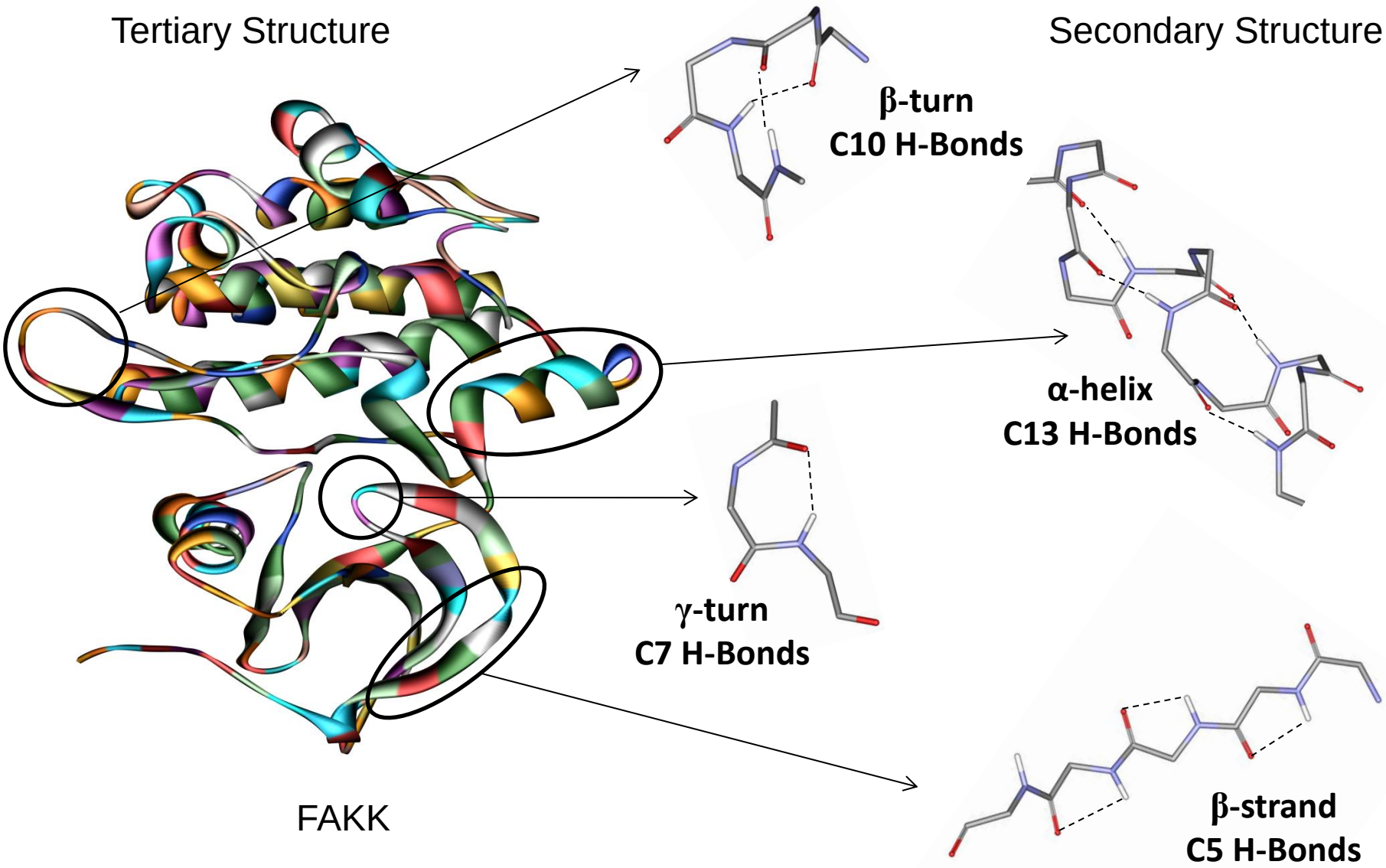
Unravelling Non Covalent Interactions within Flexible Biomolecules: from electron density topology to gas phase spectroscopy

Benoît de Courcy

Topological Approches to Intermolecular interactions

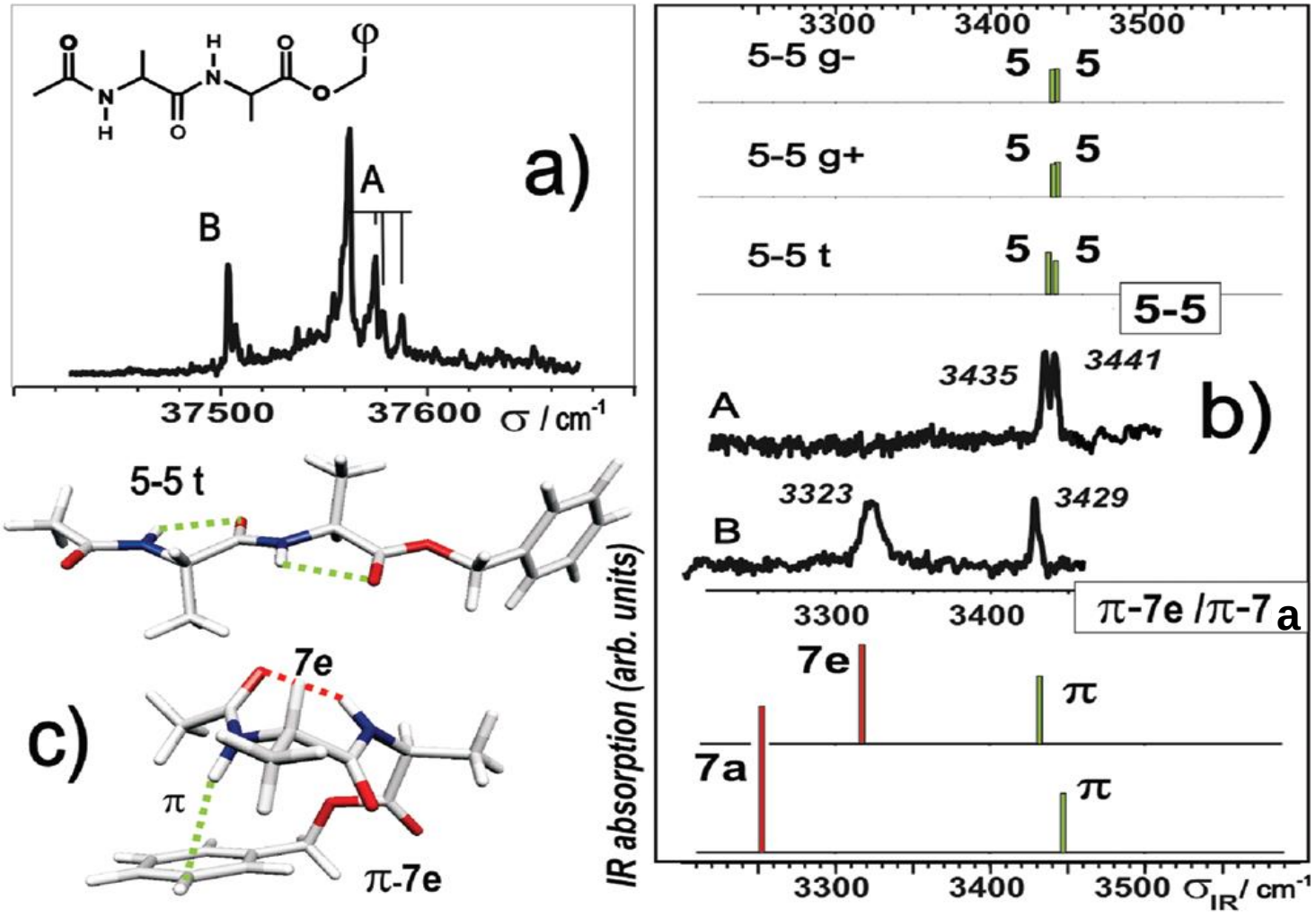
Paris, june 28th 2013

Common Binding Patterns within Proteins.



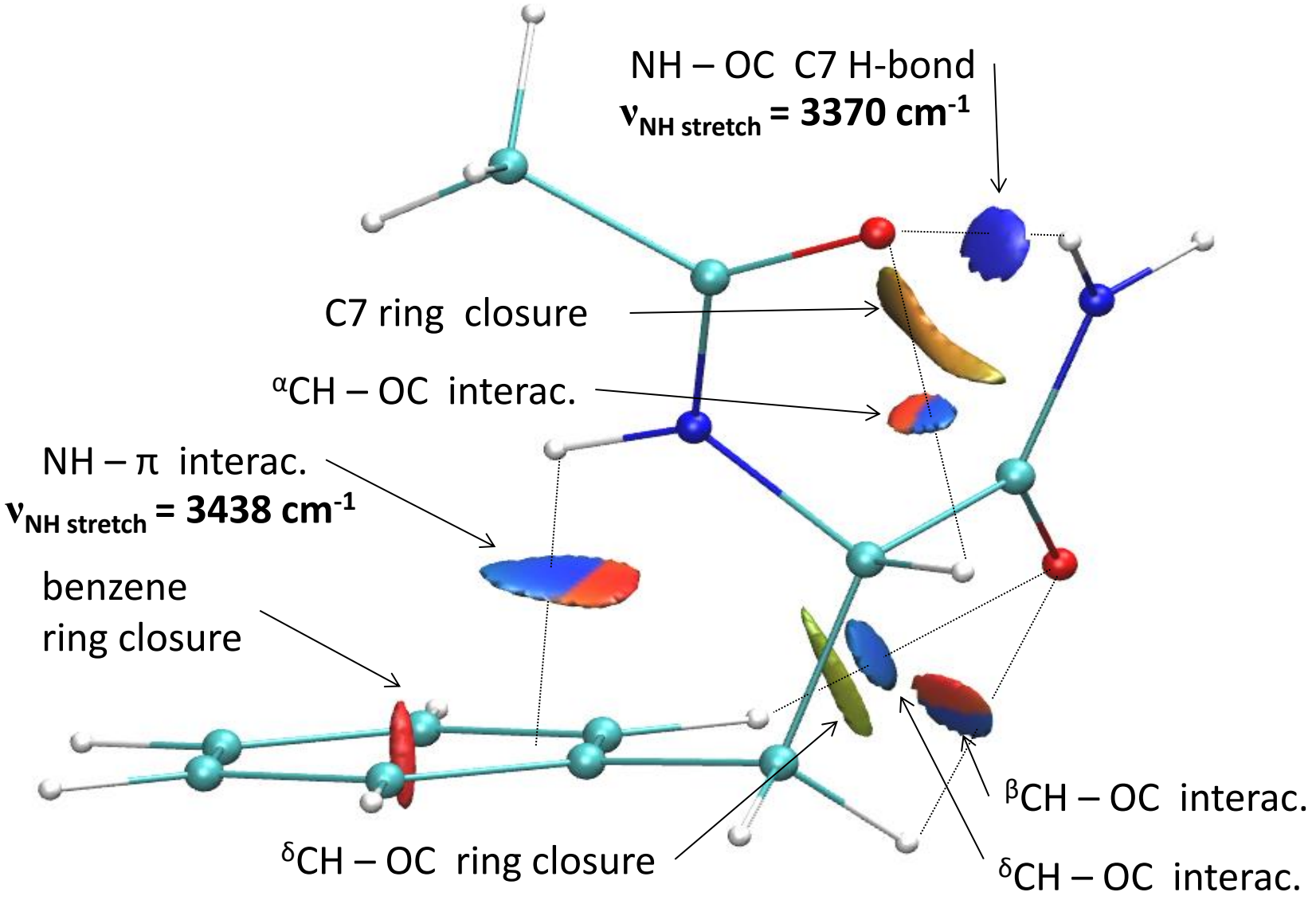
Ac-(Ala)$_2$-O-Bzl: experimental data:

Jet cooled, double resonance (UV/IR), gas phase spectroscopy



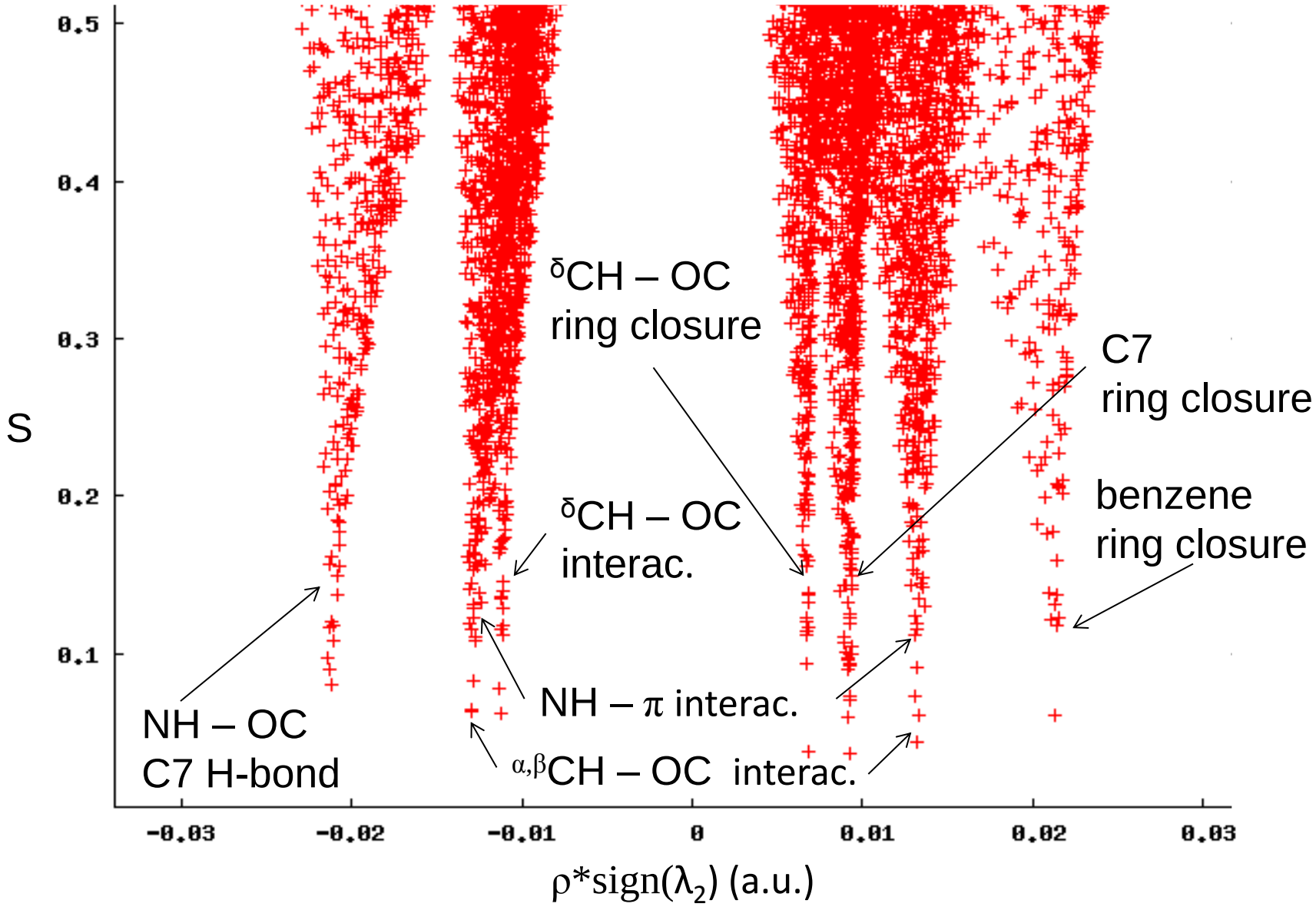
Gloaguen, E., de Courcy, B., Piquemal, J.-P., *et al.* (2010) *J. Am. Chem. Soc. (Comm.)*, **132,** 11860.

Application of the NCI index to flexible molecule: 3D NCI-plot

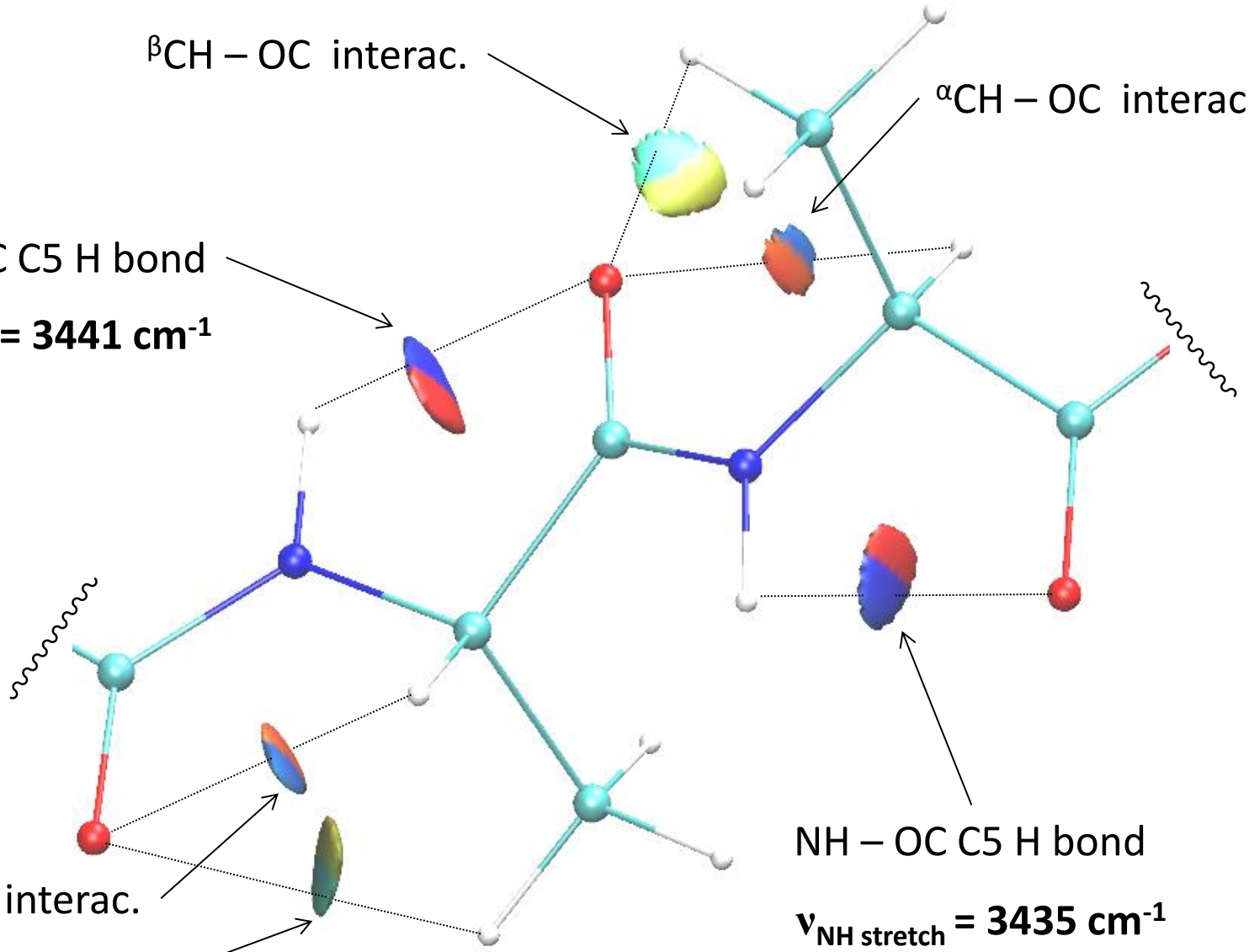


γ_L(g+) conformer of N-Acetyl-Phenylalanyl-Amide (NAPA)

Application of the NCI index to flexible molecule: 2D NCI-plot

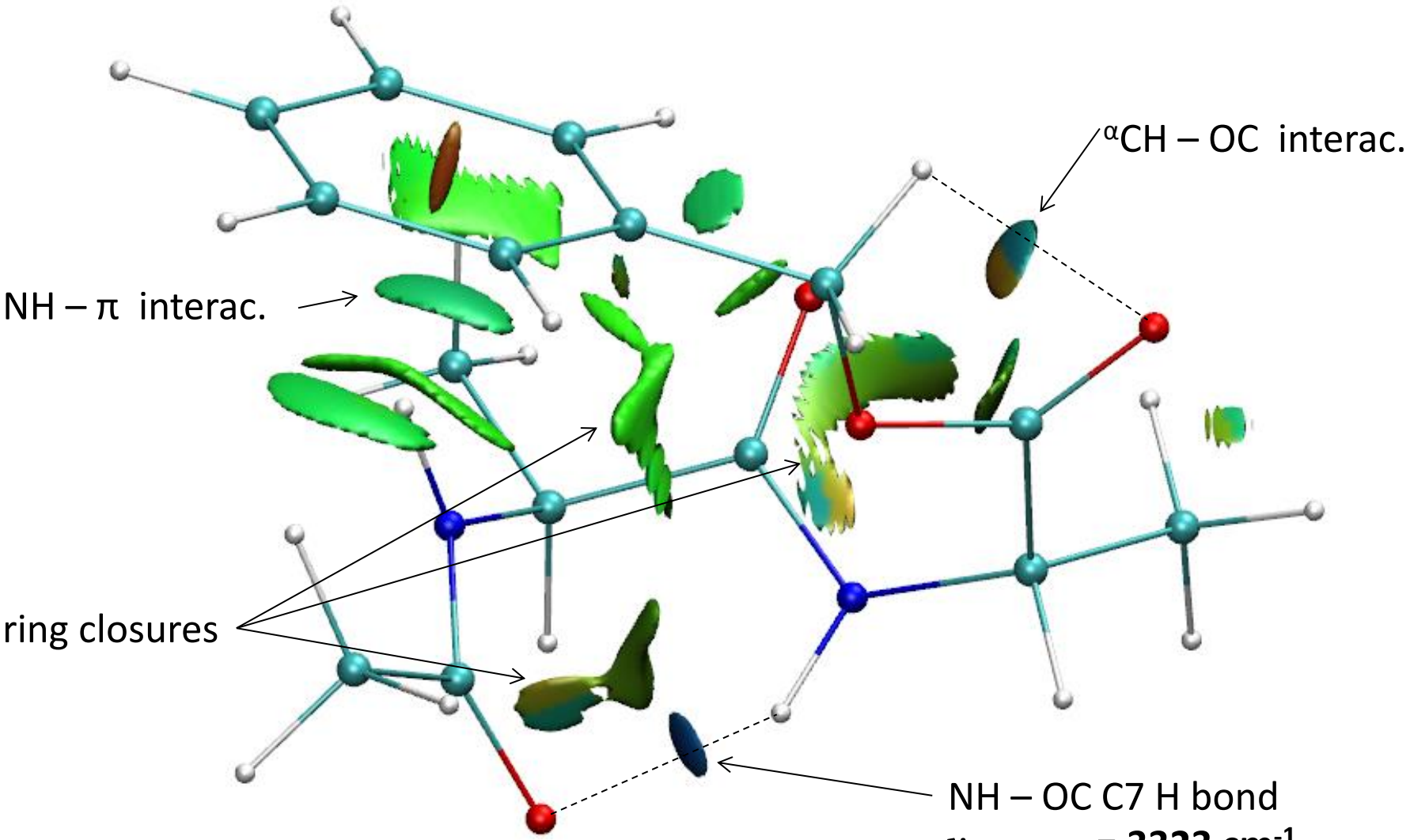


The β-strand: an example of constrained C5 NH---OC bonds



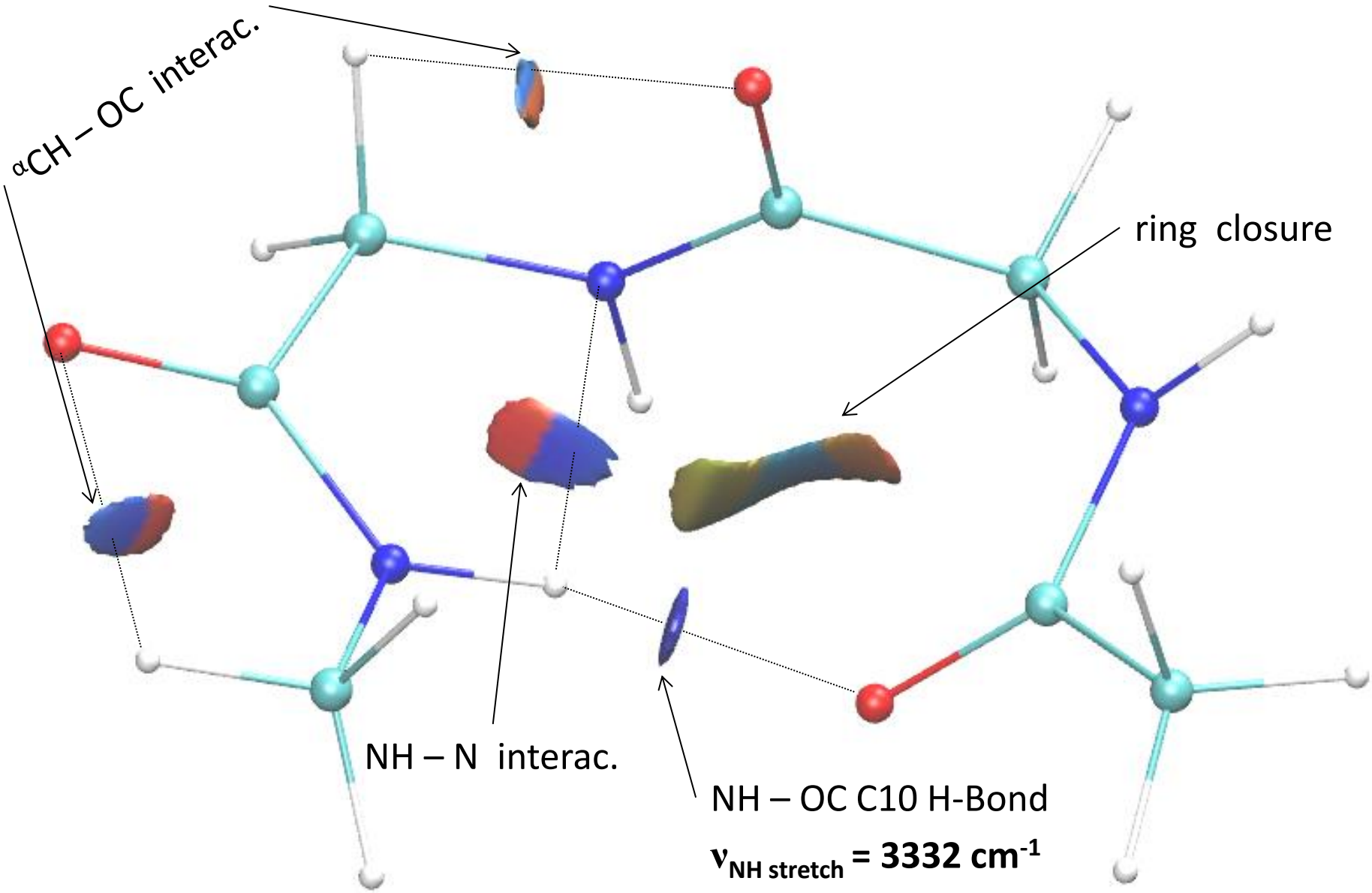
Ac-$(Ala)_2$-OBzl

γ-turns, as examples of intramolecular C7 rings

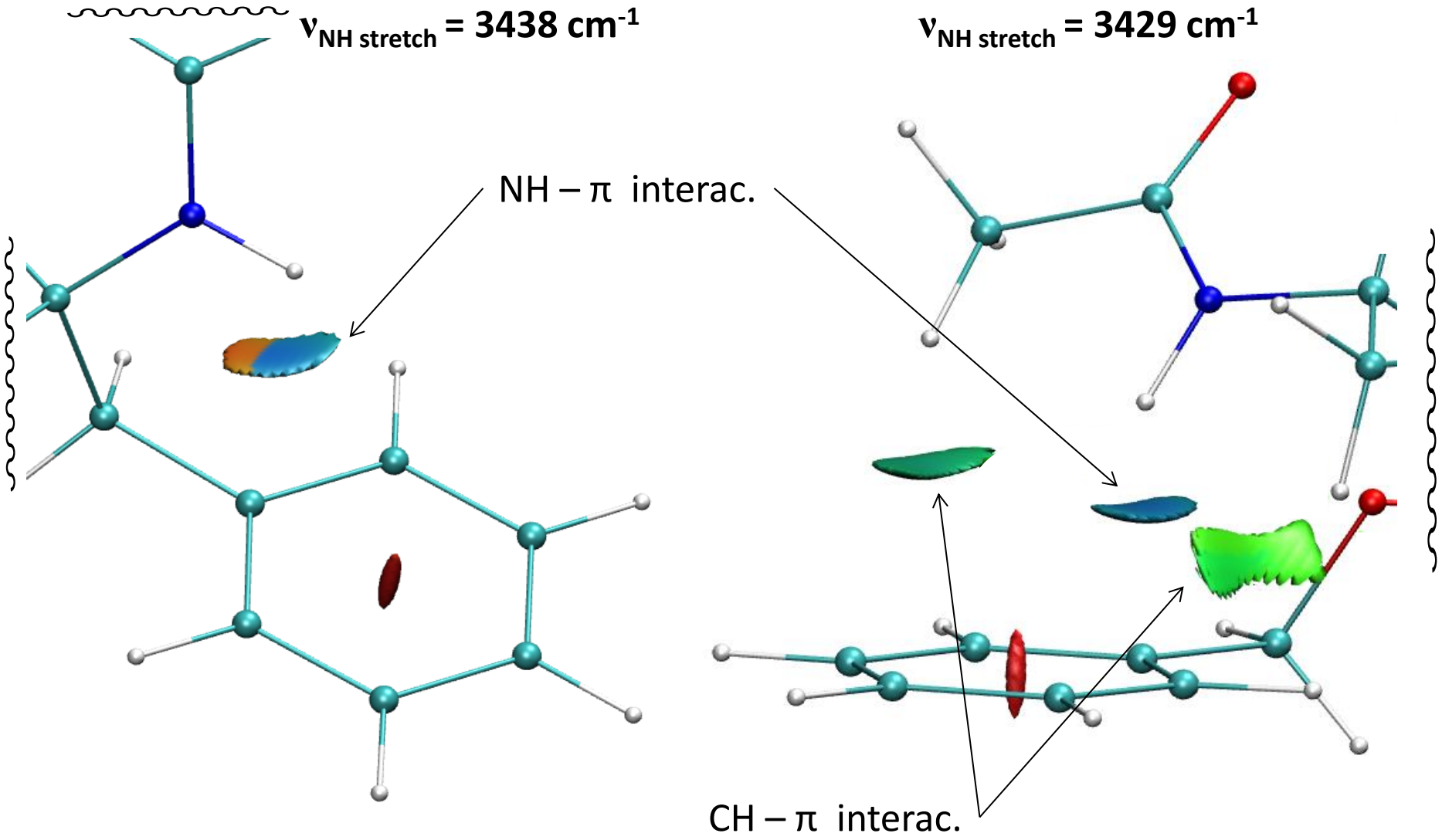


Ac-$(Ala)_2$-OBzl

β-turns, with C_{10} H-bonds



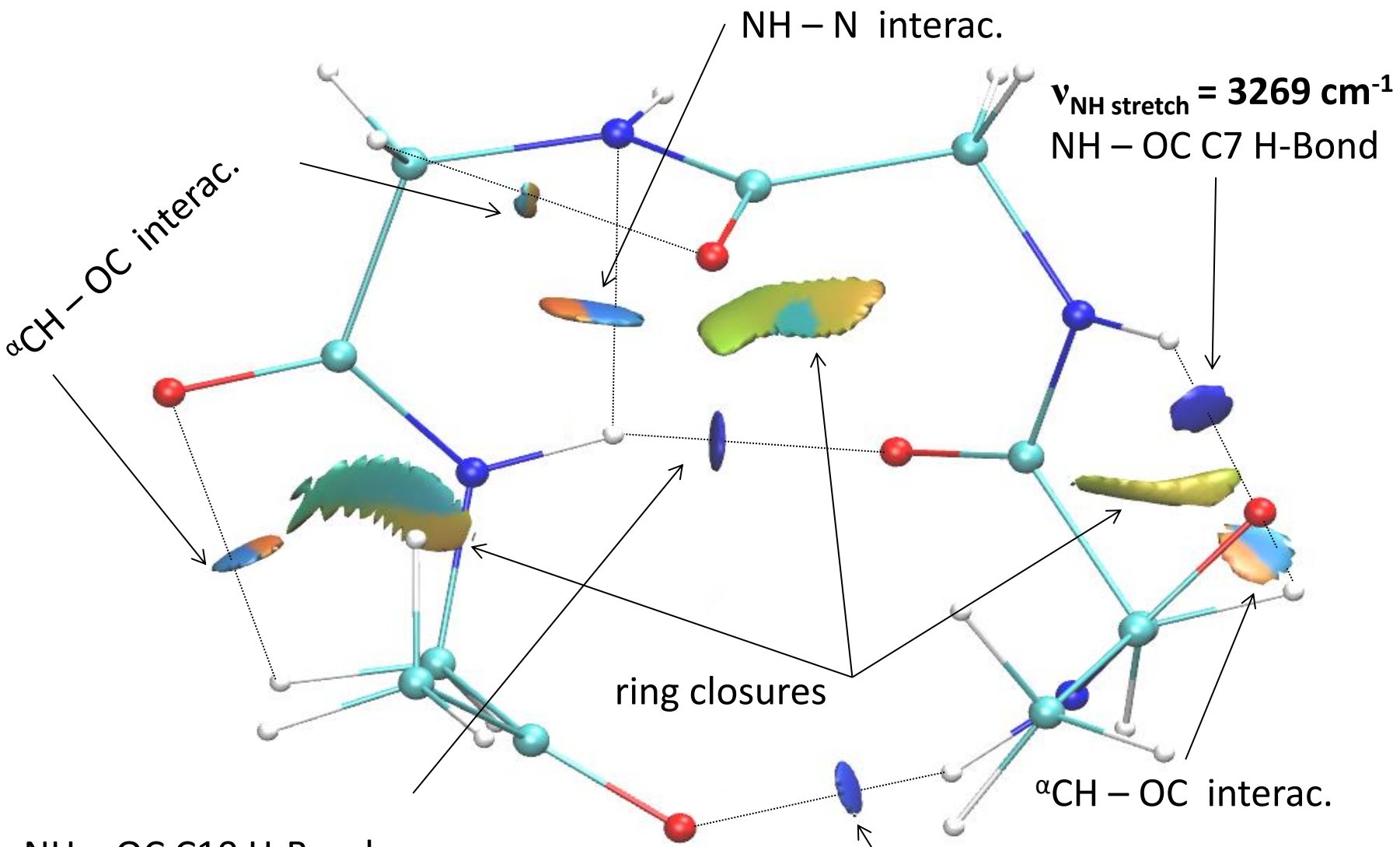
NH-π interactions



γ_L(g+) conformer of N-Acetyl-Phenylalanyl-Amide (NAPA)

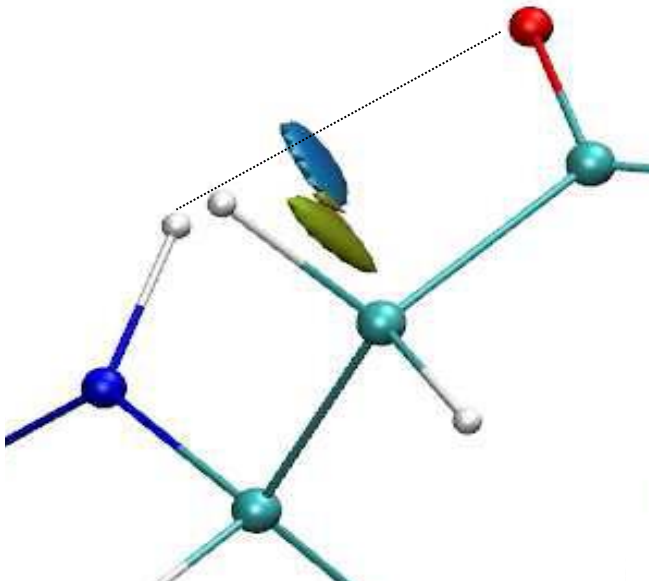
Ac-(Ala)$_2$-OBzl

Example of a large β turn conformation



1β2 conformer of Ac-$(Ala)_4$-Obzyl

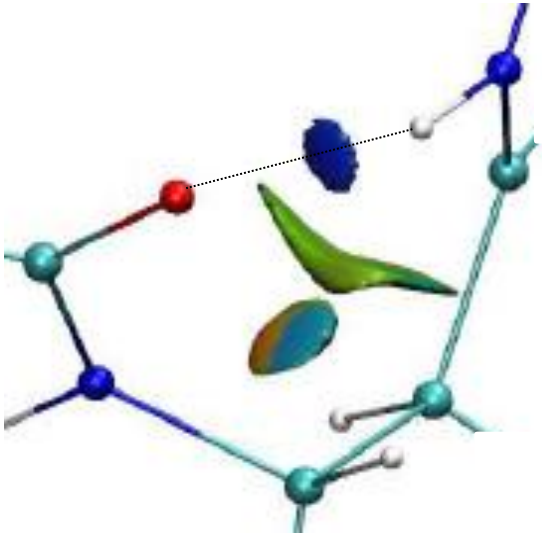
More H-bond Types within β- and γ-peptides



β-C6

$\nu_{NH\ stretch}$ = 3397 cm^{-1}

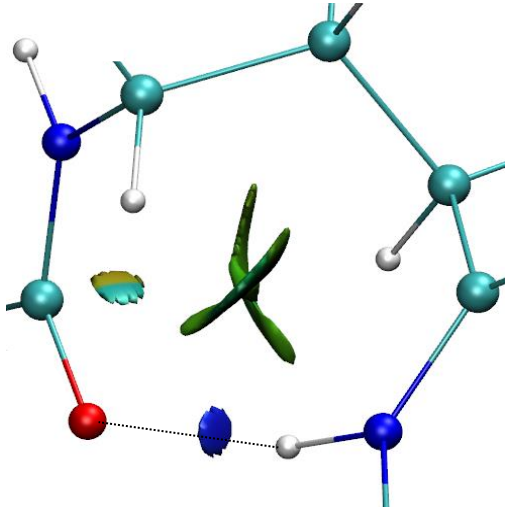
C6a(1) conformer of:
Ac-β^3-hPhe-NHMe β-peptide



β-C8

$\nu_{NH\ stretch}$ = 3339 cm^{-1}

C8a(3) conformer of:
Ac-β^3-hPhe-NHMe β-peptide



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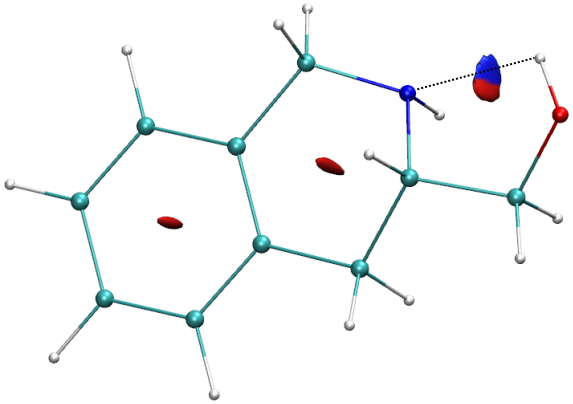
Baquero, E. E.; James, W. H.; Choi, S. H.; Gellman, S. H.; Zwier, T. S. *J.Am. Chem.Soc*. 2008, *130*, 4784

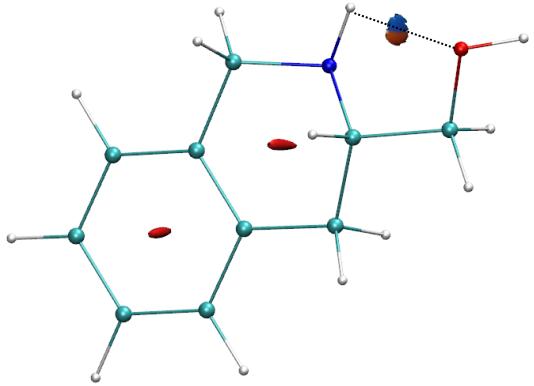
Baquero, E. E.; James, W. H., III; Choi, S. H.; Gellman, S. H.; Zwier, T. S. *J. Am. Chem. Soc*. 2008, *130*, 4795

Aminoalcohols as Examples to Consider the OH stretch Probe



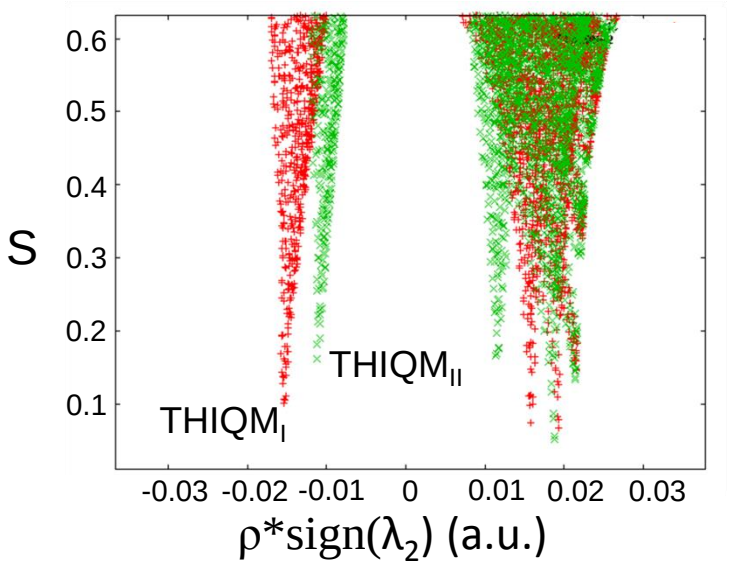
THIQM$_I$

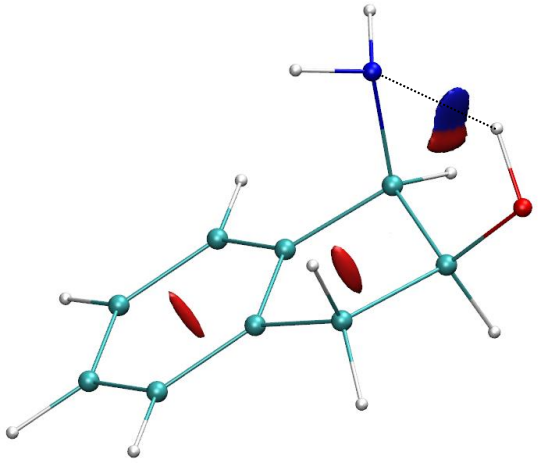
$\nu_{OH\ stretch}$ = 3566 cm^{-1}



THIQM$_{II}$

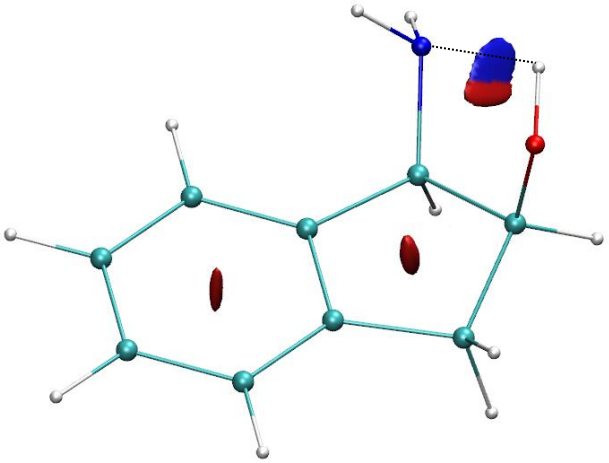
$\nu_{OH\ stretch}$ = 3686 cm^{-1}





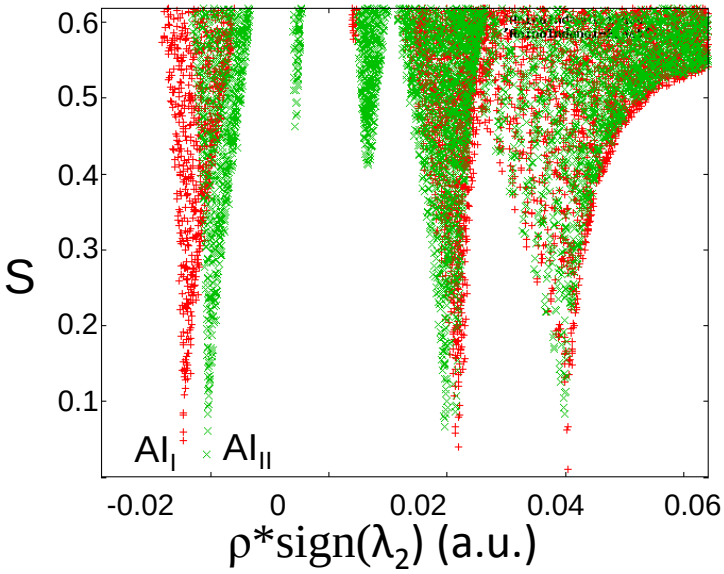
Al$_I$

$\nu_{OH\ stretch}$ = 3459 cm^{-1}

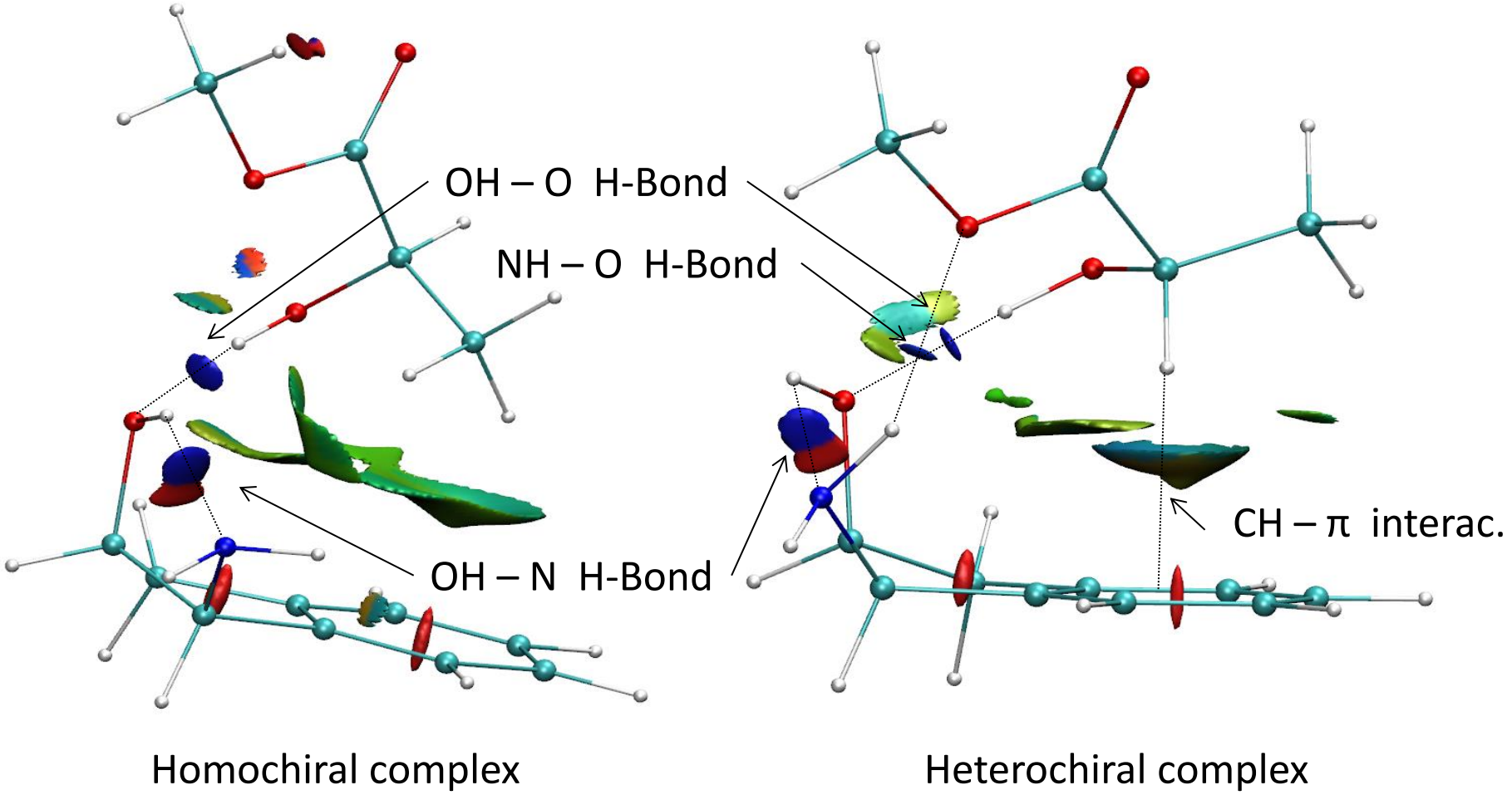


Al$_{II}$

$\nu_{OH\ stretch}$ = 3467 cm^{-1}



Chiral recognition: specific interactions in diastereomer complexes



Chaudret, R.; de Courcy, B.; Contreras-Garcia, J.; Gloaguen, E.; Zehnacker-Rentien, A.; Mons, M.; Piquemal, J.-P. *PCCP* 2013 *(submitted)*

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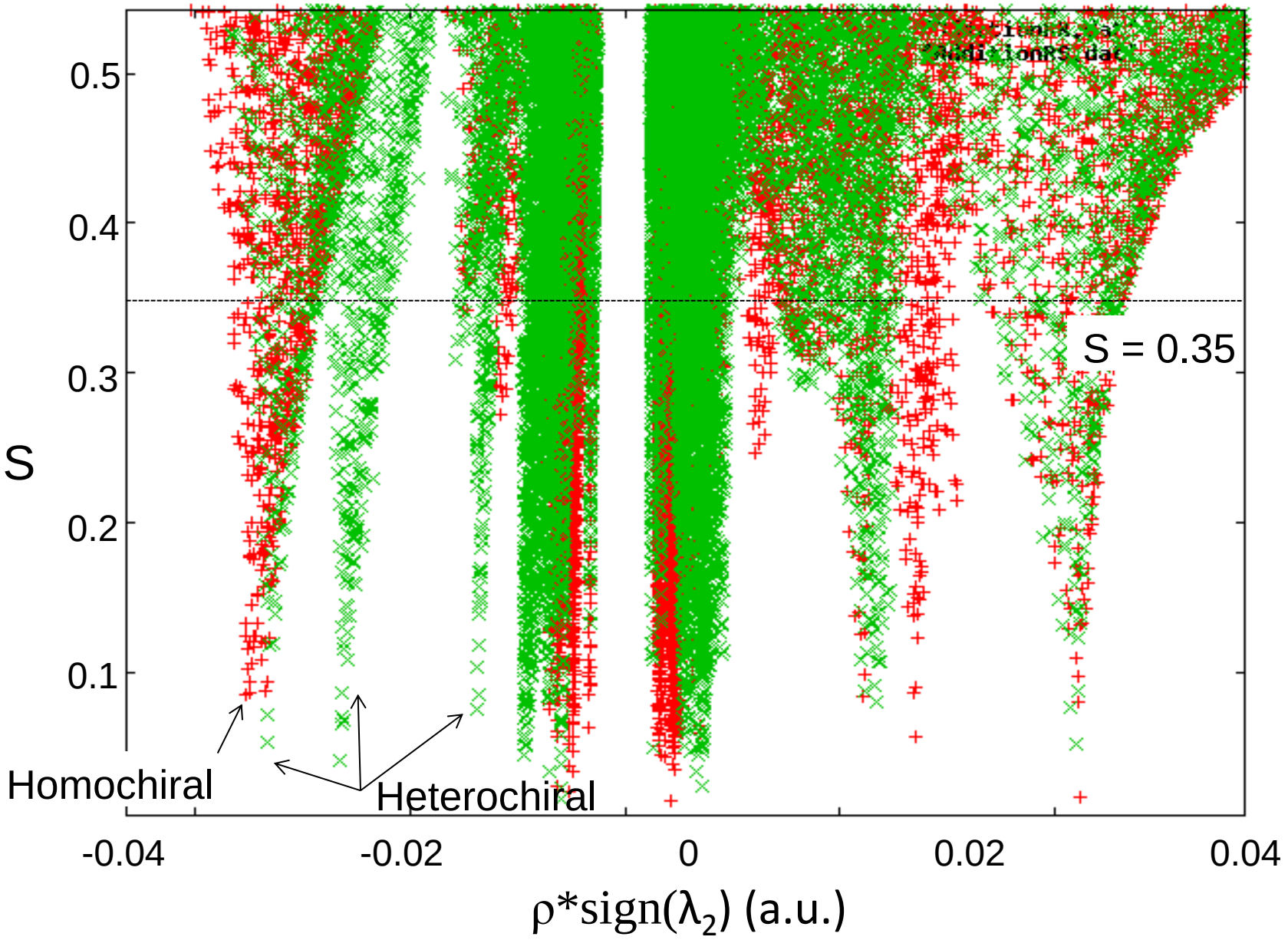
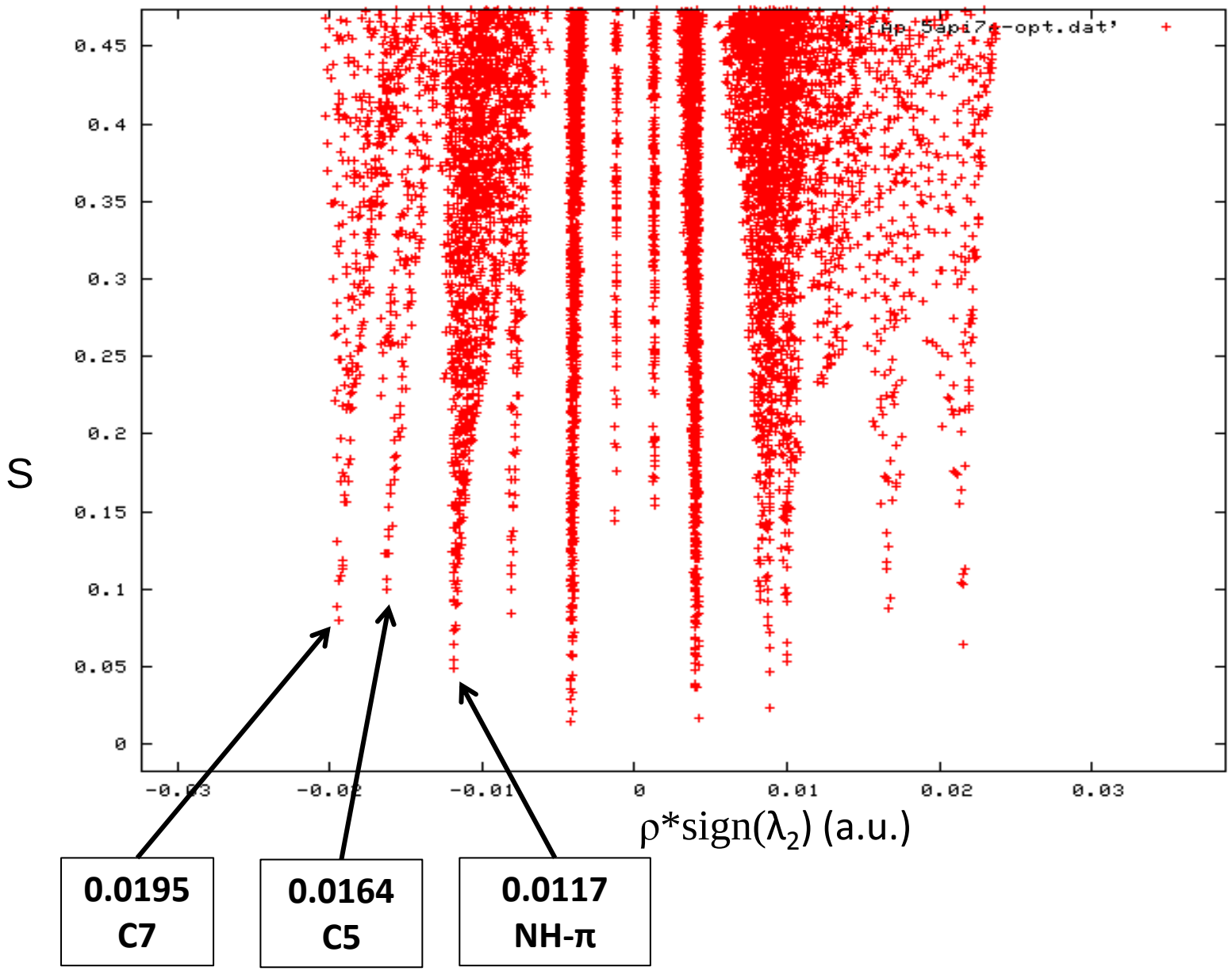
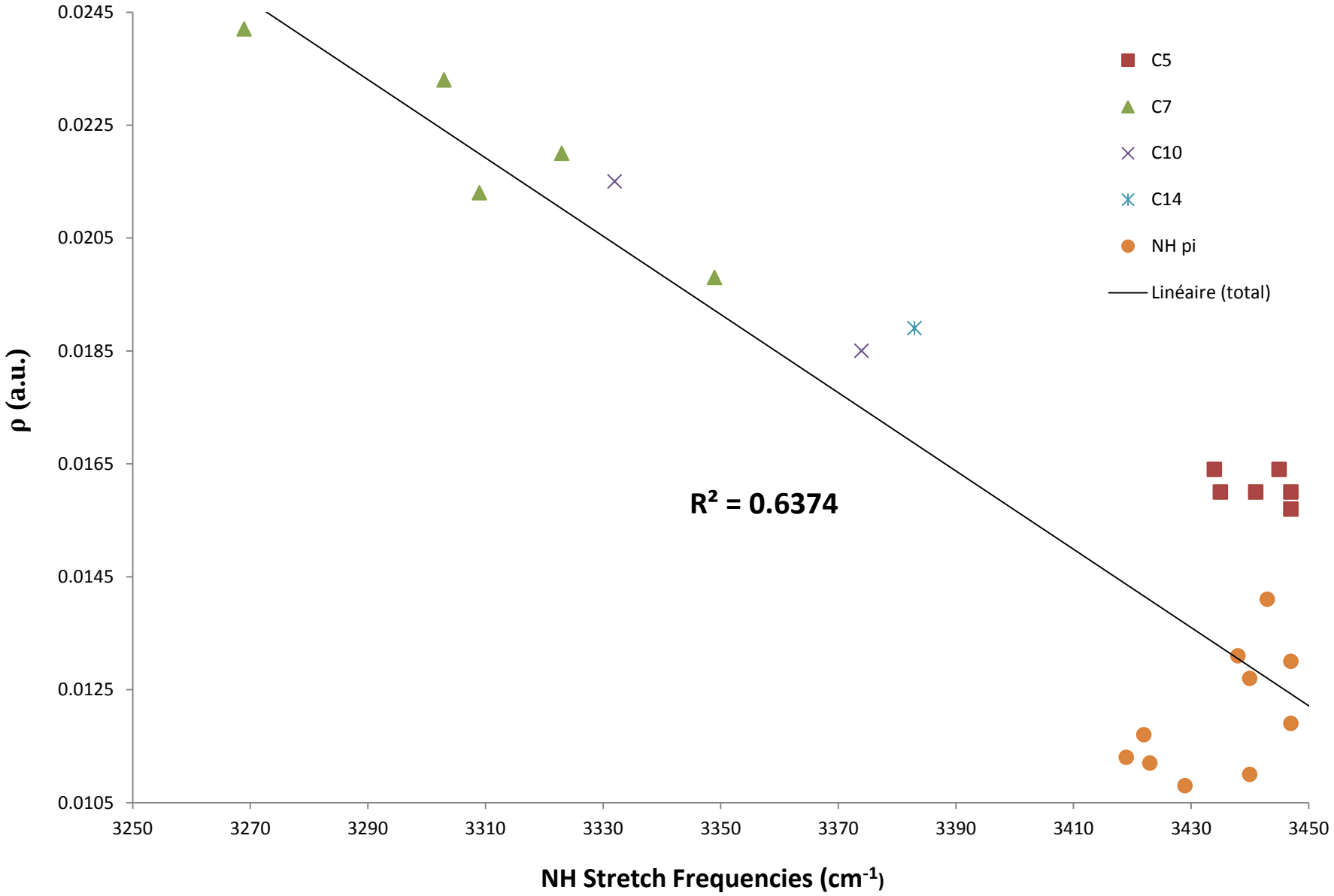


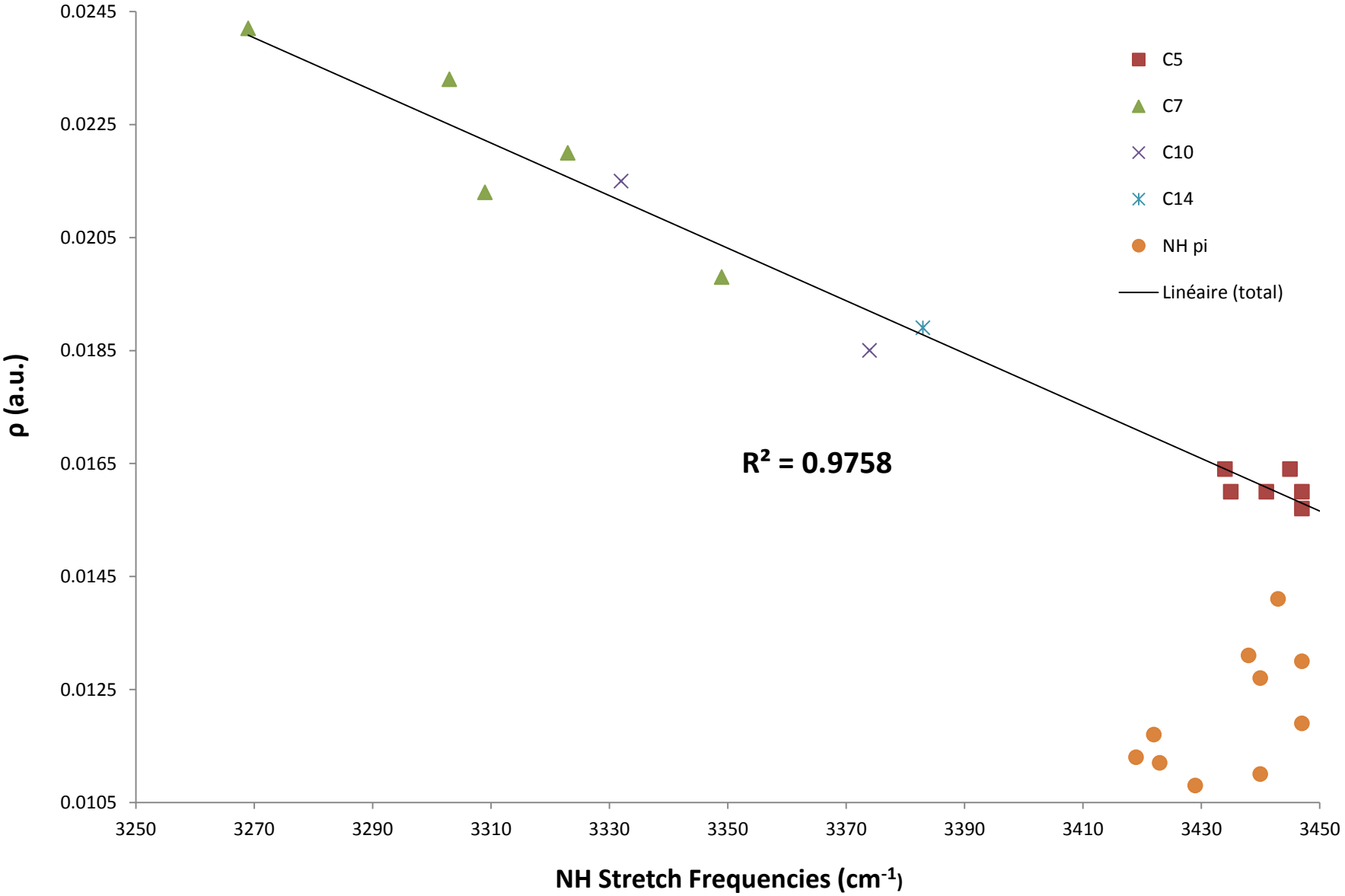
Correlation Between ρ and Experimental Frequencies



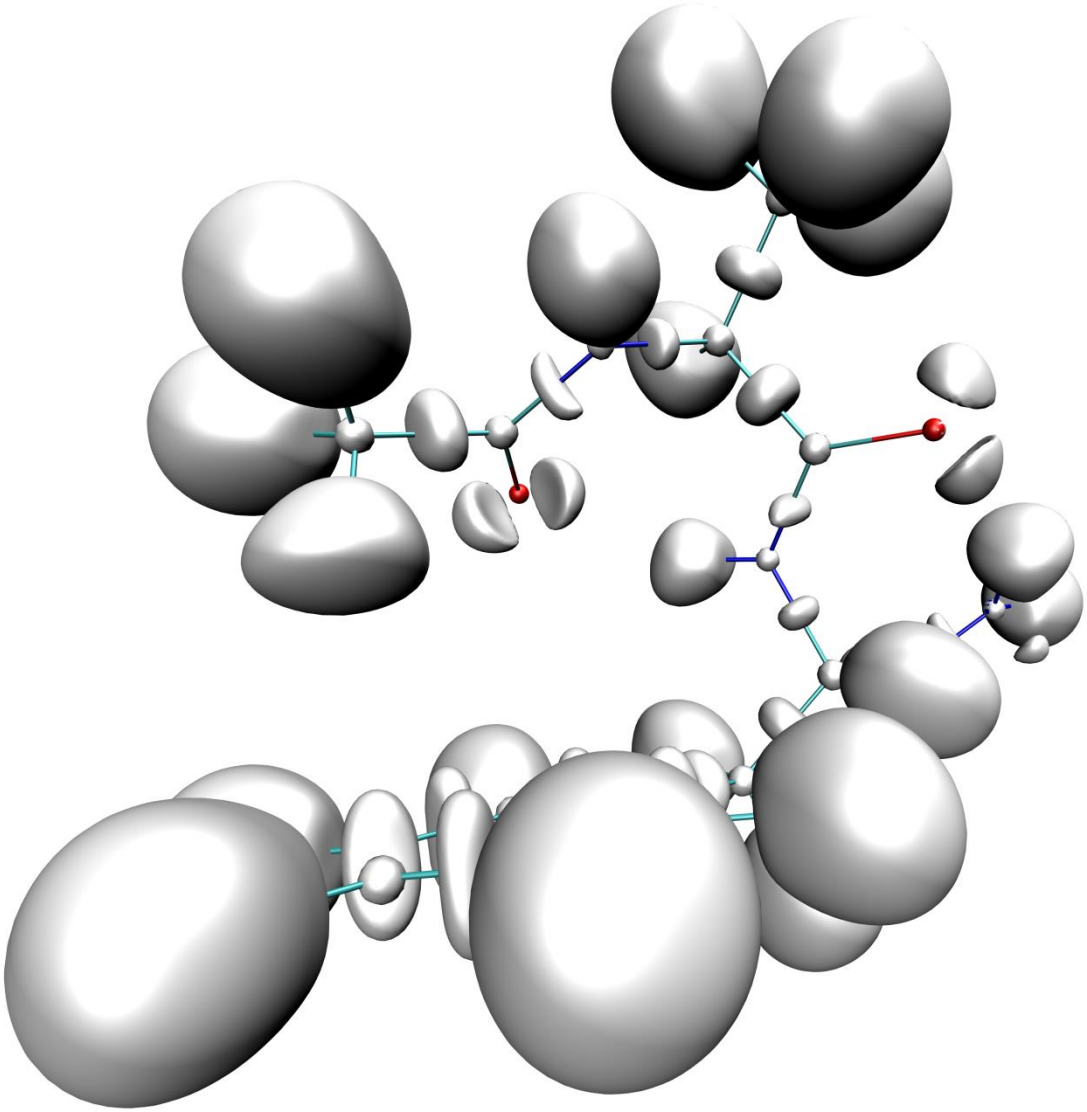
Plotting ρ vs NH Stretch Frequencies



Plotting ρ vs NH Stretch Frequencies, Disregarding NH-π Interactions



Topological Analysis: the ELF function

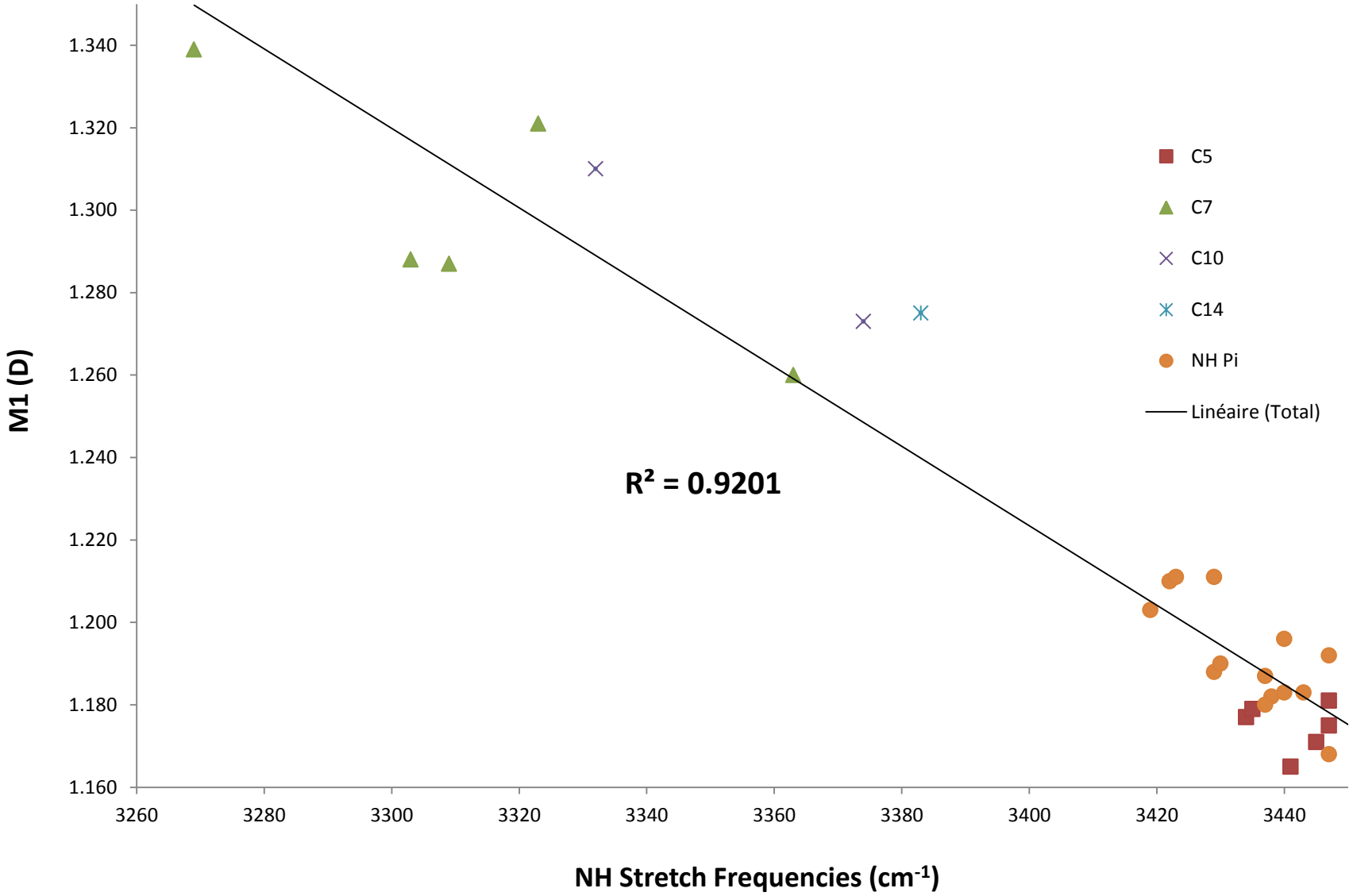


$$M1,x(\Omega)) - \int\Omega (x - Xc)F(\mathbf{r})\, d\tau$$
$$M1,y(\Omega)) - \int\Omega (y - Yc)F(\mathbf{r})\, d\tau$$
$$M1,z(\Omega)) - \int\Omega (z - Zc)F(\mathbf{r})\, d\tau$$

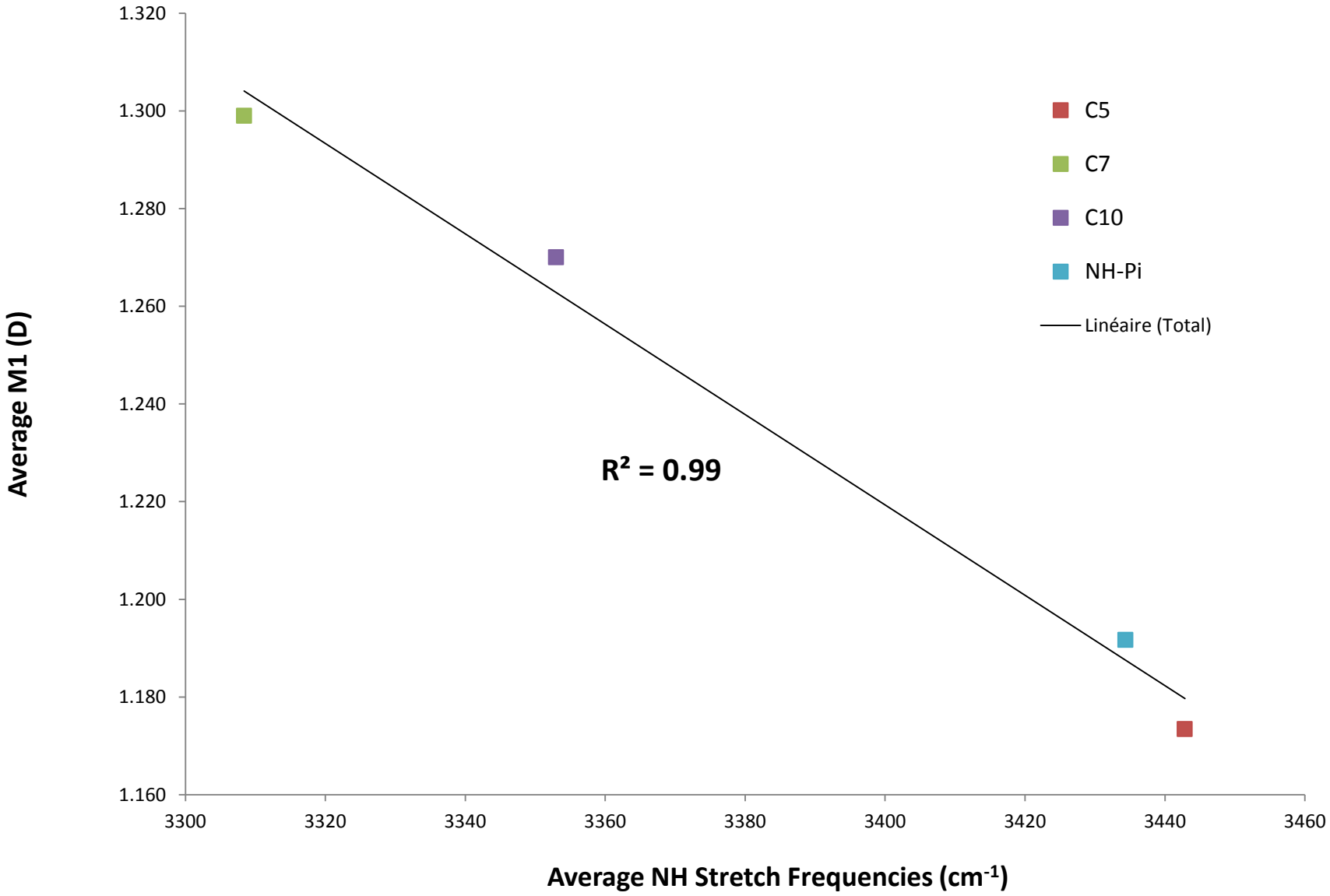
Distributed Electrostatic Moments based on the ELF Partition (DEMEP)

Pilmé, J.; Piquemal, J.-P. J Comput Chem 2008, 29, 1440.

Plotting M1 vs NH Stretch Frequencies



Plotting Average M1 vs Average NH Stretch Frequencies



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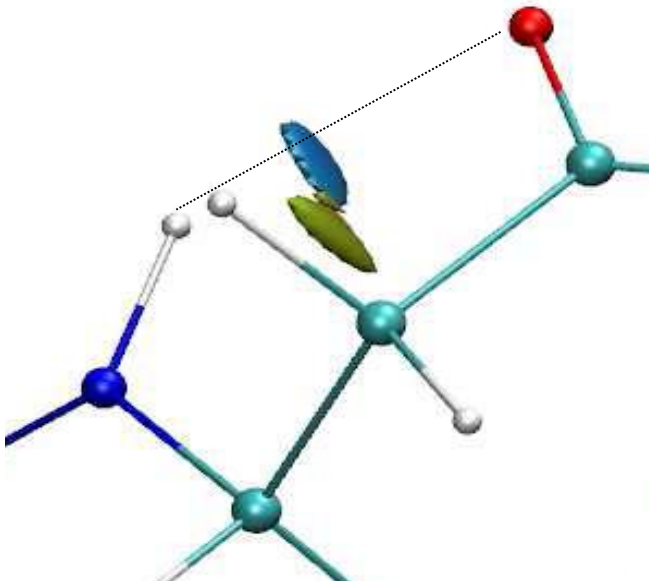

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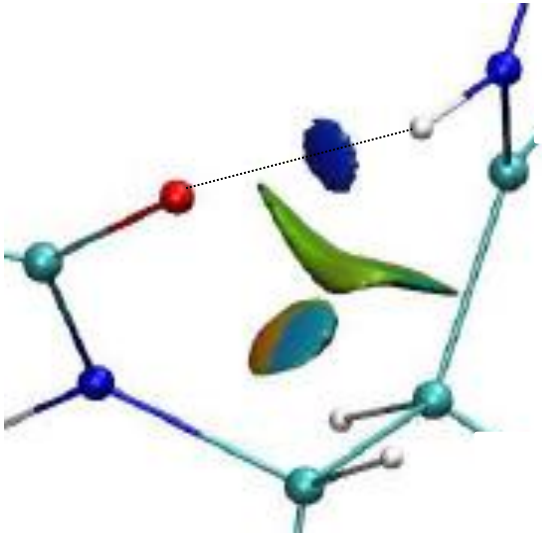

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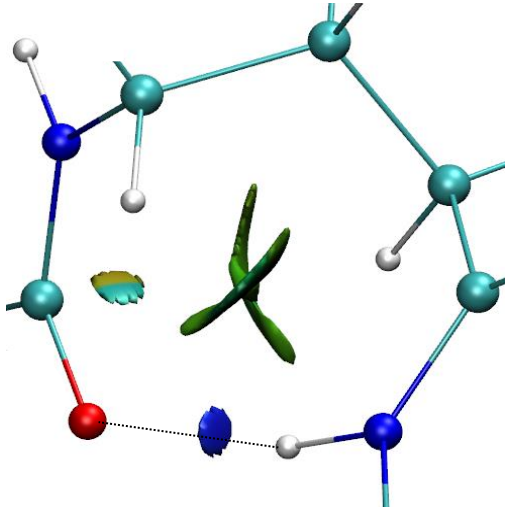

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Conclusion

To – partially at least – answer Andrea's questions:

Quantum Chemical Topology Techniques, we have used here, provide both qualitative and quantitative results.

Qualitative ones clearly highlight the capability of a quantum interpretative technique to help the experimentalists to unveil key interactions influencing the geometries and vibrational frequencies in systems difficult to interpret.

The quantitative use of such quantum interpretative techniques is aimed to facilitate the spectroscopic assignments.

Acknowledgements

Jean-Philip Piquemal	LCT
Julia Contreras-Garcia	LCT
Robin Chaudret	IFP
Anne Zehnacker-Rentien	ISMO Orsay
Michel Mons	CEA Saclay
Eric Gloaguen	CEA Saclay