



Universidad Autónoma del Estado de México

Facultad de Ciencias



Protocolo de Investigación

Análisis molecular de la influencia de micro-heterogeneidades en la tensión superficial de soluciones acuosas de disolventes polares

Para obtener el grado de :

Maestra en Ciencias (Física)

Presenta:

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Toluca, Estado de México, Marzo de 2017.

Protocolo de investigación

INTRODUCCIÓN

Los solventes o también llamados disolventes son el medio donde se disuelve un compuesto, por lo general éste se encuentra en mayor proporción en una solución. En la literatura encontramos dos grandes ramas: disolventes polares y disolventes no polares. En este trabajo de investigación nos enfocaremos en disolventes polares. El agua, etanol y ácido acético, son ejemplos de disolventes polares próticos, es decir contienen enlaces O-H y N-H. La acetona, acetonitrilo y tetrahidrofurano son ejemplos de disolventes apróticos, es decir, no contienen enlaces O-H y N-H [1].

Nos interesa analizar desde un punto de vista molecular las micro-heterogeneidades que se presentan en mezclas de disolventes polares, mayormente en soluciones acuosas. Llamamos micro-heterogeneidades a las estructuras locales que se crean en el interior del líquido de una mezcla de disolventes en las inmediaciones del punto crítico del equilibrio líquido-líquido. Estas pueden ser clúster de distintos tamaños o formas más organizadas como una micela. Nos interesa analizar este tipo de estructuras entre diferentes soluciones acuosas de disolventes próticos y apróticos y su repercusión en la tensión superficial al conseguir un equilibrio dinámico entre el líquido y el vapor de este tipo de mezclas.

Hasta donde sabemos, no existe un estudio sistemático de los efectos de los enlaces O-H y N-H en las micro-heterogeneidades de mezclas de disolventes en un equilibrio dinámico del líquido-vapor, así como tampoco hay un análisis sistemático de la influencia de las micro-heterogeneidades en la tensión superficial de este tipo de sistemas. Una de las cosas que nos llama la atención es analizar la intensidad del campo eléctrico local de estos disolventes, al menos uno prótico y uno aprótico. Una de las preguntas que queremos responder es si el campo eléctrico local nos da información acerca la formación de micro-heterogeneidades. Suponemos que sí, pero aun no sabemos como. La manera en que se estima el campo eléctrico local de manera precisa, fue publicada por Sokhan y Tildesley en 1997 [2]. Además de mostrar una forma simple de estimar el potencial eléctrico superficial del agua en fase líquida. Por otro lado, estamos interesados en estimar el campo eléctrico local en el equilibrio líquido-vapor de los sistemas etanol y acetona, así como la mezcla binaria entre ellos y las mezclas binarias con el agua. Con la intención de analizar la intensidad de estos campos eléctricos asociados a cada compuesto, y a partir de los datos intentar dar una explicación a nivel molecular de como afecta el campo eléctrico local, en mayor o menor medida, la formación de micro-heterogeneidades en la mezcla de ellos con el agua. Creemos que un campo eléctrico local intenso por parte de los disolventes apróticos promueve en mayor medida la formación de micro-heterogeneidades.

ANTECEDENTES

Los disolventes polares en general son miscibles con el agua en cualquier concentración, como es el caso del acetonitrilo o de los alcoholes primarios tales como metanol, etanol y el 1-propanol. Sin embargo, algunos disolventes polares no son completamente miscibles con el agua. Específicamente, el alcohol 1-butanol muestra una separación de fases líquido-líquido a temperatura de 20C, dentro de un régimen de concentración [10%-80%]. Esto significa que la región de dos fases esta presente en las concentraciones de 1-butanol relativamente bajas y relativamente altas, respectivamente. Es de interés el explicar por qué la interfase líquido-líquido se genera dentro de estas concentraciones de las mezclas de 1-butanol mas agua, debido a que las mezclas acuosas que son usadas como disolventes se emplean frecuentemente en la electroquímica. Así como también en otros procesos de limpieza o depuración de metales o elementos químicos de interés. Por lo que es necesario garantizar un resultado óptimo. Ha habido una gran cantidad de trabajos realizados acerca de las estructuras microscópicas de mezclas binarias de agua-alcohol a través de enfoques experimentales y teóricos, como la espectrometría de masas [3-8], difracción de neutrones [9], la difracción de rayos-X [10,11].

Cuando se mezclan dos tipos de líquidos, las mezclas binarias resultantes usualmente se desvían de la mezcla ideal. Las propiedades fisicoquímicas de las mezclas binarias, tales como el exceso de entalpía de mezcla, la presión de vapor parcial, la viscosidad de corte, la auto-difusión, etc. son bastante diferentes de los calculados sobre la base de la mezcla ideal. En general, es nuestra meta el demostrar que las propiedades físico-químicas de las mezclas líquidas binarias en la interfase liquido-vapor están estrechamente relacionados con las estructuras microheterogéneas.

HIPÓTESIS

Los enlaces O-H y N-H en la mezcla de disolventes polares y el agua, son los responsables de manera importante de la formación de micro-heterogeneidades en una región muy amplia de concentración de disolvente polar en agua. Los solventes polares presentan una organización estructural relativamente alta en la fase líquida, lo que puede ser evidenciado con un histograma de densidad y con el campo eléctrico local, un campo eléctrico local intenso no favorece una buena solubilidad de disolvente en el agua.

OBJETIVO GENERAL

Analizar la formación de micro-estructuras en las mezcla de solventes líquidos polares con el agua. Acotar en que estados termodinámicos de temperatura y presión donde se inicia la organización particular en las mezclas con agua. El análisis se realiza a través de la dinámica molecular. Se analizará la organización espacial relativamente alta de este tipo de compuestos en la superficie de la fase líquida, mostrando un campo eléctrico local intenso en la interfase liquido-vapor de la mezcla.

OBJETIVOS PARTICULARES

- Estimar la tensión superficial de los solventes polares de interés y la mezcla de ellos y con el agua.
- Estimar las densidad del equilibrio liquido-vapor de cada disolvente y las mezclas

binarias con el agua.

- Estimar el campo eléctrico local de los solventes polares analizados, la mezcla entre ellos y la mezcla binaria con el agua.

METODOLOGÍA

En el presente protocolo se plantea desarrollar el análisis generando datos del sistema de interés a través de los métodos de simulación molecular y métodos de integración numérica. En particular emplearemos la dinámica molecular. La razón de peso para elegir dinámica molecular en lugar del método directo de Montecarlo u otras, se debe a que nos interesa simular una interfase físicamente presente y además nos interesa estimar el ancho interfacial. Básicamente, la dinámica molecular consiste en estimar posiciones y velocidades finales de sistemas moleculares a partir de posiciones y velocidades iniciales, usando un modelo matemático de la forma en que interactúan los átomos de las mismas moléculas y entre distintas moléculas. En esta propuesta usaremos el software libre GROMACS para mover las moléculas en el ensamble canónico (NVT) y el ensamble isotérmico-isobárico (NPzzT) [12]. Para mantener la temperatura constante usaremos la metodología de Nosé-Hoover, cadena de termostatos. Usaremos 4 termostatos en particular con la constante de ajuste 0.5. Para mantener la presión constante usaremos el barostato de Berendsen, ciertamente este barostato no es el mejor, sin embargo este barostato da buenos resultados en el régimen de temperaturas y presiones que queremos fijar en nuestras simulaciones $T=[5\text{C}-100\text{C}]$, $P=[0\text{atm}-10\text{atm}]$. El algoritmo que usaremos será el de velocity Verlet [8] para mover las partículas en el espacio tridimensional, usaremos condiciones de frontera periódicas y la convención de mínima imagen. Emplearemos la metodología Particle Mesh Ewald [12] para estimar de manera completa la interacción de Coulomb y usaremos en todos los casos un radio de corte lo suficientemente largo $R_c=L_{\min}/2$, donde L_{\min} es la dimensión más pequeña de la caja de simulación. Dicha caja tendrá la forma de un paralelepípedo con $L_x=L_y \ll L_z$. La fuerza de van der Waals se modelará a través del potencial de Lennard-Jones. En todos los casos usaremos potenciales armónicos para modelar grados de libertad internos.

Usaremos el campo de fuerza OPLS all-atom para las moléculas empleadas en nuestro análisis: agua, etanol, acetona [1]. Para las interacciones de las partículas no iguales usaremos las reglas de combinación de Lorentz-Berthelot [12].

Usaremos la definición mecánica de la tensión superficial

$$\gamma = \frac{1}{2}L_z[\langle P_{zz} \rangle - \frac{1}{2}(\langle p_{xx} \rangle + \langle P_{yy} \rangle)] \quad (1)$$

donde P_{zz} es la componente de la presión normal a la interfase y $\frac{1}{2}(\langle p_{xx} \rangle + \langle P_{yy} \rangle)$ es la presión tangente a la interfase.

Para estimar las densidades del equilibrio líquido-vapor, construiremos histogramas de la densidad a lo largo del lado más largo de la caja de simulación (L_z). Una vez estimado el perfil de densidad, se usa como dato de entrada en el ajuste a una función tangente hiperbólica

$$\rho(z) = 0.5(r_{vap} + r_{liq}) - 0.5(r_{vap} - r_{liq})\tanh[2(z - z_0)/d] \quad (2)$$

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donde $\rho(z)$ es el perfil de densidad, r_{vap} y r_{liq} son las densidades en el vapor y el líquido, respectivamente. z_0 es la posición de la interfase (Gibbs dividing surface) y $d/2$ es el ancho de la interfase.

El campo eléctrico local lo estimaremos siguiendo la metodología propuesta por Sokhan y Tildesley [11]. Dicha metodología fue usada en el modelo del agua SPC/E con la idea de identificar las orientaciones preferenciales de la molécula del agua de manera local, este método incluso es más preciso que el método tradicionalmente usado, la generación del segundo armónico, (SHG por sus siglas en inglés, second harmonic generation),

$$E_z(z) = e - 1_0 \int_{z_0}^z dz' r_q(z') \quad (3)$$

donde $r_q(z) = \sum_i q_i r_i(z)$

es la suma sobre las diferentes especies de cargas en el modelo, cuidando la condición de electroneutralidad.



Submission Confirmation

Print

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March 13, 2017

Submitted to The Journal of Physical Chemistry

Manuscript ID jp-2017-02470a

Title The effect of dielectric constant on the solubility of acetone in water.

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Date Submitted 16-Mar-2017

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The effect of dielectric constant on the solubility of acetone in water.

March 15, 2017

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Keywords: dielectric constant, force fields, solubility

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Abstract

Molecular dynamics simulations for liquid acetone, pure component and mixed with water, are performed to analyze the effect that dielectric constant has on the solubility. The all atoms CGenFF and OPLS/AA force fields together with two TraPPE-UA models are used to simulate acetone while the TIP4P/ ϵ is applied for water. The calculated dielectric constant of acetone models at room conditions follows a linear relation with their molecular dipole moment allowing us to understand in simulations the miscibility problem of acetone in water. The experimental liquid and liquid-vapor properties as pure component are reasonable well reproduced with those force fields. The TraPPE-UA models predict for acetone in the liquid phase dielectric constants of 9 and 12, respectively. The experimental value is 21. The values obtained with the OPLS/AA and CGenFF models are 15 and 23, respectively. All the models, except CGenFF, give inhomogeneous mixtures at low and moderate concentrations of acetone.

1 Introduction

There have been a lot of efforts, during the last three decades, to improve the molecular interactions to be used in computer simulations. The widely used OPLS/AA [1], GAFF [2] and CGenFF [3] force fields to develop atomistic simulations have applied quantum chemistry methods to obtain the intramolecular parameters and the partial charges on every atom of isolated molecules. The short ranged parameters involved in the Lennard-Jones, LJ, potential are obtained with Monte Carlo or molecular dynamics simulations to reproduce the liquid density and heat of vaporization [1–3]. It has been shown that those force fields fail to reproduce experimental properties at other thermodynamic conditions [4–6]. The Transferable Potential for Phase Equilibrium, TraPPE, force field [7] was developed to improve the description of molecular interactions in a wide range of thermodynamics conditions. In that case the intramolecular parameters and atomic charges of several chemical groups are also obtained from quantum mechanical calculations. The charges are transferred to similar atoms to build new molecules. The short ranged parameters are fitted to match experimental coexisting densities, vapor pressure and critical point at the liquid-vapor phase equilibrium. The results have been obtained mainly with Monte Carlo methods combined with the histogram reweighting technique. Parameters for all atoms and united atoms versions are available [8] for several molecules.

Stubbs et al. in 2004 parameterized the TraPPE-UA for acetone [9] (here denoted as TraPPE-UA04) to obtain several properties. In what follows we use $X(\text{exp}, \text{calculated})$ to denote the experimental and calculated values of a property X . The reported values are boiling temperature (329.3, 322) K, liquid-vapor coexisting densities, vapor pressures and critical point: T_c (508.1, 508.0) K, ρ_c (0.273, 0.278) g cm^{-3} , P_c (49.2, 55.3) bars. They also reported results for acetone-hexane mixtures but the vapor pressures were overestimated respect the experimental values. A new TraPPE-UA (denoted TraPPE-UA05) was parameterized by Kamath et al. in 2005 [10] to reproduce the minimum pressure azeotropy of chloroform and acetone. They obtained the charges using the CHELPG method for dimers with the MP2 theory and the 6-31g++(3df,3pd) basis set. The new model improves the properties of the original one and they are: boiling temperature (329.3, 327.3) K, T_c (508.1, 508.2) K, ρ_c (0.273, 0.2755) g cm^{-3} , P_c (49.2, 48.5) bars.

Caleman et al in 2012 [11], performed a benchmark to evaluate the capabilities of the OPLS/AA, GAFF and CGenFF to reproduce several properties of 146 polar liquids. They obtained the liquid density, heat of vaporization, dielectric constant (15.4 for acetone using OPLS/AA), surface tension at the liquid-vapor interface, heat capacity, isothermal compressibility and volumetric expansion coefficient. They found that most of the calculated dielectric constants were systematically lower than experimental values. On the other hand, the TraPPE-UA04 force field gives [12] a dielectric constant for methanol of 23 compared with the experimental value of 32. The dielectric constant usually is used to explain miscibility, a polar molecule dissolves in a polar solvent, and it is recognized that plays an important role to describe the solubility of molecules having different degree of polarizability.

Pereyra et al. [13] studied acetone-water mixtures to reproduce the excess enthalpy as a function of concentration at 300 K and 1 atm. The CHARMM27 model of acetone was modified to scale the acetone charges with a parameter that depends on the concentration. The TIP5P-E model of water was used. Results of acetone-water, with united atom models for the methyl groups, were reported by Kesic and Perera in 2012 [14] using the OPLS, TraPPE-UA05 [10] and Weerasinge and Smith [15] force fields for acetone and the SPCE model for water [16] to analyze the micro-heterogeneous nature of the simulated mixture.

The so-called micro-heterogeneities are local arrangements of the same macromolecule or protein according to the first studies done in this respect [17]. Polar fluids such as alcohols also usually exhibit this type of properties, mainly by the formation of hydroxyl bridges promoted by the hydroxyl groups. Pozar *et al.* [18] have discussed the difference between the formation of clusters and the micro-heterogeneities and they found that they are different characteristics of complex systems. The water molecule favors the formation of hydrogen bonds between them more than with other type of molecules such as alcohols. This causes that aggregates fluctuate forming domains. However, in despite the relevant efforts to analyze the micro-structures of the water-acetone mixture through molecular simulation, there is not a systematic study where the dielectric constant is involved into the analysis.

In recent years we have developed force field parameters using as a target prop-

erty the dielectric constant. We found in water [19] that there is a linear relation between the molecular dipole moment with dielectric constant. The dipole moment can be fixed by changing the charges, geometry or both. The procedure allowed us to determine the charge distribution and geometry of water in order to reproduce the experimental dielectric constant and several density anomalies. By using that idea, we have developed a systematic procedure of parameterization that relates potential parameters with macroscopic properties [12]. In that way, the molecular dipole moment is varied until the experimental dielectric constant is reproduced. We also found that the surface tension was very sensitive to changes on the LJ energy parameter, ϵ_{LJ} , but not the dielectric constant and liquid density. Therefore, we varied the ϵ_{LJ} to reproduce the experimental surface tension. The last step in the procedure was to change the σ_{LJ} to reproduce the density. The method has been applied with success to parameterize methanol [12], formamide [5], acetamide [6], formic acid and pyridine [20]. Pérez de la Luz et al. [5] found that a correct value of dielectric constant is required to reproduce the liquid-liquid equilibrium between hexan-2-one and formamide. Aguilar et al. [6] found that a wrong value of dielectric constant does not reproduce its increase with acetamide concentrations in mixtures with water at room conditions.

In this work we have calculated the dielectric constant of acetone for two united atoms, TraPPE-UA04 and TraPPE-UA05, and two all atoms, CGenFF and OPLS/AA, force fields. We found that the dielectric constant follows an almost linear relation with molecular dipole moment. The calculated values varied from 9 for the TIP4P-UA04 to 23 for the CGenFF. The experimental value is 21. It is our interest to analyze the effect that dielectric constant has on the miscibility of acetone in water and also try to understand if the micro-heterogeneities observed in simulations are related with the poor description of the interactions in some force fields.

The work is organized as follows: Section 2 gives the potential parameter and calculated properties. The simulation details are given in section 3. The results for acetone as pure component and mixed with water are given in section 4. Finally the references and conclusions are provided.

2 Potential models and calculated properties

The parameters for the all atoms models of acetone molecules are taken from the web page <http://virtualchemistry.org>. The parameters for the two TraPPE-UA models are from the original references [9, 10]. The geometry of the all atoms models are around the same but the treatment of the angle interactions are different. The CGenFF model uses the Urey-Bradley a harmonic potential between 1-3 nonbonding interactions. The geometry of the two united atoms models is the same. The TIP4P/ ϵ water model [19], which reproduce the dielectric constant at different temperatures and pressures, was used.

The intermolecular parameters of all force fields used in this work are shown in Fig. 1. The main difference between the OPLS/AA and CGenFF parameters is in the value of ϵ_{LJ} on the oxygen atom. For the TraPPE-UA05, the charges of all atoms and ϵ_{LJ} on the carbon atom are different with respect to the original model.

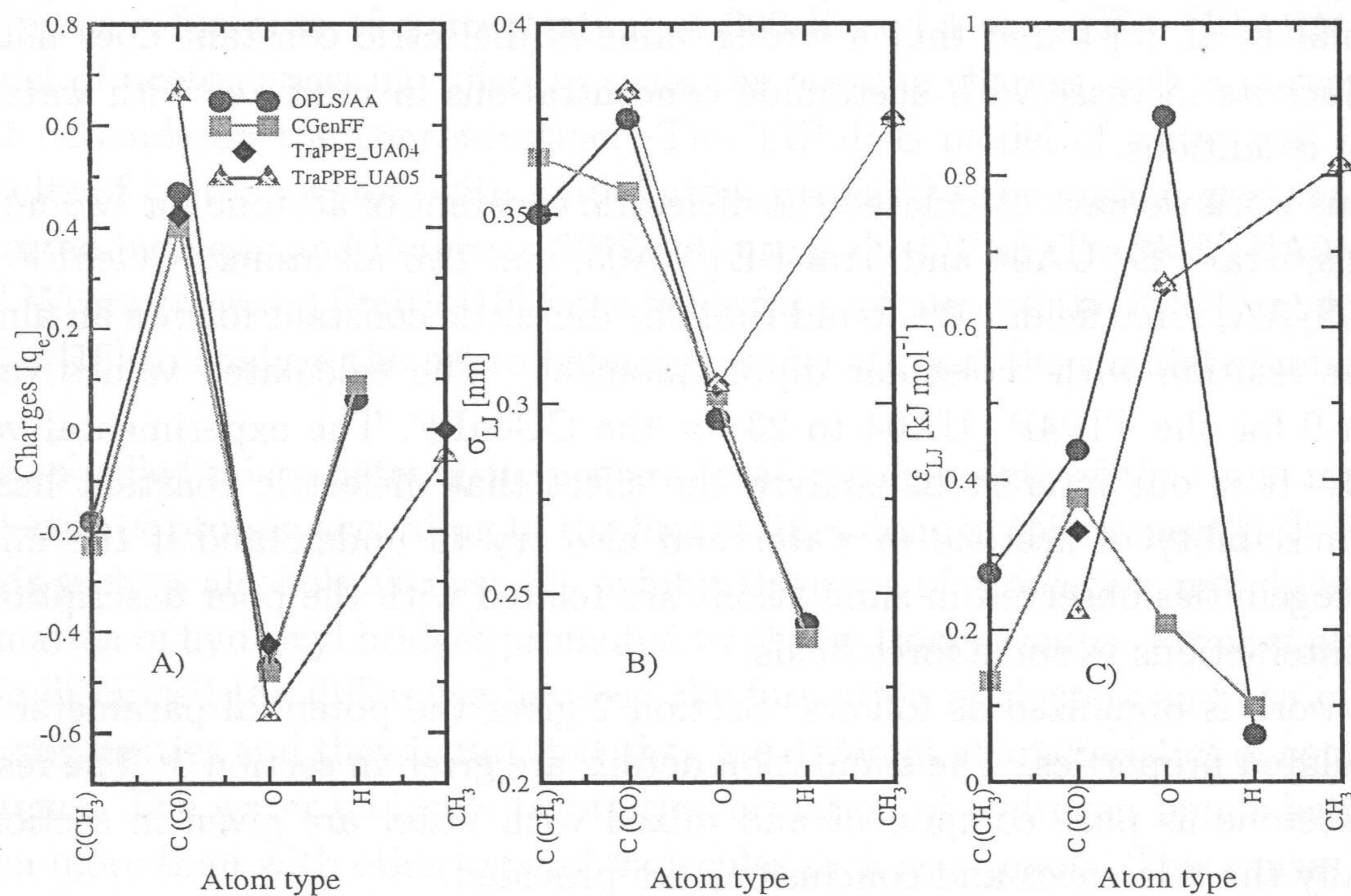


Figure 1: Intermolecular force field parameters for acetone. A) atomic charges. B) σ_{LJ} . C) ϵ_{LJ} .

The dielectric constant is calculated using the dipole moment fluctuations of

the system,

$$\epsilon = 1 + \frac{4\pi}{3k_BVT}(\langle \mathbf{M}^2 \rangle - \langle \mathbf{M} \rangle^2) \quad (1)$$

where k_B is the Boltzmann's constant, T is the absolute temperature, V is the volume of the simulation cell and \mathbf{M} is dipole moment of the system.

$$\mathbf{M} = \sum_i q_i \mathbf{r}_i \quad (2)$$

where q_i and \mathbf{r}_i are the charge and position of atom i , respectively.

2.1 Density profile, $\rho(z)$

It is defined along the Z direction of the simulation cell,

$$\rho(z) = \frac{N(z)}{L_x L_y \Delta z} \quad (3)$$

where $N(z)$ is the number of molecules with positions between z and $z + \Delta z$ in the simulation cell. The dimensions of the simulation cell are L_x , L_y and Δz is the width of the slab. In this work the number of slabs in the Z direction was around 800.

2.2 Surface tension, γ

The surface tension is obtained, as implemented in Gromacs, using the mechanical definition of the pressure for planar interfaces ,

$$\gamma = \frac{1}{2}L_z[\langle P_{zz} \rangle - \frac{1}{2}(\langle p_{xx} \rangle + \langle P_{yy} \rangle)] \quad (4)$$

where $P_{\alpha\beta}$ are the diagonal components of the pressure tensor. The simulated system have two symmetrical interfaces that is why the result is divided by 2.

2.3 Heat of vaporization, ΔH_v

It is calculated assuming the gas is ideal.

$$\Delta H_v = H_v - H_L = U_v + RT - (U_L + PV) \quad (5)$$

where H_v and H_L are the enthalpy of the gas and liquid, respectively. The potential energy of an isolated molecule at the same temperature in the gas and liquid phases are U_v and U_L , respectively. The term PV is for the liquid phase.

3 Simulation details

Simulations on the liquid phase for acetone are performed using the isothermal-isobaric ensemble [21] to obtain the density, dielectric constant, self-diffusion coefficient and heat of vaporization using the Gromacs package [22] and own programs. The number of molecules were 512 for all the force fields studied in this work. The leap-frog equations of motions were solved with a time step of 2 fs. Periodic boundary conditions were used in all directions and the bond distances were kept rigid with the LINCS procedure.

For the liquid simulations of acetone-water mixtures were used 1024 water molecules for the OPLS/AA and CGenFF but the total number of 4096 was used for the TraPPE-UA models in the semiisotropic NPT ensemble to determine properly the phase separation and miscibility of acetone. The simulation cell in the latter case were around $L_x=L_y = 5.5$ nm and L_z varied from 7.8 nm to 10.4 nm for systems with molar fractions from 0.25 to 0.75.

The gas simulations were carried out with one molecule at 298.15 K using the stochastic dynamics method and a thermostat parameter of 2 ps.

In all simulations the Ewald sum with tinfoil boundary conditions was applied to determine the electrostatic interactions with a tolerance of 10^{-6} to evaluate the real contribution. The cut-off distance was 1.2 nm for the real part and LJ interactions where analytical long range corrections were applied. The PME method was applied to evaluate the reciprocal contribution with a grid of 0.12 nm for the reciprocal vectors with a spline of order 4. The Nose-Hoover thermostat and Parrinello-Rahman barostat were applied with parameters of 0.6 ps and 1.0ps, respectively. The average properties were obtained for at least 10 millions of configurations after equilibration.

The liquid-vapor simulations were carried out with a number of molecules in the range of 4000 to 6000 depending on the particular case. The parameters for electrostatic interactions were the same as those of liquid simulations. The dimensions of the simulation cell were around $L_x=L_y$ 5.2nm and L_z between 30 nm and 50 nm. The cut-off distance for the LJ interactions was 2.5 nm without long range corrections to calculate accurately the surface tension, vapor pressure and coexisting densities. The Nose-Hoover thermostat was applied with a parameter of 0.6 ps. The average properties were calculated for at least 4 million configurations after an equilibration period of 3 million steps.

4 Results

We report results of acetone as pure component and mixed with water in the liquid phase and at the liquid-vapor phase equilibrium. The effect of temperature and acetone concentration on density, dielectric constant and surface tension is included.

4.1 Pure acetone in a liquid phase and at the liquid-vapor interface

Simulation results at room conditions are shown in Fig. 2 as a function of the molecular dipole moment, $\mu = \sum_i q\mathbf{r}_i$. The dielectric constant increases linearly with μ . The result for the CGenFF is 9.5% larger than the experimental value of 21 [23] while the TraPPE-UA04 model gives a value which is 57 % smaller. The dielectric constant of OPLS/AA and TraPPE-UA05 are 12 and 15, respectively. The low dielectric constant of the TraPPE-UA04 means the molecules have weaker interactions than molecules in the other models. That is reflected in the largest values of the self-diffusion coefficient and vapor pressure. The smallest value of the heat of vaporization is also a consequence. The CGenFF follows an opposite behavior, it gives the smallest values for those properties. The best results, which are closer to the experimental values [24, 25], are given by the TraPPE-UA05 and OPLS/AA models.

Results of pure acetone are shown in Fig. 3 to analyze the transferability of model parameters at different temperatures. The main difference of results from different models is found in the dielectric constant at all temperatures. There is a good agreement between experimental and calculated values for the liquid

density and surface tension for all the models. The surface tension obtained with the TraPPE-UA models are slightly larger than experimental data at 298.15 K.

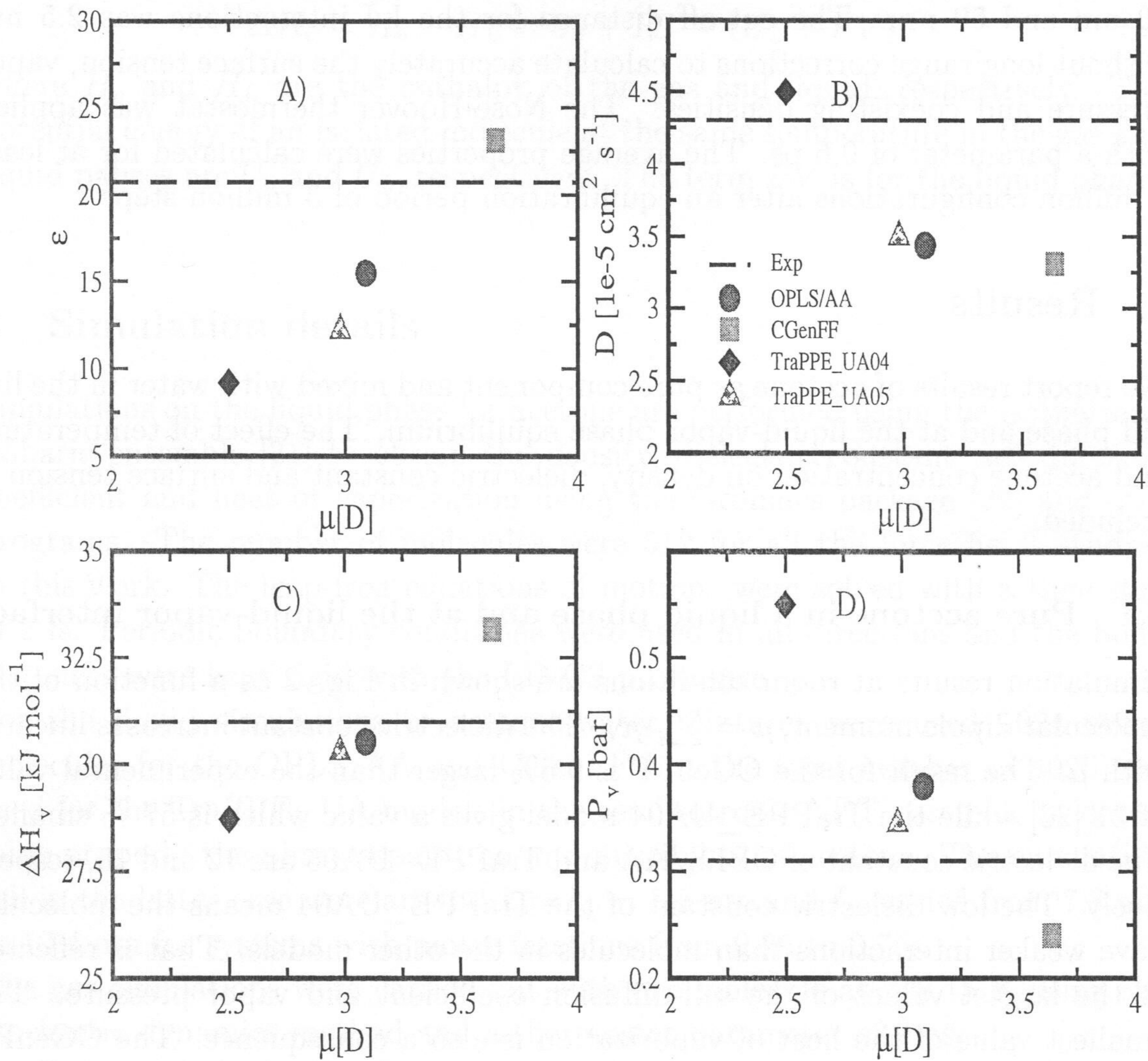


Figure 2: Results at 298.15 K as a function of the molecular dipole moment of the models compared with experimental values. A) Dielectric constant. B) Self-diffusion coefficient. C) Change of vaporization enthalpy. D) Vapor pressure at the liquid vapor interface.

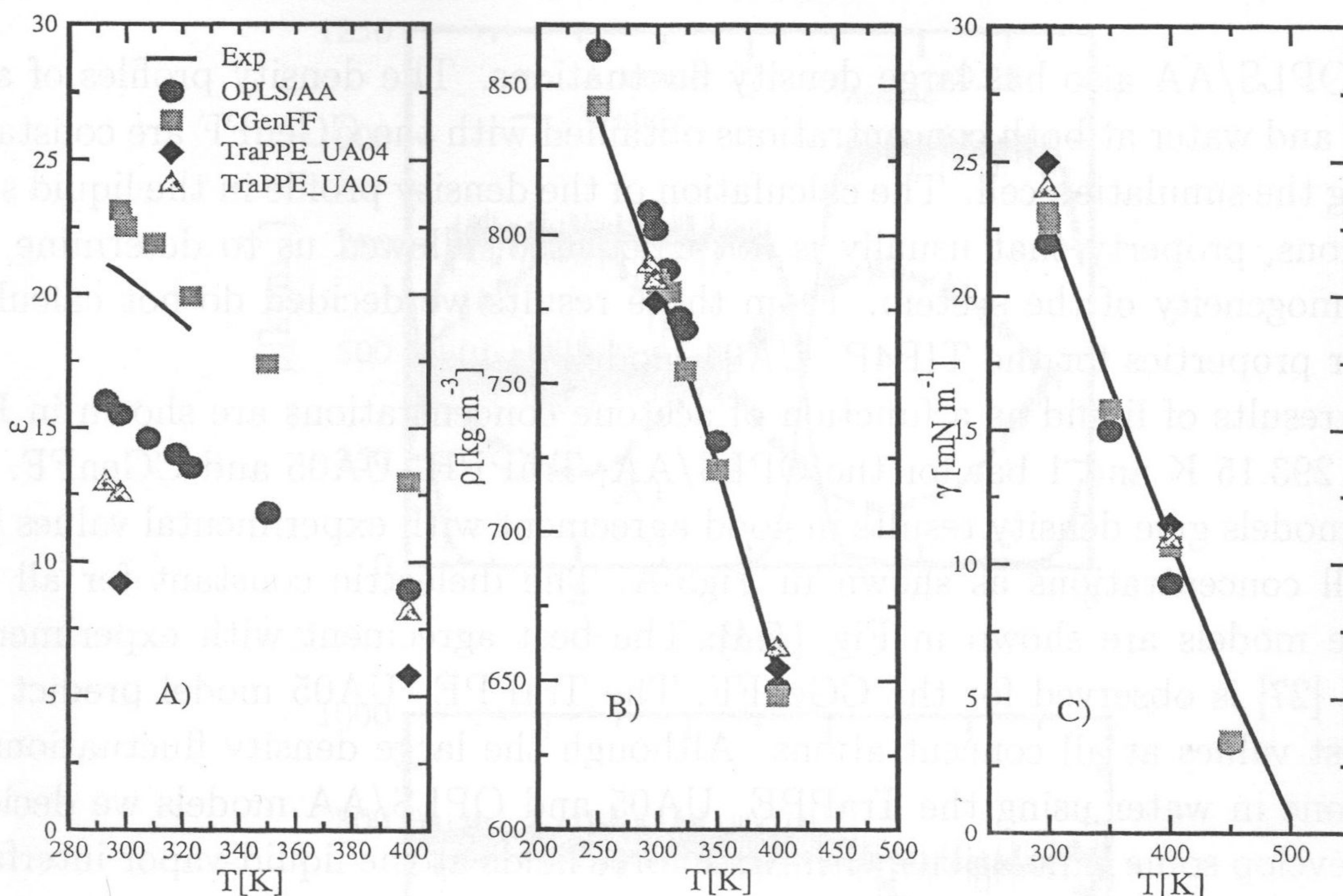


Figure 3: Results of pure acetone at different temperatures compared with experimental values [23, 25]. A) Dielectric constant, B) density. C) Surface tension at the liquid-vapor interface. The liquid simulations are performed at 1 bar.

4.2 Acetone-water mixtures in a liquid phase

Simulation results of selected density profiles of acetone-water mixtures are shown in Fig. 4 for the two TraPPE-UA models and CGenFF. The acetone concentrations are 0.25 and 0.75. The results in Fig. 4-A for the TraPPE-UA models show that the systems are not homogeneous. The TraPPE-UA04 predict a phase separation into two liquids, in complete disagreement with experiment, one phase rich in acetone and the other is rich in water. The density profiles from the TraPPE-UA05 are better than those obtained with the original model but the densities have large fluctuations along the simulation cell. The visual inspection using some snapshots shows that there are large domains of acetone in water. The results for the molar fraction of acetone of 0.75 are shown in Fig. 4-B. It is seen that, even at that high concentration, the system obtained using the TraPPE-UA04 is not homogeneous, it has large fluctuations of the density at around 8 nm. The TraPPE-UA05 has also small fluctuations at around the same position. The density profile of acetone, not shown, using

the OPLS/AA also has large density fluctuations. The density profiles of acetone and water at both concentrations obtained with the CGenFF are constants along the simulation cell. The calculation of the density profile in the liquid simulations, property that usually is not calculated, allowed us to determine the inhomogeneity of the system. From those results we decided do not calculate other properties for the TIP4P-UA04 model.

The results of liquid as a function of acetone concentrations are shown in Fig. 5 at 293.15 K and 1 bar for the OPLS/AA, TraPPE-UA05 and CGenFF. All the models give density results in good agreement with experimental values [26] at all concentrations as shown in Fig5-A. The dielectric constant for all the three models are shown in Fig. 5-B. The best agreement with experimental data [27] is observed for the CGenFF. The TraPPE-UA05 model predict the lowest values at all concentrations. Although the large density fluctuations of acetone in water using the TraPPE-UA05 and OPLS/AA models we decided to develop some simulations with those force fields at the liquid-vapor interface.

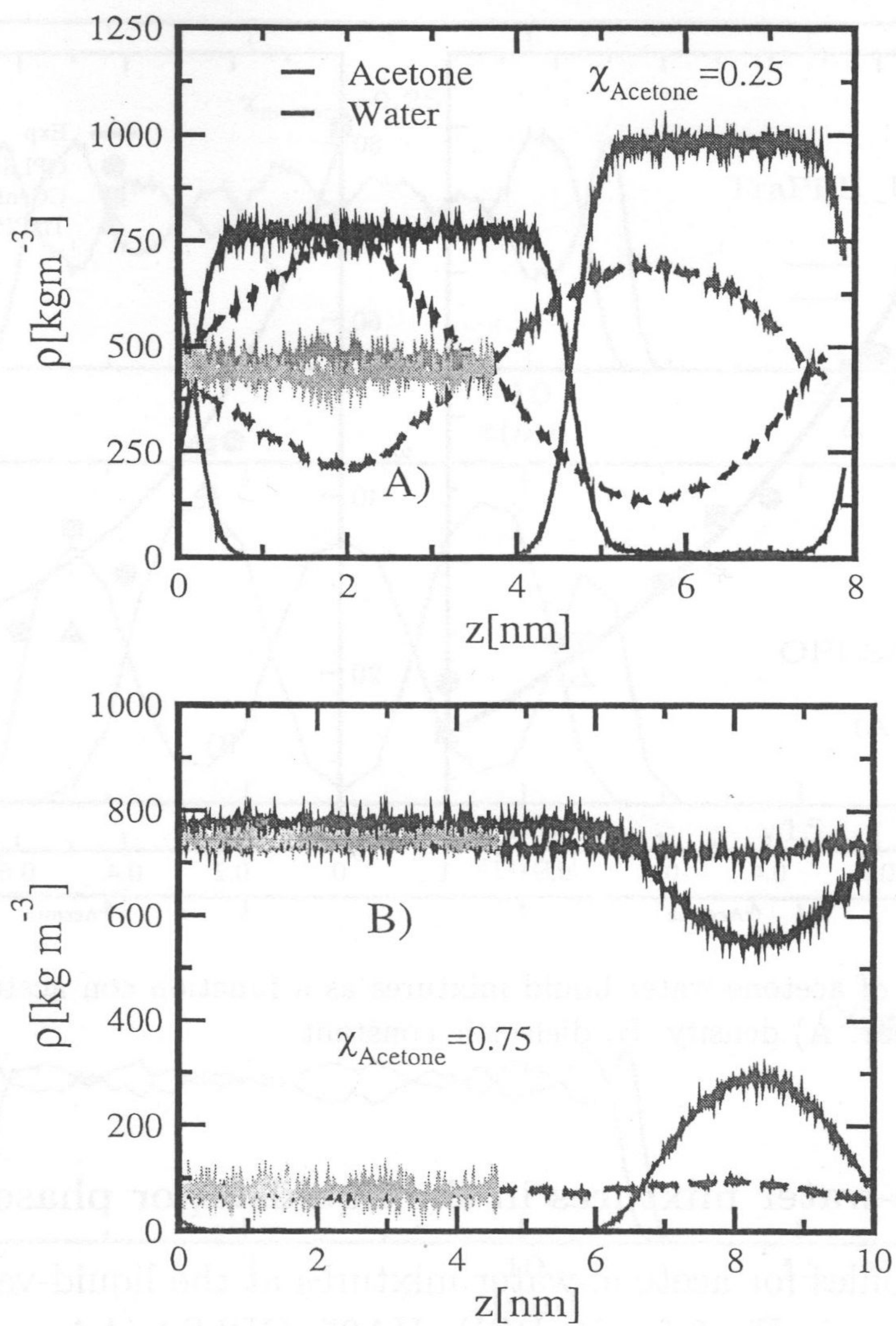


Figure 4: Density profiles of acetone-water mixtures at 298.15 K and 1 bar for TraPPE-UA04, TraPPE-UA05 and CGenFF. A) Acetone molar fraction of 0.25. B) Acetone molar fraction of 0.75. The simulations of CGenFF were performed in the isotropic NPT ensemble in a cubic cell with 1024 molecules. The simulations for the TraPPE-UA model were carried out in the semi-isotropic NPT ensemble in an elongated cell in the Z direction using 4096 molecules.

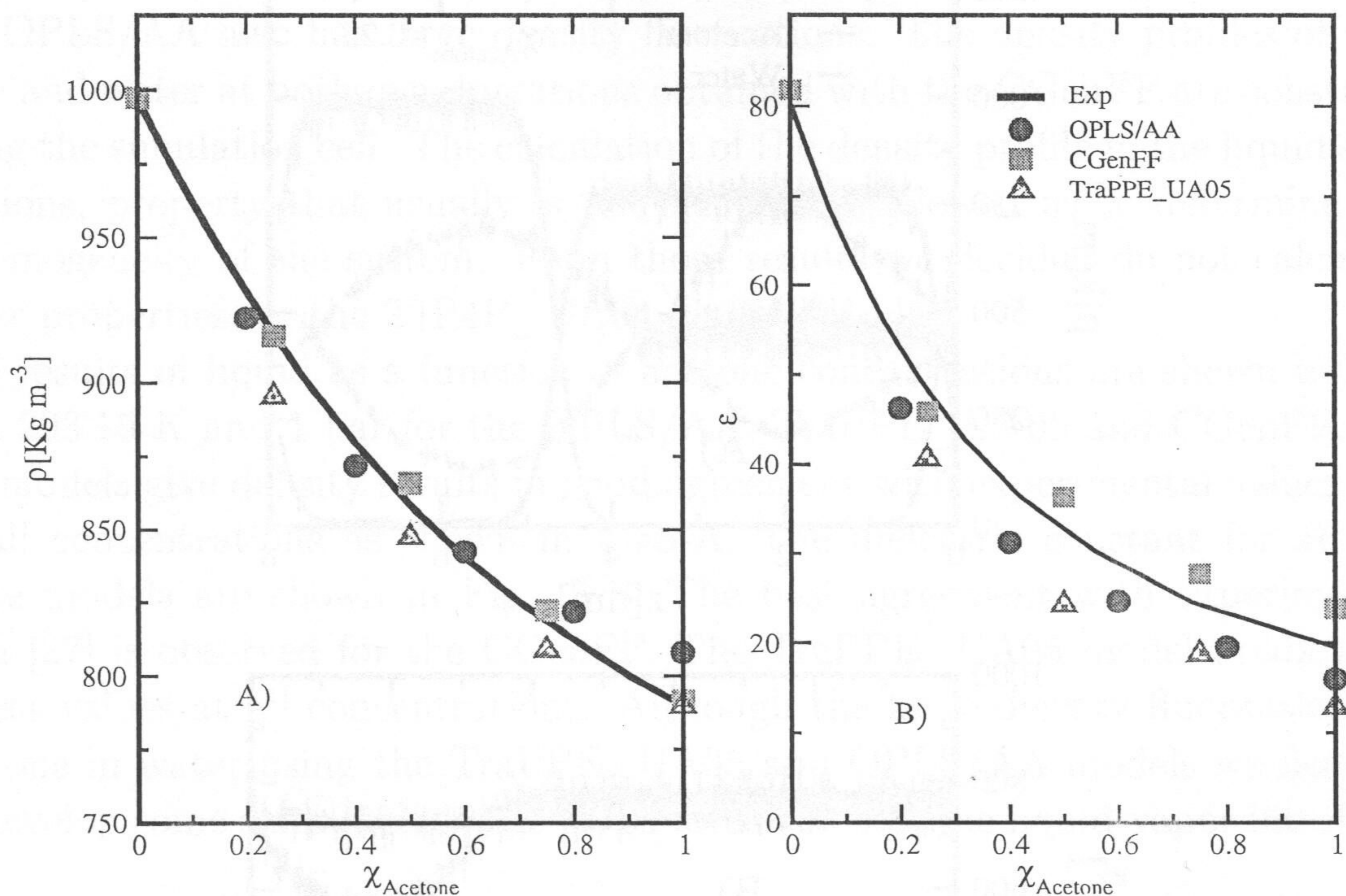


Figure 5: Results of acetone-water liquid mixtures as a function of acetone concentration at 293.2K and 1 bar. A) density. B) dielectric constant.

4.3 Acetone-water mixtures in the liquid-vapor phase equilibrium

The density profiles for acetone-water mixtures at the liquid-vapor phase equilibrium are shown in Fig.6 for TraPPE-UA05, OPLSA/AA and CGenFF with acetone molar fraction of 0.25 at 298.15 K. The results obtained using the TraPPE-UA05 and OPLS/AA have large fluctuations and the bulk region is not homogeneous. The results from CGenFF has a slight adsorption of acetone molecules at the liquid-vapor interface but the liquid phase is homogeneous. From those results we decided to calculate the surface tension for the acetone-water mixtures only for the CGenFF. The results are shown in Figure 7 and they have an excellent agreement with experimental data.

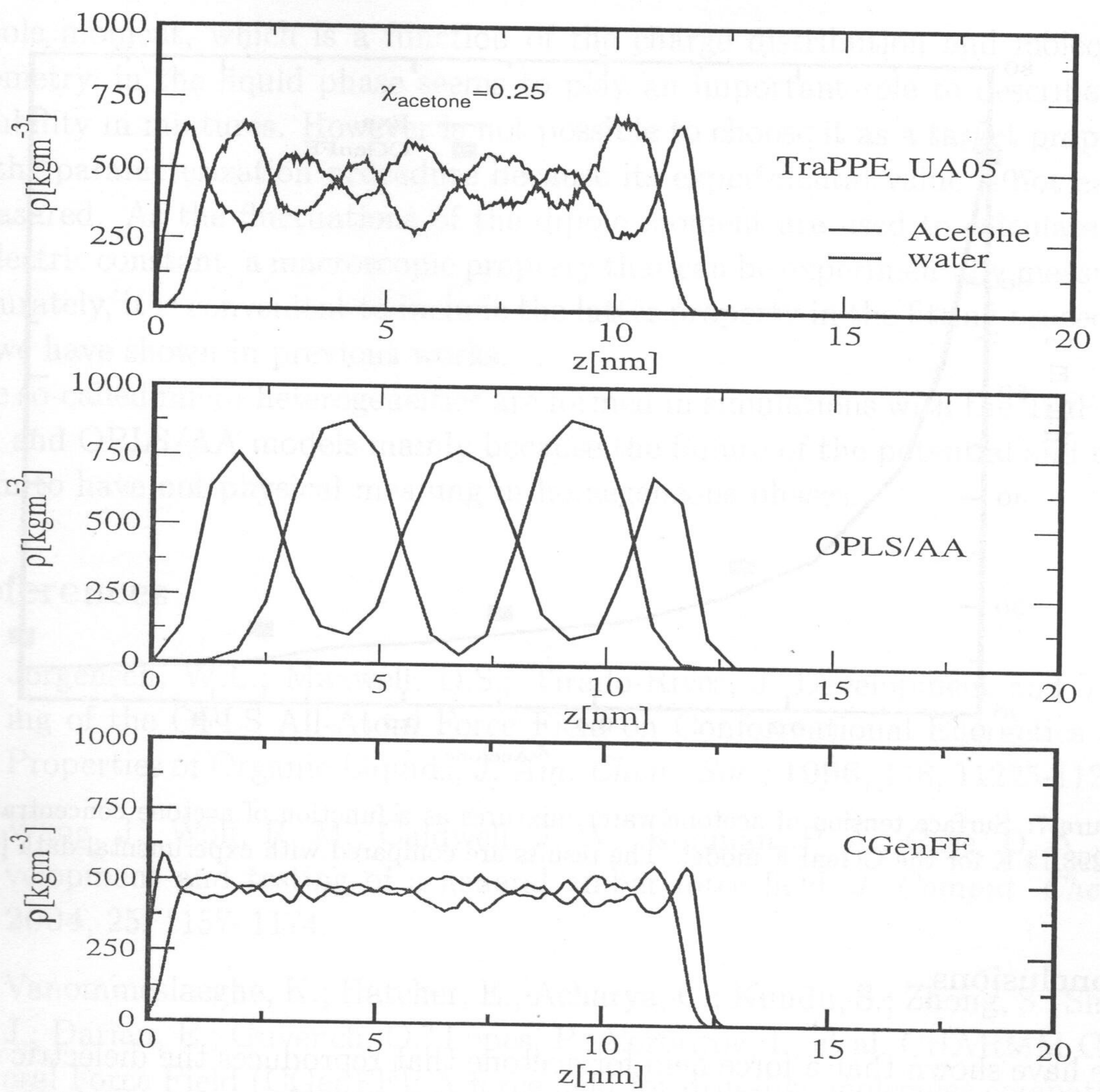


Figure 6: Density profiles of acetone-water mixtures at 298.15 K at acetone concentration of 0.25. A) TraPPE-UA05. B) OPLS/AA. C) CGenFF

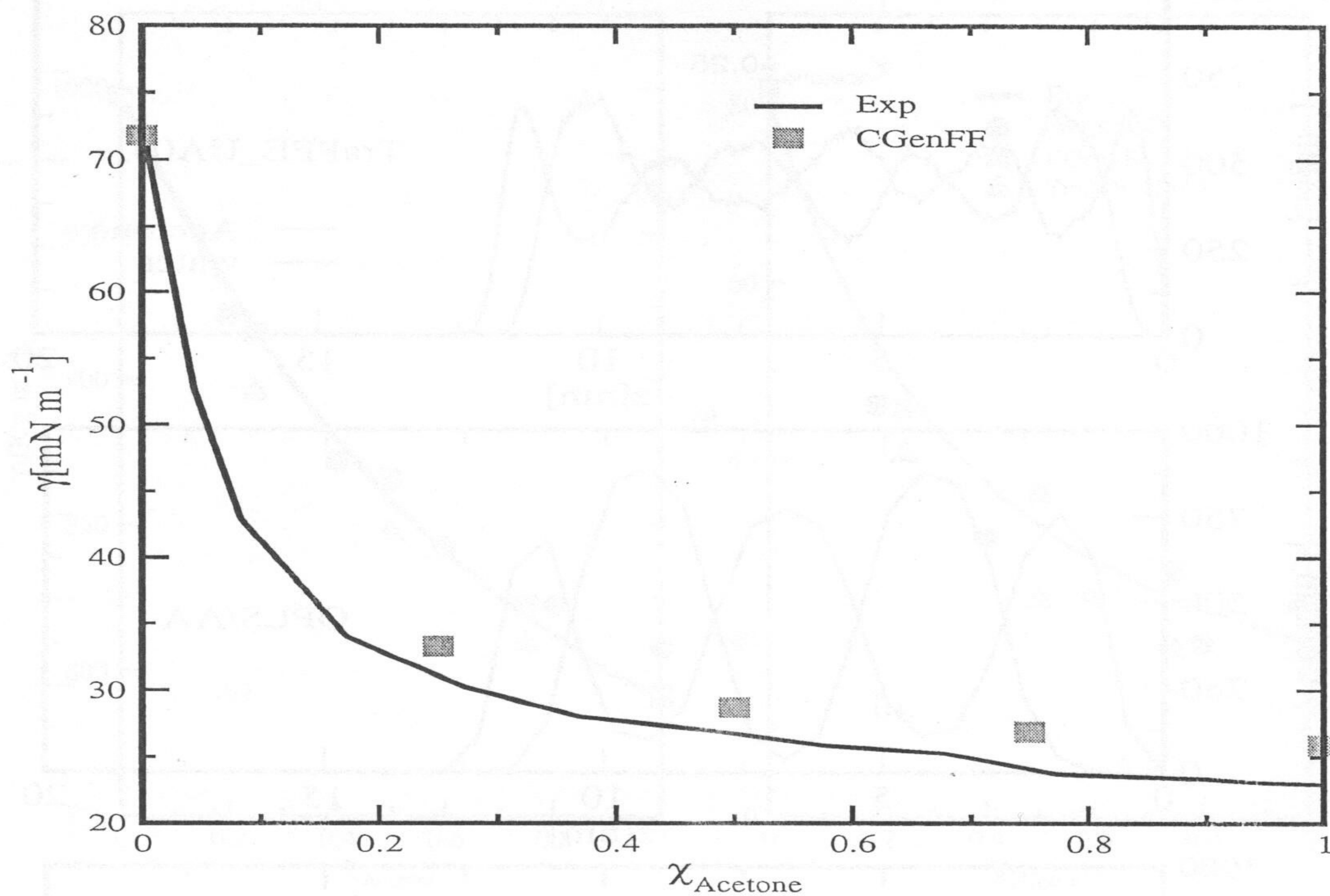


Figure 7: Surface tension of acetone-water mixtures as a function of acetone concentration at 298.15 K for the CGenFF model. The results are compared with experimental data [26]

Conclusions

We have shown that a force field for acetone that reproduces the dielectric constant at room conditions gives also a good description of macroscopic properties for pure component at different temperatures and mixed with water at several concentrations.

The TraPPE-UA models give excellent results for the pure component at all temperatures but they fail to describe the correct miscibility of acetone in water in a wide range of concentrations. The obtained results show that in order to parameterize a force field is not enough to reproduce thermodynamic properties of pure components and mixtures with fluids which have around the same dielectric constant but it is required to test the models with solvents like water which have a larger value.

The results from this work and others reported by our group also show that the use of polarizable force fields might not be needed to obtain the dielectric constant and the correct solubility of polar molecules in mixtures. The molecular

dipole moment, which is a function of the charge distribution and molecular geometry, in the liquid phase seems to play an important role to describe the solubility in mixtures. However is not possible to choose it as a target property in the parameterization procedure because its experimental value is not easily measured. As the fluctuations of the dipole moment are used to calculate the dielectric constant, a macroscopic property that can be experimentally measured accurately, it is convenient to include the latter property in the fitting procedure as we have shown in previous works.

The so-called micro-heterogeneities are formed in simulations with the TraPPE-UA and OPLS/AA models mainly because the failure of the potential and they seem to have not physical meaning in homogeneous phases.

References

- [1] Jorgensen, W.L.; Maxwell, D.S.; Tirado-Rives, J. Development and Testing of the OPLS All-Atom Force Field on Conformational Energetics and Properties of Organic Liquids, *J. Am. Chem. Soc.*; **1996**, 118, 11225-11236.
- [2] Wang, J.; Wolf, R. M.; Caldwell, J. W.; Kollman, P. A.; Case, D. A. Development and testing of a general amber force field. *J. Comput. Chem.*; **2004**, 25, 1157-1174.
- [3] Vanommeslaeghe, K.; Hatcher, E.; Acharya, C.; Kundu, S.; Zhong, S.; Shim, J.; Darian, E.; Guvench, O.; Lopes, P.; Vorobyov, I.; et al. CHARMM General Force Field (CGenFF): A force field for drug-like molecules compatible with the CHARMM all-atom additive biological force fields *J. Comput. Chem.*; **2010**, 31(4), 671-690.
- [4] van Leeuwen, M. E.; Smit, B.; Molecular simulation of the vapor-liquid curve of methanol *J. Phys. Chem.*; **1995**, 99, 1831.
- [5] Pérez de la Luz, A.; Méndez-Maldonado, G.A.; Núñez-Rojas, E.; Bresme, F.; Alexandre, J. A New Force Field of Formamide and the Effect of the Dielectric Constant on Miscibility *J. Chem. Theory Comput.*; **2015**, 11 (6), 2792-2800.
- [6] Aguilar-Pineda, J. A.; Méndez-Maldonado, G. A.; Núñez-Rojas, E.; Alexandre, J. Parametrisation of a force field of acetamide for simulations of the liquid phase.; *Mol. Phys.*; **2015**, 113, 17-18.

- [7] Martin, M. G.; Siepmann, J.; Transferable Potentials for Phase Equilibria. 1. United-Atom Description of n-Alkanes *J. Phys. Chem. B.*; **1998**, 102, 2569 - 2577.
- [8] <http://chem-siepmann.oit.umn.edu/siepmann/trappe/index.html>.
- [9] Stubbs, M.; Potoff, J.; Siepmann, J.; Transferable Potentials for Phase Equilibria. 6. United-atom description for ethers, glycols, ketones and aldehydes *J. Phys. Chem. B.*; **2004**, 108, 17596-17605.
- [10] Kamath, G.; Georgiev, G.; Potoff, J. Molecular Modeling of Phase Behavior and Microstructure of Acetone-Chloroform-Methanol Binary Mixtures, *J. Phys. Chem. B.*; **2005**, 109, 19463-19473.
- [11] Caleman, C.; van Maaren Paul, J.; Hong, M.; Jochen, S.; Luciano T.; Van der Spoel, D. Force Field Benchmark of Organic Liquids: Density, Enthalpy of Vaporization, Heat Capacities, Surface Tension, Isothermal Compressibility, Volumetric Expansion Coefficient, and Dielectric Constant, *J. Chem. Theory Comput.*; **2012**, 8, 61-74.
- [12] Salas, F.J.; Méndez-Maldonado, G.A.; Núñez-Rojas, E.; Aguilar-Pineda, J.A.; Domínguez, H.; Alejandre, J. *J. Chem. Theory and Comput.*; **2015**, 11, 683.
- [13] Pereyra, R. G.; Asar, M. L.; Carignano, M. A., The role of acetone dipole moment in acetone-water mixture. *Chem. Phys. Lett.* ; **2011**, 507, 240-243.
- [14] Kesic. B.; Perera, A.; Revisiting aqueous-acetone mixtures through the concept of molecular emulsions *J. Chem. Phys.*; **2012**, 137, 134502.
- [15] Weerasinghe, S.; Smith, P.E.; Kirkwood-Buff derived force field for mixtures of acetone and water, *J. Chem. Phys.*; **2003**, 118, 10663.
- [16] Berendsen, H. J. C.; Grigera, J. R.; Straatsma, T. P.; The missing term in effective pair potentials. *J. Phys. Chem.*; **1987** , 91, 6269-6271.
- [17] Colvin, J. R.; Smith, D.B.; and Cook, W.H. The microheterogeneity of proteins, *Chem. Rev.*; **1954** , 54, 687-711.
- [18] Pozar, M.; Lovrinevic, B.; Zoranic, L.; Primorac, T.; Sokolica, F.; Perera, A. Micro-heterogeneity versus clustering in binary mixtures of ethanol with water or alkanes, *Phys. Chem. Phys.*; **2016**, 18, 23971.

- [19] Fuentes-Azcatl, R.; Alejandre, J. Non-Polarizable Force Field of Water Based on the Dielectric Constant: TIP4P/ ϵ , *J. Phys. Chem. B.*; **2014**, 118, 1263-1272.
- [20] Salas, F. J.; Núñez-Rojas, E.; Alejandre, J. Stability of formic acid/pyridine and isonicotinamide/formamide cocrystals by molecular dynamics simulations. *J. Theor Chem Acc.*; **2017**, 17, 136.
- [21] Tuckerman, M. E.; *Statistical Mechanics: Theory and Molecular Simulation.*; Oxford University Press, **2010**.
- [22] Hess, B.; Kutzner, C.; van der Spoel, D.; Lindahl, E. GROMACS 4: Algorithms for highly efficient, load-balanced, and scalable molecular simulation. *J. Chem. Theory. Comput.*; **2008**, 4, 435-447.
- [23] Lide, D.R. *CRC Handbook of Chemistry and Physics*; CRC Press: Cleveland, Ohio, **2009**.
- [24] Kamei, Y.; Oishi, Y. Self-Diffusion Coefficients and Interdiffusion Coefficient in Acetone-Benzene System. *Bulletin of the Chem. Soc. of Japan*, **1972**, 45, 2437-2439.
- [25] Yaws, K.L. *Chemical Properties Handbook*; McGraw-Hill, **1999**.
- [26] Sabine, E.; Heike, K.; Jochen, W. Surface Tension of the Ternary System Water+Acetone+Toluene. *J. Chem. Eng. Data.*; **2007**, 52, 1072-1079.
- [27] Wang, P.; Anderko, A.; Computation of dielectric constants of solvent mixtures and electrolyte solutions. *Fluid Phase Eq.*; **2001**, 186, 103-122.

Discusión general y conclusiones

Uno de los objetivos de éste trabajo de investigación es analizar la formación de micro-heterogeneidades en mezclas de acetona-agua, las micro-heterogeneidades son arreglos locales que se presentan en sistemas formados por moléculas de gran tamaño, la formación de estas estructuras se observó por primera vez en un estudio realizado con proteínas [13]. En 2015 Pozar M.; et. al. [14] realizó un estudio en mezclas de benceno-acetona y benceno-alcoholes en donde se observó la formación de dominios moleculares, cuando se tienen varios dominios moleculares, se da origen a las micro-heterogeneidades. Particularmente, en este trabajo analizamos la relación entre la constante dieléctrica de cada modelo de acetona usado y la aparición de los dominios moleculares.

Se realizó el estudio de mezclas acuosas de acetona empleando simulación con dinámica molecular, esta metodología consiste en resolver las ecuaciones de movimiento de Newton de manera simultánea para todas y cada una de las moléculas presentes en el sistema de estudio, uno de los principales problemas al emplear métodos de simulación por computadora consiste en contar con campos de fuerza que reproduzcan de manera adecuada todas las propiedades importantes del sistema, incluida la constante dieléctrica. El problema que se observa aquí, es que la mayoría de los campos de fuerza existentes en la literatura son reparametrizados para reproducir propiedades específicas en líquido puro, en este caso se emplearon cuatro distintos campos de fuerza: OPLS/AA (Optimized Potential for Liquid Simulations /All Atom) [15] y CGenFF (CHARMM Generalize Force Field) [16] que fueron parametrizados para reproducir densidad de líquido y ΔH_{vap} , también se emplearon dos modelos de átomo unido (TraPPE-UA04 [17], TraPPE-UA05 [18]) los cuales fueron reparametrizados para reproducir densidades de líquido-vapor, presión de vapor y algunas propiedades críticas de fluidos puros. Además, para nuestro análisis tomamos en cuenta el modelo de agua TIP4P/ ϵ [19] que reproduce la constante dieléctrica experimental del agua a condiciones de temperatura ambiente.

Cada uno de estos modelos de acetona considerados aquí arroja un valor diferente para la constante dieléctrica a temperatura ambiente. Hallamos que los modelos de acetona con una constante dieléctrica baja promueven la formación de dominios moleculares, y por el contrario el modelo de acetona que reproduce la constante dieléctrica experimental no promueve dichos arreglos. Esto nos deja ver que los dominios moleculares no tienen un fundamento físico.

Para confirmar esta conclusion hicimos simulaciones extras en la fase líquida de la mezcla agua-acetona a condiciones de temperatura ambiente y 1atm de presión, usando todos y cada uno de los campos de fuerza considerados aqui. Como un resultado importante en la mezcla acuosa observamos que los modelos de acetona con una pobre constante dielectrica (lejos del dato experimental) mostraban perfiles de densidad con dominios moleculares y en donde se observaba claramente un fluido inhomogeneo, es decir, una separacion de fases, esto representa un grave problema debido a que no se reproduce el comportamiento físico del sistema ya que experimentalmente se sabe que esta mezcla es completamente soluble.

Como conclusion final diremos que para construir un buen campo de fuerza de alguna molecula es necesario reproducir la constante dieléctrica experimental tambien, y no basta con exigirle al modelo que reproduzca el momento dipolar, para garantizar una buena solubilidad en agua o en otro disolvente.

[1] A. Wakisaka, D. A. Cooke, Y. Sugimoto and T. Kajimura, *J. Chem. Phys.*, **124**, 124701 (2006)

[2] A. Wakisaka, S. Kamada and T. Ueno, *J. Chem. Phys.*, **124**, 124702 (2006)

[3] T. Takayama, I. Tamura and H. Wakabayashi, *J. Chem. Phys.*, **119**, 2004 (2004)

[4] H. Nishida and K. Yamamoto, *J. Chem. Phys.*, **109**, 7347 (1998)

[5] M. Nishi, H. Koga, G. Ohshima, K. Yamamoto, T. Takayama and H. Nishida, *J. Chem. Phys.*, **113**, 2987 (2000)

[6] M. Matsumoto, N. Nishi, T. Furusawa, M. Iwata, T. Takayama, M. Yamamoto and G. Ohshima, *Bull. Chem. Soc. Jpn.*, **71**, 1211 (1998)

[7] E. Diner, J. Oren, W. C. K. Poon, J. L. Barral and A. M. S. Silva, *Phys. Rev. E*, **61**, 036102 (2000)

[8] G. Nandoriya, Y. Kodera and T. Sugita, *J. Chem. Phys.*, **117**, 3184 (2002)

[9] K. Nomura, H. Harashina and T. Sugita, *J. Phys. Chem. B*, **10**, 6594 (2006)

[10] M.P. Allen and D.J. Tildesley, *Computer Simulation of Liquids*, Clarendon Press Oxford, 1997

[11] J. R. Challa, D. B. Smith, and W. H. Stock, *Chem. Rev.*, **54**, 1559 (1954)

[12] M. Jiang, H. Lyubchik, I. Yermak, T. Illmer, M. P. Siskin, A. Poma, *Phys. Chem. Phys.*, **28**, 2018 (2016)

[13] W. L. Jorgensen, D. S. Maxwell, J. Tirado-Rives, *J. Am. Chem. Soc.*, **114**, 1099 (1992)

[14] S. Vignuzzi, S. G. Hatcher, C. Acharyo, S. Kundu, S. Zheng, J. Zhang, S. Datta, O. Guvench, P. Datta, I. Yermak, et al. *J. Comput. Chem.*, **31**, 17 (2010)

[15] ...

Bibliografía

- [1] C. Reichardt, T. Welton, *Solvents and Solvent Effects in Organic Chemistry*, John Wiley & Sons, 2011.
- [2] V.P. Sokhan and D.J. Tildesley, *Mol. Phys.* 92 (1997) 625.
- [3] A. Wakisaka, H. A. Carime, Y. Yamamoto and Y. Kiyozumi, *J. Chem. Soc., Faraday Trans.*, 94 (1998) 369.
- [4] A. Wakisaka, S. Komatsu and Y. Usui, *J. Mol. Liq.*, 90 (2001) 175.
- [5] T. Fukasawa, Y. Tominaga and A. Wakisaka, *J. Phys. Chem. A*, 108 (2004) 59.
- [6] N. Nishi and K. Yamamoto, *J. Am. Chem. Soc.*, 109 (1987) 7353.
- [7] N. Nishi, K. Koga, C. Ohshima, K. Yamamoto, U. Nagashima and K. Nagami, *J. Am. Chem. Soc.*, 110 (1988) 5246.
- [8] M. Matsumoto, N. Nishi, T. Furusawa, M. Saita, T. Takamuku, M. Yamagami and T. Yamaguchi, *Bull. Chem. Soc. Jpn.*, 68 (1995) 68, 1775.
- [9] S. Dixit, J. Crain, W. C. K. Poon, J. L. Finney and A. K. Soper, *Nature*, 416 (2002) 829.
- [10] K. Nishikawa, Y. Koderu and T. Iijima, *J. Phys. Chem.*, 91 (1987) 3694.
- [11] K. Nishikawa, H. Hayashi and T. Iijima, *J. Phys. Chem.*, 93 (1989) 6559.
- [12] M.P. Allen and D.J. Tildesley, *Computer simulations of liquids*, Clarendon Press Oxford 1991.
- [13] J. R. Colvin, D.B. Smith, and W.H. Cook, *Chem. Rev.*; 54, (1954) 687.
- [14] M. Pozar, B. Lovrinevic, L. Zoranic, T. Primorac, F. Sokolica, A. Perera, *Phys. Chem. Phys.*; 18,(2016) 23971.
- [15] W.L. Jorgensen, D.S. Maxwell, J. Tirado-Rives, *J. Am. Chem. Soc.*; 118, (1996), 11225.
- [16] K. Vanommeslaeghe, E. Hatcher, C. Acharya, S. Kundu, S. Zhong, J. Shim, E. Darian, O. Guvench, P. Lopes, I. Vorobyov, et al. *J. Comput. Chem.*; 31(4), (2010) 671.

[17] M. Stubbs, J. Potoff, J. Siepmann, *J. Phys. Chem. B*; 108, (2004) 17596.

[18] M. G. Martin, J. Siepmann *J. Phys. Chem. B.*; 102, 1998, 2569.

[19] R. Fuentes-Azcatl, J. Alexandre, *J. Phys. Chem. B.*; 118, 2014, 1263.