Supporting Information

Noncovalent Interactions between the Second Coordination Sphere and the Active Site of [NiFeSe] Hydrogenase

Swaminathan Angeline Vedha, Gunasekaran Velmurugan and

*Ponnambalam Venuvanalingam**

*Theoretical and Computational Chemistry Laboratory

School of Chemistry

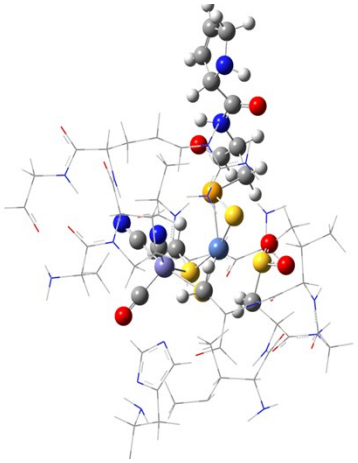
Bharathidasan University

Tiruchirappalli- 620 024

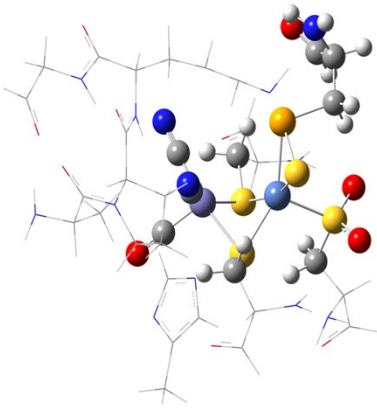
*Author for correspondence

E-Mail: venuvanalingam@yahoo.com, Ph: ++91-431-2407053, Fax: ++91-431-2407045

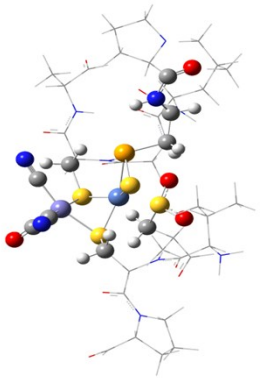
Figure S1a-e QM/MM optimized geometries of the seven models studied



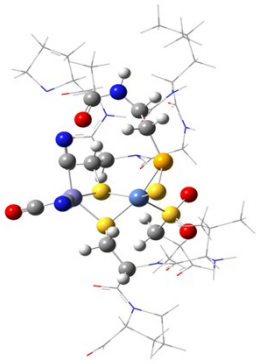
LARG



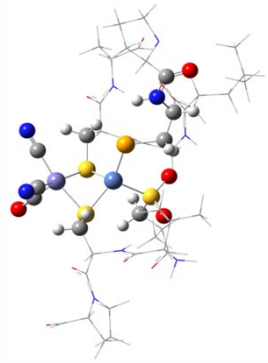
SML



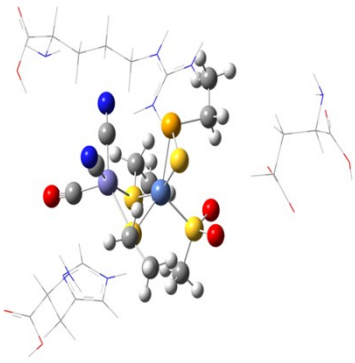
MDM-Conf1



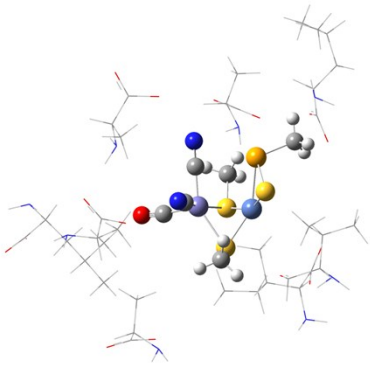
MDM-Conf2



MDM-Conf3

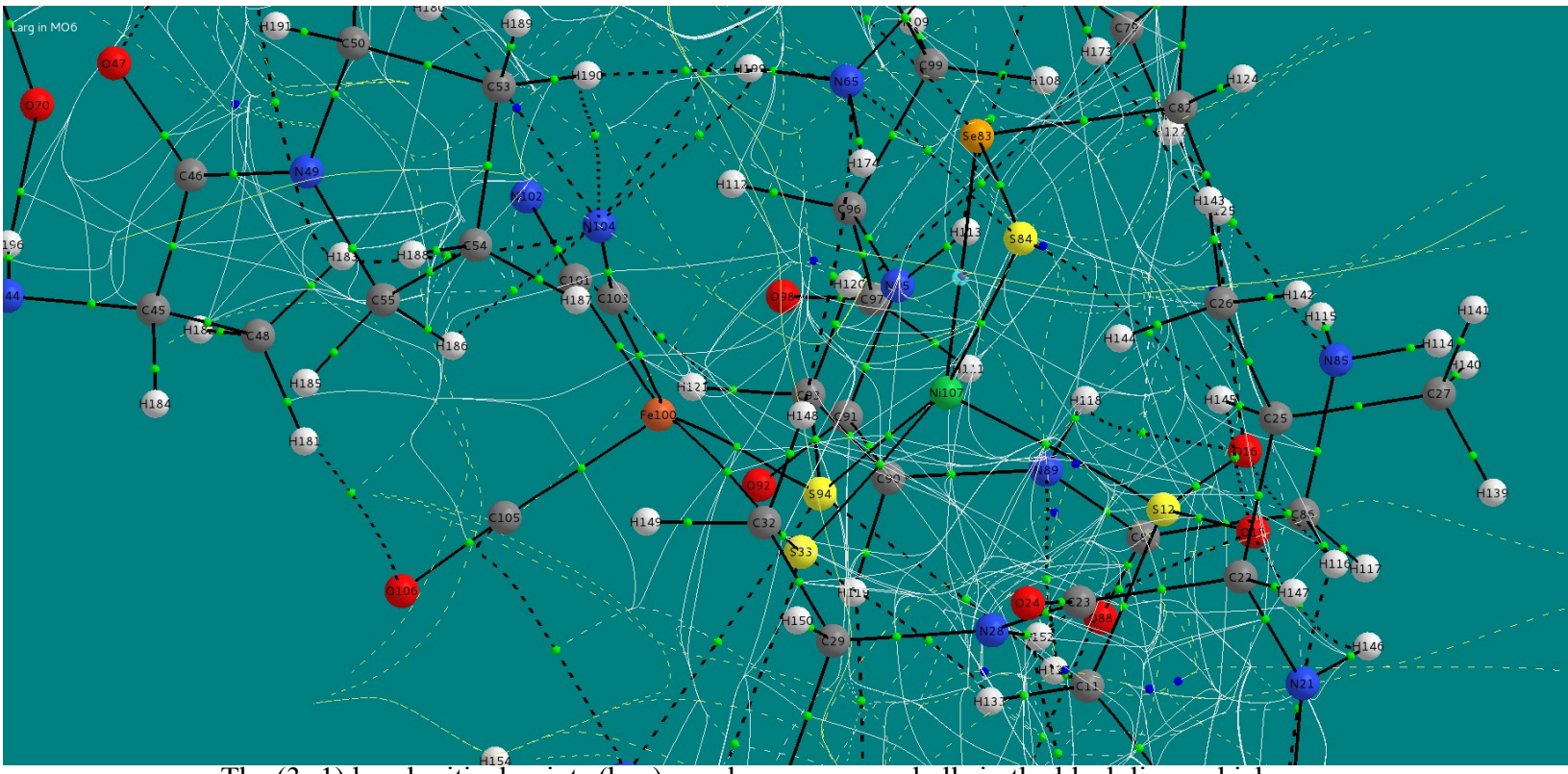


HyL



HyP

Figure S2. Molecular graph of the LARG model computed at the M06 where C, H, O & N are treated at the 6-31g(d), Ni & Fe atoms were treated at the 6-311G(3df) level and S and Se atoms were treated at the 6-311g(dp) level.



The (3,-1) bond critical points (bcp) are shown as green balls in the black lines which are the bonds. The bond paths that connect two atoms through the bcp are indicated as black dotted lines. The lines that connect the cage and ring critical points are indicated by yellow and white dotted and thin lines respectively.

Table ST1. Topological Properties at the BCPs of H-bonds formed between hydrophobic residues and the CO (in a.u).

CO···H	rho	Lapl	G(r)	H(r)	V(r)	ε	V/G
Ile 1(CH3)	0.0042	-0.0042	0.0033	0.0009	0.0024	0.0366	0.73
Ile2(CH3)	0.0029	-0.0030	0.0022	0.0007	0.0015	0.0958	0.66
Ile3(CH2)	0.0016	-0.0018	0.0013	0.0005	0.0008	0.7224	0.62
Ala1(CH3)	0.0049	-0.0048	0.0039	0.0010	0.0029	0.5558	0.75
Ala2(CH3)	0.0013	-0.0014	0.0010	0.0004	0.0006	0.5558	0.59

A brief discussion about QTAIM and NCI analysis.

QTAIM

Quantum Theory of Atoms in Molecules (QTAIM) proposed by Bader is based on the observable Ψ^2 or ρ. It is strongly rooted on– Hellman-Feynman theorem, Virial theorem and Ehrenfest theorem. Accordingly, atoms in molecules are considered as part of a open system, glued together by the electron densities in a chemical bond and all properties of the molecule are ultimately determined by the electron density distribution. A critical point (cp) in the electron density is a point in space at which the first derivative of the density vanishes. i.e., $\nabla\rho(r).n(r) = 0$ and in all other points this is a non zero quantity The second derivative of the electron density ($\nabla^2\rho$ or -L(r)) would reveal the local minimum, local maximum, and the saddle points between the two Bond path (Bp) is the universal indicator of chemical bonding in all types of bonds usually defined as weak, strong, closed shell (ionic) or shared (covalent) interactions. A point where the bond path intersects the zero-flux surface separating the two bonded atoms is the bcp.

NCI Analysis

Reduced Density Gradient methods have been in vogue for many decades. Recently, an index for identifying and analyzing the noncovalent interactions (NCI) based on the electron density and its reduced gradients has been introduced by Yang *et al.* recently.

When a weak inter- or intramolecular interaction is present, there is a crucial change in the reduced gradient between the interacting atoms, and therefore density critical points between interacting fragments are observed.

The NCI plot depicts the strength of interactions through colour codes: red signifies strong repulsion, green stands for weak interactions and blue signifies strong attractions.