# A Computational Analysis of the DMSO-Water Interaction: Toward the Implementation of an Accurate Force Field

Luca Mancini[1], Andrea Lombardi[1,3], Fernando Pirani[2], Leonardo Pacifici[3], Marzio Rosi[2,3], and Noelia Faginas-Lago[1,3(✉)]

[1] Dipartimento di Chimica, Biologia e Biotecnologie, Università degli Studi di Perugia, 06123 Perugia, Italy
luca.mancini@unipg.it

[2] Dipartimento di Ingegneria Civile ed Ambientale, Università degli Studi di Perugia, 06125 Perugia, Italy

[3] Istituto CNR di Scienze e Tecnologie Chimiche Giulio Natta (CNR-SCITEC), 06123 Perugia, Italy
noelia.faginaslago@unipg.it

**Abstract.** Molecular dynamics (MD) simulations represent an essential tool for the investigation of the chemical and physical properties of a large variety of systems, with a plethora of possible applications ranging from medicine to the development of new nanomaterials for energy purposes and carbon neutrality. The implementation of an accurate force field represents a key step in the overall theoretical analysis, allowing a correct representation of all the non-covalent interactions in the target system. The Improved Lennard-Jones potential (ILJ), developed to have a better representation of van der Waals interactions, represents a feasible methodology for the implementation of accurate force fields. The validity of the proposed methodology has been assessed by performing a theoretical investigation considering a mixture of dimethyl sulfoxide (DMSO) in water, which represents a strong cryoprotecting agent for biological samples. The ease of implementation and the low computational cost makes ILJ an excellent technique for the analysis of non-covalent interactions and the production of accurate MD force fields.

**Keywords:** Molecular Dynamics · Force Field · Improved Lennard-Jones

## 1 Introduction

Molecular dynamics represents a powerful tool in order to model the structure and predict properties of big systems which are difficult, or even impossible, to study through accurate ab initio investigations and/or experimental analysis. Molecular dynamics (MD) simulations allow to predict the position of the different atoms in a system as a function of time, by calculating the forces applied

© The Author(s), under exclusive license to Springer Nature Switzerland AG 2024
O. Gervasi et al. (Eds.): ICCSA 2024 Workshops, LNCS 14823, pp. 361–374, 2024.
https://doi.org/10.1007/978-3-031-65329-2_24

using simple formulations based on Newton's laws of motion. For this reason, MD simulations are widely spread in a variety of different fields, ranging from molecular biology and medicine to nanomaterials for energy and carbon neutrality. A clear example is represented by graphene, a carbo-nanostructure composed of a single atomic layer organized in an hexagonal lattice structure. In the last years, MD simulations unveiled the importance of graphene and graphene-like structures (such as carbon nanotubes and $\gamma$-graphynes) as possible precursors for the design of materials able to capture and selectively adsorb small molecules, including carbon dioxide and methane [1–4].

One of the main challenges in molecular dynamics simulations is represented by the implementation of a force field, which must be able to correctly reproduce the interactions of the systems under investigation. Force fields are a variety of interatomic potentials. More precisely, the force field refers to the functional form and parameter sets used to calculate the potential energy of a system at the atomistic level. The parameters for a chosen energy function may be derived from classical laboratory experiment data, calculations in quantum mechanics, or both. Force fields utilize the same concept as force fields in classical physics, with the main difference that the force field parameters in the MD simulations describe the energy landscape on the atomistic level. From a force field, the acting forces on every particle are derived as a gradient of the potential energy with respect to the particle coordinates. Typically, a MD force field, which is necessary to treat non-covalent interactions, is composed by two main components: the electrostatic (Coulombic) contribution between atoms and the non-electrostatic one. One of the most challenging task in developing accurate force fields is represented by the correct modeling of intermolecular interactions (non electrostatic contribution), in particular the van der Waals component, which is always present and plays a pivotal role in the overall dynamics.

From the non-electrostatic part, a new formulation of the classical Lennard-Jones (LJ) potential has been provided in the last years in order to have a better representation of both long-range attraction and short-range repulsion in the analysis of non-covalent interaction. The so called Improved Lennard-Jones (ILJ) [5] potential represents, indeed, an extension of the previously mentioned LJ treatment, formulated considering additional parameters which can be easily calculated on the basis of atomic and molecular properties (such as dipole moment and polarizability) [6]. Different investigations have been performed to assess the viability of the ILJ formulation and to check the correctness of the predicted results, considering the outcomes coming from both high level ab initio calculations and experimental investigations, performed through molecular beams scattering techniques [7,8].

The excellent agreement between theoretical predictions and experimental results confirmed the accuracy of the new implementation. Recently, the same formulation has been used to characterize the nature of the initial interaction between the reactants of gas phase bimolecular reactions [9,10]. The remarkable results obtained helped to clarify the reaction micro-mechanism and allowed a better understanding of how long-range non-covalent interactions drive the

chemical reactivity. The use of simple formulations, such as the semiempirical ILJ model, allowed to obtain values of rate constants in agreement with the experimental results, showing how the method is portable and can be easily adapted to different cases.

In the present contributon, the ILJ model has been used to develop an accurate preliminary force field to run MD simulations in order to characterize the interaction of dimethyl sulfoxide (DMSO, $CH_3SOCH_3$) in water, with pivotal applications in the field of medicine and biology [11–14]. Dimethyl sulfoxide is, indeed, a key species in medicinal chemistry and biology and shows a strong pharmacological potential. In the last decades, $CH_3SOCH_3$ showed important features in different fields, including analgesia, but also as possible anti-viral and anti-bacterial agent. It is also considered important in the field of anti-inflammatory and radioprotection. Together as a possible agent for the increasing of membrane permeability [15,16, & references therein], DMSO is considered an important cryoprotectant. The extreme drop in the freezing point of solutions of DMSO in water, leads to a very efficient action of dimetyl sulfoxide to preserve biological samples in extreme conditions, such as very low temperatures, increasing the possibility of survival of cryoconserved cells. Despite the strong effect of DMSO in the field has been extensively investigated, the main mechanism of action is still lacking. For this reason, different investigations have been already performed, both through experimental analysis and molecular dynamic simulations [15,17–23].

The present work is focused in order to implement an accurate preliminary force field using the Improved Lennard-Jones potential to describe the intermolecular interactions to run MD simulation of DMSO-water mixtures. Here, we will present, only, the Force Field.

## 2 Theoretical Methods

The preliminary force field to be used in molecular dynamics (MD) simulations, has been built considering a global potential ($V_{tot}$) composed of two main contributions: a first term representing the electrostatic potential ($V_{elec}$) and a second term ($V_{nelec}$), accounting for the non-electrostatic contribution of the interaction. The electrostatic contribution has been evaluated considering the atomic charges of the two interacting molecules, as expressed by the Coulomb laws. The non-electrostatic contribution has been defined exploiting proposed semi-empirical potential (ILJ), described in the next sections.

### 2.1 Electronic Structure Calculations

In details, an initial geometry optimization on the two separated molecules has been performed at the DFT level, using the B3LYP functional [24,25] in conjunction with the correlation consistent valence polarized set aug-cc-pVTZ [26–28]. Previous works on reactions involving small organic/inorganic molecules

showed the robustness and affordability of the functional for geometry optimizations [29–31]. Harmonic vibrational frequencies calculations have been performed at the same level of theory, in order to check the accuracy of the optimized molecules, i.e. a minimum shows all real frequencies. Finally, the optimized geometry has been used to evaluate the electrostatic potential atomic charges (ESP). In this regard, a benchmark analysis has been performed considering the same B3LYP functional and different basis sets: the Pople basis sets 6-31 G and 6-311++G(d,p) and four difference correlation consistent valence polarized sets aug-cc-pVDZ, aug-cc-pVTZ, aug-cc-pVQZ and aug-cc-pV5Z. All the calculations have been performed using GAUSSIAN09 [32] while the analysis of the molecular structures has been carried out using Avogadro [33].

### 2.2 Potential Energy Surface to Describe the Intermolecular Interactions

The intermolecular forces of interest in this work are those occurred between $H_2O$ molecules pair and between the $H_2O$ and the DMSO. For each pair, the total intermolecular interaction energy component is further decomposed in terms of molecule-molecule pair contribution, which are non-electrostatic and electrostatic contributions.

$$V_{tot}(r) = V_{nelec} + V_{elec} \tag{1}$$

The non-electrostatic contribution ($V_{nelec}$) is measured by taking into consideration the strength of induced dipoles attraction and the average molecular sizes repulsion. This can be done by assigning a value of polarizability to both interacting centers. On the other hand, the electrostatic contribution ($V_{elec}$) is evaluated by employing the Coulomb's law.

The non electrostatic contribution has been then evaluated considering the previously mentioned Improved Lennard-Jones (ILJ) model [5,34–37].

In details, ($V_{nelec}$) is considered as a sum of pairwise ILJ potential energy functions, formulated as:

$$V_{nelec} = V_{ILJ} = \varepsilon \left[ \frac{m}{n(r) - m} \left( \frac{r_m}{r} \right)^{n(r)} - \frac{n(r)}{n(r) - m} \left( \frac{r_m}{r} \right)^{m} \right] \tag{2}$$

where $\varepsilon$ and $r_m$ represents the well depth and its location, respectively, while $m$ assumes the value of 6 for neutral-neutral systems and 4 in the case of ion-neutral interactions. The values are estimated on the basis of the value of the polarizability, evaluated considering each interaction center at a certain distance $r$. The term $n(r)$ shows a dependence on the distance $r$, defined as:

$$n(r) = \beta + 4 \left( \frac{r}{r_m} \right)^2 \tag{3}$$

where the $\beta$ parameter represents the hardness of the two interacting fragments and can be properly modulated. This newly introduced parameter is what makes ILJ potential (Eq. 3) able to indirectly take into account some effects of

atom clustering, induction and charge transfer and to improve the Lennard-Jones function at asymptotic regions. Nevertheless, while ILJ improves the description of the present system, other effects should be included in the intermolecular potential for enhancing the model of the system.

## 3 Results

### Geometry Optimization

As reported in the previous section, the geometry of the two interacting molecules has been optimized through density functional theory calculations. In Fig. 1 are reported the main geometrical parameters obtained for dimethyl sulfoxide and water at the B3LYP/aug-cc-pVTZ level of theory. As already seen in several cases before, the use of the B3LYP functional, in conjunction with the aug-cc-pVTZ basis set, represents a good compromise between computational cost and chemical accuracy [38]. The same level of theory has been used for geometry optimization and frequencies calculations in several works [39–41].

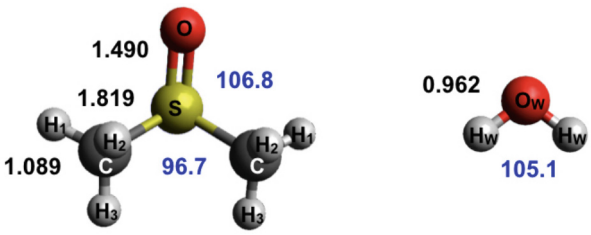


**Fig. 1.** Structural details of the molecular models of water and DMSO system. The optimized structure of the dimethyl sulfoxde and water molecules have been obtained at the B3LYP/aug-cc-pVTZ level of theory. In this figure appears labeled the different pair centers for the potential interaction.

In order to check the validity of the present calculations, the obtained data have been compared with standard reference values present in the NIST chemistry database [42]. The comparison is reported in Table 1.

As can be seen from the data reported in Table 1, the values of bond distances obtained at the B3LYP/aug-cc-pVTZ level are in very good agreement with the ones reported in the NIST database, being the differences negligible. The maximum deviation is, indeed, represented by the C-S bond, which differs from the reference in 0.02 $\mathring{A}$. As a consequence, the present level of calculation can be considered a good compromise between chemical accuracy and computational cost.

**Table 1.** Comparison between bond distances (in Å) and angles (in degrees) derived through DFT calculations and values present in the NIST database.

| Bond Distance | B3LYP/aug-cc-pVTZ | NIST |
|---|---|---|
| C-H | 1.089 | 1.092 |
| C-S | 1.819 | 1.799 |
| S-O | 1.490 | 1.485 |
| $O_W$-$H_W$ | 0.962 | 0.958 |
| **Angles** | | |
| $O_W$-$O_W$-$H_W$ | 105.1 | 104.5 |
| C-S-C | 96.7 | 96.56 |
| O-S-C | 106.8 | 106.65 |

### Atomic Charges Analysis

ElectroStatic Potential atomic charges (ESP) have been calculated at the DFT level, using the B3LYP functional and considering different basis sets, in order to identify the one which allows a better analysis and a correct representation of the dipole moment and polarizability values, which are essential for the derivation of the Improved Lennard-Jones parameters. The data obtained for the six different cases are reported in Table 2, where $H_1$, $H_2$ and $H_3$ are referred to the three hydrogen atoms of each methyl group, while the atoms of the water molecule are labelled as $O_W$ and $H_W$ (see Fig. 1).

**Table 2.** Atomic charges (in a.u.) obtained for the $H_2O$ and DMSO molecules, evaluated at different levels of theory (see text for details).

| Atom | 6-31G | 6-311+ +G(d,p) | aug-cc -pVDZ | aug-cc -pVTZ | aug-cc -pVQZ | aug-cc -PV5Z |
|---|---|---|---|---|---|---|
| C | −0.406 | −0.465 | −0.493 | −0.463 | −0.458 | −0.456 |
| $H_1$ | 0.151 | 0.158 | 0.170 | 0.160 | 0.158 | 0.158 |
| $H_2$ | 0.180 | 0.195 | 0.205 | 0.195 | 0.193 | 0.192 |
| $H_3$ | 0.164 | 0.187 | 0.195 | 0.186 | 0.184 | 0.183 |
| S | 0.280 | 0.323 | 0.293 | 0.274 | 0.268 | 0.261 |
| O | −0.482 | −0.473 | −0.446 | −0.431 | −0.424 | −0.417 |
| $O_W$ | −0.887 | −0.800 | −0.679 | −0.683 | −0.683 | −0.683 |
| $H_W$ | 0.444 | 0.400 | 0.339 | 0.341 | 0.341 | 0.342 |

The values of atomic charges obtained are then used to analyse the contribution of the dipole moment ($\mu$) and polarizability ($\alpha$) of the two interacting

molecules. In Table 3 are reported the values of $\mu$ and $\alpha$ obtained during the analysis. Atomic charges and molecular polarizabilities have been obtained through frequancies calculations, performed at the B3LYP/aug-cc-pVTZ level of theory.

**Table 3.** Dypole moment (in Debye) and molecular polarizability (in $Å^3$) obtained for the $H_2O$ and DMSO molecules, evaluated at different levels of theory (see text for details).

| Molecule | | 6-31G | 6-311+ +G(d,p) | aug-cc -pVDZ | aug-cc -pVTZ | aug-cc -pVQZ | aug-cc -PV5Z | NIST |
|---|---|---|---|---|---|---|---|---|
| DMSO | $\mu$ (D) | 4.918 | 4.403 | 4.318 | 4.125 | 4.062 | 4.011 | 3.960 |
| | $\alpha(Å^3)$ | 6.619 | 7.602 | 8.252 | 8.126 | 8.094 | 8.067 | 7.969 |
| $H_2O$ | $\mu$ (D) | 2.398 | 2.187 | 1.852 | 1.847 | 1.847 | 1.847 | 1.857 |
| | $\alpha(Å^3)$ | 0.674 | 1.068 | 1.403 | 1.453 | 1.471 | 1.478 | 1.501 |

As can be seen from the data reported in Tables 2 and 3, the values calculated with the correlation consistent valence polarized basis sets provide a better description of the physical quantities (charges, dipole, and polarizability) with respect to the Pople basis sets. In particular, also in this case, the best compromise between accuracy of the results and computational cost is represented by the use of the triple zeta (aug-cc-pVTZ) basis set. Therefore, the data reported in column 5 of Table 2, can be used for the generation of the force field necessary to run MD calculations. The values of ESP atomic charges appear to be quite similar to those obtained by Stachura et al. [17], through the use of the AMBER force field [43].

**Preliminary Force Field** Atomic charges for the two interacting molecules have been calculated, allowing a correct representation of the dipole and/or quadrupole moments of the molecules in the gas phase, in accordance with the values calculated through ab initio calculations (reported in Sect. 3). In Fig. 2, are reported the final parameters of DMSO and water, together with the ESP charges to be used to model the electrostatic part of the MD force field.

The Improved Lennard-Jones potential is formulated considering the atomic and molecular polarizabilities. The $\varepsilon$ and $r_m$ parameters are indeed calculated on the basis of correlation formulas, which relates the values of the polarizability ($\alpha$) and dipole moment ($\mu$) of the interacting species with the main features of the potential. As a consequence, the derived parameters show a high level of portability, allowing to easily pass from a system to another. The validity of the ILJ model has been assessed considering the comparison with theoretical predictions (obtained through high level ab initio calculations) and experimental analysis, for different systems [5]. An additional advantage of the formulation is represented by the possibility to study complex systems, by simply decomposing the main molecular structure in different moieties, which are representative of

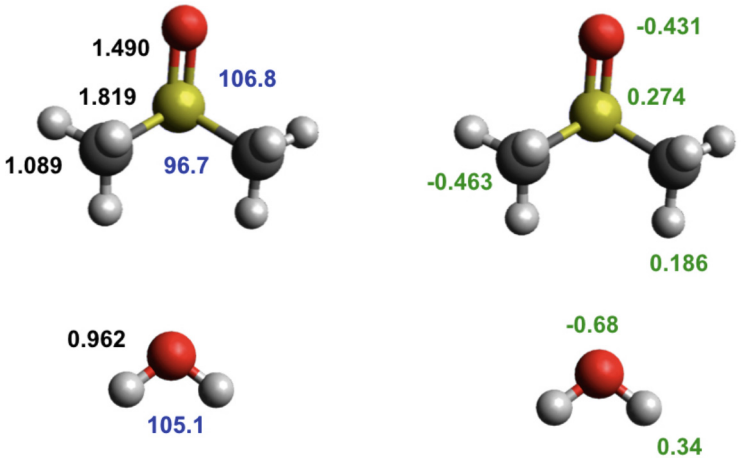


**Fig. 2.** Final parameters used to derive the MD Force Field. Left panel: bond lenght (in black, in Å) and angles (in blue, in degrees). Right panel: ESP charges (in green, in a.u.). All the data have been calculated at the B3LYP/aug-cc-pVTZ level of theory (Color figure online)

the interaction centers, allowing a relatively simple formulation also in the case of big interacting systems. In Table 4 are reported the ILJ parameters (in the form of $\varepsilon$ and $r_m$) for the interaction of dimethyl sulfoxide with water. In details, in the case of DMSO, the methyl group has been considered as an "effective" carbon atom, which has the mass and the polarizability of a $CH_3$ moiety. Similarly, the interaction with the water molecules has been formulated considering only one center, represented by the O atom, reported as $O_W$ [44].

**Table 4.** List of the parameters ($\varepsilon$ and $r_m$) used for the representation of each interacting pair in the ILJ formulation

| Interacting Centers | $\varepsilon$ (meV) | $r_m(\AA)$ |
|---|---|---|
| C-$O_W$ | 9.881 | 3.908 |
| S-$O_W$ | 10.914 | 3.921 |
| O-$O_W$ | 7.577 | 3.640 |
| $O_W$-$O_W$ | 9.060 | 3.730 |

Usually, the $\beta$ parameter is considered to be in the interval $8.5 \pm 2.5$ and can be properly modulated considering the fluctuations of $V_{elec}$. Moreover, the same parameter can be used to compensate and include the role of other different contributions which are less important and are not directly included in the formulation, such as other additive terms of the interaction at long distances which are indirectly included. Due to the relative role played by $\beta$ and the dipole

moment ($\mu$), the specific values selected for $\beta$ can depend on the selected value of $\mu$ [45]. In fact, small modifications of $\beta$ can be compensated by varying $\mu$. Due to this fact, in the present paper we have analized the modulation of the $\beta$ parameter as a function of various charge distributions assigned to the water molecules. The modulation of $\beta$ can also partially compensate the case of different representations of the charge distributions and indirectly include other less important interaction effects at intermediate and short distances [45].

### 3.1 Ab Initio Calculations for the Initial Geometry

Finally, in order to have a clear idea of the initial configuration of the system, necessary to run the MD simulations, the geometry of the two interacting fragments has been preliminary optimized through DFT calculations, performed at the B3LYP/aug-cc-pVTZ level of theory. Two different cases have been considered, composed of one DMSO molecule interacting with one and two water molecules, respectively. The optimized geometry obtained for the two cases are reported in Figs. 3 and 4.

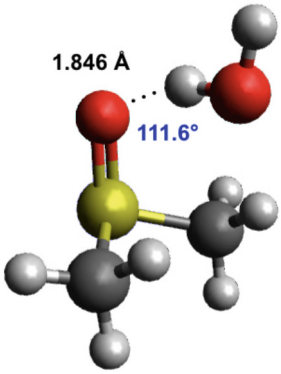


**Fig. 3.** Optimized geometry for the DMSO-$H_2O$ interacting system obtained at the B3LYP/aug-cc-pVTZ level of theory

As can be seen from the structure reported, the interaction of DMSO with a water molecule is driven by the formation of an hydrogen bond between the oxygen atom of the DMSO and one of the two hydrogen atoms of the $H_2O$ molecule. The related O-H bond distance is equal to 1.846 $\mathring{A}$ and the S-O-H angle is equal to 111.6°C. The inclusion of a second water molecule leads to the formation of a new H-bond interaction. In this case the two O-H bond distances appears to be slightly increased (reaching values of 1.898 $\mathring{A}$ and 1.875 $\mathring{A}$, respectively), while the H-O-H angle assumes a value of 106.4°C. As expected, the introduction of water molecules leads to the formation of strong H-bonds, considering the nature of the atoms in the system. This leads to a condition of

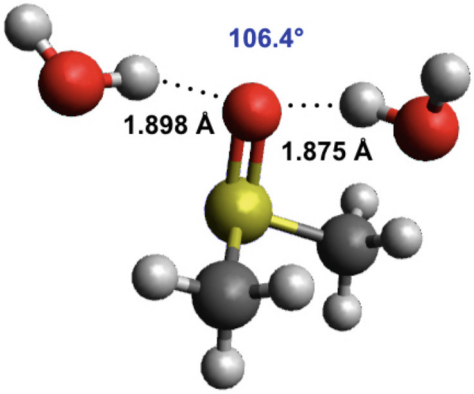


**Fig. 4.** Optimized geometry for the DMSO-2$H_2O$ interacting system obtained at the B3LYP/aug-cc-pVTZ level of theory

solvation of the DMSO molecule, which can be properly analyzed through MD calculations. The main goal of the future works is investigate in a successive order the spatial solvation and structure and topological features in the different molar ratio mixture of dimethyl sulfoxide and water using the MD simulations. At this end, it is necessary an accurate force field that describes these interactions.

## 4 Conclusions

In the present contribution, a preliminary theoretical analysis has been performed in order to develop an accurate force field for the system composed of dimethyl sulfoxide in water analyzing the properties by classical MD simulations, with a plethora of possible applications, mainly in medicine and molecular biology. High-level ab initio calculations have been performed in order to assess the main geometrical parameters and evaluate the atomic charges, as well as dipole moment and polarizability for both DMSO and $H_2O$. The comparison between the obtained data and the standard reference, reported in the NIST database, shows very small differences, almost negligible. Therefore, according to the present results, the use of the B3LYP functional, already used for the analysis of several systems [10,39–41,46,47], in conjunction with the aug-cc-pVTZ basis set, represents the best compromise between chemical accuracy and computational cost. The non electrostatic component of the interaction, which accounts for the van der Waals long-range region of the potential energy surface has been evaluated using the semi-empirical Improved Lennard-Jones formulation, proposed to have a better representation of the forces ruling the potential at long distances. The combination of electrostatic and non electrostatic parameters allowed us to derive a new force field to be used in MD simulations, which will be the focus of a future investigation. Finally, ab initio calculations allowed to derive the optimized structure representing the initial configuration

for the system composed of a DMSO molecule interacting with one and two water molecules, respectively. Thanks to the portability of the formulation, once tested, the present methodology can be used for the development of accurate force fields, to model and derive properties of a new generation of carbon-based nanomaterials, particularly relevant for carbon neutrality applications. The work in progress is devoted to use the parameters in order to evaluate the total interaction contribution using the MD simulations to obtain the properties of the system we are studying.

**Acknowledgements.** This work has been funded by the European Union - NextGenerationEU under the Italian Ministry of University and Research (MUR) National Innovation Ecosystem grant ECS00000041 - VITALITY - CUP J97G22000170005. M. R and N. F-L acknowledge financial support under the National Recovery and Resilience Plan (NRRP), Mission 4, Component 2, Investment 1.1, Call for tender No. 104 published on 2.2.2022 by the Italian Ministry of University and Research (MUR), funded by the European Union - NextGenerationEU- Project Title 2022JC2Y93 ChemicalOrigins: linking the fossil composition of the Solar System with the chemistry of protoplanetary disks - CUP J53D23001600006 - Grant Assignment Decree No. 962 adopted on 30.06.2023 by the Italian Ministry of Ministry of University and Research (MUR).

## References

1. Faginas-Lago, N., Apriliyanto, Y.B., Lombardi, A.: Confinement of $CO_2$ inside carbon nanotubes. Eur. Phys. J. D **75**(5), 161 (2021)
2. Faginas-Lago, N., Yeamin, M.B., Sánchez-Marín, J., Cuesta, I., Albertí, M., Sanchez de Meras, A.: Modelization of the $H_2$ adsorption on graphene and molecular dynamics simulation. Theor. Chem. Acc. **136**(8), 91 (2017)
3. Vekeman, J., Faginas-Lago, N., Lombardi, A., Sánchez de Merás, A., García Cuesta, I., Rosi, M.: Molecular dynamics of $CH_4/textN_2$ mixtures on a flexible graphene layer: adsorption and selectivity case study. Front. Chem. 386 (2019)
4. Apriliyanto, Y.B., et al.: Nanostructure selectivity for molecular adsorption and separation: the case of Graphyne layers. J. Phys. Chem. C **122**(28), 16195–16208 (2018)
5. Pirani, F., Brizi, S., Roncaratti, L.F., Casavecchia, P., Cappelletti, D., Vecchiocattivi, F.: Beyond the lennard-jones model: a simple and accurate potential function probed by high resolution scattering data useful for molecular dynamics simulations. Phys. Chem. Chem. Phys. **10**(36), 5489–5503 (2008)
6. Liuti, G., Pirani, F.: Regularities in van der waals forces: correlation between the potential parameters and polarizability. Chem. Phys. Lett. **122**(3), 245–250 (1985)
7. Pirani, F., Maciel, G.S., Cappelletti, D., Aquilanti, V.: Experimental benchmarks and phenomenology of interatomic forces: open-shell and electronic anisotropy effects. Int. Rev. Phys. Chem. **25**(1–2), 165–199 (2006)
8. Pirani, F., Albertı, M., Castro, A., Teixidor, M.M., Cappelletti, D.: Atom-bond pairwise additive representation for intermolecular potential energy surfaces. Chem. Phys. Lett. **394**(1–3), 37–44 (2004)
9. Richardson, V., et al.: Fragmentation of interstellar methanol by collisions with $He^{+\cdot}$: an experimental and computational study. Phys. Chem. Chem. Phys. **24**(37), 22437–22452 (2022)

10. Marchione, D., et al.: Unsaturated dinitriles formation routes in extraterrestrial environments: a combined experimental and theoretical investigation of the reaction between Cyano radicals and cyanoethene $C_2H_3CN$. J. Phys. Chem. A **126**(22), 3569–3582 (2022)
11. Chaytor, J.L., et al.: Inhibiting ice recrystallization and optimization of cell viability after cryopreservation. Glycobiology **22**(1), 123–133 (2012)
12. Wolfe, J., Bryant, G.: Freezing, drying, and/or vitrification of membrane-solute-water systems. Cryobiology **39**(2), 103–129 (1999)
13. Lenné, T.: The effects of solutes on the phase behaviour of phospholipid membranes. Ph.D. thesis, RMIT University (2008)
14. Wolfe, J., Bryant, G.: Cellular cryobiology: thermodynamic and mechanical effects. Int. J. Refrig **24**(5), 438–450 (2001)
15. Vaisman, I.I., Berkowitz, M.L.: Local structural order and molecular associations in water-DMSO mixtures. molecular dynamics study. J. Am. Chem. Soc. **114**(20), 7889–7896 (1992)
16. Strader, M.L., Feller, S.E.: A flexible all-atom model of dimethyl sulfoxide for molecular dynamics simulations. J. Phys. Chem. A **106**(6), 1074–1080 (2002)
17. Stachura, S.S., Malajczuk, C.J., Mancera, R.L.: Molecular dynamics simulations of a dmso/water mixture using the amber force field. J. Mol. Model. **24**, 1–8 (2018)
18. Kirchner, B., Reiher, M.: The secret of dimethyl sulfoxide-water mixtures. A quantum chemical study of 1dmso- n water clusters. J. Am. Chem. Soc. **124**(21), 6206–6215 (2002)
19. Geerke, D.P., Oostenbrink, C., van der Vegt, N.F., van Gunsteren, W.F.: An effective force field for molecular dynamics simulations of dimethyl sulfoxide and dimethyl sulfoxide-water mixtures. J. Phys. Chem. B **108**(4), 1436–1445 (2004)
20. Liu, H., Mueller-Plathe, F., van Gunsteren, W.F.: A force field for liquid dimethyl sulfoxide and physical properties of liquid dimethyl sulfoxide calculated using molecular dynamics simulation. J. Am. Chem. Soc. **117**(15), 4363–4366 (1995)
21. Bachmann, S.J., van Gunsteren, W.F.: Polarizable model for DMSO and DMSO-water mixtures. J. Phys. Chem. B **118**(34), 10175–10186 (2014)
22. Bordat, P., Sacristan, J., Reith, D., Girard, S., Glättli, A., Müller-Plathe, F.: An improved dimethyl sulfoxide force field for molecular dynamics simulations. Chem. Phys. Lett. **374**(3–4), 201–205 (2003)
23. Vishnyakov, A., Lyubartsev, A.P., Laaksonen, A.: Molecular dynamics simulations of dimethyl sulfoxide and dimethyl sulfoxide- water mixture. J. Phys. Chem. A **105**(10), 1702–1710 (2001)
24. Becke, A.D.: A new mixing of Hartree-Fock and local density-functional theories. J. Chem. Phys. **98**(2), 1372–1377 (1993)
25. Stephens, P.J., Devlin, F.J., Chabalowski, C.F., Frisch, M.J.: Ab initio calculation of vibrational absorption and circular dichroism spectra using density functional force fields. J. Phys. Chem. **98**(45), 11623–11627 (1994)
26. Dunning Jr, T.H.: Gaussian basis sets for use in correlated molecular calculations. I. The atoms boron through neon and hydrogen. J. Chem. Phys. **90**(2), 1007–1023 (1989)
27. Woon, D.E., Dunning Jr, T.H.: Gaussian basis sets for use in correlated molecular calculations. III. The atoms aluminum through argon. J. Chem. Phys. **98**(2), 1358–1371 (1993)
28. Kendall, R.A., Dunning Jr, T.H., Harrison, R.J.: Electron affinities of the first-row atoms revisited. systematic basis sets and wave functions. J. Chem. Phys. **96**(9), 6796–6806 (1992)

29. Mancini, L., et al.: A computational characterization of the reaction mechanisms for the reactions n (2d)+ ch3cn and hc3n and implications for the nitrogen-rich organic chemistry of titan. Comput. Theor. Chem. **1229**, 114341 (2023)
30. Rosi, M., et al.: Electronic structure and kinetics calculations for the Si+SH reaction, a possible route of SiS formation in star-forming regions. In: Misra, S., et al. (eds.) ICCSA 2019. LNCS, vol. 11621, pp. 306–315. Springer, Cham (2019). https://doi.org/10.1007/978-3-030-24302-9_22
31. Liang, P., et al.: Combined crossed molecular beams and computational study on the n (2d)+ hcccn (x1$\sigma$+) reaction and implications for extra-terrestrial environments. Mol. Phys. **120**(1–2), e1948126 (2022)
32. Frisch, M., et al.: Gaussian 09, Revision A. 02, 2009. Gaussian. Inc., Wallingford (2009)
33. Hanwell, M.D., Curtis, D.E., Lonie, D.C., Vandermeersch, T., Zurek, E., Hutchison, G.R.: Avogadro: an advanced semantic chemical editor, visualization, and analysis platform. J. Cheminformatics **4**(1), 1–17 (2012)
34. Lombardi, A., Laganà, A., Pirani, F., Palazzetti, F., Lago, N.F.: Carbon oxides in gas flows and earth and planetary atmospheres: state-to-state simulations of energy transfer and dissociation reactions. In: Murgante, B., et al. (eds.) ICCSA 2013. LNCS, vol. 7972, pp. 17–31. Springer, Heidelberg (2013). https://doi.org/10.1007/978-3-642-39643-4_2
35. Faginas-Lago, N., Albertí, M., Lombardi, A., Pirani, F.: A force field for acetone: the transition from small clusters to liquid phase investigated by molecular dynamics simulations. Theor. Chem. Acc. **135**(7) (2016). https://doi.org/10.1007/s00214-016-1914-9
36. Lombardi, A., Faginas-Lago, N., Gaia, G., Federico, P. Aquilanti, V.: Collisional energy exchange in $CO_2$–$N_2$ gaseous mixtures. In: Gervasi, O., et al. (eds.) ICCSA 2016. LNCS, vol. 9786, pp. 246–257. Springer, Cham (2016). https://doi.org/10.1007/978-3-319-42085-1_19
37. Albertí, M., Faginas-Lago, N.: Ion size influence on the Ar solvation shells of $M^+C_6F_6$ clusters (M = Na, K, Rb, Cs). J. Phys. Chem. A **116**(12), 3094–3102 (2012). https://doi.org/10.1021/jp300156k
38. Mancini, L., de Aragão, E.V.F.: A computational analysis of the reaction of atomic oxygen O($^3$P) with acrylonitrile. In: Gervasi, O., et al. (eds.) ICCSA 2021. LNCS, vol. 12958, pp. 339–350. Springer, Cham (2021). https://doi.org/10.1007/978-3-030-87016-4_25
39. Mancini, L., et al.: The reaction N($^2$D) + $CH_3CCH$ (methylacetylene): a combined crossed molecular beams and theoretical investigation and implications for the atmosphere of titan. J. Phys. Chem. A **125**(40), 8846–8859 (2021)
40. Pannacci, G., et al.: A combined crossed molecular beam and theoretical study of the O($^3$P,$^1$ D)+ acrylonitrile ($CH_2CHCN$) reactions and implications for combustion and extraterrestrial environments. Phys. Chem. Chem. Phys. **25**(30), 20194–20211 (2023)
41. Rosi, M., et al.: Possible scenarios for SiS formation in the interstellar medium: electronic structure calculations of the potential energy surfaces for the reactions of the sih radical with atomic sulphur and $S_2$. Chem. Phys. Lett. **695**, 87–93 (2018)
42. Johnson, R.D., et al.: Nist computational chemistry comparison and benchmark database (2006). http://srdata.nist.gov/cccbdb
43. Cornell, W.D., et al.: A second generation force field for the simulation of proteins, nucleic acids, and organic molecules. J. Am. Chem. Soc. **117**(19), 5179–5197 (1995)
44. Albertí, M., et al.: Phys. Script. **78**, 058108 (2008)

45. Faginas-Lago, N., Huarte Larrañaga, F., Albertí, M.: On the suitability of the ilj function to match different formulations of the electrostatic potential for water-water interactions. Eur. Phys. J. D **55**(1), 75 (2009)
46. Vanuzzo, G., et al.: Reaction $N(^2D) + CH_2CCH_2$ (allene): an experimental and theoretical investigation and implications for the photochemical models of titan. ACS Earth Space Chem. **6**(10), 2305–2321 (2022)
47. Vanuzzo, G., et al.: The $N(^2D) + CH_2CHCN$ (vinyl cyanide) reaction: a combined crossed molecular beam and theoretical study and implications for the atmosphere of titan. J. Phys. Chem. A **126**(36), 6110–6123 (2022)