

Showcasing research from the Sun lab at the KTH Royal Institute of Technology in Stockholm, Sweden.

Why nature chose the  $\text{Mn}_4\text{CaO}_5$  cluster as water-splitting catalyst in photosystem II: a new hypothesis for the mechanism of O–O bond formation

A new hypothesis was proposed for the water-oxidation mechanism by the OEC in PSII, involving a charge-rearrangement-induced  $\text{Mn}^{\text{VII}}$ –dioxo species on the dangling  $\text{Mn}^{\text{IV}}$  during the  $\text{S}_3 \rightarrow \text{S}_4$  transition. The O–O bond is formed within this  $\text{Mn}^{\text{VII}}$ –dioxo site.

As featured in:



See Biaobiao Zhang and Licheng Sun, *Dalton Trans.*, 2018, 47, 14381.



Cite this: *Dalton Trans.*, 2018, **47**, 14381

## Why nature chose the $\text{Mn}_4\text{CaO}_5$ cluster as water-splitting catalyst in photosystem II: a new hypothesis for the mechanism of O–O bond formation

Biaobiao Zhang <sup>a</sup> and Licheng Sun <sup>\*a,b</sup>

Resolving the questions, namely, the selection of Mn by nature to build the oxygen-evolving complex (OEC) and the presence of a cubic  $\text{Mn}_3\text{CaO}_4$  structure in OEC coupled with an additional dangling Mn (Mn4) *via*  $\mu$ -O atom are not only important to uncover the secret of water oxidation in nature, but also essential to achieve a blueprint for developing advanced water-oxidation catalysts for artificial photosynthesis. Based on the important experimental results reported so far in the literature and on our own findings, we propose a new hypothesis for the water oxidation mechanism in OEC. In this new hypothesis, we propose for the first time, a complete catalytic cycle involving a charge-rearrangement-induced  $\text{Mn}^{\text{VII}}$ -dioxo species on the dangling Mn4 during the  $S_3 \rightarrow S_4$  transition. Moreover, the O–O bond is formed within this  $\text{Mn}^{\text{VII}}$ -dioxo site, which is totally different from that discussed in other existing proposals.

Received 13th May 2018,  
Accepted 6th August 2018

DOI: 10.1039/c8dt01931b

rsc.li/dalton

## Introduction

The oxygen-evolving complex (OEC) of photosystem II (PSII), which is the most important natural complex for maintaining aerobic life, has existed in photosynthetic organisms on Earth for almost three billion years.<sup>1,2</sup> Understanding the structure and catalytic mechanism of OEC is motivated not only by humans' desire to discover the secret of natural photosynthesis. It can also provide a blueprint to advance the development of water-oxidation catalysts (WOCs) for artificial photosynthesis for renewable fuel production using solar energy.<sup>1</sup>

The general structure of OEC has been determined by a series of X-ray techniques.<sup>3–7</sup> Fig. 1A shows that the core of OEC comprises a cubic  $\text{Mn}_3\text{CaO}_4$  structure coupled with an additional dangling Mn (Mn4) *via*  $\mu$ -O atom. The entire  $\text{Mn}_4\text{CaO}_5$  cluster is surrounded by amino acid residues ( $\text{Y}_Z$ , D1–D61, D1–H190, *etc.*), two  $\text{Cl}^-$  ions, and many  $\text{H}_2\text{O}$  molecules. However, the pathway of water-oxidation mechanism at the OEC, which proceeds through the Kok cycle *via* five intermediates (called  $S_i$  ( $i = 0–4$ ) states),<sup>8</sup> remains unknown. Although researchers studying PSII are generally in agreement on the oxidation states<sup>9</sup> and structures of the meta-

stable  $S_0$ ,  $S_1$ , and  $S_2$  intermediates (Fig. 1B),<sup>3,4,10,11</sup> details of O–O bond formation are still unclear. This is due to lack of experimental evidence for the most important  $S_3 \rightarrow S_4$  and  $S_4 \rightarrow S_0$  steps, which directly involve the highest oxidized  $S_4$  state that produces oxygen.<sup>12–14</sup> Currently, two O–O bond formation pathways are widely discussed: water nucleophilic attack mechanism<sup>14,15</sup> and oxo-oxyl radical coupling mechanism,<sup>16–18</sup> which involve a  $\text{Mn}^{\text{V}}$ -oxo electrophile and a  $\text{Mn}^{\text{IV}}$ -oxyl radical as the active  $S_4$  intermediate (Fig. 1B), respectively. However, the existence of a  $\text{Mn}^{\text{V}}$ -oxo electrophile or  $\text{Mn}^{\text{IV}}$ -oxyl radical in OEC catalysis has not been experimentally proved. Hence, mechanism of water oxidation by the  $\text{Mn}_4\text{CaO}_5$  cluster is still an open question, requiring scientists to propose more appropriate answers.

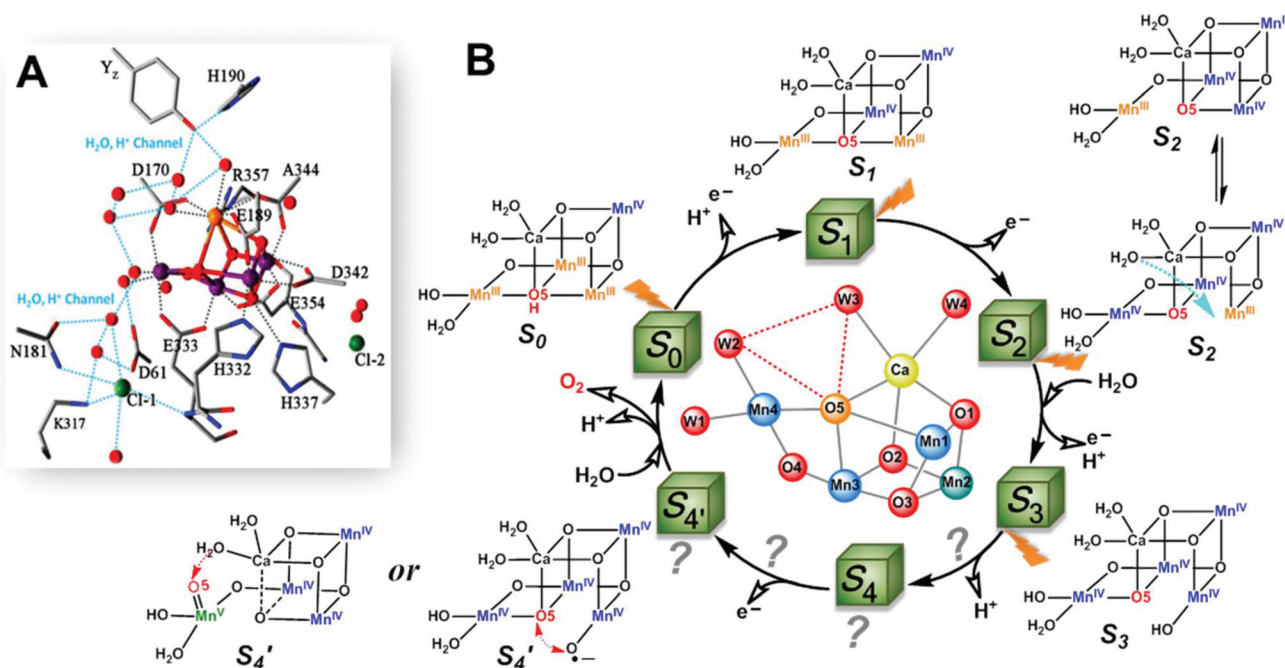
The current proposed mechanism for water oxidation by the  $\text{Mn}_4\text{CaO}_5$  cluster is far from complete and cannot effectively explain the selection of Mn by nature, the construction of OEC from multiple Mn ions, and the presence of a dangling Mn4 outside the cubic structure. Herein, we propose a  $\text{Mn}^{\text{VII}}$ -dioxo-based mechanism for O–O bond formation by the  $\text{Mn}_4\text{CaO}_5$  cluster. This mechanism is distinct from the widely discussed water nucleophilic attack and oxo-oxyl radical coupling mechanisms. Our mechanism suggests that after charge accumulation in the first three steps, charge rearrangement occurs in the fourth step to form a  $\text{Mn}^{\text{VII}}$ -dioxo site on the dangling Mn4, where the O–O bond forms in the  $S_4$  state. This  $\text{Mn}^{\text{VII}}$ -dioxo-based mechanism may open new possibilities for revealing the actual mechanism of water oxidation in PSII, and

<sup>a</sup>Department of Chemistry, KTH Royal Institute of Technology, 10044 Stockholm, Sweden. E-mail: lichengs@kth.se

<sup>b</sup>State Key Laboratory of Fine Chemicals, Institute of Artificial Photosynthesis, DUT-KTH Joint Education and Research Center on Molecular Devices, Dalian University of Technology (DUT), 116024 Dalian, China







**Fig. 1** (A) Structure of Mn<sub>4</sub>CaO<sub>5</sub> cluster of the OEC in PSII.<sup>3</sup> (B) Extended classic Kok cycle<sup>8,19</sup> for water oxidation in PSII, involving electron transfer and proton release, and the widely proposed structures of intermediate “S” states. S<sub>*i*</sub> (*i* = 0–4) states represent oxidation states of the Mn<sub>4</sub>CaO<sub>5</sub> cluster relative to the S<sub>0</sub> state. S<sub>1</sub> is the only dark-stable state. S<sub>2</sub> state exists as two interconverting isomers: “open” and “closed” configurations.<sup>10</sup> A significant structural change occurs in the S<sub>3</sub> state.<sup>19–23</sup> S<sub>4</sub> and S<sub>4</sub>' states are hypothetical states without experimental evidence, due to their ultra-short life-times<sup>14,19</sup> and related reaction steps being unclear.

consequently offer cogent guidance for developing more efficient synthetic WOCs for artificial photosynthesis.

### Proposing the Mn<sup>VII</sup> species involved mechanism

Aside from the abundance of Mn on Earth, a fundamental reason for nature to incorporate Mn in OEC could be the specificity of its redox chemistry.<sup>24,25</sup> It is reasonable to consider mechanism of water oxidation by the Mn<sub>4</sub>CaO<sub>5</sub> cluster in terms of the particular redox chemistry of Mn. For first-row transition metals in the periodic table, from Sc to Zn, the highest accessible valency and number of accessible valencies first increase up to Mn and then decrease toward Zn, which only has a valency of +2.<sup>24</sup> Therefore, Mn has the highest oxidation state (Mn<sup>VII</sup>), and the largest number of oxidation states, *i.e.*, Mn is the only metal (at least among those involved in plants) that can carry five charges (from Mn<sup>II</sup> to Mn<sup>VII</sup>). Furthermore, Mn participates in many disproportionation reactions between two or multiple Mn ions. The unique redox chemistry of Mn makes it an ideal element for building the OEC, in which accumulation of four charges is needed to oxidize two water molecules to molecular oxygen. Based on these unique features of Mn and experimental evidences presented below, we propose a new mechanism for water oxidation by the Mn<sub>4</sub>CaO<sub>5</sub> cluster in PSII, which involves charge-rearrangement-induced Mn<sup>VII</sup>-dioxo species.

In this new mechanism, we propose that first three steps, *i.e.*, S<sub>0</sub> → S<sub>1</sub>, S<sub>1</sub> → S<sub>2</sub>, and S<sub>2</sub> → S<sub>3</sub>, are the charge accumulation steps. As shown in Fig. 2, electron transfers, proton transfers,

and structural changes during these three steps are consistent with the widely accepted processes with abundant experimental evidences.<sup>9,12–14</sup> The dark-stable S<sub>1</sub> [III, IV, IV, III] state, which evolves from the S<sub>0</sub> [III, IV, III, III] state *via* a proton-coupled electron-transfer process, is transformed into the S<sub>2</sub> state after loss of one electron (please note that the order of oxidation states follows the numbering of Mn atoms in Fig. 2). In the following crucial S<sub>2</sub> → S<sub>3</sub> step, W3 H<sub>2</sub>O on the Ca site inserts into the open position between Ca and O5<sup>17,20,26</sup> and forms a new O5 for the next catalytic cycle. The original O5 is pulled towards Mn4 as a π-donating ligand. Loss of one proton and another electron gives the S<sub>3</sub> intermediate with oxidation states [IV, IV, IV, IV]. We believe that charge accumulation on the Mn<sub>4</sub>CaO<sub>5</sub> cluster is the driving force for insertion of the W3 H<sub>2</sub>O, because one negatively charged ligand is needed to stabilize the S<sub>3</sub> [IV, IV, IV, IV] state. The insertion of W3 H<sub>2</sub>O and subsequent deprotonation help to balance the positive charges accumulated on the Mn core structure after the first three steps of oxidation.

After accumulation of three charges on the Mn<sub>4</sub>CaO<sub>5</sub> cluster at the S<sub>3</sub> state, the oxidation state of Mn ions in the Mn<sub>4</sub>CaO<sub>5</sub> cluster is [IV, IV, IV, and IV]. According to the Latimer diagram of Mn, this is the highest state that can be reached through a one-electron oxidation (Scheme 1). Thus, in contrast to the first three oxidation steps, during the S<sub>3</sub> → S<sub>4</sub> step, the fourth charge obtained from P680<sup>+</sup> is retained for a longer period on Y<sub>Z</sub><sup>•</sup> than that in the first three steps. This results in the observation of a S<sub>3</sub>-Y<sub>Z</sub><sup>•</sup> state<sup>19,21</sup> because the



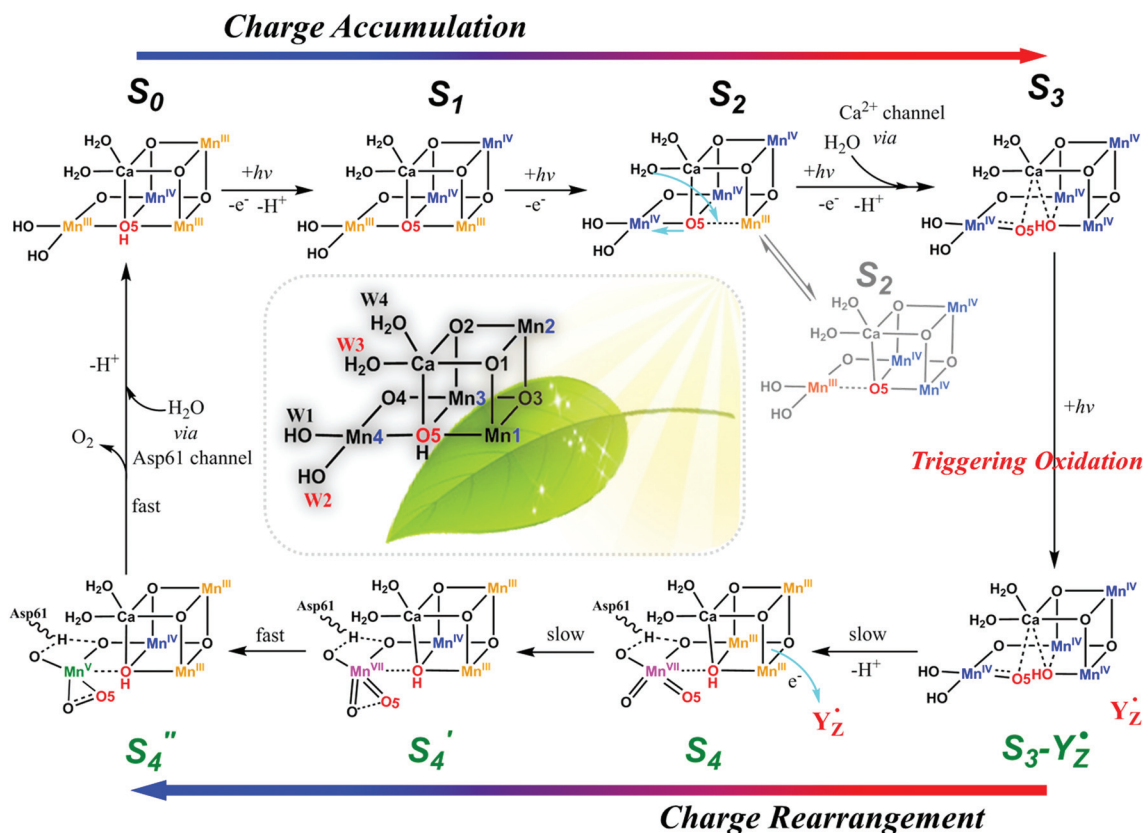
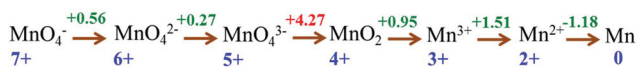


Fig. 2 Proposed catalytic mechanism for water oxidation by  $\text{Mn}_4\text{CaO}_5$  cluster in PSII involving  $\text{Mn}^{\text{VII}}$ -dioxo species. Charge disproportionation of  $\text{Mn}_4\text{CaO}_5$  cluster at the  $\text{S}_3\text{-Y}_Z^*$  state after accumulation of three charges, i.e., charge rearrangement, leads to the formation of a super-active  $\text{S}'_4$  [III, III, IV, VII] state after the  $\text{S}_3 \rightarrow \text{S}_4$  step. An O–O bond forms within the  $\text{Mn}^{\text{VII}}$ -dioxo site (between W2 and O5) during the  $\text{S}_4 \rightarrow \text{S}'_4$  step. W2, O5, and W3 all participate in  $\text{O}_2$  evolution.



Scheme 1 The Latimer diagram for Mn illustrates its standard reduction potentials (in 1 M acid) at oxidation states from +7 to 0.

direct oxidation of [IV, IV, IV, IV] to [V, IV, IV, IV] by  $\text{Y}_Z^*$  may not be the lowest energy pathway. To accept the fourth charge from  $\text{Y}_Z^*$ , i.e., to further oxidize the  $\text{Mn}_4\text{CaO}_5$  cluster, a charge rearrangement (i.e. disproportionation) occurs within the four  $\text{Mn}^{\text{IV}}$  ions in the  $\text{S}_3$  state. This is accompanied with release of a proton, resulting in an  $\text{S}_4$  [III, III, III, VII] resting state with a  $\text{Mn}^{\text{VII}}$ -dioxo site. The fourth oxidation by the  $\text{P680}^+$  can be a driving force that triggers the acceleration of charge rearrangement because it introduces the  $\text{Y}_Z^*$ , which changes the positively charged environment around the  $\text{Mn}_4\text{CaO}_5$  cluster and the  $\text{pK}_a$  balance of proton transfer channels.<sup>20,27,28</sup>

These multiple processes involved in the  $\text{S}_3 \rightarrow \text{S}_4$  step, including storage of one charge on  $\text{Y}_Z^*$ , release of one proton, charge rearrangement, and formation of the  $\text{Mn}^{\text{VII}}$ -dioxo site, are crucial for restoring the severely charged Mn cluster and producing a standby state to accept a fourth charge and form the O–O bond. Indeed, significant structural rearrangements

have been experimentally observed during the  $\text{S}_3\text{-Y}_Z^* \rightarrow \text{S}_4 \rightarrow \text{S}_0$  steps.<sup>19,21</sup> After such charge rearrangement, the  $\text{S}_4$  transition state [III, III, III, VII] is easily oxidized by its paired  $\text{Y}_Z^*$  to the active  $\text{S}'_4$  [III, III, IV, VII] state. This highly active  $\text{S}'_4$  species immediately releases a molecular oxygen via a peroxo transition state  $\text{S}''_4$  [III, III, IV, V] and is transformed back to the  $\text{S}_0$  [III, IV, III, III] state by binding one ready  $\text{H}_2\text{O}$ , supplied from the ASP61/ $\text{Cl}^-$  water channel, to vacant sites on the dangling Mn4 and losing one proton, thus completing one catalytic cycle.

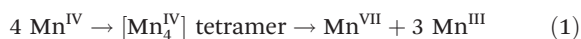
In this new mechanism, two unique and attractive points are to be necessarily discussed in detail: (1) charge rearrangement involving disproportionation of 4  $\text{Mn}^{\text{IV}}$  into 3  $\text{Mn}^{\text{III}}$  and 1  $\text{Mn}^{\text{VII}}$  (i.e.,  $\text{Mn}^{\text{IV}}\text{-Mn}^{\text{IV}}\text{-Mn}^{\text{IV}}\text{-Mn}^{\text{IV}} \rightarrow \text{Mn}^{\text{VII}}\text{-Mn}^{\text{III}}\text{-Mn}^{\text{III}}\text{-Mn}^{\text{III}}$ ), and (2) O–O bond formation at the  $\text{Mn}^{\text{VII}}$ -dioxo site. Although we did not perform special verifiable experimental studies for this article, there are sufficient published experimental results to support these two essential proposals.

#### Disproportionation of $\text{Mn}^{\text{IV}}\text{-Mn}^{\text{IV}}\text{-Mn}^{\text{IV}}\text{-Mn}^{\text{IV}}$ to $\text{Mn}^{\text{VII}}\text{-Mn}^{\text{III}}\text{-Mn}^{\text{III}}\text{-Mn}^{\text{III}}$

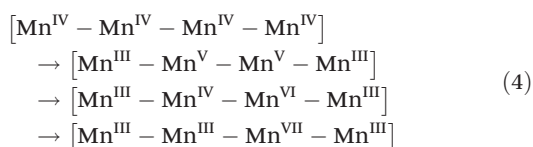
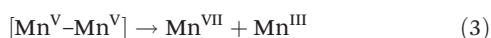
The mechanism of water oxidation by  $\text{Mn}^{\text{IV}}$  sulphate was investigated by Shilov *et al.* ca. 40 years ago.<sup>29</sup> Their experimental



results showed that the intermediate involved in oxygen evolution is a  $\text{Mn}^{\text{VII}}$  species generated by disproportionation of  $\text{Mn}^{\text{IV}}$  ions.<sup>29,30</sup> The detailed kinetic study of this reaction indicated that charge disproportionation of 4  $\text{Mn}^{\text{IV}}$  to 1  $\text{Mn}^{\text{VII}}$  and 3  $\text{Mn}^{\text{III}}$  regularly happens under  $\text{Mn}^{\text{IV}}$ -rich conditions. Furthermore, a kinetic study by Dzhabiev *et al.* showed that a tetranuclear  $\text{Mn}^{\text{IV}}$  intermediate may be involved in the charge disproportionation of 4  $\text{Mn}^{\text{IV}}$  to 1  $\text{Mn}^{\text{VII}}$  and 3  $\text{Mn}^{\text{III}}$  (eqn (1)).<sup>31</sup>



Moreover, formation of  $\text{MnO}_4^-$  species has been observed during water oxidation using several Mn based catalytic systems.<sup>32–36</sup> For example, Kaneko *et al.* reported that  $\text{MnO}_4^-$  was formed from the oxidation of  $[(\text{bpy})_2\text{Mn}(\mu\text{-O})_2\text{Mn}(\text{bpy})_2]$  ( $\text{Mn-bpy}$ ,  $\text{bpy} = 2,2'$ -bipyridine).<sup>33</sup> As shown in eqn (2), they suggested that two molecules of  $\text{Mn-bpy}$  dimer, *i.e.*, four Mn cores, are involved in  $\text{MnO}_4^-$  formation.



Similarly, Brudvig *et al.* observed the formation of  $\text{MnO}_4^-$  while studying water oxidation by  $[(\text{H}_2\text{O})(\text{tpy})\text{Mn}(\mu\text{-O})_2\text{Mn}(\text{tpy})(\text{H}_2\text{O})]$  ( $\text{Mn-tpy}$ ,  $\text{tpy} = 2,2':6',2''$ -terpyridine) dimer catalysts.<sup>32,34</sup> They proposed that  $\text{MnO}_4^-$  formed *via* disproportionation of  $[(\text{tpy})(\text{O})\text{Mn}^{\text{V}}(\mu\text{-O})_2\text{Mn}^{\text{V}}(\text{tpy})(\text{H}_2\text{O})]$  (eqn (3)). Furthermore, Yagi *et al.* found that two molecules of  $\text{Mn-tpy}$  dimer were involved in the rate-determining step of  $\text{MnO}_4^-$  formation by kinetic analysis. This is consistent with proposal by Kaneko *et al.* These experimental observations strongly support that one possible evolution pathway for a [IV, IV, IV, IV] state is to disproportionate into a [VII, III, III, III] state. A detailed process of charge rearrangement is proposed as shown in eqn (4), in which the transformation from  $\text{Mn}^{\text{IV}}\text{-Mn}^{\text{VI}}$  to  $\text{Mn}^{\text{VII}}\text{-Mn}^{\text{III}}$  is a fast step.<sup>30</sup>

Although theoretical studies are not sufficient to explain this complicated process, a Latimer diagram of Mn can preliminarily help us understand why multiple Mn ions are involved in the generation of  $\text{Mn}^{\text{VII}}$  species instead of a step by step one-electron oxidation (Scheme 1). The Latimer diagram of Mn shows that oxidation potential from  $\text{Mn}^{\text{IV}}$  to  $\text{Mn}^{\text{V}}$  is 4.27 V, which is much higher than all other redox potentials of Mn. This implies that the stepwise one-electron oxidation of  $\text{Mn}^{\text{IV}}$  to  $\text{Mn}^{\text{VII}}$  may need very high energy. This also explains why  $\text{Mn}^{\text{V}}$  is the only species missing in the Pourbaix diagram of Mn and why  $\text{MnO}_4^-$  lies in close proximity to  $\text{MnO}_2$ .

However, the oxidation potentials of PSII are sufficient to generate a high-valent  $\text{Mn}^{\text{VII}}$  site in the  $\text{Mn}_4\text{CaO}_5$  cluster. In the Pourbaix diagram for Mn, theoretical potential for the formation of  $\text{MnO}_4^-$  at pH 7 is 1.05 V.<sup>36</sup> The estimated redox

potentials for  $\text{P680}^+$  and  $\text{Y}_Z/\text{Y}_Z^+$  are approximately +1.26 and +1.21 V, respectively,<sup>37</sup> and are thermodynamically adequate for initiating the formation of  $\text{Mn}^{\text{VII}}$  species. Indeed,  $\text{Mn}^{\text{II}}$  can be oxidized to  $\text{Mn}^{\text{VII}}$  by moderate one-electron oxidants<sup>29</sup> such as  $\text{Ru}(\text{bipyridine})_3^{3+}$  with an oxidation potential of +1.26 V, which is close to the potentials of  $\text{P680}^+$  and  $\text{Y}_Z^+$ .

These analyses together with the consideration of the facts of PSII, *i.e.*, the unique dangling Mn4 site and existence of the  $\text{S}_3\text{-Y}_Z^+$  state, reasonably support the disproportionation of the [IV, IV, IV, IV] state to a [III, III, III, VII] state during the  $\text{S}_3 \rightarrow \text{S}_4$  transition.

### O–O bond formation within the $\text{Mn}^{\text{VII}}$ -dioxo site

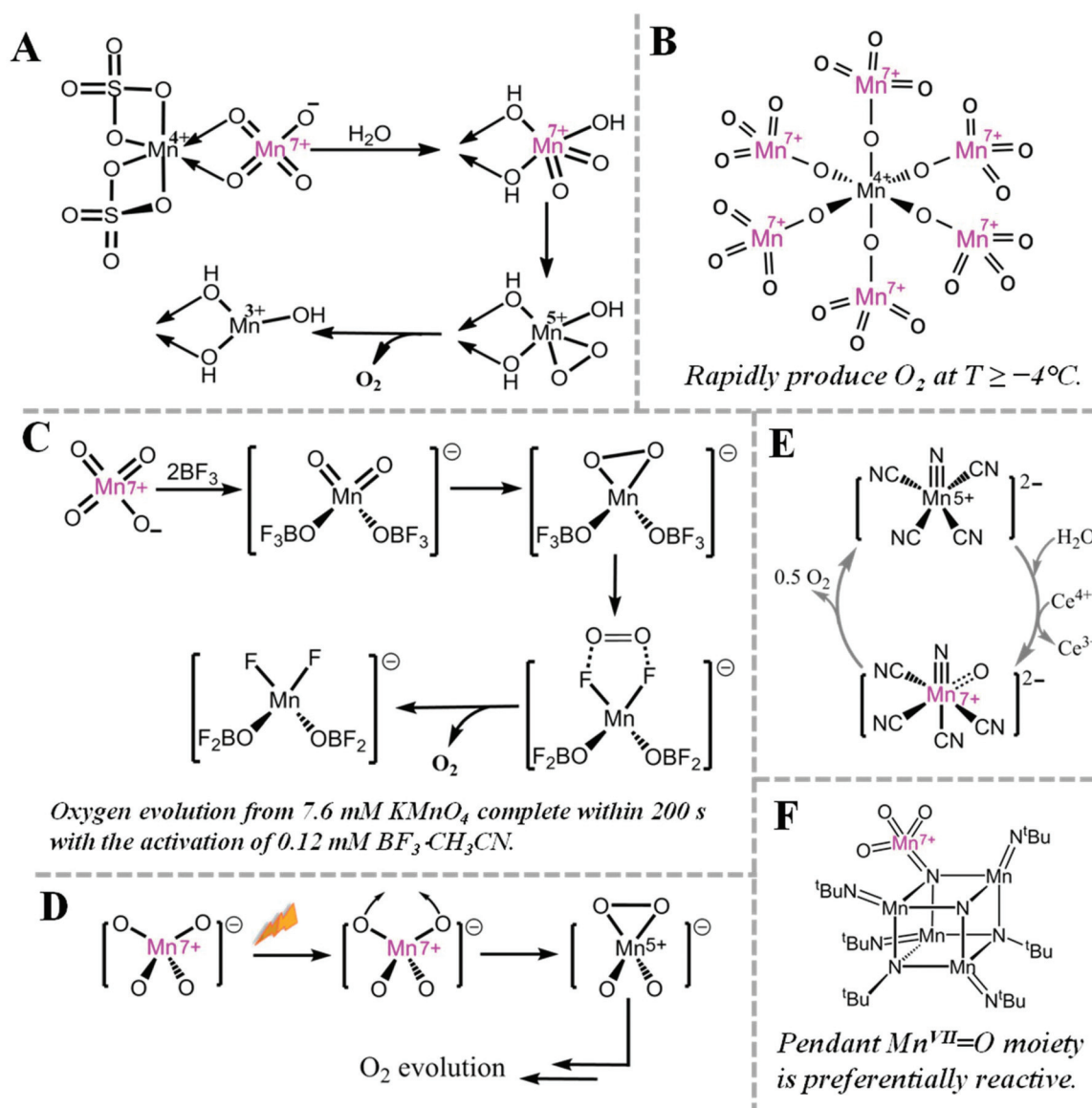
Oxygen evolution at  $\text{Mn}^{\text{VII}}$ -dioxo site is thermodynamically possible, but kinetically hampered. For example, it is well known that  $\text{MnO}_4^-$  can evolve  $\text{O}_2$ , but the rate is very slow.<sup>38</sup>

However, the rate of oxygen evolution from  $\text{Mn}^{\text{VII}}$ -dioxo site can be greatly enhanced by various promoters. For example,  $\text{MnO}_2$  has been known as a catalyst for oxygen evolution from  $\text{MnO}_4^-$  by Skrabal since 1910.<sup>38</sup> Shafirovich *et al.* studied the mechanism of oxygen formation during oxidation of water by  $\text{Mn}^{\text{IV}}$  sulfate. They suggested a mechanism (Fig. 3A) where a  $\text{Mn}^{\text{IV}}\text{-Mn}^{\text{VII}}$  surface complex is the active intermediate for O–O bond formation.<sup>29–31</sup> Interestingly, a crystalline  $\text{Mn}^{\text{IV}}\text{-Mn}^{\text{VII}}$  complex,  $(\text{H}_3\text{O})_2\text{-}[\text{Mn}^{\text{IV}}(\text{Mn}^{\text{VII}}\text{O}_4)_6] \cdot 11\text{H}_2\text{O}$ , immediately evolves oxygen when kept at or over  $-4^\circ\text{C}$  (Fig. 3B).<sup>39</sup> When  $\text{MnO}_4^-$  is activated by a strong Lewis acid such as  $\text{BF}_3$ ,  $\text{O}_2$  is rapidly evolved *via* intramolecular coupling of  $\text{Mn}^{\text{VII}}$ -dioxo site (Fig. 3C).<sup>40</sup> During photo-induced oxygen evolution from  $\text{MnO}_4^-$ , Lee *et al.* investigated the presence of an excited state of  $\text{MnO}_4^-$ , which is a much more active oxidant than permanganate itself and the subsequent formation of a  $\text{Mn}^{\text{V}}$ -dioxo intermediate prior to oxygen evolution (Fig. 3D).<sup>41</sup> A  $\text{Mn}^{\text{VII}}=\text{O}$  species has also been proposed as an essential intermediate for a  $\text{Mn}^{\text{V}}$ -nitrido complex during  $\text{Ce}^{\text{IV}}$ -driven water oxidation (Fig. 3E).<sup>42</sup> In 2017, a highly reactive pendant  $\text{Mn}^{\text{VII}}=\text{O}$  moiety on a cubic Mn-nitride complex has been reported as a synthetic structural model of the proposed  $\text{S}_4$  state in PSII (Fig. 3F).<sup>43</sup>

Very recently, we reported the presence of an essential  $\text{Mn}^{\text{VII}}$ -dioxo intermediate in a synthetic *c*-disordered  $\delta\text{-MnO}_x$ -based water oxidation catalyst (*i.e.*,  $\text{MnO}_x\text{-300}$ ),<sup>45</sup> where a  $\text{Mn}^{\text{IV}}\text{-O-Mn}^{\text{VII}}=\text{O}$  was proposed as the active species for O–O bond formation.<sup>44</sup> As shown in Fig. 4, one active Mn site and three related Mn atoms of the manganese oxides are suggested to participate actively in the catalysis. After multiple electrochemical oxidations of the active site, the initial  $[\text{Mn}^{\text{III}}\text{Mn}^{\text{III}}\text{Mn}^{\text{IV}}(\text{HO-Mn}^{\text{III}}\text{-OH}_2)]$  state is oxidized to  $[\text{Mn}^{\text{IV}}\text{Mn}^{\text{IV}}\text{Mn}^{\text{IV}}(\text{HO-Mn}^{\text{IV}}=\text{O})]$  accompanied by the loss of three electrons and two protons.  $[\text{Mn}^{\text{IV}}\text{Mn}^{\text{IV}}\text{Mn}^{\text{IV}}(\text{HO-Mn}^{\text{IV}}=\text{O})]$  is assumed to undergo charge rearrangement with release of one proton, resulting in a resting  $[\text{Mn}^{\text{III}}\text{Mn}^{\text{III}}\text{Mn}^{\text{III}}\text{Mn}^{\text{VII}}(=\text{O})_2]$  state. A structural moiety of this intermediate has been proved by a characteristic CV reduction peak at 0.93 V and an IR absorption frequency of  $912\text{ cm}^{-1}$ , which strictly corresponds to the occurrence of water-oxidation







**Fig. 3** Highly reactive  $\text{Mn}^{\text{VII}}$  species and related  $O_2$  evolution reactions. (A) Pathway for oxygen evolution from  $\text{MnO}_4^-$ , catalysed by  $\text{Mn}^{\text{IV}}$  ion.<sup>29</sup> (B) Structure of  $[\text{Mn}^{\text{IV}}(\text{Mn}^{\text{VII}}\text{O}_4)_6]^{2-}$  complex.<sup>39</sup> (C) Mechanism for fast oxygen evolution from  $\text{MnO}_4^-$ , activated by  $\text{BF}_3$ , a strong Lewis acid.<sup>40</sup> (D) Proposed structures of intermediates for  $O_2$  evolution from photodecomposition of  $\text{MnO}_4^-$ .<sup>41</sup> (E) Mechanism for water oxidation by  $\text{Mn}^{\text{V}}$ -nitrido molecular catalyst.<sup>42</sup> (F) Structure of cubic Mn-nitride complex with pendant  $\text{Mn}^{\text{VII}}=\text{O}$  moiety.<sup>43</sup>

reaction. Moreover, several experimental evidences demonstrated that this surface-bonded  $\text{Mn}^{\text{VII}}$ -dioxo intermediate is more prone to oxidation than the free  $\text{MnO}_4^-$ . However, we consider it as a resting state instead of a final active species for O–O bond formation since this  $\text{Mn}^{\text{VII}}$ -dioxo intermediate has a long life time. Subsequently, the  $\text{Mn}^{\text{III}}$  ion directly bonded to the dangling  $\text{Mn}^{\text{VII}}=\text{O}$  site is thought to be further oxidized to  $\text{Mn}^{\text{IV}}$ , which drastically increases reactivity of the  $\text{Mn}^{\text{VII}}=\text{O}$  site, forming the active state  $[\text{Mn}^{\text{III}}\text{Mn}^{\text{III}}\text{Mn}^{\text{IV}}\text{Mn}^{\text{VII}}(=\text{O})_2]$  state for oxygen evolution. Results of this study can be experimental evidences to support the assumption that an activated permanganate-like  $\text{Mn}^{\text{VII}}=\text{O}$  moiety is highly reactive and it may be present during the catalytic cycle of water oxidation in PSII.

The above examples clearly show that O–O bond formation from species with activated permanganate-like  $\text{Mn}^{\text{VII}}=\text{O}$  moiety is a fast and efficient pathway for oxygen evolution. In contrast, a fast O–O bond formation mechanism from  $\text{Mn}^{\text{IV}}=\text{O}$  or  $\text{Mn}^{\text{V}}=\text{O}$  species is not commonly available in the published studies on oxygen evolution reaction. Since the turnover frequency of PSII is about  $100\text{--}400\text{ s}^{-1}$ ,<sup>36</sup> it is necessary to consider a fast pathway for the O–O bond formation, involved in the mechanism of water oxidation by PSII.

Lastly, we emphasize that in this new proposed mechanism, the essential charge rearrangement involved in the steps of  $\text{S}_3\text{-Y}_Z^* \rightarrow \text{S}_4 \rightarrow \text{S}_0$  is consistent with the kinetic studies where a slow kinetic phase involving a structural rearrangement has



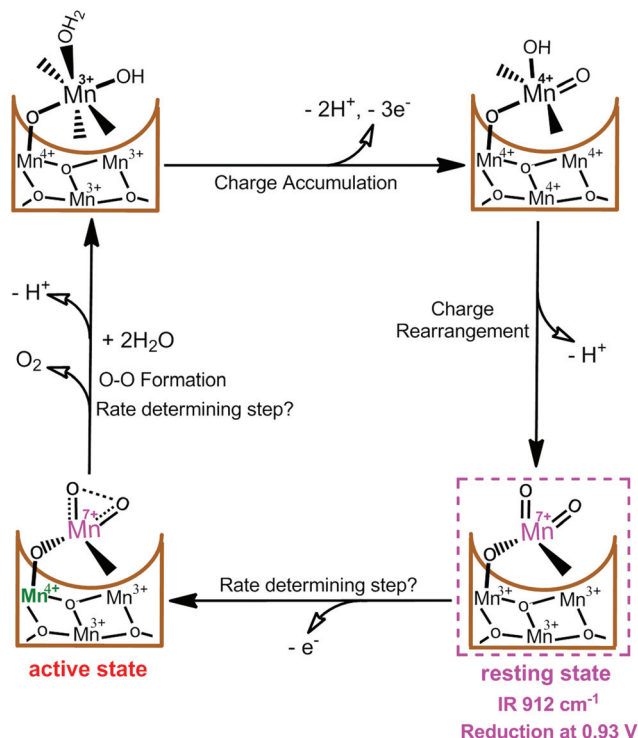


Fig. 4 Proposed catalytic cycle in  $\text{MnO}_x\text{-300}$ -catalyzed water-oxidation reaction.<sup>44</sup>

been strongly suggested,<sup>19,21–23,27,28</sup> giving a possible explanation to this slow kinetic phase. Two molecules of water are transferred into the  $\text{Mn}_4\text{CaO}_5$  cluster during each catalytic cycle: one from the Ca water channel (as the successor of O5 for the next catalytic cycle) and one from the Asp61 water channel (for the new W2) consumed for forming  $\text{O}_2$ . This is consistent with the fact that the proton/water channels in PSII are closely related to the Ca site and the Mn4 site.<sup>46</sup> This finding also agrees with the fact that W2, W3 and O5 are usually considered as the O substrates involved in O–O bond formation.<sup>46</sup>

Based on our findings, we prefer this mechanism that involves  $\text{Mn}^{\text{VII}}=\text{O}$  moiety and O–O bond formation compared to the coupling of O5 and O of W2 for water oxidation by the OEC. However, without experimental evidence from direct studies on the OEC, particularly for the  $\text{S}_3 \rightarrow \text{S}_4$  step, other potential O–O bond formation pathways may be possible, for example, O–O bond formation from O5 and the new O (O6) on Mn1<sup>17,18,47</sup> or from O4 and O of W1.<sup>48</sup>

## Conclusions

Involvement of  $\text{Mn}^{\text{VII}}$  in the O–O bond formation step is a highly appropriate alternative mechanism for water-oxidation catalysis by the  $\text{Mn}_4\text{CaO}_5$  cluster. This mechanism involves a complete catalytic cycle with reasonable valency changes, structural transformations, and O–O bond formation steps. In this new mechanism, we propose that Mn4 is the active site for the O–O bond formation in the  $\text{S}_4$  state by forming an essential

$\text{Mn}^{\text{VII}}$ -dioxo species. This Mn4 site also functions as a gate for releasing protons from the  $\text{Mn}_4\text{CaO}_5$  cluster. Mn1, Mn2, and Mn3 sites, within the cubane, function as a battery for charge storage in the first three steps. During the  $\text{S}_3 \rightarrow \text{S}_4$  step, all stored charges accumulate on Mn4 to form the appropriate  $\text{Mn}^{\text{VII}}$ -dioxo state, which subsequently triggers O–O bond formation and oxygen evolution. Hence, OEC is constructed as a  $\text{Mn}_3\text{CaO}_4$  cubane coupled with a dangling Mn4. In addition, OEC has an extremely open coordination sphere that is located in the water and proton channels and approaches the redox mediator  $\text{Y}_Z$ .

Therefore, we suggest that synthetic multinuclear Mn complexes could be promising candidates for efficient artificial WOCs. Different coordination environments should be considered in the ligand structure design for different types of Mn cores with specific roles, *i.e.*, multiple Mn cores for charge storage and Mn with open coordination sites for handling substrate water, proton release, and O–O bond formation. Furthermore, special attention should be paid to the ligands that are needed to stabilize the  $\text{Mn}^{\text{VII}}$  site.

Finally, on the basis of our new mechanistic proposal, we can answer the question in the title: why did nature choose the  $\text{Mn}_4\text{CaO}_5$  cluster as the catalyst for water oxidation in PSII?

- Mn is abundant in the Earth, has rich redox chemistry, and can bear four charges by varying its valencies between  $\text{Mn}^{\text{III}}$  and  $\text{Mn}^{\text{VII}}$ .

- Four Mn can coordinate and create the  $\text{Mn}^{\text{VII}}$ -dioxo site *via* charge disproportionation of four  $\text{Mn}^{\text{IV}}$ , which is unique, *i.e.*, distinguishable from other 3 Mn ions by being placed outside the cubane structure.

- Five  $\mu$ -oxo bridges are essential, with one (O5) available for O–O bond formation and the other four for balancing the positive charges. These bridges can also prevent the integral  $\text{Mn}_4\text{CaO}_5$  cluster structure from falling apart (maintaining cooperation among four Mn and one Ca).

- Ca is needed as a “taxi stand” for the essential substrate water molecules before they are transferred to the open site during the  $\text{S}_2 \rightarrow \text{S}_3$  step to regenerate a new O5 for the next catalytic cycle.

Therefore, as an economic and perfect “team-playing” catalyst, the  $\text{Mn}_4\text{CaO}_5$  cluster was chosen by nature for water oxidation in PSII three billion years ago. Since investigations and conclusions on the mechanism of oxygen evolution in PSII are still far from clear, we hope our new hypothesis opens new possibilities for uncovering the secrets of water oxidation in PSII.

## Conflicts of interest

The authors declare no competing interests.

## Acknowledgements

We acknowledge financial support of this work by the Swedish Research Council (2017-00935), Swedish Energy Agency, Knut



and Alice Wallenberg Foundation, and the National Basic Research Program of China (973 program, 2014CB239402). We thank Professor Christina Moberg at KTH for reviewing the manuscript and the valuable discussions.

## References

- 1 J. P. McEvoy and G. W. Brudvig, *Chem. Rev.*, 2006, **106**, 4455–4483.
- 2 S. A. Crowe, L. N. Dossing, N. J. Beukes, M. Bau, S. J. Kruger, R. Frei and D. E. Canfield, *Nature*, 2013, **501**, 535–538.
- 3 M. Suga, F. Akita, K. Hirata, G. Ueno, H. Murakami, Y. Nakajima, T. Shimizu, K. Yamashita, M. Yamamoto, H. Ago and J. R. Shen, *Nature*, 2015, **517**, 99–103.
- 4 Y. Umena, K. Kawakami, J. R. Shen and N. Kamiya, *Nature*, 2011, **473**, 55–60.
- 5 K. N. Ferreira, T. M. Iverson, K. Maghlaoui, J. Barber and S. Iwata, *Science*, 2004, **303**, 1831–1838.
- 6 A. Zouni, H.-T. Witt, J. Kern, P. Fromme, N. Krauß, W. Saenger and P. Orth, *Nature*, 2001, **409**, 739–743.
- 7 B. Loll, J. Kern, W. Saenger, A. Zouni and J. Biesiadka, *Nature*, 2005, **438**, 1040–1044.
- 8 B. Kok, B. Forbush and M. McGloin, *Photochem. Photobiol.*, 1970, **11**, 457–475.
- 9 V. Krewald, M. Retegan, N. Cox, J. Messinger, W. Lubitz, S. DeBeer, F. Neese and D. A. Pantazis, *Chem. Sci.*, 2015, **6**, 1676–1695.
- 10 D. A. Pantazis, W. Ames, N. Cox, W. Lubitz and F. Neese, *Angew. Chem., Int. Ed.*, 2012, **51**, 9935–9940.
- 11 T. Lohmiller, V. Krewald, A. Sedoud, A. W. Rutherford, F. Neese, W. Lubitz, D. A. Pantazis and N. Cox, *J. Am. Chem. Soc.*, 2017, **139**, 14412–14424.
- 12 J. Yano and V. Yachandra, *Chem. Rev.*, 2014, **114**, 4175–4205.
- 13 M. Perez-Navarro, F. Neese, W. Lubitz, D. A. Pantazis and N. Cox, *Curr. Opin. Chem. Biol.*, 2016, **31**, 113–119.
- 14 D. J. Vinyard, S. Khan and G. W. Brudvig, *Faraday Discuss.*, 2015, **185**, 37–50.
- 15 J. Barber, *Nat. Plants*, 2017, **3**, 17041.
- 16 P. E. M. Siegbahn, *Acc. Chem. Res.*, 2009, **42**, 1871–1880.
- 17 M. Suga, F. Akita, M. Sugahara, M. Kubo, Y. Nakajima, T. Nakane, K. Yamashita, Y. Umena, M. Nakabayashi, T. Yamane, T. Nakano, M. Suzuki, T. Masuda, S. Inoue, T. Kimura, T. Nomura, S. Yonekura, L.-J. Yu, T. Sakamoto, T. Motomura, J.-H. Chen, Y. Kato, T. Noguchi, K. Tono, Y. Joti, T. Kameshima, T. Hatsui, E. Nango, R. Tanaka, H. Naitow, Y. Matsuura, A. Yamashita, M. Yamamoto, O. Nureki, M. Yabashi, T. Ishikawa, S. Iwata and J.-R. Shen, *Nature*, 2017, **543**, 131–135.
- 18 P. E. M. Siegbahn, *Proc. Natl. Acad. Sci. U. S. A.*, 2017, **114**, 4966–4968.
- 19 M. Haumann, P. Liebisch, C. Müller, M. Barra, M. Grabolle and H. Dau, *Science*, 2005, **310**, 1019–1021.
- 20 H. Sakamoto, T. Shimizu, R. Nagao and T. Noguchi, *J. Am. Chem. Soc.*, 2017, **139**, 2022–2029.
- 21 H. Bao and R. L. Burnap, *Proc. Natl. Acad. Sci. U. S. A.*, 2015, **112**, E6139–E6147.
- 22 I. Zaharieva, H. Dau and M. Haumann, *Biochemistry*, 2016, **55**, 6996–7004.
- 23 M. Haumann, C. Müller, P. Liebisch, L. Iuzzolino, J. Dittmer, M. Grabolle, T. Neisius, W. Meyer-Klaucke and H. Dau, *Biochemistry*, 2005, **44**, 1894–1908.
- 24 F. A. Armstrong, *Philos. Trans. R. Soc., B*, 2008, **363**, 1263–1270.
- 25 R. J. Pace, R. Stranger and S. Petrie, *Dalton Trans.*, 2012, **41**, 7179–7189.
- 26 M. Capone, D. Narzi, D. Bovi and L. Guidoni, *J. Phys. Chem. Lett.*, 2016, **7**, 592–596.
- 27 M. R. Razeghifard and R. J. Pace, *Biochemistry*, 1999, **38**, 1252–1257.
- 28 G. Renger, *Biochim. Biophys. Acta*, 2001, **1503**, 210–228.
- 29 V. Y. Shafirovich, N. K. Khannanov and A. E. Shilov, *J. Inorg. Biochem.*, 1981, **15**, 113–129.
- 30 V. Y. Shafirovich, *Kinet. Katal.*, 1978, **19**, 1502–1507.
- 31 T. S. Dzhabiev, *Kinet. Katal.*, 1989, **30**, 1219–1224.
- 32 J. Limburg, J. S. Vrettos, L. M. Liable-Sands, A. L. Rheingold, R. H. Crabtree and G. W. Brudvig, *Science*, 1999, **283**, 1524–1527.
- 33 R. Ramaraj, A. Kira and M. Kaneko, *Chem. Lett.*, 1987, **16**, 261–264.
- 34 J. Limburg, G. W. Brudvig and R. H. Crabtree, *J. Am. Chem. Soc.*, 1997, **119**, 2761–2762.
- 35 M. Yagi and K. Narita, *J. Am. Chem. Soc.*, 2004, **126**, 8084–8085.
- 36 M. M. Najafpour, G. Renger, M. Holynska, A. N. Moghaddam, E. M. Aro, R. Carpentier, H. Nishihara, J. J. Eaton-Rye, J. R. Shen and S. I. Allakhverdiev, *Chem. Rev.*, 2016, **116**, 2886–2936.
- 37 M. Grabolle and H. Dau, *Biochim. Biophys. Acta*, 2005, **1708**, 209–218.
- 38 A. Skrabal, *Anorg. Allg. Chem.*, 1910, **68**, 48–51.
- 39 B. Krebs and K.-D. Hasse, *Angew. Chem., Int. Ed. Engl.*, 1974, **13**, 603.
- 40 S. M. Yiu, W. L. Man, X. Wang, W. W. Lam, S. M. Ng, H. K. Kwong, K. C. Lau and T. C. Lau, *Chem. Commun.*, 2011, **47**, 4159–4161.
- 41 D. G. Lee, C. R. Moylan, T. Hayashi and J. I. Braurnan, *J. Am. Chem. Soc.*, 1987, **109**, 3003–3010.
- 42 L. Ma, Q. Wang, W. L. Man, H. K. Kwong, C. C. Ko and T. C. Lau, *Angew. Chem., Int. Ed.*, 2015, **54**, 5246–5249.
- 43 S. Vaddypally, S. K. Kondaveeti, S. Karki, M. M. Van Vliet, R. J. Levis and M. J. Zdilla, *J. Am. Chem. Soc.*, 2017, **139**, 4675–4681.
- 44 B. Zhang, Q. Daniel, L. Fan, T. Liu, Q. Meng and L. Sun, *iScience*, 2018, **4**, 144–152.
- 45 B. Zhang, H. Chen, Q. Daniel, B. Philippe, F. Yu, M. Valvo, Y. Li, R. B. Ambre, P. Zhang, F. Li, H. Rensmo and L. Sun, *ACS Catal.*, 2017, **7**, 6311–6322.
- 46 J. R. Shen, *Annu. Rev. Plant Biol.*, 2015, **66**, 23–48.
- 47 H. Isobe, M. Shoji, J. R. Shen and K. Yamaguchi, *Inorg. Chem.*, 2016, **55**, 502–511.
- 48 K. Kawashima, T. Takaoka, H. Kimura, K. Saito and H. Ishikita, *Nat. Commun.*, 2018, **9**, 1247.

