



Simulation of fully anharmonic IR spectra for flexible peptides

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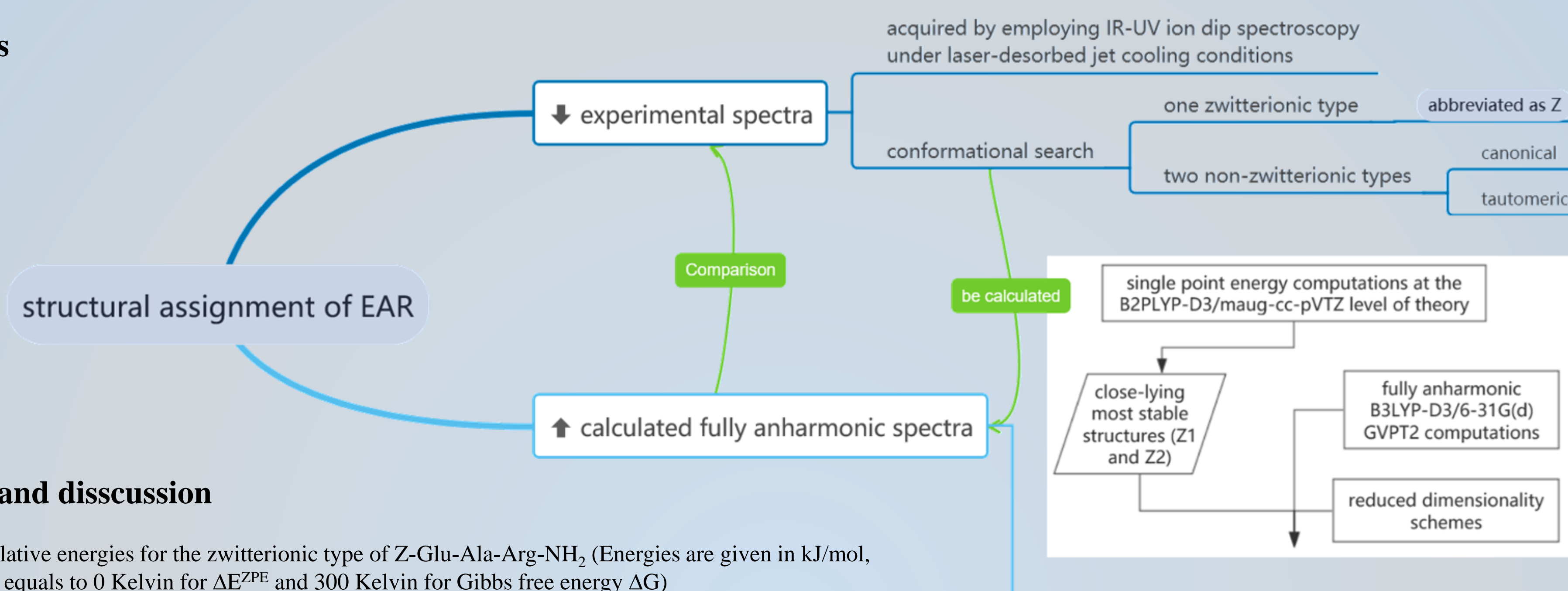
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Abstract

The conformational preference of the capped tripeptide EAR (Glu-Ala-Arg-NH₂) is complicated due to the high flexibility and presence of several weak interactions. Among the various types of investigations spectroscopies are the most powerful tools, allowing direct detection of different binding schemes and three-dimensional (3D) conformation via microwave (MW) measurements or indirect analysis through finger-print vibrational features in infrared (IR), Raman, Resonance Raman, UV-vis or fluorescence spectra, including also their chiral counterparts. These sophisticated experiments call for accurate and reliable theoretical support in order to link the rich experimental data to the desired information on the structure and properties of complex molecular systems. In this work the structural assignment of EAR was performed via the comparison between the calculated fully anharmonic spectra with the experimental one, in the NH stretching region (3150-3700 cm⁻¹). The latter was acquired by employing IR-UV ion dip spectroscopy under laser-desorbed jet cooling conditions. The conformational search include three different families depending on the form of the Arginine side chain: two non-zwitterionic types (canonical and tautomeric structures) and one zwitterionic type with a deprotonated Glu and protonated Arg side chain (abbreviated as Z). Their relative energies were determined by single point energy computations at the B2PLYP-D3/maug-cc-pVTZ level of theory, and for the close-lying most stable structures (Z1 and Z2) followed by fully anharmonic B3LYP-D3/6-31G(d) GVPT2 computations, employing also the reduced dimensionality schemes. The computed spectrum of the lowest energy conformer Z1 shows many more features, some due to the non-fundamental transitions, in good agreement with the experimental results.

Methods



Results and discussion

Table. 1. Relative energies for the zwitterionic type of Z-Glu-Ala-Arg-NH₂ (Energies are given in kJ/mol, temperature equals to 0 Kelvin for ΔE_{ZPE} and 300 Kelvin for Gibbs free energy ΔG)

B2PL YP-D3	ΔE_{ZPE}	0.00	8.21	11.62	13.98	14.37	23.28	27.36	23.83	31.30	29.83	37.51	33.35
	ΔG	0.00	3.19	8.63	9.08	11.16	45.11	44.93	24.69	23.81	50.17	61.18	56.31
		EAR _Z1	EAR _Z2	EAR _Z3	EAR _Z4	EAR _Z5	EAR _Z6	EAR _Z7	EAR _Z8	EAR _Z9	EAR _Z10	EAR _Z11	EAR _Z12

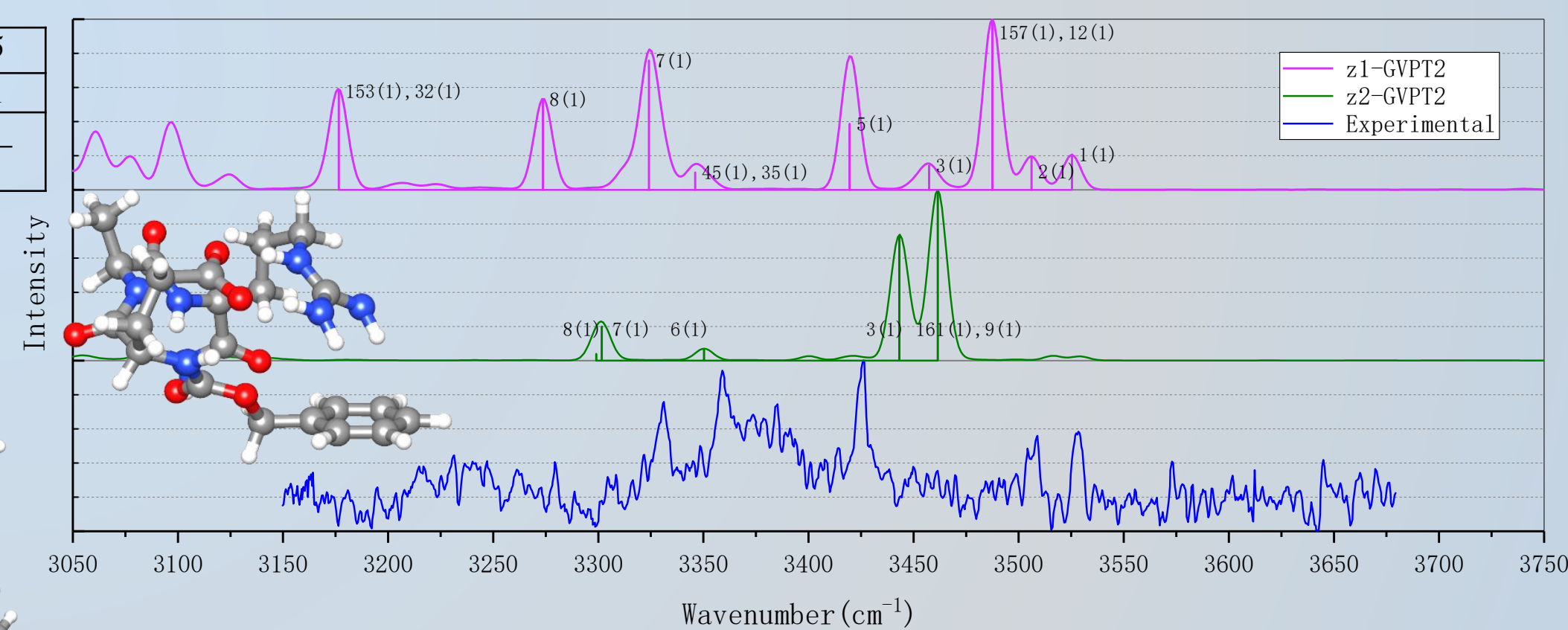
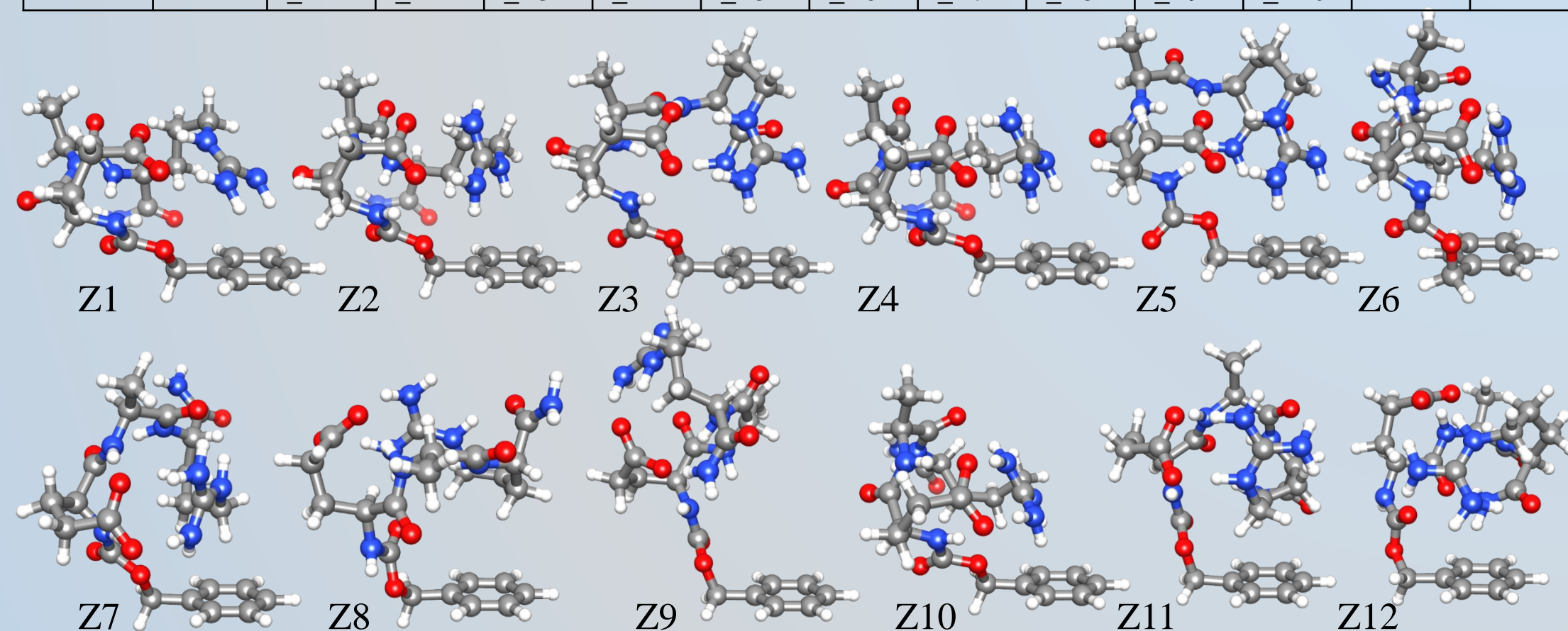


Fig. 2: Experimental spectrum of Glu-Ala-Arg-NH₂ compared to the GVPT2-RD24 computations for the two lowest energy conformers.

Table. 1. shows the relative energies for the 12 conformers of zwitterionic type of Z-Glu-Ala-Arg-NH₂. Those single point energies were calculated at the B2PLYP-D3/maug-cc-pVTZ level of theory. The results shows that the energies of most two stable structures (Z1 and Z2) are quite close.

Then the fully anharmonic B3LYP-D3/6-31G(d) GVPT2 computations were applied on the two conformers, employing also the reduced dimensionality schemes. Fig. 1. shows the spectra of Z1 with different reduced dimensionality parameters compared to experimental one. The curves were broadened by Lorentzian function with hwhm=2 cm⁻¹. Peaks are labeled (*n*(*m*)) according to the final vibrational state with *m* quanta associated to mode *n*. As Fig. 1. shows, there is no much difference within reduced dimensionality options with N equal to 12, 24, 34. And they all keep sufficient information. The similar goes for conformer Z2.

From Fig. 2. we can see that the computed spectrum of the lowest energy conformer Z1 shows many more features than that of Z2, some due to the non-fundamental transitions, in good agreement with the experimental results.

Improved accuracy is to be obtained by the hybrid scheme, with harmonic wavenumbers corrected at the higher level of theory.

References:

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Fig. 1: Experimental spectrum of Glu-Ala-Arg-NH₂ compared to the GVPT2 computations for Z1 with different reduced dimensionality (RDN) schemes. N corresponds to the number of lowest energy modes excluded from the VPT2 treatment (RedDim=(Passive=N)).