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Anharmonic C−H and C=O Interactions in Peptide and Sugar[†]

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C−H and C=O stretching modes are two among many structural and dynamic probes of proteins and peptides in condensed phases. Anharmonic properties of these two modes in peptide and sugar have been examined using a second-order perturbative vibrational approach. High order force constants were obtained and examined to find how crucial they are in determining the degree of mode localization and the nature of mode anharmonicity of the two stretching modes. It is found that the C−H mode is highly localized, and its diagonal anharmonicity is mainly determined by the mode itself. However, the C=O mode is largely delocalized, and the diagonal anharmonicity involves contributions from other modes. The off-diagonal anharmonicity between C−D and C=O modes is found to be negative in deuterated species, differing from those of the non-deuterated ones. It is also found that inter-mode interaction between each of the two modes with low-frequency modes contribute significantly to the off-diagonal anharmonicity. These low-frequency modes give rise to a network of energy relaxation or intramolecular vibrational energy redistribution pathways which can be used to examine temporal behavior of intramolecular vibration energy flow, provided a femtosecond broadband two-dimensional infrared spectroscopy is available.

Key words: Anharmonicity, Two-dimensional infrared spectroscopy, Peptide, Sugar, Vibrational interaction

I. INTRODUCTION

C−H stretching modes has been recognized as a potential probe of structures and dynamics in a molecule complex in condensed phases [1]. Its deuterated form, C−D, appears to have a vibration frequency that does not likely to overlap with most of other normal mode vibrations in mid-infrared region. C=O stretching mode, on the other hand, has been known to be a useful and reliable backbone conformation reporter for protein and peptide [2]. More interestingly, it has been found that the two species, C−H(D) especially C_α−H(D), and C=O, may form an intermolecular hydrogen bond in certain proteins that have a framework provided by two glycine residues separated by three intervening residues (GxxxG). An example of such is a glycoprotein called glycophorin A [3]. Therefore the anharmonic properties of the C−D and C=O modes and their combination band, have been a subject of recent two-dimensional infrared (2D IR) studies [4,5].

The 2D IR technique is useful in revealing inter-mode interactions of anharmonic vibrations of peptide, from which angular and distance information about two species could be obtained [6-9]. There are quite extensive studies of the nature of the anharmonicities and couplings among C=O stretching modes (such as found in the amide-I mode of a protein), however, little is known about the anharmonic nature of the

C−H(D) stretching modes, especially in biomolecules such as proteins and sugars. For polyatomic system, it is well known that incorporating anharmonicity in a quantum chemical calculation of vibrational frequency could bring better agreement between theory and gas-phase measurement, since all the polyatomic vibrational modes are intrinsically anharmonic. Recently we have examined the anharmonic properties of the amide modes in small model peptide, using one of the elegant computational methods, the second-order perturbative vibrational treatment [10-15]. It was found that theoretical predictions of the anharmonicities of amide modes are consistent with measureables obtained from recent 2D IR experiments.

The goal of this work is to learn about the anharmonicities and inter-mode interaction between C−H(D) and C=O stretching modes. The molecules we have chosen are formamide and N,N-dimethylformamide, both being the smallest peptide model compounds; and glycolaldehyde, the smallest diose. The gas-phase geometry and harmonic vibrational frequencies of formamide monomer and oligomers have been well studied by quantum chemical calculations [16-19]. Structures and dynamics of liquid formamide have also been investigated using classical molecular dynamics simulation [20,21] and *ab initio* molecular dynamics simulation [22,23]. The anharmonic frequencies of formamide monomer and dimer in the gas phase have also been reported [24-27]. The gas-phase experimental studies of glycolaldehyde have also been reported [28,29].

In this work, the harmonic and anharmonic vibrational frequencies of these molecules and their deuterated isotopomers are examined using a quantum chemical approach. The diagonal and mixed-mode off-

diagonal anharmonicities of C−H(D) and C=O stretching modes are obtained. We analyzed the factors that influence these anharmonicities, and identify intermode interactions that contribute most to the anharmonicity. The localization nature of the C−H(D) and C=O stretching modes for these molecules have been examined by potential energy distribution analysis. Efforts have also been made to explain the negative mixed-mode anharmonicity of C−D and C=O stretching modes.

II. METHODS

The anharmonic vibrational frequencies of three chosen molecules, formamide (NH_2CHO), N,N-dimethylformamide ($N(CH_3)_2CHO$), and glycolaldehyde (CH_2OHCHO) were calculated using density functional theory (DFT), at the B3LYP level of theory with the 6-311++G** basis set. Their deuterated isotopomers, ND_2CDO (formamide-d_3), $N(CH_3)_2CDO$, and CH_2OHCDO were also considered. A tight convergence was used during the geometry optimization and harmonic and anharmonic frequency calculations. All calculations were carried out using Gaussian03 [17]. The structures of these three molecules are given in Fig.1.
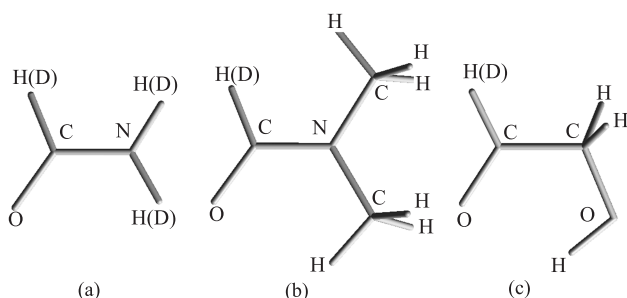

FIG. 1 Optimized molecular structures of (a) formamide, (b) N,N-dimethylformamide, and (c) glycolaldehyde.

The diagonal anharmonicity and the mixed-mode anharmonicity are obtained in a straightforward way. In the normal mode basis, the vibrational energy of fundamentals, overtones and combination bands of a polyatomic molecule can be written as [30]

$$E(n_i, n_j) = E_0 + hc \sum_i^{3N-6} \omega_i \left(n_i + \frac{1}{2}\right)$$
$$+ hc \sum_{i \le j}^{3N-6} x_{ij} \left(n_i + \frac{1}{2}\right)\left(n_j + \frac{1}{2}\right) \quad (1)$$

here ω_i is the harmonic frequency, n_i is the vibrational quantum number of the ith mode, and x_{ij} is the anharmonic correction term. In Eq.(1), h is plank's constant and c is speed of light. Using the second-order perturbation approach [10,11,15], x_{ij} and x_{ii} can be obtained

in terms of the cubic and quartic force constants:

$$x_{ii} = -\frac{1}{16}\left[-\Phi_{iiii} + \frac{5\Phi_{iii}^2}{3\omega_i} + \sum_{k \ne i=1}^{3N-7} \frac{\Phi_{iik}^2 \left(8\omega_i^2 - 3\omega_k^2\right)}{\omega_k \left(4\omega_i^2 - \omega_k^2\right)}\right] \quad (2)$$

$$x'_{ij} = -\frac{1}{4}\left(-\Phi_{iijj} + \frac{\Phi_{iii}\Phi_{ijj}}{\omega_i} + \frac{\Phi_{jjj}\Phi_{iij}}{\omega_j} + \frac{2\Phi_{iij}^2\omega_i}{4\omega_i^2 - \omega_j^2} + \frac{2\Phi_{jji}^2\omega_j}{4\omega_j^2 - \omega_i^2}\right) \quad (3)$$

$$x''_{ij} = -\frac{1}{4}\sum_{k \ne j \ne i=1}^{3N-8}\left[\frac{\Phi_{iik}\Phi_{jjk}}{\omega_k} - \frac{2\Phi_{ijk}^2(\omega_i^2 + \omega_j^2 - \omega_k^2)\omega_k}{\omega_i^4 + \omega_j^4 + \omega_k^4 - 2(\omega_i^2\omega_j^2 + \omega_i^2\omega_k^2 + \omega_j^2\omega_k^2)}\right] \quad (4)$$

here coefficients Φ_{ijk} and Φ_{ijkl} are general form of the third and fourth derivatives of the potential that involve various normal coordinates. The mixed-mode off-diagonal anharmonic term is $x_{ij} = x'_{ij} + x''_{ij}$. The anharmonic fundamental, the overtone and the combination band frequencies are given by

$$\nu_i = \omega_i + 2x_{ii} + \frac{1}{2}\sum_{j \ne i} x_{ij} \quad (5)$$

$$\nu_{2i} = 2\nu_i + 2x_{ii} \quad (6)$$

$$\nu_{ij} = \nu_i + \nu_j + x_{ij} \quad (7)$$

therefore the diagonal anharmonicity Δ_i can be obtained as

$$\Delta_i = -2x_{ii} \quad (8)$$

Using Eqs.(2) and (8), one is able to examine the composition of the diagonal anharmonicity: the first two terms in Eq.(2) involve exclusively energy derivatives with respect to the mode i, which can be denoted as x'_{ii} and the third term in Eq.(2) can be denoted as x''_{ii}, so that $x_i = x'_{ii} + x''_{ii}$ and $\Delta_i = \Delta'_i + \Delta''_i$. Similarly, using Eqs.(3) and (4), one is able to examine the detailed composition of the mixed-mode anharmonicity:

$$\Delta'_{ij} = -x'_{ij} \quad (9)$$
$$\Delta''_{ij} = -x''_{ij} \quad (10)$$

and we have a total mixed-mode anharmonicity as $\Delta_{ij} = \Delta'_{ij} + \Delta''_{ij}$. For any two vibrators i and j, the mixed-mode anharmonicity contains contribution from solely the interaction between the two vibrators which can also be expressed in terms of the cubic and quartic force constants and harmonic frequencies, shown in Eqs.(3) and (9). The contribution to the mixed-mode anharmonicity from the interaction of the modes i and j with the remaining 3N-8 modes is given in Eqs.(4) and (10). Using these equations, a detailed numerical analysis of the anharmonicities was carried out.

TABLE I Calculated harmonic (ω) and anharmonic (ν) frequencies (in cm^{-1}) of the C−H(D) and C=O stretching modes, their overtones, combination bands, and diagonal anharmonicities ($\Delta_{C-H(D)}$ and $\Delta_{C=O}$) and off-diagonal anharmonicities ($\Delta_{C-H(D)+C=O}$) of the two modes in peptides and sugars in gas phase

Molecule	Formamide		N,N-dimethylformamide		Glycolaldehyde	
Isotopomer	H-form	D$_3$-form	H-form	D-form	H-form	D-form
$\omega_{C-H(D)}$	2945.307	2179.160	2944.569	2176.493	2927.788	2167.162
$\omega_{C=O}$	1790.590	1761.589	1752.253	1734.683	1792.322	1774.894
$\nu_{C-H(D)}$	2795.707	2097.832	2797.799	2099.592	2761.078	2028.947
$\nu_{2C-H(D)}$	5449.013	4120.572	5452.815	4121.754	5386.094	3980.232
$\nu_{C=O}$	1756.862	1742.069	1724.463	1714.167	1768.271	1744.594
$\nu_{2C=O}$	3495.676	3464.832	3428.387	3410.475	3515.845	3469.346
$\nu_{C-H(D)+C=O}$	4549.262	3840.517	4514.436	3815.195	4528.826	3774.508
$\Delta_{C-H(D)}$	142.4010	75.0920	142.7830	77.4300	136.0620	77.6620
$\Delta_{C=O}$	18.0480	19.3060	20.5390	17.8590	20.6970	19.8420
$\Delta_{C-H(D)+C=O}$	3.3070	−0.6160	7.8260	−1.4360	0.5230	−0.9670

III. RESULTS AND DISCUSSION

A. Calculated harmonic and anharmonic frequencies of the C−H(D) and C=O stretching modes

Table I listed the calculated gas-phase harmonic (ω) and anharmonic (ν) frequencies of C−H stretching and C=O stretching modes, their overtones and combinations bands for formamide, N,N-dimethylformamide, and glycolaldehyde. We are interested in the anharmonic properties of the C−H(D) and C=O stretching modes mainly arising from the left side of the molecule, that is, the O−C−H(D) species. The C−D and C=O frequencies of their isotopomers, ND$_2$CDO, N(CH$_3$)$_2$CDO, and CH$_2$OHCDO were also calculated. It is found that when anharmonic is incorporated the C−H and C−D transition frequencies decreases by ca. 150-180 cm^{-1} in these three molecules and their deuterium isotopomers, suggesting a similar anharmonic behavior of the C−H (and C−D) stretching modes in peptide and sugar. On the other hand, the C=O stretching frequency only decreases by 20-35 cm^{-1} in both the H- and D-isotopomers of these three molecules, indicating that the C=O modes are less anharmonic than the C−H(D) modes.

The calculated anharmonic frequencies are expected to be in better reasonable agreement with gas-phase experimental results. Using the formamide as an example, the gas-phase measurements yield $\nu_{C=O}$=1755 cm^{-1} [28], whereas the calculated frequency is $\nu_{C=O}$=1753.9 cm^{-1}. For glycolaldehyde, the C=O stretching frequency was found to be 1753 cm^{-1} in gas phase [29] and 1744 cm^{-1} in aqueous solution [31]. Our calculation shows the C=O stretching frequencies are 1768.3 and 1744.6 cm^{-1} for the H- and D-form respectively, which are very close to the gas-phase values.

B. Calculated anharmonicities

Table I also summarizes the calculated anharmonicities of the C−H(D) and C=O stretching modes for six isotopomers. The anharmonicity of the C−H modes is always around 140 cm^{-1}, and that of the C−D modes is around 75 cm^{-1}. These results indicate that the anharmonicity of the C−H stretching mode is very sensitive to the deuterium replacement. The ratio of these two anharmonicities is near 1.9 in all cases, suggesting the vibrational potentials of these vibrators are alike Morse potential. The anharmonicity of the C=O stretching mode is less affected by the deuterium replacement: the values are between 17 and 20 cm^{-1} for these isotopomers. A similar value is found experimentally for the amide-I mode (essentially C=O stretching motion) of peptide [32]. These results indicate that the anharmonicity of the C=O stretching mode is not too sensitive to the H/D exchange of its nearby chemical groups. The most striking observation is the value of the C−H(D) and C=O mixed-mode anharmonicity in these six isotopomers: it is positive for the H-form isotopomer but negative for the D-form isotopomers. A detailed analysis is needed to understand such behavior (see the following section). The results shown in Table I also suggest that as far as only the −CHO species are concerned, the anharmonicities of these two types of stretching modes in sugar molecules are quite similar to those in peptide.

C. Composition of the diagonal anharmonicities

It is of interest to understand the intrinsic nature of the diagonal anharmonicity of certain modes in a molecule. As have been seen in our recent 2D IR study of a β-hairpin, the diagonal anharmonicity is very sensitive to peptide local conformation [33]. The composition of the diagonal anharmonicity has been examined

TABLE II Harmonic frequencies, cubic and quartic force constants (in cm^{-1}) and their contributions to the diagonal anharmonicities of the C−H(D) and C=O modes in these compounds

Isotopomer	Vibrator i	Species	ω_i	Φ_{iiii}	Φ_{iii}	Δ'_i	Δ_i	Δ'_i/Δ_i
H-form	C−H	Formamide	2945.307	1083.3999	−1974.3343	140.2958	142.401	0.9852
		N,N-dimethylformamide	2944.569	1062.3093	1964.8278	140.3518	142.783	0.9830
		Glycolaldehyde	2927.788	968.8722	−1844.9370	121.0955	136.062	0.8900
	C=O	Formamide	1790.590	143.9462	−472.8089	8.0163	18.048	0.4442
		N,N-dimethylformamide	1752.253	153.1620	−474.6602	7.6420	20.539	0.3721
		Glycolaldehyde	1792.322	172.7989	−572.9934	16.5631	20.697	0.8003
D-form	C−D	Formamide	2179.160	560.96541	−1209.1390	69.6519	75.092	0.9276
		N,N-dimethylformamide	2176.493	561.4332	1225.3068	73.5322	77.430	0.9497
		Glycolaldehyde	2167.162	537.2004	−1202.3504	71.8226	77.662	0.9248
	C=O	Formamide	1761.589	143.7577	−466.0941	7.7225	19.306	0.4000
		N,N-dimethylformamide	1734.683	142.5423	−434.9071	4.8982	17.859	0.2743
		Glycolaldehyde	1774.894	156.7451	−535.2371	14.0331	19.842	0.7072

for the C−H(D) and C=O modes in the three molecules and their deuterium isotopomers, to investigate the localization of the anharmonic forces. The results are given in Table II, which includes calculated harmonic frequencies, the cubic and quartic force constants, and the contributions of those terms in Eqs.(2) and (8) to the diagonal anharmonicities of C−H(D) and C=O modes of the six isotopomers. For the C−H stretching mode, it is seen that more than 89.0% of Δ_i come from Δ'_i, suggesting that the C−H mode is a highly localized mode, and the interaction between the C−H mode and other normal modes only contribute to a small extent to the diagonal anharmonicity of this vibrator. The Δ'_i/Δ_i ratio is also in the range of 0.92-0.94 for the C−D stretching mode, suggesting a similar localization nature of the C−D mode. In both the H-form and D-form, the Δ'_i/Δ_i ratio of glycolaldehyde was found to be the lowest, indicating a smaller degree of localization of the C−H(D) stretching mode in the sugar molecule. For the C=O stretching mode, the Δ'_i/Δ_i ratio was found to be less than 0.44 in peptides but as high as 0.80 in glycolaldehyde, suggesting that the C=O modes in peptide and sugar molecules have completely different localization situation. These results suggest that although the C−H(D) mode seems to be localized and the C=O mode seems to be delocalized, there is actually no pure local mode in these molecules, the diagonal anharmonicities of the C−H(D) and C=O stretching modes are always dependent on the inter-mode interactions to some extent.

D. Composition of the mixed-mode anharmonicities

We have also examined the mixed-mode anharmonicities between the C−H(D) and C=O stretching modes in these molecules. The calculated harmonic frequencies, the cubic and quartic force constants and their contributions to the mixed-mode anharmonicities are

listed in Table III. The magnitude of Δ'_{ij} for the six pairs of C−H(D) and C=O modes are shown, along with the Δ'_{ij} values taken from Table I. The Δ'_{ij}/Δ_{ij} is of no much meaning in these cases, because either the magnitude of Δ'_{ij} is larger than Δ_{ij}, or different signs are seen for these two parameters. These results suggest that the interaction of the two modes is not the only parameter that determines the mixed-mode anharmonicities. This argument is further supported by the fact that Φ_{iijj} is not as significant as other force constants listed in the table, and also by the fact that cubic force constants Φ_{iii} and Φ_{jjj} have different signs, so do Φ_{jjj} and Φ_{iij}. Because of these reasons, the calculated Δ'_{ij}, using Eqs.(3) and (9) becomes largely negative. In addition, these results show that the total off-diagonal anharmonicity is influenced by the force field and hence is isotope dependent.

E. Inter-mode interaction and anharmonicity

It is very interesting to find out how much the inter-mode interaction contributes to or influences the sign and magnitude of the diagonal and mixed-mode off-diagonal anharmonicities. For this, we examine the composition of Δ''_i and Δ''_{ij} by plotting the composition of them as a function of the anharmonic normal mode frequencies of the entire 3N-6 modes of a molecule. The influence of the different modes, according to Eqs.(2) and (8) and Eqs.(4) and (10), on the diagonal and off-diagonal anharmonicities can be thus examined explicitly. The results are given in Fig.2 and Fig.3.

Figure 2 shows the calculated Δ''_i of the C=O mode versus the frequency of the normal modes for three deuterated molecules. As can be seen that almost all modes contribute to Δ''_i, most significant contributions are all positive and mostly from low-frequency modes. It is also noticed that the C−D stretching modes play a significant role in contributing to Δ''_i of C=O stretching

TABLE III Harmonic frequencies, cubic and quartic force constants (in cm^{-1}), and their contributions to the mixed-mode anharmonicity of C−H(D) and C=O modes in these compounds

Vibrator i/j pair	Compound	ω_i	ω_j	Φ_{iijj}	Φ_{iii}	Φ_{jjj}
C−H/C=O	Formamide	2945.307	1790.590	−48.9859	−1974.3343	−472.8089
	N,N-dimethylformamide	2944.569	1752.253	−48.3489	1964.8278	−474.6602
	Glycolaldehyde	2927.788	1792.322	−34.1498	−1844.9370	−572.9934
C−D/C=O	Formamide	2179.160	1761.589	−2.4492	−1209.1390	−466.094
	N,N-dimethylformamide	2176.493	1734.683	−6.8942	1225.3068	−434.9071
	Glycolaldehyde	2167.162	1774.894	−1.0760	−1202.3504	−535.2371
		Φ_{iij}	Φ_{ijj}	Δ'_{ij}	Δ_{ij}	
C−H/C=O	Formamide	42.1216	83.0965	−2.8871	3.3070	
	N,N-dimethylformamide	49.1878	−80.7146	−3.0152	7.8260	
	Glycolaldehyde	56.1972	58.0288	−4.2415	0.5230	
C−D/C=O	Formamide	−160.1137	140.5565	−4.2660	−0.6160	
	N,N-dimethylformamide	−126.5759	−132.6539	−5.8282	−1.4360	
	Glycolaldehyde	−151.44798	129.73140	−2.8281	−0.9670	

* The value of Δ'_{ij}/Δ_{ij} was not calculated because Δ'_{ij} and Δ_{ij} have different signs.

mode in all three cases. Band assignment has been carried out. For formamide the largest contribution is coming from the C−N stretching plus ND$_2$ in-plane-bending motions, but it is C−N stretching plus NC$_2$ in-plane-bending motions in the case of N,N-dimethylformamide. For Glycolaldehyde, it is C−D in-plane-bending that has the largest contribution.

Figure 3 shows the calculated Δ''_{ij} of the C−D and C=O mixed mode versus the frequency of the normal modes for three deuterated molecules. As can be seen, almost all the modes contribute to Δ''_{ij}, a large percentage of the contribution is from low-frequency modes and the sum of the contribution is positive. The largest contribution is also coming from the ND$_2$ in-plane-bending motion in the case of formamide. In the case of N,N-dimethylformamide, the contribution from the CH$_n$ stretching modes is also significant. Therefore the anharmonic shift of the C−H(D) and C=O combination band depends not only on the interaction of the specific pair, but also on the interaction of each of the two modes with the remaining 3N-8 normal modes. From normal mode analysis, it is found that the C−N stretching plus ND$_2$ in-plane-bending motions contributes most to the mixed-mode anharmonicity in the case of formamide. For N,N-dimethylformamide, it is shown that C−N stretching plus NC$_2$ in-plane-bending motions give the largest contribution. For glycolaldehyde, the C−D in-plane-bending motion contributes dominantly. Essentially these contributors are the same as those in the Δ''_i as shown in Fig.2.

These results are of fundamental interest in understanding the intrinsic properties of the anharmonic C−H(D) and C=O stretching modes. First, the occurrence of off-diagonal forces involving other modes, suggests that simple, local model picture of the an-

harmonicity could easily miss some essential molecular structural content. Second, the complexity of the anharmonic coupling matrix in the normal mode basis suggests also a complex set of vibration energy relaxation pathways for these modes once being excited [30]. And third, because there is a great deal of coupled modes in a molecules, one may expect to build a network of interactions and vibration energy relaxation pathways by means of time-dependent 2D IR spectra so as to reveal the temporal behavior of internal vibration redistribution, and one may be able to get a complete picture of energy flow channels for vibration energy relaxation within the same molecule, or even within solute-solvent molecular complexes.

The off-diagonal anharmonicity of the C−D and C=O stretching modes in formamide-d$_3$ has been studied very recently [4]. A negative Δ_{ij} was obtained (−0.85±0.2 cm^{-1}), which falls into the range of the predicted values in all three deuterated species (Table I), indicating that *ab initio* calculations at a reasonable level of theory, is able to predict certain anharmonic vibrational parameters quite satisfactorily. This also implies that the mixed-mode anharmonicity of C−D and C=O stretching modes are quite similar in peptides and sugars. Thus, one may begin exploring the structures and dynamics of molecular complexes of sugars and other biomolecules as well, by using these structural probes in combination of femtosecond 2D IR spectroscopy.

F. Potential energy distributions

To verify the degree of localization of the C−H(D) and C=O stretching modes, we finally examined the potential energy distributions (PED) in the normal mode
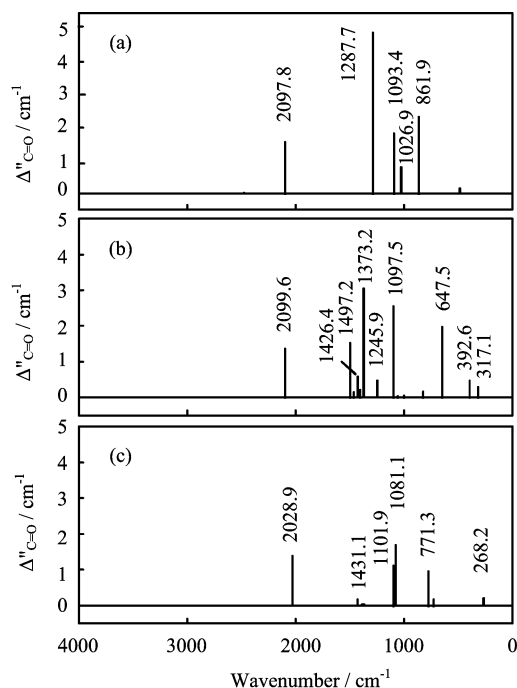
FIG. 2 Calculated contributions of the cubic force constants to the diagonal anharmonicity (Δ''_i) of the C=O stretching mode versus the anharmonic frequency of the normal modes. (a) Deuterated formamide. Bands assignments are: 2097.8 (C−D stretching), 1287.7 (C−N stretching plus N−D$_2$ in-plane bending), 1093.4 (N−D$_2$ in-plane bending plus C−D in-plane bending), 1026.9 (C−D in-plane bending), and 861.9 (N−C=O deformation plus C−D in-plane bending). (b) Deuterated N,N-dimethylformamide. Major bands assignments are: 2099.6 (C−D stretching), 1497.2 (C−D$_3$ rocking), 1373.2 (C−N stretching), 1097.5 (C−D in-plane bending), and 647.5 (CNC in-plane bending). (c) Deuterated glycolaldehyde. Major bands have been assigned: 2028.9 (C−D stretching), 1101.9 (C−D stretching), 1081.1 (C−D in plane bending) and 771.3 (C−C stretching).

FIG. 3 Calculated contributions of the cubic force constants to the off-diagonal anharmonicity (Δ''_{ij}) of the C−D and C=O stretching modes versus the anharmonic frequency of the normal modes. (a) Deuterated formamide. (b) Deuterated N,N-dimethylformamide. (c) Deuterated glycolaldehyde. Major bands can be assigned similarly as in Fig.2. Two low-frequency bands giving negative contributions are 317.1 (C=O in plane bending plus C−N−C in-plane bending) in (b) and 268.2 (C=O in plane bending plus C−O−H in-plane bending) in (c), respectively.

TABLE IV Potential energy distributions (PED) of C−H(D) and C=O stretching modes calculated in the normal mode basis for the six isotopomers

	Species	C−H(D)	C=O
Non-deuterated	Formamide	0.9997	0.5160
	N,N-dimethylformamide	0.9931	0.5833
	Glycolaldehyde	0.9599	0.7178
Deuterated	Formamide	0.9978	0.6773
	N,N-dimethylformamide	0.9982	0.6012
	Glycolaldehyde	0.9951	0.6569

basis. The PED values of the C−H(D) stretching modes were calculated by summarizing the wave function coefficients (the normal coordinates) of the C and H (or D) atoms, whereas the PED values of the C=O stretching modes were obtained by summarizing the wave function coefficients of the C and O atoms. Similar calculations
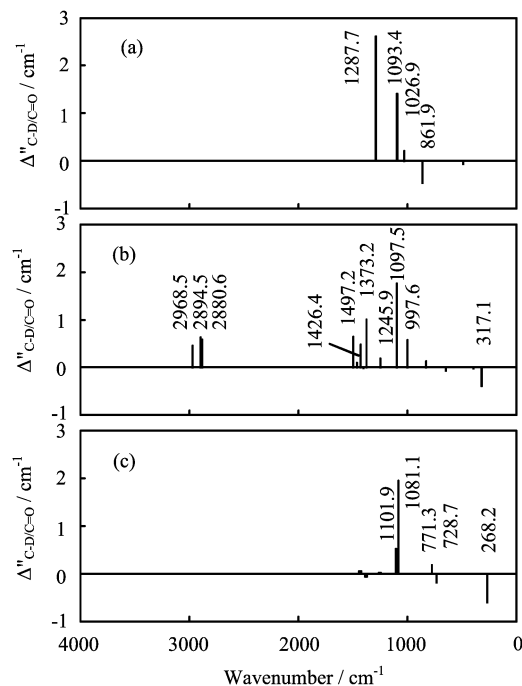
can be done in terms of internal coordinates, however we chose to use the Cartesian coordinates. Table IV summarizes the PED values of C−H(D) and C=O stretching modes for the six isotopomers. Values are the sum of wave functions of C and H(D) atoms for the C−H(D) mode, and that of C and O atoms for the C=O mode. It is not surprising to note that the C−H(D) stretching mode is indeed highly localized onto C and H(D) atoms, whereas the C=O stretching mode is only partially localized. These results are in agreement with the composition analysis performed on the diagonal anharmonicities given in Table II.

G. Anharmonicity and delocalization

The findings that the diagonal anharmonicity of the C=O stretching mode contains substantial contributions from modes other than the mode itself, is closely related to the nature of the normal mode: the C=O mode is significantly delocalized in these molecules. Results are shown quite convincingly in Fig.2. Thus, it is not a surprise that a mixed-mode anharmonicity involving this normal mode would also show low-

frequency contributions from modes other than the two modes themselves. This is clearly shown in the case of C=O/C−D. By comparing Fig.2(a) and Fig.3(a) it can be seen that the identities of four major low-frequency contributors are essentially the same. Similar results are also seen in Fig.2(b) and Fig.3(b), and Fig.2(c) and Fig.3(c) respectively, strongly suggesting that the mixed-mode anharmonicity is significantly influenced by the delocalization of one or two of the two modes involved. The sum of the force field-dependent contributions in each panel of Fig.3 is positive, making a big difference in the sign of the total mixed-mode anharmonicity.

IV. CONCLUSION

In this work, the second-order perturbative vibrational treatment was employed to calculate the vibrational frequencies of peptide and sugar molecules in the fundamental, overtone, and combination regions. The anharmonic potential parameters of the C−H(D) and C=O modes in peptide and sugar were examined specifically. A detailed composition analysis of the anharmonicity was performed to reveal the intrinsic characteristics of the anharmonicity of these two types of modes using the *ab initio* computational results.

Theory suggests that the diagonal anharmonicity of the C−H(D) transitions is insensitive to the interaction between the C−H(D) mode and other normal modes. However, the diagonal anharmonicity of the C=O transitions is much sensitive to such inter-mode interactions and thus involves essentially all the normal modes in a molecule. These results can be explained by the delocalization nature of vibrational modes: the C−H(D) stretching modes are very much localized, whereas the C=O stretching modes are very much delocalized, a conclusion also drawn from their potential energy distributions.

Theory also suggests that the anharmonic properties of both the C−H(D) and C=O stretching modes are quite similar in peptide and in sugar, suggesting that these two types of biomolecules could share a common theoretical and experimental library of anharmonic parameters in structural determinations and dynamical characterizations, even though the chemical environment is somewhat different in peptide and sugar for both the C−H(D) and C=O species.

Theory also suggests that the off-diagonal anharmonicity of the C−H(D) and C=O stretching modes are isotopomers dependent: positive in C−H and C=O pair, but negative in C−D and C=O pair, and the latter is found to be in reasonable agreement with a recent 2D IR experimental study. The isotope-dependent off-diagonal anharmonicity is due to the isotope-dependent force field, which is an intrinsic property of the force field. Our results indicate that quantum chemical computations at a reasonable level of theory can apparently

be a useful tool in describing or predicting the anharmonic parameters for modeling or analyzing 2D IR experimental results. Moreover, almost all the normal modes were found to contribute to the diagonal and off-diagonal anharmonicities of the modes studied here to some extent, implying that a network of vibrational modes are responsible for the vibration energy relaxation within a molecule. One may expect to utilize such a network of information and be able to track the vibrational energy relaxation and especially the inter-molecular vibration redistribution pathways, by collecting a series of time-dependent 2D IR spectra in a broad spectral range, as is the ultimate goal of the ultrafast 2D IR spectroscopy.

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