The Supplementary Materials for

A Fixed Multi-Sites Interaction Charge Model for Accurate Prediction of the QM/MM Interactions

Xianwei Wang[1,3], Xilong Li[2], Xiao He[3], John Z.H. Zhang[3,4,5*]*

[1]College of Science, Zhejiang University of Technology, Hangzhou, Zhejiang 310023, China

[2]College of Computer Science and Technology, Zhejiang University of Technology, Hangzhou, Zhejiang 310023, China

[3]Shanghai Engineering Research Center for Molecular Therapeutics and New Drug Development, Shanghai Key Laboratory of Green Chemistry and Chemical Process, School of Chemistry and Molecular Engineering, East China Normal University, Shanghai 200062, China

[4]NYU-ECNU Center for Computational Chemistry at NYU Shanghai, Shanghai 200062, China

[5]Department of Chemistry, New York University, New York, New York 10003, USA

* To whom correspondence should be addressed: xwwang@zjut.edu.cn; xiaohe@phy.ecnu.edu.cn; John.zhang@nyu.edu

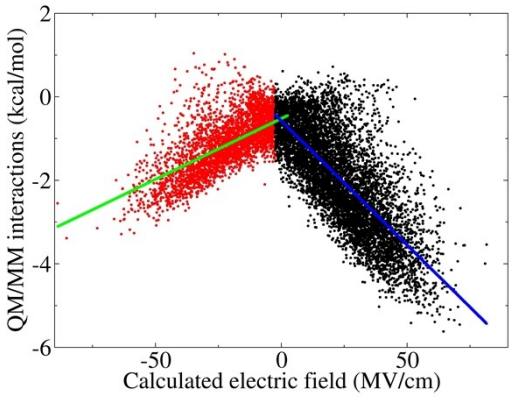

Figure S1. Distribution of the calculated QM/MM interaction energies between CO and the wild type Mb protein environment as a function of the electric fields along the CO bond.

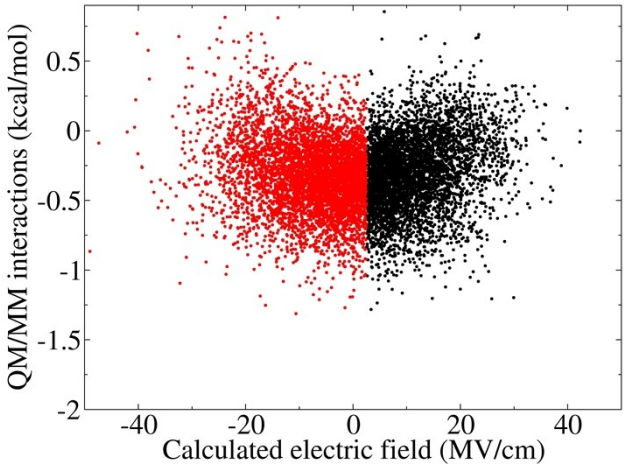

Figure S2. Distribution of the calculated QM/MM interaction energies between CO and the H64L Mb protein environment as a function of the electric fields along the CO bond.

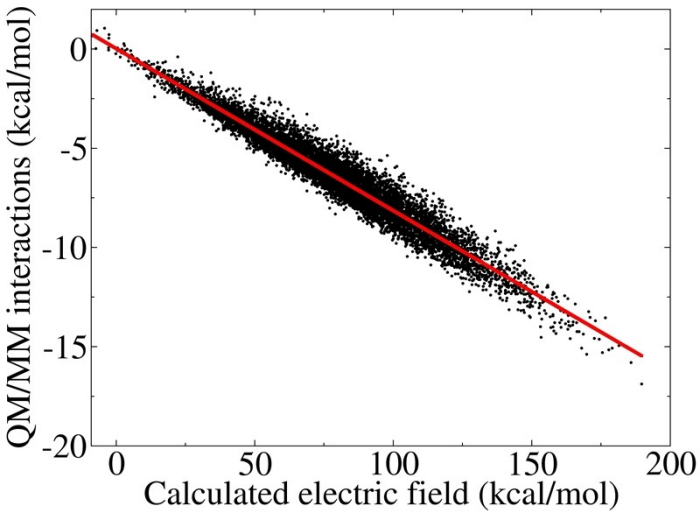

Figure S3. QM/MM interaction energies between the HF molecule and 492 TIP3P waters as a function of the electric field (the positive direction of the electric field is defined from F to H) along the F-H bond. The best fit line was shown in red (y=-0.08168x+0.026123). The obtained electrostatic energy-based atomic charges (EEC) are $H^{0.42674}F^{-0.42674}$ given that the equilibrium bond length of the F-H is 0.83 Å. The QM/MM calculations were performed at the electrostatic embedding B3LYP/aug-cc-pVDZ/TIP3P level. 10,000 different structures generated from 10 ns classical MD simulation were employed.