

INTRODUCTION

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“A theory is something nobody believes, except the person who made it. An experiment is something everybody believes, except the person who made it”.

Albert Einstein

Transition metal complexes (TMCs) are playing important role in many areas of research, including catalysis, materials synthesis, photochemistry, and medicine. Unique properties of TMCs are making them irreplaceable for various industrial branches. Transition metals are essential to biological processes. They are involved in a form of complexes as cofactors in vitally important processes of living organisms. Cells rely on several transition metals to regulate their metabolic and signaling functions. It is a specificity of the transition metal properties, which is determining the diversity and efficiency of the physiological functions of the cells. Due to the ability of transition metals to exist in different oxidation states and to form complexes with charged and neutral molecules, nature selected them as key elements for enzymatic reactions and as electron transport agents in biological systems, respectively. Thus, the interest of many experimental and theoretical research groups to study TMCs is not surprising.

Many of transition metal complexes involved as cofactors in the active centers of proteins are redox-active. Therefore, it is important to characterize the redox properties of these cofactors to understand the electron-transfer (ET) reactions and/or mechanism of their catalytic action in such biochemical systems. A direct measurement of cofactor redox potentials in proteins is generally limited to equilibrium situations by establishing contact with the solvent redox potential. If the cofactor is buried deeply in the protein this contact is hampered, which may have an influence on the measured redox potential. Furthermore, action redox potentials referring to non-equilibrium situations, which are typical for ET processes and transient redox states occurring in chemical reactions, cannot be measured directly. In such instances, one can only estimate the action redox potential of an electron-donor group from measured ET rates, assuming the validity of standard ET theory, knowing the redox potential of the electron-acceptor group and approximating the reorganization energy. Because of these limitations the development

of reliable theoretical methods to calculate redox potentials of TMCs is of great interest. Recent works^[1-5] on the calculation of the redox potentials of TMCs are based on density functional theory (DFT), which has proved to be a most suitable method for computations on TMCs^[6-10]. The concept to combine DFT with continuum dielectric theories was implemented by Chen et al.^[11] and used effectively in several studies^[1-5], where the best result yielded a mean absolute deviation (MAD) between computed and measured redox potential that was found to be about 150 mV, corresponding to 3.46 kcal/mol^[2]. However, ET processes in biological systems often proceed between redox-active species with energy gaps of less than 0.100 eV. Hence, enhancement of the computational accuracy of the DFT/continuum hybrid approach so that it may be applied reliably to ET processes of biological relevance is a challenging task.

Recent procedures^[12-15] to compute redox potentials of different organic compounds (excluding TMCs) showed agreement with experiment in a range of an RMSD of 170 mV^[12] (calibrated method of combined DFT and electrostatics computation) or 58 mV^[14] (*ab initio* quantum chemistry with independent continuum electrostatics). Although *ab initio* quantum chemical methods are very accurate, they are computationally demanding for the large molecular systems of interest here. On the other hand, DFT has proved to be an efficient and relatively accurate tool for the description of large molecular systems. From the DFT functionals that have been developed over the years, B3LYP^[16-19] has become the most popular and successful DFT functional. It is given by

$$E_0^{\text{B3LYP}} = a_0 E_x^{\text{exact}} + (1 - a_0) E_x^{\text{LSDA}} + a_x \Delta E_x^{\text{B88}} + a_c E_c^{\text{LYP}} + (1 - a_c) E_c^{\text{VWN}}, \quad (1.1)$$

where the five individual terms are defined as follows: E_x^{exact} , the exact exchange energy; E_x^{LSDA} , the Slater local exchange energy^[16]; ΔE_x^{B88} , Becke's 1988 non-local gradient correction to the local spin-density approximation (LSDA) for exchange^[18]; E_c^{LYP} , the Lee-Yang-Parr local and non-local correlation functional^[19]; and E_c^{VWN} , the Vosko-Wilk-Nusair local correlation functional^[17]. The three parameters were determined to be $a_0 = 0.20$, $a_x = 0.72$ and $a_c = 0.81$ ^[20]. Although the B3LYP functional yields good results for energies and geometries, it is not able to reproduce reliably the spin multiplicity of the electronic ground state for TMCs^[21, 22]. While hybrid density functionals such as B3LYP generally favor high-spin states, pure density functionals favor low-spin states^[21, 22]. The recently suggested density functional B3LYP*^[21, 22], which is essentially equivalent to B3LYP, overcomes this problem. Hess and co-workers^[21, 22] demonstrated that the low-spin/high-spin energy splitting for the TMCs depends linearly on the coefficient a_0 of the exact exchange energy E_x^{exact} . The B3LYP* density functional, for which the value of a_0 is reduced from 0.20 to 0.15, yields the proper experimental spin multiplicities for the TMCs studied by Reiher et al.^[21, 22].

Analysis of the computed redox potentials given in Refs. [2, 12, 14] shows that DFT computations with the B3LYP functional generally yield redox potentials that are lower than the measured values. Furthermore, it was recently shown that computed ionization potentials for 270 organic molecules systematically underestimated the measured values^[12]. Underestimated redox potentials calculated using DFT were recently attributed to incomplete cancellation of spurious self-Coulomb terms by the corresponding approximate exchange-correlation counterparts^[23].

The aim of the present work is to develop a procedure based on density functional theory that allows computation of redox potentials of TMCs most accurately with root mean square deviation (RMSD) from experiment of less than 0.100 V. For this purpose, an additional functional has been introduced, which partially replaces the Hartree-Fock exchange term E_x^{exact} , to correct deficiencies in the conventional B3LYP functional. Since its exact functional form is unknown, it has been evaluated after the self-consistent DFT procedure as a charge-dependent correction term. This correction procedure is analogous to recently introduced high-level spin-dependent corrections, which are applied in combination with Møller-Plesset perturbation approaches after the self-consistent quantum-chemical computation^[24-26].