

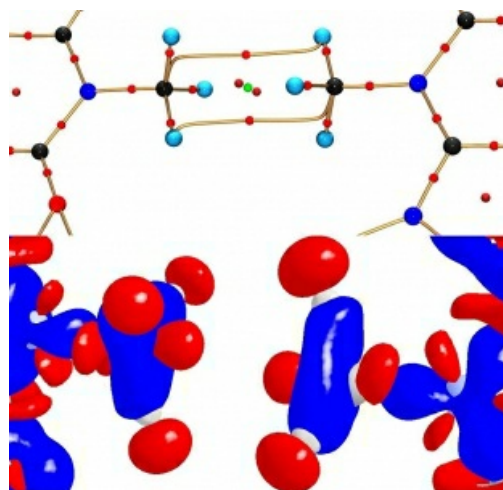
*Decoding the nature of hydrophobic interactions in caffeine molecular complexes*Sounak Sarkar¹, Sajesh P. Thomas², T.N.Guru Row¹¹Soild State And Structural Chemistry Unit And Indian Institute Of Science, Bangalore, India, ²School of Chemistry and Biochemistry, The University of Western Australia, Perth, Australia
E-mail: sarkar.sounak009@gmail.com

Hydrophobic interactions are ubiquitous in existence and they play an important role in protein folding, protein ligand binding, formation of lipid bilayers in cell walls and micelle formation. In the present work, we have attempted to unravel the chemical nature of hydrophobic interactions in short Me-Me (methyl-methyl) contacts in three reported molecules-complexes of biologically active caffeine and theophylline (co-crystal of caffeine and 3-hydroxy-2-naphthoic acid; co-crystal of caffeine and 3,5-pyrazole dicarboxylic acid and co-crystal of theophylline and 3,5-pyrazole dicarboxylic acid) from experimental charge density in combination with periodic and gas phase ab-initio calculations. The common characteristic observed in all interacting Me groups is the 'staggered conformation' with respect to each other. The strength and the electronic features of these hydrophobic interactions are quantified and qualified from Bader's QTAIM theory (Bader, 1990). The bond path for this interaction shows an unusual curved trajectory from H nuclei of one methyl group to the C nuclei of the other inversely related counterpart. 3D static deformation map depicts the interaction zone similar to a Type I halogen contact (Hathwar & Row, 2010). ¹³C ssNMR is performed to further characterise the variation in the chemical shift of the Me groups participating in hydrophobic interactions. We have used Turner's approach for calculating the energy corresponding to the hydrophobic interaction between whole molecules using Crystal explorer and accurate estimates of various component like electrostatic, dispersive, polarization and repulsive energy contributing to the interaction energy are also obtained. (Turner et al., 2014)

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[3].Turner, M. J., Grabowsky, S., Jayatilaka, D. & Spackman, M. A. (2014). J. Phys. Chem. Lett. 5, 4249-4255.

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