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Short Review

# Recent theoretical studies of water oxidation in photosystem II

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ABSTRACT

In the present mini-review, computational work over the past decade on water oxidation in photosystem II (PSII) is summarized. The size of the chemical model used for the oxygen evolving complex (OEC) has during this time increased from the initial 20 atoms to the present day 220 atoms. The electronic structure methods used have during the same period only undergone minor improvements. It is concluded that the results have now reached a high level of convergence and the predictions for both the structure of the OEC and the O–O bond formation mechanism are most probably of higher accuracy than presently available from experiments.



**Contents**



## 1. Introduction

Photosystem II is the only system in nature capable of forming dioxygen from water and sunlight. The oxygen evolving complex (OEC), located close to the lumenal side in the membrane, is the catalyst for the step where the O–O bond is formed. The OEC complex contains four manganese and one calcium atom. X-ray diffraction studies during the past seven years have considerably clarified the detailed structure of the OEC [1–3]. In the first of these studies [1], it was shown that three of the manganese and the calcium atom form a cuboidal structure, with the fourth manganese situated outside the cube. The amino acids most likely to be ligated to the complex were also assigned. Waters were assumed to fill up the remaining coordination sites. Since the resolution was rather low (3.5 Å), the positions of the bridging oxo-groups and the ligation pattern could only be suggested. In the more recent X-ray structures the resolution was slightly higher (2.9-3.0 Å) [2,3], and a different ligation pattern was suggested with most of the carboxylate amino acid ligands assumed to bind bidentately between two different metal atoms. This means that hardly any water derived ligands had to be added to saturate the metal coordinations. The positions of the metal atoms were similar to the ones in the earlier X-ray structure, with the exception of the outside manganese which was placed farther out from the $Mn_3Ca$-cube. No positions for the oxo-groups were suggested. These two X-ray structures will in the following be termed the London and the Berlin structures. One problem with the X-ray structures is that they do not agree with EXAFS experiments [4,5]. It has been suggested that this is due to radiation damage [6], but could also come from the low resolution.

Parallel to the experimental structural work, significant progress has been made on the mechanism for O–O bond formation using density functional theory (DFT). In the quantum mechanical (QM) cluster approach [7], discussed in the present paper, a model of the OEC has been used with up to 200 atoms. Back-bone atoms were fixed to the positions obtained in the London X-ray structure. Another approach [8] has been to use the QM/MM (Quantum Mechanics/Molecular Mechanics) methodology. A small QM part

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was surrounded by a large MM part, together making up the entire protein. Several recent reviews have been written about the stepwise improvements of the cluster approach, both concerning the structure of the OEC and the mechanism for O–O bond formation [9–11].

In the present mini-review, the more recent findings using the cluster approach will be described. A significant addition to the models previously used is the inclusion of the critical $Tyr_Z$-His190 amino acids in the model. In each S-transition of water oxidation $P680^+$ in the reaction center first oxidizes $Tyr_Z$. In this process the $Tyr_Z$-OH proton concertedly goes to His190 to form a neutral $Tyr_Z$ radical and a positively charged His190. The next step is the oxidation of a manganese atom of the OEC by the $Tyr_Z$ radical. Some time ago it was suggested that both an electron and a proton would be transferred from the OEC to the neutral $Tyr_Z$ radical, in a so called hydrogen atom transfer (HAT) process [12]. Data based on electrochromic measurements argued against this mechanism [13]. Energetic considerations have also shown that a HAT step between the OEC and $Tyr_Z$ is unlikely to happen [14].

Methods similar to those adopted previously have been used for the present calculations, with one important addition. Recent theoretical work [15] has made it possible to include also dispersion effects in a simple way for the energies. These effects are generally small for the different reaction steps, but can be substantial when the water substrate becomes bound and dioxygen is released [16].

## 2. Methods and models

The Density Functional Theory (DFT) calculations discussed here were made using the hybrid functional B3LYP*, which is a modification of the original B3LYP functional [17] with a reduction of the exact exchange to 15% [18]. Procedures were used very similar to those in previous studies [7,9], with polarized basis sets for the geometries (lacvp*), large basis sets for energies (cc-pvtz(-f)), and a surrounding dielectric medium with dielectric constant equal to 6.0 (basis lacvp*). The performance of the B3LYP functional for the present type of problems has recently been reviewed [19], indicating a typical accuracy within 3–5 kcal/mol, normally overestimating barriers. A different procedure than used by other workers for obtaining redox potentials and $pK_a$ values is a key feature of the present approach [7,9,22]. Using experimental information about the driving force (measured redox potentials), and a single adjustable parameter, it is possible to determine accurate values for these properties without explicitly describing the enzyme surrounding the active site. The results are essentially independent of the choice of dielectric constant.

The addition of dispersion effects, neglected in DFT, is an important modification compared to previous studies. These are calculated using the simple empirical formula of Grimme [15]. This formula depends only on the geometric and not on the electronic structure. With a cutoff for short distances, the dispersion contribution depends on the number of intermediate distances in the structure. This means that when molecules are added, such as water, there will be an increase of dispersion, and a decrease when molecules, such as $O_2$, leave. The calculations were performed with the programs Jaguar [20] and Gaussian 03 [21].

The chemical models used here are built on the X-ray structures [1,2]. A ligand pattern close to the one from the Berlin structure was adopted as the chemically most reasonable starting point. Some variations of this ligand pattern were tested energetically, and it was, for example, found that Glu189 should have a monodentate, rather than a bidentate, bridging mode [9].

The chemical model used in most of the calculations discussed here is shown in Fig. 1. Thirteen amino acids were included in the model with three of its atoms, the α-carbon and two hydrogens

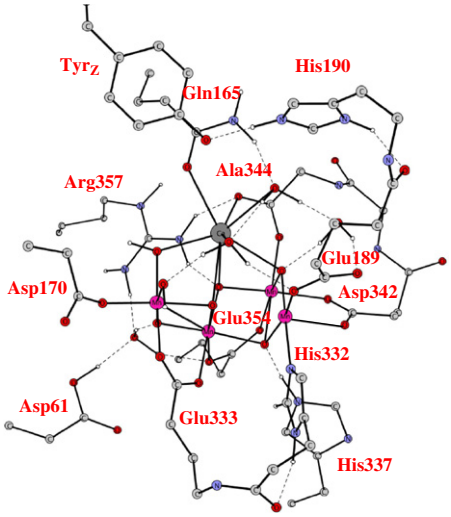


**Fig. 1.** Most recent model used for the oxygen evolving complex of PSII containing about 220 atoms.

along the back-bone, held fixed from the X-ray structure in the geometry optimizations. The main difference compared to the previous studies [7,9] is the inclusion of the $Tyr_Z$ and His190 amino acids. The nomenclature for the S-states used in the discussion below is slightly different from the one in previous studies. $S_n^m$ means that $n$ is the number of the S-state, as before, but $m$ is now the charge of the complex not only including direct ligands to the OEC but also His337. The reason for this change is that a proton alternates between the OEC and His337 during the S-transitions.

## 3. Results

### 3.1. O–O bond formation

The first computational attempts to understand water oxidation were made already before the first X-ray structures. Therefore, the starting point had to be rather crude models, where the only goal was to understand the general chemical requirements for forming an O–O bond [23,24]. The most important result from these studies was that the initial creation of an oxygen radical ligand appears to be necessary for a low-barrier O–O bond formation. This type of result was obtained essentially independently of the model used for the OEC. An important conclusion concerning electron and proton transfers could also be drawn based on these studies and those of other enzymes. The general rule found is that for processes in enzymes where protons and electrons are removed or added, a metal complex tries to minimize changes of the total charge [22,25]. This means that two electron transfer steps cannot occur after each other without a proton transfer in between. The same idea has more recently been advocated based on experiments [26].

The earliest studies of O–O bond formation all led to a mechanism with a nucleophilic attack, where a preformed oxygen radical reacts with an external water in the $S_4$-state. However, the barrier for this mechanism was much too high compared to experiments [25]. An important step toward a low-barrier mechanism was taken when essentially all possibilities to form the O–O bond with the oxygen radical were investigated for the best available $S_4$-state, which had four Mn(IV)-centers [27]. Rather surprisingly, the by far lowest barrier was found for a reaction between the terminal oxygen radical and a bridging oxo-group, see Figs. 2 and 3. What was even more surprising in the new mechanism was a spin-requirement for a low barrier, also shown in the figure. This requirement means that the directions of the spins on the four most directly