[FeFe]hydrogenase mimics for proton reduction catalysis: Supramolecular proton reduction catalysts with appended redox-active and proton-responsive ligands towards application in a molecular artificial leaf

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Introduction
The Transition from a Fossil Fuel Economy to a Hydrogen Economy

Early human life developed alongside a system of production and consumption of food. Our earliest ancestors were hunter-gatherers, and as long as populations remained small, the natural abundance of animals and plants was sufficient to give human life the necessary boost to develop society. However, when populations grew and societies organized themselves in settlements, the natural food supplies became limiting and people had to invent agriculture – the large-scale production of food. Producing food by means of natural photosynthesis using a combination of water, carbon dioxide and solar energy, and releasing the energy in the body through the Krebs cycle whilst releasing carbon dioxide, we created the first sustainable, circular (closed-cycle) economy. However, to build a society based on farming, humankind first harvested the available food from nature, then used it – instinctively – to invest it in building a sustainable society.

Roughly 10,000 years later, our society faces a similar challenge, but this time with fuel instead of food. The natural abundance of fossil fuels gave us the possibility to industrialize the world in a very short time, which brought the world great overall prosperity. These fossil fuel reserves have – for the largest part – been used as a technological investment into global society as such. Now that the industrial revolution is ending and the world has changed in a profound way, it becomes evident that depleting the remaining fossil fuels has a huge detrimental impact on the global environmental, societal and economic structures. Luckily, most people nowadays realize that we have to make the transition back to a sustainable, circu-
lar economy. This paradigm shift has now brought about the discussion what this sustainable economy should look like.

Just as the agricultural revolution, the industrial revolution will eventually lead to the development of a global system of fuel ‘farming’ to replace fuel ‘gathering’. A practical and likely candidate for a long-term sustainable, circular economy is based on sunlight due to its abundance and its availability anywhere on the planet. Through photovoltaics we can convert sunlight into electricity and use it to power industry, transportation and home appliances. However, the intermittency of sunlight necessitates the transport and storage of electricity. Transporting electricity over large distances leads to energy losses, but storage in (redox flow) battery-type devices has recently started to show great potential. For mobile applications (cell phones, cars, aeroplanes, etc.) it is at present difficult to predict what viable energy carriers would look like, and current research is equally strongly devoted to developing batteries as it is to storing electricity in chemical bonds (creating gaseous or liquid fuels).

A straightforward way to store electricity in chemical bonds is by electrolysis of water. In this process two water molecules are converted to one molecule of oxygen. The remaining four protons and four electrons (which contain the converted electrical energy) can then be used to create a fuel. The most straightforward fuel is hydrogen gas (H₂), produced by combining two electrons and two protons, but these protons and electrons can also be used to convert an existing low-energy molecule (e.g. carbon dioxide; CO₂) to a higher-energy molecule such as methanol (CH₃OH) or methane (CH₄). These different forms of fuel all have their pros and cons. For example, hydrogen can be made without the use of carbon dioxide, avoiding the need for CO₂ capture from the air. On the other hand, methanol is a liquid at room temperature, which is easy to handle but also quite toxic, and for methane the existing natural gas infrastructure can be used after some adaptation, but its production from CO₂ and protons/electrons is challenging.

An excellent review of reviews by McDowall and Eames summarizes the main

![Figure 2. A schematic depiction of the circular reaction scheme in the hydrogen economy.](image-url)
(short term) drivers towards a hydrogen economy and barriers that slow down its implementation in our current society. The drivers are more or less self-explanatory, with climate change and air quality being serious threats to our health and the environment. The availability of solar energy all over the planet leads to a situation where energy is inherently decoupled from (geo)politics and where everyone with the ability to finance infrastructure can be a competitor on the global energy market. The drivers can therefore be summarized as factors increasing health and independence. The barriers are mainly of financial and technological origin. In developed countries, niche applications tend to stimulate the hydrogen market development. Fuel cell vehicles are one of these niche applications that have come to life in the past decade, speeding up the deployment of hydrogen fuel stations and their infrastructure.

However, past investments in existing fossil fuel-based infrastructure are at this moment largely suppressing the development of non-fossil fuel-based technologies in developed countries. For this reason, it is expected that the hydrogen economy will first be operational in developing countries, where little infrastructure yet exists but the demand for energy is steadily increasing. Decentralized hydrogen production in these parts of the world largely avoids the need of expensive infrastructure. However, the more widespread and decentralized hydrogen production becomes, the higher the need for new infrastructure will become. Many studies have been published on hydrogen infrastructure focussing on hydrogen production, compression, transportation and fuelling stations. An interesting example of a new-era power grid is the idea of a hydrogen-filled SuperGrid, where electricity and
hydrogen are simultaneously transported, with liquid hydrogen cooling to make the grid superconducting.\textsuperscript{12}

Apart from infrastructural issues, the high costs of hydrogen production and fuel cells is a challenging issue to be solved. In a rather simplistic view, hydrogen production devices and fuel cells can be regarded as the same thing, as they do the same job, albeit in opposite directions. A hydrogen production device requires energy to split water into oxygen and hydrogen, whereas a fuel cell combines hydrogen and oxygen (or air) into water, thereby releasing electrical energy. For a large part, the high cost of these devices is due to the use of expensive catalysts – the materials that actively interconvert protons and electrons with hydrogen. The most widely used catalyst nowadays is platinum, which is both scarce and expensive. A lot of effort is put in the development of novel catalysts to replace platinum with a cheaper, more abundant material.

The artificial leaf

The production of hydrogen through splitting of water requires energy, which can be either thermal (thermolysis), electrical (electrolysis) or electromagnetic (photolysis) in nature. Common commercial hydrogen production devices are high-temperature, alkaline or proton-exchange membrane (PEM) electrolysers, often based on platinum (proton reduction) and iridium (water oxidation) as active catalysts.\textsuperscript{13,14} When operated in a sustainable fashion, these electrolysers can be powered by photovoltaics to obtain an overall device that can produce hydrogen from water and sunlight. In this method, light is first converted to electricity, which is then converted to fuel. However, these two steps can also be combined into one, avoiding the use of electricity. This direct conversion of water and light into hydrogen is strikingly similar to natural photosynthesis. For this reason, devices that try to accomplish this task are commonly dubbed \textit{artificial leaves}.\textsuperscript{15}

In photosynthetic organisms, the thylakoid membrane contains all the building blocks to capture sunlight and spatially separate charges into electron-hole pairs.
that are subsequently used to oxidize water on one side and generate energy carriers (‘fuel’) such as NADPH on the other side. Charge separation occurs over a redox gradient, which is organized in a so-called ‘Z-scheme’.\textsuperscript{16,17} Starting from the left side of the scheme, the oxygen evolving complex (OEC) oxidizes water to release oxygen, protons and electrons. On excitation with red light, the antenna system of photosystem II (PSII) accepts an electron from the OEC while donating an electron to plastoquinone (QH\textsubscript{2}). This electron then travels down the redox gradient, into cytochrome \textit{bf} (Cyt \textit{bf}) via [2Fe-2S] clusters and haem, into a copper-containing plastocyanine (Pc) and down into the second photosystem (PSI). After excitation with light, the antenna system of PSI can then donate its high-energy electron into a [4Fe-4S] ferredoxin (Fd) electron acceptor. These electrons are used to generate NADPH, which can be seen as the cell’s dihydrogen (H\textsubscript{2}) equivalent. The redox levels in the Z-scheme are all properly matched to ultimately deliver electron-hole pairs that have the right redox levels to split water (+0.81 V and –0.42 V vs. SHE at pH 7). These redox levels are perfectly balanced to obtain reduced and oxidized states that have the proper lifetime for the desired reaction to occur, as well as the right driving force to ensure proper kinetics.

Photosynthetic organisms have to continuously adapt to changing conditions, repair themselves when damaged and are limited in design by the synthetic toolbox supplied by nature, leading to a meager 1%-3% overall light conversion efficiency.\textsuperscript{18} In contrast, an artificial leaf can be designed to operate under a limited set of con-

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Figure 5. Simplified depiction of the Z-scheme in photosynthesis. Redox levels (vs. SHE) are approximate and rounded to 0.1 V. Only the redox-active parts of the structures are shown. P680/P700, Phe a and haem all follow the same general (porphyrinic) structure, but containing different metals (M = Mg, H\textsubscript{2} and Fe, respectively).
Introduction

ditions, while the versatility of synthetic chemistry can be fully exploited to find suitable materials unknown to nature. However, the basic design principles remain the same: the redox levels in an artificial leaf should be sufficient to drive water splitting, and the kinetics of the system should be matched to the solar flux under which the device operates.

The building blocks needed to create an artificial leaf can be divided into three parts: (a) the chromophoric part (‘photosensitizer’ or PS) that captures light, (b) two catalysts for water oxidation (WOC) and proton reduction (PRC), respectively, and (c) an electron transfer chain (ETC) connecting the catalysts and photosensitizers. These systems are often studied as half-reactions, where water oxidation and proton reduction are studied separately. The rationale is that these half-reactions can in principle be seen as black boxes, that can be connected together provided the potentials and currents are matched. Most reported systems can be classified as either a triad (both PRC and WOC are coupled to the same PS) or dyad/dyad (two PS-catalyst dyads are connected together). The advantage of using multiple chromophoric systems is that a larger part of the solar spectrum can be captured. However, this comes at the cost of using multiple photons per electron, so an increase in overall efficiency is only expected in well-matched systems, such as the light-harvesting

Figure 6. Simplified redox level diagram of molecular triad and dyad/dyad systems, and their respective use of the solar spectrum.
complexes in photosystem I and II. Within these natural systems, additional chromophores are assembled around the main chromophore, and their excited states are harvested by the central chromophores through resonant energy transfer.\textsuperscript{19}

**Inorganic artificial leaves**

In 1912, the Italian chemist Giacomo Giamician published an article in Science entitled “The photochemistry of the future”, elaborating on using solar energy to surpass the use of fossil fuels.\textsuperscript{20} Little did he know, that only 60 years later a proof of concept for his ideas would be realized. In 1972, Fujishima and Honda published the first stand-alone device that could split water into its constituents by irradiation of a titania (TiO\textsubscript{2}) photoanode using visible light ($h\nu < 415$ nm).\textsuperscript{21} This device used a single light-absorbing entity, analogous to the triad model discussed before. A quarter century later, Khaselev and Turner reported on an integrated, monolithic photoelectrochemical cell for water splitting with a dual light absorber analogous to the dyad/dyad model, reaching a hydrogen production efficiency of 12.4\% using white light irradiation.\textsuperscript{22} The core of this artificial leaf consisted of a gallium-arsenide (GaAs) photovoltaic cell coupled to a platinum anode for water oxidation on one side and a p-doped gallium-indium-phosphide (GaInP\textsubscript{2}) photocathode for photocatalytic proton reduction. In 2011, Nocera \textit{et al.} reported the first artificial leaf based on earth-abundant metals using triple-junction amorphous silicon photovoltaics, a cobalt-based water oxidation catalyst and a nickel-molybdenum-zinc proton reduction catalyst, reaching a maximum efficiency of 4.7\%.\textsuperscript{23} This design concept

**Figure 7. Selected examples of inorganic artificial leaves.**
was further extended to the use of a new generation of photoanodes such as bismuth vanadate (BiVO$_4$) and photovoltaic materials such as organic semiconductors and lead perovskite (CH$_3$NH$_3$PbI$_3$), leading to a current record solar-to-fuel efficiency of 12.3%.

Biohybrid artificial leaves

Artificial leaves (or parts thereof) can be completely synthetic in nature, but can also partly contain structures isolated from nature. Some of these hybrid systems use parts of the thylakoid membrane, whereas others use parts of non-photosynthetic organisms. A variety of reported biohybrid proton reduction dyads use isolated photosystem I coupled to synthetic proton reduction catalysts based on nickel, cobalt or platinum, or even coupled to isolated iron-iron hydrogenase ([FeFe]H$_2$ase) – a naturally occurring enzyme that reversibly reduces protons to hydrogen with rates similar to platinum, the best synthetic catalyst known to date. In another type of hybrid dyad, this [FeFe]H$_2$ase enzyme has been coupled to (inorganic) semiconducting photocathodes such as cadmium sulfide and cadmium telluride quantum dots, exemplifying the wide variety of systems into which biomolecules have been integrated.

On the water oxidation side, the complete PSII system has been isolated and immobilized on gold, nanostructured titania (TiO$_2$) and mesoporous indium-doped tin oxide (ITO) electrodes to create fully functional biohybrid water oxidation photoanodes. Although some of these systems show remarkable efficiencies and stabilities, the use of biomolecules in artificial leaves is still hampered by troublesome isolation and purification methods. To avoid these issues, researchers often try to make synthetic mimics of the active site of photosystems and enzymes. These mimics ideally behave identical to the natural system, with the ease of synthetic accessibility.

Molecular artificial leaves

Over the past years, numerous reviews have been published that focused on the development of synthetic, molecular artificial leaves and their sub-systems. A recent review by Sun and co-workers outlines the progress made in molecular photocatalytic water splitting, where dyes are often anchored to electron (TiO$_2$) or hole (NiO$_2$) accepting semiconductors, with catalysts anchored to the respective dyes.
On the water oxidation side, most photosensitizers are ruthenium-based because of their high oxidation potential and long-living exited states, making them (in effect) photo-generated chemical oxidants. Water oxidation catalysts are often based on ruthenium or iridium. On the proton reduction side, a variety of (in)organic photosensitizers have been shown to work, either in combination with a cobaloxime PRC or as a photocatalyst by itself.

As these molecular systems are generally soluble in either an organic solvent, water or a mixture thereof, they are often first studied as a multi-component system in solution, using a sacrificial reductant or oxidant to mimic the respective electrode. In a next step, the multiple components are connected together and immobilized on an electrode or, alternatively, the components are co-immobilized on an electrode. For these reasons, most reviews on molecular water splitting generally focus on either electrocatalysis or photocatalytic systems for proton reduction or water oxidation. The general rationale is that electrocatalysts can in most cases also be used as photocatalysts when coupled to a suitable photosensitizer – catalysis can then in principle occur in a similar fashion, with electrons being supplied by the photosensitizer instead of an electrode. Likewise, photocatalytic systems that work in solution using a sacrificial reductant or oxidant, can in principle be immobilized on an electrode to obtain a similarly behaving system. It should be stressed here that while this is the case in principle, in practice the immobilization of catalysts or photocatalytic assemblies onto electrodes turns out to be much less straightforward than it is on paper. One of the complicating factors lies in the inherent different nature of the electron accepting/donating moieties: sacrificial reductants and oxidants generally display quite rich (follow-up) chemistry, whereas electrodes are merely a

![Diagram of photocatalytic proton reduction half-reaction](image)

**Figure 8.** Schematic depiction of a photocatalytic proton reduction half-reaction. Studied as (left) multicomponent in solution, (middle) co-immobilized on an electrode and (right) immobilization of a dyad system on an electrode.
Introduction

— 11 —

‘pool of electrons’ at a certain potential.

**Molecular catalysts for water splitting – electrocatalysis**

A recent review on molecular water oxidation catalysts (WOCs) nicely illustrates the often-found diagonal relationship in the periodic table of elements, with the best performing WOCs containing manganese, ruthenium or iridium (and, to a lesser extent, iron and cobalt). However, despite its scarcity and price, ruthenium is the element that is still most often used in WOCs. Electro catalysts for proton reduction (PRCs) are most often based on cobalt, nickel or iron, with polypyridyl ligands recently gaining a lot of attention. These molecular catalysts are most often studied electrochemically, whereby electrons are removed from or added to the catalyst from an electrode. The formed oxidized or reduced catalysts can then activate the desired substrate (water or protons) and undergo sequential redox or chemical processes. By carefully choosing the operating conditions, it is possible to extract kinetic and thermodynamic data from the obtained current responses, as well as stability constants. This data is most often provided in the form of a turnover number (TON), a turnover frequency (TOF) and an overpotential (η), which can be used for the recently published rational benchmarking approaches for molecular electrocatalysts.
Before photosensitizers and catalysts are used for the construction of an artificial leaf, they are most often studied in homogeneous solution with a molecular sacrificial reductant/oxidant instead of an electrode. These three-component systems are then irradiated with a suitable light source and the cell’s head space is sampled over time to monitor evolved hydrogen or oxygen gas. From these data, typical figures of merit are again TON and TOF, with additional factors such as the photon-to-fuel conversion efficiency. However, as molecular catalysts and photosensitizers for water oxidation are still relatively under-developed, current literature and reviews thereof generally focus more on proton reduction. Recent reviews on photocatalytic proton reduction focus on the use of porphyrins, rhenium-based photosensitizers, photoactive semiconductors or molecular dye-sensitized structures – all in conjunction with or coupled to suitable proton reduction catalysts. Additionally, as the field matured, enough data became available to study the linker between photosensitizers and catalysts, which can be altered to affect the rate as well as the directionality of electron transfer.

Figure 10. Proton reduction and water oxidation catalysts.
Commonly used PRCs based on nickel, cobalt and iron and WOCs based on ruthenium (isoq = isoquinoline), iridium and manganese.


Synthetic mimics

Reverting from artificial, molecular systems back to the natural photosynthetic system, we can easily see that all the components to construct a well-functioning artificial leaf are already present in nature. Looking at the simplified photosynthetic scheme from Figure 5, we could modify the right part of the scheme by taking out the part that produces NADPH (ferredoxin-NADP$^+$ reductase) and introduce a part that uses the same electrons and protons to produce hydrogen: the hydrogenase (H$_2$ase) enzyme. Golbeck et al. coupled photosystem I to the [FeFe]H$_2$ase enzyme using a dithiol linker to obtain a system that outperforms natural photosynthesis by a factor two in terms of electron transfer rates.$^{34,63}$ The beauty of this system is exemplified by the fact that the electron transport chains of both PS I and [FeFe]H$_2$ase are constructed of [4Fe-4S] clusters and are thus fully compatible.

However, for large-scale deployment of artificial leaves the use of isolated biomolecules is hampered by elaborate (costly) isolation and purification steps. For this reason, a lot of research is devoted to mimicking nature by attempting to synthesize mimics of the active sites present in photosynthetic reaction centers and enzymes. These compounds are generally classified as being either structural or functional mimics of the natural system, where the first is as close as possible to the original structure and the latter a mimic of the functionality the natural system displays. In most practical cases, reported mimics are a mix of both structural and functional mimicry.

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Figure 11. Schematic depiction of PS 1 and [FeFe]H$_2$ase immobilized on an electrode. The electron transport chain (ETC) of PS 1 and [FeFe]H$_2$ase is depicted in pink. The active sites of the enzymes consist of chlorophyll pigments and an [2Fe-2S] cluster, respectively.
Mimicking the [FeFe]H\textsubscript{2}ase enzyme

The all-iron hydrogenase enzyme is the most efficient proton reduction catalyst found in nature, with catalytic turnover rates comparable to platinum at around 10,000 s\textsuperscript{-1} with minimal overpotential.\textsuperscript{64} The active site of the enzyme consists of a [2Fe-2S] cluster bound to three carbonyl and two cyanide ligands, which are in turn hydrogen bonded to the apoenzyme. The two sulfur atoms are connected by a three-atom long fragment whose chemical composition was until recently debated,\textsuperscript{65} but has now been established to be a nitrogen atom in-between two carbon atoms.\textsuperscript{66} A cysteine residue connects the [2Fe-2S] cluster through its sulfur atom to a [4Fe-4S] cluster which is part of the electron transport chain, accepting electrons and donating them into the active site. This assembly of [2Fe-2S] and [4Fe-4S] clusters is commonly referred to as the H-cluster.

In recent years, attention has been drawn to two functionalities of the H-cluster. The nitrogen atom in the active sites bridgehead is a Brønsted base and pre-organizes protons close to the active site, a functionality commonly called ‘proton relay’. The [4Fe-4S] cluster functions as an electron reservoir, accepting electrons from the electron transport chain and donating them into the active site during catalysis.\textsuperscript{69} Within the catalytic cycle for proton reduction (neglecting CO-inhibited

Figure 12. Selected [FeFe]H\textsubscript{2}ase mimics.
The H-cluster framework of the [FeFe]H\textsubscript{2}ase (top left), a structural mimic reported by Tard and Pickett (bottom left)\textsuperscript{67} and a functional mimic reported by Rauchfuss (right).\textsuperscript{68}
states), the H-cluster in its $H_{\text{ox}}$ state accepts an electron and a proton to form the $H_{\text{red}}$ state. This added electron is first located on the [4Fe-4S] subsite, followed by electron transfer to the distal iron atom of the [2Fe-2S] subsite\textsuperscript{70} – the added proton is located on the bridgehead amine. One-electron reduction of the $H_{\text{red}}$ state to the super-reduced $H_{\text{sred}}$ state leads to the reduction of the [4Fe-4S] co-factor. Interestingly, on protonation of this $H_{\text{sred}}$ state, this electron on the electron reservoir is shuttled to the distal iron atom. After loss of hydrogen, the $H_{\text{ox}}$ state is reformed. It can thus be seen that both electrons needed in the reaction are supplied by the electron transport chain, mediated by [4Fe-4S] clusters. Moreover, it seems that the low overpotential of proton reduction by [FeFe]H$_2$ase requires proton-coupled electron transfer steps,\textsuperscript{71} whereby electrons and protons are transported together to the active site, which is energetically more favorable than stepwise transfer of protons and electrons.\textsuperscript{72}

The desired properties of [FeFe]H$_2$ase mimics (or PRCs in general) resemble those of the enzyme, in that the catalyst should catalyze the reduction of protons:

- With high efficiency:
  - High enough turnover rate ($\text{TOF}$) to keep up with the supply of photons from the sun: $10^2$-$10^3$ s$^{-1}$ is generally deemed sufficiently fast.
  - At a potential close to the thermodynamic potential of proton reduction (0.41 V vs. NHE at pH 7), or (alternatively stated) at minimal overpotential ($\eta$).
- With decent turnover numbers ($\text{TON}$):
  - Tolerance to the presence of oxygen (this is not the case for [FeFe]H$_2$ase enzymes).
  - No intrinsic deactivation pathways.
  - Operate in water at (close to) neutral pH.

A lot of research has been devoted to elucidating the structure-function relation-
ship of the various hydrogenase enzymes, leading to a plethora of structural and functional mimics of the enzyme’s active site. When research interest into these mimics sprouted in 1999, the exact configuration of the bridgehead (connecting the dithiolate fragment) had not yet been elucidated, but was thought to contain only carbon. For this reason, the groups of Darensbourg, Pickett and Rauchfuss started on mimics containing propanedithiolato (μ-pdt) bridges. Fortunately, the chemistry to access these structures was already established in 1982, when the iron carbonyl precursor Fe₃(CO)₁₂ was reacted with a small library of α,ω-dithiols to give the respective hexacarbonyl clusters (μ-dithiolato)Fe₂(CO)₆. This led to the first family of synthetic pdt-functionalized [2Fe-2S] clusters as biomimetic catalysts for H₂ production and to the first structural mimic of the complete H-cluster framework. The next generation of mimics operated along different paths, with the group of Rauchfuss mainly focusing on structural mimics containing the azadithiolato (μ-adt) bridge, and other groups focusing on mimics containing aromatic bridges such as the benzenedithiolato (μ-bdt) bridge. In 2011, the group of Rauchfuss published a [FeFe]H₂ase mimic containing both an electron relay and a proton relay that are both operative under catalytic conditions. Since the presence of proton relays and electron reservoirs could in principle benefit any proton reduction catalyst, mimicking hydrogenases has found its way outside the realm of iron-sulfur clusters into various catalytic systems incorporating proton relays and electron relays. However, the ideal molecular proton reduction catalyst has still not been reported, as in most cases the catalysts either operate at high overpotential or low rate, they are only active in organic solvents or are oxygen sensitive.

The three main families of H₂ase mimics discussed before (with bridge moieties denoted as pdt, adt and bdt) all consist of a similar [2Fe-2S] core, but differ in the dithiolate bridge. The parent compounds contain six carbonyl ligands and are thus dubbed ‘hexacarboxyls’. In absence of acid, the hexacarboxyl complexes follow quite different redox chemistry, depending on the nature of the bridge (Figure 15).
In the hexacarbonyl complex with the fully aliphatic carbon (pdt) bridge, the first one-electron reduction process occurs at −1.62 V with no major structural changes in the mono-anion compared to the neutral complex. This mono-anion is susceptible to a wide variety of rearrangements and dimerizations, and although the reduction of the mono-anion to the di-anion can be probed (it occurs around −1.81 V), the rich follow-up chemistry after reduction generally limits the use of this H$_2$ase mimic. On replacing the central bridge carbon in pdt mimics with a nitrogen atom, the first reduction potential and follow-up chemistry do not change appreciably. However, the presence of the nitrogen atom changes the overall reduction chemistry, since the second reduction potential is at roughly the same potential as the first (Figure 15), and the mono-anion is kinetically protected against detrimental follow-up chemistry. After overall two-electron reduction, the [2Fe-2S] butterfly structure in (μ-adt)Fe$_2$(CO)$_6$ opens up in favor of a bridging carbonyl ligand, which has been postulated as being of great importance in the formation of terminal hydrides, stabilized by the nitrogen bridgehead atom. The benzenedithiolato hexacarbonyl complex (μ-bdt)Fe$_2$(CO)$_6$ follows similar chemistry as the adt mimic, but with the second reduction at even more positive potentials. This behavior has been attributed to the aromatic character of the bridge, and similar potential in-

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**Figure 15.** Redox processes in hexacarbonyl complexes.
Reduction potentials (in CH$_3$CN vs. Fc/Fc$^+$) and molecular structures of the anions (simplified) of pdt, adt and bdt hexacarbonyl complexes in absence of acid. (R = -CH$_2$CH$_2$OCH$_3$).
versions have been observed in various mimics containing aromatic bridges.\textsuperscript{87}

In presence of weak to moderately strong acids – a desired condition for application in an artificial leaf – all aforementioned complexes have to be activated by reduction before entering a catalytic cycle. The mono-anion of the (μ-pdt)Fe$_2$(CO)$_6$ complex is basic enough to react with $p$-toluenesulfonic acid ($pK_a$ 8.6 in CH$_3$CN), leading to an overall (E)CECE\textsuperscript{1} catalytic mechanism at potentials close to the first reduction potential.\textsuperscript{88} For the (μ-adt)Fe$_2$(CO)$_6$ mimic, weak acid catalysis occurs via two competing mechanisms (ECEC and ECCE for ClCH$_2$COOH in CH$_3$CN, $pK_a$ 15.3) at similarly mild potentials.\textsuperscript{89} When employing an acid that is strong enough to protonate the bridgehead amine (e.g. $p$-toluenesulfonic acid), catalysis occurs via a CECE mechanism, but at potentials milder than the reduction potential in absence of acid. Weak acid catalysis using (μ-bdt)Fe$_2$(CO)$_6$ leads to an (E)ECEC mechanism (acetic acid in CH$_3$CN),\textsuperscript{51} whereas employing a stronger acid (HOTs in CH$_3$CN) allows direct protonation of the hydride species – eliminating one electron transfer in the catalytic cycle – leading to an EECC mechanism. An important observation is that whereas the mono-anions of the pdt and adt mimics are basic enough to be protonated by weak acid, the mono-anion of the bdt mimic does not get protonated, due to a structural transformation after reduction.\textsuperscript{51} It should be noted here that a bridging carbonyl in the mono-reduced state has recently been experimentally disproven in favor of a mono-anion with a ruptured Fe-S bond, but with all CO fragments in a terminal binding mode.\textsuperscript{90} Following the rational benchmarking approach, a log$TOF$-overpotential (‘Tafel’) plot can be constructed for all three catalysts using a range of dif-

The terminology for electrocatalytic mechanisms generally follows the form (A) XXXX, with X=E for electron transfer and X=C for proton transfer. The activation step A follows (E)XXXX for weak acids through activation by electron transfer. In strong acid-catalysis, pre-protonation can lead to (C)XXXX (unimolecular) or (C)XX (bimolecular) mechanisms.
ferent acids (Figure 16).\textsuperscript{47,48,89} From this plot it can be seen that within the hexacarbonyl complexes, the azadithiolate complex is the better catalyst, especially when weak acids are employed.

The Brønsted basicity of the (reduced) hexacarbonyl complexes can be increased by substituting one or more carbonyl ligands (good \(\pi\)-acceptors) for e.g. phosphine ligands (good \(\sigma\)-donors).\textsuperscript{86,91} However, care must be taken, since substitution of CO for \(\text{PPh}_3\) generally shifts the reduction potential negatively by around 0.2 to 0.3 V.\textsuperscript{92} If the potential increase is more than 59 mV per pK\textsubscript{a} increase (at standard conditions) of the reduced species, the overall effect can be detrimental, even though reactivity seems to increase. This effect has been observed for the reduction of HOTs in CH\textsubscript{3}CN by (\(\mu\)-bdt)Fe\textsubscript{2}(CO)\textsubscript{6} and the trimethylphosphite substituted complex (\(\mu\)-bdt)Fe\textsubscript{2}(CO)\textsubscript{5}(P(OMe)\textsubscript{3}) where under the applied conditions the substituted complex attains a higher turnover rate, although careful analysis shows that the hexacarbonyl complex is in fact the better catalyst of the two.\textsuperscript{93} It therefore seems that tuning of the electronics of a proton reduction catalyst is in general only beneficial for catalysis if it opens up novel reactivity (protonation pathways, internal transformations).

**Mimicking photosystem I**

The crystal structure of photosystem I shows that its core antenna system is comprised of around 100 chlorophyll a and 15 \(\beta\)-carotene units.\textsuperscript{94} These highly conjugated pigments harvest incoming light and funnel the energy down into the core of the photosystem: the chlorophyll dimer PsaA/PsaB. The resulting excited states are then efficiently transformed into spatially separated electron-hole pairs by transfer-
ring the electrons to quinone moieties and even further-lying [4Fe-4S] electron acceptors. Photosystem mimics are often constructed of molecules closely resembling the structure of chlorophyll, such as porphyrins, which are relatively readily accessible, with functionalization possible at various positions and metalation achieved with a variety of metals.55,95

One way to use porphyrins in artificial leaves is to sensitize porphyrins that are attached to semiconductor nanoparticles, which in turn can be used for electron transfer to a suitable PRC.56 This strategy can be extended to antenna-like systems which can be built up on electrode surfaces, avoiding the need for nanostructured electrodes. This strategy has been applied by the group of Dinolfo using a layer-by-layer (LbL) approach based on copper-catalyzed azide-alkyne cycloaddition (CuAAC ‘click’ chemistry).96

Recently, the use of metal-organic frameworks (MOFs) has entered the field of artificial leaves.97 The advantage of these materials is that they are relatively easy to make, provide a heterogeneous yet porous structure to support catalysts and can be grown or deposited on electrodes. The incorporation of porphyrins into MOFs that are stable under acidic conditions has also been established.98 Growing of porphyrin MOFs onto electrodes can be done either under solvothermal conditions99,100 or by employing a layer-by-layer method.101,102 After solvothermal synthesis, MOFs can be deposited onto electrodes by electrophoresis.103 Most of these methods yield MOF thin films with redox centers that are electrochemically addressable, a necessary feature for solar harvesting applications.
Thesis scope and outline

This thesis is the result of a research project within the BioSolar Cells consortium of the Netherlands, which aims at creating novel approaches for solar-to-fuel conversion. This research project entailed the development of novel supramolecular proton reduction catalysts, which could be anchored to electrodes or to photosensitizers, allowing for modular system building and rapid screening.

Chapter 2 discusses in detail the electrochemical methods and data analysis techniques used throughout the thesis. The chapter starts with an introduction into electrochemistry and cyclic voltammetry, and shows how the shape of a cyclic voltammogram can be easily explained by the Nernst equilibrium and diffusive mass transfer. It then shows how electron transfer processes can be elucidated, in absence and presence of a reaction substrate. The last part of the chapter is devoted to the determination of catalytic efficiencies, both for ideally behaving systems and systems displaying interfering side-effects. Various ways of forcing a system into a kinetic region apt for analysis are discussed. The chapter is by no means exhaustive, but aims to outline the general principles and techniques that can be employed for a variety of cases typically encountered when studying electrocatalysts by cyclic voltammetry.

Chapter 3 studies a phosphoramidite modified [FeFe]H\textsubscript{2}ase mimic as a model for photodriven production of H\textsubscript{2}. On cathodic activation, the pyridyl-phosphoramidite complex exhibits a strongly enhanced rate of proton reduction over the previously reported pyridylphosphine model at the same overpotential. Analysis of the cyclic voltammograms shows an apparent H\textsubscript{2} evolution rate strongly influenced by the presence of both side-bound pyridyl and phosphorus-bound dimethylamino moieties at the phosphoramidite ligands. This difference is ascribed to the basic amines acting as proton relays.

Chapter 4 reports on a synthetic H\textsubscript{2}ase mimic that contains a redox-active phosphole ligand as an electron reservoir, a feature also crucial for the operation of the natural enzyme. Using a combination of (spectro)electrochemistry and time-resolved infrared spectroscopy we elucidate the unique redox behaviour of the catalyst. We find that the electron reservoir actively partakes in the reduction of protons and that its electron-rich redox states are stabilized through ligand protonation. In dilute sulfuric acid, the catalyst has a turnover frequency of 7.0×10\textsuperscript{4} s\textsuperscript{-1} at an overpotential of 0.66 V. This catalyst is tolerant to the presence of oxygen, thereby paving the way for a new generation of synthetic H\textsubscript{2}ase mimics that combine the benefits
of the enzyme with synthetic versatility and improved stability.

Chapter 5 describes in more detail the effect of redox-non-innocent phosphole ligands on the redox properties and proton reactivity of [FeFe]H₂ase mimics equipped with such a moiety. We show that after reduction, the structural integrity of the phosphole complexes is retained through electron delocalization onto the phosphole backbone, opening up weak-acid protonation pathways that are inaccessible in the reference phosphine and all-carbonyl complexes.

Chapter 6 summarizes our efforts in designing functional porphyrinic materials for the construction of a photocathode for use in an artificial leaf.
References

Chapter 1


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Introduction


