

## Reply to reviewer 4

We strongly disagree with the reviewer that the science in this paper is “already presented”, “imprecise”, “over-interpreted”, “speculative”, or irrelevant. Instead, we consider this an extremely important and rigorous contribution to understanding high-valent iron-oxo systems.

However, we have considered the comments and suggestions very carefully and address each of them in the following as they were raised by the reviewer:

### 1<sup>st</sup> paragraph

- The reviewer is not correct in that there is a large number of prior publications. We have published one communication (ref. 2, JACS 2004,124,5378-9) describing the MCD data on only one complex,  $[(\text{Fe}^{\text{IV}}(\text{O})(\text{TMC})(\text{NCMe}))^{2+}]$ , where we did not deal with the vibronic structure. The introduction, pages 3-4, exactly itemizes what we did previously (in ref 2) and what is new and done here.
- We do not agree that the TD-DFT results are over-interpreted. Not only do they qualitatively agree with the  $\Delta\text{SCF}$  calculations carried out with ADF, but we present spectroscopic data of these excitation energies and use these experimental data to evaluate the quality of the computations.
- We have greatly condensed and restructured the discussion section to clarify the connection between the model complexes studied here and the enzyme intermediates. However, the purpose of biomimetic model systems lies in their extension to biological systems.
- We have tried to clarify our use of standard bonding terminology (see as well first point of 2<sup>nd</sup> paragraph)

### 2<sup>nd</sup> paragraph

- We have tried to clarify our use of standard bonding terminology. We understand the “strength of the Fe-O bond” as it is reflected by the stretching frequency as well as by its covalency given in MO theory by the energy splitting of the bonding and corresponding antibonding orbitals. Both frequency and orbital splitting can be and have been determined experimentally, in contrast to the Fe-O dissociation energies for which there are no experimental data.

- We have changed our wording regarding the use of “significant” throughout the manuscript in order to avoid ambiguities.
- We have spectroscopic data probing the unoccupied orbitals, i.e. the transition energies, and use the calculations only after correlation to experiments. In addition, the electronic structures and bonding interactions can be analyzed by means of the unoccupied antibonding molecular orbitals, since these reflect the uncompensated electron density involved in bonding interactions.
- We have restructured and tightened the discussion section for clarification: In this study we have connected the electronic structure to the reactivities of  $\text{Fe}^{\text{IV}}=\text{O}$  (S=1) model complexes. Now, we correlate them to both the electronic structure and reactivity (studied experimentally and computationally in the given reference) of a  $\text{Fe}^{\text{IV}}=\text{O}$  (S=1) biological system (bleomycin). In the next step, the extension to the electronic structure and reactivity (studied both experimental and computationally in the given references) to  $\text{Fe}^{\text{IV}}=\text{O}$  (S=2) enzyme intermediates are made. We believe this is a tight chain of logic, not irrelevant or beyond the scope of this study.

## Scientific Issues

### 1<sup>st</sup> paragraph

- As described in the given reference (Rohde, Angew. Chem. 2005), the reaction of complex **1**,  $[\text{Fe}^{\text{IV}}(\text{O})(\text{TMC})(\text{NCMe})]^{2+}$  with 10 equivalents of  $\text{NEt}_4\text{CF}_3\text{CO}_2$  in acetonitrile affords complex **2**,  $[\text{Fe}^{\text{IV}}(\text{O})(\text{TMC})(\text{OC}(\text{O})\text{CF}_3)]^+$ , which has been characterized spectroscopically. Thus, no ligand exchange in butyronitrile has occurred. We have spectroscopically verified that the complex we have studied is indeed **2**.
- Even though complex **3** can abstract the hydrogen atoms from cyclohexane, there is no abstraction of the activated C-H bond next to the nitrile group of the butyronitrile solvent. This question was dealt with computationally (with acetonitrile as the solvent) in Hirao et al, JACS 2006, reference 86.

### 2<sup>nd</sup> paragraph

- How can the fact, that the computational results correlating to data are better than expected, be a point of criticism?

- The multi-determinant nature of the system does not pose to a problem. Spin-contamination in these complexes is negligible. We have added a sentence in the computational methodology section in this regard.
- We have left INDO/S semi-empirical calculations a long time ago and do not intend to return to them.

**Abstract, lines 9-11**

- As pointed out in the text as well by the reviewer himself, the “inherent contradiction” between the strength of the Fe-O bond, i.e. the stability of the reactant, and the higher reactivity only holds if other aspects governing the reactivity are not considered. This study deals in a thorough and detailed way with the modes of activation and how they relate to reactivity in these  $\text{Fe}^{\text{IV}}=\text{O}$  complexes.
- We experimentally measure the frequency of the vibrational Fe-O stretching mode in the excited state, and thus we understand the “strength of the Fe-O bond” as it is reflected by the stretching frequency as well as by its covalency given in MO theory and related to the energy splitting of the bonding and corresponding antibonding orbitals.

**Page 13, lines 7-9**

- Yes, the excitation of an electron itself is not a reflection of the Fe-O  $\pi$ -bond strength. It is the energy of this transition which is a direct measure of the strength of the Fe-O  $\pi$ -bond. We have changed the wording accordingly.

**Page 14, lines 3-8**

- It is indeed better to imagine the Fe-O  $\pi$ -interaction as two “half- $\pi$ ” bonds, as we explain in the introduction on page 3. We have repeated this description at the beginning of section 3.3 for clarification.

**Page 16, lines 16-19**

- To avoid misunderstandings, we changed the wording “significantly” throughout the text.

**Page 17, lines 3-7**

- We certainly do not “over interpret” the experimental data. To avoid misunderstandings, we changed the wording.

**Pages 17-19**

- The section “3.4 Experimental trends”, connects the results from the VT-MCD to the vibronic analysis and compares the trends in the spectra and the electronic structures of all three complexes. We do think that this is necessary to develop the trends and generalize the bonding scheme.

**Page 21**

- The fact that the energy splitting between the S=1 ground state and the S=2 excited state in these complexes is dependent on the density functional is not connected to the electronic structure descriptions of either S=1 or S=2 systems obtained by DFT. Thus, we do not agree with this point of criticism.

**Page 24, lines 1-3**

- Stability checks were not performed, as those would undoubtedly return the system to the ground state (as they should). The point was to converge to this specific excited state.

**Page 28, lines 20-22**

- We have added values for the two types of C-H bond dissociation energies for clarification and quantification.
- 2,3-dimethylbutane was used as a general model for a tertiary C-H bond with a typical C-H bond strength of a tertiary hydrogen.
- Yes, there are experimental data for C-H abstraction by these complexes in references 16 and 22.
- These experimental data in the given references support the DFT calculations, as stated on the next page.

**Pages 29-31**

- Transition state structures have been calculated for several  $\text{Fe}^{\text{IV}}=\text{O}$  complexes, and are given in references 80-82 (as mentioned in the text, pages 29-31). They suggest an angle of Fe-O-H/C angle of  $\sim 120^\circ$  (given in the text) which supports the notion of steric hindrance in **1**.

### **Minor Points**

- Page 3, lines 2-3: The sentence referring to heme enzymes highlights that this type of intermediate does not only occur in non-heme enzymes, but is common among other iron enzymes, too. The sentence was slightly modified to clarify this point.
- Figure 1: This figure shows the Fe-d based orbitals which are the important FMOs for the interaction with the ligands as well as the reactivity of the complex. The caption was modified for clarification.
- Page 7, lines 12-15: Yes, the influence of solvent is included directly in these calculations. the sentence was slightly modified to avoid confusion.
- The Endnote-generated errors were corrected.