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REVIEW

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# Application of gas diffusion electrodes in bioeconomy: An update

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## Abstract

The transition of today's fossil fuel based chemical industry toward sustainable production requires improvement of established production processes as well as development of new sustainable and bio-based synthesis routes within a circular economy. Thereby, the combination of electrochemical and biotechnological advantages in such routes represents one important keystone. For the electrochemical generation of reactants from gaseous substrates such as $O_2$ or $CO_2$, gas diffusion electrodes (GDE) represent the electrodes of choice since they overcome solubility-based mass transport limitations. Within this article, we illustrate the architecture, function principle and fabrication of GDE. We highlight the application of GDE for conversion of $CO_2$ using abiotic catalysts for subsequent biosynthesis as well as the application of microbial catalysts at GDE for $CO_2$ conversion. The reduction of oxygen at GDE is summarized for the application of oxygen depolarized cathodes in microbial fuel cells and generation of $H_2O_2$ to drive enzymatic reactions. Finally, engineering aspects such as scale-up and the modeling of GDE-based processes are described. This review presents an update on the application of GDE in bio-based production systems and emphasizes their large potential for sustainable development of new pathways in bioeconomy.

**KEYWORDS**

bioeconomy, C1-biotechnology, $CO_2$ conversion, electrobiotechnology, gas diffusion electrode, hydrogen peroxide dependent enzymes

## 1 | INTRODUCTION

The combination of electrochemical and microbial as well as enzymatic reactions is well-established in the field of biosensors (Bedendi et al., 2022). In bioeconomy in general, this combination is believed to be highly effective to optimize established processes or to setup new production routes (Harnisch & Urban, 2018). Often, the high selectivity of the biocatalysts is combined with a high energy efficiency of the electrochemical reaction step. Common examples are the electrochemical substitution or regeneration of cofactors (Castañeda-Losada et al., 2021; Çekiç et al., 2010; Dong et al., 2020; El Housseini et al., 2021; Tosstorff et al., 2014; Xu et al., 2021; Yuan et al., 2019; C. Zhang et al., 2022) and the electrochemical generation of reactants for biotransformations (Haas et al., 2018;

Hegner et al., 2020; Horst, Bormann, et al., 2016; Kracke et al., 2021; Krieg et al., 2018; Stöckl et al., 2020; Teetz et al., 2022; Tremblay et al., 2019). High Technology Readiness Levels (TRL) and high relevance to achieve the Sustainable Development Goals of the United Nations were demonstrated, especially for the electrochemical production of reactants and the subsequent microbial and enzymatic conversion (Fruehauf et al., 2020; Stöckl et al., 2022). Different processes are now transitioning from well-characterized conditions and optimized reaction systems in the laboratory setting toward realization of technical production sites with similar performance indicators (e.g., Haas et al., 2018; Kopljar et al., 2016). The development toward technical scale is a grand challenge and hence scaling-up is increasingly becoming a focus of research. To realize high productivity and energy efficiencies, three main issues must be addressed: (i) high mass transport, (ii) large specific electrode area per volume ($A_e$; ratio between the electrode surface and the reaction volume), and (iii) high reaction selectivity. In "classical" electrochemical engineering, targeting abiotic reactions only, technical electrolysis cells with three-dimensional electrodes are well established. These electrochemical cells provide an enlarged specific electrode area and improved mass transport due to the specific fluid dynamics inside the three-dimensional electrode structure. Typical examples of such three-dimensional reaction systems are porous flow-through reactors, packed- and fluidized bed cells and gas diffusion electrode (GDE) designed setups. To generate reactants for subsequent biotransformations, gaseous substrates are often reduced, exemplarily, for the reduction of $CO_2$ to CO and formate or $O_2$ to $H_2O$ or $H_2O_2$. Driven by the generally low solubility of gases in aqueous reaction systems, GDE were invented and designed to circumvent this intrinsic mass transport limitation (Hernandez-Aldave & Andreoli, 2020; S. Lu et al., 2022). In 2016 we summarized the application of GDE for biosynthesis using enzymatic and microbial energy conversions (Horst, Mangold, et al., 2016). In the last years, the application fields of GDE in biotechnology have been significantly expanded, calling for this update.

GDE are based on nano-porous materials which serve as a three-phase interphase between a gas, a liquid and a solid electrocatalyst. Through the combination of different materials, GDE provide three-dimensional hydrophilic and hydrophobic networks, which enable the electrochemical conversion of gases by circumventing their low solubility in an aqueous electrolyte solution. A schematic of a cross section of a GDE is presented in Figure 1. Technically, formation of hydrophobic and hydrophilic regions inside the GDE is realized by combining hydrophobic materials such as polytetrafluoroethylene (PTFE) with hydrophilic and electric conductivity increasing additives such as carbon-based materials and electrocatalysts. The hydrophobic PTFE allows the formation of a porous three-dimensional gas passage network throughout the GDE. The remaining components, such as carbon-based additives and electrocatalyst materials, form hydrophilic pores, which allow a transport of electrolyte solution inside the GDE. Under ideal operation conditions (pressure equilibrium between gas and liquid), the GDE is partially flooded with gas

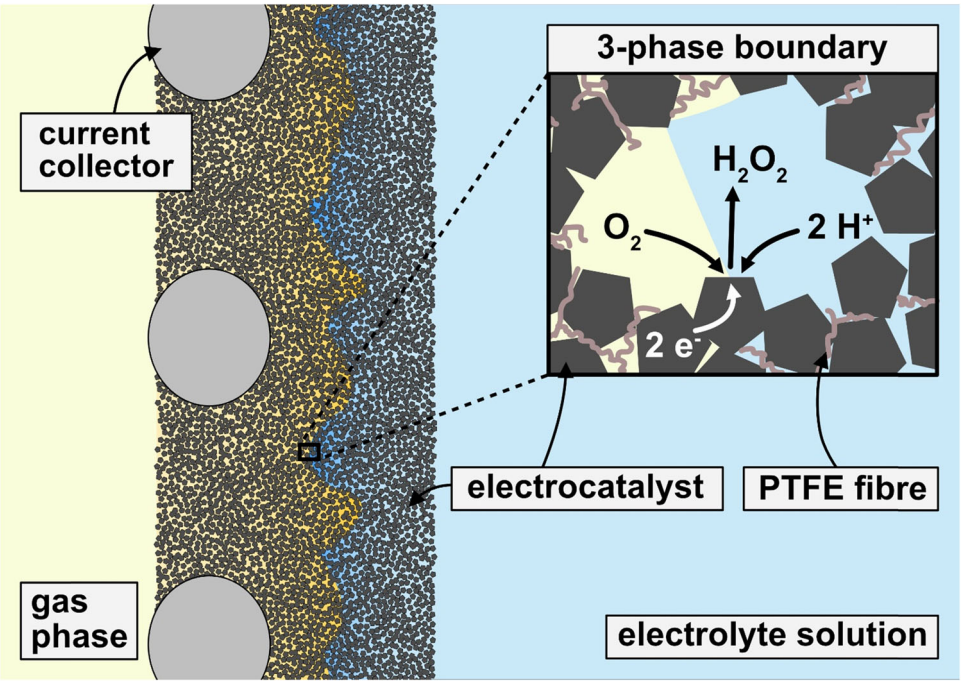


**FIGURE 1** Schematic cross section illustration of a gas diffusion electrodes (GDE). Description from left to right: gas phase; porous GDE system comprised of a current collector (current collector mesh schematically illustrated as a cross section of single metal mesh fibers) and electrocatalyst particles. A curved pattern inside the GDE schematically shows the vertical pattern of the 3-phase boundary, electrolyte solution at the right side of the GDE. Insert: schematic of the 3-phase boundary, where the gas phase, the liquid electrolyte phase and the solid electrocatalyst phase are in direct contact. Exemplarily, the cathodic hydrogen peroxide synthesis from oxygen is shown.

and electrolyte solution, respectively, which leads to the formation of three-phase boundaries inside the GDE (see insert in Figure 1), where the gas phase, the aqueous phase and the solid electrocatalyst phase are in direct contact with each other. This allows the electrocatalytic conversion of gases with solutes on one moiety, regardless of the solubility of the gas in the electrolyte solution. The architecture of GDE depends on the fabrication method and on the size of the GDE. Small-scale (up to few $cm^2$) GDE are often comprised of a layered design, where the electrocatalyst is applied on a hydrophobic (carbon-based) gas diffusion layer, for example, by spraying of an ink, which contains the catalyst or its precursor. Usually, PTFE and an ionomer (e.g., Nafion®) are part of the catalyst ink to adjust the hydrophobicity of the catalyst layer and transport, respectively. Large-scale electrodes such as silver-based oxygen depolarization electrodes or carbon black-based GDE for $H_2O_2$ synthesis are composed of mechanically stabilizing and current collecting metal grids (Figure 1) and the hydrophobic, conducting and electrocatalytic materials. Usually, the respective materials are provided as a homogenous particle mixture and are combined with the current collector mesh under pressure and increased temperature (e.g., via calendering) to prepare the GDE (Bidault et al., 2009).

## 2 | CONVERSION OF $CO_2$ AT GDE USING ABIOTIC CATALYSTS

The electrochemical conversion of $CO_2$ is considered as one of the most promising strategies for converting $CO_2$ into value-added chemicals. For the realization of $CO_2$-based industrial processes, the electrochemical conversion should present high product concentrations, productivities, current densities and long-term operation stabilities. Furthermore, high Faradaic efficiencies (FE; indicates the amount/ratio of current/electrons, which participate in the electrochemical target reaction; also referred as coulombic efficiency and sometimes current efficiency, CE) are desired to minimize the fraction of electrochemical by- and/or side-products. Electrocatalysts for the selective electrochemical reduction of $CO_2$ and the underlying reaction mechanism have been intensely researched in the last decades. Table 1 summarizes the currently most important and promising electrochemical $CO_2$ reduction reactions ($eCO_2RR$) to produce possible feedstock for subsequent bioprocesses.

**TABLE 1** Electrochemical reactions, number of transferred electrons (z) and standard equilibrium potentials (E°) at pH = 0 for the $CO_2$ conversion to biotechnological relevant products (Kortlever et al., 2015).

| Product | Reaction | z | $E^0$ vs. RHE |
|---|---|---|---|
| Carbon monoxide | $CO_2 + 2H_3O^+ + 2e^- \rightarrow CO + 3H_2O$ | 2 | −0.10 V |
| Formic acid | $CO_2 + 2H_3O^+ + 2e^- \rightarrow HCOOH + 2H_2O$ | 2 | −0.20 V |
| Methanol | $CO_2 + 6H_3O^+ + 6\ e^- \rightarrow CH_3OH + 5H_2O$ | 6 | 0.02 V |

The $eCO_2RR$ to CO at GDE gained an increasing interest in the scientific and industrial communities within the last decade since process performance parameters point toward promising commercialization (Masel et al., 2021). Typical catalysts for CO generation are silver (Ag) (Kim et al., 2016), gold (Au) (Verma et al., 2018), and platinum (Pt) (Du et al., 2013), (see Table 2). Thereby the most applied electrocatalyst material for CO formation by $eCO_2RR$ by far is Ag due to its high selectivity for CO, relatively high abundance and comparably low price (Enzmann et al., 2022). Kutz et al. achieved high FE of 96.9% at −100 mA $cm^{-2}$ and outstanding long-term performance of several 1000 h with Ag-based carbon GDE (Kutz et al., 2017). This was accomplished by using an imidazolium functionalized styrene vinylbenzyl chloride co-polymer as an anion exchange membrane. Further optimization was realized by adding porous carbon and imidazolium functionalized monomer to an Ag-containing ink used to spray paint onto the carbon support (Liu et al., 2018). The optimized Ag-based carbon GDE cathode could be operated at −200 mA $cm^{-2}$, a cell voltage of 3 V, and a CO selectivity of 98%. Dinh et al. used an Ag-coated porous PTFE membrane being spray coated with carbon as a current collector and compared the $CO_2$ reduction to CO at different pH (Dinh et al., 2018). They achieved FE to CO of more than 90% at current densities of more than −150 mA $cm^{-2}$ in neutral and alkaline electrolyte solutions and longtime stability of more than 100 h. The gaseous electrolysis-originating CO stream can be combined with hydrogen produced via water electrolysis to obtain syngas (CO and $H_2$ mixture) serving as a sustainable feedstock for a biotechnological process, as illustrated in Figure 2b. Both gaseous products can be generated separately or simultaneously within the same electrolysis set-up (co-electrolysis) to directly achieve syngas. The respective co-electrolysis has been demonstrated by Haas and co-workers with Ag-based electrodes from Covestro (Haas et al., 2018), achieving a stable syngas production throughout more than 1000 h at a high current density of −300 mA $cm^{-2}$ with constant cell voltage within 7.0–7.5 V. Furthermore, using a mixed culture of *Clostridium autoethanogenum* and *Clostridium kluyveri*, they impressively demonstrated the production of butanol and hexanol directly from electrolysis-originating syngas in a separate bioreactor.

Similar attempts to optimize the overall process can be seen for the electrochemical $CO_2$ reduction to formic acid/formate, even though the TRL is currently not as high as it is for the $eCO_2RR$ to CO. Like CO synthesis, the $eCO_2RR$ to formic acid/formate requires two electrons (Table 1). The most widely used electrocatalysts are tin (Sn) or tin oxide ($SnO_x$) (Löwe et al., 2021) and modified Sn-based materials (Lin et al., 2022). Other reported selective catalysts are indium (In) (Bitar et al., 2016; Hegner et al., 2018), amalgams (Park & Shin, 2021) and bismuth-based materials (García de Arquer et al., 2018; Wang et al., 2021), whereby the latter shows increased catalysts stability toward alkaline catalyst corrosion (Bienen et al., 2021). In a comprehensive and well-structured review, Han and co-workers summarized the achievements on metal-based nano-structured electrocatalysts for formate synthesis (Han et al., 2020). For instance, with a three-compartment electrolyzer using an imidazole functionalized Sustainion™ membrane technology, Yang and co-workers produced formic acid directly with 5–20 wt%, high FE and current densities at Sn-based GDE (H. Yang et al., 2017). After further

**TABLE 2** Examples of the commonly used catalysts in GDE for the $CO_2$ reduction to CO and Formate.

| Active center/electro catalysts | Support material | Main product | Current density [mA $cm^{-2}$] | Faraday efficiency [%] | Literature |
|---|---|---|---|---|---|
| Au | Carbon | CO | 158 | 99 | Verma et al. (2018) |
| Ag | GDE/XA-9 ionomer | CO | 200 | 98 | Liu et al. (2018) |
| Ni | Carbon substrate | CO | 308.4 | 88 | H. Yang, Lin, et al. (2020) |
| Sn | PTFE + Carbon | $HCOO^-$ | 400 | 75 | Kopljar et al. (2016) |
| Bi | Carbon substrate | $HCOO^-$ | 200 | 90 | García de Arquer et al. (2018) |
| Sn | PTFE + Carbon | $HCOO^-$ | 800 | 85 | Löwe et al. (2019) |
| Sn | Carbon + PTFE + Nafion | $HCOO^-$ | 1800 | 70 | Löwe et al. (2021) |

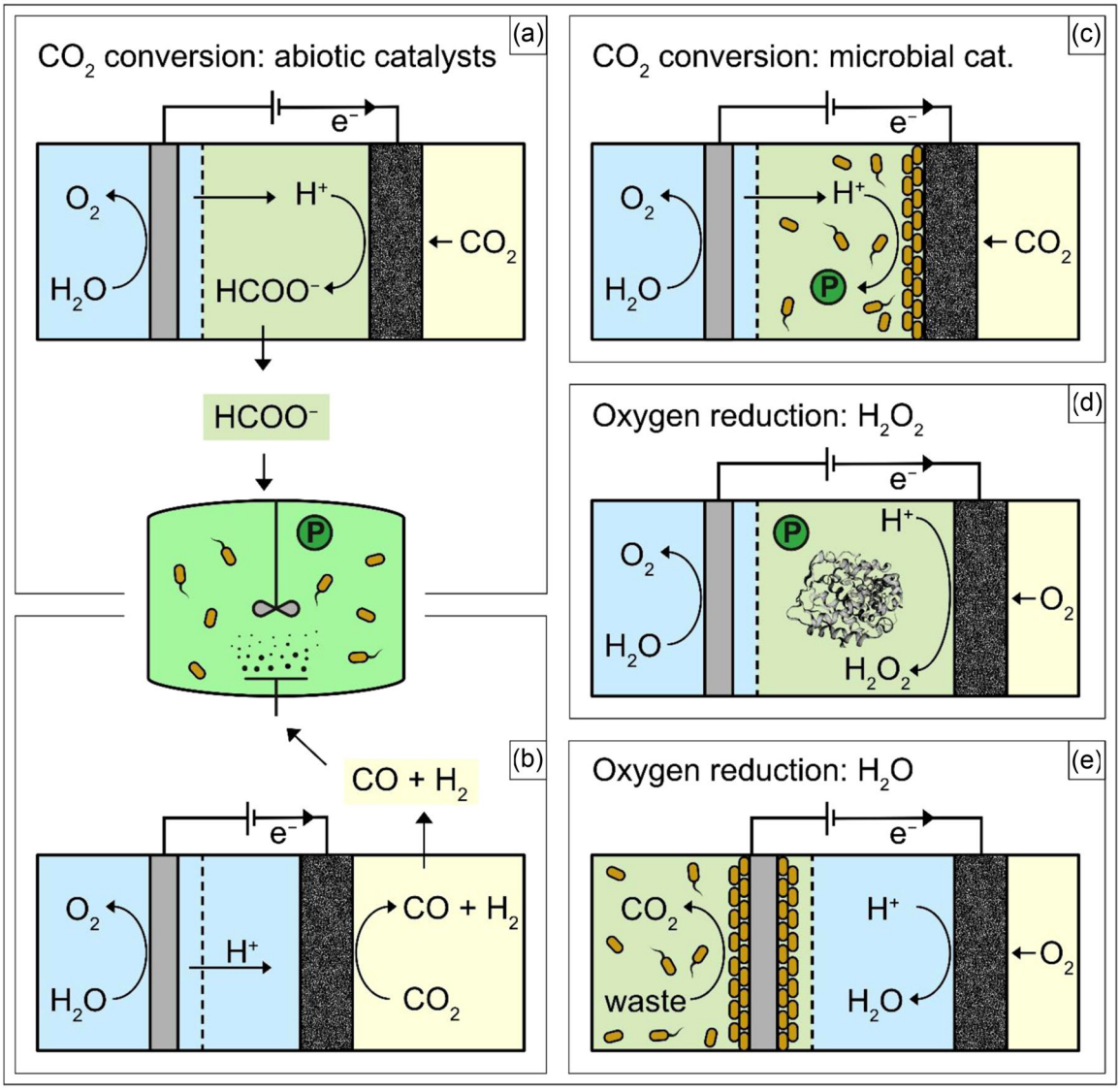


**FIGURE 2** Schematic illustration of different applications of gas diffusion electrodes (GDE) in bioeconomy. GDE is illustrated by porous black electrode of the respective schemes. Oxygen evolution reaction is displayed as anodic counter reaction, except for scheme E. (a) $CO_2$ reduction with abiotic electrocatalysts to formate ($COOH^-$) coupled with a formate-based fermentation to bio-products (P). (b) Co-electrolysis of $CO_2$ and water with abiotic electrocatalysts to obtain carbon monoxide and hydrogen gas mixture ($CO + H_2$), which is fed to a syngas-based fermentation. (c) $CO_2$ conversion with microbial catalysts. Microbial catalysts displayed as GDE associated biofilm and planktonic cells. (d) Oxygen reduction for hydrogen peroxide ($H_2O_2$) synthesis, which is subsequently consumed enzymatically for product generation. (e) Oxygen reduction at oxygen depolarization electrodes to water as cathodic counter reaction for the microbially catalyzed wastewater oxidation in microbial fuel cells.

optimization, they yielded a long-term stability of 1000 h at 200 mA $cm^{-2}$, which titers of 1.3–2.8 M formic acid, depending on operational conditions (H. Yang, Lin, et al., 2020). In contrast to the syngas-based processes (Figure 2b), formic acid/formate represents a less toxic and liquid/solid feedstock, which can be beneficial in terms of feedstock storage and process safety. The respective $eCO_2RR$ to formate at GDE for providing microbial feedstock combined with the biosynthesis is displayed in Figure 2a. A perspective on the use of formate as sole carbon source for the production of value-added chemicals has been published by Yishai and co-workers (Yishai et al., 2016). Exemplarily, the formate-based bioproduction with formate originating from the $eCO_2RR$ at Sn-based GDE has been demonstrated to produce the polymer polyhydroxy butyrate (PHB) by *Cupriavidus necator*. Furthermore, the formate-containing electrolyte was used as a biological feedstock without any intermediate purification step respectively downstream processing (Stöckl et al., 2020).

As mentioned before, the $eCO_2RR$ to CO and formic acid/formate at GDE represent processes to provide sustainable feedstock for biosynthesis. However, both feedstocks come with a relatively low energy content (high degree of reduction), which either requires a high substrate-to-product ratio or limits the product spectrum of the bioprocess. Therefore, $eCO_2RR$ products of higher energy/electron content, such as alcohols, represent a desirable sustainable feedstock from the mid- to long-term perspective since they can be used in already established processes such as methanol-based biotechnology (Schrader et al., 2009; Singh et al., 2022; W. Zhang et al., 2018). The synthesis of alcohols by $eCO_2RR$ requires the transfer of multiple electrons, and the selectivity to alcohols is generally much lower than that to CO, formic acid and even ethylene. Currently, developments on the selective $eCO_2RR$ to alcohols such as methanol are on a low TRL and reviewed by Al-Rowaili and co-workers (Al-Rowaili et al., 2018). Reported catalysts for the methanol synthesis are based on copper (Cu) (Azenha et al., 2020; Hazarika & Manna, 2019; L. Lu et al., 2018; D. Yang et al., 2019; H. Yang et al., 2019), cobalt (Co) (Wu et al., 2019) or boron phosphide materials (Mou et al., 2019). So far, the results reported for alcohol synthesis via $eCO_2RR$ are very promising in terms of selectivity and show increasing current densities. However, catalyst and/or electrode stabilities are not comparable with CO and formic acid/formate electrodes, and the transfer from dispersed electrodes and catalyst development to GDE (Azenha et al., 2020) is often unpredictable and currently on an early development stage. Thus, intensive academia and industry-driven research is required to successfully apply GDE for alcohol synthesis via $eCO_2RR$ for biological feedstocks and to close the gaps between both processes (Stöckl et al., 2022).

## 3 | CONVERSION OF $CO_2$ AT GDE USING MICROBIAL CATALYSTS

Conversion of $CO_2$ to value-added chemicals can also be achieved by using microbial electrocatalysts which is called microbial electrosynthesis (MES) (Figure 2c). These electroactive microorganisms are able to wire their metabolisms to an electron flow at the electrode (Schröder et al., 2015; Sydow et al., 2014). This concept of MES is also denominated as a primary microbial electrochemical technology (MET) and has to be distinguished from approaches using a secondary MET. Secondary MET approaches are based on abiotic electrocatalysis and indirectly connected to microbial synthesis, for example, by the electrochemical generation of feedstock (see above) (Izadi & Harnisch, 2022; Schröder et al., 2015). For MES in primary MET, the GDE design aims to allow sufficient supply of $CO_2$ for the microorganisms. Further, it shall provide the suitable interface between the gas and cathode solution for the biofilm formation at the electrode surface, where $CO_2$ enters the cathodic compartment. Only few studies have exploited GDE for MES, and in most it remains uncertain, whether the microbial electrocatalysts reduce $CO_2$ directly or use electrochemical hydrogen generated at the cathode as a mediator/reducing agent. This is probably due to the challenges involved in controlling the microbial activities in such complex reactor designs compared to conventional reactor setups like H-cells or stirred tank reactors. One of the first studies on MES using GDE was reported by Bajracharya et al (Bajracharya et al., 2016). In this study, a GDE reactor using a porous activated carbon electrode was inoculated with a mixed microbial culture and operated at the cathodic potential of −1.1 V versus Ag/AgCl using a circular Pt sheet as a counter electrode. The inoculum was assumed to be dominated by homoacetogenic bacteria after a four-stage enrichment from a wastewater sludge (including heating the sludge, heterotrophic and autotrophic growth, followed by four autotrophic growth transfers) (Mohanakrishna et al., 2015). The authors discussed the faster $CO_2$ mass transfer in the GDE setup compared to the conventional $CO_2$ sparging reactor, and therefore the higher production rate. Mass transfer coefficient for $CO_2$ in the reactor with a GDE was estimated almost two times higher than that in the reactor with a sparger (estimated mass transfer coefficient of 3.92 compared to 1.81 per h), leading to maximum $CO_2$ transfer rates of 91 mg $L^{-1}$ $min^{-1}$ and 42 mg $L^{-1}$ $min^{-1}$ (at 25°C), respectively. Detecting acetate as the main and ethanol and butyrate as the secondary products, the maximum acetate production rate in this study was 238 mg $L^{-1}$ $d^{-1}$. Afterwards, Srikanth et al. studied a similar setup for MES from $CO_2$ using a microbial mixed culture (Srikanth et al., 2018). As the pH was not controlled during the 90 days of experiment and due to the accumulation of formate and acetate, more diverse compounds such as ethanol, butyrate and butanol were produced. Overall production rates of 233 mg $L^{-1}$ $d^{-1}$ alcohols and 144 mg $L^{-1}$ $d^{-1}$ organic acids were reported. The effect of three different flow rates of $CO_2$ (5, 10, and 20 mL $min^{-1}$) was also compared in both H-cells and GDE reactors using mixed population of microorganisms (Rojas et al., 2021). Although increase in the flow rate of gaseous $CO_2$ improved the acetate production rate in the H-cell reaching a maximum value of 270 mg $L^{-1}$ $d^{-1}$, the lower $CO_2$ flow rate allowed the higher gas-liquid transfer in the GDE reactors. As a result, the highest acetate production rate (85 mg $L^{-1}$ $d^{-1}$) in the GDE reactors was achieved at the lowest $CO_2$ flow rate (5 mL $min^{-1}$). In addition, Fontmorin et al. reported the modification of a GDE using binary-doped polyaniline

polymer (Fontmorin et al., 2021). The key role of microbial biofilms formed at the cathode for MES from $CO_2$ was previously shown (Izadi et al., 2020). Following that, Fontmorin et al. showed the effect of polyaniline polymer on increasing the hydrophilicity and biocompatibility of the electrode, leading to a rapid biofilm formation from the mixed population of microorganisms at the GDE for $eCO_2RR$. As a result, faster start-up and higher production of acetate and subsequently butyrate was observed. The authors showed the increase in acetate and butyrate production rates from maximum 17 and 1 mg $L^{-1}$ $d^{-1}$ when a plain carbon GDE was used to maximum 183 and 6 mg $L^{-1}$ $d^{-1}$ when using a polymer coating with polyaniline at the GDE, respectively. Although not many studies focused on MES by primary MET using GDE, in all available studies the GDE design increased the production when compared to conventional setups.

## 4 | REDUCTION OF OXYGEN AT GDE—OXYGEN CATHODES AND THE GENERATION OF $H_2O_2$

The oxygen reduction reactions (ORR) are important cathode reactions for the synthesis of chemicals and energy storage (e.g., proton exchange membrane fuel cells or metal-air batteries). Depending on the pH, the electrolyte composition, the electrocatalyst, the applied potential and further parameters, different reactions take place (Table 3). The 4-electron reduction pathway from $O_2$ to $H_2O$ is often used as cathode reaction in microbial fuel cells (MFC, Figure 2e). Here, the main advantages are the harmless reaction product water as well as the high potential difference between the anode and the cathode making the MFC a source of electric power. In electroenzymatic processes, the 2-electron reduction pathway is used to produce hydrogen peroxide as reactant for $H_2O_2$-dependent enzymes ([Burek et al., 2019], [Figure 2d]). This 2-electron reduction also occurs as a side reaction of the 4-electron pathway, leading to a decrease in performance of the MFC (Zhao et al., 2006). Typical electrocatalysts for the 4-electron pathway are Pt and further elements from the Pt-group. In the last decade, significant achievements have been made to use non-Pt group elements (e.g., [Shao et al., 2016; Tian et al., 2020]). The most common electrocatalyst for the production of $H_2O_2$ is carbon material in various configurations and modifications (Rozendal et al., 2009).

As mentioned before, GDE are often used as cathodes for the ORR to water in MFC, (Figure 2e). The major reason is the need of a cathode in MFC that does not limit the microbially catalyzed anodic reactions, like it is often found with non-gas diffusion cathodes (Rossi et al., 2019). GDE-based MFC (also known as air cathode MFC) have been shown to be a suitable configuration to overcome limitations due to oxygen solubility. This is particularly advantageous when microorganisms catalyze ORR, as one of the key factors controlling the performance of aerobic biocathodes was shown to be the mass transfer of $O_2$ (Ter Heijne et al., 2010). In addition, GDE design discards the need for a constant aeration using an air pump, which is an economic burden (Rossi et al., 2022). Previously, air cathode MFC were used in different research fields such as COD removal (X. Zhang et al., 2015), monitoring of water or wastewater quality (Di Lorenzo et al., 2014; Holtmann & Sell, 2002), wastewater treatment (Feng et al., 2008; Sevda et al., 2013), and so forth, and to improve reactor designs (Fan et al., 2007; You et al., 2007). Only few studies have evaluated the performance of MFC based on gas diffusion cathodes using microbial catalysts for ORR. Xia et al. studied the development of biocathodes in a GDE reactor, which was initially enriched in a dual chamber electrochemical cell (Xia et al., 2013). Additionally, the authors discussed the higher maximum current density generated in the air cathode MFC with biocathode (1 A $m^{-2}$) than that generated in the dual chamber MFC (0.49 A $m^{-2}$). Izadi et al. also studied the MFC with iron-oxidizing bacteria (IOB) as a biocathode enriched from iron-rich river sediment using a GDE (Izadi et al., 2019). After developing the biocathode in the GDE setup under 3-electrode configuration, the authors discussed that GDE was responsible for regeneration of ferrous ion required as an energy source for IOB, which provided constant available oxygen needed for their metabolisms. Using the developed biocathode in an air cathode MFC led to maximum power of 1100 mW $m^{-2}$. This result was higher than the maximum power produced in the similar MFC, but with a Pt (5 mg $cm^{-2}$) coated GDE, which was 500 mW $m^{-2}$. Apart from the aforementioned reports, the majority of studies on GDE used abiotic electrocatalysts in MFC. Platinised graphite paper GDE was one of the common electrode materials used for ORR in GDE designed MFC previously, for example, (Cheng et al., 2006; Logan et al., 2007). However, over the past decade several studies focused on the development of different electrocatalysts suitable for GDE reactors. For instance, stainless-steel mesh and a cobalt oxide hybrid electrode (Gong et al., 2014) were utilized to achieve a stable and efficient ORR

**TABLE 3** Products, electrochemical reactions, number of transferred electrons (z) and potentials for the reduction of O2 at different pH (selected examples, [Senarathna et al., 2016]).

| Reaction product(s) and condition | Reaction | z | E vs. SHE |
|---|---|---|---|
| Water, acidic electrolyte solution (pH = 0, $[H^+_{(aq)}]$ = 1 mol L) | $O_2 + 4H^+ + 4e^- \rightarrow 2H_2O$ | 4 | 1.229 V |
| Hydrogen peroxide, acidic electrolyte (pH = 0, $[H^+_{(aq)}]$ = 1 mol L) solution | $O_2 + 2H^+ + 2e^- \rightarrow H_2O_2$ | 2 | 0.670 V |
| Hydroxide ion, alkaline electrolyte solution (pH = 14, $[OH^-_{(aq)}]$ = 1 mol L) | $O_2 + 4e^- + 2H_2O \rightarrow 4OH^-$ | 4 | 0.401 V |
| Hydroxide ion + hydroperoxyl, alkaline electrolyte (pH = 14, $[OH^-_{(aq)}]$ = 1 mol L) solution | $O_2 + 2e^- + H_2O \rightarrow HO_2^- + OH^-$ | 2 | −0.065 V |

to improve the MFC performance (Carrillo-Rodríguez et al., 2019; Santoro et al., 2016; Srikanth et al., 2016).

As mentioned before, hydrogen peroxide ($H_2O_2$) can be generated in a 2-electron reduction of oxygen and subsequently applied in enzymatic processes with $H_2O_2$-dependent enzymes (Figure 2d). In these processes, $H_2O_2$ acts as a co-substrate for a wide range of enzymatic reactions (e.g., hydroxylations, epoxidations, sulfoxidations, halogenations, Baeyer–Villiger oxidations, decarboxylations) (Burek et al., 2019). However, in addition to serving as a co-substrate, the $H_2O_2$ could also show negative effect on the enzyme stability. In particular, heme-dependent peroxidases and peroxygenases tend to irreversible oxidative inactivation by $H_2O_2$. This effect was investigated in detail by using the heme-containing chloroperoxidase from *Caldariomyces fumago* (*Cfu*CPO). While the theoretical ratio of $H_2O_2$ to the substrate monochlorodimedone is 1:1, it has been shown that the highest operational stability is achieved at a ratio of 0.1:1 (Holtmann et al., 2014). This indicates that high enzyme stabilities can preferentially be achieved in a hydrogen peroxide limited process. One major challenge in the technical application of the $H_2O_2$-dependent enzymes is to control the $H_2O_2$ concentration at levels that enable efficient catalytic turnover of the enzyme while simultaneously minimizing the undesired inactivation reaction (Burek et al., 2019). Besides other supply methods, the electrochemical in-situ generation of $H_2O_2$ in scalable reactors was evaluated as an energy and resource efficient process (Bormann et al., 2019, 2021; Getrey et al., 2014; Holtmann et al., 2014; Horst, Bormann, et al., 2016; Krieg et al., 2011; Lütz et al., 2007). Lütz et al used a fixed bed electrode and the *Cfu*CPO to oxidize thioanisole to (*R*)-methylphenylsulfoxide (Lütz et al., 2007). GDE-based reactors were used as an alternative concept to fixed bed electrodes. High oxygen concentration next to the catalyst improved mass transfer in the electrode, high specific electrode surface areas and the avoidance of gassing the reactor are claimed to be the main advantages. Table 4 shows different electroenzymatic processes based on hydrogen peroxide dependent enzymes and GDE. The aim of most of these studies was to improve the operational stability of the enzymes and to broaden the product portfolio. The FE depend on the applied electrolyte/buffer system. The measured FE in sodium acetate buffer (pH 5.0) with addition of 50 mM sodium sulfate or 100 mM citrate buffer (pH 2.75) with addition of 10 mM sodium chloride as electrolyte were 88 ± 4% and 55%, respectively (Krieg et al., 2011). Organic co-solvents are often used to realize sufficient concentration of hydrophobic substrates in enzymatic reactions. By using a buffer containing 100 mM potassium phosphate (pH 7.0) and 3% acetone, the FE was approx. Seventy-one percent (Horst, Bormann, et al., 2016). One particular challenge when using organic solvents is the hydrophilicity of the GDE. Hydrophobic solvents and substrates can prevent establishing a proper 3-phase boundary between the electrolyte solution, electrocatalyst and the gas phase. Furthermore, leakage problems could occur (Getrey et al., 2014; Horst, Bormann, et al., 2016). These effects can only be addressed by electrode engineering. This has only been done to a small extent, as in most investigations commercial electrodes were used. However, the large capabilities provided by optimized electrodes have already been used to decrease overpotentials. The coating of a GDE with oxidized carbon nanotubes can lead to a decreased overpotential by around 100 mV, compared to unmodified electrodes, during ORR to $H_2O_2$ (Bormann et al., 2019). Recently, a process model was introduced which allows to predict optimized reaction conditions of electroenzymatic processes with $H_2O_2$-dependend enzymes (Bormann et al., 2021). The developed model can also be used for efficient process development with different enzymes. Furthermore, the use of GDE in electroenzymatic processes was extended further. Schuhmann and co-workers modified a GDE with a viologen-based redox polymer and tungsten dependent formate dehydrogenase (Szczesny et al., 2020). This system was used to produce formate from $CO_2$.

A further future-oriented combination is the use of a cathodic hydrogen peroxide-producing GDE and an anodic microbial fuel cell in wastewater treatment (Rozendal et al., 2009; Sim et al., 2018). In such microbial electrolysis cells (MECs) the anodic conversion of organic wastewater components provides the majority of energy for the cathodic conversion of $O_2$ to $H_2O_2$. $H_2O_2$-producing MECs can yield significant profits over other MECs due to high cost and demand of hydrogen peroxide (Sim et al., 2018).

## 5 | ENGINEERING ASPECTS—SCALE-UP AND MODELING OF GDE-BASED PROCESSES

As demonstrated, the majority of GDE-based processes are showing promising key performance indicators. The next step toward industrial realization is now to increase the scale and especially overall production volume of the processes. While "conventional" bioprocesses are typically volume dependent, electrobiotechnological processes are in first instance surface-dependent (Enzmann et al., 2019). This scale-up challenge is reduced in the case of the GDE-based processes, as here the reactants are mostly generated electrochemically in the electrode while the subsequent biological reaction takes place in the reactor volume. The technical realization of a large scale GDE-based process was demonstrated for the abiotic electrochemical chlorine production (press release from thyssenkrupp Uhde and Bayer MaterialScience from June 2013, [Moussallem et al., 2008]). The specific challenge in electrobiotechnology will be to adapt requirements and performances of the respective electrochemical and microbial or enzymatic processes to each other. In particular, model-based approaches can be used for both a knowledge-based design of the individual steps as well as for a conceptual design of the overall processes. As most prominent example, Able and Clark developed a multiphysics model to analyze a formate-mediated microbial electrosynthesis with the aerobic "Knallgas" bacteria *Cupriavidus necator* (Abel & Clark, 2021). The comprehensive model includes transport phenomena, electrochemical and microbial reactions, thermodynamic and kinetic effects, temperature effects, and gas/liquid mass transfer. This showed that

**TABLE 4** Electrochemical reactions, number of transferred electrons and standard potentials for reduction of $O_2$ (selected examples, ttn = total turnover number, ratio between the total moles of product yield per mole of added biocatalyst).

| Enzyme | Enzymatic conversion | Reaction conditions | Key performance indicators | Literature |
|---|---|---|---|---|
| Heme-containing chloroperoxidase from *Caldariomyces fumago* (*Cfu*CPO) | Thioanisole to methyl phenyl sulfoxide | 100 or 600 nM *Cfu*CPO, 100 mM sodium acetate buffer pH 5 + 50 mM $Na_2SO_4$, carbon-based commercial GDE, 16.5 $cm^{2,a}$, 1.8 or 5.5 mA $cm^{-2}$ | $ttn_{Enzyme}$ = 83,600, productivity 19.8 g $L^{-1}$ $d^{-1}$ (100 nM enzyme and 1.8 mA $cm^{-2}$), $ttn_{Enzyme}$ = 3120, productivity 23 g $L^{-1}$ $d^{-1}$ (600 nM enzyme and 5.5 mA $cm^{-2}$) | Krieg et al. (2011) |
| *Cfu*CPO | Indole to oxindole | 100 nM *Cfu*CPO, 100 mM citrate buffer pH 2.75 + 10 mM NaCl, carbon-based commercial GDE, 16.5 $cm^{2,a}$, 1.8 mA $cm^{-2}$ | $ttn_{Enzyme}$ = 39,000, productivity 8.3 g $L^{-1}$ $d^{-1}$ | Krieg et al. (2011) |
| *Cfu*CPO | Monochlorodimedone (MCD, surrogate substrate) to dichlorodimedone | 5–30 nM *Cfu*CPO, 100 mM citrate buffer pH 2.75/3.5, carbon-based commercial GDE, 5.5 $cm^{2,a}$, 2.7–5.5 mA $cm^{-2}$ | $ttn_{Enzyme}$ = 1,150,000 | Holtmann et al. (2014) |
| *Cfu*CPO | Thymol to chlorothymol | 100 nM *Cfu*CPO, 100 mM citrate buffer + 50 mM NaCl, pH 3.5, carbon-based commercial GDE, 5.5 $cm^{2,a}$, 8.2 mA $cm^{-2}$ | Productivity 20.4 g $L^{-1}$ $d^{-1}$ | Getrey et al. (2014) |
| Recombinant unspecific peroxygenase from *Agrocybe aegerita* (r*Aae*UPO) | Ethylbenzene to 1-phenethyl alcohol | 50 nM r*Aae*UPO, 100 mM potassium phosphate buffer pH 7.0 + 3% acetone as second phase, carbon-based commercial GDE, 2 $cm^{2,a}$, 5–30 mA $cm^{-2}$ | ttn = 400,000 (at 10 mA $cm^{-2}$), productivity 25 g $L^{-1}$ $d^{-1}$ (at 25 mA $cm^{-2}$) | Horst, Bormann, et al. (2016) |
| Vanadium chloroperoxidase from *Curvularia inaequalis* (*Ci*VCPO) | 4-Pentenoic acid to bromolactone | 100 nM *Ci*VCPO, 100 mM sodium citrate (pH 5) with 100 mM KBr, GDE modified with oxidized carbon nanotubes (oCNTs), 4.5 $cm^{2,a}$, −0.35 V versus Ag/AgCl | Productivity 3.4 g $L^{-1}$ $d^{-1}$ | Bormann et al. (2019) |
| r*Aae*UPO | 4-ethylbenzoic acid to 4-(1-Hydroxy-ethyl)benzoic acid | 12.5 nM r*Aae*UPO, 100 mM potassium phosphate buffer pH 7.0, carbon-based commercial GDE, 5.5 $cm^{2,a}$, 1.8–14.5 mA $cm^{-2}$ | ttn approx. 400,000 (at 1.8 mA $cm^{-2}$), turnover frequency up to 135 $s^{-1}$ (at 10.9 mA $cm^{-2}$) | Bormann et al. (2021) |

[a]Geometrical surface.

formate-mediated microbial electrosynthesis reactors needed for this specific bacterium are mainly limited by the trade-off between $O_2$ gas/liquid mass transfer and $CO_2$ transport to the cathode surface (Abel & Clark, 2021). They concluded that the decoupling of the electrochemical and microbial processes into separate reactors overcomes this limitation. Further modeling includes for example, the model-based improvement of GDE (Heßelmann et al., 2022), model-based upscaling of GDE based $CO_2$-reduction systems (Z. Yang et al., 2021) and a multi-criteria optimization of $H_2O_2$ synthesis in GDE (von Kurnatowski & Bortz, 2021).

## 6 | CONCLUSION AND OUTLOOK

For improvement of established production processes as well as development of new sustainable and biobased synthesis routes within a circular economy, the combination of biotechnology and electrochemistry is a powerful tool. Whenever electrochemically or electromicrobially catalyzed (cathodic) reactions involve the consumption of gaseous compounds, applying GDE can significantly improve the overall process, since GDE circumvent the poor solubility of gases in aqueous and biocompatible electrolyte solution. GDE are the electrode of choice for the $eCO_2RR$ to different carbon-based chemicals, which can be used as a sustainable feedstock for biotechnological synthesis. Especially for syngas-based fermentations, this elegant coupling of electrochemical $CO_2$ fixation to CO and microbial synthesis is currently in the transition to larger-scale industrial realization (press release from the companies Evonik and Siemens, from October 10, 2019). Although not many studies focused on MES in primary MET using GDE, in all available studies the GDE design showed improved production compared to conventional setups. In $H_2O_2$-dependent enzyme-based systems, GDE were successfully used for the energy and resource-efficient in-situ $H_2O_2$ production from $O_2$ at levels that enable efficient catalytic turnover of the enzyme while simultaneously minimizing the undesired inactivation reaction.

This wide variety of applications shows that GDE are one of the key engineering components for the successful electrification of the bioeconomy (Harnisch & Urban, 2018). In both academic research and industry-driven biobased process development, GDE engineering provides the possibility to enhance the conversion of gaseous feedstock sustainably and significantly. The development of GDE and their application in the bioeconomy is an ongoing process, involving for instance electrode and process scale-up, process and electrode stability and reaction design for the integration and interconnection of electrochemical and biobased reactions (Harnisch & Holtmann, 2019).

## AUTHOR CONTRIBUTIONS

*Conceptualization of the review, supervision, and funding acquisition*: Markus Stöckl and Falk Harnisch und Dirk Holtmann. *Contribution to the concept*: All authors. *Literature mining*: All authors. *Writing of the review*: All authors. *Preparation of tables and figures, and validation of the manuscript*: All authors

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## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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