Mapping the Extra Solvent Power of Ionic Liquids for Monomers, Polymers, and Dry / Wet Globular Single-Chain Polymer Nanoparticles

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ABSTRACT: Ionic liquids (ILs) have shown advantages in organic synthesis and catalysis, energy storage and conversion, as well as a variety of pharmaceutical applications. Understanding the miscibility behavior of IL / monomer, IL / polymer and IL / polymer nanoparticle mixtures is critical for the use of ILs as green solvents in polymerization processes, as well as to rationalize recent observations concerning the superior solubility of some proteins in ILs when compared to standard solvents. In this work, the most relevant results obtained in terms of an extended three-component Flory-Huggins theory concerning the Extra Solvent Power (ESP) of ILs when compared to traditional non-ionic solvents for monomeric solutes (Case I), linear polymers (Case II), dry (*i.e.*, without IL inside) globular single-chain polymer nanoparticles (SCNPs) (Case III) and wet (*i.e.*, with IL inside) globular SCNPs (Case IV) are presented. Moreover, useful ESP maps are drawn for the first time for IL mixtures corresponding to Case I, II, III and IV at constant temperature and pressure. Finally, a potential pathway to improve the miscibility of non-ionic polymers in ILs is proposed.

1. INTRODUCTION

Ionic liquids (ILs) exhibit unique properties such as high ionic conductivity, thermal and (electro)chemical stability, non-flammability, broad liquid temperature range, almost negligible vapor pressure and good solvent power for a wide range of both organic and inorganic solutes.¹⁻⁶ The difference in solubility between ordinary solvents and ILs as ionic solvents is called the “Extra Solvent Power” (ESP) of ILs. Understanding the miscibility behavior of IL / polymer (P) mixtures is critical for the use of ILs as green solvents in polymerization processes. Additionally, quantification of the ESP (extra solvent power) of ILs for globular single-chain polymer nanoparticles (SCNPs),⁷ as very simple models of natural globular proteins (*e.g.*, enzymes), is essential for many potential end-use applications of these soft nano-objects. Thermodynamic models accounting for the ESP of ILs when compared to traditional non-ionic solvents are thus very useful tools for both academy and industry. In fact, the increased solvent power of ILs and their superior ionic conductivity, electrochemical stability and non-flammability have been advantageous for several organic synthesis and catalysis uses,⁸ pharmaceutical applications,⁹ and energy storage and conversion enhancement,¹⁰ among other uses. Nevertheless, as recently highlighted by the groups of Yu¹¹ and Zhu¹² not all ILs are green solvents due to potential bioaccumulation, toxicity, and degradability issues of some of them, that might cause water or soil pollution as other commonly used chemicals.

To rationalize the solubility of organic solutes¹³⁻¹⁸ in ILs with a simple but effective model, a three-component Flory-Huggins (FH) theory comprising anions, cations, and neutral solute molecules of the same size was originally introduced by Aerov *et al.*¹⁹ (see Figure 1, Case I). In this model, each ion was considered to consist of a charged group surrounded by a neutral

Figure 1. Ionic liquid (IL) mixtures comprising a monomeric solute (S) (Case I), a linear polymer (P) of polymerization degree N (Case II), a dry (*i.e.*, without IL inside) globular single-chain polymer nanoparticle of radius R (Case III) and a wet (*i.e.*, with IL inside) globular single-chain polymer nanoparticle of radius R^* (Case IV). Case II, III and IV have not been addressed previously.

“bulky” shell. The interactions of the shells of the ions with the solute are described in terms of a classical Flory-Huggins χ parameter. The interaction of the shells of the ions with each other is assumed to involve short-range (non-Coulomb) forces and described in the model through an additional, effective χ_{+-} parameter. According to this theory the solvent power of ILs is enhanced if short-range interactions between the shells of the anions and cations are repulsive (*i.e.*, $\chi_{+-} > 0$)

when compared to an equivalent non-ionic liquid having the same χ value with respect to the solute but, obviously, $\chi_{+-} \equiv 0$.¹⁹ In this sense, based on cohesive energy measurements reported for *n*-alkyl-3-methylimidazolium bis(trifluoromethyl sulfonyl)-imide ILs, an absolute change in χ_{+-} as large as $\Delta\chi_{+-} = 4.5$ can be estimated on passing from $n = 2$ to $n = 8$.²⁰ Hence, in terms of this simple model, the shielding of the repulsive short-range cation-anion interaction by the neutral solute molecules should be responsible of the ESP of ionic liquids when compared to conventional mixtures. Recently, the theory has been successfully refined to consider the miscibility of ILs with different sizes of anion and cation,²¹ to predict micro-phase separation in a mixture of ionic and non-ionic liquids,²² to investigate the structure and surface tension coefficient of the boundary between ionic and non-ionic liquids,²³ and to determine the conditions for cluster formation in a mixture composed of an “amphiphilic” ionic liquid and a non-ionic liquid.^{24,25}

In spite of its potential utility for organic synthesis and catalysis, energy storage and conversion as well as pharmaceutical applications, quantification of the ESP of ILs for linear polymers (Figure 1, Case II) and compact SCNPs (Figure 1, Cases III and IV) when compared to the corresponding equivalent non-ionic liquid mixtures has not been performed yet. In this work, we highlight the most important results obtained in terms of an extended three-component Flory-Huggins theory concerning the ESP of ILs for linear polymers and globular single-chain polymer nanoparticles (both dry and wet SCNPs). The results are compared to those obtained for the case of IL / monomeric solute (S) mixtures, as a reference. Useful ESP maps are drawn for the first time for IL mixtures corresponding to Case I, II, III and IV at constant temperature and pressure. As a corollary, a potential pathway to improve the miscibility of non-ionic polymers in ILs is proposed.

2. THEORETICAL SECTION

A comprehensive description of the fundamentals of the three-component Flory-Huggins (FH) theory (Figure 1, Case I) can be found in refs. 19 and 21, and a detailed description of the original FH theory in ref. 26. For homogeneous IL / S mixtures (*i.e.*, miscible systems), it is well-known that the change in free energy upon mixing (f) must be negative (see equation 1.1 in Table 1).²⁷ In this sense, equation 1.2 provides one of the two necessary conditions for thermodynamic miscibility (*i.e.*, $f < 0$). Additionally, the second derivative of the free energy of mixing with composition ($f^{(2)} \equiv \left(\frac{d^2 f}{d \phi_1^2} \right)_T$) must be positive (eq. 1.3) for the mixture to be stable against small fluctuations in composition, which leads to equation 1.4 as the second necessary condition for miscibility.²⁷

Extension of this three-component Flory-Huggins theory to Case II (IL / P mixtures) and Case III (IL / dry globular SCNP mixtures) is relatively straightforward. The main results obtained are displayed in Table 1. For Case II, the introduction of the degree of polymerization, N , as an additional parameter is necessary,²⁶ whereas for Case III (see Figure 1) the ratio of the radius of the nanoparticle to the radius of the ions (R / r) must be introduced.²⁸⁻³⁰ As explained in refs. 28-30, the R / r ratio is needed to account for the interaction of the solvent with the external surface of the globular, dry nanoparticle. For Case IV (wet nanoparticle), an additional term is necessary arising from the swelling of the SCNP from size R (dry state, Case III) to R^* in terms of the parameter $\xi \equiv R^* / R$. To a simple first approximation, the change in free energy associated

to SCNP swelling can be estimated as:²⁶ $\left(\frac{f}{kT} \right)_{swelling} \approx \left[\left(\frac{R^*}{R} \right)^2 - 1 \right] \phi_1 \phi_2 = (\xi^2 - 1) \phi_1 \phi_2$. Note that

$\left(\frac{f}{kT}\right)_{\text{swelling}} = 0$ for $R^* = R$, as it is expected. This expression should be valid only at low content

of IL inside the globule, since it completely neglects enthalpic contributions.

Table 1. Thermodynamic miscibility conditions for different mixtures containing ILs in terms of the extended three-component FH theory^a

Case I: IL / S	
$\frac{f}{kT} = \phi_1 \ln \frac{\phi_1}{2} + \phi_2 \ln \phi_2 + \chi_{+-} \frac{\phi_1^2}{4} + \chi \phi_1 \phi_2 < 0$	(1.1) ^b
$\chi < -\left(\frac{\ln(\phi_1/2)}{\phi_2} + \frac{\ln \phi_2}{\phi_1} + \frac{\chi_{+-}\phi_1}{4\phi_2}\right)$	(1.2) ^c
$\frac{f^{(2)}}{kT} = \frac{1}{\phi_1 \phi_2} - 2\left(\chi - \frac{\chi_{+-}}{4}\right) > 0$	(1.3) ^b
$\chi < \left(\frac{1}{2\phi_1 \phi_2} + \frac{\chi_{+-}}{4}\right)$	(1.4) ^b
Case II: IL / P	
$\frac{f}{kT} = \phi_1 \ln \frac{\phi_1}{2} + \frac{\phi_2}{N} \ln \phi_2 + \chi_{+-} \frac{\phi_1^2}{4} + \chi \phi_1 \phi_2 < 0$	(2.1) ^c
$\chi < -\left(\frac{\ln(\phi_1/2)}{\phi_2} + \frac{\ln \phi_2}{N\phi_1} + \frac{\chi_{+-}\phi_1}{4\phi_2}\right)$	(2.2) ^c
$\frac{f^{(2)}}{kT} = \frac{1}{\phi_1} + \frac{1}{N\phi_2} - 2\left(\chi - \frac{\chi_{+-}}{4}\right) > 0$	(2.3) ^c
$\chi < \left(\frac{1}{2\phi_1} + \frac{1}{2N\phi_2} + \frac{\chi_{+-}}{4}\right)$	(2.4) ^c

Case III: IL / DRY SCNP

$$\frac{f}{kT} = \phi_1 \ln \frac{\phi_1}{2} + \frac{\phi_2}{(R/r)^3} \ln \phi_2 + \chi_{+-} \frac{\phi_1^2}{4} + \left(\frac{r}{R} \right) \chi \phi_1 \phi_2 < 0 \quad (3.1)^c$$

$$\chi < -\frac{R}{r} \left(\frac{\ln(\phi_1/2)}{\phi_2} + \frac{\ln \phi_2}{(R/r)^3 \phi_1} + \frac{\chi_{+-} \phi_1}{4 \phi_2} \right) \quad (3.2)^c$$

$$\frac{f^{(2)}}{kT} = \frac{1}{\phi_1} + \frac{1}{(R/r)^3 \phi_2} - 2 \left(\frac{r}{R} \chi - \frac{\chi_{+-}}{4} \right) > 0 \quad (3.3)^c$$

$$\chi < \frac{R}{r} \left(\frac{1}{2\phi_1} + \frac{1}{2(R/r)^3 \phi_2} + \frac{\chi_{+-}}{4} \right) \quad (3.4)^c$$

Case IV: IL / WET SCNP

$$\frac{f}{kT} = \phi_1 \ln \frac{\phi_1}{2} + \frac{\phi_2}{(R/r)^3} \ln \phi_2 + \chi_{+-} \frac{\phi_1^2}{4} + \left[\left(\frac{r}{R} \right) \chi + \xi^2 - 1 \right] \phi_1 \phi_2 < 0 \quad (3.5)^c$$

$$\chi < -\frac{R}{r} \left(\frac{\ln(\phi_1/2)}{\phi_2} + \frac{\ln \phi_2}{(R/r)^3 \phi_1} + \frac{\chi_{+-} \phi_1}{4 \phi_2} + \xi^2 - 1 \right) \quad (3.6)^c$$

$$\frac{f^{(2)}}{kT} = \frac{1}{\phi_1} + \frac{1}{(R/r)^3 \phi_2} - 2 \left[\left(\frac{r}{R} \right) \chi + \xi^2 - 1 \right] - \frac{\chi_{+-}}{4} > 0 \quad (3.7)^c$$

$$\chi < \frac{R}{r} \left(\frac{1}{2\phi_1} + \frac{1}{2(R/r)^3 \phi_2} + \frac{\chi_{+-}}{4} + \xi^2 - 1 \right) \quad (3.8)^c$$

^a $f^{(2)} \equiv \left(\frac{d^2 f}{d \phi_1^2} \right)_T$; $\phi_2 = 1 - \phi_1$; ϕ_1 = Volume fraction of IL in the mixture; IL = Ionic liquid; S = Non-ionic

solute; P = Polymer; SCNP = Single-chain polymer nanoparticle; k = Boltzmann's constant; T = Absolute temperature; $\xi = (R^*/R)$ where R^* = Wet SCNP radius; R = Dry SCNP radius. ^b Ref. 19. ^c This work.

3. RESULTS AND DISCUSSION

We are interested to know how the interplay between the specific values of χ and χ_{+-} affect the Extra Solvent Power (ESP) of IL / S mixtures (Case I), IL / P mixtures (Case II), IL / dry SCNP mixtures (Case III) and IL / wet SCNP mixtures (Case IV) when compared with non-ionic solvents of exactly the same value of χ but $\chi_{+-} \equiv 0$. Within the framework of the extended three-component FH model we will restrict our analysis to the most interesting scenario of non-athermal mixtures with $\chi > 0$ and $\chi_{+-} > 0$. This scenario is characterized by unfavorable enthalpic interactions (*i.e.*, $\chi > 0$) that take place between the IL and the second component in the mixture, and repulsive short-range (non-Coulomb) interactions between the shells of the anions and cations (*i.e.*, $\chi_{+-} > 0$). Our main aim is to understand how both the miscibility behavior and ESP depend on χ_{+-} and composition for Cases I – IV in Table 1.

3.1. Case I: IL / S Mixtures. It is worth of mention that miscibility for IL / monomeric solute (S) mixtures is only possible when $\chi < \chi_c$, where χ_c is the critical Flory-Huggins χ parameter of an IL / S mixture which satisfy both the free energy and spinodal criteria^{27,31} (see Section 2). Previously, only a simplified analysis based exclusively on the second thermodynamic criterion (*i.e.*, $\left(\frac{d^2 f}{d \phi_1^2}\right)_T > 0$) was performed by Aerov *et al.*¹⁹ By taking into account both the free energy and spinodal criteria we obtain (see SI):

$$\chi_c = \left(\frac{1}{2\phi_1\phi_2} + \frac{\chi_{+-}}{4} \right); \quad \text{for } \chi_{+-} \leq \chi_{+-}^m \quad (3.9)$$

$$\chi_c = - \left(\frac{\ln(\phi_1/2)}{\phi_2} + \frac{\ln \phi_2}{\phi_1} + \frac{\chi_{+-}\phi_1}{4\phi_2} \right); \quad \text{for } \chi_{+-} \geq \chi_{+-}^m \quad (3.10)$$

$$\chi_{+-}^m = 4\Delta\chi^{max} \quad (3.11)$$

$$\Delta\chi^{max} = -\left(\ln(\phi_1/2) + \frac{\phi_2 \ln \phi_2}{\phi_1} + \frac{1}{2\phi_1}\right) \quad (3.12)$$

where χ_{+-}^m is the *optimum* value of the cation / anion interaction parameter, $\Delta\chi^{max}$ is the *maximum* ESP, and ϕ_1 and $\phi_2 = 1 - \phi_1$ are the volume fraction of IL and solute in the mixture, respectively.

The volume fraction of IL which provides the highest value of $\Delta\chi^{max}$, denoted as ϕ_1^m , is obtained

by solving the equation $\left(\frac{d\Delta\chi^{max}}{d\phi_1}\right) = 0$. It is given for IL / S mixtures by $\phi_1^m = 1 - e^{-1/2} = 0.394$.

Figure 2 illustrates the ESP calculated as the difference between the value of χ_c for a IL/S mixture which satisfy both the free energy and spinodal criteria (equation 1.1 and equation 1.3 in Table 1)^{27,31} and the value of χ_c for an equivalent non-ionic liquid mixture (see SI):

$$\Delta\chi = \left(\frac{\chi_{+-}}{4}\right); \quad \text{for } \chi_{+-} \leq \chi_{+-}^m \quad (3.13)$$

$$\Delta\chi = -\left(\frac{\ln(\phi_1/2)}{\phi_2} + \frac{\ln \phi_2}{\phi_1} + \frac{\chi_{+-}\phi_1}{4\phi_2} + \frac{1}{2\phi_1\phi_2}\right); \quad \text{for } \chi_{+-} \geq \chi_{+-}^m \quad (3.14)$$

As illustrated in Figure 2, at low values of the cation / anion interaction parameter χ_{+-} , the ESP in the IL / S mixture is controlled by the spinodal criterion (equation 1.3 and 3.13) whereas for high values of χ_{+-} the ESP becomes limited by the free energy criterion (equation 1.1 and 3.14). By definition, the concept of “Extra Solvent Power” has physical meaning only if the condition $\Delta\chi > 0$ is fulfilled. Note that the value of χ_{+-}^m results by equating the r.h.s. of equation 3.13 and 3.14.

Figure 2. The “Extra Solvent Power, ESP ($\Delta\chi > 0$)” of ILs is limited by the full criteria for thermodynamic miscibility: negative free energy of mixing and positive second derivative of the free energy of mixing with composition at fixed temperature (equation 1.1 - 1.4 in Table 1). See text for definition of $\Delta\chi$ and $\Delta\chi^{\max}$ as well as SI for calculations. Data shown correspond to a volume fraction of IL in the IL / S mixture of $\phi_1 = 0.5$ (see Table 1, Case I).

The dependence of $\Delta\chi^{\max}$ and χ_{+-}^m with respect to the content of IL in the mixture (ϕ_1) is illustrated in Figure 3A. A detailed analysis of Figure 3A reveals several important trends: i) no ESP is observed at low IL content ($\phi_1 < 0.15$), ii) the maximum ESP ($\Delta\chi^{\max} = 1.125$) takes place at $\phi_1^m \approx 0.4$ for IL/S mixtures having $\chi_{+-}^m \approx 4.5$, and iii) at $\phi_1 > \phi_1^m$ the maximum ESP, as well as the corresponding optimum value of the cation / anion interaction parameter reduce progressively when compared to the values at ϕ_1^m .

Figure 3. A) Optimum value of cation/anion interaction parameter (χ_{+-}^m , blue solid circles) and maximum ESP ($\Delta\chi^{max}$, red solid circles) as a function of the volume fraction of IL in the mixture (ϕ_1) for IL / S mixtures. B) ESP map for IL / S mixtures ($\phi_1 = 0.5$). Open circles: Combination of (χ_{+-}, χ) data providing ESP (*i.e.*, $\Delta\chi > 0$).

Additionally, as illustrated in Figure 3B for a given composition ($\phi_1 = 0.5$), a useful ESP map can be easily constructed by considering the free energy and spinodal criteria for miscibility in the three-component FH theory of IL/S mixtures at constant temperature and pressure.

3.2. Case II: IL / P Mixtures. For IL mixtures in which the solute is a linear polymer (P) having a polymerization degree N (Case II in Figure 1) the expressions for the free energy of mixing and second derivative of the free energy with composition, as well as the corresponding free energy and spinodal criteria for miscibility are given in Table 1. A close inspection of equation 2.1 - 2.4 in Table 1 reveals that they reduce, as they must, to equation 1.1 - 1.4 for the limiting case of $N = 1$ (*i.e.*, for the case of monomeric solute). According to this model, in the limit of very large polymer size ($N \rightarrow \infty$) we have (see SI):

$$\chi_c = \left(\frac{1}{2\phi_1} + \frac{\chi_{+-}}{4} \right); \quad \text{for } \chi_{+-} \leq \chi_{+-}^m \quad (3.15)$$

$$\chi_c = - \left(\frac{\ln(\phi_1/2)}{\phi_2} + \frac{\chi_{+-}\phi_1}{4\phi_2} \right); \quad \text{for } \chi_{+-} \geq \chi_{+-}^m \quad (3.16)$$

$$\chi_{+-}^m = 4\Delta\chi^{max} \quad (3.17)$$

$$\Delta\chi^{max} = - \left(\ln(\phi_1/2) + \frac{\phi_2}{2\phi_1} \right) \quad (3.18)$$

$$\phi_1^m = 1/2 \quad (3.19)$$

$$\Delta\chi = \left(\frac{\chi_{+-}}{4} \right); \quad \text{for } \chi_{+-} \leq \chi_{+-}^m \quad (3.20)$$

$$\Delta\chi = - \left(\frac{\ln(\phi_1/2)}{\phi_2} + \frac{\chi_{+-}\phi_1}{4\phi_2} + \frac{1}{2\phi_1} \right); \quad \text{for } \chi_{+-} \geq \chi_{+-}^m \quad (3.21)$$

Figure 4. A) Dependence of $\Delta\chi^{\max}$ (red solid circles) and χ_{+-}^m (blue solid circles) with respect to ϕ_1 for IL / P mixtures for the case of $N \rightarrow \infty$. B) ESP map for IL / P mixtures ($N \rightarrow \infty$; $\phi_1 = 0.5$). Open circles: Combination of (χ_{+-}, χ) data providing ESP (*i.e.*, $\Delta\chi > 0$).

Figure 4A shows the dependence of $\Delta\chi^{max}$ and χ_{+-}^m with respect to ϕ_1 for IL / P mixtures in the limit of very large polymer size ($N \rightarrow \infty$) and Figure 4B illustrates the corresponding ESP map for $\phi_1 = 0.5$. Several trends are observed in Figure 4: i) similar to the results obtained for IL / S mixtures, no ESP is observed at low IL content in the mixture ($\phi_1 < 0.15$) and ii) the maximum ESP takes place at $\phi_1^m = 0.5$ instead at $\phi_1^m \approx 0.4$ (IL / S mixtures), with a reduction of 18 % in the values of both $\Delta\chi^{max}$ and χ_{+-}^m .

A comparison of Figure 4B and Figure 3B illustrates the significant reduction in the ESP region (open circles) on passing from a conventional low molecular weight solute to a very high molecular weight polymeric solute. Experimentally, this trend has been observed during the polymerization of some vinyl monomers in ILs (*i.e.*, immiscibility of the resulting polymer in the IL)³² and can be rationalized within this extended three-component FH model.

3.3. Case III: IL / Dry SCNP Mixtures. A special case is related to the solubility of ultrafine globular single-chain polymer particles in ILs, which can be taken as a very simplified model for globular proteins.⁷ Referred to IL / SCNP mixtures (see Figure 1), we consider first the simple case of dry globular SCNPs, each of a radius R placed in a mixture with ions (cations and anions) of radii $r < R$ that interact exclusively with the surface of the compact SCNP (*i.e.*, no IL inside the SCNP). Inspection of equation 3.1 - 3.4 in Table 1 reveals that these expressions reduce to equation 1.1 - 1.4 in the limit of $r = R$, as they must. It can be easily shown that according to this model (see SI):

$$\chi_c = \frac{R}{r} \left(\frac{1}{2\phi_1} + \frac{1}{2(R/r)^3 \phi_2} + \frac{\chi_{+-}}{4} \right); \quad \text{for } \chi_{+-} \leq \chi_{+-}^m \quad (3.22)$$

$$\chi_c = -\frac{R}{r} \left(\frac{\ln(\phi_1/2)}{\phi_2} + \frac{\ln \phi_2}{(R/r)^3 \phi_1} + \frac{\chi_{+-}\phi_1}{4\phi_2} \right); \quad \text{for } \chi_{+-} \geq \chi_{+-}^m \quad (3.23)$$

$$\chi_{+-}^m = 4 \left(\frac{r}{R} \right) \Delta\chi^{max} \quad (3.24)$$

$$\Delta\chi^{max} = -\frac{R}{r} \left(\ln(\phi_1/2) + \frac{\phi_2}{2\phi_1} + \left(\frac{r}{R} \right)^3 \left[\frac{\phi_2 \ln \phi_2}{\phi_1} + \frac{1}{2} \right] \right) \quad (3.25)$$

$$\phi_1^m = 1/2 \quad (3.26)$$

$$\Delta\chi = \frac{R}{r} \left(\frac{\chi_{+-}}{4} \right); \quad \text{for } \chi_{+-} \leq \chi_{+-}^m \quad (3.27)$$

$$\Delta\chi = -\frac{R}{r} \left(\frac{\ln(\phi_1/2)}{\phi_2} + \left(\frac{r}{R} \right)^3 \left[\frac{\ln \phi_2}{\phi_1} + \frac{1}{2\phi_2} \right] + \frac{\chi_{+-}\phi_1}{4\phi_2} + \frac{1}{2\phi_1} \right); \quad (3.28)$$

for $\chi_{+-} \geq \chi_{+-}^m$

The dependence of $\Delta\chi^{max}$ and χ_{+-}^m with respect to ϕ_1 is illustrated in Figure 5A for the relevant case of $R/r = 5$. According to this simple model, for a given value of ϕ_1 , on passing from a linear polymer to a dry globular single-chain nanoparticle we have a notable increase in the value of maximum ESP which now is given by $\Delta\chi^{max} = \left(\frac{R}{r} \right) \left(\frac{\chi_{+-}^m}{4} \right)$ involving the R/r ratio (see equation 3.24). By taking the typical value of $r = 0.4 - 0.6 \text{ nm}^{21}$ we are considering here the most relevant case of globular SCNPs with a size ($R = 2 - 3 \text{ nm}$) similar to that typically found in natural enzymes ($R = 1.5 - 3.5 \text{ nm}$). Unfortunately, there are not experimental data available about the solubility of large ($R/r \gg 5$) globular nanoparticles in ILs, so in this work we restrict our analysis to the natural case of $R/r = 5$. Moreover, the FH theory is known to give incorrect results when the R/r ratio is very large.³³

Figure 5. A) Dependence of $\Delta\chi^{\max}$ (red solid circles) and χ^m_{+-} (blue solid circles) with respect to ϕ_1 for IL / dry globular SCNPs ($r / R = 5$). B) ESP map for IL / dry globular SCNPs mixtures ($R / r = 5$; $\phi_1 = 0.5$). Open circles: Combination of (χ^m_{+-}, χ) data providing ESP (*i.e.*, $\Delta\chi > 0$).

The miscibility enhancement observed in Figure 5B is related to a reduction in the total number of IL / repeat unit interactions in the case of IL / dry SCNP mixtures, when compared to IL / P mixtures. Consequently, a potential way to improve the miscibility of non-ionic polymers in ILs could be their folding / collapse to globular nanoparticles *via* single chain technology.³⁴ Remarkably, this work provides a simple framework to understand a recent observation concerning the superior solubility of corn protein zein in imidazolium-based ILs when compared to its solubility in reference solvents.³⁵

3.4. Case IV: IL / Wet SCNP Mixtures. Let us consider the case in which the IL comes inside the SCNP giving rise to a wet globular SCNP. Swelling the SCNP from radius R to R^* has associated a free energy penalty that can be estimated to a first approximation (by neglecting enthalpic interactions) through $\left(\frac{f}{kT}\right)_{swelling} \approx (\xi^2 - 1)\phi_1\phi_2$, where $\xi \equiv R^* / R \geq 1$ (see equation 3.5 - 3.8 in Table 1). It is worth of mention that ξ can be related to the volume fraction of IL inside the globule (θ) through $\theta = \left(1 - \frac{1}{\xi^3}\right)$.³⁶ We have determined the ESP of IL / wet SCNP mixtures containing a volume fraction of IL inside the SCNP of ~25%, since the present model is presumably valid only at very low content of IL inside the globule.

According to this model, for IL / wet SCNPs we have (see SI):

$$\chi_c = \frac{R}{r} \left(\frac{1}{2\phi_1} + \frac{1}{2(R/r)^3\phi_2} + \frac{\chi_{+-}}{4} + \xi^2 - 1 \right); \quad \text{for } \chi_{+-} \leq \chi_{+-}^m \quad (3.29)$$

$$\chi_c = -\frac{R}{r} \left(\frac{\ln(\phi_1/2)}{\phi_2} + \frac{\ln\phi_2}{(R/r)^3\phi_1} + \frac{\chi_{+-}\phi_1}{4\phi_2} + \xi^2 - 1 \right); \quad (3.30)$$

for $\chi_{+-} \geq \chi_{+-}^m$

Figure 6. A) Dependence of $\Delta\chi^{\max}$ (red solid circles) and χ_{+-}^m (blue solid circles) with respect to ϕ_1 for IL / wet globular SCNP mixtures for $r/R = 5$ and $\theta \approx 0.25$ (*i.e.*, $\xi = 1.1$). B) ESP map for IL / wet globular SCNP mixtures ($R/r = 5$; $\xi = 1.1$; $\phi_1 = 0.5$). Open circles: Combination of (χ_{+-}, χ) data providing ESP (*i.e.*, $\Delta\chi > 0$).

$$\chi_{+-}^m = 4 \left[\left(\frac{r}{R} \right) \Delta\chi^{max} - \xi^2 + 1 \right] \quad (3.31)$$

$$\Delta\chi^{max} = -\frac{R}{r} \left(\ln(\phi_1/2) + \frac{\phi_2}{2\phi_1} + \left(\frac{r}{R} \right)^3 \left[\frac{\phi_2 \ln \phi_2}{\phi_1} + \frac{1}{2} \right] + (\xi^2 - 1)(2\phi_2 - 1) \right) \quad (3.32)$$

$$\phi_1^m = \frac{1 - \sqrt{1 - 4(\xi^2 - 1)}}{4(\xi^2 - 1)}; \text{ for } 1 < \xi < \sqrt{5/4} \approx 1.118 \quad (3.33)$$

$$\Delta\chi = \frac{R}{r} \left(\frac{\chi_{+-}}{4} \right); \text{ for } \chi_{+-} \leq \chi_{+-}^m \quad (3.34)$$

$$\Delta\chi = -\frac{R}{r} \left(\frac{\ln(\phi_1/2)}{\phi_2} + \left(\frac{r}{R} \right)^3 \left[\frac{\ln \phi_2}{\phi_1} + \frac{1}{2\phi_2} \right] + \frac{\chi_{+-}\phi_1}{4\phi_2} + \frac{1}{2\phi_1} \right); \quad (3.35)$$

for $\chi_{+-} \geq \chi_{+-}^m$

The dependence of $\Delta\chi^{max}$ and χ_{+-}^m with respect to ϕ_1 is illustrated in Figure 6A for IL / wet globular SCNP mixtures with $R / r = 5$ and $\xi = 1.1$ (*i.e.*, $\theta \approx 0.25$, that is 25% of IL inside the SCNP) and the corresponding ESP map ($\phi_1 = 0.5$) is shown in Figure 6B. No significant changes are observed when compared to the case of IL / dry globular SCNP mixtures, so we can conclude that both the ESP and miscibility behavior are not modified to a large extent by incorporating a low content of IL inside the globule.

Further works will be devoted to refine the treatment of globule swelling to afford the case of high content of IL inside the globule, as well as to incorporate free volume effects into the three-component FH theory which are known to play a significant role in the change of miscibility behavior with temperature.

4. CONCLUSIONS

In summary, we have quantified the “Extra Solvent Power, ESP” of ILs when compared to traditional non-ionic solvents for monomeric solutes (Case I), linear polymers (Case II), dry globular single-chain nanoparticles (Case III) and wet globular SCNPs at low content of IL inside the globule (Case IV) in terms of an extended three-component FH theory. ESP maps were drawn, for the first time, for IL mixtures corresponding to Case I, II III and IV at constant temperature and pressure. On one hand, on passing from monomeric to polymeric mixtures with ILs, a significant reduction in ESP was observed. Interestingly, the opposite trend was found on passing from linear polymer to globular single-chain nanoparticle mixtures with ILs, either with or without IL inside the SCNPs. Quantification of the ESP of ILs for globular SCNPs, as very simple models of natural globular proteins, is essential for many potential end-use applications of these soft nano-objects as bioinspired catalysts. In this sense, this work provides a useful framework for the investigation of the miscibility behavior of IL / globular SCNP mixtures, as well as to understand recent observations concerning the superior solubility of some proteins in ILs when compared to other standard solvents.

ASSOCIATED CONTENT

Supporting Information. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.langmuir.xxxxxxx

Calculations for Case I, II, III and IV (PDF)

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Notes

The authors declare no competing financial interest.

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