individual polyions has been characterized by their radius of gyration, whereas the composition of the complexes has been investigated by their net charge and their internal topological structure by a novel analysis describing how the shorter polycations link to monomers of the longer polyanion. Conditions have been found at which the polyanion and a given number of polycations form distinguishable complexes differing in (i) the polyanion conformation and (ii) the fraction of polycations being in extended and collapsed states. Thus, at equilibrium, these PECs display a stepwise variation of the degree of intrachain disproportionation within the polyanion (also referred to as intrachain segregation), concomitant with the interchain disproportionation of the polycations, which is in agreement with previous theoretical predictions. The coexistence of the different polyelectrolyte complex structures appears, generally, at mixing ratios close to but different from charge equivalence and, as a consequence, broad polyelectrolyte size distributions are commonly obtained.


Key words: Intrachain and interchain segregation; coexistence; Monte Carlo simulations; polyplexes; DNA condensation

Introduction

The interactions between oppositely charged polyelectrolytes (PEs) and the formation of polyelectrolyte complex (PEC) have attracted much interest in the past decade, and a vast amount of experimental work has been performed as summarized in several reviews.1–3 Part of the interest in these systems derives from the fact that PECs prepared using DNA (polyplexes) are considered promising gene delivery vehicles in gene transfection. Also, the formation of films and capsules containing oppositely charged PEs made by the layer-by-layer method4,5 has potential applications in biosensing,6 catalysis,7 optical devices,8 and drug delivery.9–11

A number of simulation techniques have been used to study the interactions between oppositely charged PEs and concomitant formation of PECs using linear chains with the same length and varying (i) the interaction strength,12,13 (ii) the size of the chains,13,14 and (iii) the charge density of one of the chains.15,16 It was found that on the interaction of the oppositely charged PEs, there was a considerable reduction on the extension of the chains.14 Studies were also performed on solutions containing 10 positively charged PEs (polycations, PCs) and zero, two, or five negatively charged PEs (polyanions, PAs) with the same length.15 For the systems with the larger number of PAs, the formation of stable and rather monodisperse 2:1 complexes was observed. With two PAs, a coexistence between such 2:1 complexes and free PCs was reported. The nature of the PECs was found to depend on the linear charge density of the chains; increasing the bond length leads to larger and stoichiometric less defined complexes.15 The influence of the asymmetry in the bond length on the structure of the PECs was studied further, now considering solely one PA and one PC with the same number of monomers.16 In the symmetric case, the distribution of positive and negative monomers in the complex is identical, producing clusters that are on average locally neutral. However, deviations from the symmetric case lead to net-charge oscillations inside the complex.16

Systems containing PEs of different chain lengths have also been considered. The effect of the stiffness of the polyanion,17 and of the length, charge density, and number of the compacting agents on the degree of compaction18,19 and the coil-to-globule transition20 of a

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single PA were looked upon. The size, number, and size polydispersity of the PAs on PA–PC cluster formation were also examined.\textsuperscript{21,22} It was found that the strongest tendency to form large complexes appeared slightly before charge equivalence, whereas at charge equivalence the large clusters were partly broken up. Small and neutral complexes dominated the solution at charge equivalence in a monodisperse system, whereas larger clusters dominated the solutions of polydisperse polymers.\textsuperscript{21}

The multilayer formation of PEs at charged surfaces with different geometries was additionally considered.\textsuperscript{23} The layer-to-layer adsorption of short PEs at planar surfaces was achieved up to three layers. An increase of the PE length increased the number of layers.\textsuperscript{24} The formation of multilayer structures at cylindrical surfaces was unfavorable, due to the entropic penalty of adsorption on a surface with low dimensionality and strong curvature. In fact, true bilayering could only occur if an additional and attractive short-range polymer–surface potential was included.\textsuperscript{25} The results with spherical surfaces were very similar to those with the cylindrical one. Without the short-range attraction, the formation of globular PECs in bulk solution, of which some were adsorbed onto the charged sphere, was typically observed.\textsuperscript{26}

Theoretical work has also been conducted to determine phase diagrams of oppositely charged PEs, both for symmetrical PEs where the length and charge density of the PEs were the same,\textsuperscript{27,28} and cases where the PEs possessed different length.\textsuperscript{29–32} Considering specifically the studies on the compaction of a long PE by shorter oppositely charged ones, little attention has been paid to the way the shorter PEs are distributed along the longer PE and how this affects the characteristics of the PECs, with the exception of a study, where the formation of highly charged and extended complexes was reported for charge ratios reasonably below or above the charge equivalence, and nearly neutral and compact complexes, as well as a “tadpole” configuration, around charge equivalence.\textsuperscript{29}

The tadpole configuration is characterized by a neutralized and compact part, whereas the rest of the complex is charged and extended. Tadpole structures arise from “intrachain disproportionation,” also commonly denominated “intrachain segregation,” and have been observed experimentally using fluorescence microscopy.\textsuperscript{33–37} Coexistence regions containing tadpole configurations and extended or compact structures were later included in the theoretical phase diagrams.\textsuperscript{31}

In a previous communication, we have shown that for systems below charge equivalence, PECs containing 30 monomers are preferentially positioned along a four times longer PA with some degree of repulsion between the PCs.\textsuperscript{18} At charge equivalence, the distribution of positively charged monomers along the PA becomes uniform. Recently, using similar systems, we have observed that for charge ratios close to but off charge equivalence, there is a coexistence of compact and extended conformations that enhances the large size distribution of the complexes, and which is related to the number of smaller PCs present in the systems.\textsuperscript{19}

In this work, we study the characteristics of PECs formed by a long PA of variable length and different numbers of shorter PCs, also of variable length, by Monte Carlo simulations. Of particular interest is the phenomenon of intrachain disproportionation, observed for the polyanion in the presence of sufficiently large PCs, and concomitant increase in the size distribution of the complexes in systems close to but different from charge equivalence. A novel linking analysis has been used to identify these conformations, which are not visible through the use of more common tools for structural analysis.

Model and Systems

\textbf{Model}

A simple coarse-grained model has been adopted to describe the structure of complexes appearing in a solution containing oppositely charged PEs confined in a spherical volume. A PE is composed of a polyanion (PI) and simple counterions. A PI consists of a sequence of charged hard spheres (monomers) connected by harmonic bonds with the chain flexibility regulated by angular force terms. The solvent enters the model only through its relative permittivity.

All interactions are taken as pairwise additive. The total potential energy \( U \) of a system can be expressed as a sum of three contributions according to

\[
U = U_{\text{nonbond}} + U_{\text{bond}} + U_{\text{ang}}.
\]

The nonbonded potential energy, \( U_{\text{nonbond}} \), is given by

\[
U_{\text{nonbond}} = \sum_{i<j} u_{ij}(r_{ij}),
\]

where the summation extends over the PI monomers and simple ions with \( u_{ij} \) representing the electrostatic potential plus hard-sphere repulsion according to

\[
u_{ij}(r_{ij}) = \begin{cases} \infty, & r_{ij} < R_i + R_j \\ \frac{Z_i Z_j e^2}{4 \pi \epsilon_0 \epsilon_r r_{ij}}, & r_{ij} \geq R_i + R_j \end{cases}
\]

with \( Z_i \) being the valence of particle \( i \), \( R_i \) the radius of particle \( i \), \( r_{ij} \) the distance between particles \( i \) and \( j \), \( e \) the elementary charge, \( \epsilon_0 \) the permittivity of vacuum, and \( \epsilon_r \) the relative permittivity of the solvent.

The bond potential energy of the chains, \( U_{\text{bond}} \), is given by

\[
U_{\text{bond}} = \sum_{c=1}^{N_c} \sum_{i=1}^{N_{\text{mon},c} - 1} \frac{k_{\text{bond}}}{2} (r_{c,i+1} - r_0)^2,
\]

where \( N_c \) is the number of chains, and \( N_{\text{mon},c} \) the number of monomers of chain \( c \). Furthermore, \( r_{c,i+1} \) is the distance between two connected monomers of chain \( c \), \( k_{\text{bond}} = 0.4 \text{ Nm}^{-1} \) is the bond force constant, and \( r_0 \) is the equilibrium separation of a bond. We have used \( r_0 = 5.0 \text{ Å} \) for the PA and \( r_0 = 5.6 \text{ Å} \) for the PCs, the latter being found in polyanines. The angular potential energy of the chains, \( U_{\text{ang}} \), is given by

\[
U_{\text{ang}} = \sum_{c=1}^{N_c} \sum_{i=2}^{N_{\text{mon},c} - 1} \frac{k_{\text{ang}}}{2} (\alpha_{c,i} - \alpha_0)^2,
\]

where \( \alpha_{c,i} \) is the angle between two bond vectors of chain \( c \), and \( k_{\text{ang}} = 1.0 \text{ Nm} \) is the force constant.
The PEC comprises the PA and one or several PCs, for which the distance between at least one of the monomers of the complexed PC and one monomer of the PA is smaller than 8 Å. The net charge of the PEC, $z_{\text{PEC}}$, was evaluated according to

$$ z_{\text{PEC}} = \frac{N_{\text{PC}} N_{\text{PEC}} N_{\text{mon,PC}}}{N_{\text{mon,PA}}} $$

where $N_{\text{PC}}$, $N_{\text{PEC}}$, and $N_{\text{mon,PC}}$, at a distance smaller than 8 Å from at least one PA monomer was made to analyze the positioning of the shorter PCs on the PA.

Finally, a characterization of the topological relation between a complexed PC and the PA was made by the calculation of the number of PA monomers, $L$, in a PA subchain, whose ends are linked to a PC (referred to as a linking analysis). For that reason, we assign a sequential number (referred to as a rank) to each of the PA monomers. Two slightly different definitions of $L$ have been used, namely,

$$ L_{\text{hl}} = m_h - m_1 + 1 $$

$$ L_{\text{ee}} = m_{e2} - m_{e1} + 1 $$

where $m_h$ and $m_1$ are the highest and lowest rank of monomers at a distance smaller than 8 Å from any monomer of the PC and

$$ L_{\text{hl}} = m_h - m_1 + 1 $$

where $m_{e2}$ and $m_{e1}$ are the highest and lowest rank of monomers at a distance smaller than 8 Å from the end monomers of the PC. Thus, $L_{\text{hl}}$ provides the maximum number of PA monomers linked to a PC, because every monomer of the PC is considered to potentially give the largest number of linked PA monomers (Fig. 1a), whereas $L_{\text{ee}}$ represents the number of PA monomers linked by the PC considering only the end monomers of the PC (Fig. 1b).

### Results and Discussion

The first part of this section comprises properties of systems containing a PA composed of $N_{\text{mon,PA}} = 120$ monomers and PCs composed of $N_{\text{mon,PC}} = 3, 5, 10, 40$ monomers at $\beta$ varying between 0.0 and 2.0 (3.0 for $N_{\text{mon,PC}} = 3$ and 5). In the second part, results are given for systems with $N_{\text{mon,PA}} = 30, 90$, and 120 monomers and the number of monomers of a PC is varied such that $N_{\text{mon,PA}}/N_{\text{mon,PC}} = 3$, again with $\beta$ ranging from 0.0 to 2.0.

### Complexes Containing a long PA

Figure 2 shows the probability distributions of the radius of gyration, $P(R_G)$, of the PA (left column) and PCs (right column) in systems containing a PA with 120 monomers and a different number of shorter PC chains with varying number of monomers ($N_{\text{mon,PC}}$ increases from top to bottom). Most often $P(R_G)$ displays a single maximum, giving the most probable radius of gyration, whereas the width provides information on the fluctuations of the polymer extension.

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### Table 1. Investigated Systems.

<table>
<thead>
<tr>
<th>System</th>
<th>$N_{\text{mon,PA}}$</th>
<th>$N_{\text{mon,PC}}$</th>
<th>$\beta$</th>
</tr>
</thead>
<tbody>
<tr>
<td>120:3:1</td>
<td>120</td>
<td>3</td>
<td>0.0, 0.5, 0.75, 1.0, 1.5, 2.0</td>
</tr>
<tr>
<td>120:5:1</td>
<td>120</td>
<td>5</td>
<td>0.0, 0.5, 0.75, 1.0, 2.0</td>
</tr>
<tr>
<td>120:10:1</td>
<td>120</td>
<td>10</td>
<td>0.0, 0.5, 0.75, 1.0, 2.0</td>
</tr>
<tr>
<td>120:40:1</td>
<td>120</td>
<td>40</td>
<td>0.0, 0.33, 0.67, 1.0, 2.0</td>
</tr>
<tr>
<td>90:30:1</td>
<td>90</td>
<td>30</td>
<td>0.0, 0.33, 0.67, 1.0, 2.0</td>
</tr>
<tr>
<td>30:10:1</td>
<td>30</td>
<td>10</td>
<td>0.0, 0.33, 0.67, 1.0, 2.0</td>
</tr>
</tbody>
</table>

where $\alpha_{i,j}$ is the angle formed by the vectors $\mathbf{r}_{i+1} - \mathbf{r}_{i}$ and $\mathbf{r}_{i-1} - \mathbf{r}_{j}$ of chain $c$, $k_{\text{ang}} = 1.7 \times 10^{-24}$ J deg$^{-2}$ the angular force constant, and $\alpha_0 = 180^\circ$ the equilibrium angle.

For simplicity, the same hard-sphere radius $R_l = 2$ Å has been used for the chain monomers and simple ions. Moreover, all charged particles are monovalently charged.

The particles are enclosed in a spherical cell with a radius of 300 Å. Throughout, $T = 298$ K and $\epsilon_r = 78.4$ have been used.

In this work, systems containing one PA, several PCs, and their counterions are considered. We have varied (i) the number of monomers of the PA ($N_{\text{mon,PA}}$), (ii) the number of monomers of each PC ($N_{\text{mon,PC}}$), and (iii) the number of PCs ($N_{\text{PC}}$). Table 1 summarizes the systems studied, referred to as $N_{\text{mon,PA}} : N_{\text{mon,PC}} : \beta$, where $\beta$ denotes the stoichiometric charge ratio of PC and PA according to

$$ \beta = \frac{N_{\text{PC}} N_{\text{mon,PC}}}{N_{\text{mon,PA}}} $$

In particular, the stoichiometric charge ratio $\beta = 1.0$ is referred to as charge equivalence.

### Simulation Details

All Monte Carlo simulations were performed in the canonical ensemble using the standard Metropolis algorithm. Three different types of MC trial moves were used for the PIs: (i) single monomer move, (ii) translation of the entire chain, and (iii) slithering move. The single-particle trial move was attempted 10 times more often than the other two types of trial moves. The counterions were subjected to translational trial moves only.

Each simulation included an equilibration of at least $1.4 \times 10^6$ trial moves per particle followed by a production run of at least $2 \times 10^6$ trial moves per particle. Statistical uncertainties were evaluated by dividing the total simulation into subbatches. All the simulations were performed using the simulation package MOLSIM.

### Characterization of Complexes

The structure of the PEC formed by the oppositely charged PIs was characterized using different properties. The extension of the PIs was monitored by calculating the radius of gyration $R_G$ of the two types of PIs separately with $R_G$ being defined according to

$$ R_G^2 = \frac{1}{N_{\text{mon}}} \sum_{i=1}^{N_{\text{mon}}} |\mathbf{r}_i - \mathbf{r}_{CM}|^2, $$

where $\mathbf{r}_i$ denotes the position of particle $i$, and $\mathbf{r}_{CM}$ denotes the position of the center of mass of the chain.
In general, all systems display similar trends. In a solution with a PA and its counterions without PCs (β = 0.0), the extension of the PA is much larger than that of the corresponding uncharged polymer (dotted curves labeled NP). At increasing number of PCs (increasing β), the maximum of P(RG) of the PA is successively shifted toward smaller RG, indicating a compaction of PA. Except for Nmon,PC = 3, the smallest size and size fluctuation occur at charge equivalence (β = 1.0). Moreover, the extension of the PA becomes smaller than that of the corresponding uncharged polymer, implying that the electrostatic effect of the PCs is different from a pure electrostatic screening of the repulsion between like-charged PA monomers. Further addition of PCs beyond charge equivalence (β > 1.0), leads to a re-expansion of the PA. The absolute size fluctuations appear to be only marginally affected on the addition of PCs up to β = 1.0, where these fluctuations are strongly reduced.

Systems with the shortest PCs (Nmon,PC = 3) display some deviation from this general behavior (Fig. 2a). The largest PA compaction appears at β = 1.5 and no substantial expansion of the PA occurs on further addition of PCs. As P(RG) at β = 1.5 is similar to that of the corresponding uncharged polymer, the compaction is smaller. As discussed earlier,18 the compaction of the PA occurs when the PCs are closer to the negative chain. These shorter PCs are, however, more loosely bound, and a larger amount is required to induce PA compaction, as observed in the cases of spermine and spermidine.40,41 This behavior has also been observed using trivalent ions as compacting agents.42 However, polymers with trivalent counterions without additional small ions typically display a smaller extension than that of corresponding uncharged polymers.43

An increasing number of PC monomers shifts the distribution P(RG) of PA to smaller sizes, that is, larger PCs promote a stronger PA compaction (Figs. 2a, 2c, 2e, and 2g). The most compacted PA, also showing the smallest size fluctuations, is obtained with the longest PCs considered (Nmon,PC = 40).

Beyond charge equivalence in systems containing PCs having five or more monomers (Nmon,PC ≥ 5), the PA undergoes some expansion at increasing β. In more detail, for Nmon,PC = 5 the P(RG) distributions for β = 2.0 and 1.0 are very similar, except for the presence of a second small maximum corresponding to a much more extended PA conformation (Fig. 2c). As the PCs are made even longer, the probability of finding compact conformations becomes progressively smaller for β = 2.0 (Figs. 2e and 2g).

The general behavior of P(RG) of PCs, given in Figure 2 (right column), is similar to that observed for the PA. The PCs undergo similar compaction in the presence of the longer and oppositely charged PA, and, in particular, for longer PCs, the maximum of P(RG) is shifted toward smaller RG as further PC chains are added. The strongest PC compaction appears again at charge equivalence (β = 1.0). For the shortest PCs (Nmon,PC = 3), no significant variation in P(RG) is observed (Fig. 2b), which is not surprising, considering that they are only trimers. The size distributions at all β are shifted to larger sizes when compared with the corresponding uncharged chain. In fact, only for Nmon,PC = 40 and β ≥ 1.0 is the extension of the PCs smaller than that of the corresponding uncharged polymer.

The reason for the size expansion of the PCs beyond charge equivalence is twofold: (i) PCs complexing the PA expand due to the expansion of the PA and (ii) the number of PCs not belonging to the complex increases, and these PCs have a more expanded conformation. The distribution of P(RG) of the PCs for system 120:40:2.0 (Fig. 2h) displays two maxima: one located at RG ≈ 20 Å, arising from the PCs complexed with the PA, while the other at RG ≈ 50 Å originating from PCs that are free in solution. Obviously, when the PCs are sufficiently long the two contributions become separable.

Figure 3 presents the ratio of the net charge of the PEC and that of the PA as function of β. As the limiting net charge ratio at large β for PA’s with three monomers is positive, the PC’s are not able to fully neutralize the PA, which is in good agreement with results given in Figure 2a. However, PCs with a larger number of monomers (Nmon,PC ≥ 5) are able to induce overcharged PECs. For the longest PCs considered (Nmon,PC = 40), at β ≥ 1.33, we observe zPEC/zPA ∼ −0.33, implying that beyond charge neutralization one additional PC is incorporated in the PEC. At Nmon,PC = 5 and 10, we have also a charge excess corresponding to, most often, one additional PC. We rationalize the spatial expansion of the PA beyond charge equivalence (β > 1.0), observed in Figure 2, to the overcharging of the PA by the excess of one PC, as assumed in other model systems.44 It should be noted that additional calculations were performed to examine how sensitive zPEC/zPA is on the threshold distance defining a complex. Not surprisingly, systems with shorter PCs were the most sensitive. For example, the system Nmon,PC = 3 and β = 3.0 gave zPEC/zPA = 0.23, 0.13, and 0.10 using the threshold distances 6, 8, and 10 Å, respectively. No difference among these threshold distances was found for Nmon,PC = 10 and 40. A similar behavior to that depicted in Figure 3 has been observed experimentally using, for example, poly(propylene imine) dendrimers of different generations.45 Dendrimers of generations 4 and 5, the most charged of the study, formed positively charged
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Figure 2. Probability distribution of the radius of gyration $P(R_G)$ of the PA (left) and PCs (right) for $N_{\text{mon,PA}} = 120$ and (a, b) $N_{\text{mon,PC}} = 3$, (c, d) 5, (e, f) 10, and (g, h) 40 at indicated $\beta$. The corresponding distribution for an uncharged PI (dotted curves labeled NP) and for a system containing one PC and its counterions (dashed curves labeled PC) are also shown.

PECs when added in excess to a DNA solution, whereas dendrimers of smaller generations formed electroneutral complexes even at high $\beta$ values.

Figure 4 shows the average number of PC monomers $\langle N_{\text{mon,PC}} \rangle$ in the vicinity of each PA monomer at increasing PC length (top to bottom) at various $\beta$. Generally, the number of PC monomers in the vicinity of the PA monomers (i) increases at increasing $\beta$ up to, at least, $\beta = 1.0$, (ii) is lower at the ends of the PA, and (iii) increases with increasing length of the PCs at a given $\beta$. Observation (i) is of course a consequence of the increasing number of PCs complexed to the PA (see Fig. 3), whereas (ii), the drop at the ends, is attributed to a weaker electrostatic attraction to the PA. Similar observation has been made for the distribution of counterions along a polyion.46, 47 The final observation implies that longer PCs form tighter complexes with the PA, a consequence of the stronger attraction between the oppositely charged PIs.
Interestingly, $\langle N_{\text{mon,PC}} \rangle$ versus the rank of PA monomer displays further details that provide a deeper insight into the complex. For systems below charge neutralization ($\beta < 1.0$), we find small maxima near the ends with the shortest PCs ($N_{\text{mon,PC}} = 3$; Fig. 4a). With an increasing length of the PCs, damped oscillations start to propagate toward the middle of the PA (Fig. 4b) and with PCs having 10 monomers ($N_{\text{mon,PC}} = 10$) the oscillations appear for the whole PA (Fig. 4c). In fact, for system 120:10:0.5 with six PCs complexing the PA, the six maxima indicate that there is a larger probability of finding the six PCs located separately along the PA chain rather than being close to each other. The same type of oscillation is observed for the 120:10:0.75 system, now with nine maxima corresponding to the nine complexed PCs. The snapshots in Figure 5 illustrate these topological arrangements. Considering the systems with the longest PCs ($N_{\text{mon,PC}} = 40$), a single PC favors complexation at the central part of the PA chain and with two PCs a dip is found at the center of the PA chain (Fig. 4d). Thus, below charge equivalence, the complexation of not too short PCs to a longer PA is similar to that of beads on a string. Such oscillatory features with the same interpretation have also been observed in systems containing complexes formed by a polyanion and oppositely charged macroions.48

At charge equivalence ($\beta = 1.0$), these finer details are absent. That is understood as being a consequence of the much more compact PA (Fig. 2), making it likely that the PCs do not appear, any longer, as discrete entities.

Beyond charge equivalence ($\beta > 1.0$), the average number of PC monomers in the vicinity of each PA monomer still increases with increasing $\beta$ for PCs having three monomers. This occurs because the complex is not yet electroneutral at charge equivalence and displays further contraction as additional PCs are added and become complexed. Perhaps more unexpected is that the $\langle N_{\text{mon,PC}} \rangle$ of the overcharged complexes remains constant at increasing $\beta$ for PCs with 5 and 10 monomers but decreases for PCs with 40 monomers. We suggest that $\langle N_{\text{mon,PC}} \rangle$ is determined by two opposing effects. The presence of an additional PC should lead to (i) an increase of $\langle N_{\text{mon,PC}} \rangle$ solely by the fact there is a larger number of complexed PC monomers and (ii) a decrease of $\langle N_{\text{mon,PC}} \rangle$ owing to the expansion of the PA, making a PC monomer neighbor to fewer PA monomers. Obviously, the importance of these two effects differs among the systems with PCs of different lengths.

We will now further characterize the PECs by examining the probability distributions $P(L_{hl})$ and $P(L_{ee})$. According to the definitions of $L_{hl}$ and $L_{ee}$ [eqs. (9) and (10)], they provide the length of a PA subchain that complexes a PC, either maximally ($L_{hl}$) or by the end monomers of the PC ($L_{ee}$). Such probability distributions are given in Figure 6 for PCs with 10 (top row) and 40 (bottom row) monomers. The results obtained for PCs with three or five monomers

![Figure 3](image_url)  
Figure 3. Ratio of the net charge of the PEC and of the PA, $z_{\text{PEC}}/z_{\text{PA}}$, versus the stoichiometric charge ratio, $\beta$, for $N_{\text{mon,PA}} = 120$ at indicated $N_{\text{mon,PC}}$. In particular, $z_{\text{PEC}}/z_{\text{PA}} = 0$ represents a neutral complex and $\beta = 1.0$ charge equivalence.

![Figure 4](image_url)  
Figure 4. Average number of PC monomers at a distance smaller than 8 Å from a PA monomer, $\langle N_{\text{mon,PC}} \rangle$, versus the rank of PA monomer for $N_{\text{mon,PA}} = 120$ with (a) $N_{\text{mon,PC}} = 3$, (b) 5, (c) 10, and (d) 40 at indicated $\beta$.  
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Figure 5. Representative snapshots of system (a) 120:10:0.5 and (b) 120:10:0.75, displaying PA monomers (dark gray), PC monomers (light gray), PA counterions (light gray), and PC counterions (dark gray).

arere very similar to those with 10 monomers (data not shown) and will not be discussed further.

Consider first the set of systems 120:10:β (Figs. 6a and 6b). At β = 0.5, P(Lhl) and P(Lee) are very similar and relatively narrow with maxima at L ≈ 14, indicating that the six PCs are stretched and aligned parallel to the PA, as suggested by the contact analysis in Figure 4 and the snapshot in Figure 5a. At charge equivalence (β = 1), the probability of finding longer PA subchains linked to a PC is enhanced as well as the probability of Lee < 10, that is, nearby PA monomers are linked to the two ends of a PC. This implies an compaction of the PA and, since the ends of a PC are spatially close to each other, also the compaction of the PC. Beyond charge equivalence (β > 1.0), both linking analyses display an increase in the probability maximum, now occurring at L ≈ 10, and concomitant decrease of the probabilities of large L consistent with the reexpansion of the PEC.

Turning to the set of systems 120:40:β (Figs. 6c and 6d), the linking analyses display new features revealing internal structuring of the PEC. With one PC present (β = 0.33), there is again a strong resemblance between the two linking analyses, indicating that the PC is essentially stretched along the PA. Furthermore, P(Lee) possesses a left-side tail, displaying some propensity for the PC to adopt more compact conformations, in agreement with the P(Rg) of the PC (Fig. 2h) that also presents this tail.

At charge equivalence (β = 1.0), P(Lhl) is very different from that of systems with shorter PCs. The largest probability occurs for the maximal linking length Lhl = 120, and there is no indication of linking lengths shorter than 30 monomers. Hence, most likely a PC is simultaneously in contact with PA monomers that reside near the two ends of the PA. In addition, P(Lee) displays a broad length distribution, indicating that the end monomers of a PC often link to nearby PA monomers. These results suggest a strong intermixing of PC and PA monomers in a compact PEC.

Beyond charge equivalence with a PEC having a charge excess of one PC, we again encounter different features in the P(Lhl) linking analysis. Now, P(Lhl) displays four maxima at Lhl ≈ 30, 60, 90, and 120 with decreasing amplitudes, denoted by (i)–(iv) in Figure 6c. Maximum (i) corresponds to PCs that link about a forth of the PA chain and are therefore expected to be stretched along the PA chain and spatially separated from other PCs. Maximum (ii) occurs for PCs that link about half of the PA chain and are therefore expected to be stretched along the PA chain and spatially separated from other PCs. Maximum (ii) occurs for PCs that link about half of the PA chain and which requires that the

Figure 6. Probability distributions of (left) P(Lhl) and (right) P(Lee) with (a, b) Nmon,PC = 10 and (c, d) 40 for Nmon,PA = 120 at indicated β. In (c), (i)–(iv) denote maxima of the distribution at β = 2.0.

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PA chain is, at least, partially compact such that these PCs can
embrace half of it. Maximum (iii) corresponds to PCs, which link
approximately three-fourth of the PA, which hence has to be even
further compacted, whereas maximum (iv) implies that all four PCs
are in contact with both ends of the PA, which suggests that the
PA is completely compacted. The appearance of both stretched and
compacted PCs in the PEC is consistent with the broad distribution
of $L_{cc}$ of the PCs.

Figure 7 provides snapshots illustrating four structures of PECs
corresponding to the four maxima of $P(L_{hl})$ in Figure 6c as follows:
(i) four PCs separately complexing the PA chain (Fig. 7a) contribut-
ing to the first maximum of $P(L_{hl})$; (ii) two PCs and half of the PA
intermixed and compacted and two PCs separately located along a
stretched part of the PA (Fig. 7b) contributing to the first and second
maxima; (iii) three PCs and three-fourth of the PA intermixed and
compacted and one PC separately located along a stretched part of
the PA (Fig. 7c) contributing to the first and third maxima; and (iv)
all PCs and the full PA intermixed and compacted (Fig. 7d) con-
tributing to the fourth maximum. Moreover, the appearance of four
plateaus separated by shallow minima of the contact analysis given
in Figure 4d is consistent with a finite probability of fully separated
PCs along the PA chain as shown in Figure 7a. The appearance of
a number of different characteristic and distinguishable structures
of the PEC with different PA and PC conformations rationalizes the
broad and rather uniform distribution of the $R_G$ of the PA (Fig. 2g),
and the right shoulder of the maximum located to lower values of
$R_G$ of the PC (Fig. 2h).

The aforementioned analyses show that the overcharged complex
with PCs having 40 monomers undergoes significant fluctuations
between four different and separable equilibrium structures. The two
extreme ones involve (i) a stretched PA with the four PCs separated
and aligned with the PA, and consequently, the excess PC charge
is well distributed along the PA, and (ii) a compact PEC with PA
and PC monomers strongly intermixed with the excess PC charge
more localized in space. From Figure 7d, it could be discerned that
the excess PC charge is predominantly located on the surface of the
PEC. The two intermediate structures are composed of stretched and
compacted subchains of the PA. Here, we have no information of
how the excess PC charge is distributed between these two parts.

Phase diagrams of solutions containing long PAs and shorter PCs
at various ionic strength have been obtained using theoretical anal-
ysis. At charge equivalence, the authors predict the appearance
of neutral complexes composed of one PA and many PCs condensed
in a “liquid drop.” More related to our work, a study of a single
PA and many shorter PCs, at off charge equivalence conditions,
shows the appearance of a complex formed by “a neutral head and
a charged tail” referred to as a “tadpole.” The head is neutral and
composed of a part of the PA and PCs, both compact, whereas the
stretched tail is charged and composed of the remaining part of the
PA and other PCs, for example, an interchain disproportionation
of the PC chains in the complex and concomitant intrachain dispro-
portionation of the PA forming a complex composed of two parts
with unequal structure and net charge. The two intermediate structures
in Figures 7b and 7c are very striking realizations of tadpoles based
on a coarse-grained model.

Tadpole observations in coarse-grained models have appeared in
a few different systems. Simulations of a solution containing
polyampholytes and PEs of similar lengths showed that the (ran-
dom) polyampholyte resides preferentially at the end of the PE with
an elongated conformation and aligned along the PE backbone. When
the ionic strength was increased, the compacted part of the
complex moved toward the center of the PE backbone. Diblock
polyampholyte–PE complexes also showed a tadpole-like structure
with part of the block that possesses equal charge of the PE form-
ing the tail and the other block intermixing with the PE, forming
the head of the tadpole. Clearly, in these cases, the asymmetry
of the system induces such conformations. Similar observations
were made on linear PI and dendrimer (or star-like polymer) sys-
tems, where one-tail (tadpole) conformations were shown to be
more energetically favorable when the linear PI length was

Figure 7. Representative snapshots of system 120:40:2.0 illustrating four different PEC structures: (a) four
PCs are separately located along a stretched PA, (b) two PCs intermix and compact half of the PA while
two PCs are separately located along the stretch part of the PA, (c) three PCs intermix and compact three
fourths of the PA while one PC is separately located along the stretch part of the PA, and (d) all four PCs
intermix and compact the whole PA. PA and PC monomers are represented by red and green, respectively,
and PA and PC counterions by blue and black, respectively.
Figure 8. Average number of PC monomers at a distance smaller than 8 Å from a PA monomer, \( \langle N_{\text{mon,PC}} \rangle \), versus the rank of PA monomer for \( N_{\text{mon,PA}} = 30 \) and \( N_{\text{mon,PC}} = 10 \) at indicated \( \beta \).

In this section, we consider systems with PAs of different lengths (30, 90, and 120 monomers) while keeping \( N_{\text{mon,PA}} / N_{\text{mon,PC}} = 3 \).

The overall compaction behavior, at least in what concerns the probability distributions of the \( R_G \), is preserved when the length of the PA is reduced from 120 to 30 monomers (not shown). As both PIs are made shorter, their compaction degree decreases.

The average number of PC monomers \( \langle N_{\text{mon,PC}} \rangle \) in the vicinity of each PA monomer was evaluated for the different sets of systems under study. Systems 120:40: \( \beta \) and 90:30: \( \beta \) are very similar both qualitative and quantitatively, illustrating (i) the complexation of a single PC chain in the middle of the PA chain, (ii) the preferential placement of the PCs separately along the PA chain for \( \beta = 0.67 \) and 2.0, and (iii) an uniform distribution of the PC monomers along the PA chain at charge equivalence. Set of systems 30:10: \( \beta \) preserves features (i) and (ii). However, for \( \beta = 1.0 \) the distribution of the PC monomers along the PA chain is not uniform. Instead, it shows three maxima, one for each PC chain complexed to the PA (Fig. 8). This suggests that the intermixing between PA and PC monomers is not very strong and that a reasonable number of conformations includes the PC chains spatially separated along the PA.

The PECs formed by the systems under consideration have been further characterized by examining the distributions \( P(L_{hl}) \) and \( P(L_{ee}) \). The general features obtained for systems 120:40: \( \beta \), 90:30: \( \beta \), and 30:10: \( \beta \) are again very similar. However, system 30:10:1.0, in contrast to what was obtained with the longer PAs, shows no predominance of very compacted structures in the \( P(L_{hl}) \) distribution (Fig. 9a). Instead, a broad maximum is obtained at about 10 monomers followed by a nearly uniform distribution where two other features can be deconvoluted for 20 and 30 monomers. Also, the \( P(L_{ee}) \) distribution (Fig. 9b) shows a large contribution of \( L_{ee} \) values below 15. This indicates again the coexistence of different PEC structures and is in good agreement with the two minima observed in the contact analysis (Fig. 8). Representative snapshots in Figure 10 show the variety of PEC structures that can be obtained for 30:10:1.0, ranging from extended to compact PA conformations, while the longer PA systems display essentially compact structures and small size fluctuations at charge equivalence.

Clearly, the 30 monomer-long PA does not undergo as strong compaction as the 120 and 90 monomer-long ones. Experiments

Figure 9. Probability distributions of (a) \( P(L_{hl}) \) and (b) \( P(L_{ee}) \) for \( N_{\text{mon,PA}} = 30 \) and \( N_{\text{mon,PC}} = 10 \) at indicated \( \beta \).

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were additionally conducted using a 30 monomer-long PC or two PC chains with 15 monomers and, again, very extended structures were occasionally obtained.

Intrachain and interchain disproportionations are also present in system 30:10:2.0, as shown by the reminiscences of local maxima in $P(L_{\text{Pa}})$ (Fig. 9a) and, the already mentioned, maxima in the contact analysis (Fig. 8).

Conclusions

We have studied the structure of the complexes formed on the interaction of oppositely charged polyions with emphasis on the compaction of the individual polyions and the internal structure of the complexes.

Systems with relatively long PA chains and very short PCs, display PCs that are loosely bound, having a very small and local effect on the longer chain. Such PECs retain some negative charge and behave close to an uncharged chain even for PC concentrations much above charge equivalence. An increase in the PC chain length leads to the increase of the PA compaction. Below charge equivalence, the PC chains are preferentially aligned with the PA chain. The most compact PEC structure is found at charge equivalence, and further addition of PCs leads to an expansion of the complex due to overcharging of the PA.

For sufficiently long PCs, the topology of the complexes is strongly dependent on the number of PC chains. When few compacting chains are present, these are, again, predominantly distributed along the PA. However, for systems close to but off-charge equivalence, there is a large variation in complex topology with the coexistence of extended, compact, and intermediate structures showing disproportionation. This leads to an increase in the size dispersion of the complexes.

Short PAs do not undergo strong compaction, and the coexistence of complex structures with different degrees of PA extension is obtained even at charge equivalence.

The linking analyses introduced in this work, together with the contact analysis and the probability distributions of the radius of gyration of the PA and PCs, offer unique information, demonstrating an equilibrium of PECs with different structures. These structures range from extended PECs where all PCs are stretched, to compact PECs where all PCs are collapsed. In between, we found PECs with both stretched and collapsed PCs that we referred to as interchain disproportionation of the PCs and concomitant intrachain disproportionation of the PA.

References

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