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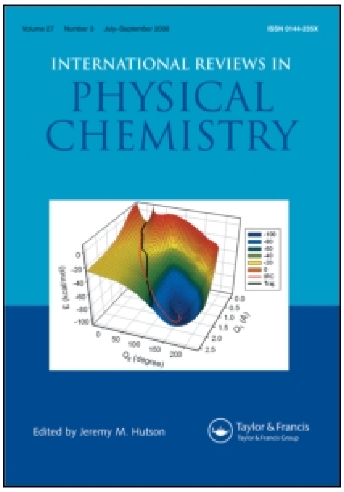

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# Understanding polyelectrolyte solutions: macroion condensation with emphasis on the presence of neutral co-solutes

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The multi-faceted applications of polyelectrolyte solution systems to a kaleidoscope of technological and biological processes make the understanding of these systems important and of interest. The highly relevant issue of instabilities that may occur in a polyelectrolyte solution and the ensuing macroion condensation constitute the premise of this review. An abundance of experimental and numerical simulation results in recent years provide evidence that a net electrostatic attractive force may exist between macroions and may lead to a phase separation. Specifically, in this review, three different types of instability involving macroions of spherical geometry are discussed. (i) The instability arising out of strong Coulomb correlations between counterions in the solution; this is most likely to occur in solutions containing multivalent counterions and/or in the presence of solvents of low relative permittivity. (ii) The instability caused by the macroion surface-charge fluctuations; the resultant charge correlations may induce an effective attraction between the weakly charged macroions. (iii) The instability due to the combined effect of electrostatic and *crowding* interactions when an inert co-solute is added to the solution. A sufficient increase in the concentration of the neutral species leads to a gradual change in the nature of the interaction between two macroions, from being repulsive to less repulsive and ultimately attractive. The structural features and thermodynamics in these complex systems are shaped by the collective and often competing effects of the species.

## Contents

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## 1. Introduction

Solutions of surfactant micelles, globular proteins, microemulsions and suspensions of charged colloids, in other words polyelectrolyte systems, currently constitute a rapidly expanding area of physical chemistry/chemical physics. This interest is stimulated by the many applications these substances have in the food, textile and pharmaceutical industries. In addition, understanding of polyelectrolytes is vital to studies of important bio-polymers such as DNA and RNA and of many other biological processes.

Polyelectrolytes can be complex in general and modelling them theoretically poses a challenge. In the simplest case the aqueous solution (or suspension) contains large and often highly charged macroions and the related number of counterions to render the system electroneutral. The strong attractive interaction between a charged macroion and small, simple ions of the opposite sign (counterions) in the solution leads to the accumulation of counterions in the vicinity of a macroion. In polyelectrolyte–electrolyte mixtures small ions having the same sign of charge (coions) as that for the macroions will also be present in the solution. In contrast to the case of counterions, Coulomb repulsion will now tend to push these coions away from the macroions. In these solutions the activity and the mobility of the counterions are reduced well below their bulk values. Also, when an external electric field is applied to the solution a fraction of the counterions moves as an integral part of the macroion. The increased concentration of counterions near a macroion, called an electrical double layer in the literature, strongly modulates the bare Coulomb interaction between the macroions. Systems of biological relevance are even more complex; in addition to the aqueous polyelectrolyte–electrolyte mixture, large concentrations of neutral macromolecules are often present in solution. It is quite clear that an addition of simple electrolyte, or any other change in the composition of the solution, would further affect the stability of the system. Although in such charged systems the Coulomb interaction may most often be the dominant interaction, it is not the only one that governs the properties of these systems. In general, the detailed physico-chemical behaviour of polyelectrolyte solutions results from the competing effects of the various types of interaction.

The problem of stability of charged colloids, solutions of globular proteins and surfactant micelles is of considerable importance for science and technology. The problem is most often considered in the framework of the Deryaguin–Landau–Verwey–Overbeek (DLVO) theory. Deryaguin and Landau (1941) and Verwey and Overbeek (1948) independently developed a quantitative theory to treat the stability of lyophobic sols in relation to an added electrolyte. In brief, according to this approach, the solution is described as an effective one-component fluid. The effects of solvent and a dissolved simple electrolyte are amalgamated in a continuum approximation with only the macroion–macroion interactions being considered explicitly. In the Hamiltonian the interaction potential between two macroions in such a one-component model has two contributions

$$u(r) = u_{\mathrm{R}}(r) + u_{\mathrm{A}}(r). \tag{1}$$

The term $u_{\mathrm{R}}(r)$ is a long-range repulsive contribution which originates from an overlap of the electrical double layers. The second term, $u_{\mathrm{A}}(r)$, is the van der Waals energy and is attractive in nature. In the Poisson–Boltzmann (PB) and related mean-field theories an overlap of the electrical double layers always yields a repulsive interaction (see, for example, Kjellander (1996)) which may be approximated by the screened Coulomb potential. This term ($u_R$) therefore stabilizes the system. On the other hand, the short-range van der Waals term ($u_A$) is solely responsible for attraction and possible coagulation of the macroions.

Recent experimental and theoretical studies have raised doubts on the validity of the DLVO theory under certain conditions (for reviews see Schmitz (1993), Ise (1999), Vlachy (1999), Belloni (2000) and Spalla (2000)). At present these phenomena are being studied intensively by various experimental techniques, perhaps the most recent paper being that of Gröhn and Antonietti (2000). According to Gröhn and Antonietti the solution structuring, phase-separation behaviour and other properties prove the presence of electrostatic attractive forces between spherical polyelectrolyte microgels. These experimental results are consistent with recent numerical simulation studies of primitive model asymmetric electrolytes which have predicted an existence of attractive net interaction of electrostatic origin between like-charged spherical macroions (Hribar and Vlachy 1997, 2000a, Gronbech-Jensen *et al.* 1998, Wu *et al.* 1998, Linse and Lobaskin 1999, Linse 2000).

Nature provides polyelectrolytes with myriads of shapes. The fact that the conclusions arrived at, for example, in studies of cylindrical polyelectrolytes may not always be applied to situations involving spherical geometry, is not always appreciated. As stressed by Allahyarov *et al.* (1998), the behaviour of a polyelectrolyte solution depends on the geometric shape of the macroions. In this review we shall consider model macroions of spherical geometry; note, however, that some globular proteins and even micelles may be of ellipsoidal shape. Colloidal suspensions have been reviewed elsewhere (Schmitz 1993, Hansen and Löwen 1999, Ise 1999, Belloni 2000, Spalla 2000) and will therefore not be considered here. Rather, in this review we focus on three different types of instability that may occur in spherical polyelectrolyte solutions.

First, the instability caused by strong correlations between counterions in the solution. It has been known for some time that divalent (or trivalent) counterions precipitate polyelectrolytes. The effect has been ascribed to the efficient screening of the Coulomb interaction between macroions by the multivalent counterions allowing the attractive van der Waals forces to become more prominent. Recent computer simulation results (Hribar and Vlachy 1997, 2000a, Gronbech-Jensen *et al.* 1998, Wu *et al.* 1998, Linse and Lobaskin 1999, Linse 2000) show unambiguously the existence of the short-range attractive electrostatic force between like-charged macroions in solution. This kind of situation is most likely to happen in aqueous solutions containing divalent or trivalent counterions, and/or in the presence of solvents of low dielectric constant. As a consequence of strong inter-ionic correlations in these systems the charged macroions form dimers and higher clusters that may eventually yield to a phase separation (Linse and Lobaskin 1999, 2000, Linse 2000, Reščič and Linse 2001). The results suggest that the van der Waals attractive interaction is not the only source of instability in these systems and, indeed, may play a minor or negligible role in explaining the clustering of macroions.

Most of the existing models used to interpret experimental results assume that the surface charge of a macroion is constant and independent of the approach of other particles. This assumption fails for many experimental systems where, for instance, the surface charge results from a chemical adsorption of ions on to the surface sites. In § 3 of the review we discuss the effects of the second type of instability, surface-charge fluctuation, on the stability of polyelectrolyte solutions. The idea that the electrostatic interaction that arises from the fluctuations in charge could give rise to an attractive force between protein molecules was first proposed by Kirkwood and Shumaker (1952). More recently, Spalla and Belloni (1995) proposed a statistical-mechanical model to account for this effect. In this model the surface charge on the macroions results from the adsorption of positive and/or negative ions on to the colloidal particle (see also, Belloni and Spalla (1996)). The correlation between charges on different macroions may induce an effective attraction between the weakly charged (or even neutral) macroions and destabilizes the system. These results are helpful in the interpretation of experimental data for solutions of globular proteins and, according to Spalla and Belloni (1995), offer an explanation for the so-called hydrophobic force measured experimentally (Israelachvilli and Pashley 1982).

Much of the chemistry of life, as opposed to the chemistry in the laboratory, takes place in media that generally contain a substantial volume fraction of both charged and neutral macromolecules. The third instability concerns the combined effect of the electrostatic and 'crowding' interactions in these systems. The term 'crowding' interaction in the literature is reserved for situations where a large amount of inert co-solute is added to influence the interactions between the species originally present. One example of practical interest is the phase separation of globular proteins caused by the addition of a non-adsorbing polymer (polyethylene glycol (PEG) for example) to the aqueous solution. This phase separation often takes place in the presence of a low-molecular electrolyte and thus we need to consider the combined effect of electrostatic and non-electrostatic forces. Recently Reščič *et al.* (1998, 1999) have studied an equilibrium mixture of macroions, counterions and neutral particles using Monte Carlo (MC) simulations and other formal statistical mechanical approaches such as the hypernetted chain (HNC), symmetric Poisson–Boltzmann (SPB) and modified Poisson–Boltzmann (MPB) theories. A significant result of the studies is that a sufficient increase of the neutral species concentration leads to a gradual change in the qualitative nature of the interaction between two macroions from being repulsive to less repulsive and ultimately attractive. The theoretical results may be of help in choosing the optimal conditions in procedures such as colloid precipitation, purification of water, or separation of globular proteins (Wu and Prausnitz 1999).

## 2. Effects of multivalent counterions

In determining the stability of a polyelectrolyte solution important physical variables that must come into play are the charges and sizes of the macroions and the small ions, the concentration of all solute components and also the nature of the solvent. A goal of polyelectrolyte research has been to quantify the influence of different physical parameters in the measurable properties of a solution. To this end there have been at least three different levels of theoretical description used to analyse the experimental results in polyelectrolyte solutions and colloidal dispersions.

The first theoretical model is essentially given by equation (1), which describes the system as an effective one-component fluid. The effects of the solvent and the simple ions are included in a continuum approximation. Thus at this level of description, while the macroion–macroion interaction is considered explicitly, all information about the macroion–small ion correlation is precluded. The second model is the so-called cell model (Bell and Dunning 1970) (see also Rebolj *et al.* (1997) and the references therein) which builds on the natural asymmetry in size and charge between the macroions and the simple ions. In spherical geometry—the domain of our discussion here—the (spherical) cell model would be made up of a macroion being caged in a spherical cell that includes an appropriate number of simple ions so as to make the cell electroneutral. The whole polyelectrolyte solution is divided into such cells, the sizes of which are determined by the macroion concentration and aggregation number. Application of the cell model is limited to situations where the macroion concentration is not too high and the macroions are distributed rather uniformly throughout the solution, as discussed elsewhere (Rebolj *et al.* 1997, Hribar and Vlachy 2000a). The third level of description treats the polyelectrolyte solution as a highly asymmetric electrolyte solution. The solution is described as a mixture of charged hard (or sometimes soft) spheres, while the solvent is still considered to be a continuum dielectric. This is known in the literature as the primitive model (PM), which treats all the species present, with the exception of the solvent, explicitly and on an equal footing. Recent theoretical results based on this popular model are reviewed in the present paper.

Seminal computer simulations for highly asymmetric (both in charge and size) model electrolytes were performed by Linse and Jönsson (1983). In parallel, more analytical theories (see, for example, the review by Vlachy (1999)) were adapted to polyelectrolyte solutions. Among these theories the HNC theory was found to be well suited for electrolyte solutions (for a review see Rasaiah (1988)). Patey (1980) and Teubner (1981) applied the HNC approximation to a pair of spherical macroions immersed in an electrolyte solution. Later Belloni (1985) extended the HNC calculations to a finite concentration of macroions. Vlachy *et al.* (1989) provided a well converged MC simulation of model asymmetric electrolytes with asymmetry (between the macroions and the counterions) in size of 10:1 and in charge of $-10:+1$ and $-15:+1$. These computer simulations were used to examine the accuracy of the HNC theory for these systems. Systematic discrepancies with the simulation results were found as the charge asymmetry was increased. The most important conclusion of the study is that the HNC theory predicts the counterions to be too close to each other and also too close to the highly charged macroions. This leads to an underestimation of the macroion–macroion repulsion. One consequence of this defect manifests itself in the numerical instability of the HNC approximation; for instance, for dilute solutions and/or in presence of divalent counterions the HNC approximation does not yield convergent solutions. Hribar *et al.* (1997) performed extensive computer simulations for dilute solutions of counterions and macroions with asymmetry in charge of $-10:+1$ ($-10:+2$) and $-20:+1$ ($-20:+2$). These results were used to compare and contrast theoretical predictions from the HNC, the cluster expansion approach and the two density theories (Kalyuzhnyi and Vlachy 1993) in the associated HNC approximation and mean spherical approximation (MSA). The conclusion is that these theories yield fair agreement with the MC data for only low charge asymmetry between macroions and counterions, and/or for solutions with monovalent counterions. For example, none of the theories examined by Hribar *et al.* (1997) was able to describe quantitatively the structure of dilute $-20:+2$ electrolytes. For this reason at present the computer simulations seem to be the only reliable tool to investigate such systems.

An important development in our understanding of highly asymmetric electrolytes, the one that concerns us here, came through the work of Hribar and Vlachy (1997), where the results are suggestive of the fact that strong Coulomb correlations can lead to an attractive interaction between two like macroions. This is in stark

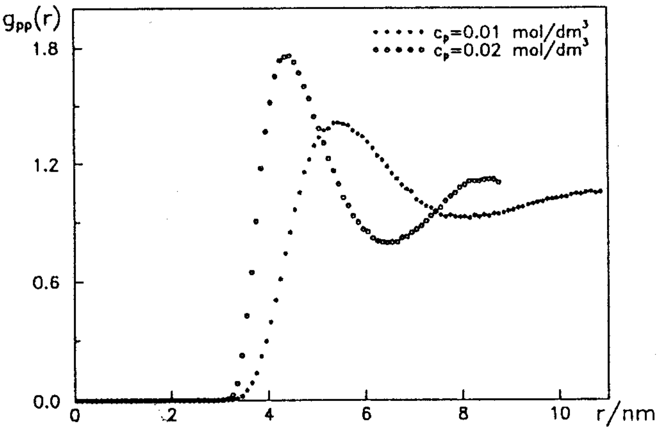

Figure 1. The macroion–macroion pair distribution functions $g_{\mathrm{pp}}(r)(= g_{\mathrm{mm}}(r))$ obtained from MC simulations for a $-20:+1$ electrolyte at macroion concentration $c_{\mathrm{p}}(= c_{\mathrm{m}}) = 0.01\,\mathrm{mol\,dm^{-3}}$ ($\star$, lower curve) and $c_{\mathrm{p}}(= c_{\mathrm{m}}) = 0.02\,\mathrm{mol\,dm^{-3}}$ ($\circ$, upper curve). Reproduced with permission from Hribar, B., and Vlachy, V., 1997, *J. phys. Chem.* B, **101**, 3457–3459. Copyright (1997) American Chemical Society.

contrast to the classical DLVO prediction, which says no attractive interaction can be observed between highly charged macroions immersed in an electrolyte solution. Evidence of electrostatic attraction between equally charged macroions induced by divalent counterions has been examined in depth in a series of papers by Hribar and Vlachy (1997, 2000a,b,c, 2001). These authors investigated a system composed of macroions (m), counterions (c), and, in a few cases, also of coions (k). These ionic species are represented by charged hard spheres of different diameters $\sigma_s$ (of species $s$) embedded in a continuous dielectric with relative permittivity $\varepsilon_{\mathrm{r}}$ (primitive model). The interaction pair potential for two ions of valences $z_i$ and $z_j$, separated by distance $r_{ij}$, is assumed to be

$$u_{ij}(r) = \begin{cases} z_i z_j \dfrac{L_{\mathrm{B}}}{r_{ij}} & r \geq \sigma_{ij}, \\ \infty & r < \sigma_{ij}, \end{cases} \tag{2}$$

$$L_{\mathrm{B}} = \frac{\beta e^2}{4\pi\varepsilon_0\varepsilon_{\mathrm{r}}}, \tag{3}$$

with $\sigma_{ij} = (\sigma_i + \sigma_j)/2$ and $\varepsilon_0$ the vacuum permittivity. As usual, $\beta = 1/(k_{\mathrm{B}}T)$, where $k_{\mathrm{B}}$ is Boltzmann's constant and $T$ the absolute temperature. Hribar and Vlachy (1997) applied the MC method in conjunction with equations (2) and (3). In this study the macroions are assumed to carry 20 negative charges ($z_{\mathrm{m}} = -20$, $\sigma_{\mathrm{m}} = 30 \times 10^{-10}\,\mathrm{m}$) and the counterions have charge $z_{\mathrm{c}} = +1$ or $+2$. The diameter of the counterions $\sigma_{\mathrm{c}} = 4\times10^{-10}\,\mathrm{m}$. The simulation results apply to $T = 298\,\mathrm{K}$ where the Bjerrum length $L_{\mathrm{B}} = 7.15\times10^{-10}\,\mathrm{m}$. Pair distribution functions $g(r)$ and some thermodynamic properties were calculated for macroion concentrations of 0.01 and $0.02\,\mathrm{mol\,dm^{-3}}$.

The macroion–macroion pair distribution functions are shown in figures 1 and 2 (figures 1 and 2 of Hribar and Vlachy (1997)). Figure 1 shows the macroion–macroion $g(r)$ for monovalent counterions, that is for $-20:+1$ electrolytes as described above. As we can see, the first peak in the $g(r)$ is shifted towards larger

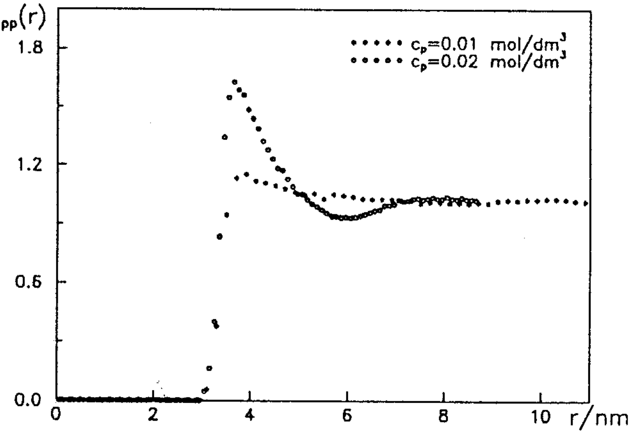

Figure 2. The macroion–macroion pair distribution functions $g_{\mathrm{pp}}(r)(=g_{\mathrm{mm}}(r))$ obtained from MC simulations for a $-20:+2$ electrolyte at macroion concentration $c_{\mathrm{p}}(=c_{\mathrm{m}})=0.01\,\mathrm{mol\,dm^{-3}}$ ($\star$, lower curve) and $c_{\mathrm{p}}(=c_{\mathrm{m}})=0.02\,\mathrm{mol\,dm^{-3}}$ ($\circ$, upper curve). Reproduced with permission from Hribar, B., and Vlachy, V., 1997, *J. phys. Chem.* B, **101**, 3457-3459. Copyright (1997) American Chemical Society.

distances upon dilution from 0.02 to 0.01 mol dm$^{-3}$. This result is a consequence of the repulsion between the macroions. More interesting are the results for $-20:+2$ electrolytes shown in figure 2. In this case the first peak of the macroion–macroion $g(r)$ does not change its position when the solution is diluted. For both concentrations this peak is located around $38\times10^{-10}$ m, so that there are on the average one or two layers of counterions between two macroions. Clearly, the structures of the $-20:+1$ and $-20:+2$ solutions are very different. In a subsequent paper Hribar and Vlachy (2000b) extended the study to a macroion system with a mixture of monovalent and divalent counterions. Structural and thermodynamic results (excess internal energy $E^{\mathrm{ex}}$ and osmotic coefficient) were presented for various mixtures of $-20:+1$ and $-20:+2$ electrolytes. It is shown that by increasing the fraction of divalent counterions in the solution the first peak of the macroion–macroion $g(r)$ is gradually shifted towards smaller distances. Thermodynamic considerations indicate that for solutions with divalent counterions the energy ($\Delta E$) and entropy ($T\Delta S$) contributions to the free energy of dilution from 0.02 to 0.01 mol dm$^{-3}$ roughly cancel each other. These results indicate an important role of correlated interaction between divalent counterions.

Interactions between two isolated charged spherical particles in their counterions solution were studied in several papers (Allahyarov *et al.* 1998, Gronbech-Jensen *et al.* 1998, Wu *et al.* 1988). According to Wu *et al.* (1988) the motivation for these studies was the suspicion that the attraction described above may be arising partly due to the correlation among many macroions present in the solution. The studies of infinitely dilute systems provide the potential of mean force between macroions, which can be compared with the classical DLVO theory. Allahyarov *et al.* (1998) used computer simulations of the PM to propose a mechanism for the counterion-mediated attraction between like-charged macroions. According to their explanation, there is a depletion zone between nearly touching macroions and this effect dominates over the electrostatic contribution. Gronbech-Jensen *et al.* (1998) demonstrated a strong attractive effective potential between two like-charged spheres

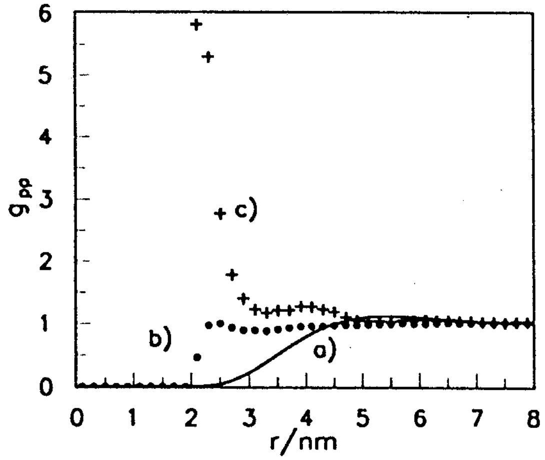

Figure 3. The macroion–macroion pair distribution functions $g_{pp}(=g_{mm})$ at macroion concentration $c_m = 0.01\,\mathrm{mol\,dm^{-3}}$: (a) $-12:+1$, (b) $-12:+2$ and (c) $-12:+3$ electrolytes. Reproduced with permission from Hribar, B., and Vlachy, V., 2000, *Biophys. J.*, **78**, 694–698. Copyright (2000) Biophysical Society.

in the presence of divalent counterions. The results are again in contrast to the always repulsive DLVO potential.

Insight into calculations of the potential of mean force between a pair of isolated spherical macroions immersed in an electrolyte solution was provided by the calculations of Wu *et al.* (1998, 1999). In their first paper, Wu *et al.* (1998) presented MC results for the potential of mean force between macroions in $+1:-1$ and $+2:-2$ PM electrolyte solutions. Comparison with the DLVO approach and the Sogami–Ise (1984) theory indicates that none of the theories are able to describe the simulation results for a system with divalent simple ions. In a subsequent paper Wu *et al.* (1999) extended their study to include electrolyte solutions with valences $+1:-2$, $+2:-1$ and $+2:-2$. Their conclusion is that macroions of the same charge can attract each other in the presence of divalent counterions. The attraction between macroions is of energetic origin; the entropic contribution to the potential of mean force is generally repulsive under the conditions studied. These results have been discussed *vis-à-vis* experimental data for globular proteins (Wu and Prausnitz 1999).

The ion–ion correlation is expected to be even stronger in solutions with trivalent counterions. This expectation is confirmed in several studies (Linse and Lobaskin 1999, Hribar and Vlachy 2000a,c, 2001). Hribar and Vlachy (2000a) presented MC results for a PM asymmetric electrolyte (see equations (2) and (3)) with asymmetry in size of $20\times10^{-10}\,\mathrm{m}/2\times10^{-10}\,\mathrm{m}$. The macroions were assumed to carry 12 negative charges ($z_m = -12$) while the counterion species had charges $z_c = +1, +2$ or $+3$. The results for the macroion–macroion pair distribution function are shown in figure 3 (figure 1 of Hribar and Vlachy (2000a)). This figure displays the results for (a) $-12:+1$, (b) $-12:+2$ and (c) $-12:+3$ solutions at $c_m = 0.01\,\mathrm{mol\,dm^{-3}}$ and clearly brings out the essential role the valency of counterions plays in determining the structure of the solution. In solutions with monovalent counterions (curve (a), figure 3) the interaction is purely repulsive and the macroions are distributed at large distances from each other. The position of the very broad first peak is estimated to be

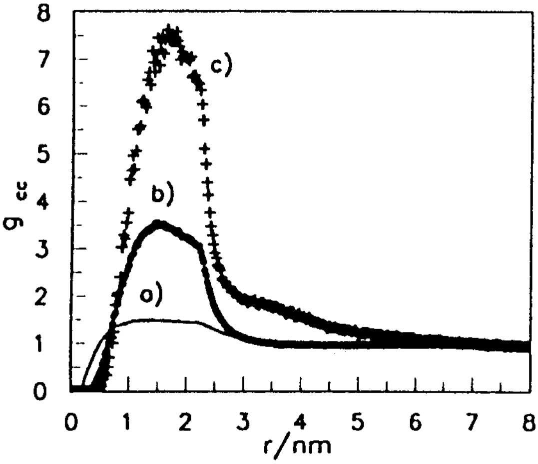

Figure 4. The counterion–counterion pair distribution functions $g_{cc}$ at macroion concentration $c_m = 0.005\,\mathrm{mol\,dm^{-3}}$: (a) $-12:+1$, (b) $-12:+2$ and (c) $-12:+3$ electrolytes. Reproduced with permission from Hribar, B., and Vlachy, V., 2000, *Biophys. J.*, **78**, 694–698. Copyright (2000) Biophysical Society.

at $54\times10^{-10}$ m. In the case with divalent counterions (curve (b), figure 3) the peak in $g(r)$ is shifted towards a smaller distance and is located at $24\times10^{-10}$ m. Here two macroions share a layer of counterions. Curve (c) in figure 3, which shows the macroion–macroion $g(r)$ in solutions with trivalent counterions, reflects a high probability for two macroions being in contact. In order to better illustrate the structural features that are obtained in the solution, we show also the counterion–counterion distribution function in figure 4 (figure 4 of Hribar and Vlachy (2000a)), which indicates a very strong correlation between trivalent counterions. The same holds true for the macroion–counterion correlation. The values of the macroion–counterion pair distribution function $g_{mc}$ in contact are around 29, 120 and 250 for respectively $-12:+1$, $-12:+2$ and $-12:+3$ solutions at $c_m = 0.005\,\mathrm{mol\,dm^{-3}}$.

Figures 5 and 6 (figures 6 and 7 of Hribar and Vlachy (2000a)) show typical equilibrium arrangements of macroions attained in the simulation for two different solutions, one (figure 5) with monovalent and the other (figure 6) with trivalent counterions both at $c_m = 0.005\,\mathrm{mol\,dm^{-3}}$. By comparing the two figures we can see that strong inter-ionic correlations yield a very non-uniform distribution (clusters and voids) of macroions in the case where trivalent counterions (figure 6) are present. Hribar and Vlachy have also discussed some thermodynamic properties; for example, the MC values of the osmotic coefficient for $-12:+1$, $-12:+2$ and $-12:+3$ solutions at $c_m = 0.005\,\mathrm{mol\,dm^{-3}}$ are $0.57\pm0.005$, $0.31\pm0.01$ and $0.14\pm0.04$ respectively. In addition, the results for the internal energy, entropy and free energy changes upon dilution from $c_m = 0.02$ to $0.01\,\mathrm{mol\,dm^{-3}}$ were calculated. The results presented in table 1 (table 1 of Hribar and Vlachy (2000a)) indicate an energy–entropy compensation for solutions with divalent and trivalent counterions.

In a recent paper Hribar and Vlachy (2001) have extended their MC simulations to solutions with a mixture of monovalent and trivalent counterions. Structure and thermodynamics of this system were studied for several values of the composition

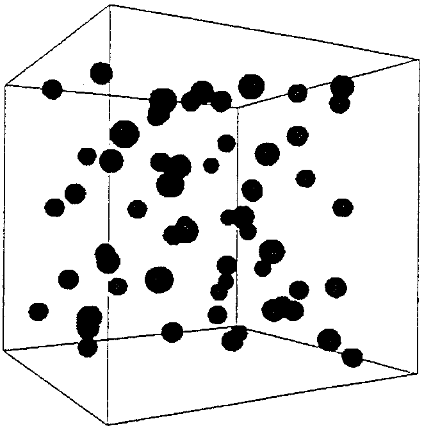

Figure 5. An example of an equilibrium distribution of macroions for a $-12:+1$ electrolyte at macroion concentration $c_m = 0.005\,\mathrm{mol\,dm^{-3}}$. Reproduced with permission from Hribar, B., and Vlachy, V., 2000, *Biophys. J.*, **78**, 694–698. Copyright (2000) Biophysical Society.

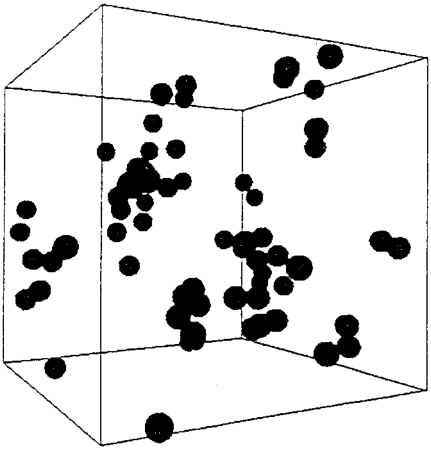

Figure 6. An example of an equilibrium distribution of macroions for a $-12:+3$ electrolyte at macroion concentration $c_m = 0.005\,\mathrm{mol\,dm^{-3}}$ Reproduced with permission from Hribar, B., and Vlachy, V., 2000, *Biophys. J.*, **78**, 694–698. Copyright (2000) Biophysical Society.

parameter $x_3$, defined as $x_3 = 3c_3/(c_1 + 3c_3)$, where $c_1$ is the concentration of monovalent and $c_3$ the concentration of trivalent counterions. It is interesting to note that for low macroion concentrations ($c_m = 0.0005$ and $0.001\,\mathrm{mol\,dm^{-3}}$) the osmotic coefficient, presented as a function of $x_3$, exhibits a small maximum, whereas at higher concentration the osmotic coefficient is seen to be a monotonic function of the composition parameter. Hribar and Vlachy (2000c) have also studied the effect of addition of a simple electrolyte to the stability of $-12:+3$ solutions. The results indicate that when the clusters (mostly pairs) are formed, they are not very sensitive to addition of a simple electrolyte, which must be added in excess to modify the structure of the solution substantially.

Table 1. The internal energy, $E/Nk_BT$, entropy, $S/Nk_B$ and free energy, $A/Nk_BT$, changes upon dilution from macroion concentration $c_m = 0.02$ to 0.01 mol dm$^{-3}$. Reproduced with permission from Hribar, B., and Vlachy, V., 2000, *Biophys. J.*, **78**, 694–698. Copyright (2000) Biophysical Society.

| $z_c$ | $\Delta E/Nk_BT$ | $\Delta S/Nk_B$ | $\Delta A/Nk_BT$ |
|---|---|---|---|
| +1 | $0.260 \pm 0.003$ | $0.621 \pm 0.006$ | $-0.362 \pm 0.003$ |
| +2 | $0.27 \pm 0.01$ | $0.36 \pm 0.02$ | $-0.10 \pm 0.01$ |
| +3 | $0.3 \pm 0.1$ | $0.3 \pm 0.2$ | $0.0 \pm 0.1$ |

So far most of the theoretical information about structure and thermodynamics of these systems comes from the MC method. Very recently, the asymmetric electrolytes have been studied by the molecular dynamics (MD) simulations (Spohr *et al.* 2001). In this calculation the ions were treated as soft spheres and the solvent was considered as a continuum with a permittivity of water at $T = 298$ K. Only the solutions of macroions and counterions were studied; the macroions carried in one case 12 and in the other 24 negative charges, while the valencies of counterions were $z_c = +1$, $+2$ or $+3$. The asymmetries in size between the macroions and the counterions were 5:1 in the first example and 7:1 in the second. The MD results showed clustering of macroions when trivalent counterions were present in solution and this confirmed the earlier MC simulations of Hribar and Vlachy (2000a). Detailed analysis of both static and dynamic properties showed that macroion dimerization (and formation of higher clusters) proceeds in two steps. In the first step the trivalent counterions neutralize the macroions, practically all the counterions residing on macroions and most of the macroions having an effective charge zero or $-3$. These 'neutralized' macroions serve as precursors for the clustering process in the second step: most macroion pairs are formed by combining either two neutral macroion species, or one neutral and one '$-3$ charged' (that is partly neutralized) macroion. The MD simulations indicate that the formation of clusters between like-charged macroions requires the existence of neutralized or almost neutralized macroions as precursors. In solutions with monovalent counterions the formation of these neutralized precursors is highly unlikely to happen, owing to unfavourable entropic contribution to the free energy. Note, that only four trivalent counterions are needed to neutralize the macroion in comparison with 12 monovalent counterions. Spohr *et al.* (2001) calculated also the self-diffusion coefficients of the macroion ($D_m$) and counterion ($D_c$) species. In solutions with monovalent counterions the ratio $D_c/D_m$ was in the range from 5 to 10, depending on the concentration of the solution. Interestingly, in solutions with trivalent counterions the same ratio $D_c/D_m$ was close to unity and almost independent of the polyelectrolyte concentration.

The studies reviewed above apply to asymmetric electrolytes of relatively low to moderate asymmetry in charge. Higher asymmetries in both charge and size have been treated by Linse and Lobaskin (1999, 2000) and Linse (2000). For example, a sodium dodecyl sulphate micelle has at concentrations slightly above the critical micelle concentration (cmc) about 64 negative charges. This is approximately the range of parameters studied by Linse and Lobaskin (1999, 2000) using MC simulations in the presence of either monovalent, divalent or trivalent counterions. The ions are, as in the earlier studies, assumed to interact solely through hard core and Coulomb forces (cf. equations (2) and (3)). In the first paper Linse and Lobaskin

(1999) studied a system of macroions ($z_m = -60$) and counterions ($z_c = 1$, 2 or 3) with diameters $40 \times 10^{-10}$ m and $4 \times 10^{-10}$ m at $T = 298$ K and $\varepsilon_r = 78.4$ at macroion volume fraction of $\phi_m = 0.0168$. The results, obtained for a system of 80 macroions, reinforce the Hribar and Vlachy (2000a) finding that in solutions with monovalent counterions the macroions are well separated from each other. In the case of divalent counterions Linse and Lobaskin observed a tendency of macroion pairing and substantial accumulation of counterions in the vicinity of macroions. Finally, with trivalent counterions the macroions formed a large aggregate, with occasionally a few macroions being free. In addition, most of the counterions were associated with macroions. A more extensive study of the same system is presented in Linse and Lobaskin (2000). The results of both studies are clearly consistent with those obtained for systems with smaller asymmetry in charge (Hribar and Vlachy 1999, 2000a).

The limiting size-asymmetric case of macroions and point ions was simulated by Linse (2000). The structure and thermodynamics of the system were investigated at different macroion volume fractions (ranging from 0.001 25 to 0.08) and different macroion–point ion charge ratios (ranging from 10 to 80). Apart from the macroion–macroion attraction and macroion aggregation, the gas–liquid two-phase region was also observed (see below). It is worth mentioning here that within the framework of the PM, even for a single electrolyte at normal temperature and pressure conditions there is *like attraction* (Sloth and Sorensen 1990, Outhwaite *et al.* 1993), namely, $g_{++}$(contact) $> 1$ or $g_{--}$(contact) $> 1$ for (a) 1:1 valency unequal size, for larger ions at high concentrations, and, (b) 2:1 valency equal size, for univalent ions at high concentrations. This would suggest that charge asymmetry and large variation in ion size both encourage attraction between like ions. Evidently, macroions with point counterions are an extreme case of (a) + (b), but one can essentially see that *attraction* could well be a consequence in certain parameter ranges.

A significant conclusion from the above simulation studies is that macroions form a single aggregate in the case of trivalent counterions (Linse and Lobaskin 2000), or in the case of solvents with low dielectric permittivity (Linse 2000). It is therefore of interest to determine the fluid–fluid two-phase region for this system. This has been done by Linse (2000) and in a more recent paper by Reščič and Linse (2001). In these studies the density scaling MC technique was applied to a system of spherical macroions and point counterions. The modification of the MC method allows for a determination of the relative free energies of thermodynamic states. Reščič and Linse (2001) determined the relative free energies for the macroion volume fraction interval $0.04 < \phi_m < 0.24$ at different values of the plasma coupling parameter $\Gamma$ defined as $2z_c^2 L_B/\sigma_m$. The binodal curve separating the one-phase system and a gas–liquid two-phase region was determined. These results are presented in figure 7 (figure 5 of Reščič and Linse (2001)). The critical values of parameters were estimated to be $\phi_m^{crit} = 0.15$ and $\Gamma = 2.6$.

Although there is a considerable body of experimental evidence for the electrostatic attraction between like-charged cylindrical macroions in solution (see, for example, Bloomfield (1991) and Tang *et al.* (1996), the breakdown of the classical PB description for the planar electrical double layer in the presence of trivalent phosphotungstate ions has been documented experimentally by Cuvillier and Rondelez (1998)), such results for the corresponding spherical macroions are beginning to be available. An important piece of experimental evidence for the

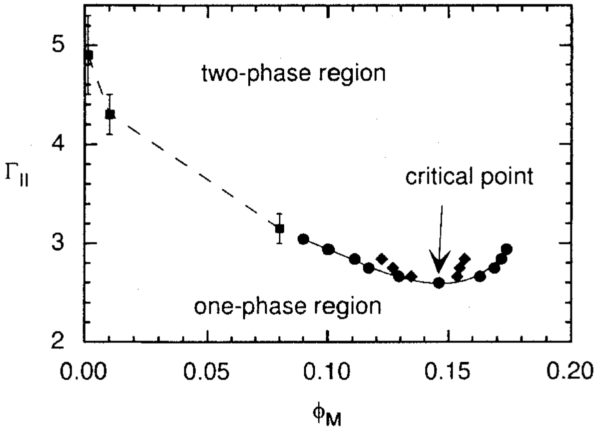

Figure 7. Gas–liquid binodal curve with interpolated critical point (circles with fitted solid curve) and spinodal curve (diamonds) for $Z_r = 10$ ($Z_r = -z_M/z_I$), as determined using the temperature and density scaling MC approach with 10 macroions. Subscripts M and I denote macroions and counterions respectively and $\Gamma_{II} = \Gamma$. The low-density part of the gas branch of the binodal curve (squares with error bars connected with dashed lines) was obtained by standard Metropolis MC simulations using 40 macroions. Reprinted with permission from Reščič, J., and Linse, P., 2001, *J. chem. Phys.*, **114**, 10 131–10 136. Copyright (2001) American Institute of Physics.

attraction between equally charged spherical macroions has been recently provided by Gröhn and Antonietti (2000). These authors investigated salt-free solutions of highly charged spherical polyelectrolyte microgels with radii between $60\times10^{-10}$ and $700\times10^{-10}$ m. By using a static light scattering experiment, Gröhn and Antonietti (2000) explored an important range of particle sizes between small ions and latex suspensions. The experimental results indicate a microheterogeneity of the solution. According to the authors, domains with long-range ordering coexist with a polymer-poor phase (voids). At low concentrations, the aqueous salt-free solutions separate into two phases of widely different (factor of 200) concentration.

The experimental results for large colloidal particles, not consistent with the DLVO theory, have been reviewed by several authors (Schmitz 1993, Ise 1999, Belloni 2000, Hansen and Löwen 2000, Spalla 2000) and will not be repeated here. However, in passing, we note a recent interesting development since these reviews, which might be of relevance here. There exists a class of theories, the so-called volume-term theories (van Roij and Hansen 1997, 1998, Denton 1999, van Roij *et al.* 1999, Warren 2000), which purport to explain the two-state structure observed in colloidal suspensions. A prototype is the theory developed by van Roij, Hansen and co-workers. In their approach, the techniques of the density functional formalism are applied to a free energy functional (of the simple ion density profiles) to obtain the effective macroion interaction energy and hence the free energy of the system. The phase diagram corresponding to the effective interaction energy is then constructed following standard procedure. The density functional theory has proved useful in studies of phase transitions in complex fluid systems (see, for example, the reviews by Evans (1993) and Hansen (1995)). In charge-stabilized colloidal suspensions the source of spinodal instability in the phase diagrams is linked to certain terms in the free energy expression (see, for example, van Roij and Hansen (1998)), which are independent of the macroion coordinates but depend on the system volume through the average number density of the species. An important feature of these theories is that the DLVO repulsive screened Coulomb interaction between macroions is retained. Sogami and Ise (1984) on the other hand, had earlier proposed an effective pair potential between the macroions, which has a counterion mediated attractive tail. In a recent paper Schmitz and Bhuiyan (2000) have reconciled the two approaches by showing from fundamental thermodynamic arguments that a long-range attractive term in the pair potential between macroions is consistent within the volume-term formalism.

## 3. Surface-charge fluctuations

Popular models for micellar and colloidal system such as the PM discussed in the previous section, assume that the surface charge of a macroion is constant and independent of the proximity of other particles. This assumption fails for many experimental systems where the surface charge results from a chemical adsorption of ions on to the surface sites. Examples are mineral systems such as oxides, or biological systems, where the charge on the surface is sensitive to solution conditions. Note, in this regard, that the DLVO theory treats the macroion charge as an adjustable parameter.

The idea that the electrostatic interaction arising out of fluctuations in surface charge can give rise to an attractive force between protein molecules was first proposed by Kirkwood and Shumaker (1952). Further analysis was performed by Phillies (1974), who derived an expression relating the charge fluctuations to the potential of mean force and hence the pair correlation function. The conclusion of these studies is that charge fluctuations can yield an attractive potential proportional to the variance in the average charge on the macroion. In the Phillies theory, the variance in the average charge is not known *a priori*, rather it is used as an adjustable parameter. One example of the application of these ideas is the work of Haynes *et al.* (1992). These authors used the charge-fluctuation correction of Phillies in their analysis of the osmometric measurements of $\alpha$-chymotrypsin solutions. Inclusion of the contribution due to the protein charge fluctuations yielded a better agreement with experimental data (Haynes *et al.* 1992).

The *charge-regulation* model to calculate the fraction of ionized sites for a given thermodynamic condition at the mean field level has been proposed by Ninham and Parsegian (1971). They wrote down a local law of mass action for a given constant which involves the local number densities calculated from the solution of the PB equation. The approach accounts for the observed strong interweaving of electrostatics and chemistry, however, owing to the mean-field nature of the theory, it is not able to predict macroion–macroion attraction.

Recently, a more rigorous statistical-mechanical treatment of the surface-charge regulation process in colloidal suspensions was proposed by Spalla and Belloni (1991, 1995) and Belloni and Spalla (1996, 1997). A novel aspect of the theory is that it seeks to account for the surface chemistry and the ion–ion correlation simultaneously. The starting point is a new version of the PM for asymmetric electrolytes, called charge regulated primitive model (CRPM), which relaxes the constant charge approximation of the standard PM. In this model therefore, the charge on a macroion is not constant (nor is it uniform), but follows from the calculation itself. Belloni and Spalla (1996, 1997) considered a three-component mixture of ions. The species are small ions of valencies $z_+ = +1$ and $z_- = -1$ and the macroions ($z_m$)

immersed in the continuum dielectric as for the PM. The pair interaction between two ions of species $i$ and $j$ ($i, j = +, -, \mathrm{m}$) is

$$u_{ij}(r) = \begin{cases} z_i z_j \dfrac{L_\mathrm{B}}{r} & r \geq \sigma_{ij}, \\ \infty & r < \sigma_{ij}. \end{cases} \tag{4}$$

As before $\sigma_{ij} = (\sigma_i + \sigma_j)/2$, where $\sigma_i$ is the diameter of ionic species $i$. The essential ingredient of the CRPM is that there is an additional short-range potential $V_i$ acting between small ions and macroions over and above that given by equation (4), namely,

$$\mathrm{e}^{-\beta v_{\mathrm{m}i}(r)} = \begin{cases} V_i \delta(r - L_i) & r < \sigma_{\mathrm{m}i}, \\ 1 & r > \sigma_{\mathrm{m}i}, \end{cases} \tag{5}$$

where the subscript $i$ denotes a small ion species (+ or −). The infinitely deep and narrow potential well between the macroion and an ion of type $i$ is located at distance $r = L_i = (\sigma_\mathrm{m} - \sigma_i)/2$. This potential mimics the chemical reaction between these two species: the macroions may be initially neutral, however, they acquire their equilibrium charge via a chemical reaction with the small ions present. The strength of the potential is characterized by $V_i$, thus the assumption of the macroions being neutral initially would imply that for a pure PM electrolyte $V_i = 0$. It is important to note that several ions can attach themselves to the same macroion, however, the choice of $L_i$ ( $L_i < \sigma_\mathrm{m}/2$ ) and the macroion–macroion excluded volume, prevent the simultaneous *reaction* of one counterion with two different macroions. In this approach, the average number of chemically adsorbed ions of species $i$ per macroion $n_i$ and the net average charge of the macroion $ze$, which is a sum of the fixed charge $z_\mathrm{m}e$ (which may be zero) and of the adsorbed charges $n_+e$ and $n_-e$ ($z = z_\mathrm{m} + n_+ - n_-$), are results of the calculation.

Belloni and Spalla (1997) have derived certain asymptotic expressions using a diagramatic expansion. These expressions are quite informative in that they help in understanding the physics behind numerical results. For example, in the special case of small macroions ( $\kappa\sigma_\mathrm{m} \ll 1$ ) the following approximate expressions for the long-range behaviour ($\kappa r \to \infty$) of the potential of mean force between macroion and ion $w_{\mathrm{m}i}(r)$

$$w_{\mathrm{m}i}(r) \approx z_i z L_\mathrm{B} \frac{\mathrm{e}^{-\kappa r}}{r} - X \frac{L_\mathrm{B}^2}{2} \frac{\mathrm{e}^{-2\kappa r}}{r^2}, \tag{6}$$

and between two macroions $w_\mathrm{mm}(r)$

$$w_\mathrm{mm}(r) \approx z^2 L_\mathrm{B} \frac{\mathrm{e}^{-\kappa r}}{r} - X^2 \frac{L_\mathrm{B}^2}{2} \frac{\mathrm{e}^{-2\kappa r}}{r^2} \tag{7}$$

have been derived. In these equations $\kappa$ is the screening constant defined as $\kappa^2 = 8\pi L_\mathrm{B} \rho_\mathrm{s}$, $X = (n_+ + n_- - 2\phi)$ with $\phi = \frac{4}{3}\pi a^3 \rho_\mathrm{s}$ where the mean number density $\rho_\mathrm{s} = \rho_+ = \rho_-$ for a symmetric electrolyte, and $a = \sigma_\mathrm{m}/2$. Note, that the two equations were derived using only the first long-range diagram (enumerated as 1 in figure 1 of Belloni and Spalla (1997)) and therefore apply to low values of adsorption. They must be understood as first terms in the asymptotic expansion ($\kappa r \to \infty$) of $w_{\mathrm{m}i}$ and $w_\mathrm{mm}$ in increasing powers of $n = (n_+ + n_-)$ and $\phi$. The factor $X = (n - 2\phi)$ is a dimensionless quantity related to the difference between the number of adsorbed ions contained in the volume occupied by a macroion and the number of ions in the bulk electrolyte of concentration $\rho_s$ contained in an identical volume.

Equations (6) and (7) each have two terms. The first term represents the usual screened Coulomb interaction (this could be the term $u_R$ in equation (1)) being always repulsive for the like-charge ions, whereas the second term is related to the quadratic term in the ion–ion correlations. In equation (6), the latter term is repulsive for low adsorption but attractive at high adsorption. An interesting result is contained in equation (7): the second term in this equation is always negative and it therefore yields an attractive contribution to $w_{mm}(r)$. When the average macroion charge $z = 0$, this term yields an attraction not seen in the DLVO or any other linear theory. For the PM though, there is no adsorption ($n_+ = n_- = 0$) and for $z = 0$, the potential of mean force between the macroions is negative. For $n_+ + n_- = 2\phi$, the attractive contribution in equation (7) vanishes for all values of the net average charge $z$.

Belloni and Spalla (1997) next considered the contribution of the second diagram (enumerated as 2 in their figure 1) in the expansion of the excess macroion–ion potential of mean force. This approximation is therefore not limited to the case of very low adsorption. The inclusion of the second diagram in the calculation merely yields a slightly different prefactor $X$ in equations (6) and (7); in other words, the $r$-dependence does not change. The new prefactor indicates a saturation effect; as the ionic adsorption increases, the macroion–macroion attraction becomes weaker than that predicted by the limiting result contained in equation (7).

Belloni and Spalla (1997) further employed the HNC integral equation (see also § 2) to calculate the pair distribution functions for the above system and to test the new approximations. They investigated the case of infinite dilution of the macroions, $\rho_m = 0$, while $\rho_+ = \rho_- = \rho_s$ and the bulk electrolyte concentration $c_s$ was $10^{-3}$ mol dm$^{-3}$. Both symmetric ($V_+ = V_-$) and asymmetric absorption were considered. In most of the calculations the following values of parameters were used: $\sigma_m = 68 \times 10^{-10}$ m, $\sigma_+ = \sigma_- = 4 \times 10^{-10}$ m. The authors considered several sets of parameters, perhaps the most important being the case for $z_m = 0$. Good agreement with the asymptotic predictions of equations (6) and (7) valid for large distances $r$ and small adsorption was obtained. This finding suggests, among other things, that these limiting expressions based on the diagrammatic expansion capture essentially the correct physics.

Further investigations of Belloni and Spalla (1997) focused on including the leading bridge graph in the HNC calculation, what they called the HNCB approximation. As has been shown before (Bacquet and Rossky 1983, Reščič *et al.* 1990) inclusion of this graph significantly improves the accuracy of the HNC calculation. According to Belloni and Spalla (1997), at low adsorption the HNCB approximation reduces slightly the non-DLVO attraction predicted by the HNC. At high adsorption the two approximate theories yield qualitatively different behaviour and no attraction is found in the HNCB calculation. A quantitative test of the proposed theories is only possible through a detailed comparison with computer simulations which, to our knowledge, are presently not available.

In summary, the CRPM, which considers the macroion charge to be a consequence of ionic adsorption, yields a new attraction contribution in the macroion–macroion potential of mean force. The attraction exists at low adsorption (low charge) and for solutions with monovalent counterions. In this respect the effect is different from that due to strong Coulomb correlations (cf. § 2) seen in the presence of highly charged macroions and/or multivalent counterions. We share the opinion of Belloni and Spalla that the charge regulation model may prove helpful in situations where the charge on macroions is not expected to be constant. This feature would seem to be useful in interpreting experimental data for mineral oxides and globular proteins (Haynes *et al.* 1992). The attraction mechanism suggested above also offers an explanation for the so-called hydrophobic force measured experimentally (Israelachvilli and Pashley 1982).

## 4. Effects of neutral co-solute

We now turn our attention to the instability in a polyelectrolyte solution caused by the presence of a neutral polymer—a neutral co-solute and in particular to the changes in the interaction between the ionic species brought about as a consequence. As mentioned in the Introduction, most natural process chemistry occurs in the presence of substantial volume fractions of inert macromolecules (Minton 1995). Terms such as *crowding reactions* or *macromolecular crowding* are used to describe the effects (of the addition) of such inert co-solutes upon the equilibrium and non-equilibrium behaviour of the solution. It has been demonstrated that a crowded environment yields conditions that lead to properties hitherto not seen in dilute solutions (Zimmerman and Minton 1993, *Biophys. Chem.* 1995). Examples of practical interest are the effects of a neutral macromolecular co-solute on the stability of globular proteins against denaturation (Zhou and Hall 1996, Minton 2000) and their biochemical equilibrium (Minton 1998) and on the condensation of large duplex-DNA (Kidoaki and Yoshikawa 1999). The phase separation processes of globular proteins caused by the addition of a non-adsorbing polymer (PEG) to the aqueous solution are important further examples. A second protein purification method consists of adding a mixture of PEG and a low molecular weight electrolyte such as dextran mixed above some critical concentration to a protein solution whereupon the proteins precipitate. It is perhaps relevant to note here that an entire issue of the journal *Biophysical Chemistry* was recently devoted to the phenomenon of crowding reactions (*Biophys. Chem.* 1995).

It is customary to assume that the neutral particles in a polyelectrolyte solution interact non-specifically. However, there will still be a complex interplay between, for example, long-range Coulomb interactions, short-range interactions and steric effects. This renders theoretical studies of macromolecular crowding a challenging endeavour and, as noted by Minton (1995), the properties of such systems cannot be deduced simply from the properties of individual components at low concentrations.

An early theoretical effort at understanding colloidal particle coagulation and phase separation in a macromolecular (polymer) solution was provided by the pioneering work of Asakura and Oosawa (1954, 1958) nearly five decades ago. They showed through a simple, elegant derivation that considered the relative geometry of the constituent species, that a depletion of macromolecules in the region between two colloidal particles leads to a local anisotropy and a reduction in osmotic pressure of the polymer solution in this region relative to the corresponding bulk value. This in turn leads to an *osmotic force* on the outer surfaces of the particles and hence an *osmotic attraction* between the colloidal particles. Note that the origin of this attraction is quite independent of the usual forces such as those due to the overlap of the electrical double layers and the van der Waals force.

The Asakura–Oosawa ideas coupled with the relevance of protein precipitation in pharmaceutical industries (Bjurstrom 1985) inspired a whole generation of theoretical physicists and chemists in the 1970s through to the 1990s who investigated both experimentally (Vrij 1976, Vincent *et al.* 1980, Atha and Ingham 1981, de Hek and Vrij 1981, Sperry *et al.* 1981, Haire *et al.* 1984, Forciniti *et al.* 1991) and theoretically (Vrij 1976, de Hek and Vrij 1981, Gast *et al.* 1983, Lekkerkerker 1990, Mahadevan and Hall 1990, 1992, Vlachy and Prausnitz 1992, Vlachy 1993, Vlachy *et al.* 1993) (see also the review by Russel *et al.* (1991)) the phenomenon of phase separation of globular proteins and other colloids induced by the addition of a non-adsorbing co-solute to the suspension. In general, the experiments tend to support the conjecture that osmotic attraction in the Asakura–Oosawa sense is responsible for phase separation in such systems. Although the theories differ in details (see below), a common thread running through them is the fact that in the Hamiltonian, an osmotic attraction term enters in the pair potential between two macroionic particles. It is instructive to view this term closely. Assuming the protein (colloid)–electrolyte–polymer mixture to be described as a *one-component fluid* of colloidal particles—the premise of many a theory—the pair interaction between two particles would now be

$$u(r) = u_{\mathrm{R}}(r) + u_{\mathrm{A}}(r) + u_{\mathrm{AO}}(r) \tag{8}$$

where the extra term $u_{\mathrm{AO}}(r)$ on the right-hand side is the Asakura–Oosawa attractive term. Following Asakura and Oosawa (1958), this can be written as

$$u_{\mathrm{AO}}(r) = \begin{cases} \infty & r < \sigma_{\mathrm{m}} \\ -\frac{4}{3}\pi\sigma_{\mathrm{mp}}^3 P_{\mathrm{osm}}\left(1 - \dfrac{3r}{4\sigma_{\mathrm{mp}}} + \dfrac{r^3}{16\sigma_{\mathrm{mp}}^3}\right) & \sigma_{\mathrm{m}} < r < 2\sigma_{\mathrm{mp}} \\ 0 & r > 2\sigma_{\mathrm{mp}} \end{cases} \tag{9}$$

where $\sigma_{\mathrm{mp}} = (\sigma_{\mathrm{m}} + \sigma_{\mathrm{p}})/2$, $\sigma_{\mathrm{m}}$ and $\sigma_{\mathrm{p}}$ are the diameters of the macroion and the polymer particle respectively and $P_{\mathrm{osm}}$ is the osmotic pressure of the pure polymer solution. It is clear that for $\sigma_{\mathrm{m}} < r < 2\sigma_{\mathrm{mp}}$ polymer molecules do not enter the region between two macroions, leading to a depletion of polymers here. This causes a net attraction, often called the *depletion interaction* in the literature, between the two macroions. However, the attraction vanishes when $r > \sigma_{\mathrm{mp}}$ as polymers can now freely enter the region between the two macroions with the polymer concentration in the region equalling its bulk value. It is worth noting here that more formal theories (Joanny *et al.* 1979, Russel *et al.* 1991) have confirmed the simple geometric analysis of Asakura and Oosawa.

Gast *et al.* (1983) and Hall and co-workers (Mahadevan and Hall 1990, 1992, Forciniti *et al.* 1991) have utilized the Asakura–Oosawa osmotic attraction potential in conjunction with the perturbation theory of liquids (Barker and Henderson 1967) in studies of protein precipitation induced by neutral polymer particles. The Gast *et al.* work predicts flocculation of colloids besides other general experimental trends (de Hek and Vrij 1981). Hall's group, on the other hand, have calculated protein solubility as a function of protein to polymer size ratio and have also incorporated into their theory pH and ionic strength effects. Again, the results are in qualitative accord with experiments.

A different approach, one based on the random phase approximation (RPA) and the Asakura–Oosawa model, was adopted by Vlachy *et al.* (1993). The RPA is simple

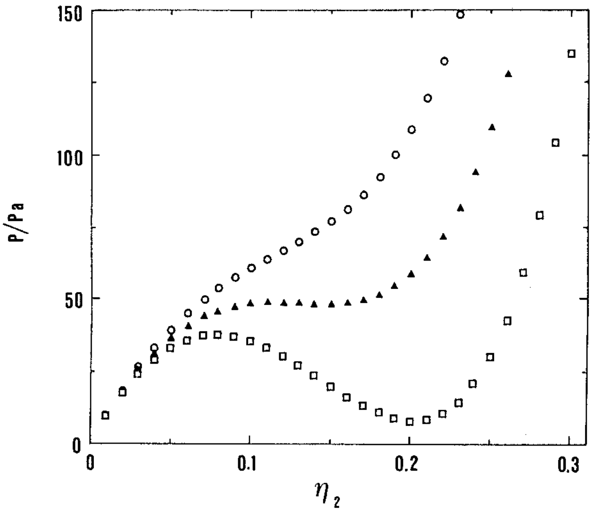

Figure 8. Osmotic pressure (in pascals) in colloid–polymer mixtures as a function of the volume fraction of colloid $\eta_2(=\eta_m)$. The volume fractions of the neutral polymer $\eta_n$ are 0.2 (o), 0.225 ($\triangle$) and 0.25 ($\diamond$). Reproduced with permission of the American Institute of Chemical Engineers (Vlachy, V., Blanch, H. W., and Prausnitz, J. M., 1993, *AIChE J.*, **39**, 215–223). Copyright (1993) AIChE. All rights reserved.

to use, an attractive feature being that it affords analytical expressions for many quantities of interest, namely, pressure and chemical potential. Among other things, Vlachy *et al.* studied phase separations in colloidal suspensions by non-ionic polymers in both non-aqueous and aqueous solvents. In the latter case an electrolyte at moderate concentrations ($< 0.8\,\mathrm{mol\,dm^{-3}}$) was also present. Calculations were performed for the osmotic pressure in the colloid–polymer mixture, the concentration of polymer needed to induce phase separation and the partitioning of the colloid between the coexisting phases. An important result is that the critical polymer concentration needed to induce phase separation decreases with increasing size of the polymer particle, or increasing volume fraction of the colloid, or increasing concentration of the electrolyte (cf. figures 2, 3 and 4 respectively of Vlachy *et al.* (1993)). In figure 8 (figure 1 of Vlachy *et al.* (1993)) the osmotic pressure of the colloid–polymer system as a function of colloid volume fraction is seen at volume fractions 0.20, 0.225 and 0.25 of the polymer. The curves clearly indicate the onset of van der Waals loops in the pressure isotherms (beyond some critical concentration (volume fraction) of the added polymers) heralding criticality in the system. This is interesting for as we shall see later in the discussion on multicomponent models, it has implications on the nature of interaction between two colloidal particles. Overall, the Vlachy *et al.* (1993) results show the correct experimental trends with respect to the physical variables such as species' size, charge and concentration.

Notwithstanding the fact that the one-component models along with the Asakura–Oosawa attractive term in the pair potential lead to a fair interpretation of experimentally observed properties of a colloid–polymer mixture, from a theoretical perspective a drawback of the model is the unevenness with which the various species in the solution are treated (cf. §2). Further, it may be noted that the Asakura–Oosawa potential is essentially a *volume exclusion potential.* It has been shown (Meijer and Frenkel 1991, Barlett and Ottewill 1992) that such a potential neglects entropic effects of polymers and can be a poor approximation for long molecules. Some recent MC simulations by Dickman *et al.* (1997) and Wu *et al.* (1999) have lent support to their arguments. A comparative study by Vlachy (1993) of the one-component versus multicomponent models within the PM framework for systems consisting of macroions, counterions and neutral polymers also reveals sharp differences between the predictions from the two models. For instance, a much more structured potential of mean force is seen in the multicomponent model than in the one-component model (cf. figures 2 and 3 of Vlachy (1993)).

Vlachy's (1993) work was also one of the initial studies to apply the PM to a polyelectrolyte solution modelled as a three (or more) component mixture of hard core ions (and neutral spheres representing non-ionic polymers when necessary). Vlachy applied the HNC approximation to solve both the one-component and multicomponent models. For our purposes some of the results involving a three-component mixture of macroion–neutral particle–counterion are of relevance. The physical parameters were $T = 298\,\mathrm{K}$ and $L_\mathrm{B} = 7.14 \times 10^{-10}\,\mathrm{m}$, with the diameters of the macroion, uncharged particle and counterion being $40\times10^{-10}$, $16\times10^{-10}$ and $4 \times 10^{-10}\,\mathrm{m}$, respectively. The macroion at concentration $0.002\,\mathrm{mol\,dm^{-3}}$ carried a charge $5e$ while the concentration of the neutral species was variable. A rather interesting result is the variation of the macroion–macroion contact value as a function of the neutral species packing fraction $\eta_\mathrm{n}$. The contact value increases monotonically, being less than unity for $\eta_\mathrm{n} \leq 0.18$ and greater than unity for $\eta_\mathrm{n} > 0.18$ (cf. figure 1, Vlachy (1993)). This is an indication that the nature of macroion–macroion interaction is gradually changing from being repulsive at low concentrations of the neutral species to attractive at higher concentrations of the neutral species. Although the later MC simulations would reveal that the HNC probably overestimates the attraction at the higher neutral species concentrations, the effect is real.

A more detailed investigation of the structure and thermodynamics in the three-component PM with one neutral component was taken up by Forciniti and Hall (1994). They also applied the HNC approximation covering a fairly wide range of ionic species' charge, size and concentration as well as size and concentration of the neutral species. They found generally a complex inter-dependence of electrostatic and non-electrostatic interactions on system properties. Importantly, the nature of interaction between the charged species underwent changes upon the introduction of the neutral component, echoing similar findings by Vlachy (1993). The contact values of the like-ion distribution functions increase with increasing volume fractions of the neutral components (see tables I–VII of Forciniti and Hall (1994)). Furthermore, the excess chemical potential of the ions and inverse isothermal compressibility increase with the increase in concentration of the neutral species which suggest that the tendency of the neutral particles would be to push the solution towards instability. Although Forciniti and Hall (1994) do not mention an attractive interaction between like ions, they do observe 'an attractive region in the potential of mean force' between the like ions in some cases.

Caccamo *et al.* (1993) and Kenkare *et al.* (1995) have investigated the phase stability of rigid ion–neutral sphere mixtures using the MSA. Although the MSA is not quite as accurate as the HNC, the analytic nature of the MSA implies that a broad region of the phase space can be scanned with ease and dependence of the phase diagrams on the physical variables established. Caccamo *et al.* focused on the dense phase regime applicable to molten silicate mixtures whereas Kenkare *et al.*

treated the low density electrolyte solution regime relevant to colloidal dispersions. Both the studies attest that the neutral species influences phase stability substantially. This is a significant result for it emphasizes the importance of neutral co-solutes in shaping the stability of a polyelectrolyte solution over a very broad concentration range.

Caccamo *et al.* (1993) calculated the Gibbs free energy of mixing $G_{\text{mix}}$ as a function of the plasma coupling parameter $\Gamma$, the ionic and the neutral species concentrations. A surprising result is that $G_{\text{mix}}$ changes dramatically from being negative to positive upon addition of neutral component or upon increasing $\Gamma$ at a fixed neutral concentration (cf. figures 1 and 2 of Caccamo *et al.* (1993)). Thus demixing can be avoided only by keeping the solution very dilute with respect to the neutral particles and/or by keeping the coupling parameter low. Since the latter situation is typical of the electrolyte solution regime, it follows that dilute polyelectrolyte solutions would tend to be more stable than high density solutions with regard to addition of a neutral polymer. Kenkare *et al.* (1995) determined the dependence of the phase diagrams on charge asymmetry of the ionic components, the size of the neutral component and the solution pressure. Increases in both the charge asymmetry and the neutral species size result in an increase in the critical temperature (inverse coupling parameter) of the mixture and hence are less favourable to phase stability.

Around the early to mid-1990s theoretical approaches based on the mean electrostatic potential formulation began to be applied to the multicomponent ($\geq$3) PM. Schmidt and Ruckenstein (1992) and Outhwaite and Molero (1992) used a symmetric Poisson–Boltzmann (SPB) theory to analyse multicomponent models involving three charged species. An important result of their studies was that the theory can predict an attraction between two like-charged colloidal particles. Since the mean field result for two isolated colloids (Sanchez-Sanchez and Lozada-Cassou 1992) does not show such attraction, the conclusion was that the phenomenon is due to the collective effects of all the charged species. We note further a recent relevant result due to Trizac (2000), who has suggested that mean field theories relying solely on the local density approximation can only predict repulsion between colloidal particles.

The SPB arose out of attempts to symmetrize the pair correlation function $g_{st}(r)$ appearing in the classical, standard PB theory with respect to the interchange of the indices $s$ and $t$ for asymmetric systems (Outhwaite 1978, 1987, Martinez *et al.* 1990, Outhwaite *et al.* 1991). We recall that in the traditional PB theory, $g_{st}(r) \neq g_{ts}(r)$ for any asymmetry in size and/or charge in the system. In contrast, in the SPB the (symmetric) $g_{st}(r)$ is given by

$$g_{st}(r) = g^0_{st} \exp\left[-\frac{1}{2k_{\text{B}}T}(e_s(\psi_t(r) + \psi^0_t(r)) + e_t(\psi_s(r) + \psi^0_s(r)))\right] \tag{10}$$

where $e_s = z_s e$, $\psi_s(r)$ is the mean electrostatic potential at a distance $r$ about an ion $s$ with $\psi^0_s(r)$ being the corresponding discharged potential $\psi^0_s(r) = \psi_s(r; e_s = 0)$ and $g^0_{st}(r) = g_{st}(r; e_s = e_t = 0)$ is the exclusion volume term. The discharged potentials vanish if all the constituent components have the same size. The SPB theory is formed by utilizing the above $g_{st}(r)$ in Poisson's equation

$$\nabla^2 \psi_s(r) = -\frac{1}{\varepsilon_0 \varepsilon_{\text{r}}} \sum_t e_t \rho_t g_{st}(r). \tag{11}$$

For $n$ species, once $g^0_{st}$ is known, only $n$ coupled equations need to be solved in contrast to the $n(n+1)/2$ coupled equations for the HNC equation. In Schmidt and Ruckenstein's (1992) version of the SPB, $g^0_{st}(r) = 1$ and $\psi^0_s(r) = 0$.

The SPB theory was applied to a three-component mixture of macroion, neutral polymer and counterion by Outhwaite *et al.* (1994) and the results compared with the HNC predictions. The diameters of the three species were assigned the values $40 \times 10^{-10}$, $16 \times 10^{-10}$ and $4 \times 10^{-10}$ m respectively with macroion valency 5 and counterion valency $-1$. The other parameters were $T = 298$ K, $\varepsilon_r = 78.54$ and the macroion concentration fixed at 0.002 mol dm$^{-3}$. The exclusion volume term was approximated by the Percus–Yevick (PY) uncharged hard sphere pair correlations, namely, $g^0_{st}(r) = g^{PY}_{st}(r)$ (Lebowitz 1964, Hansen and McDonald 1990). That structural changes in the system are driven by neutral polymers can be ascertained from the steady monotonic increase in the probability of two macroions being in contact with increase in the neutral species concentration (cf. figure 1 of Outhwaite *et al.* (1994)). The SPB is in qualitative agreement with the HNC, both predicting an attraction between two macroions beyond some critical value of the neutral species concentration. However, no such attraction occurs with the SPB when the $g^0_{st}(r) = 1$. This is suggestive of the phenomenon owing its origin to size correlations in the system leading to a depletion interaction between two macroions.

Bhuiyan and Outhwaite (1996) undertook another study of the three-component PM mixture using now the modified Poisson–Boltzmann (MPB) theory in addition to the SPB and made comparisons with the HNC. The MPB seeks to incorporate inter-ionic correlation effects through the fluctuation potential terms, which are neglected in the SPB formulation. In the MPB theory, the $g_{st}(r)$ reads (see, for example, Outhwaite *et al.* (1991, 1993, 1994))

$$g_{st}(r) = g^0_{st}(r) \exp\left\{ -\frac{1}{2k_B T} \left( e_s(L_s(u_t) + L_s(u^0_t)) + e_t(L_t(u_s) + L_t(u^0_s)) \right) \right\} \quad (12)$$

$$L_t(u_s) = \frac{1}{2r(1 + \kappa\sigma_{is})} \left\{ u_s(r + \sigma_{is}) + u_s(r - \sigma_{is}) + \kappa \int_{r-\sigma_{is}}^{r+\sigma_{is}} u_s(r)\, dR \right\} \quad (13)$$

$$u^0_s = u_s(e_s = 0) \quad (14)$$

$$\kappa^2 = \frac{1}{\varepsilon_0 \varepsilon_r k_B T} \sum_s \rho_s e_s^2 \quad (15)$$

where $u_s(r) = r\psi_s(r)$, $i$ denotes the smallest species and $\kappa$ is the Debye–Hückel parameter. The exclusion volume term was again taken to be $g^{PY}_{st}(r)$.

Two different systems were investigated, (i) a polyelectrolyte–electrolyte solution and (ii) a macroion–neutral polymer–counterion mixture, at the same physical parameters as in the earlier Outhwaite *et al.* (1994) SPB work. Apart from the Donnan equilibrium properties of system (i), the variation of the contact value of the macroion–macroion pair distribution function with the coion concentration was calculated. At higher coion concentrations both the SPB and the MPB (as well as the HNC) show an attraction between two macroions (see also the SPB work of Schmidt and Ruckenstein (1992) and Outhwaite and Molero (1992)). Of more interest and significance to this review are the results for system (ii). The effect of the neutral component on the solution structure is clearly noticeable in figure 9 (figure 7 of Bhuiyan and Outhwaite (1996)) where the macroion–macroion contact value rises above unity at higher neutral polymer concentrations. All of the theories, SPB, MPB

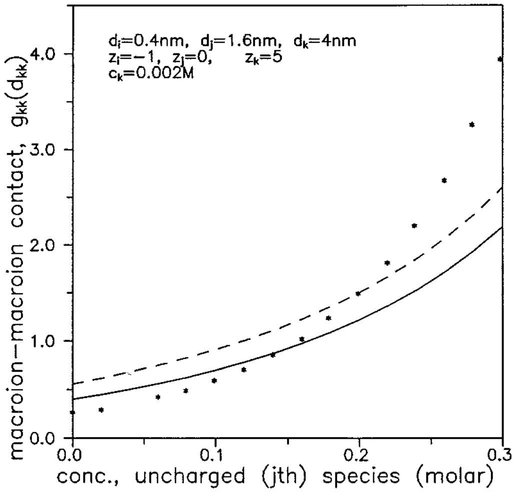

Figure 9. The contact value of the macroion–macroion pair distribution function for a (three-component) macroion–neutral species–counterion mixture as a function of the concentration of the neutral species $c_j(=c_\mathrm{n})$. The macroion concentration is $c_k(=c_\mathrm{m}) = 0.002\,\mathrm{mol\,dm^{-3}}$ with valency $z_k(=z_\mathrm{m}) = 5$, while the valency of the counterion is $z_i(=z_\mathrm{c}) = -1$. The diameters of the species are, macroion $d_k(=\sigma_\mathrm{m}) = 40 \times 10^{-10}\,\mathrm{m}$, neutral species $d_j(=\sigma_\mathrm{n}) = 16 \times 10^{-10}\,\mathrm{m}$ and counterion $d_i(=\sigma_\mathrm{n}) = 4 \times 10^{-10}\,\mathrm{m}$. (——), MPB results; (– – –), SPB results; (✱), HNC results. Reprinted with permission from Bhuiyan, L. B., and Outhwaite, C. W., 1996, *Molec. Phys.*, **87**, 625–635. Copyright (1996) Taylor & Francis Ltd, http://www.tandf.co.uk.

and HNC, reveal the same qualitative feature that at sufficiently high neutral species concentration an attractive interaction sets in between two like-charged macroions. Quantitatively, the MPB and the HNC results are close for uncharged species of concentration less than $0.18\,\mathrm{mol\,dm^{-3}}$, while above this value the HNC results overestimate both the SPB and MPB results. Further, small differences between the SPB and MPB predictions, especially at higher neutral species concentrations, indicate that the collective effects of the species manifested in the exclusion volume terms are perhaps more important here than the fluctuation potential corrections.

The SPB, MPB and HNC calculations for the system (ii) above considered monovalent counterions only. An extension to multivalent counterions (−2 and −3) was made by Vlachy *et al.* (1997). In the SPB and MPB formalisms somewhat better bulk hard sphere distributions, namely, PY $g_{st}(r)$ plus the Verlet–Weis (VW) corrections (Grundke and Henderson 1972, Verlet and Weis 1972, Lee and Levesque 1973) were used for the exclusion volume term. Some novel results, shown in figure 10 (figure 10 of Vlachy *et al.* (1997)), are (i) that for all counterion valencies considered an attractive interaction between two macroions ensues at sufficiently high neutral species concentrations and (ii) that this (attraction) is a consistent prediction of the potential based and integral equation theories even for strongly correlated solutions with trivalent counterions. Multivalent counterions tend to screen the macroions more efficiently leading to diminished repulsion between the macroions. Addition of a neutral polymer now triggers depletion forces at lower values of the polymer concentration than would be the case with monovalent counterions. This is clearly evident from figure 10 (see also figures 1, 4 and 7 of

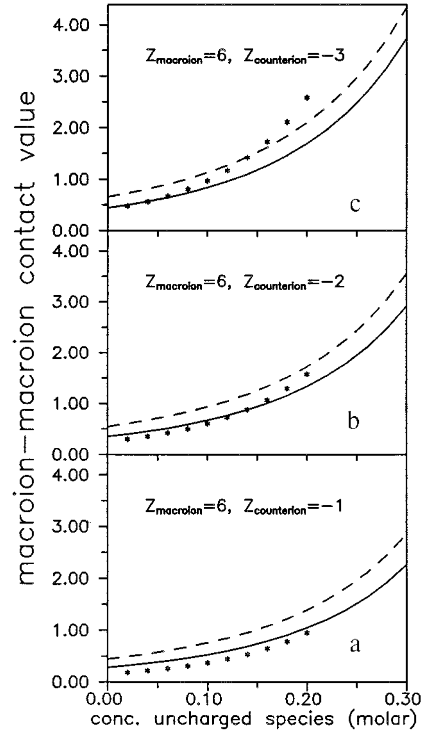

Figure 10. Contact value of the macroion–macroion pair distribution function for a (three-component) macroion–neutral species–counterion mixture as a function of the concentration of the neutral species $c_n$. The macroion concentration is $c_k (= c_m) = 0.002\,\mathrm{mol\,dm^{-3}}$ with valency $z_k (= z_m) = 6$: the valency of the counterion is (*a*) $z_c = -1$, (*b*) $z_c = -2$ and (*c*) $z_c = -3$. The diameters of the species are, macroion $\sigma_m = 40 \times 10^{-10}\,\mathrm{m}$, neutral species $\sigma_n = 16 \times 10^{-10}\,\mathrm{m}$ and counterion $\sigma_c = 4 \times 10^{-10}\,\mathrm{m}$. (——), MPB results; (– – –), SPB results; (✱), HNC results. Reprinted with permission from Vlachy, V., Bhuiyan, L. B., and Outhwaite, C. W., 1997, *Molec. Phys.*, **90**, 553–561. Copyright (1996) Taylor & Francis Ltd, http://www.tandf.co.uk.

Vlachy *et al.* (1997)). It is noted again that the HNC overestimates the macroion–macroion attraction relative to the other two theories, which is probably somewhat exaggerated (Rossky *et al.* 1980). Vlachy *et al.* (1997) also calculated the excess internal energy and osmotic coefficients of the systems as functions of the added neutral species (see table of Vlachy *et al.* (1997)). Not unexpectedly, the internal energy becomes less negative while the osmotic pressure increases with increasing amounts of the neutral polymer present. Some experimental support for the theories may be found in the direct force measurements (Kjellander *et al.* 1990, Parker *et al.* 1992, Kekicheff *et al.* 1993, Sober and Walz 1995); for instance, in the more recent experiments of Sober and Walz (1995) the measured force between a colloid and a plate in the presence of a surfactant remains repulsive below the cmc but becomes attractive above it. It has been demonstrated (Vlachy 1996) that a multicomponent model, where the ions are represented as soft charged spheres differing widely in charge and size, reproduces the main features of the experimental results reported by Sober and Walz (1995).

The first comprehensive and systematic explorations of the equilibrium properties of a three-component PM mixture of an electrolyte and a neutral species through computer simulations were reported by Reščič *et al.* (1997, 1998). They applied the MC methods to study the structure and thermodynamics of the model solutions over a fairly wide range of concentrations and valencies of the species. These simulations show unmistakable evidence for what was predicted earlier by the SPB, MPB and HNC theories (Vlachy 1993, Outhwaite *et al.* 1994, Bhuiyan and Outhwaite 1996, Vlachy *et al.* 1997) that beyond some threshold concentration of the added neutral species, there is an attractive interaction between two macroions and that the addition of the neutral component is energetically unfavourable. Reščič *et al.* (1997) focused on a $1:-1$ valency, size-symmetric electrolyte mixed with a variable sized uncharged particle. The system parameters were $L_B = 7.15 \times 10^{-10}$ m, $\sigma_{\text{ion}} = 4.25 \times 10^{-10}$ m and $\sigma_{\text{neutral}} = 4.25 \times 10^{-10}$ or $8.50 \times 10^{-10}$ m. Although owing to limitations in the computer facilities the highest packing fraction for the uncharged species was $\eta_n = 0.03$, for the unequal mixture this value could be raised to 0.5. For the latter case figure 11 (figure 4 of Reščič *et al.* (1997)) shows the gradual transformation in the like-ion distributions ($g_{++}$ or $g_{--}$) from being repulsive and structureless in a pure electrolyte ($\eta_n = 0$) to attractive and quite structured at $\eta_n = 0.4$. The change is attributed to the collective effects of the species with the depletion interaction playing a likely, crucial role. The SPB, MPB and the HNC

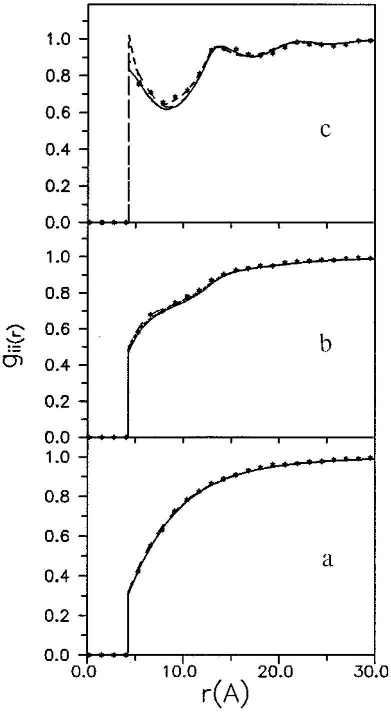

Figure 11. The like-ion pair distribution functions, $g_{ii}(r) (= g_{++}(r)$ or $g_{--}(r))$ for the unequal-sized mixture of a single electrolyte and a neutral species ($\sigma_{\text{ion}} (= \sigma_+ = \sigma_-) = 4.25 \times 10^{-10}$ m, $\sigma_n = 8.5 \times 10^{-10}$ m). The electrolyte concentration is $c_{\text{elec}} (= c_+ = c_-) = 0.1\,\text{mol}\,\text{dm}^{-3}$, while (*a*) $\eta_n = 0$, (*b*) $\eta_n = 0.2$ and (*c*) $\eta_n = 0.4$. (✱), MC data; (——), MPB results; (– – –), SPB results; (⋯⋯), HNC results. Reprinted with permission from Reščič, J., Vlachy, V., Bhuiyan, L. B., and Outhwaite, C. W., 1997, *J. chem. Phys.*, **107**, 3611–3618. Copyright (1997) American Institute of Physics.

Table 2. The osmotic coefficient and the excess internal energy for an equisized three-component mixture of a +1 : − 1 electrolyte and neutral particles at different volume fractions $\eta_{\mathrm{neutral}}(=\eta_{\mathrm{n}})$ of the neutral species. The concentration of the electrolyte is $c_{\mathrm{elec}}(=c_{+}=c_{-})=0.1\,\mathrm{mol\,dm^{-3}}$. The theoretical values of the osmotic coefficient are obtained through the virial route. In the MC entries for internal energy the uncertainty is less than 0.5% and for the osmotic coefficient the uncertainty is about 1%. Reprinted with permission from Reščič, J., Vlachy, V., Bhuiyan, L. B., and Outhwaite, C. W., 1997, *J. chem. Phys.*, **107**, 3611–3618. Copyright (1997) American Institute of Physics.

| | −Internal energy | | | | Osmotic coefficient | | | |
|---|---|---|---|---|---|---|---|---|
| $\eta_{\mathrm{neutral}}$ | SPB | MPB | HNC | MC | SPB | MPB | HNC | MC |
| 0 | 0.263 | 0.271 | 0.273 | 0.267 | 0.946 | 0.945 | 0.944 | 0.945 |
| 0.000 05 | 0.261 | 0.268 | 0.271 | – | 0.947 | 0.946 | 0.944 | – |
| 0.001 | 0.218 | 0.225 | 0.227 | 0.225 | 0.963 | 0.962 | 0.961 | 0.962 |
| 0.005 | 0.130 | 0.133 | 0.135 | 0.134 | 1.00 | 1.00 | 1.00 | 1.00 |
| 0.01 | 0.0862 | 0.0886 | 0.0894 | 0.0889 | 1.04 | 1.04 | 1.04 | 1.04 |
| 0.02 | 0.0516 | 0.0530 | 0.0535 | 0.0531 | 1.09 | 1.09 | 1.09 | 1.09 |
| 0.03 | 0.0369 | 0.0379 | 0.0382 | 0.0382 | 1.14 | 1.14 | 1.14 | 1.14 |

Table 3. The osmotic coefficient and the excess internal energy for an unequal-sized three-component mixture of a +1 : − 1 electrolyte and neutral particles at different values of electrolyte concentration $c_{\mathrm{elec}}(=c_{+}=c_{-})$ and different volume fractions $\eta_{\mathrm{neutral}}(=\eta_{\mathrm{n}})$ of the neutral species. The theoretical values of the osmotic coefficient are obtained through the virial route. In the MC entries for internal energy the uncertainty is less than 0.5% and for the osmotic coefficient the uncertainty is about 1%. Reprinted with permission from Reščič, J., Vlachy, V., Bhuiyan, L. B., and Outhwaite, C. W., 1997, *J. chem. Phys.*, **107**, 3611–3618. Copyright (1997) American Institute of Physics.

| | −Internal energy | | | | Osmotic coefficient | | | |
|---|---|---|---|---|---|---|---|---|
| $\eta_{\mathrm{neutral}}$ | SPB | MPB | HNC | MC | SPB | MPB | HNC | MC |
| $c_{\mathrm{elec}}=0.1\,\mathrm{mol\,dm^{-3}}$ | | | | | | | | |
| 0.005 | 0.234 | 0.240 | 0.239 | 0.242 | 0.97 | 0.969 | 0.969 | 0.97 |
| 0.01 | 0.210 | 0.216 | 0.215 | 0.217 | 0.994 | 0.993 | 0.992 | 0.99 |
| 0.05 | 0.117 | 0.120 | 0.119 | 0.120 | 1.19 | 1.19 | 1.19 | 1.19 |
| 0.1 | 0.0755 | 0.0778 | 0.0771 | 0.0777 | 1.49 | 1.49 | 1.50 | 1.49 |
| 0.2 | 0.0450 | 0.0465 | 0.0459 | 0.0462 | 2.37 | 2.37 | 2.47 | 2.38 |
| 0.3 | 0.0325 | 0.0337 | 0.0331 | 0.0331 | 3.95 | 3.95 | 4.34 | 3.96 |
| 0.4 | 0.0257 | 0.0267 | 0.0262 | 0.0260 | 6.92 | 6.92 | 8.16 | 6.96 |
| 0.5 | 0.0214 | 0.0224 | 0.0219 | – | 13.1 | 13.1 | 16.7 | – |
| $c_{\mathrm{elec}}=0.05\,\mathrm{mol\,dm^{-3}}$ | | | | | | | | |
| 0.2 | 0.0190 | 0.0193 | 0.0194 | 0.0194 | 2.39 | 2.39 | 2.48 | 2.39 |
| $c_{\mathrm{elec}}=0.2\,\mathrm{mol\,dm^{-3}}$ | | | | | | | | |
| 0.2 | 0.0974 | 0.102 | 0.102 | 0.102 | 2.36 | 2.36 | 2.45 | 2.36 |

theories follow the MC results closely (see figures 1–3, 5–11 of Reščič *et al.* (1997)), the agreement being semi-quantitative or better. In tables 2 and 3 (tables I and II of Reščič *et al.* (1997)), the increase in the internal energy with added uncharged particle is observed. The SPB tends to overestimate the energy but gives a surprisingly good fit to the simulated pressure while the HNC overestimates the pressure for the unequal mixture at higher values of $\eta_{\mathrm{n}}$.

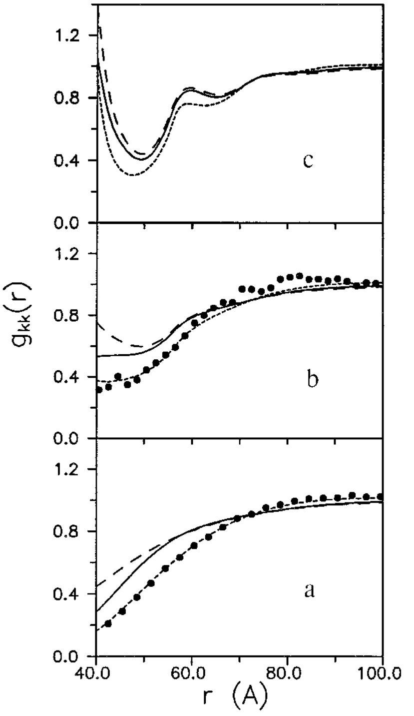

Figure 12. The macroion–macroion pair distribution function $g_{kk}(r)(=g_{\mathrm{mm}}(r))$ for a (three-component) macroion–neutral species–counterion mixture at macroion concentration $c_k(=c_{\mathrm{m}})=0.002\,\mathrm{mol\,dm^{-3}}$, macroion valency $z_k(=z_{\mathrm{m}})=6$, counterion valency $z_i(=z_{\mathrm{c}})=-1$ and neutral species concentration of (*a*) $c_j(=c_{\mathrm{n}})=0$, (*b*) $c_j(=c_n)=0.1\,\mathrm{mol\,dm^{-3}}$ and (*c*) $c_j(=c_n)=0.2\,\mathrm{mol\,dm^{-3}}$. (●), MC data; (——), MPB results; (– – –), SPB results; and (- - - -), HNC results. Reprinted with permission from Reščič, J., Vlachy, V., Bhuiyan, L. B., and Outhwaite, C. W., 1998, *Molec. Phys.*, **95**, 233–242. Copyright (1999) Taylor & Francis Ltd, http://www.tandf.co.uk.

In a second paper (Reščič *et al.* 1998) the focus was shifted to an asymmetric mixture of a macroion ($\sigma_{\mathrm{m}}=40\times10^{-10}\,\mathrm{m}$), a counterion ($\sigma_c=4\times10^{-10}\,\mathrm{m}$) and a neutral sphere ($\sigma_{\mathrm{neutral}}=16\times10^{-10}\,\mathrm{m}$) with elaborate variations (limited by available computer resources) in the species' concentration and charge. For example, macroion valencies of 6, 8 and 10 and counterion valencies ranging from $-1$ to $-5$ were used, while the neutral species concentration $c_{\mathrm{n}}$ was varied in the interval $0<c_{\mathrm{n}}<0.15\,\mathrm{mol\,dm^{-3}}$. A principal result, shown in figure 12 (figure 1 of Reščič *et al.* (1998)) is again the change in the nature of the mean force between two macroions from repulsive (at $c_{\mathrm{n}}=0$) to less repulsive upon addition of neutral particles and to ultimately attractive at sufficiently high $c_{\mathrm{n}}$. The variations in the physical parameters highlight further the complex interlinking of the collective effects in shaping system properties. These effects can sometimes be competing, for instance, whereas increasing $c_{\mathrm{n}}$ raises the contact value of $g_{\mathrm{mm}}$, increasing macroion charge suppresses it. The MPB, the HNC and to lesser degree the SPB theories were found to reproduce the MC structural details to a reasonable degree of accuracy. The MC thermodynamics shown in tables 4 and 5 (tables 1 and 2 of Reščič *et al.* (1998)) reveal interesting details. Adding a neutral species to a polyelectrolyte solution is energetically costly so that a more stable solution would be one that is more dilute

Table 4. The osmotic coefficient and the excess internal energy in a (three-component) macroion–neutral species–counterion mixture for different values of the neutral species concentration $c_j (= c_n)$ (in mol dm$^{-3}$) for mono-, di- or trivalent counterions. The concentration of the macroion is fixed at $c_m = 0.01$ mol dm$^{-3}$. The relative uncertainty in the MC entries is ±2% for the excess internal energy and ±5% for the osmotic coefficient. Reprinted with permission from Reščič, J., Vlachy, V., Bhuiyan, L. B., and Outhwaite, C. W., 1998, *Molec. Phys.*, **95**, 233–242. Copyright (1999) Taylor & Francis Ltd, http://www.tandf.co.uk

| | −Internal energy | | | | Osmotic coefficient | | | |
|---|---|---|---|---|---|---|---|---|
| $c_j$ | SPB | MPB | HNC | MC | SPB | MPB | HNC | MC |
| Monovalent counterions | | | | | | | | |
| 0.0 | 0.700 | 0.728 | 0.784 | 0.803 | 1.72 | 1.42 | 1.38 | 1.35 |
| 0.05 | 0.411 | 0.430 | 0.464 | 0.470 | 2.45 | 2.17 | 2.15 | 2.05 |
| 0.1 | 0.292 | 0.307 | 0.330 | 0.335 | 3.43 | 3.20 | 3.32 | 3.03 |
| 0.15 | 0.228 | 0.240 | 0.257 | 0.263 | 4.88 | 4.75 | 5.23 | 4.53 |
| Divalent counterions | | | | | | | | |
| 0.0 | 1.50 | 1.60 | 1.79 | 1.80 | 1.67 | 1.36 | 1.29 | 1.24 |
| 0.05 | 0.674 | 0.721 | 0.803 | 0.811 | 2.52 | 2.29 | 2.27 | 2.14 |
| 0.1 | 0.437 | 0.470 | 0.521 | 0.527 | 3.55 | 3.41 | 3.55 | 3.22 |
| 0.15 | 0.324 | 0.351 | 0.388 | 0.393 | 5.08 | 5.06 | 5.59 | 4.81 |
| Trivalent counterions | | | | | | | | |
| 0.0 | 2.33 | 2.52 | 2.88 | 2.88 | 1.58 | 1.30 | 1.16 | 1.14 |
| 0.05 | 0.881 | 0.958 | 1.09 | 1.09 | 2.52 | 2.35 | 2.30 | 2.17 |
| 0.1 | 0.546 | 0.598 | 0.676 | 0.679 | 3.57 | 3.49 | 3.64 | 3.28 |
| 0.15 | 0.398 | 0.438 | 0.493 | 0.496 | 5.12 | 5.17 | 5.72 | 4.92 |

with respect to the added polymer. The HNC seems more efficient in predicting the internal energy while the MPB (and the SPB) are better in predicting the osmotic pressures especially at higher volume fractions of the neutral component. The SPB would appear to be useful in giving a fair, first description of such asymmetric systems. One other comment on the relative performance of the theories is in order. For certain ranges of solution parameters the HNC numerical scheme does not lead to convergence (see also § 2): the $+8 : -4$ and $+10 : -5$ valency mixtures at all $c_n$ (cf. table 5) and $+6 : -1$, $+6 : -2$, $+6 : -3$ cases for $c_n \geq 0.20$ (cf. figure 10). Similar convergence problems with the HNC have also been detected by Vlachy (1993). In contrast, no such problems have been found with the SPB or MPB.

In a more recent third study, Reščič *et al.* (1999) have extended the MC simulations to four-component asymmetric mixtures of (i) two electrolytes with a common ion plus a neutral species and (ii) one electrolyte and two neutral species. An extension of the SPB theory up to a six-component PM mixture (Mukherjee 1998) was used to analyse the data. Although the general structural and thermodynamic details follow the pattern seen with the three-component model, because of the presence of an extra component the collective effects are more involved. Figure 13 (figure 3 of Reščič *et al.* (1999)) shows the like-ion distributions for a $1 : -1$–$1 : -2$–neutral species mixture. Significantly all the four distributions become more structured (in a couple of cases $g_{1- : 1-}$ and $g_{1+ : 1+}$ showing beginnings of an attraction) as the lone neutral species volume fraction is increased from zero. It is entirely possible that in a practical situation the neutral component will be

Table 5. The osmotic coefficient and the excess internal energy in a (three-component) macroion–neutral species–counterion mixture at a fixed neutral species concentration $c_j(= c_{\mathrm{n}})$ (in mol dm$^{-3}$) for mono-, di- or trivalent counterions, and at different macroion concentration $c_j(= c_{\mathrm{m}})$ (in mol dm$^{-3}$) and macroion valency $z_{\mathrm{m}}$. The relative uncertainty in the MC entries is ±2% for the excess internal energy and ±5% for the osmotic coefficient. Reprinted with permission from Reščič, J., Vlachy, V., Bhuiyan, L. B., and Outhwaite, C. W., 1998, *Molec. Phys.*, **95**, 233–242. Copyright (1999) Taylor & Francis Ltd, http://www.tandf.co.uk

| | | −Internal energy | | | | Osmotic coefficient | | | |
|---|---|---|---|---|---|---|---|---|---|
| $Z_j$ | $c_k$ | SPB | MPB | HNC | MC | SPB | MPB | HNC | MC |
| $c_j = 0, Z_k = 6$ | | | | | | | | | |
| −1 | 0.002 | 0.491 | 0.513 | 0.550 | 0.552 | 0.970 | 0.954 | 0.943 | 0.941 |
| | 0.005 | 0.600 | 0.633 | 0.683 | 0.682 | 1.17 | 1.09 | 1.06 | 1.06 |
| −2 | 0.002 | 1.12 | 1.19 | 1.27 | 1.28 | 0.839 | 0.819 | 0.806 | 0.802 |
| | 0.005 | 1.33 | 1.42 | 1.55 | 1.55 | 1.06 | 0.967 | 0.925 | 0.920 |
| −3 | 0.002 | 1.84 | 1.99 | 2.12 | 2.13 | 0.699 | 0.678 | 0.666 | 0.670 |
| | 0.005 | 2.11 | 2.29 | 2.52 | 2.52 | 0.929 | 0.839 | 0.783 | 0.771 |
| $c_j = 0.1, Z_k = 6$ | | | | | | | | | |
| −1 | 0.002 | 0.0613 | 0.0644 | 0.0688 | 0.0683 | 1.93 | 1.92 | 1.94 | 1.90 |
| | 0.005 | 0.158 | 0.168 | 0.180 | 0.182 | 2.37 | 2.28 | 2.31 | 2.22 |
| −2 | 0.002 | 0.0847 | 0.0907 | 0.0962 | 0.0954 | 1.95 | 1.94 | 1.97 | 1.92 |
| | 0.005 | 0.225 | 0.244 | 0.264 | 0.266 | 2.42 | 2.35 | 2.39 | 2.28 |
| −3 | 0.002 | 0.106 | 0.116 | 0.122 | 0.121 | 1.96 | 1.94 | 1.97 | 1.93 |
| | 0.005 | 0.280 | 0.307 | 0.335 | 0.334 | 2.42 | 2.37 | 2.41 | 2.30 |
| $c_j = 0, Z_k = 8$ | | | | | | | | | |
| −1 | 0.002 | 0.687 | 0.726 | 0.776 | 0.792 | 0.930 | 0.907 | 0.899 | 0.890 |
| | 0.005 | 0.828 | 0.883 | 0.961 | 0.960 | 1.15 | 1.04 | 1.01 | 1.00 |
| −2 | 0.002 | 1.57 | 1.70 | 1.85 | 1.86 | 0.747 | 0.725 | 0.711 | 0.709 |
| | 0.005 | 1.83 | 1.99 | 2.19 | 2.19 | 0.972 | 0.866 | 0.818 | 0.807 |
| −4 | 0.002 | 3.67 | 4.14 | – | – | 0.359 | 0.362 | – | – |
| | 0.005 | 4.04 | 4.54 | – | – | 0.606 | 0.536 | – | – |
| $c_j = 0.1, Z_k = 8$ | | | | | | | | | |
| −1 | 0.002 | 0.106 | 0.113 | 0.123 | 0.122 | 1.93 | 1.90 | 1.91 | 1.87 |
| | 0.005 | 0.260 | 0.280 | 0.304 | 0.302 | 2.37 | 2.24 | 2.24 | 2.16 |
| −2 | 0.002 | 0.145 | 0.158 | 0.171 | 0.172 | 1.95 | 1.92 | 1.94 | 1.90 |
| | 0.005 | 0.370 | 0.408 | 0.447 | 0.447 | 2.42 | 2.32 | 2.32 | 2.22 |
| −4 | 0.002 | 0.211 | 0.241 | 0.258 | – | 1.95 | 1.93 | 1.95 | – |
| | 0.005 | 0.534 | 0.606 | 0.674 | – | 2.41 | 2.35 | 2.35 | – |
| $c_j = 0, Z_k = 10$ | | | | | | | | | |
| −1 | 0.002 | 0.883 | 0.940 | 1.04 | 1.05 | 0.893 | 0.862 | 0.849 | 0.839 |
| | 0.005 | 1.05 | 1.14 | 1.25 | 1.25 | 1.14 | 0.993 | 0.958 | 0.953 |
| −2 | 0.002 | 2.01 | 2.21 | 2.46 | 2.47 | 0.659 | 0.636 | 0.628 | 0.620 |
| | 0.005 | 2.32 | 2.56 | 2.85 | 2.84 | 0.897 | 0.778 | 0.726 | 0.713 |
| −5 | 0.002 | 6.20 | 7.28 | – | – | −0.0833 | 0.0151 | – | – |
| | 0.005 | 6.63 | 7.68 | – | – | 0.182 | 0.227 | – | – |
| $c_j = 0.1, Z_k = 10$ | | | | | | | | | |
| −1 | 0.002 | 0.161 | 0.173 | 0.186 | 0.194 | 1.92 | 1.88 | 1.88 | 1.84 |
| | 0.005 | 0.378 | 0.412 | 0.451 | 0.451 | 2.38 | 2.20 | 2.17 | 2.08 |
| −2 | 0.002 | 0.218 | 0.243 | 0.267 | 0.270 | 1.94 | 1.91 | 1.92 | 1.87 |
| | 0.005 | 0.541 | 0.605 | 0.670 | 0.669 | 2.42 | 2.28 | 2.25 | 2.16 |
| −5 | 0.002 | 0.355 | 0.420 | – | – | 1.93 | 1.92 | – | – |
| | 0.005 | 0.874 | 1.02 | – | – | 2.38 | 2.34 | – | – |

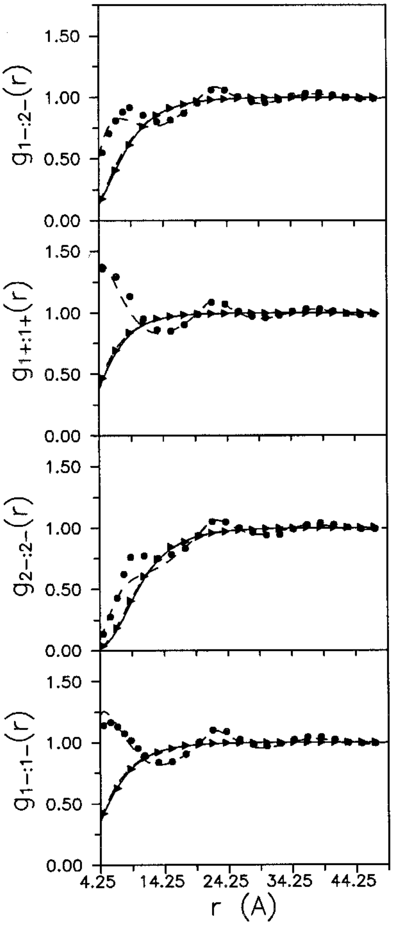

Figure 13. The like-ion pair distribution functions for a mixture consisting of a $+1:-1$ electrolyte at 0.1 mol dm$^{-3}$ concentration, a $+1:-2$ electrolyte at 0.05 mol dm$^{-3}$ concentration, and a neutral species at zero (lower curves) and 0.275 mol dm$^{-3}$ concentration respectively. The ions have the common diameter $4.25 \times 10^{-10}$ m while the neutral component has the diameter $17 \times 10^{-10}$ m. (▲), MC data for $c_n = 0$; (●), MC data for $c_n = 0.275$ mol dm$^{-3}$; (——), MPB results; and (– – –), SPB results. Reprinted with permission from Reščič, J., Vlachy, V., Outhwaite, C. W., Bhuiyan, L. B., and Mukherjee, A. K., 1999, *J. chem. Phys.*, **111**, 5514–5521. Copyright (1999) American Institute of Physics.

inhomogeneous in terms of size with a distribution of molecular weights. This scenario was simulated using the second model above. In figure 14 (figure 9 of Reščič *et al.* (1999)) is shown the contact value of like-ion distributions for a $1:-1$ electrolyte as a function of the bigger neutral species concentration where the smaller neutral species concentration is held fixed. This figure and tables 6 and 7 (tables I and II of Reščič *et al.* (1999)) show the substantial effects of the neutral particles on the solution properties. The SPB again affords a useful description of the model mixtures at the concentrations studied.

In an alternative viewpoint, perhaps with some justification, the neutral particles are assumed to mimic the solvent thereby imparting some structure to the solvent. The continuum solvent character of the PM implies all solvent effects are subsumed

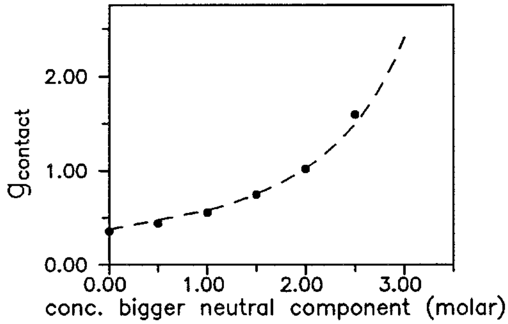

Figure 14. The contact value of like-ion pair distribution functions, $g_{1+:1+}$ or $g_{1-:1-}$, for a four-component mixture consisting of a 1:1 electrolyte at 0.2 mol dm$^{-3}$ concentration and two neutral species, one of which (diameter $4.25 \times 10^{-10}$ m) is held fixed at 0.2 mol dm$^{-3}$ concentration while the concentration of the other (diameter $8.5 \times 10^{-10}$ m) is varied. All the ions have the common diameter of $4.25 \times 10^{-10}$ m. (●), MC data; (– – –), SPB results. Reprinted with permission from Reščič, J., Vlachy, V., Outhwaite, C. W., Bhuiyan, L. B., and Mukherjee, A. K., 1999, *J. chem. Phys.*, **111**, 5514–5521. Copyright (1999) American Institute of Physics.

Table 6. The osmotic coefficient and the excess internal energy for different four-component PM mixtures consisting of two electrolytes with a common ion and a neutral species. All concentrations ($c$) are in mol dm$^{-3}$ and the species size (given in radius $a$) is in $10^{-10}$ m. The relative uncertainty in general in the MC entries is ±2% for the excess internal energy and ±5% for the osmotic coefficient. The entries within parentheses correspond to the modified Poisson–Boltzmann calculations. Reprinted with permission from Reščič, J., Vlachy, V., Outhwaite, C. W., Bhuiyan, L. B., and Mukherjee, A. K., 1999, *J. chem. Phys.*, **111**, 5514–5521. Copyright (1999) American Institute of Physics

| | | | | | −Internal energy | | Osmotic coefficient | |
|---|---|---|---|---|---|---|---|---|
| $c_{elec}$ (1:1) | $c_{elec}$ (1:2) | $c_{neutral}$ | $a_{elec}$ | $a_{neutral}$ | SPB | MC | SPB | MC |
| 1:1 electrolyte + 1:2 electrolyte + neutral species | | | | | | | | |
| 0.1 | 0.05 | 1 | 2.125 | 2.125 | 0.133 | – | 1.11 | – |
| 0.1 | 0.05 | 1 | 2.125 | 4.25 | 0.140 | – | 2.26 | – |
| 0.1 | 0.05 | 0 | 2.125 | 8.5 | 0.510 (0.539) | 0.535 | 0.904 (0.900) | 0.898 |
| 0.1 | 0.05 | 0.1 | 2.125 | 8.5 | 0.415 | 0.435 | 1.47 | 1.46 |
| 0.1 | 0.05 | 0.15 | 2.125 | 8.5 | 0.383 | 0.402 | 2.02 | 2.01 |
| 0.1 | 0.05 | 0.275 | 2.125 | 8.5 | 0.328 | 0.344 | 5.21 | 5.56 |

| | | | | | | | −Internal energy | | Osmotic coeffficient | |
|---|---|---|---|---|---|---|---|---|---|---|
| $c_{elec}$ (1:1) | $c_{elec}$ (1:1) | $c_{neutral}$ | $a_+$ | $a_-$ | $a_+$ | $a_{neutral}$ | SPB | MC | SPB | MC |
| 1:1 electrolyte + 1:1 electrolyte + neutral species | | | | | | | | | | |
| 0.1 | 0.1 | 0 | 2.125 | 2.125 | 3.71875 | 8.5 | 0.309 (0.323) | 0.324 | 0.996 (0.995) | 0.992 |
| 0.1 | 0.1 | 0.1 | 2.125 | 2.125 | 3.71875 | 8.5 | 0.259 | 0.324 | 1.62 | 1.61 |
| 0.1 | 0.1 | 0.2 | 2.125 | 2.125 | 3.71875 | 8.5 | 0.227 | 0.236 | 3.15 | 3.22 |
| 0.1 | 0.1 | 0.275 | 2.125 | 2.125 | 3.71875 | 8.5 | 0.211 | 0.219 | 5.77 | 6.15 |

Table 7. The osmotic coefficient and the excess internal energy for different four-component PM mixtures (one electrolyte plus two neutral species). All concentrations ($c$) are in $\mathrm{mol\,dm^{-3}}$ and the species size (given in radius $a$) is in $10^{-10}$ m. The relative uncertainty in general in the MC entries is ±2% for the excess internal energy and ±5% for the osmotic coefficient. Reprinted with permission from Reščič, J., Vlachy, V., Outhwaite, C. W., Bhuiyan, L. B., and Mukherjee, A. K., 1999, *J. chem. Phys.*, **111**, 5514–5521. Copyright (1999) American Institute of Physics

| | | | | | | −Internal energy | | Osmotic coefficient | |
|---|---|---|---|---|---|---|---|---|---|
| $c_{\mathrm{elec}}$ | $c_{\mathrm{neutral1}}$ | $c_{\mathrm{neutral2}}$ | $a_{\mathrm{elec}}$ | $a_{\mathrm{neutral1}}$ | $a_{\mathrm{neutral2}}$ | SPB | MC | SPB | MC |
| 1:1 electrolyte +2 neutral species | | | | | | | | | |
| 0.05 | 0.025 | 0.025 | 2.125 | 2.125 | 2.125 | 0.137 | 0.139 | 0.975 | 0.974 |
| 0.05 | 0.05 | 0.5 | 2.125 | 2.125 | 4.25 | 0.0320 | 0.0327 | 1.48 | 1.48 |
| 0.1 | 0.1 | 0.25 | 2.125 | 2.125 | 4.25 | 0.0870 | 0.100 | 1.19 | 1.19 |
| 0.1 | 0.1 | 1 | 2.125 | 2.125 | 4.25 | 0.0460 | 0.0460 | 2.28 | 2.31 |
| 0.2 | 0.2 | 0 | 2.125 | 2.125 | 4.25 | 0.220 | 0.229 | 1.00 | 0.999 |
| 0.2 | 0.2 | 0.5 | 2.125 | 2.125 | 4.25 | 0.123 | 0.128 | 1.48 | 1.48 |
| 0.2 | 0.2 | 1 | 2.125 | 2.125 | 4.25 | 0.0870 | 0.0902 | 2.29 | 2.31 |
| 0.2 | 0.2 | 1.5 | 2.125 | 2.125 | 4.25 | 0.0680 | 0.0706 | 3.67 | 3.79 |
| 0.2 | 0.2 | 2 | 2.125 | 2.125 | 4.25 | 0.0570 | 0.0595 | 6.13 | 6.52 |
| 0.2 | 0.2 | 2.5 | 2.125 | 2.125 | 4.25 | 0.0490 | 0.0528 | 10.76 | 11.83 |
| 1 | 2 | 1 | 2.125 | 2.125 | 4.25 | 0.214 | 0.235 | 3.18 | 3.08 |
| 1:2 electrolyte +2 neutral species | | | | | | | | | |
| 0.05 | 0.025 | 0.025 | 2.125 | 2.125 | 2.125 | 0.454 | 0.476 | 0.869 | 0.899 |
| 0.05 | 0.05 | 0.5 | 2.125 | 2.125 | 4.25 | 0.133 | 0.140 | 1.45 | 1.45 |
| 0.1 | 0.1 | 0.25 | 2.125 | 2.125 | 4.25 | 0.345 | 0.368 | 1.14 | 1.11 |
| 0.1 | 0.1 | 1 | 2.125 | 2.125 | 4.25 | 0.167 | 0.178 | 2.26 | 2.29 |
| 0.2 | 0.2 | 1 | 2.125 | 2.125 | 4.25 | 0.309 | 0.334 | 2.27 | 2.26 |
| 1 | 2 | 1 | 2.125 | 2.125 | 4.25 | 0.635 | 0.743 | 3.54 | 2.97 |

into an effective permittivity of the medium in the Coulomb interactions. In both the bulk and interfacial electric double layers there have been theoretical works aimed at incorporating the solvent as a separate entity on an even footing with the solute (Carnie and Chan 1980, Blum and Henderson 1981, Outhwaite 1983, Torrie and Patey 1993, Wei *et al.* 1993) by treating the solvent as consisting of dipoles and higher order multipoles. A notable result is the fact that the high density of the solvent molecules drives the structure in the solutions. However, the basic problems associated with the majority of the multipolar solvent models are, (i) a poor value of the relative permittivity calculated from first principles and (ii) the complex numerics needed to affect a solution. A hybrid model, which tends to overcome some of the problems associated with solvent polarization while at the same time retaining the *discreteness-of-the-solvent*, is the solvent primitive model (SPM). The charged fluid is a mixture of rigid ions and rigid spheres with the latter playing the role of the solvent (see, for example, Krienke and Thamm (1992)). The relative permittivity is still fed in as an input parameter and in this sense the model might be aesthetically lacking. Note also that the model approximations have not been clearly delineated as has been done for the PM. However, it is expected that the model would bring out the steric role of the solvent molecules. The usefulness of the SPM in some studies of the double layer is a case in point (Groot 1988, Groot and van der Earden 1988, Tang *et al.* 1992, Patra and Ghosh 1993, 1994a,b, Zhang *et al.* 1993, Lamperski *et al.* 1996).

## 5. Concluding remarks

In this review we have tried to detail the development of our understanding of the mechanism of macroion condensation in spherically symmetric polyelectrolyte solutions. The likely mechanisms that may lead to phase instability in a solution are classifiable into three broad categories:

(a) strong Coulomb correlations in the presence of multivalent counterions,
(b) fluctuations in the surface charge of the macroions, and,
(c) steric and depletion effects associated with the addition of a neutral co-solute.

The structural changes that occur in the solution, which are often precursors of condensation, are the manifestations of the highly interesting, intuitively inconsistent attractive forces between like-charged ionic species, ion-pairing and higher order clustering and the consequent appearance of inhomogeneity in the solution in the form of clusters and voids. Thermodynamically, the changes can be increases in the (i) solution internal energy, (ii) excess chemical potential of the ions, (iii) inverse isothermal compressibility and (iv) Gibbs energy of mixing, all suggestive of a decrease in the solution stability.

The enormous significance of macroion condensation in protein precipitation and other important biological processes, the significance of macromolecular crowding reactions in pharmaceutical industries in particular, can only point to a persistent research interest in the subject. Indeed, as we have seen in the course of this discussion, sophisticated, precision experimental techniques coupled with ever increasing computer power continue to unearth fascinating and novel properties (of such complex fluids) the explanations of some of which remain a theoretical challenge.

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*Note added in proof*:—The interest in the nature of macroion–macroion interaction in polyelectrolyte solutions continues to be substantial. Some relevant publications since the submission of this manuscript include the following.

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