

Isabela Quintela Matos

**Partition Coefficient Calculations of  
Molecules Mimicking Asphaltenes Through  
Molecular Simulation Using The  
Coarse-Grained SAFT- $\gamma$  Mie Force Field**

Rio de Janeiro

2018

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Dissertação de Mestrado apresentada ao  
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Escola de Química, Universidade Federal  
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Universidade Federal do Rio de Janeiro

Escola de Química

Programa de Pós-Graduação em Tecnologia de Processos Químicos e Bioquímicos

Supervisor: Charlles Rubber de Almeida Abreu

Co-supervisor: Papa Matar Ndiaye

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Elemento opcional da [ABNT](#) (2011, 4.2.1.2). Exemplo:

FERRIGNO, C. R. A. **Tratamento de neoplasias ósseas apendiculares com reimplantação de enxerto ósseo autólogo autoclavado associado ao plasma rico em plaquetas**: estudo crítico na cirurgia de preservação de membro em cães. 2011. 128 f. Tese (Livre-Docência) - Faculdade de Medicina Veterinária e Zootecnia, Universidade de São Paulo, São Paulo, 2011.

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**Charles Rubber de Almeida Abreu**  
Orientador

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**Professor**  
Convidado 1

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**Professor**  
Convidado 2

Rio de Janeiro  
2018

*Este trabalho é dedicado às crianças adultas que,  
quando pequenas, sonharam em se tornar cientistas.*

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<sup>1</sup> Os nomes dos integrantes do primeiro projeto *abnT<sub>E</sub>X* foram extraídos de <<http://codigolivres.org.br/projects/abntex/>>

<sup>2</sup> <<http://www.cpai.unb.br/>>

<sup>3</sup> <<http://groups.google.com/group/latex-br>>

<sup>4</sup> <<http://groups.google.com/group/abntex2>> e <<http://www.abntex.net.br/>>

*“Não vos amoldeis às estruturas deste mundo,  
mas transformai-vos pela renovação da mente,  
a fim de distinguir qual é a vontade de Deus:  
o que é bom, o que Lhe é agradável, o que é perfeito.  
(Bíblia Sagrada, Romanos 12, 2)*



# Abstract

Segundo a [ABNT \(2003, 3.1-3.2\)](#), o resumo deve ressaltar o objetivo, o método, os resultados e as conclusões do documento. A ordem e a extensão destes itens dependem do tipo de resumo (informativo ou indicativo) e do tratamento que cada item recebe no documento original. O resumo deve ser precedido da referência do documento, com exceção do resumo inserido no próprio documento. (...) As palavras-chave devem figurar logo abaixo do resumo, antecedidas da expressão Palavras-chave:, separadas entre si por ponto e finalizadas também por ponto.

**Palavras-chave:** latex. abntex. editoração de texto.

# Abstract

This is the english abstract.

**Keywords:** latex. abntex. text editoration.

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# List of symbols

$\Gamma$	Letra grega Gama
$\Lambda$	Lambda
$\zeta$	Letra grega minúscula zeta
$\in$	Pertence

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# 1 Literature Review

## 1.1 Coarse Grained Force Fields

Molecular simulations can be carried out at different levels of descriptions. The detailed atomistic level or *ab initio* level is described by the laws of quantum mechanics. The system consists of a set of subatomic particulars in which Schrodinger's equation is solved for all of them. The next level is the atomistic description. It considers that the system is made up of atoms following the laws of statistical mechanics. Force fields at this level are based on pair potentials with Coulombic charged sites, which account for the molecular interactions. The contributions due to intramolecular interactions like bond-stretching, angle-bending and torsion are also usually accounted by these kind of force fields. When the scale of the simulations needs to be increased and the atomistic simulations become too computationally expensive, the coarse-grained (CG) description is more suited. It considers that the system is made up of pseudo atoms or beads that contain multiple atoms.

There is a obvious loss of information in grouping atoms, hence it is necessary to assure that the process of eliminating unnecessary or unimportant information ('coarse graining') doesn't affect the system's physical behavior. The coarse grained force fields are developed by mapping the atomistic model to define the pseudo atoms with the intetion of assuring that the model has accuracy, transferability, robustness, and computational efficiency. This mapping is normally done by grouping similar funcional groups. The level of coarse-graining also needs to be defined, up to 6 heavy atoms (non-hydrogen atoms) per bead in order to not loose much detail and maintain isotropic representations of the beads (SHINODA; DEVANE; KLEIN, 2007; MARRINK *et al.*, 2007; HADLEY; MCCABE, 2012). The CG force field can be parametrized following two different approaches: bottoms up and top down. The bottoms up approach uses information of a more detailed scale such as the *ab initio* description or the atomistic description to obtain the information necessary to the parametrization. This method depends highly of the quality of the detailed model to succeed. Meanwhile, the top down methodology obtains the parameters from one larger scales. This information at larger scales could be experimentally observed data like thermodynamic properties or native-structure based properties.

One of the first applications of coarse grained models is the study of protein folding (LEVITT; WARSHE, 1975; LEVITT, 1976). These earlier protein CG models were based on the structure of the molecule and they contributed for the knowledge of the physicochemical forces associated with protein folding and protein interactions

(KOGA; TAKADA, 2001). More recent models focused on retaining the protein's chemical specificity. The Bereau and Deresmo model (BEREAU; DESERNO, 2009) has a up to four-bead representation and was used in studies of protein folding and aggregation. However, this model still needs tuning to improve stability of proteins (BEREAU; BACHMANN; DESERNO, 2010). The OPEP (Optimized Potential for Efficient Protein Structure Prediction) model (STERPONE *et al.*, 2014; STERPONE; DERREUMAUX; MELCHIONNA, 2015) has up to six-bead representation. It was used to investigate a variety of phenomena, ranging from protein folding to *ab initio* peptide structure prediction (BARDUCCI; BONOMI; DERREUMAUX, 2011; CHEBARO *et al.*, 2009b; CHEBARO *et al.*, 2009a). Other CG protein models used in the literature are the Scorpion (solvated coarse-grained protein interaction) (BASDEVANT; BORGIS; HA-DUONG, 2013), the UNRES (united residue) (ADAM *et al.*, 2014) and the MARTINI model (LARS *et al.*, 2013). The later one is the most popular model for the CG modeling of membrane proteins (MARRINK; TIELEMAN, 2013). The MARTINI model is also extensively used as CG model for water. This model represents four water molecules as one bead using a shifted Lennard Jones potential for the non bonded interactions. Though its extensive use, the MARTINI water model doesn't properly represent properties as interfacial tension and compressibility (HE *et al.*, 2010) and can freeze at room temperature (WINGER *et al.*, 2009; MARRINK *et al.*, 2007), what makes necessary the use of anti-freeze agents during the simulations. This behavior can be explained by the high level of coarse graining (4:1), the lack of explicit charges and the use of the 12-6 potential. With the idea of improving the MARTINI model, Chiu, Scott e Jakobsson (2010) used the Morse Potential, which is softer than the LJ potential. Meanwhile, Shinoda, Devane e Klein (2007) used different forms of the Mie potential. They concluded that a 12-4 Mie Potential was ideal for the all water cross interactions and a 9-6 Mie Potential was suited for all the solute-solute interactions.

Outside of the Martini framework, He *et al.* (2010) studied different levels of coarse-graining for water ranging for one to 4 molecules per bead using different Mie and Morse potentials. Other works also assessed the use of Soft-core potentials to study aqueous solutions of surfactants (SHINODA; DEVANE; KLEIN, 2007), ionic liquids (BHARGAVA; KLEIN, 2009), lipids (SHINODA; DEVANE; KLEIN, 2010) and membranes (PANTANO; KLEIN, 2009). Other CG force field for water based on the Mie Potential is the SAFT- $\gamma$  Mie (LOBANOVA *et al.*, 2015). In this model, the water molecule can be represented by two different one isotropic bead interacting via a 8-6 Mie Potential models. The CGW1-vle model was parametrized using saturated-liquid density and vapor pressure data, and should be used for simulations of aqueous systems' fluid-phase equilibria at high temperatures and pressures. This model still suffers from premature freezing with a triple point at 343 K. The other model, CGW1-ift, was parametrized using saturated-liquid density and vapor-liquid interfacial tension, hence it is best



suited for interfacial properties calculations. Both models have temperature-dependent size and energy parameters and performed well for these properties over the entire temperature range of the liquid. The SAFT- $\gamma$  Mie force field have also been applied to other compounds with satisfactory results. Müller e Mejía (2017) parametrized the force field for aromatic compounds and tested it with simulations of fluid phase equilibrium. Herdes, Totton e Müller (2015) carried out simulations of alkanes and light gases with this force fields. Binary and ternary mixtures of water, carbon-dioxide and water (LOBANOVA *et al.*, 2016), thermodynamic and transport properties of carbon dioxide and methane (AIMOLI; MAGINN; ABREU, 2014a; AIMOLI; MAGINN; ABREU, 2014b) and water/oil interfacial tension (HERDES *et al.*, 2017) were also studied with this force field.

## 1.2 Solvation Free Energies Based on Molecular Dynamics

Free energies can be expressed as averages over ensembles of atomic configurations generated using Monte Carlo or molecular dynamics techniques. In the canonical ensemble, the free energy is given by:

$$F(N, V, T) = -\kappa_b T \ln Q(N, V, T) \quad (1.1)$$

where  $Q(N, V, T)$  is the partition function of the canonical ensemble. Meanwhile, the average over the isothermal-isobaric ensemble gives the Gibbs free energy:

$$G(N, P, T) = -\kappa_b T \ln \int_0^\infty dV \exp(-\kappa_b T P V) Q(N, V, T) \quad (1.2)$$

Since it is only possible to obtain free energy differences, Solvation free energy calculations based on molecular dynamics estimate the difference between the Gibbs free energies of end states, more specifically the difference between the solute alone in the gas phase and the solute interacting with the solvent. In order to these energy differences between be accurate, the states' phase integral must have sufficient overlap (KLIMOVICH; SHIRTS; MOBLEY, 2015). This can be achieved by calculating the free energy difference between a series of intermediates states. The result of these differences are independent of the intermediate states chosen since the free energy is a state function. That's why the states chosen typically don't have a physical sense, they are alchemical states which are only linking the physical states of interest.

The solvation free energy calculations follow a thermodynamic cycle to gradually insert the solute molecule into the solvent as illustrated in the Figure 1.2.1. According to

this cycle, the free energy of solvation can be expressed as:

$$\Delta G_{solv} = \Delta G_{1 \rightarrow 4} = \Delta G_{1 \rightarrow 2} + \Delta G_{2 \rightarrow 3} + \Delta G_{3 \rightarrow 4} \quad (1.3)$$

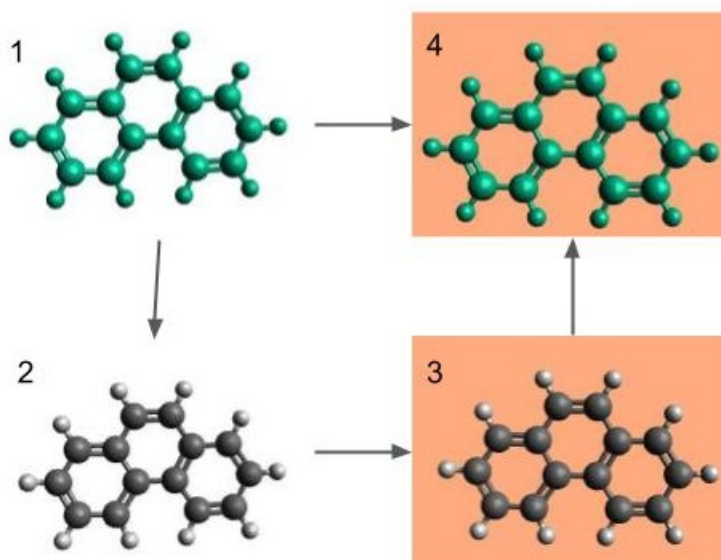


Figure 1.2.1 – Thermodynamic cycle for solvation free energy calculations with molecular dynamics (KLIMOVICH; SHIRTS; MOBLEY, 2015)

The solvation free energy between states 1 and 2 in the cycle is the one associated with turning off the molecule's non bonded interactions in the gas phase. The following transformation,  $\Delta G_{2 \rightarrow 3}$ , is the free energy of moving the non-interacting molecule in the gas phase to the solvent and is equal to zero. Lastly,  $\Delta G_{3 \rightarrow 4}$  is the free energy required to the the non-interaction molecule in the aqueous phase regain its non-bonded interactions.

If both the non-bonded interactions with the environment and the internal interactions are turned of, this is the annihilation free energy. Meanwhile, if only the non-bonded interactions with the environment are turned off, this is the decoupling free energy. In this later case,  $\Delta G_{1 \rightarrow 2} = 0$  since no gas transformation is needed.

benchmark Specifically, in some situations, free energy calculations appear to be capable of achieving RMS errors in the 1-2 kcal/mol range with current force fields, even in prospective applications.

The most immediate application of these techniques is to guide synthesis for lead optimization, but applications to scaffold hopping and in other areas also appear possible.

At the same time, it is clear that not all situations are so favorable, so it is worth asking what level of accuracy is actually needed

The present review focuses on a class of methods in which free energy differences are computed with simulations that sample Boltzmann distributions of molecular configurations. These samples are usually generated by molecular dynamics (MD) simulations [92], with the system effectively coupled to a heat bath at constant temperature, but Monte Carlo methods may also be used [32, 120, 121].

In either case, the energy of a given configuration is provided by a potential function, or force field, which estimates the potential energy of a system of solute and solvent molecules as a function of the coordinates of all of its atoms.

In all cases, however, the calculations yield the free energy difference between two states of a molecular system, and they do so by computing the reversible work for changing the initial state to the final one.

## 2 SAFT- $\gamma$ Mie Force Field

### 2.1 SAFT-VR Mie EoS

The SAFT-VR Mie equation of state (LAFITTE *et al.*, 2013) is the basis for the SAFT- $\gamma$  Mie coarse grained force field (AVENDAÑO *et al.*, 2011). This EoS was initially developed to describe chain molecule formed from fused Mie segments using the Mie attractive and repulsive potential. The Mie potential is a type of generalized Lennard-Jones potential that can be used to describe explicitly repulsive interactions of different hardness/softness and attractive interactions of different ranges, and is given by:

$$U_{Mie}(r) = \epsilon \frac{\lambda_r}{\lambda_r - \lambda_a} \left( \frac{\lambda_r}{\lambda_a} \right)^{\left( \frac{\lambda_a}{\lambda_r - \lambda_a} \right)} \left[ \left( \frac{\sigma}{r} \right)^{\lambda_r} - \left( \frac{\sigma}{r} \right)^{\lambda_a} \right] \quad (2.1)$$

where  $\epsilon$  is the potential well depth,  $\sigma$  is the segment diameter,  $r$  is the distance between the spherical segments,  $\lambda_r$  is the repulsive exponent and  $\lambda_a$  is the attractive exponent. This equation uses the Barker e Henderson (1976) high perturbation expansion of the Helmholtz free energy up to third order and an improved expression for the radial distribution function (RDF) of Mie monomers at contact to obtain a equation able to give an accurate theoretical description of the vapor-liquid equilibria and second derivative properties (LAFITTE *et al.*, 2013). For a non-associating fluid, the Helmholtz free energy is:

$$\frac{A}{N\kappa_b T} = a = a^{IDEAL} + a^{MONO} + a^{CHAIN} \quad (2.2)$$

#### 2.1.1 Ideal Contribution

The ideal contribution for a mixture is given by:

$$a^{IDEAL} = \sum_{i=1}^{N_c} x_i \ln (\rho_i \Lambda_i^3) - 1 \quad (2.3)$$

where  $x_i = N_i/N$  is the molar fraction of component  $i$ ,  $\rho_i = N_i/V$  is the number density,  $N_i$  is the number of molecules of each component and  $\Lambda_i^3$  is de Broglie wavelength.

#### 2.1.2 Monomer Contribution

The monomer contribution describes the interactions between Mie segments and can be expressed for a mixture as:

$$a^{MONO} = \left( \sum_{i=1}^{N_c} x_i m_{s,i} \right) a^M \quad (2.4)$$

In the equation above,  $m_{s,i}$  is the number of spherical segments making up the molecule  $i$  and  $a^M$  is the monomer dimensionless Helmholtz free energy and it is expressed as a third order perturbation expansion in the inverse temperature (BARKER; HENDERSON, 1976):

$$a^M = a^{HS} + \beta a_1 + \beta a_2^2 + \beta a_3^3 \quad (2.5)$$

where  $\beta = \kappa_b T$  and  $a^{HS}$  is the hard-sphere dimensionless Helmholtz free energy for a mixture :

$$a^{HS} = \frac{6}{\pi \rho_s} \left[ \left( \frac{\zeta_2^3}{\zeta_3^2} - \zeta_0 \right) \ln(1 - \zeta_3) + \frac{3\zeta_1\zeta_2}{1 - \zeta_3} + \frac{\zeta_2^3}{\zeta_3(1 - \zeta_3)^2} \right] \quad (2.6)$$

The variable  $\rho_s = \rho \sum_i^{N_c} x_i m_{s,i}$  is the total number density of spherical segments and  $\zeta_l$  are the moments of the number density:

$$\zeta_l = \frac{\pi \rho_s}{6} \left( \sum_{i=1}^{N_c} x_{s,i} d_{ii}^l \right), l = 0, 1, 2, 3 \quad (2.7)$$

where  $x_{s,i}$  is the mole fraction of the segments and is related through the mole fraction of component  $i$  ( $x_i$ ) by:

$$x_{s,i} = \frac{m_{s,i} x_i}{\sum_{k=1}^{N_c} m_{s,k} x_k} \quad (2.8)$$

The effective hard-sphere diameter  $d_{ii}$  for the segments is:

$$d_{ii} = \int_0^{\sigma_{ii}} (1 - \exp(-\beta U_{ii}^{Mie}(r))) dr \quad (2.9)$$

The integral in Eq. (2.9) is normally obtained by means of Gauss-Legendre with a 5-point quadrature (PAPAIOANNOU *et al.*, 2014). The detailing of the terms of Eq. (2.4) can be found in Lafitte *et al.* (2013).

### 2.1.3 Chain Contribution

The chain formation of  $m_s$  tangentially bonded Mie segments contribution is based on the first-order perturbation theory (TPT1) (PAPAIOANNOU *et al.*, 2014) and can be expressed as:

$$a^{CHAIN} = - \sum_{i=1}^{N_c} x_i (m_{s,i} - 1) \ln(g_{ii}^{Mie}(\sigma_{ii})) \quad (2.10)$$

The  $g_{ij}^{Mie}(\sigma_{ij})$  term correspond to the value of the radial distribution function (RDF) of the hypothetical Mie system evaluated at the effective diameter and can be obtained with the perturbation expansion:

$$g_{ij}^{Mie}(\sigma_{ij}) = g_{d,ij}^{HS}(\sigma_{ij}) \exp[\beta \epsilon g_{1,ij}(\sigma_{ij}) / g_{d,ij}^{HS}(\sigma_{ij}) + (\beta \epsilon)^2 g_{2,ij}(\sigma_{ij}) / g_{d,ij}^{HS}(\sigma_{ij})] \quad (2.11)$$

The other terms in the equations above are explicitly exposed in the original article (LAFITTE *et al.*, 2013).

### 2.1.4 Ring Contribution

There are two forms for the Helmholtz free energy for rings formed from  $m_s$  tangentially bonded segments in the literature. The first one (LAFITTE *et al.*, 2012) considered that the difference between a chain and a ring molecule is that the latter one has one more bond that is connecting the first segment to the last. With this assumption, the Eq. (2.10) can be adapted to rings by:

$$a^{RING} = - \sum_{i=1}^{N_c} x_i m_{s,i} \ln(g_{ii}^{Mie}(\sigma_{ii})) \quad (2.12)$$

According to Lafitte *et al.* (2012), Eq. (2.12) needs an additional parametrization with molecular simulation data so the EoS can be used in molecular simulations, but this procedure is not the necessary for chain molecules. Recently Müller e Mejía (2017) tried to correct this inconsistency by means of developing the ring free energy based on the work of Müller e Gubbins (1993) who obtained rigorous expressions for molecular geometries of rings of  $m_s = 3$  for hard fluids. The final expression developed for the ring dimensionless Helmholtz free energy is:

$$a^{RING} = - \sum_{i=1}^{N_c} x_i (m_{s,i} - 1 + \chi_i \eta_i) \ln(g_{ii}^{Mie}(\sigma_{ii})) \quad (2.13)$$

$\eta_i = m_{s,i} \rho_i \sigma_{ii}^3 / 6$  is the packing fraction and  $\chi_i$  is a parameter which depends on  $m_{s,i}$  and on the geometry of the ring of each component  $i$ . For a value of  $\chi = 0$  Eq. (2.13) is equal to Eq. (2.10) and the system corresponds to a hard sphere system of triangles when  $\chi = 1.3827$ . Müller e Mejía (2017) also calculated values of  $\zeta$  for values of  $m_s = 3, m_s = 4, m_s = 5, m_s = 7$  with pseudo-experimental data from molecular dynamics (MD) for a defined pure fluid. The values of  $\chi$  for each geometry estimated can be seen in the Figure 2.1.1.

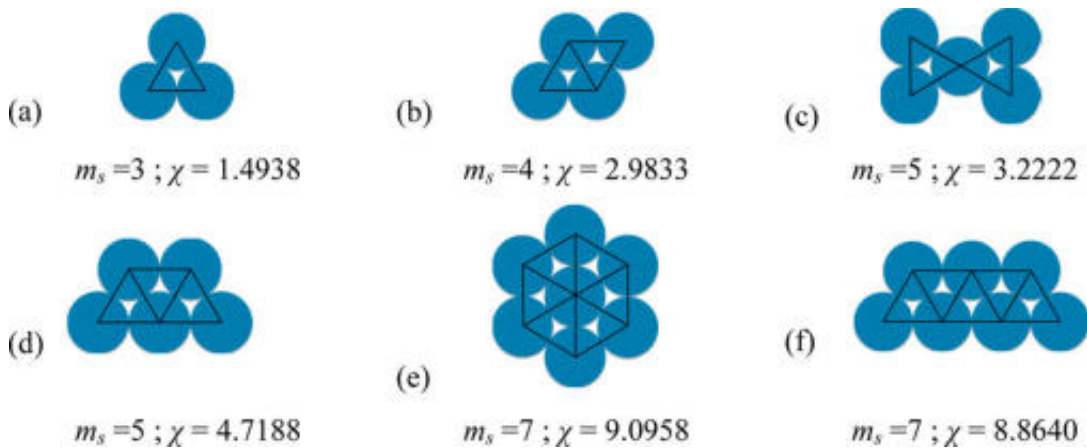


Figure 2.1.1 – Values for parameter  $\chi$  according to the ring geometry (MÜLLER; MEJÍA, 2017)

### 2.1.5 Combining rules for the intermolecular potential parameters

Lafitte *et al.* (2013) also suggested mixing rules for the potential parameters based on Lorentz-Berthelot combining rules (ROWLINSON; SWINTON, 1982):

$$\sigma_{ij} = \frac{\sigma_{ii} + \sigma_{jj}}{2} \quad (2.14)$$

$$\lambda_{k,ij} - 3 = \sqrt{(\lambda_{k,ii} - 3)(\lambda_{k,jj} - 3)}, k = r, a \quad (2.15)$$

$$\epsilon_{ij} = (1 - k_{ij}) \frac{\sqrt{\sigma_{ii}^3 \sigma_{jj}^3}}{\sigma_{ij}^3} \sqrt{\epsilon_{ii} \epsilon_{jj}} \quad (2.16)$$

The  $k_{ij}$  is a binary interaction parameter to correct the deviations of the Lorentz-Berthelot rule for chemically distinct compounds. This parameter can also be fitted to experimental data or pseudo experimental data.

## 2.2 Parameter Estimation for the SAFT- $\gamma$ Mie Force Field

The SAFT- $\gamma$  Mie is a force field that uses a coarse graining top down methodology in its parameterization. This methodology aims to obtain the intermolecular parameters from macroscopic experimental data like fluid-phase equilibrium or superficial tension data. The idea is that the force field's parameters estimated with the equation of state can be used on molecular simulations since both the SAFT-VR Mie EoS and the force field use the same explicit intermolecular potential model (Mie potential). This correspondence between models has already been seen for a variety of fluids in which this force field was parameterized and this success in the representation of the properties of real fluids can be imputed to the degrees of freedom of Mie Potential (HERDES; TOTTON; MÜLLER, 2015). This flexibility also provides an exploration of a very large parameter space without using a iterative simulation scheme (AVENDAÑO *et al.*, 2011).

Each substance has initially five parameters to be estimated ( $m_s, \sigma, \epsilon, \lambda_r$  and  $\lambda_a$ ) according to Eq. (2.1). The number of segments are usually fixed in an integer value so it can be used in the coarse grained simulations. The attractive parameter can also be fixed since there is a high correlation between the attractive and repulsive parameter. Usually, the parameter is fixed in the London value of 6, which is expected to be a good representation of the dispersion scale of most simple fluids that don't have strong polar interactions (RAMRATTAN *et al.*, 2015; HERDES; TOTTON; MÜLLER, 2015). There are two strategies to obtain the parameters of each substance: one is by fitting the Saft-Vr Mie EoS to experimental data as vapor pressure and liquid density and the

other is using correspondent state parametrization. The first one, generally, minimizes the following unweighted least-squares objective function:

$$\min_{\sigma, \epsilon, \lambda_r} F_{obj}(\sigma, \epsilon, \lambda_r) = \sum_{i=1}^{N_p} \left( \frac{P_v^{SAFT}(T_i, \sigma, \epsilon, \lambda_r) - P_v^{exp}(T_i)}{P_v^{exp}(T_i)} \right)^2 + \sum_{i=1}^{N_p} \left( \frac{\rho_l^{SAFT}(T_i, \sigma, \epsilon, \lambda_r) - \rho_l^{exp}(T_i)}{\rho_l^{exp}(T_i)} \right)^2 \quad (2.17)$$

where  $N_p$  is the number of experimental points,  $P_v$  is the vapor pressure and  $\rho_l$  is the saturated liquid density. The minimized properties can also change and other possible properties as superficial tension and speed of sound can also be taken into account. These multiple parameters make it necessary the use of a wide range of experimental data since multiple solutions can be found for the fit. So one need to be careful in deciding the level of coarse graining (i.e. the parameter  $m_s$ ) and subsequent parameter space that will not result in some physical inconsistencies like a fluid with premature freezing.

Lafitte *et al.* (2012) suggested that the two corrections factors ( $c_\sigma$  and  $c_\epsilon$ ) should be estimated with simulation data when using Eq. (2.12) for the ring contribution. They are related to the EoS parameters by scaled parameters:

$$\sigma^{scaled} = c_\sigma \sigma^{SAFT} \quad (2.18)$$

$$\epsilon^{scaled} = c_\epsilon \epsilon^{SAFT} \quad (2.19)$$

According to Lafitte *et al.* (2012), these corrections are necessary because the approximations employed in the EoS theory generate discrepancies between molecular simulations and the EoS results for ring molecules modeled with Eq. (2.12). The objective function for this second estimation is given by:

$$\min_{c_\sigma, c_\epsilon} F_{obj}(c_\sigma, c_\epsilon) = \sum_{i=1}^{N_p} \left( \frac{P_v^{sim}(T_i, \sigma^{SAFT}, \epsilon^{SAFT}) - P_v^{SAFT}(T_i, \sigma^{scaled}, \epsilon^{scaled})}{P_v^{sim}(T_i, \sigma^{SAFT}, \epsilon^{SAFT})} \right)^2 + \sum_{i=1}^{N_p} \left( \frac{\rho_{liq}^{sim}(T_i, \sigma^{SAFT}, \epsilon^{SAFT}) - \rho_{liq}^{SAFT}(T_i, \sigma^{scaled}, \epsilon^{scaled})}{\rho_{liq}^{sim}(T_i, \sigma^{SAFT}, \epsilon^{SAFT})} \right)^2 \quad (2.20)$$

The repulsive parameter is maintained in the value found on the minimization of Eq. (2.17), so the refined values for the force field are:

$$\sigma^{sim} = \sigma^{SAFT} / c_\sigma \quad (2.21)$$



$$\epsilon^{scaled} = \epsilon^{SAFT} / c_\epsilon \quad (2.22)$$

It is interesting to point out that this new parametrization is not necessary when using Eq. (2.13) as the ring contribution. The other method to obtain the force field parameters is the correspondent state parametrization for the EoS SAFT-VR Mie (MEJÍA; HERDES; MÜLLER, 2014). This method considers that the unweighted volume average of the attractive contribution to the Mie intermolecular potential,  $a_1$ , can be given a mean field approximation:

$$a_1 = 2\pi\rho\sigma^3\epsilon\alpha \quad (2.23)$$

The van der Waals constant,  $\alpha$ , considering  $\lambda_a = 6$  is related by the Mie exponents by:

$$\alpha = \frac{1}{\epsilon\sigma^3} \int_{\sigma}^{\infty} \phi(r)r^2 dr = \frac{\lambda_r}{3(\lambda_r - 3)} \left( \frac{\lambda_r}{6} \right)^{6/(\lambda_r - 6)} \quad (2.24)$$

The parametrization in this method starts by using the experimental acentric factor,  $\omega$ , for each molecule with a fixed value of  $m_s$  to obtain the value of the repulsive exponent with the following Padé series:

$$\lambda_r = \frac{\sum_{i=0} a_i \omega^i}{1 + \sum_{i=1} b_i \omega^i} \quad (2.25)$$

$a_i$  and  $b_i$  are dependent parameters of the number of segments and a table with its values is presented in the original paper (MEJÍA; HERDES; MÜLLER, 2014). Substituting  $\lambda_r$  into Eq. (2.24), the van der Waals constant can be found. The reduced critical potential  $T_c^*$  can also be related to  $\alpha$  by a Padé series:

$$T_c^* = \frac{\sum_{i=0} c_i \alpha^i}{1 + \sum_{i=1} d_i \alpha^i} \quad (2.26)$$

The values of  $c_i$  and  $d_i$  are also available in the original paper. The reduced temperature of the equation above is used in conjunction with the experimental critical temperature,  $T_c$ , to find the energy parameter with the relation below:

$$T_c^* = \frac{\kappa_b T_c}{\epsilon} \quad (2.27)$$

The diameter parameter, however, is not obtained with the critical properties, but with the reduced liquid density,  $\rho_{T_r=0.7}$ , at the reduced temperature,  $T_r$ , of 0.7. This

density is also obtained with a Padé series using parameters obtained by [Mejía, Herdes e Müller \(2014\)](#):

$$\rho_{T_r=0.7}^* = \frac{\sum_{i=0} j_i \alpha^i}{1 + \sum_{i=1} k_i \alpha^i} \quad (2.28)$$

The relation among the equation above,  $\sigma$  and the experimental density is given by:

$$\rho_{T_r=0.7}^* = \rho_{T_r=0.7} \sigma^3 N_{av} \quad (2.29)$$

where  $N_{av}$  is The Avogadro number. This correspondent state method has the advantage of only requiring critical data, that it is available for a great range of fluids, and one liquid density point. In addition to that, there is an available online parameter database obtained with this strategy ([ERVIK; MEJÍA; MÜLLER, 2016](#)).

The binary interaction parameter  $k_{ij}$  of Eq. (2.16) is necessary to adjust the mixture behaviour of chemically distinct components. Normally, it is fitted to experimental binary vapor liquid equilibrium or superficial tension data with the SAFT-VR Mie EoS ([MÜLLER; MEJÍA, 2017](#); [LOBANOVA et al., 2016](#)). However, [Ervik et al. \(2016\)](#) used molecular simulation results to fit the parameter to the superficial tension data of the mixture water-toluene. The strategy followed by them was to do simulations in three values of  $k_{ij}$  and then refine the parameter value until a value in good agreement with the experimental data was found.

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# Appendix

## APPENDIX A – Quisque libero justo

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## APPENDIX B – Nullam elementum urna vel imperdiet sodales elit ipsum pharetra ligula ac pretium ante justo a nulla curabitur tristique arcu eu metus

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# Annex

## ANNEX A – Morbi ultrices rutrum lorem.

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# ANNEX B – Cras non urna sed feugiat cum sociis natoque penatibus et magnis dis parturient montes nascetur ridiculus mus

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## ANNEX C – Fusce facilisis lacinia dui

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