

Cylindrical DNA with positive and negative surfactants

Paulo Sérgio Kuhn
Departamento de Física
Instituto de Física e Matemática, UFPel

February 6, 2024

1 Introduction

In the last few decades polyelectrolyte solutions have been intensively studied, both theoretical and experimentally [1]. The applications of these macromolecules range from flocculation in colloidal suspensions to their use as emulsifiers, water treatment and oil recovery. Many industrial products as soaps or cosmetics incorporate polyelectrolytes. Biologically important molecules as DNA and many proteins are polyelectrolytes [2]. Although all their importance, polyelectrolytes are still a difficult branch of research. We may cite as main sources of complexity the long range nature of the Coulomb interaction and the flexibility of the chains. The long range nature of electrostatic interactions makes these systems much different compared to neutral polymers, and the flexibility of chains allows for a great number of spatial configurations of the molecules [3]-[5].

Polyelectrolytes are large molecules whose monomers become ionized in solution, being an example of a complex charged system [6, 7]. The most common solvent is water, but eventually other substances, as organic compounds or ionic liquids, may be used. Besides the long ranged electrostatic interaction and the flexibility of chains, other sources of difficulties are the interaction between the macromolecules, and the macromolecules and the solvent. Nevertheless, some simulations have been made [8].

Regarding symmetric electrolyte solutions, they have been described successfully by Debye-Huckel theory [9]. Ion pair formation has been included in the theory by Bjerrum [10]. This treatment was mainly used as a limiting theory, and recently has been extended to finite densities, allowing for a detailed study of phase transitions in charged symmetric solutions [11, 12]. By

applying Debye-Huckel theory to dilute polyelectrolyte solutions, Manning has derived a very useful set of limiting relations [13]. This treatment has also been extended to finite densities of cylindrical polyelectrolytes [14]-[16]. All this work refers to rigid polyelectrolytes, with cylindrical symmetry, although flexible chains has also been studied [17]-[19].

In this work we consider solutions of cylindrical polyelectrolytes with salt and surfactants, both positive and negative. Such systems are of great importance, as for example solutions of DNA with surfactants [20]-[23]. Much interesting features occur in such systems, as binding and collapse transition. An important application is the developing of gene delivery systems [24]. Adsorption isotherms for DNA with positive surfactants have been evaluated in the context of Debye-Huckel, Bjerrum and Manning theories [25]. Here we include both positive and negative surfactants, allowing for micelle formation in solution. This is a very broad research area, with a large amount of experimental and theoretical work [26]-[38].

The association of positive surfactants to DNA molecules is cooperative, in the sense that, after the first surfactant binds electrostatically to DNA, the second is attracted not only by positive monomers of DNA, but also by hydrophobic attraction to an already bound surfactant [25]. We represent this interaction by an energy parameter ε , which is used only in the complexes. In solution the formation of micelles is also driven by hydrophobic interaction, which is modeled by an energy parameter ε_m . We do not attempt to establish here a new theory on surfactants in solution. These systems may form micelles, vesicles, monolayers, bilayers, etc. We symplify the problem here by considering only spherical mixed micelles in solution, since our main concern is to evaluate the binding isotherms of DNA complexes, but without neglecting surfactant association in solution.

2 The model

The model used here for the system is essentially the same we have used before for evaluating association isotherms of cylindrical polyelectrolytes with counterions or surfactants [14]-[16],[25]. The polyelectrolyte chains are cylinders of length $L = Zb$, where Z is the number of charged monomers and b the distance between adjacent monomers. Since we are mainly concerned with DNA solutions we take $b = 1.7 \text{ \AA}$, and the monomers are negative, while counterions are positive. All ions and monomers are supposed to have the same diameter $\sigma = b$. The salt if present is monovalent, and the solvent is taken as a continuum. Besides chains and ions there are also surfactants in solution, both positive and negative. The surfactant molecule dissociates in a

chain and an ion. The chain has an end monomer charged and the remaining monomers are neutral. The system as a whole is neutral. The strong electrostatic interactions between the charged monomers of the polyelectrolyte chain and ions in solution leads to formation of complexes. The positive surfactant also binds to the polyelectrolyte chain, first by electrostatic interaction, and then by hydrophobic attraction between associated surfactants. Besides complex formation, positive and negative surfactants form micelles in solution. Here is also present the short ranged hydrophobic attraction between neutral monomers of surfactants.

The mixed micelles are considered all to have the same number of surfactants, which we denote by g . From these p are positive and n are negative, hence $p + n = g$. The micelles are all supposed to be spherical with radius R_g . We define the fraction x of surfactants bound in the micelles,

$$x \equiv \frac{g\rho_g}{\rho_p + \rho_n}, \quad (1)$$

where ρ_g is the number density of micelles, ρ_p is the number density of positive surfactants, and ρ_n is the number density of negative surfactants. We choose p and n to be proportional to the respective surfactant densities,

$$p = \frac{g\rho_p}{\rho_p + \rho_n}, \quad n = \frac{g\rho_n}{\rho_p + \rho_n}. \quad (2)$$

With this choice of p and n we may express x alternatively as

$$x = \frac{p}{\rho_p}\rho_g = \frac{n}{\rho_n}\rho_g. \quad (3)$$

The complexes are formed by one polyelectrolyte molecule with n_c bounded positive ions and n_a bounded positive surfactants. Denoting the corresponding association fractions by $m_c = n_c/Z$ and $m_a = n_a/Z$ we have the densities of free surfactants given by

$$\begin{aligned} \rho_p^f &= \rho_p - Zm_a\rho_{ch} - p\rho_g, \\ \rho_n^f &= \rho_n - n\rho_g, \end{aligned} \quad (4)$$

where $\rho_{ch} = N_{ch}/V$ is the number density of polyelectrolyte chains, with N_{ch} being the number of polyelectrolyte chains and V the total volume of the system. Hence the monomer density is $Z\rho_{ch}$. These equations are simple consequence of conservation of total number of particles. The analog equations for free ions must take into account the possibility of micelles being positive or negative. If $p = n$ the micelles are neutral and no ion bounds. For positive micelles, $p > n$ and we have

$$\begin{aligned}
\rho_+ &= \rho_s + \rho_n + Z(1 - m_c)\rho_{ch}, \\
\rho_- &= \rho_s + \rho_p - Z_g m_g \rho_g.
\end{aligned}
\tag{5}$$

If the micelles are negative, $p < n$ and we have

$$\begin{aligned}
\rho_+ &= \rho_s + \rho_n + Z(1 - m_c)\rho_{ch} - Z_g m_g \rho_g, \\
\rho_- &= \rho_s + \rho_p.
\end{aligned}
\tag{6}$$

In both cases the number of associated ions on the micelle is n_g , and the association fraction is $m_g = n_g/Z_g$, where $Z_g = |p - n|$. The inverse Debye screening length is defined in the usual way by

$$\kappa^2 = 4\pi\lambda_B(\rho_+ + \rho_- + \rho_p^f + \rho_n^f),
\tag{7}$$

with $\lambda_B = \beta q^2/4\pi\varepsilon$ the Bjerrum length. Here q is the proton charge, ε is the permittivity constant of solvent, $\beta = 1/kT$, k is the Boltzmann constant, and T is the Kelvin temperature.

3 The mixed micelles

We evaluate the size of micelles in the following way. The number of neutral monomers of positive surfactant is denoted by z_p , while the number of neutral monomers of negative surfactant is denoted by z_n . The average number of neutral monomers in a surfactant molecule is then

$$z_m = \frac{z_p \rho_p + z_n \rho_n}{\rho_p + \rho_n},
\tag{8}$$

and the volume of one surfactant molecule is

$$v_1 = (z_m + 1) \frac{\pi}{6} \sigma^3.
\tag{9}$$

The radius of a micelle can be written as

$$R_g = f(z_m + 1)\sigma,
\tag{10}$$

where f is a fixed parameter. If $f = 1$ we have the maximum radius, with the surfactants fully extended. But in general we may suppose $f < 1$. With these quantities we have the volume of a micelle,

$$V_g = \frac{4\pi R_g^3}{3}, \quad (11)$$

and then the number g of surfactants in a micelle,

$$g = \frac{V_g}{v_1}. \quad (12)$$

The free energy of micelles in solution is written in the most simplified form as possible. We follow here the main lines used in [19]. Hence, apart the ideal term, the free energy for micelles in solution can be written as

$$F_m = F_m^{ent} + F_m^{el} + F_m^h, \quad (13)$$

where the different terms are respectively the entropic, electrostatic and hydrophobic contributions. This is a great simplification of the problem, but sufficient for our purposes, which is to estimate the amount of surfactants in solution that form micelles, and hence its influence in the association of surfactants in DNA molecules.

The entropic free energy, due to all possible configurations of associated ions on micells is [16]

$$\beta F_m^{ent} = N_g Z_g [m_g \ln m_g + (1 - m_g) \ln(1 - m_g)]. \quad (14)$$

The electrostatic repulsion in the spherical micell may be written as [39]

$$\beta F_m^{el} = N_g Z_g^2 (1 - m_g)^2 \frac{\lambda_B}{2R_g}. \quad (15)$$

Finally, we have the hydrophobic attraction between the surfactants in the micell, modelled as a square well potential [34],

$$\beta F_m^h = -N_g a_m g^2 \frac{z_m \sigma^3}{V_g}, \quad (16)$$

with

$$a_m = \frac{2\pi}{3} \beta \varepsilon_m (\lambda^3 - 1). \quad (17)$$

Here ε_m is the energy depth of the potential well, and λ defines the range of attraction,

$$u = -\varepsilon_m, \quad \sigma_m < r < \lambda \sigma_m, \quad (18)$$

with $\sigma_m = z_m^{1/3} \sigma$. We use $\lambda = 2$.

4 The polyelectrolyte solution and complete free energy

In this section we write the contribution of polyelectrolyte chains to the free energy of the system. We follow along the lines of previous work [16, 25]. Therefore the Helmholtz free energy corresponding to polyelectrolyte chains in solution is given by a sum of terms,

$$F_p = F_{ent} + F_{ion} + F_h + F_{el}, \quad (19)$$

The entropic term due do different configurations of associated particles on the chain is

$$\begin{aligned} \beta F_{ent} = & N_p Z [m_c \ln m_c + m_a \ln m_a \\ & + (1 - m_c - m_a) \ln(1 - m_c - m_a)]. \end{aligned} \quad (20)$$

The electrostatic interaction between charged sites is

$$\beta F_{ion} = N_p \frac{\lambda_B}{b} p^2 S, \quad (21)$$

where the valence of each site of the polyelectrolyte chain is

$$p = -1 + m_c + m_a, \quad (22)$$

and

$$S = Z[\psi(z) - \psi(1)] - Z + 1, \quad (23)$$

and ψ is the digamma function [40]. The electrostatic interaction of complexes with the ionic solution is described by

$$\beta F_{el} = N_p \frac{\lambda_B}{L} (Zp)^2 \frac{K_0(\kappa R)}{\kappa R K_1(\kappa R)}, \quad (24)$$

where K_n is the modified Bessel function of second kind [40]. Finally, the hydrophobic interaction between associated surfactants on the chain, which leaves to the cooperative association, is given by [25]

$$\beta F_h = -N_p \beta \varepsilon (Z - 1) m_a^2. \quad (25)$$

The complete free energy of the system is then

$$F = F_{id} + F_p + F_m, \quad (26)$$

where the ideal contribution is

$$\beta F_{id} = \sum N_j [\ln \rho_j^* - 1], \quad (27)$$

with the index j denoting all species present in solution, polyelectrolytes, free ions, and surfactants. The reduced density is $\rho_j^* = \rho_j \sigma^3$.

5 Results and Conclusions

The equilibrium configuration of the system for given temperature and densities is found minimizing the complete free energy with respect to x , m_c , m_a and m_g . We have chosen $Z = 100$, $\rho_{ch} = 1 \mu\text{M}$, $\rho_p = 10^{-4} \text{ M}$, $\rho_s = 0$, $\beta\varepsilon = 1.5$, $\beta\varepsilon_m = 0.7$, $z_p = z_n = 12$, $T = 25^\circ\text{C}$. The results are shown as functions of ρ_n , the density of negative surfactants, for different values of f , the parameter determining the radius of micelles.

Figure 1 shows the fraction x of surfactants in micelles. We see that the maximum value of x corresponds to equimolarity of surfactants. Small micelles are formed before the large ones. That is reasonable, since more surfactants are needed to form big micelles. Table 1 shows the size g and the radius R_g of micelles as functions of f . In general we have g and R_g dependent of density, since z_m depends on densities ρ_p and ρ_n , but if $z_p = z_n$, as we have chosen here, g and R_g become constants, independent of surfactant densities. Figure 2 shows the fraction m_c of associated counter-ions on DNA molecules, and figure 3 the fraction m_a of associated positive surfactants on DNA molecules. The results for x and m_a are complementary, as expected, since the number of associated surfactants on the DNA molecules reduces if more surfactants form micelles in solution.

f	g	R_g/σ
0.4	86	5.2
0.5	169	6.5
0.6	292	7.8
0.8	692	10.4
1	1352	13.0

Table 1: Number g of surfactants in a micelle and the radius R_g , for the values of f used in this work.

Figure 4 shows the fraction m_g of associated ions on micelles, which can be positive or negative, according to the net charge of the micelle. For positive micelles ($\rho_p > \rho_n$ and $p > n$) we have association of negative ions.

For negative micelles ($\rho_p < \rho_n$ and $p < n$) we have association of positive ions. Figure 5 shows, for $f = 1$, the number p of positive surfactants on a micelle and the number n of negative surfactants on a micelle. If $p > n$ the micelle is positive, and if $p < n$ the micelle is negative. Only the case $f = 1$ is shown here for clarity, but for other values the results are qualitatively similar. Figure 6 shows the net charge of micelles, in absolute value. We may also construct three dimensional figures with the surfactant densities as axes. The results for x , m_a , m_c and m_g are shown in figures 7-10 for $f = 0.5$. The remaining parameters have the same value as above.

In summary, we conclude that micelle formation reduces the number of positive surfactants available for association in DNA complexes. Hence the size of polyelectrolyte-surfactant complexes depends on the densities of surfactants in solution. Besides this, two energy parameters are of fundamental importance in the system. One is the hydrophobic attraction energy between associated positive surfactants on polyelectrolyte chains, denoted by ε . The other is the hydrophobic attraction between positive and negative surfactants in micelles, denoted by ε_m . These two energy parameters may be used as adjusting parameters in order to reproduce experiments with DNA surfactant solutions.

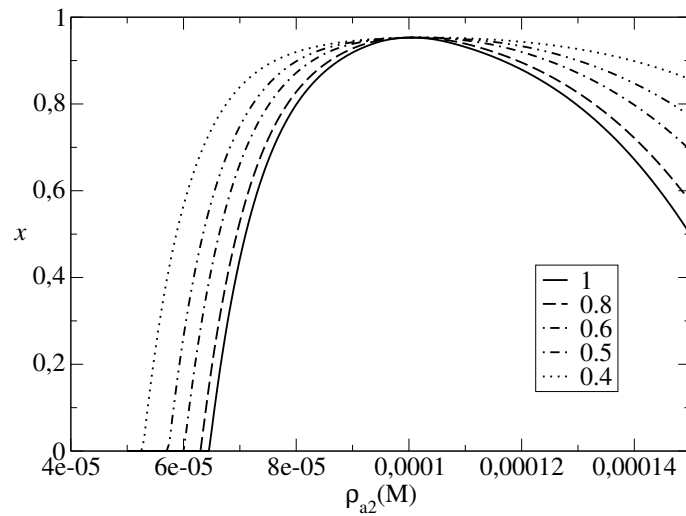


Figure 1: Fraction x of surfactants in micelles as function of negative surfactant density, for different values of f .

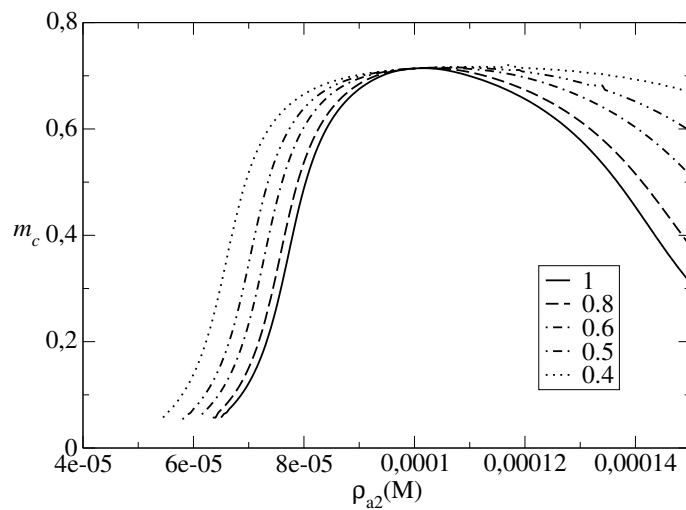


Figure 2: Fraction m_c of associated counter-ions in DNA molecules, as function of negative surfactant density, for different values of f .

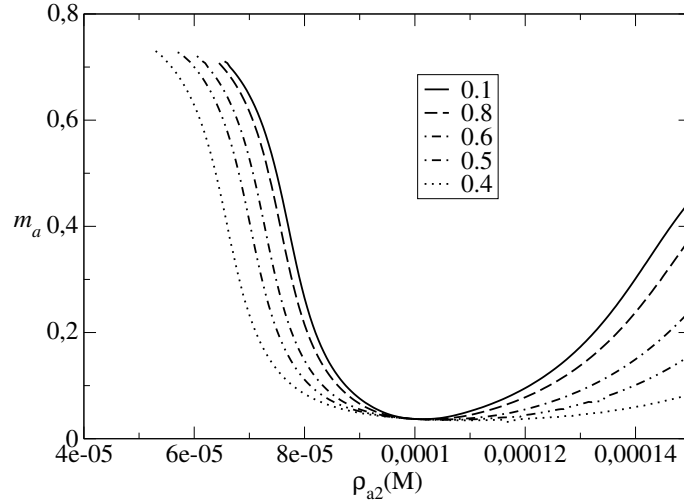


Figure 3: Fraction m_a of associated surfactants in DNA molecules, as function of negative surfactant density, for different values of f .

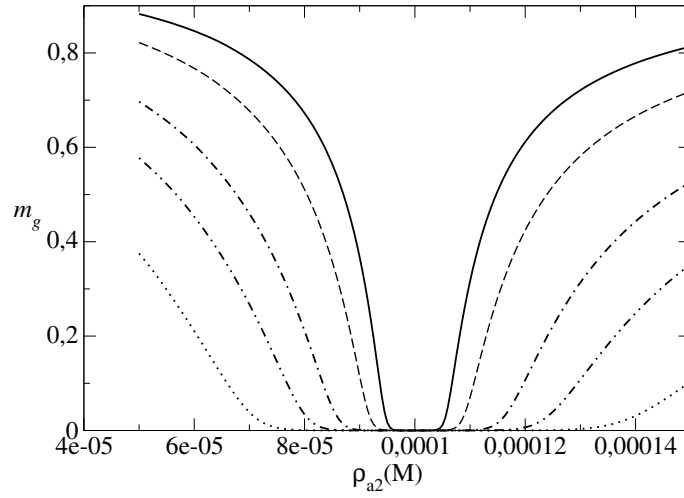


Figure 4: Fraction m_g of associated ions on micelles, as function of negative surfactant density, for different values of f . Note that micelles are positive for $\rho_n < \rho_p$ ($p > n$), with association of negative ions, and the micelles are negative for $\rho_n > \rho_p$ ($p < n$), with association of positive ions.

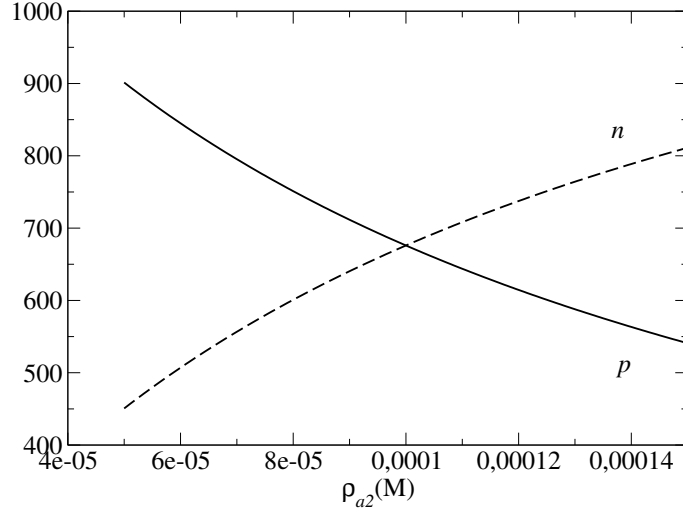


Figure 5: Values of p and n , as functions of negative surfactant density, for $f = 1$. Note that micelles are positive for $\rho_n < \rho_p$ ($p > n$), with association of negative ions, and the micelles are negative for $\rho_n > \rho_p$ ($p < n$), with association of positive ions.

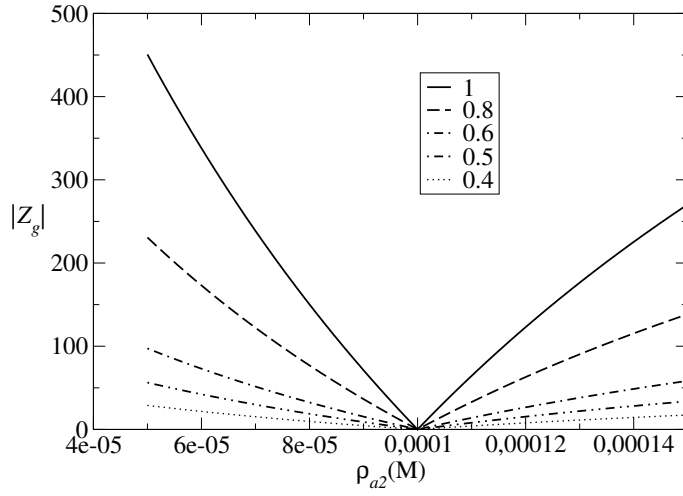


Figure 6: The value of $Z_g = |p - n|$ in micelles, as function of negative surfactant density, for different values of f . Note that micelles are positive for $\rho_n < \rho_p$ ($p > n$), with association of negative ions, and the micelles are negative for $\rho_n > \rho_p$ ($p < n$), with association of positive ions.

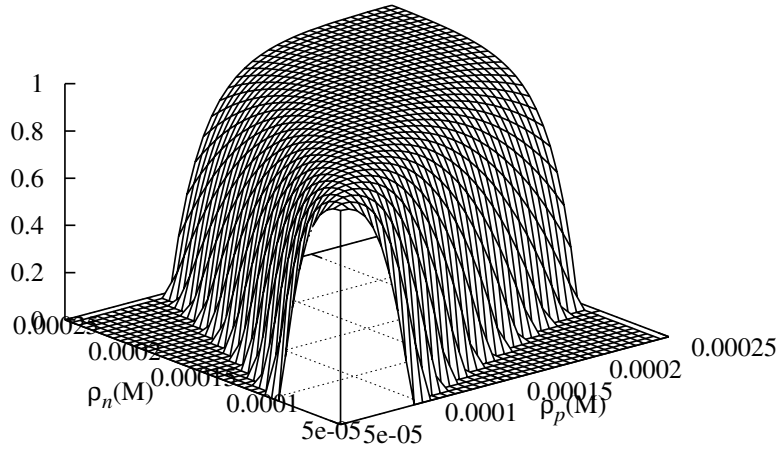


Figure 7: Fraction x of surfactants in micelles, as function of surfactant densities ρ_p and ρ_n .

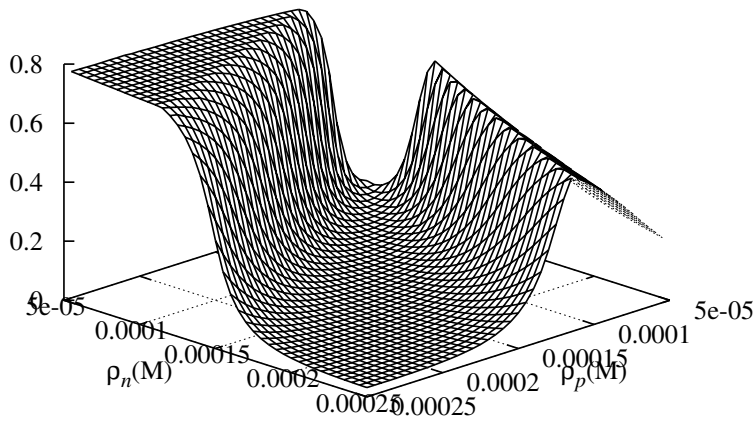


Figure 8: Fraction m_a of associated surfactants in polyelectrolyte complexes, as function of surfactant densities ρ_p and ρ_n .

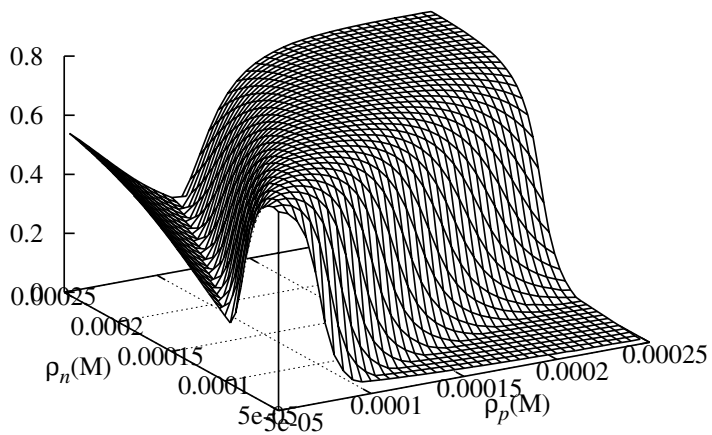


Figure 9: Fraction m_c of associated counterions in polyelectrolyte complexes, as function of surfactant densities ρ_p and ρ_n .

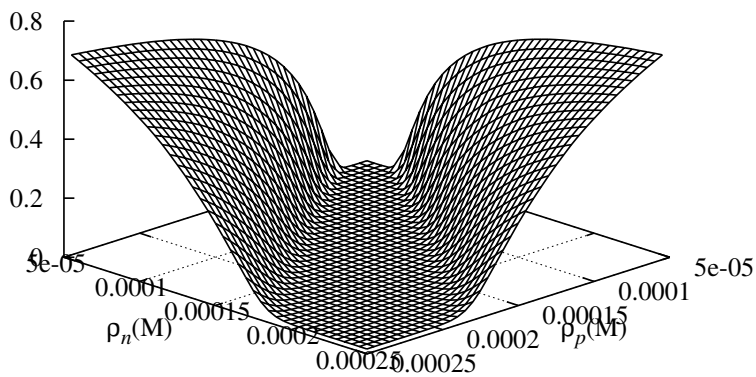


Figure 10: Fraction m_g of associated counterions in polyelectrolyte complexes, as function of surfactant densities ρ_p and ρ_n .

References

- [1] A. V. Dobrynin, M. Rubinstein, *Prog. Polym. Sci.* 30 (2005) 1049-1118.
- [2] D. Frank-Kamenetskii, *Phys. Rep.* 288 (1997) 13-60.
- [3] P. J. Flory, *Principles of Polymer Chemistry* (Cornell University Press, Ithaca, New York, 1971).
- [4] P. J. Flory, *Statistical Mechanics of Chain Molecules* (John Wiley & Sons, New York, 1969).
- [5] D. S. McKenzie, *Phys. Rep.* 27(2) (1976) 35-88.
- [6] Y. Levin, *Rep. Prog. Phys.* 65 (2002) 1577-1632.
- [7] H. Lowen, *Phys. Rep.* 237(5) (1994) 249-324.
- [8] M. J. Stevens, K. Kremer, *Phys. Rev. Lett.* 71 (1993) 2228-2231.
- [9] P. W. Debye, E. Huckel, *Phys. Zeits.* **24**(3), 185 (1923).
- [10] N. Bjerrum, *K. Dan. Vidensk. Selsk. Mat. Fys. Medd.* 7, (1926) 1.
- [11] M. E. Fischer, Y. Levin, *Phys. Rev. Lett.* 71 (1993) 3826-3829.
- [12] Y. Levin, M. E. Fischer, *Physica A* 225 (1996) 164.
- [13] G. S. Manning, *J. Chem. Phys.* 51(3) (1969) 924-933.
- [14] Y. Levin, *Europhys. Lett.* 34 (1996) 405.
- [15] Y. Levin, M. C. Barbosa, *J. Phys. II (Fr.)* 7 (1997) 37.
- [16] P. S. Kuhn, Y. Levin, M. C. Barbosa, *Macromolecules* 31 (1998) 8347-8355.
- [17] P. S. Kuhn, M. C. Barbosa, *Phys. A* 357 (2005) 142-149.
- [18] P. S. Kuhn, A. Diehl, *Phys. Rev. E* 76 (2007) 041807(6).
- [19] A. Diehl, P. S. Kuhn, *Phys. Rev. E* 79 (2009) 011805(6).
- [20] D. Langevin, *Adv. Coll. Int. Sci.* 147-148 (2009) 170-177.
- [21] D. Matulis, I. Rouzina, V. A. Bloomfield, *J. Am. Chem. Soc.* 124 (2002) 7331-7342.

- [22] R. Dias, M. Rosa, A. C. Pais, M. Miguel, B. Lindman, *J. Chin. Chem. Soc.* 51 (2004) 447-469.
- [23] C. von Ferber, H. Löwen, *Faraday Discuss.* **128**, 389 (2005).
- [24] J. Zabner, *Adv. Drug Del. Rev.* 27 (1997) 17-28.
- [25] P. S. Kuhn, Y. Levin, M. C. Barbosa, *Chem. Phys. Lett.* 298 (1998) 51-56.
- [26] M. T. Yacilla, K. L. Herrington, L. L. Brasher, E. W. Kaler, S. Chiruvolu, J. A. Zasadzinski, *J. Phys. Chem.* 100 (1996) 5874-5879.
- [27] L. L. Brasher, K. L. Herrington, E. W. Kaler, *Langmuir* 11(11) (1995) 4267-4277.
- [28] E. F. Marques, O. Regev, A. Khan, M. G. Miguel, B. Lindman, *J. Phys. Chem. B* 102 (1998) 6746-6758.
- [29] A. Shiloach, D. Blankschtein, *Langmuir* 14 (1998) 7166-7182.
- [30] J. L. L.-Fontán, M. J. Suárez, V. Mosquera, F. Sarmiento, *Phys. Chem. Chem. Phys.* 1 (1999) 3583-3587.
- [31] V. Tomasic, I. Stefanic, N. F.-Vincekovic, *Coll. Polym. Sci.* 277 (1999) 153-163.
- [32] A. Khan, E. F. Marques, *Curr. Opp. Coll. Int. Sci.* 4 (2000) 402-410.
- [33] E. W. Kaler, K. L. Herrington, A. K. Murty, J. A. N. Zasadzinski, *J. Phys. Chem.* 96 (1992) 6698-6707.
- [34] T. L. Hill, *An Introduction to Statistical Thermodynamics* (Dover, New York, 1986).
- [35] R. Nagarajan, *Langmuir* 1 (1985) 331-341.
- [36] R. Nagarajan, E. Ruckenstein, *J. Coll. Int. Sci.* 60(2) (1977) 221-231.
- [37] C. Tanford, *Proc. Natl. Acad. Sci. USA* 79(9) (1979) 4175-4176.
- [38] C. Tanford, *J. Phys. Chem.* 78(24) (1974) 2469-2479.
- [39] R. K. Wangsness, *Electromagnetic Fields* (John Wiley & Sons, 1986).
- [40] I. S. Gradshteyn, I. M. Ryzhik, *Table of Integrals, Series, and Products*, 7n. ed. (Academic Press, 2007).