

Theoretical insight of Cyanide as a ligand of Myoglobin: Ligand binding and vibrational relaxation - Supplemental Information

Jonas Danielsson and Markus Meuwly

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In this supplemental information we describe the convergence problems encountered at larger R distances, *i.e* when the ligand dissociates from the heme group. Although convergence could be achieved by geometrical perturbations or by using a quadratic convergence tool, additional analysis of spin contamination was carried out. The S^2 expectation values turned out to deteriorate more and more from their ideal value of 0.75 as R increased. A plot of the calculated S^2 values for the different radial scans at different angles are shown in figure 1.

Inspection of the Mulliken spin density of the ligand revealed that at larger

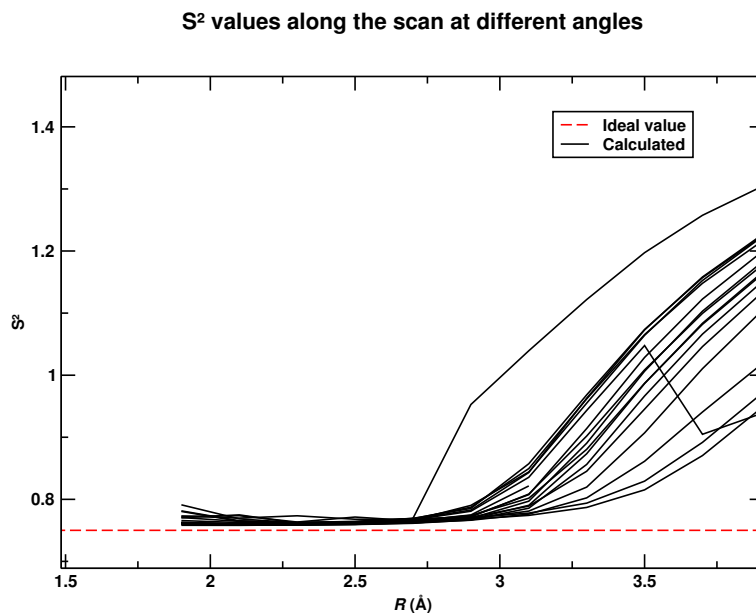


Figure 1: S^2 values of ligand heme complex along radial scans at different angles

distances the ligand acquires a radical character instead of dissociating to Fe^+ and CN^- . The reason for this shift in electronic structure is the inherent energetic cost of charge separation in vacuum, which pushes the Fe(II) - cyanide radical dissociation curve below that of Fe(III) - cyanide anion. Calculating the energies of the two pairs of dissociation products gives an energetical preference of 60 kcal/mol for the cyanide radical - ferrous heme pair. However, this effect is a result of treating the system in vacuum rather than in an environment more closely mimicking the one in the protein. One possible way to include the bulk effect of the protein is to calculate quantum chemical energies in the presence of a dielectric continuum. This is done by using the polarizable continuum model (PCM)[1], and choosing ether as solvent, which has a dielectric constant close to 4 (4.335) comparable to that in proteins. Using this model pushes the total energy of the $\text{Fe}^+ \text{-} \text{CN}^-$ dissociation limit 30 kcal/mol below that of Fe-CN^\bullet . A computation of the entire complex with a heme ligand separation of 15 Å now gives a spin density on the ligand of 0.00 and a charge of -1.00, as would be expected for full ionic dissociation. We recalculated the energetics of one of the radial scans to see if this qualitatively changed the binding surface. For the energetics, the interaction energy with the dielectric was not included, but rather the expectation value of the internal molecular Hamiltonian evaluated with the polarized density was used since only the internal energy is of interest to construct a forcefield. As can be seen in figure 3 in the paper the two curves diverges when $r_{\text{FeCOM}} \approx 3.3$ Å. However, around the minimum, the region most relevant to our simulations, the points lie very close.

References

- [1] S. Miertus, E. Scrocco, and J. Tomasi. Electrostatic interaction of a solute with a continuum. a direct utilization of ab initio molecular potentials for the prevision of solvent effects. *Chem Phys.*, 55:117–129, 1981.