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DFT Studies of NO Activation of Heme Proteins. A. BARABANSCHIKOV, J.T. SAGE, Northeastern University, N.J. SILVERNAIL, W.R. SCHEIDT, University of Notre Dame, J. ZHAO, WOLFGANG STURHAHN, E.E. ALP, Advanced Photon Source, Argonne, IL — Many important cardiovascular and neural system processes are triggered by activation of the enzyme soluble guanylate cyclase (sGC), a sensor of NO widely thought to be activated through binding of NO to heme. Our understanding of these processes will remain incomplete without knowing why NO activates sGC more effectively than other diatomic ligands. We report DFT calculations on various porphyrins and heme protein active sites to test the hypothesis that activation of sGC is associated with disruption of the Fe-histidine bond to the protein. We demonstrate that NO binding significantly weakens this bond. Also, comparing the predicted vibrational spectra of these compounds with nuclear resonance vibrational spectroscopy (NRVS) measurements allows us to identify the Fe- histidine stretching mode, a reaction coordinate for histidine dissociation in NO-ligated heme proteins. Comparison of 5-coordinate and 6-coordinate NO and CO compounds provides additional tests of the hypothesis.

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