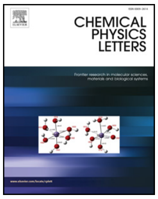
Chemical Physics Letters 713 (2018) 15–20

Contents lists available at ScienceDirect

Chemical Physics Letters

journal homepage: www.elsevier.com/locate/cplett



Research paper

Raman spectra of aqueous uracil stacked dimer: First principle molecular dynamics simulation

B. Milovanović, M. Petković, M. Etinski*

Faculty of Physical Chemistry, University of Belgrade, Studentski trg 12-16, 11000 Belgrade, Serbia

HIGHLIGHTS

- Wannier orbital localization prevents the simulation of aqueous uracil's Raman spectra.
- Mechanical anharmonicity has modest impact on the carbonyl stretching peak positions in the gas phase dimer.
- The discrepancies between the simulated and experimental Raman spectra are larger compared to the infrared counterparts.

ARTICLE INFO

Keywords:
Density functional theory
Aggregation
Nucleobases

ABSTRACT

Raman spectra of aqueous uracil stacked dimer have been studied by employing density functional theory based molecular dynamics simulation together with the maximally localized Wannier functions. The unpolarized spectra are in a reasonable good agreement with the available experimental spectrum. The discrepancies are attributed to the used density functional approximation. Static quantum chemical calculations reveal that the coupling of the carbonyl stretching modes is significantly weaker than the one of the amide modes. The non-coincidence effect of the ring breathing mode is explained in terms of repulsive steric interactions.

1. Introduction

The secondary and tertiary structures of nucleic acids are mainly determined by hydrogen bonding and π-π stacking interactions of nucleobases [1]. On the other hand, in the absence of backbone, nucleobase association depends on solvent hydrogen bonding capacity [2]. In aprotic solvents and gas phase, planar hydrogen-bonded dimers are found to be dominant aggregates [3,4] whereas in protic solvents, the association proceeds via formation of stacked dimers or multimers. Since water molecules are excellent hydrogen bond donors and acceptors, nucleobase association in aqueous solution results in formation of vertical stacks. This association occurs due to enthalpy change since entropy is found to be negative and thus opposes the stacking [2]. Cancellation of the enthalpic and entropic contributions results in the small stacking free energy, which is of the order ~ -1 kcal/mol.

The origin of the thermodynamic forces responsible for the stacking is still under debate. Most of the studies argue that base-base dispersion [1,5] and solvent mediated interactions [6–8] contribute to the stacking stabilization, although several investigations [9,10] pointed out that polar interactions are also important. By employing first principle molecular dynamics, we recently examined structure and infrared spectra of uracil monomer and dimer solvated with water molecules [11]. Our findings revealed that uracil stacking leads to polarization of monomers in a dimer, which consequently increases uracil-water hydrogen bonding and modifies rearrangement of water molecules around the monomers in a dimer. In addition, we simulated and assigned infrared absorption spectra of both species. The simulation reproduced all experimental infrared transitions, although with red-shifted frequencies.

Raman spectroscopy is generally more suitable than infrared absorption spectroscopy for probing nucleobases and their aggregates in biologically relevant environment since water is a notoriously strong infrared absorbing medium. It also might be used to extract information about the interaction potential between the monomers in aggregates using the shapes and the positions of transitions in the polarized Raman spectra. Namely, the anisotropic and isotropic components of the Raman scattering tensor are related to the angular and the spherically symmetric averages of the intramolecular interactions, respectively [12,13]. Thus, the noncoincidence of anisotropic and isotropic Raman spectra originates from the variations in the angular dependence of the intramolecular interactions. If the difference between a peak position in the anisotropic and in the isotropic spectra is positive/negative, the

---

* Corresponding author.
E-mail address: etinski@ffh.bg.ac.rs (M. Etinski).

https://doi.org/10.1016/j.cplett.2018.10.015
Received 9 July 2018; Accepted 4 October 2018

phenomenon is called the positive/negative noncoincidence effect. The sign and the magnitude of the noncoincidence effect are sensitive probes for the structure and the relative orientation of the monomers in aggregates [14,15,13,16,17]. Tavagnacco et al. used this fact to study caffeine stacking in aqueous solution [10]. By analyzing the frequency shifts between the anisotropic and isotropic Raman bands of totally symmetric breathing modes of the purine rings and bending modes of the methyl groups, they concluded that caffeine aggregation occurred by planar stacking of the hydrophobic faces. Besides, they found the caffeine molecules avoided a perpendicular orientation of the permanent dipole moment vectors of adjacent molecules.

For a proper understanding of Raman spectra, a reliable simulation of vibrational transitions and intensities is essential. This could be a formidable task in aqueous solutions because solvent hydrogen bonding and thermal fluctuations together with mechanical and electrical anharmonicity of the solute are necessary to be included for a proper description of the Raman response. In the beginning of this work, we intended to simulate the unpolarized and the polarized Raman spectra of aqueous uracil monomer and stacked dimer by employing first principle molecular dynamics. During the simulation of the monomer Raman spectrum, we came across difficulties recently reported by Thomas et al. [18] related to numerical calculation of aromatic molecules' polarizability with the maximally localized Wannier orbitals. These authors showed that different localizations of the Wannier orbitals in the two electronic structure calculations with and without the electric field might artificially increase the polarizability of an aromatic molecule by orders of magnitude and thus provide inaccurate Raman spectra. Although pyrimidine ring is not formally aromatic, we observed the same issue as Thomas et al. [18] for the monomer system since hydration causes bond length alternation and formation of zwitter-ionic resonance structures. On the other hand, the different orbital localization issue was absent in the case of the dimer system, which is most likely due to enhanced rigidity of the pyrimidine ring caused by stacking [11]. To overcome this problem, Thomas et al. suggested [18] partitioning of the electron density by radical Voronoi tessellation to compute molecular dipole moments and polarizabilities. Nevertheless, in this work we only report uracil stacked dimer Raman spectra. Up to our knowledge, ab initio molecular dynamics has not been employed to simulate the Raman spectra of aqueous uracil, although its spectra were extensively experimentally and theoretically studied [19–23]. The majority of quantum chemical studies [24,19,25,21,26,22] used the linear dipole and harmonic oscillator approximation as well as dielectric continuum models to simulate uracil's vibrational response, although sometimes higher level theoretical models were also employed [27–31]. Therefore, it is of interest to examine the extent to which first principle molecular dynamics might reproduce the Raman spectrum. In addition, the simulation of the polarized spectra offers a possibility to examine the sign and the magnitude of the noncoincidence effect in the dimer.

2. Theoretical methods

In order to compute Raman spectra of aqueous stacked uracil dimer, we employed the trajectory collected in our previous work [11]. Here, we briefly recapitulate the computational setup, whereas more details are provided elsewhere [11]. The molecular dynamics simulations were performed with the CP2K [32] program package. We utilized the BLYP functional [33,34] based on the generalized gradient approximation together with Grimme's D3 correction for dispersion interactions [35] and mixed Gaussian (DZVP) and plane waves basis set [36]. The dimer was solvated with 63 water molecules under periodic conditions in a cubic box of 12.94 Å and equilibrated in the canonical ensemble for 10 ps to temperature of 300 K. Afterwards, a production run was performed in a microcanonical ensemble together with calculation of maximally localized Wannier orbitals. We selected the first 15 ps of the production run and recomputed the Wannier orbitals applying an electric field along positive and negative directions of x, y, and z axes with the intensity 0.0005 a.u. The orbitals were recomputed every 2.5 ps, resulting in 6000 points along the trajectory. Uracil's polarizability tensor was subsequently computed numerically. The orientational averaging of the polarizability tensor was applied for the calculation of spectra. Raman intensities were computed by employing excitation wavelength 1.06 μm. The spectra were calculated using the TRAVIS program package [37,38]. The assignment of the spectrum was performed by using the power spectra from our previous work [11].

Static quantum chemical calculations were performed with the Turbomole program package [39]. We employed density functional theory with the same functional as in the molecular dynamics simulations and Dunning's [40,41] correlation-consistent basis set aug-cc-pVDZ (C, O: 10s5p2d/4s3p2d; H: 5s2p/3s2p). Cubic and quartic anharmonic coefficients for the C═O stretching modes of the uracil monomer and the FB72 dimer (see next section) were estimated with the finite difference procedure from analytic second derivatives[42,43] computed with the Gaussian program package[44] at the BLYP-D3/aug-cc-pVDZ level. Raman intensities were evaluated by using excitation wavelength 0.51 μm. The reduced density gradient was computed at BLYP/aug-cc-pVDZ//BLYP-D3//aug-cc-pVDZ level, whereas its analysis was performed with the AIMAll program package [45].

3. Results and discussion

3.1. The coupling of the carbonyl stretching modes

In our previous work, we reported that the N—H stretching modes of stacked 1-methylthymine dimer were strongly coupled [3]. For each examined stacked dimer, there were several cubic anharmonic force constants above 500 cm^{-1}, which usually included interaction with the out-of-plane N—H bending modes. The one-dimensional potential energy curves along N—H stretching modes revealed that the anharmonic frequency shifts amounted up to 170 cm^{-1}. On the other hand, first principle molecular dynamics simulations showed that aqueous uracil exhibited much smaller frequency shifts in the region from 500 to 1800 cm^{-1} upon stacking. The largest discrepancies are found for the C2═O2 stretching mode (~ 30 cm^{-1}), C4═O4 and C5═C6 (8–18 cm^{-1}), whereas other modes were modified by less than 10 cm^{-1} (see Fig. 1. in Ref. [11] for the atomic labels). Nevertheless, the limited timescale of the molecular dynamics simulation did not allow us to examine all conformers of the stacked dimer.

Here, we examine the stretching carbonyl modes since we previously found that these modes are sensitive to uracil aggregation [11]. Particularly, we are interested into what extent different orientations of monomers in the dimer influences positions and intensities of the carbonyl stretching modes in infrared and Raman spectra. The static quantum chemical calculations in the gas phase allow us to directly examine all dimer conformers. To this end, we computed the harmonic frequencies, anharmonic coupling terms and the Raman and infrared responses of the C═O stretching modes of stacked dimers in the gas phase.

Let us first briefly discuss the two C═O stretching modes in the monomer. For simplicity, we will consider absolute values of all anharmonic coefficients. The harmonic values for the C2═O2 and C4═O4 stretching frequencies amount to 1711 and 1675 cm^{-1}, respectively. The diagonal cubic terms (407 and 397 cm^{-1}) are more pronounced than the diagonal quartic terms which are significantly below 200 cm^{-1} (136 and 116 cm^{-1}). All mixed terms (both cubic and quartic) are considerably lower than 200 cm^{-1}. Thus, the two C═O stretching modes in the monomer are basically uncoupled.

The stacked dimers might be found in face-to-back (FB) or face-to-face (FF) configurations. The former configuration corresponds to the case in which one base is on the top of the other, whereas in the later configuration one base is flipped by 180 degrees. Hunter and van Mourik [46] reported three face-to-back (FB72, FB180, FB288) and two