Electrostatic DFT Map for the Amide I, II, III and A Vibrational Bands of NMA

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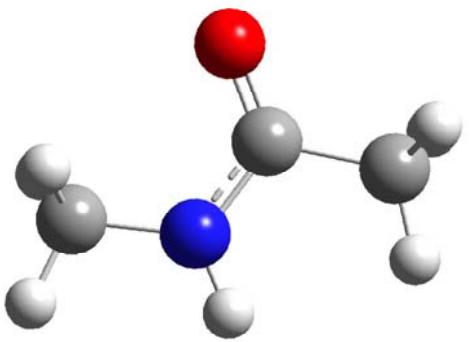
Goal and Outline

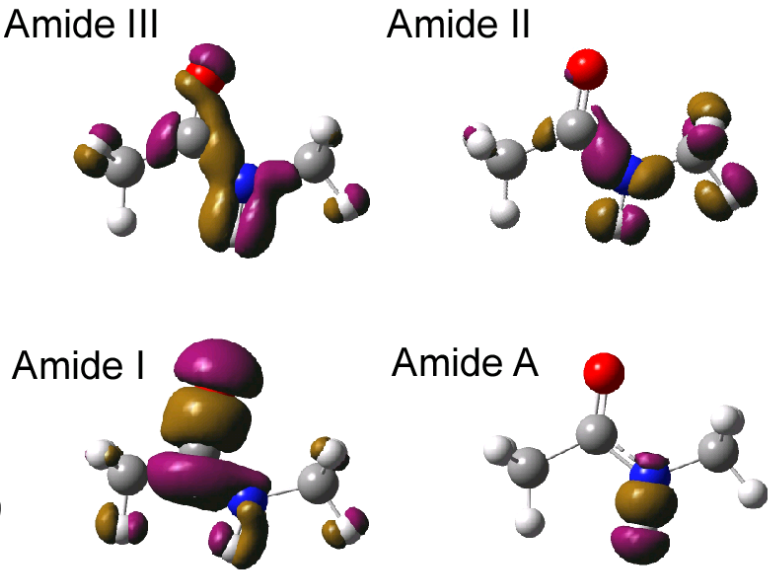
- N-methyl acetamide (NMA): simplest model system for the peptide bond
- High level anharmonic vibrational Hamiltonian of NMA is crucial for simulating the vibrational dynamics of proteins (SPECTRON code).
  - Transition Charge Densities (TCDs)
  - Electrostatic Fluctuations and Electrostatic Samplings
  - Electrostatic DFT map
  - Infrared Absorption
  - Anharmonicities
  - Collective solvent coordinates
  - Photon Echo Spectra



Transition Charge Densities (TCDs)

- TCDs

$$\rho(\mathbf{r}) = \rho^{(0)}(\mathbf{r}) + \sum_i \left(\frac{\partial \rho(\mathbf{r})}{\partial Q_i} \right) Q_i + \cdots$$



- Amide I, A:
  localized on 4 amide atoms
- Amide III:
  delocalized (amide, methyls)
- Amide II:
  most highly delocalized (amide, methyls)

Electrostatic Samplings

- Least-square fit of the 19 electrostatic components at sets of sampling points, S1(global) and S2(atom positions).

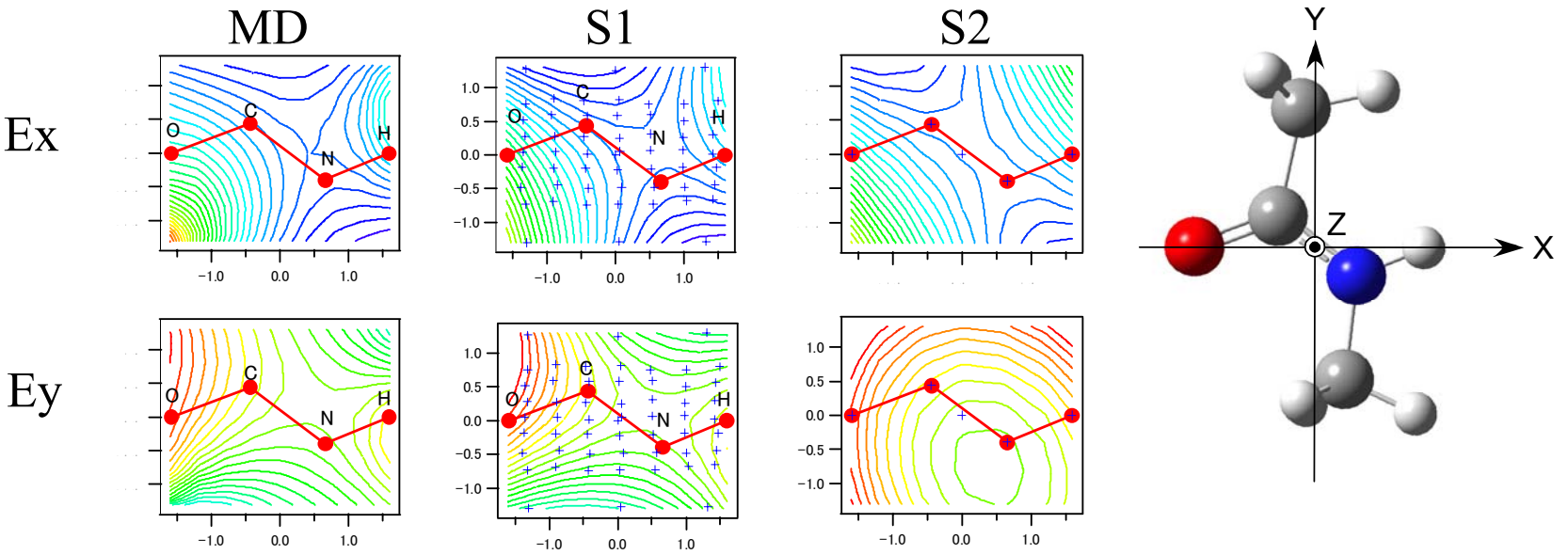
$$U(\mathbf{X}) = U_0 - \sum_{\alpha} E_{\alpha} X_{\alpha} - \frac{1}{2}\sum_{\alpha,\beta} E_{\alpha\beta} X_{\alpha} X_{\beta} - \frac{1}{6}\sum_{\alpha,\beta,\gamma} E_{\alpha\beta\gamma} X_{\alpha} X_{\beta} X_{\gamma}$$

19 independent variables

$$\mathbf{C} = (E_x, E_y, E_z, E_{xx}, \cdots, E_{xxx}, \cdots)$$

S1: 65 points (59 grid points in -1.4<x<1.4,-1.3<y<1.3, 6 out-of-plane)

S2: 7 points (4 atom positions, origin, 2 out-of-plane)



Anharmonic Vibrational Hamiltonian of an isolated NMA molecule

- 6th order anharmonic vibrational Hamiltonian expanded in 5 normal coordinates at DFT (BPW91/6-31G(d,p)) level.

$$V(\mathbf{Q};\mathbf{C}) = \sum_i f_i^{(1)}(\mathbf{C})Q_i + \sum_{i,j} f_{ij}^{(2)}(\mathbf{C})Q_iQ_j + \cdots + \sum_{ijklmn} f_{ijklm}^{(6)}(C)Q_iQ_jQ_kQ_lQ_mQ_n$$

Mode	Harmonic Freq.	Description
1	1081.6	N-H bend, methyl def.
2	1241.2	Amide III
3	1506.6	Amide II
4	1732.8	Amide I
5	3582.8	Amide A

- Expansion coeffieicnts $f^{(1)}\cdots f^{(6)}$ depend parametrically on the electrostatic component vector **C** resulting that the equilibrium geometry changes depending on **C**.
- Eigenstates calculation including up to 12 total number of excitations (6183 states) in harmonic oscillator basis set.

Vibrational Eigenstates in Gas Phase (BPW91/6-31G(d,p), 10 amide states)

- Calculated fundamental frequencies are in good agreement with experiment without scaling (e.g. calc: 1724, obs: 1728 cm^{-1} for amide I).
- Calculated anharmonicities are in good agreements with experiment (e.g. calc:11, obs 16 cm^{-1} for amide I).

State	Frequency		Intensity	Description	Eigenvector
	Calc	Obs			
1	0.0		-		+0.99(00000)
3	1229.2	(1258[a],1255[b])	92.83	amide III	+0.99(01000)
4	1495.4	(1500[a],1499[b])	273.30	amide II	+0.99(00100)
5	1723.9	(1728[a])	352.74	amide I	−0.98(00010)−0.12(00020)
8	2451.5	(2504[a])	0.01	amide III×2	+0.98(02000) +0.12(01100)
10	2716.6	(2758[a])	0.68	amide III+II	−0.12(00200)−0.97(01100)
12	2955.2	(2971[a])	0.19	amide I+III	+0.98(01010)
13	2981.1		0.15	amide II×2	−0.98(00200) +0.13(01100)
14	3222.2		0.18	amide I+II	−0.98(00110)−0.10(00120)
17	3428.1	(3498)	24.20	amide A	+0.93(00001) +0.28(00002)
18	3436.8	(3440[a])	1.25	amide I×2	+0.95(00020) +0.23(00030)

[a]: Mayne,L.C, and Hudson,B., *J.Phys.Chem.***95**,2962

[b]: Kubelka,J. and Keiderling,T.A., *J.Phys.Chem.A.***105**,10922

Electrostatic DFT Map

- Vibrational transition frequencies ω^{ν} and transition moments $\mu^{\nu\nu'}$ of 10 amide states are parametrized with 19 electrostatic components C=(Ex,Ey,Ez,..) based on the anharmonic vibrational Hamiltonian of a single isolated molecule in a nonuniform electric field.

$$\omega^{\nu}_{\mathrm{map}} = \omega^{\nu}_{\mathrm{gas}} + \mathbf{O}^{\nu(1)\dagger}\mathbf{C} + \frac{1}{2}\mathbf{C}^{\dagger}\mathbf{O}^{\nu(2)}\mathbf{C}$$

$$\mu^{\nu\nu'}_{\alpha} = \mu^{\nu\nu'}_{\mathrm{gas}\,\alpha} + \mathbf{M}^{\nu\nu'(1)\dagger}_{\alpha}\mathbf{C} + \frac{1}{2}\mathbf{C}^{\dagger}\mathbf{M}^{\nu\nu'(2)}_{\alpha}\mathbf{C}$$

where

$$(\mathbf{O}^{\nu(1)+})_i \propto \frac{\partial\omega^{\nu}}{\partial E_i}, \qquad (\mathbf{O}^{\nu(2)})_{ij} \propto \left(\frac{\partial^2\omega^{\nu}}{\partial E_i \partial E_j}\right)$$

10 amide states

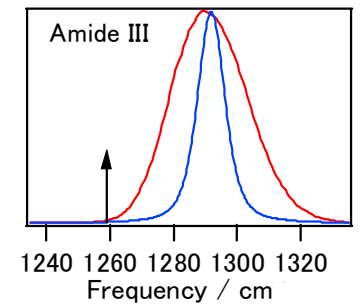
I, II, III, A	4 fundamentals
2xI,2xII,2xIII	3 overtones
I+II,I+III,II+III	3 combinations

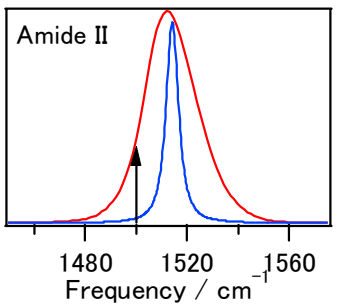
- The map includes the geometry change of NMA due to the external field induced polarization which has been found significant in earlier studies[1].

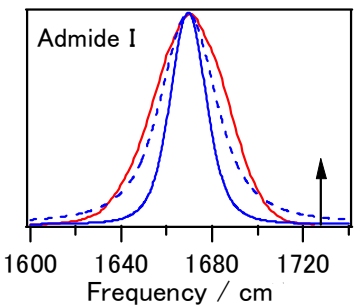
[1]: Guo, H. and Karplus, J. Phys. Chem. **96**, 7273 (1992)

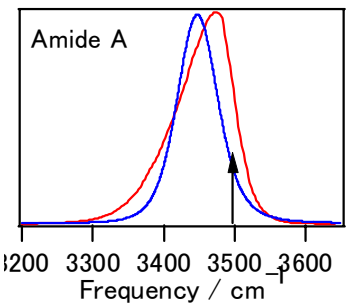
Infrared Absorption in TIP3 water
(59 point sampling)

Red: static distributions, blue: infrared bandshapes

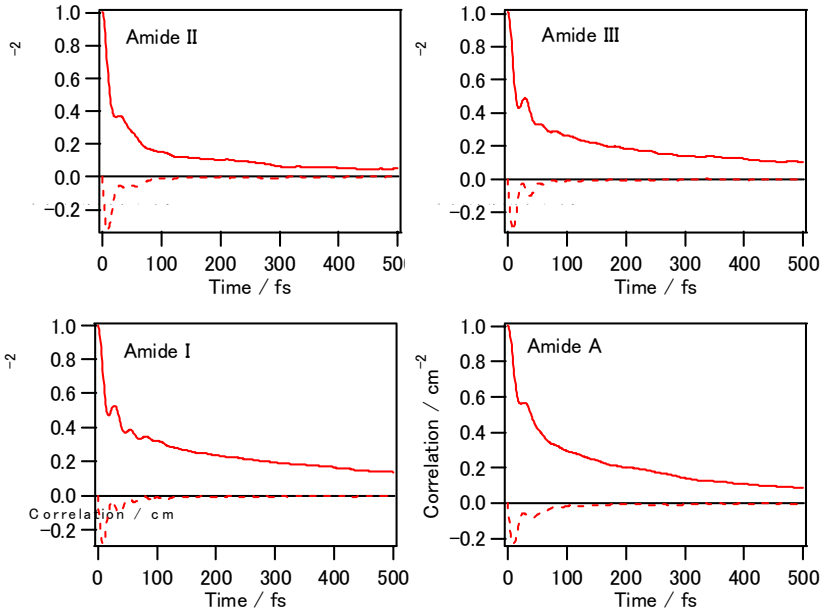








Frequency correlation functions



Statistics of Infrared Absorption

- S2 does not reproduce experiment in bending modes (amide II and III).
- Calculated solvent shifts of Amide I, III, and A with S1 are in good agreement with experiment.
- Calculated solvent shift of Amide II is not satisfactory.

	Amide I				Amide II				Amide III				Amide A			
	Gas	Shift	fwhm	Int.	Gas	Shift	fwhm	Int.	Gas	Shift	fwhm	Int.	Gas	Shift	fwhm	Int.
S1	1724	−59	29	1.0	1497	+14	19	0.656	1232	+33	22	0.215	3428	−51	77	0.338
S2	1724	−57	28	1.0	1497	−16	37		1232	+10	33		3428	−72	116	
EM[a]	-	−78	25	-	-	-	-	-	-	-	-	-	-	-	-	-
NM[b]	1738	−102	-	-	1533	+47	-	-	1240	+92	-	-	-	-	-	-
Exp.	1728[c]	−87[c,f]	29	1.0	1500[c]	+76[c,d]	36	0.803	1259[c]	+53[c,d]	32	0.205	3498[e]	−78[f]	-	

[a]: Kwac,K and Cho, M.H. J.Chem.Phys. **119**, 2247

[b,d]: Kubelka,J. and Keiderling,T.A., *J.Phys.Chem.A*.**105**,10922

[c]: Mayne,L.C, and Hudson,B., *J.Phys.Chem*.**95**,2962

[f]: Zhang, R., Li, H.R.,Lei,Y., and Han,S.J., *J.Mol.Struct*. **693**, 17

Frequency Correlation Functions

- Fitting of the real part of the frequency autocorrelation functions

$$\langle \delta\omega(t)\delta\omega(0)\rangle / \langle \delta\omega^2 \rangle = \sum_{i=1}^{3} A_i \exp(-t/T_i)$$

$$+ \sum_{i=4}^{5} A_i [\cos(\Omega_i t) + 1/(T_i\Omega_i)\sin(\Omega_i t)]\exp(-t/T_i)$$

- Oscillation frequencies (660-1100 cm^{-1}) correspond to the two hydrogen bonding vibrations (674,726 cm^{-1}) obtained from the normal mode calculation of a NMA-$3H_2O$ cluster
- Amide II and III bending modes are more close to the motional narrowing limit than amide I and A stretches.

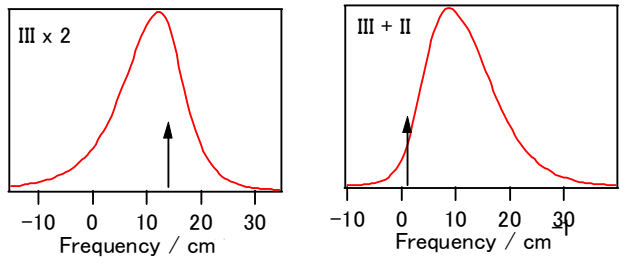
	Amide III	amide II	amide I	amide A
A_1/cm^{-2}	0.481	0.584	0.503	0.521
T_1/fs	17.65	30.87	16.36	27.79
A_2/cm^{-2}	0.273	0.172	0.273	0.367
T_2/fs	155.7	297.7	210.6	250.2
A_3/cm^{-2}	0.122	-	0.151	0.038
T_3/fs	1888	-	1820	4277
A_4/cm^{-2}	0.170	0.250	0.218	0.081
Ω_4/fs^{-1}	0.183	0.187	0.213	0.158
T_4/fs	22.64	17.44	21.29	32.92
A_5/cm^{-2}	0.040	0.114	-	0.054
Ω_5/fs^{-1}	0.224	0.125	-	0.094
T_5/fs	59.48	38.96	-	37.04
$\langle \delta\omega^2 \rangle$	140.5	146.6	266.3	2153.6
τ/fs	275.3	101.5	431.9	186.6
κ	1.62	4.32	0.75	0.61

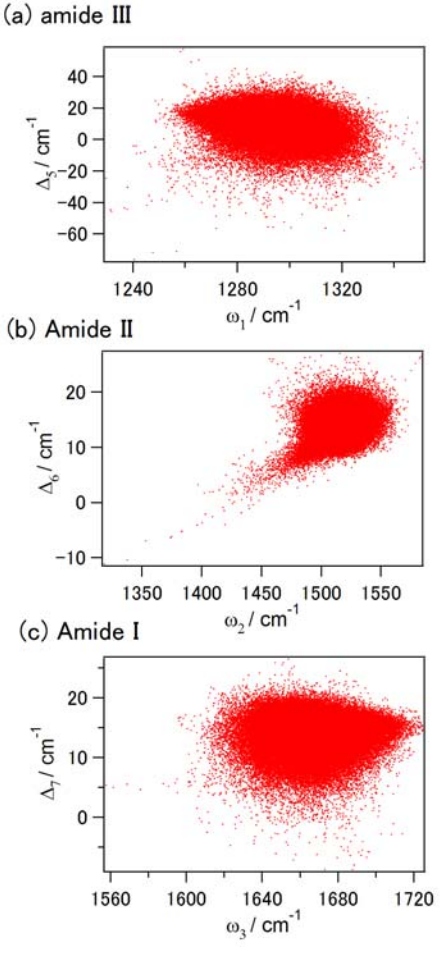
Anharmonicity Distributions and their correlation with fundamentals

- All states have narrow (5-15 cm^{-1}) asymmetric distributions.

$$\Delta^{\nu} \equiv \omega^{\nu_1} + \omega^{\nu_2} - \omega^{\nu}$$

- Correlation between anharmonicities and their fundamentals are very weak.





Collective Solvent Coordinates

- 10 collective solvent coordinates for 10 amide states

$$\Omega_\nu \equiv \sum_{i=1}^{19} L_i^\nu \delta E_i$$

where $\delta\mathbf{C} = (\delta E_1, \cdots, \delta E_{19})$ and

$$\delta\mathbf{C} = \mathbf{C} - \langle\mathbf{C}\rangle$$

$$\mathbf{L}^\nu = \mathbf{O}^{\nu(1)} + \mathbf{O}^{\nu(2)\dagger}\langle\mathbf{C}\rangle.$$

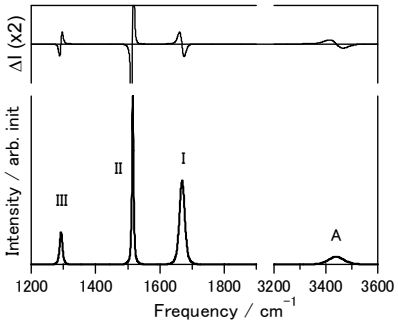
- DFT map frequency is approximated by:

$$\omega_{\mathrm{cc}}^\nu = \omega_{\mathrm{eq}}^\nu + \Omega_\nu + k\Omega_\nu^2.$$

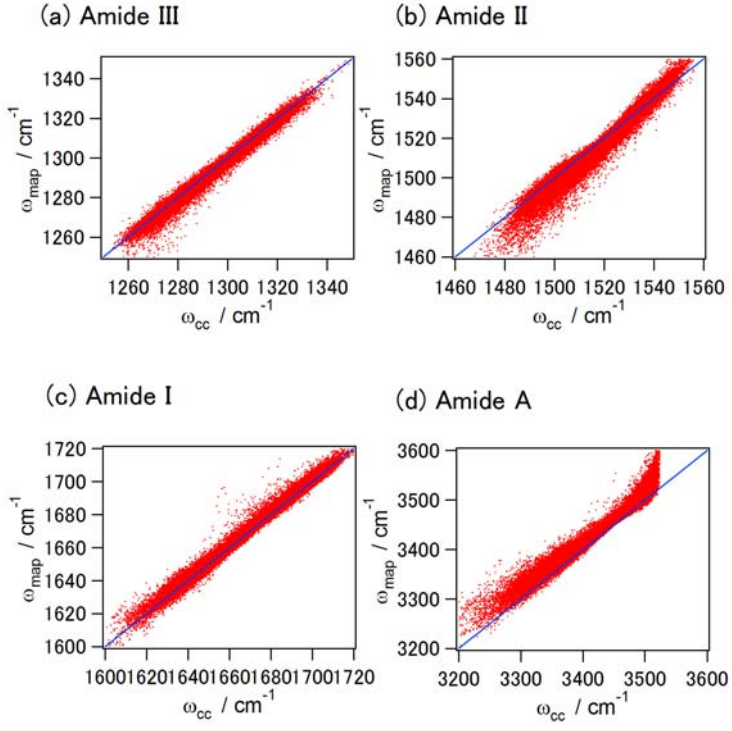
Collective coordinates of Amide I

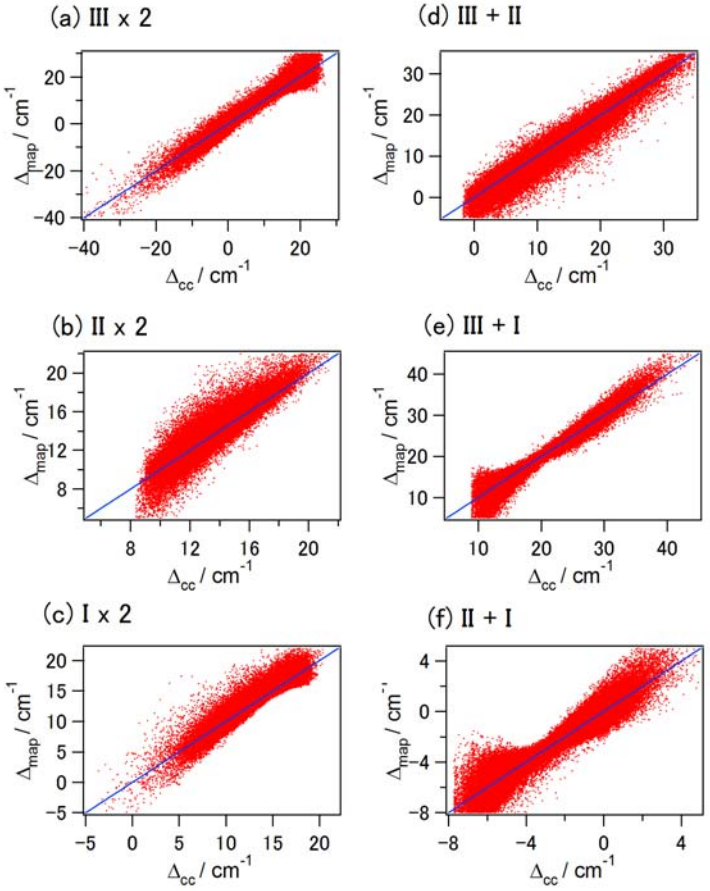
	Fundamental	Overtone
Ex	−2685	−152
Ey	−2422	−287
Ez	0	0
Exx	2392	−479
Eyy	−3182	−671
Ezz	341	18
Exy	3129	−703
Exz	−35	−20
Eyz	−223	15
Exxx	−6978	−1113
Eyyy	−3896	−614
Ezzz	0	0
Exyy	5368	−2428
Exxy	−3905	−1747
Exxz	0	0
Exzz	−2632	−136
Eyzz	−2692	34
Eyyz	0	0
Exyz	0	0

Scatter plots of $\omega_{map}(\Delta_{map})$ vs $\omega_{cc}(\Delta_{cc})$

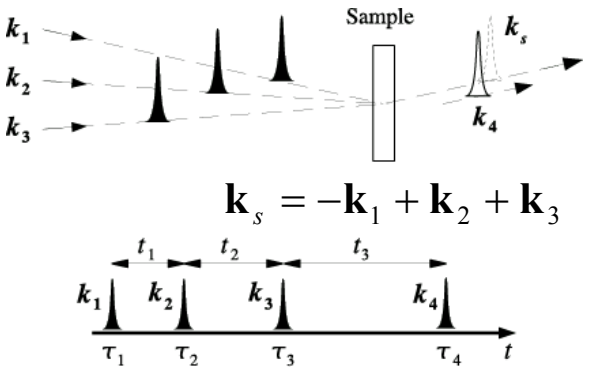


- Good agreements between DFT map and Collective coordinate frequencies.

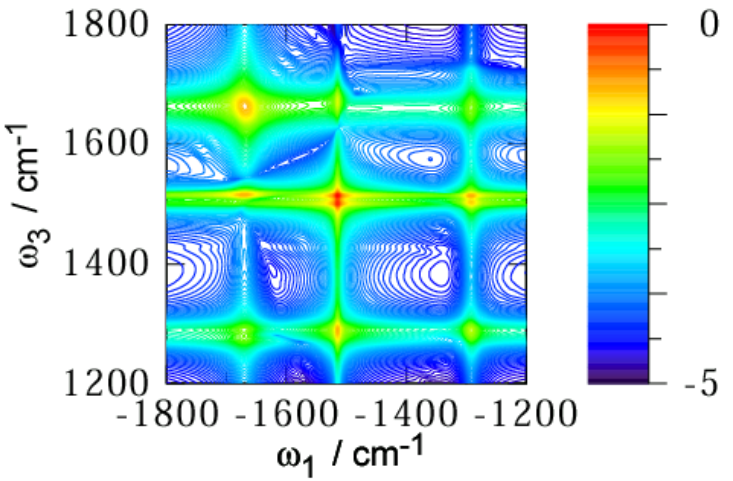


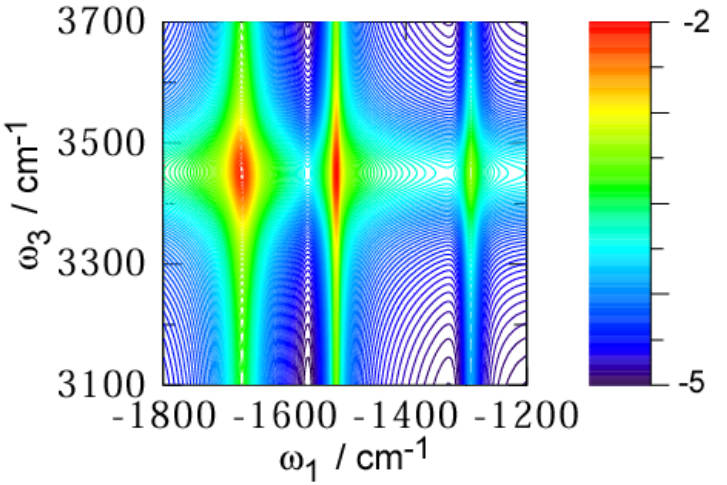


Photon Echo Spectra $\log\left|S(\omega_1, t_2 = 0, \omega_3)\right|$



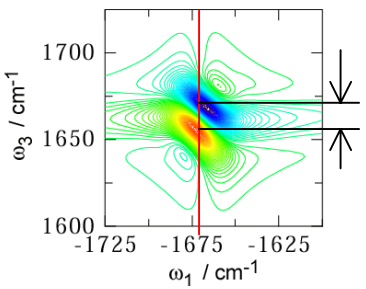
- Cumulant expansion of Gaussian fluctuations model (CGF) employed.
- Rotating wave approximation (RWA).
- ± 250 cm^{-1} rectangular pulses.



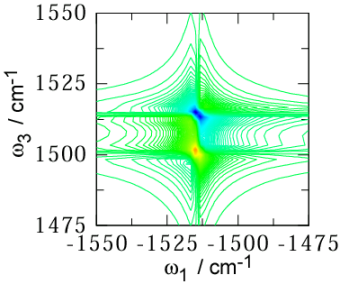


Photon Echo Spectra $\mathrm{Im}[S(\omega_1, t_2 = 0, \omega_3)]$

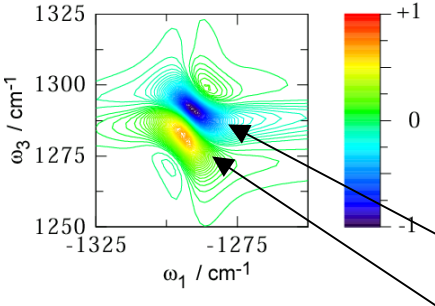
I



II



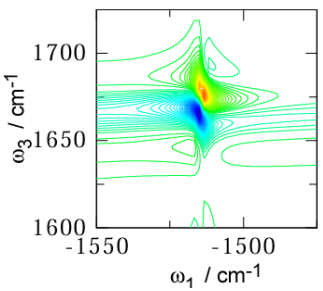
III



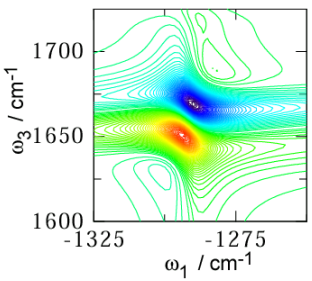
Diagonal and
off-diagonal anharmonicity
and anharmonic shift

	Anharm.	Anharm. shift
I – I	14.3	17
II – II	13.0	13
III – III	10.7	13
I – II	−3.1	−15
I – III	19.7	22
II – III	11.0	12

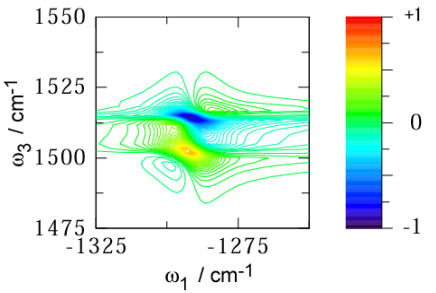
I-II

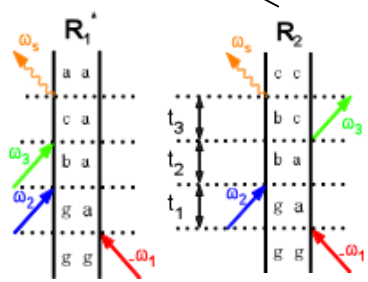


I-III



II-III





Conclusions

- Electrostatic DFT map is constructed for all amide modes (III, II, I and A) of NMA. The map includes geometry change of NMA due to the solvent induced polarization. Anharmonicity fluctuation is inherently built in the map.
- Electrostatic DFT map for amide I has been implemented to the SPECTRON code which simulate the linear and nonlinear infrared spectra of proteins.
- Correlation between anharmonicities and fundamental frequencies are very weak. Electric field derivatives are crucial for the anharmonicity fluctuations.
- Global sampling of the electric field structure in the region of the transition charge densities (TCDs) is crucial for realistic lineshape simulations. Only S1(global) gives the good amide III solvent shift and amide II blue shift as well as amide I solvent shift and bandwidth.
- Normal mode analysis of an NMA-3H_2O cluster shows that the 660 – 1100 cm^{-1} oscillation in the frequency autocorrelation functions can be ascribed to the two bending vibration of intermolecular hydrogen bonding to the amide oxygen of NMA
- Collective solvent coordinate is constructed for each of the 10 amide states. Infrared bandshapes from collective coordinates are in good agreement with the DFT map bandshapes.
- Diagonal and off-diagonal anharmonicies of photon echo spectra can give additional information to determine the protein structures.