The effect of dendrimer charge inversion in complexes with linear polyelectrolytes

Citation for published version (APA):
INTRODUCTION

One of the main lines of progress in biology, pharmacy, and medicine is the use of nanotechnologies. An example of this application is the transport of drugs and genes directly to cells for correction of genetic defects and damaged areas. The most popular vehicles used in clinical tests, or in other words, nanocontainers for drug and gene delivery, are viruses. However, the viruses themselves are a great hazard to the body. At the same time, the use of polymers, which are the best known synthetic nanomolecules, as nanocontainers is usually impractical because of their polydispersity.

Dendrimers are new polymeric materials that are free from this limitation. Their unique architecture and monodispersity makes it possible to use dendrimers as nanocontainers for the direct transport of drugs and genes. Despite their high cost, two types of dendrimer are manufactured on a rather large scale, polyamidoamine (PAAM) by the Aldrich Chemical Company and Dendritech and polypropyleneimine (PPI) or Astramol by Aldrich and DSM Fine Chemicals. The properties of these dendrimers and their potential use in various fields are being studied intensively now [1, 2]. Dendrimers have a fairly low in vivo toxicity [3]. Recently, Zinselmeyer et al. [4] showed that PPI dendrimers possess a low in vitro cytotoxicity; however, a growth in toxicity with an increase in the number of generations limits the use of these high-generation dendrimers as nanocontainers.

Investigation of the properties of dendrimers in complexes with various compounds is the first step in studying the feasibility of their application as nanocontainers. Usually, complexes of dendrimers with other compounds in aqueous solutions are stabilized by electrostatic forces. In this case, a dendrimer must have an opposite charge as compared with the guest molecule. There is a wealth of studies in which the guest was a low-molecular-mass compound. However, the amount of works on studying dendrimer complexes with polymeric molecules is small. Of these, the study by Kabanov et al. [5] should be mentioned first. The most important representative of linear macromolecules is DNA. Complexes of DNA with various compounds are being stabilized by electrostatic forces. In this case, a dendrimer must have an opposite charge as compared with the guest molecule. There is a wealth of studies in which the guest was a low-molecular-mass compound. However, the amount of works on studying dendrimer complexes with polymer molecules is small. Of these, the study by Kabanov et al. [5] should be mentioned first. The most important representative of linear macromolecules is DNA. Complexes of DNA with various compounds are being stabilized by electrostatic forces. In this case, a dendrimer must have an opposite charge as compared with the guest molecule. There is a wealth of studies in which the guest was a low-molecular-mass compound. However, the amount of works on studying dendrimer complexes with polymer molecules is small. Of these, the study by Kabanov et al. [5] should be mentioned first. The most important representative of linear macromolecules is DNA. Complexes of DNA with various compounds are being stabilized by electrostatic forces. In this case, a dendrimer must have an opposite charge as compared with the guest molecule.
plexity. Computer simulation of complexes formed by charged dendrimers and oppositely charged linear molecules was first performed by Welch and Muthukumar [11]. Special attention in their study was given to the case when a dendrimer charge exceeded the charge of the chain.

In this study, we investigated complexes of dendrimers and oppositely charged chains bearing a charge equal to or greater than the dendrimer charge. In such systems, a very interesting effect of sign inversion of the dendrimer charge may be produced.

The effect of charge inversion or overcharging of a spherical macroion in complexes with polyions or small ions is well known. The effect consists in that the amount of oppositely charged groups adsorbed on the spherical macroion exceeds the number required for its electric neutralization. The overcharging effect has been studied intensively both theoretically and experimentally [12–22]. The adsorption can be determined experimentally; for example, by measuring the mobility of the complex during electrophoresis. For complexes with polymer molecules, these measurements are made after enzymatic cutting of the free end of the adsorbed polyion [23].

The phenomenon of charge inversion on a spherical macroion, which constitutes an impenetrable charged sphere, in a complex with an oppositely charged linear chain has been considered in many works [12–16]. To describe the effect of charge inversion in such a system, correlation theories are generally used [17–21]. Chodanowski and Stoll [13] attempted Monte Carlo computer simulation of the complexes formed by a charged hard sphere and an oppositely charged freely jointed chain. Their results agree well with the theoretical predictions by Nguyen and Shklover [18]. The degree of charge inversion depends on the solvent quality, macroion radius, and polyelectrolyte flexibility [16, 22].

In a dendrimer complex with a polymer molecule, the linear polyelectrolyte must also be adsorbed on the dendrimer. Unlike a hard sphere, dendrimer is fairly flexible, does not possess a clearly defined surface, and admits penetration of a chain inside. The phenomenon of charge inversion in such a system is manifested in the charge of a part of the linear chain adsorbed on the dendrimer exceeding the charge of the dendrimer itself. There are a few reported studies in which the overcharging was examined experimentally for nonrigid macroions. For example, Yager et al. [7] showed that a negatively charged DNA molecule, while winding round a positively charged liposome, forms a complex that bears a negative net charge after the enzymatic cutting of the DNA tails.

The effect of charge inversion attracts special attention because of its importance for gene and drug delivery: it is known that the surface of a cell membrane usually bears a negative charge and a complex composed of a nanocontainer and, e.g., DNA must be positively charged in order to penetrate into the cell. However, there have been no systematic investigations of this effect for entities that can be used as nanocontainers, including dendrimers, i.e., systems penetrable to other molecules. The first attempt of this sort seems to be a study of a complex formed by a nonspherical protein and a linear chain [24].

The main aim of this study was to investigate the phenomenon of charge inversion in a complex composed of a charged dendrimer and an oppositely charged linear chain by simulation using the Brownian dynamics approach. As a model of a charged dendrimer, we consider the model used previously in [25–30]. We will study the manifestation of the effect in structural characteristics of the complex. We deal with complexes with rather long linear chains whose charge is equal to or exceeds the dendrimer charge. This study is restricted to simulation of complexes that are formed by charged linear chains and third- and fourth-generation dendrimers with charged terminal groups. An analysis of dendrimers of higher generations showed the necessity of including very long polymer chains in the complex, but this would increase the simulation time critically. Note that PAAM dendrimers of these generations have been used successfully as nanocontainers for drug delivery [31] and DNA capture [10].

**DENDRIMER AND LINEAR-CHAIN MODELS. SIMULATION METHOD**

In this study, we use the model of a freely jointed chain for a charged dendrimer [25–30] and an oppositely charged linear chain (Fig. 1). The dendrimer is represented as a system of beads with a coefficient of friction $\zeta$ linked by rods with a length $l$. Dendrimers are assumed to have a trifunctional core and trifunctional branching points. Dendrimer generations are numbered beginning from zero, with reference to the entity composed of four beads including the core. The total number of beads, $N$ in a dendrimer of the $g$th generation may be defined by the expression

$$N = 3s(2^{g+1} - 1) + 1,$$

where $s$ is the length of the spacer between branching points. In this study, we considered the case of $s = 1$. The main results were obtained for $g = 3$ and 4.

The polymer chain is a linear system composed of $N_{cl}$ beads of the same nature connected by rods with a length $l$. Excluded-volume interactions between the $i$th and $j$th beads in the complex, which are not linked by covalent bonds and occur at a distance of $r_{ij}$ from one another, are described by the modified Lennard-Jones potential in which the term responsible for attraction is omitted:

$$\tilde{U}_{LJ}(r_{ij}) = 4\varepsilon_{LJ}\left(\frac{\sigma}{r_{ij}}\right)^{12} - \left(\frac{\sigma}{r_{cut}}\right)^{12}. \quad (2)$$
Here, $r_{cut} = 2.5\sigma$ is the potential cutoff distance. Thus, the potential defined by Eq. (2) corresponds to an athermal solvent. For calculation, the earlier selected parameters of the Lennard-Jones potential, namely, the length $\sigma = 0.8l$ and the energy $\epsilon_{LJ} = 0.3k_BT$ [27–30], were used.

All of the $N_T$ terminal groups of the dendrimer are charged and bear an identical charge $+e$. This situation may be realized, for example, in aqueous solutions of PAAM and other dendrimers at neutral pH values [32–34].

Each bead of the linear chain bears a negative charge $-e$; i.e., the total charge of the chain is $-eN_{ch}$.

Each $j$th bead interacts with all the other charges in the system via the Debye–Hückel potential (screened Coulomb potential):

$$U_{ij}^C = \frac{\lambda_B}{k_BT} \sum_i \exp(-kr_{ij})$$  \hspace{1cm} (3)

where $r_{ij}$ is the distance between the charges $i$ and $j$, the summation is carried out over all the other charged beads and $\lambda_B$ is the Bjerrum length describing the Coulomb interaction force in a medium with a dielectric constant of $\varepsilon$

$$\lambda_B = \frac{\epsilon^2}{4\pi \varepsilon k_B T}.$$  \hspace{1cm} (4)

The $\lambda_B$ value in water at ambient temperature equals 7.14 Å and is close to the segment length of an ordinary flexible-chain polymer. Therefore, without loss of generality, we took $\lambda_B = l$.

The inverse Debye radius $k$ in Eq. (3) corresponds to the screening of electrostatic interactions by counterions and salt ions present in solution:

$$k^2 = 4\pi \lambda_B^2 \sum_i z_i^2 c_i.$$  \hspace{1cm} (5)

Here, $c_i$ is the concentration of the $i$th ion and $z_i$ is its valence. Electrostatic interactions are expected to have the greatest effect when the Debye radius $r_{ij}$ exceeds the dendrimer size. In this study, $r_{ij} = k^{-1} = 8.96l$, which corresponds to a salt concentration of 2.2 mol/l in an aqueous solution at room temperature [11]. This value was also used earlier in investigation of some dendrimers [27–30]. Generally speaking, in molecular systems with a high charge density, such as dendrimers, the effect of condensation of counterions is substantial [35] and the Debye–Hückel mean-field approximation is insufficiently correct. However, the dendrimer charge in the complexes in question is counterbalanced by the charge of the linear chain and the counterion condensation effect must be small.

The main results were obtained on complexes formed by the $g = 3$ ($N = 46$, $N_T = 24$) and the $g = 4$ ($N = 94$, $N_T = 48$) dendrimers and chains that have a total charge equal to or greater than the dendrimer charge, i.e., at $60 \geq N_{ch} \geq 24$ (for complexes with the $g = 3$ dendrimers) and at $90 \geq N_{ch} \geq 48$ (for complexes
with the \( g = 4 \) dendrimers). To simulate the complex, we made use of the Brownian dynamics in which the motion of all particles in the system is described by the Langevin equation. Interactions between all particles inside the complex are taken into account in an explicit form and interaction with the solvent is expressed through friction forces and random Brownian strikes.

Strictly speaking, in order to describe the polymer dynamics in solution, it is necessary to take into account the effect of hydrodynamic interactions as well. However, since the main task of this work was to study the equilibrium properties of complexes, hydrodynamic interactions that have no effect on these properties may be ignored in simulation. Therefore, in this study we consider freely draining models of the dendrimer and linear chain. The finite-difference scheme based on the Ermak–McCammon equation [25–30], which has been applied successfully in the previous studies on the properties of some charged and neutral dendrimers [27, 28]. The total force \( \mathbf{F}_j^0 \) acting on the \( j \)th bead in the system may be defined by the expression

\[
\mathbf{F}_j^0 = -\sum_{k=1}^{N} \mu_k \left( \frac{\partial \mathbf{v}_k}{\partial r_j} \right)^r - \partial \mathbf{U}_{LL}/\partial r_j^0 - \partial \mathbf{U}_{C}/\partial r_j^0,
\]

where \( \mathbf{v}_k = \frac{1}{2} (\mathbf{r}_{k+1} - \mathbf{r}_k)^2 - l^2 = 0 \) is the equation of the \( k \)th bond, \( \mu_k \) is the corresponding Lagrange multiplier,

and \( \mathbf{r}_j^0 \) is the radius vector of the \( j \)th bead before the next time step \( \Delta t \).

To retain a fixed value of the bond (rod) length \( l \), the SHAKE algorithm [36] with a tolerance of \( 2 \times 10^{-6} \) was used. As usual, we used dimensionless quantities expressed in units of length \( l \), energy \( k_B T \), frictional coefficient \( \zeta \), time \( \zeta l^2/k_B T \), and charge \( e \). The dimensionless integration step is \( \Delta t = 10^{-4} \). This value of \( \Delta t \) was selected so that the maximal displacement of the bead by one step did not exceed 10% of the rod length.

To generate the initial dendrimer configuration, we used the procedure proposed by Murat and Grest [37]. The \( g = 0 \) generation is created by linking three monomers to the central bead (core) along the axes \( OX, OY, \) and \( OZ \) of the coordinate system. The next generation is obtained by adding two monomers to each of the terminal beads of the previous generation. The new monomer is considered to be added if the distance between it and any of the already added monomers is \( r \geq r_{\text{min}} = 0.8 \sigma \). If the new monomer cannot be added after 1000 trials, the building procedure begins again.

To build the initial configuration of the linear chain, we determined the maximum value of the coordinates of beads of the constructed dendrimer: \( x_{\text{max}}, y_{\text{max}}, \) and \( z_{\text{max}} \). The first bead of the chain has the coordinates \( x_{\text{max}} + 1, y_{\text{max}}, z_{\text{max}} \). Then, we constructed the whole chain in the planar extended configuration with a bond angle of \( \theta = 90^\circ \) (Fig. 1).

After building the initial configuration, the system was brought to equilibrium over 6–11 sets of calculations, wherein each set consisted of \( 2 \times 10^6 \) steps. After that, 7 main sets of the same duration were carried out, by which the equilibrium characteristics of the system were calculated. The equilibration was monitored by following the instantaneous values of the squared radius of gyration \( R_g^2 \) for the complex as a whole and separately for the dendrimer and the chain that compose the complex:

\[
R_g^2 = \frac{1}{N+1} \sum_{n=0}^{N} (\mathbf{r}_n - \mathbf{r}_C)^2,
\]

where \( \mathbf{r}_C \) is the radius vector of the corresponding center-of-mass and \( \mathbf{r}_n \) is the radius vector of the \( n \)th bead.

Figure 2 shows a typical evolution of instantaneous values of the squared radii of gyration during the procedure of equilibration of the complex formed by the \( g = 4 \) dendrimer and the chain with \( N_{\text{ch}} = 48 \). During the equilibration time, the squared radius of gyration of the dendrimer varies to a much smaller extent than that of the linear chain and the length of the entire procedure is determined by the time of equilibration of the linear chain.
SIMULATION RESULTS

Charge Inversion Effect

As mentioned above, the overcharging of an impenetrable charged sphere interacting with an oppositely charged linear chain has been established and studied in theoretical and computer simulation works [7, 12–21, 23, 38]. The essence of the effect is that the chain charge adsorbed on the sphere exceeds the initial charge of the sphere.

The correlation theory [18] for the persistent-chain model predicts the following change in the structure of the complex with an increase in the chain length $N_{ch}$ beginning from a chain length of $N_{ch} = N_p$ that is necessary for the electric neutralization of the sphere. At $N_{ch} \geq N_p$, the linear chain is completely adsorbed on the sphere until the chain length reaches the critical value $N_C$. At $N_{ch} = N_C$, a first-order phase transition takes place when the number of chain monomeric units adsorbed on the sphere decreases dramatically, reaching the limiting value with a further increase in the chain length. Nguyen and Shklovskii [18] derived analytic expressions for the critical chain length $N_C$ at which the tail is released, the length of the tail at this point $N_{C,\text{tail}}$, and the limiting number of chain monomeric units adsorbed on the sphere $N_{\text{ov}}$. These quantities are strongly dependent on the total charge of the sphere and depend weakly on its radius. The predictions by the analytic theory agree well with the results of Monte Carlo simulation [13, 14]. Chodanowski and Stoll [13, 14] used the model of a chain composed of $N$ freely jointed charged hard spheres with a radius of $\sigma_m = 3.57$ Å and a charge $-e$. The distance between centers of the spheres in the chain (bond length) was assumed to be equal to the Bjerrum length in water, $\lambda_B = l = 2\sigma_m = 7.14$ Å. The impenetrable uniformly charged sphere was characterized by a radius $\sigma_p$ and a charge $Q$ placed at its center so that the surface charge density was fixed equal to +100 μC/m². The $\sigma_p/\sigma_m$ ratio was varied between 2 and 50. The chain monomeric unit was considered adsorbed on the sphere if the distance between its center and the center of the sphere did not exceed a distance of $\sigma_p + l = R + l$, where $l$ is the bond length. We will call this criterion for adsorption the spherical criterion.

Strictly speaking, the adsorption criterion is not defined unequivocally for macroions that are not impenetrable hard spheres, such as dendrimers. We may use the same criterion as was employed by Chodanowski and Stoll [13, 14] that represents the dendrimer as a sphere with an effective radius $r_{ov}$. As shown in [18], a persistent chain with a charge equal to that of a spherical macroion is adsorbed completely on this ion. This finding was used to determine the radius $r_{ov}$. The smallest values of $r_{ov}$ at which a chain with a length of $N_{ch} = N_T$ is adsorbed on a dendrimer within the limits of accuracy are equal to 3.2 and 4 for dendrimers of the generations $g = 3$ and 4, respectively. The found values of $r_{ov}$ exceed the corresponding values of the radius of gyration of the dendrimer in the complex. For all the examined complexes with $g = 3$ and 4 dendrimers, we found the value of $N_{ads}$ while considering the dendrimer as a sphere with the radius $r_{ov}$ as calculated by the spherical criterion for adsorption. The results obtained for the adsorption of the linear chain on the dendrimer are presented in Fig. 3.

In view that chain units penetrate the dendrimer and occur near the terminal groups, we may use another criterion for determining the number of adsorbed groups; we will call this criterion the local criterion. We consider that a chain bead is adsorbed on the dendrimer if
a dendrimer bead occurs nearby at a distance shorter than a certain value $r_c$. Taking into account the intrinsic volume of the bead, we set $r_c = l + \sigma = 1.8l$. The $N_{\text{ads}}$ values thus calculated are also shown in Fig. 3. The same plot represents the results of theoretical prediction [18] for spheres with the same radius $r_{ov}$. As is seen, both adsorption criteria (local and spherical) produce almost identical results; i.e., the calculated amount of chain monomeric units adsorbed on the dendrimer depends slightly on the choice of adsorption criterion. We found that, for chains with a length of $N_{\text{ch}} > N_T$, the total number of chain monomers adsorbed on the dendrimer exceeds the amount necessary for neutralization of the dendrimer. Thus, the phenomenon of dendrimer charge inversion exists in all the complexes considered above.

According to the theoretical predictions [18], the function $N_{\text{ads}}(N_{\text{ch}})$ is nonmonotonic (Fig. 3); however, the results obtained by the Brownian dynamics simulation differ from the theory in some aspects: the domain of values of the chain length in the complex when $N_{\text{ads}}$ begins to decrease with a further increase in $N_{\text{ch}}$ is smeared, and the chain length at which $N_{\text{ads}}$ begins to decrease is displaced to greater values as compared with the theory for the hard sphere. The values of the chain length at which $N_{\text{ads}}$ begins to decrease are $N_{\text{ch}}^{ov} \sim 45$–50 and $N_{\text{ch}}^{ov} \sim 75$–80 for the complexes with the $g = 3$ and $g = 4$ dendrimers, respectively.

Strong adsorption of the chain is seen well in Fig. 4, which presents the snapshots of the configurations of complexes formed by the $g = 3$ dendrimer and the chain of $N_{\text{ch}} = 60$. At the same time, the dendrimer is not fixed on the chain, thus allowing its migration along the chain from one end to another. The possibility of such migration was indicated earlier in [11].

To summarize, the phenomenon of inversion of dendrimer charge takes place in all complexes considered in this study when the charge of the linear chain exceeds the dendrimer charge. This phenomenon is accompanied by a nonmonotonic change in the amount of chain monomeric units adsorbed on the dendrimer with variation in the chain length. This effect manifests itself in various structural characteristics, such as the mean square radius of gyration, the monomer-density radial distribution function, and mass and charge distribution inside the monomer.

**Mean Square Radius of Gyration**

The values of the mean square radius of gyration $\langle R_g^2 \rangle$ were calculated individually for the dendrimer and the linear chain involved in the complex. The dependence of $\langle R_g^2 \rangle$ for the $g = 3$ and $g = 4$ dendrimers on the length of the chain involved in the complex is shown in Fig. 5. It is seen that the dendrimer size remains practically constant with varying the number of chain monomeric units. Figure 5 also shows the values of $\langle R_g^2 \rangle$ for individual neutral and charged dendrimers as calculated in our previous works [27, 28]. It is seen that $\langle R_g^2 \rangle$ of the dendrimer in the complex somewhat exceeds the corresponding value for an individual neutral dendrimer. Thus, the mean square radius of gyration of the dendrimer in the complex with long chains whose charge is equal to or higher than the dendrimer charge is close to the corresponding value for the individual neutral dendrimer but substantially smaller than the mean square radius of gyration of the single charged dendrimer at the same Debye radius $r_D = 8.96$. This means that the linear chain in the complex is strongly adsorbed on the dendrimer and electro-
static interactions inside the dendrimer are screened almost completely by the polion adsorbed on the dendrimer.

Figure 6 shows the plots of $\langle R_g^2 \rangle$ versus the chain length for the chains in complexes with dendrimers of the generations $g = 3$ and 4. There are two modes seen in these plots, namely, a slow growth at the beginning and a faster growth at the end. Such a behavior may be interpreted as the transition from the completely adsorbed state of the chain to the adsorbed chain with the tail. This conclusion is confirmed by the observation that the crossover from one mode to the other takes place in the region of $N_{ch}$ values close to the critical chain lengths of $N_{ch}^{ov} \approx 45$ and $N_{ch}^{ov} \approx 75$ (as specified in Fig. 6) determined earlier in the study on the charge inversion effect for complexes with dendrimers of the generations $g = 3$ and 4, respectively. In other words, in this adsorption mode, almost the whole chain is adsorbed on the dendrimer and only small tails or loops are present in the complex. As the chain length $N_{ch}$ increases further, longer tails begin to appear in the complex, thus resulting in a faster growth of the mean square radius of gyration in the second mode. This behavior is consistent with the results obtained above during study of the number of chain units adsorbed on the dendrimer.

When the total charge of the chain exceeds that of the dendrimer, the chain in the complex occurs in the compact coiled configuration at a length of $N_{ch} \leq N_{ch}^{ov}$. Longer chains occur in part in the coiled configuration with one or two tails (see Fig. 4 as an example).

Radial Distribution Function of Monomer Density

To study the distribution of various monomers inside the complex, as well as inside the dendrimer in the complex and a linear chain in the complex, we used the radial distribution function for the density of monomers $\rho(r)$. To define this function, the space is divided into concentric spheres with the center located at the center-of-mass. Then, the monomer-density radial distribution function $\rho(r)$ is defined by

$$\rho(r) = \frac{\langle n(r) \rangle}{4\pi r^2 \Delta r}, \quad (8)$$

where $\langle n(r) \rangle$ is the average number of beads in the layer formed by neighboring spheres and $\Delta r$ is the thickness of the layer.

Figure 7 shows the radial distribution functions of the density of all monomers in the complex, as well as the monomers of the dendrimer and the chain individually. Notice a high extent of penetration of the linear chain into the dendrimer. The maximum in the distribution of monomers of the linear chain is localized in the

![Fig. 5. Mean square radius of gyration $R_g$ for the (a) $g = 3$ and (b) $g = 4$ dendrimers in a complex (closed symbols) with chains of different lengths. Data for single neutral (open circles) and charged (open squares) dendrimers with a Debye radius of $r_D = 8.96$ are also given. The dashed line marks the $N_{ch}$ value equal to the number of terminal groups $N_T$.](image)

![Fig. 6. Mean square radius of gyration $R_g$ for a linear chain in a complex with (1) the $g = 3$ and (2) the $g = 4$ dendrimer as a function of the chain length $N_{ch}$. The arrows indicate the values of $N_{ch} = N_{ch}^{ov}$ at which the dependence of the number of adsorbed chain units on the chain length begins to display a nonmonotonic character.](image)
region where the density of dendrimer units is still rather high. Knowledge of the distribution of chain monomeric units inside the dendrimer is not only of theoretical importance but also of practical interest. Strong penetration of a polyelectrolyte into the interior of a nanocontainer can lead to hindrance of its subsequent release, for example, with a change in the pH of the medium.

To better study the localization of chain monomeric units inside the dendrimer, we compared the radial distribution function for chain monomers and terminal groups of the dendrimer (Fig. 8). First, it is seen clearly that the distribution of dendrimer terminal groups remains practically unchanged with variation in the length of the linear chain and is close to the corresponding function for the single neutral dendrimer. Second, in complexes where the dendrimer charge is fully neutralized by the charge of the linear chain, i.e., when \( N_{ch} = N_T \), (where \( N_{ch} = 24 \) and 48 for complexes with the \( g = 3 \) and 4 dendrimers, respectively), the \( \rho(r) \) value for chain monomers practically coincides with the values of \( \rho(r) \) for the terminal groups of the dendrimer. This implies that all chain monomeric units occur near the dendrimer terminal groups. As the chain length in the complex increases, the maximum in the chain monomer distribution is shifted to the dendrimer periphery.

An increase in the chain length in the complex slightly changes the position of the maximum in the distribution function for the terminal groups of the dendrimer, this position remaining close to that of the maximum for the neutral dendrimer.
Integral Mass-Distribution Function

Unlike the radial distribution function for the density of monomeric units, the mass-distribution function \( M(r) \) (the total number of monomers in a sphere with a radius \( r \) and the center coinciding with the center-of-mass of the system) is an integral characteristic of the monomer distribution (Fig. 9). In the region of small \( r \) values, the curves for the complexes with chains of different lengths coincide with one another and the corresponding curve for the single neutral dendrimer. In other words, dendrimer monomeric units make the major contribution to \( M(r) \) in this region. First, \( M(r) \) increases as \( \sim r^3 \). This relationship corresponds to a uniformly filled sphere. For not very long chains after a certain transition region, \( M(r) \) stops growing when the limiting value is reached. This behavior is observed for complexes with chains shorter than \( N_{ch} \approx 50 \) and 75 for the \( g = 3 \) and \( g = 4 \) dendrimers, respectively. For complexes with longer chains, the portion of the fast rise in \( M(r) \) is changed by a weaker linear dependence \( M(r) \sim r \). The appearance of this portion is due to the emergence of the tail. The presence of the tail is indicated by the fact that the \( N_{ch} \) values at which this region appears are close to the values of \( N_{ch}^{ow} \) obtained above during study of the charge inversion effect. Moreover, the behavior of \( M(r) \) becomes nonmonotonic: the linear portion for the complexes with the longer chains appears at shorter distances from the center than in the case of the shorter chains provided that \( N_{ch} > N_{ch}^{ow} \).

**Fig. 9.** Integral mass-distribution function \( M(r) \) in complexes with (a) \( g = 3 \) and (b) \( g = 4 \) dendrimers: (a) (1) the single neutral dendrimer and (2–6) \( N_{ch} = 24, 45, 48, 55, \) and 60, respectively; (b) the single neutral dendrimer and (2–5) \( N_{ch} = 48, 70, 80, \) and 90, respectively.

**Fig. 10.** Total charge \( Q_{tot}(r) \) inside a sphere with a radius \( r \) in a complex with (a) \( g = 3 \) and (b) \( g = 4 \) dendrimers as a function of the distance from the center-of-mass of the complex: (a) \( N_{ch} = (1) 24, (2) 30, (3) 35, (4) 40, (5) 45, (6) 48, (7) 60, \) and (8) 55; (b) \( N_{ch} = (1) 48, (2) 55, (3) 60, (4) 65, (5) 70, (6) 80, \) and (7) 90.
Integral Charge Distribution Function Inside the Complex

The charge inversion effect is also manifested in the behavior of another integral characteristic: the total charge $Q_{\text{tot}}(r)$ occurring in a sphere with a radius $r$ and the center at the dendrimer center-of-mass as a function of the sphere radius $r$ (Fig. 10). At small distances, $Q_{\text{tot}}$ is zero, thus indicating the absence of charged beads in the vicinity of the center-of-mass. Then, $Q_{\text{tot}}$ begins to increase and passes through a positive maximum whose position is close to that of the maximum in the distribution of terminal groups of the dendrimer. The position of the maximum remains practically unchanged with a growth in chain length, but its height nonmonotonically varies. As the distance from the center further increases, $Q_{\text{tot}}$ decreases, passes through zero, and then tends toward the limiting negative value equal to the net charge of the complex ($N_T - N_{\text{ch}}$). All curves (except for the neutral complex when $N_{\text{ch}} = 24$) pass through zero approximately at the same distance from the center. Since the dendrimer size remains practically unchanged with an increase in the chain length, we may choose as a measure of the extent of charge inversion the value of charge $Q_{\text{tot}}^0$ at the point where the net charge of the neutral complex vanishes. It is seen (Fig. 11) that this value also depends nonmonotonically on $N_{\text{ch}}$, with the $N_{\text{ch}}$ value at the minimum coinciding with the estimates made in our previous studies.

REFERENCES