Microbial electrosynthesis from CO₂: Challenges, opportunities and perspectives in the context of circular bioeconomy

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ABSTRACT
Recycling CO₂ into organic products through microbial electrosynthesis (MES) is attractive from the perspective of circular bioeconomy. However, several challenges need to be addressed before scaling-up MES systems. In this review, recent advances in electrode materials, microbe-catalyzed CO₂ reduction and MES energy consumption are discussed in detail. Anode materials are briefly reviewed first, with several strategies proposed to reduce the energy input for electron generation and enhance MES bioeconomy. This was followed by discussions on MES cathode materials and configurations for enhanced chemolithoautotroph growth and CO₂ reduction. Various chemolithoautotrophs, effective for CO₂ reduction and diverse bioproduct formation, on MES cathode were also discussed. Finally, research efforts on developing cost-effective process for bioproduct extraction from MES are presented. Future perspectives to improve product formation and reduce energy cost are discussed to realize the application of the MES as a chemical production platform in the context of building a circular economy.

1. Introduction
Global warming, mainly due to the greenhouse effect induced by the accumulation of CO₂, CH₄ and N₂O in the atmosphere, is becoming a severe problem (Bajracharya et al., 2017c). CO₂ represents the majority of greenhouse gas (GHG) emissions (63% CO₂, 24% CH₄ and 3% N₂O), and main contributor for global warming (ElMekawy et al., 2016). The annual CO₂ emission has exhibited a continuous growth trend since 1971, increasing dramatically from 14.1 gigaton to 38.2 gigaton in 2014 (Bajracharya et al., 2017c). In order to restrain the global temperature rise within 2 °C according to the Paris Agreement (Peter, 2018) and achieve worldwide carbon balance, effective control of CO₂...
emissions and gradual reduction of CO2 concentration in the atmosphere have become a priority of research and technological development. Three main strategies have been proposed to combat global warming: (1) reduction of fossil fuel usage (Liu et al., 2015b), (2) development of low-carbon renewable energy source (Granovskii et al., 2007) and (3) CO2 mitigation technologies including carbon capture and storage (CCS) and carbon capture and utilization (CCU) (Bui et al., 2018).

So far, consensus has been reached that renewable energy could be utilized to partially replace fossil fuel consumption (Chu et al., 2017). However, developing novel technologies to reduce CO2 concentration in the atmosphere and thus achieve “negative” CO2 emissions is yet a great challenge. Several techniques have emerged for CCU to transform waste CO2 stream into value-added resources, which represents a shift in our perception by considering CO2 as a resource, and hence contributing to circular economy. Unlike CCS which treats CO2 as a waste stream that requires efficient adsorption and storage (Qasem et al., 2018), CCU through catalytic or biological CO2 conversion at large industrial sites is now becoming an attractive solution to diverse chemical production in circular carbon economy globally. The thermo/electro catalytic CO2 reduction with mainly metal-based catalysts has been widely studied to convert CO2 into mono-carbon compounds (mostly CO or CH4) (Hou et al., 2006; Kas et al., 2016; Wang et al., 2019). Even though longer-chain hydrocarbons could be generated via CO and/or methanol mediator (Li et al., 2018), the long-term stability of the catalysts and novel techniques for further energy reduction are still under investigation (Wang et al., 2019). To efficiently reduce human dependence on fossil fuels, biological CO2 conversion into value-added chemicals (Savakis and Hellingwerf, 2015; Xu et al., 2019) has been regarded as a cost-effective approach to achieve circular carbon economy.

Bioelectrochemical system (BES) has been proposed in the past for waste stream treatment and resource recovery (Katuri et al., 2018). Microbial electrosynthesis (MES) has been specifically designed for cathodic CO2 reduction and diverse product generation by utilizing chemolithoautotrophs as self-sustaining and economic biocatalysts (Bajracharya et al., 2016; Jourdin et al., 2016a). This system does not face the problem of lipid extraction from microalgae cells as in microalgae-based photo-reactors, or unstable catalysts for generating organic products with relatively short carbon-chain from thermo/electro catalytic CO2 reduction. The long-term stability of MES reactors and the high coulombic efficiency of CO2 reduction to products make MES a potentially scalable technology for CO2 utilization in the circular bioeconomy and high-value biofuel generation (Liu et al., 2015a). Currently microbial electrolysissynthesis of acetate from CO2 has been progressing towards high production (> 10 g/L) (Bajracharya et al., 2016; Gildemyn et al., 2015), which is approaching the lower limit of acetic acid concentration in Chinese vinegar (3.5–4.5%) (Liu et al., 2004). This indicates the great potential of MES technology for the CO2 transformation into value-added biochemicals in food industry. Apart from acetate, more valuable bioproducts, such as butyrate (Ganigue et al., 2015), caproate (Jourdin et al., 2018) and polyhydroxybutyrate (PHB) (Sciarría et al., 2018), could be generated from CO2 in MES system. The wide diversity of biochemicals generated from CO2 in MES represents another strategic approach for material and chemical synthesis, potentially positioning biotechnology, especially MES, as an effective supplement for circular bioeconomy.

In previous studies, different aspects of MES, in terms of reactor configurations, electron transfer mechanism, electrocatalytic microbmes and cathode materials utilized in MES have been reviewed in recent years (Table 1). However, several bottlenecks, such as the high energy input, poor CO2 utilization efficiency, and end-product inhibition, are still lacking systematic analysis, which currently restrain the production rates of volatile fatty acids (VFAs) from CO2 at low costs and large scale (Gildemyn et al., 2015). Since energy consumption and product formation rates usually determine the feasibility of biotechnology for scaling up and achieving circular bioeconomy, it is essential to develop cost-effective electrode materials and configurations for reduced energy input, enhanced bacterial colonization, excellent CO2 mass transfer and bioproduct extraction in MES (Bajracharya et al., 2017b; Gildemyn et al., 2015).

In this review, we first start with the discussion about the anode materials commonly used in MES. The anode plays a significant role in lowering the energy input for the anodic water splitting. This will be followed by a thorough review of MES cathode materials and configurations for chemolithoautotroph’s growth and various VFAs generation. The impact of direct gaseous CO2 delivery on CO2 mass transfer and pH control at the cathode surface is presented in detail. The analysis of energy consumption in MES, including anodic water splitting, cathodic biocatalysis and bioproduct extraction, is discussed. Recommendations for MES system optimization to reduce the overall energy demand and enhance the VFA production are discussed at the end, in the context of translating MES into a viable technology that contributes to circular bioeconomy.

2. Anode modification for efficient electron generation in MES

MES for CO2 reduction is an electricity-driven bioproduction process catalyzed by microbes. The reactor configuration usually consists of two main compartments, anode and biocathode chambers, separated with a proton exchange membrane (Fig. 1). Currently most MES studies focus on the cathodic CO2 reduction using various microbial inocula, and different cathode materials and configurations (Aryal et al., 2017a). Cathodic CO2 conversion into acetate has been reported feasible with microbial catalysis at a relatively low cathode potential of ~ −0.4 V vs. standard hydrogen electrode (SHE) (Bian et al., 2018a; Nie et al., 2013; Zhang et al., 2013a), which represents an overpotential of 110 mV compared to the standard CO2 redox potential (~ 0.29 V vs. SHE). However, an applied voltage of at least 3 V is usually required to boost the current density and acetate production (Giddings et al., 2015), most of which is believed to bias at the MES anode to drive water splitting (Torella et al., 2015).

Oxygen evolution reaction (OER) from water is widely used in MES for proton/electron generation at the anode. OER consumes a large amount of electricity because the reaction is not kinetically favorable, which involves four-electron transfer and is believed to be much more complicated than the hydrogen evolution reaction (HER) at the cathode (Palaniselvam et al., 2017). However, despite its relevance, the development of effective MES anode is not gaining attention in MES research. Most MES anodes are made of carbonaceous materials, such as graphite stick (Chen et al., 2016; Nie et al., 2013), graphite plate (Gong et al., 2013), carbon cloth (Bian et al., 2018a) and carbon fiber brush (Alqahtani et al., 2018). However, carbon electrodes exhibit intrinsic electrocatalytic OER activity with an overpotential of more than 600 mV to drive a current density of 5 mA cm−2 (Cheng et al., 2015). To avoid the high energy input and/or reduce the cost of electrode for anodic OER in MES, several strategies have been developed as shown in Fig. 2 such as (1) deposition of small amounts of stable noble catalyst on non-noble electrode for efficient OER; (2) the utilization of photo-anodes; (3) the use of anodic reactions other than OER for electron generation; and (4) the use of biotic anode for organic or sulfide oxidation. These strategies are discussed in more detail below.

Several metal electrodes, instead of carbonaceous materials, have been utilized as MES anodes to initiate better OER. Ti and Pt metal anodes have been reported to efficiently drive the OER and maintain long-term MES performance without corrosion (Bajracharya et al., 2016; Blanchet et al., 2015). As noble-metal electrodes are usually more expensive than carbon, small amount of noble metal catalysts (Ir or Pt) have been deposited onto cheap substrates to serve as MES anodes (Bajracharya et al., 2017b; Bian et al., 2018a). To further reduce the cost for catalyst preparation, biosynthesized reduced graphene oxide doped with transition-metals using electroactive bacteria has
One of the first reviews explaining the overall concept of MES and other biocathodic production processes

A detailed description of electroautotrophic microbes that utilize electricity as electron source for CO₂ reduction

An interesting perspective on extracellular transfer of electrons to acetogenic microorganisms in MES

An overview of cathode materials for MES from carbon dioxide

The most recent advances in biocathalysts development and process design in bioelectrochemical systems for CO₂ transformations were reviewed

A quantitative analysis of the state-of-the-art on MES and its comparison with electro-fermentation concept

A state-of-the-art report on enzymatic electrochemical CO₂ reduction for chemical production

An evaluation of membrane-based technologies for effective separation of CO₂ and biogas and subsequent conversion of CO₂ using MES

Fig. 1. Schematic of a microbial electrosynthesis (MES) cell powered with different energy sources. PEM: proton exchange membrane. Reproduced with permission (Katuri et al., 2018). Copyright 2018, John Wiley & Sons, Inc.

been developed for OER with long stability and proposed for potential application in MES (Kalathil et al., 2019). However, since current MES studies mainly focused on the biocathodes with chemolithoautotrophs for CO₂ reduction, no results regarding the anodic OER overpotential have been reported for these MES anodes with noble metal catalysts, which makes it difficult to identify their long-term stability.

Light energy, one of the most abundant renewable resources, can be additionally used at the anode to overcome the overpotential of OER in MES and thus achieving so-called artificial photosynthesis (Fu et al., 2018). Photo-electrochemical (PEC) systems in recent years have been widely reported for hydrogen production through water splitting (Kistler et al., 2019; Yang et al., 2017). To efficiently harvest solar energy, titanium dioxide (TiO₂) nanowire arrays have been utilized as photo-absorber and OER catalyst in MES by Liu et al. (2015a) and Fu et al. (2018), respectively. An instant photo-response from the MES photocathode induced a current of ~1.2 mA in the absence of external bias, demonstrating the feasibility of minimized energy input for the photo-assisted MES (Fu et al., 2018). Thus it is promising to utilize solar energy in MES for efficient OER and reduced energy input at the same time.

Oxygen was reported to be able to diffuse from the anode to the cathode in a two-chamber MES reactor (Alqahtani et al., 2019). Previous studies using two-chamber MFCs revealed the negative effects of oxygen diffusion, using ion-exchange membrane, on MFC performance and electricity generation (Suzuki et al., 2016). To reduce the energy input for OER and minimize the negative impacts of oxygen intrusion on chemolithoautotrophic enrichment, chlorine evolution reaction (CIER) could potentially serve as the substitute for OER. The electro-chemical formation of chlorine and oxygen gas at the anode occurs according to the following reactions (Bard et al., 1985; Karlsson and Cornell, 2016):

\[
2\text{Cl}^- \rightarrow \text{Cl}_2 + 2e^- \quad \text{E}^- = 1.358 \text{V vs. SHE} \tag{1}
\]

\[
2\text{H}_2 \text{O} \rightarrow \text{O}_2 + 4\text{H}^+ + 4e^- \quad \text{E}^- = 1.229 \text{V vs SHE} \tag{2}
\]

By comparing the standard potentials of reaction (1) and (2), it is obvious that OER requires less activation energy versus CIER. However, high CIER selectivity over OER has been already reported with photocatalysts, since it is more kinetically favorable with only two electrons involved in chlorine evolution (Karlsson and Cornell, 2016). Finke et al. (Finke et al., 2019) systematically studied the activity of oxygen-evolution and chlorine-evolution through TiO₂ photocatalysts synthesized by atomic layer deposition (ALD). Lower anode overpotential towards CIER induced higher current density (700 mV, ~2 mA/cm²) compared to OER (900 mV, ~0.05 mA/cm²) with the same fluorine-doped tin oxide (FTO) electrode coated at 10 ALD cycles of TiO₃.

Considering the much lower overpotential to initiate CIER and the huge market size (50–60 million ton./year) of chlorine gas (Gamble, 2019), developing cost-effective anode materials for efficient CIER could be a suitable alternative for OER in MES to achieve circular bioeconomy.

Bioanodes are typically used in BESs such as MECs for the removal of chemical oxygen demand (COD) in wastewater with generation of electrons and protons (Katuri et al., 2014). An applied voltage as low as 0.7 V, which is commonly not high enough to drive OER and HER in MES, has been demonstrated to sufficiently drive HER in MEC (Katuri et al., 2014). The main reason for this low voltage is due to the low potential established at the bioanode from the oxidation of organic compounds (Gamble, 2019). An instant photo-response from the MES photocathode induced a current of ~1.2 mA in the absence of external bias, demonstrating the feasibility of minimized energy input for the photo-assisted MES (Fu et al., 2018). Thus it is promising to utilize solar energy in MES for efficient OER and reduced energy input at the same time.

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Fig. 2. A scheme of different anode strategies in MES for reducing energy input. All the values included in this scheme are based on the standard redox potential (vs. SHE) of the different anodic reactions for electron generation. ^\text{°} = 0.28 \text{V vs SHE}$ represents the oxidation potential of acetate, which is a common organic compound present in wastewater.
<table>
<thead>
<tr>
<th>Type of cathode</th>
<th>Cathode materials</th>
<th>Microbial inoculum</th>
<th>Cathode potential (V vs SHE)</th>
<th>Current density § (Am$^{-2}$)</th>
<th>Acetate production rate (gm$^{-2}$d$^{-1}$)</th>
<th>CE in acetate (%)</th>
<th>Other VFAs and alcohols (gm$^{-2}$d$^{-1}$)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unmodified carbon</td>
<td>Graphite granules</td>
<td>Enriched brewery WW sludge</td>
<td>−0.59</td>
<td>−0.8 (kA m$^{-2}$)</td>
<td>1.0§</td>
<td>69</td>
<td>−</td>
<td>(Marshall et al., 2013)</td>
</tr>
<tr>
<td>based cathode</td>
<td>Graphite disk</td>
<td>S. ovata</td>
<td>−0.68</td>
<td>−0.25 ± 0.06</td>
<td>2.25</td>
<td>79 ± 6</td>
<td>nC6 &amp; EtOH</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gas diffusion cathode VITO-Gore</td>
<td>Enriched Anaerobic sludge</td>
<td>−1</td>
<td>−20</td>
<td>36.6</td>
<td>35 ± 8</td>
<td>nC4</td>
<td>(Rajacharya et al., 2016)</td>
</tr>
<tr>
<td></td>
<td>RVC foam (Continuous mode)</td>
<td>Enriched acetogenic culture</td>
<td>−1.1 to −1.3</td>
<td>−83.3</td>
<td>196.8</td>
<td>35</td>
<td>−</td>
<td>(LaBelle and May 2017)</td>
</tr>
<tr>
<td></td>
<td>3 Carbon felts stacked together (flow through, continuous)</td>
<td>Enriched mixed culture</td>
<td>−0.85</td>
<td>−110 ± 20</td>
<td>371 ± 5</td>
<td>91 ± 9</td>
<td>nC4 (160 ± 29), nC6 (46 ± 1) VFA</td>
<td>(Jourdin et al., 2018)</td>
</tr>
<tr>
<td>Modified carbon</td>
<td>CC-SS</td>
<td>Raw + acclimated activated sludge</td>
<td>−0.95</td>
<td>−10</td>
<td>−</td>
<td>80.3 ± 0.5</td>
<td>nC6 (2.1 ± 0.01§) VFA</td>
<td>(Jiang et al., 2020)</td>
</tr>
<tr>
<td>cathodes</td>
<td>CC</td>
<td>−2 mA</td>
<td>1.4§</td>
<td>44</td>
<td>44</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CC-coated with PEDOT-PSS</td>
<td>S. ovata</td>
<td>−0.69</td>
<td>−0.47</td>
<td>13.5 ± 3.3</td>
<td>86 ± 12</td>
<td>−</td>
<td>(Jourdin et al., 2015)</td>
</tr>
<tr>
<td></td>
<td>3D Graphene carbon felt composite</td>
<td>S. ovata</td>
<td>−0.69</td>
<td>−0.23</td>
<td>62.4 ± 26.6</td>
<td>83 ± 3</td>
<td>−</td>
<td>(Jourdin et al., 2016a)</td>
</tr>
<tr>
<td></td>
<td>3D Graphene Paper</td>
<td>S. ovata</td>
<td>−0.69</td>
<td>−2.4</td>
<td>54.6 ± 1.7</td>
<td>86 ± 3</td>
<td>−</td>
<td>(Aryal et al., 2016)</td>
</tr>
<tr>
<td></td>
<td>CC coated with PEDOT-PSS</td>
<td>S. ovata</td>
<td>−0.69</td>
<td>−2.5</td>
<td>39.8</td>
<td>90.7</td>
<td>−</td>
<td>(Aryal et al., 2016b)</td>
</tr>
<tr>
<td></td>
<td>MXene Ti$_x$C$_y$T$_z$H$_w$-coated carbon felt electrode</td>
<td>Mixed culture from WWTP sludge</td>
<td>−0.6</td>
<td>−0.1742</td>
<td>12.24§</td>
<td>41</td>
<td>C3 (13.95§), nC4 (25.08§) VFA</td>
<td>(Tahir et al., 2020)</td>
</tr>
<tr>
<td></td>
<td>CC-Coated Ni nano wire</td>
<td>S. ovata</td>
<td>−0.4</td>
<td>−0.63</td>
<td>3.4</td>
<td>82 ± 14</td>
<td>−</td>
<td>(Nie et al., 2013)</td>
</tr>
<tr>
<td></td>
<td>Si-TiO$_2$ nanowire photo cathode</td>
<td>S. ovata</td>
<td>−0.59</td>
<td>−3.5</td>
<td>86 ± 9</td>
<td>−</td>
<td>−</td>
<td>(Liu et al., 2015a)</td>
</tr>
<tr>
<td></td>
<td>3D Graphene Ni-foam</td>
<td>Mix culture from MFC</td>
<td>−0.69</td>
<td>−92</td>
<td>−</td>
<td>80</td>
<td>nC4, i-C4, nC6 VFAs and their alcohols</td>
<td>(Vassilev et al., 2018)</td>
</tr>
<tr>
<td></td>
<td>Porous Ni hollow fiber with MWCNTs</td>
<td>S. ovata</td>
<td>−0.4</td>
<td>−0.33</td>
<td>1.85</td>
<td>83 ± 8</td>
<td>−</td>
<td>(Iwan et al., 2018)</td>
</tr>
<tr>
<td></td>
<td>NiMo deposition on doped Si wafer</td>
<td>S. ovata</td>
<td>−0.7</td>
<td>−10</td>
<td>6.7§</td>
<td>95-100</td>
<td>−</td>
<td>(Knacke et al., 2019)</td>
</tr>
<tr>
<td></td>
<td>NiMo deposition on doped Si wafer</td>
<td>A. woodii</td>
<td>−0.7</td>
<td>−10</td>
<td>6†</td>
<td>−100</td>
<td>−</td>
<td>(Knacke et al., 2019)</td>
</tr>
</tbody>
</table>

§ Projected surface area based current densities, ‡ unit in g L$^{-1}$ d$^{-1}$, † calculated from the provided graphs of the products, ‡ calculated from g L$^{-1}$ d$^{-1}$ value. CE: Coulombic efficiency, VFAs-Volatile fatty acids; ng-not given, 3D-Three dimensional, RVC-reticulated vitreous carbon, GC-Carbon cloth; SS-Stainless steel; AC-Activated carbon; WWTP-Wastewater treatment plant; EtOH-Ethanol; VFA C3-propionate, nC4-n-Butyrate; i-C4-isobutyrate; nC6-n-Caproate; MWCNT-Multi-walled Carbon nanotube, rGO-reduced graphene oxide, PEDOT:PSS-poly(3,4-ethylenedioxythiophene):polystyrene sulfonate polymer.
matter (for example, acetate/HCO$_3^-$, $E^0 = -0.28\ V$ vs. SHE), instead of the energy-demanding water splitting ($H_2O/O_2$, $E^0 = 0.82\ V$ vs. SHE). Since MES has been proposed to purify the biogas (mainly CH$_4$ and CO$_2$) from anaerobic digestion (AD) (Jourdin et al., 2016a) and the digested effluent from AD usually contains high strength of persistent organic substances (Ihara et al., 2006), combining bioanodes with biocathodes in MES for AD effluent treatment and biogas upgrading, respectively, could enhance the role of AD in circular bioeconomy and help reduce the energy input in MES by replacing the anodic OER reaction (Katuri et al., 2019). The utilization of bioanode has recently been reported in MES reactors with a bipolar membrane (Xiang et al., 2017), however, no details about the anode potential was provided. Another study reported that the bioanode potential could reach as low as $-0.2\ V$ vs. SHE to generate electron/proton with higher current density compared with abiotic anode in MES (Tian et al., 2019). Both studies reported a COD removal efficiency of $> 45\%$ and a coulombic efficiency of over $60\%$, demonstrating the feasibility of integrating bioanode in MES systems for both treating wastewater and reducing energy input.

Apart from electron generation via organic oxidation at bioanode (Bian et al., 2018b; Sadvukhan et al., 2016), some reduced inorganic compounds (for example, $S^2-$, $HS^-$) could also serve as electron donors through anodic oxidation at lower overpotentials. Sulfide has been converted by microbes to sulfur with electron generation to reduce the anodic overpotential in BESs (Gong et al., 2013; Ni et al., 2019; ter Heijne et al., 2018). The electrochemical oxidation of $S^2-$ is shown below (Ni et al., 2019):

$$\text{HS}^- \rightarrow \text{S}_2(\text{aq}) + 2e^- + \text{H}^+ , \ E_{\text{anode}} = -0.262\ V \text{ vs SHE (pH} = 9.1\text{M Na}^+)$$

(3)

It is obvious that sulfide oxidation is much more thermodynamically favorable than OER and CIER as shown above. Recent studies showed the electron transfer from sulfide to bioanode inoculated with sulfide-oxidizing bacteria (SOB) at anode potential of 305 mV (ter Heijne et al., 2018) or 503 mV vs SHE (Ni et al., 2019). Sulfide-driven MES process at 503 mV vs SHE has been successfully demonstrated using SOB-inoculated (*Desulfobulbus propionicus* and *Desulfuromonas*) bioanode (Gong et al., 2013).

3. MES cathodes to utilize CO$_2$ as a resource for chemical production

MES cathode represents the core of MES system as it is the central platform for CO$_2$ recycling and biochemical production. One of the key elements affecting the chemical production from CO$_2$ in MES is the selection of cathode materials because it governs the electroactivity and biocompatibility. Chemically stable cathodes with low cost, high conductivity, high HER capability, and large biocompatible surface area for cell adherence/biofilm formation are preferable for CO$_2$ reduction in MES (Aryal et al., 2017a).

The proof of principle for microbial CO$_2$ reduction at the cathode was reported with a graphite stick cathode using *Sporomus ovata* as biocatalyst (Nevin et al., 2010). The planar graphite block as a cathode in MES was not able to achieve high acetate production due to its limited surface area for biofilm development. A number of MES cathodes made from carbonaceous, metallic, and carbon-metallic materials have been recently developed in MES. These materials can come in different configurations including planar (such as cloth, plate, and rod) and porous 3D configuration (such as foam and felt). Porous 3D materials with large specific surface area can enhance microbial-electrode interaction and substrate mobility within the electrode even without surface modification (Jourdin et al., 2018). Other configurations such as flow through (Bajracharya et al., 2017d; Jourdin et al., 2018) and gas diffusion cathodes (Alqahtani et al., 2018; Bajracharya et al., 2016) are also beneficial in enhancing CO$_2$ reduction rate in MES. To further enhance the cathode-microbial interactions, cathode surface modifications have been employed (Bian et al., 2018a; Jourdin et al., 2014; Zhang et al., 2013). An overview of different cathode materials for CO$_2$ reduction in MES is presented in Table 2.

Modifications in cathode surface are intended to enhance the electrocatalytic activity and microbial cell adherence to the cathode. For example, carbon cloth electrode after modification with chitosan, an amino and hydroxyl-group rich polysaccharide, increased the acetate production rate by 7.6 folds (Zhang et al., 2013). Production of acetate from CO$_2$ reduction was boosted as a result of CO$_2$ adsorption on the porous chitosan, enhanced electron transfer pertaining to biocompatible cathode surface, and better interaction between the positive charges on chitosan and the negative charges on the external surface of bacteria. Besides, carbon nanomaterials have been widely used for the enhancement of conductivity, specific surface area and biocompatibility of MES cathodes. Multi-walled carbon nanotube (MWCNT) coating on reticulated vitreous carbon (RVC) was first utilized to efficiently provide a high specific surface area for bacterial growth and the corresponding acetate production (Jourdin et al., 2014). The high conductivity of the RVC-based cathodes induced by MWCNTs also led to ~100% electron recovery in MES (Jourdin et al., 2015). Modifying the carbon-based electrode with reduced graphene oxide (rGO) also improved the CO$_2$ reduction rates using *S. ovata* (Chen et al., 2016), enhancing the acetate formation by 11.8 times as compared to the unmodified carbon cloth cathode in MES (Chen et al., 2016). Likewise, metal–carbon complex cathodes were also applied in MES for CO$_2$ reduction. Nickel (Ni) nanowire (Nie et al., 2013), Fe$_3$O$_4$ (Cui et al., 2017) and Fe$_3$O$_4$ (Zhu et al., 2019) were reported to combine with carbonaceous materials as MES cathodes and contribute to the enhanced CO$_2$ reduction rates in MES due to the improved electrocatalytic property of cathode material. A photocathode based on silicon-titanium oxide nanowires (Si-TiO$_2$ NWs) has also been specifically designed to enrich *S. ovata* cells, which resulted in 4.4 ± 1.0 times higher cell loading compared to the planar Si electrode (Liu et al., 2015a).

In addition to cathode surface modifications, there is a need to design a better cathode architecture to address the mass transfer limitation in MES (See Table 2). Gas diffusion electrode (GDE) made from activated carbon and Polytetrafluoroethylene (PTFE), VITO-CoRe®, was thus employed in MES. The VITO-CoRe® GDE provided a gas–liquid–solid interface for the CO$_2$ diffusion, which improved CO$_2$ mass transfer (Bajracharya et al., 2016). Likewise, a forced flow-through configuration of carbon felt cathodes enhanced the production rates in MES by improving the mass transfer and electrode surface area (Bajracharya et al., 2017d; Jourdin et al., 2018). Remarkably, three layers of non-modified carbon felts as the flow-through cathode at $-0.85\ V$ vs SHE produced the highest rate of acetate production at $371 \pm 5\ g\ m^{-2}\ d^{-1}$ (Jourdin et al., 2018). This system also produced longer chain organic compounds such as n-butyrate and n-caproate at the rate of $160 \pm 29\ g\ m^{-2}\ d^{-1}$ and $46 \pm 1\ g\ m^{-2}\ d^{-1}$, respectively.

In the latest modification of cathode architecture to address CO$_2$ mass transfer limitation, direct CO$_2$ supply in dual-functional porous Ni-hollow fiber (Ni-HF) membrane cathode was demonstrated to enhance the bioelectrochemical CO$_2$ reduction in MES (Alqahtani et al., 2018; Bian et al., 2018a). Almost 84% of the electrons were recovered as methane via CO$_2$ delivery through Ni-HFs, achieving almost 4 times higher CO$_2$ conversion efficiency compared to CO$_2$ sparging into MES electrolyte (Alqahtani et al., 2018). A follow-up study depositing MWCNT on the surface of Ni-HF further confirmed the superiority of direct CO$_2$ delivery to chemolithoautothrophs on the cathode, with greatly enhanced CO$_2$ adsorption capacity and reduced electron transfer resistance, which led to higher acetate production from CO$_2$ using *S. ovata* compared to the unmodified Ni-HF (Bian et al., 2018a). The direct CO$_2$ delivery through porous hollow fiber electrodes created high CO$_2$ availability at the MES cathode surface, which resulted in higher production of methane and acetate from CO$_2$.

CO$_2$ concentration and bubble sizes may also bring variations in the performances of CO$_2$ utilization and bacterial growth in MES. The effect
of CO₂ concentration, flow rate and bubble size on CO₂ fixation was analyzed in tubular microalgae-bioreactors, and the results showed that higher CO₂ concentration induced higher cell concentration and photosynthesis productivity (Ryu et al., 2009). The authors also observed higher bacterial growth with smaller CO₂ bubble sizes ranging from 31 mm to 61 mm by using smaller pore size (5–10 μm) spargers, which could be attributed to the enhanced gas–liquid interfacial area by reducing the bubble size and thus enhancing mass transfer. The CO₂ bubble size could be further reduced using porous membrane electrodes with small pore sizes (< 1 μm), which can lead to better CO₂ mass transfer and availability will be enhanced, but the local pH at the electrode surface could be adjusted by direct CO₂ delivery through the porous membrane cathodes in MES. The pH level in MES utilizing bicarbonate as the carbon source usually increases with time, as protons are consumed to produce VFAs, methane or hydrogen (Ganigie et al., 2015). Acetate production in MES was analyzed with stepwise change in media pH (from 6.7 to 3) and the largest acetate production value was reported at a pH of 5.2 (Jourdin et al., 2016a). It is evident that a slightly acidic environment (pH 5–6) promotes the production of multi-carbon VFAs and inhibit the methane generation at the cathode (LaBelle et al., 2014). Since CO₂ sparging into media was reported to be able to create slightly acidic pH (Bajracharya et al., 2016), continuous CO₂ sparging along with bicarbonate in medium could be an excellent alternative for maintaining pH at 5–6 in MES. Considering all these findings, the future developments on cathode architecture in MES could focus more on porous membrane electrodes for direct gas delivery and small bubble production in order to achieve high CO₂ concentrations, fast mass transfer and slightly acidic pH at the cathode surface (Katuri et al., 2018).

4. Chemolithoautotrophs at MES biocathodes for CO₂ reduction

Chemolithoautotrophs can use H₂, formate, sulfide and reduced metal ions as electron donors for CO₂ reduction through Wood–Ljungdahl (WL) pathway, reverse tricarboxylic acid passing through hydroxypropionate/hydroxybutyrate pathways. Reduced electron donors, especially H₂, could be generated through HER at the cathode surface when sufficient reductive potential is imposed under electrochemical settings. In addition, microorganisms may uptake electrons directly from the cathode. Direct uptake of electrons from the cathode has been reported for some species of methanogens (Walker et al., 2019) and homoacetogens for CO₂ fixation via WL pathway (Alqahtani et al., 2019). Genome analysis revealed novel halophilic homoacetogens for CO₂ fixation via WL pathway (Alqahtani et al., 2019). The operation of MES system under saline conditions might be advantageous for scaling up as seawater is abundant and can be used as highly conductive electrolyte to reduce ohmic resistance. Selecting a robust and effective CO₂ reducing communities from saline environments, that are diverse in microbial composition such as salt marsh, mangrove, and deep sea sediments, can be useful for MES study in this aspect.

5. Diverse products obtained from CO₂ using MES platform

In general, acetate is the most common bioproduct generated from CO₂ conversion in MES. However, some other products such as butyrate, oxo-butyrate, ethanol, iso-propanol have also been produced as minor products (Ganigie et al., 2015; LaBelle et al., 2014; Nevin et al., 2011). More reduced products were formed as a result of further reduction of the accumulated acetate produced in MES (Sciarrà et al., 2018). Production of ethanol from CO₂ was reported using S. ovata pure culture when the condition became highly reductive with excess availability of hydrogen (Blanchet et al., 2015). Microbial chain elongation could be thus initiated to produce up to C4-C8 products at the presence of acetate and ethanol (Batlle-Vilanova et al., 2017). The production of longer chain fatty acids from acetate needs ethanol as an electron donor, but in MES under highly reductive condition the cathode or hydrogen also serves as an electron donor for chain elongation (Steinbusch et al., 2011). Ethanol could be produced as an intermediate through the reduction of acetate using hydrogen as depicted in Fig. 3a. Van Eerten-Jansen et al. (Van Eerten-Jansen et al., 2013) first reported the chain elongation of acetate to caproate (C6) using cathode as the electron donor.

Acetate and other VFAs produced from CO₂ in MES could be the precursor compounds for the bioproduction of other raw chemicals. Production of butyrate (0.16 g L⁻¹ d⁻¹) as the main product from CO₂ reduction was reported in MES (Ganigie et al., 2015). Butyrate production rate from CO₂ in MES was increased to 0.21 g L⁻¹ d⁻¹ under microbial adaptation (Batlle-Vilanova et al., 2017). Butyrate and caproate production rates reached as high as 160 ± 29 g m⁻² d⁻¹ and 46 ± 1 g m⁻² d⁻¹, respectively, when the acetate production was as high as 370 g m⁻² d⁻¹ in continuous mode using forced flow-through carbon felt cathode (Jourdin et al., 2018). Various other VFAs and alcohols have been discovered in MES and production rates have been enhanced with improvements in cathode material and configuration (Table 2). The aforementioned results demonstrate that MES is an attractive approach to supply in-situ electrons or H₂ for electrode-driven chain elongation process at the cathode.

MES as a production platform becomes attractive in the context of circular economy when the production can be established at high rate, and the end-product can be diversified to special and economically valuable commodities. In CO₂ reduction via Wood-Ljungdahl (WL) pathway, acetyl-CoA is a central precursor that may undergo further metabolic conversion to generate various commodity chemicals such as ethanol, butyrate, lactate, 2,3-butanediol and butanol under the appropriate conditions (Schiel-Bengelsdorf and Durre, 2012). Solventogenesis metabolism can be introduced into the MES process by changing operational conditions to produce respective alcohols from VFAs
(Vassilev et al., 2018). In addition, lactate (C3) and succinate (C4) could also be generated from the intermediate products of CO2 reduction through Krebs cycle (Venkata Mohan et al., 2016). The perspective of production of various value-added products from CO2 by integrating MES with chain elongation mechanism and other bioconversion systems is depicted in Fig. 3b. Such perspective presents the MES as the producer of precursory compounds such as H2, CH4 and acetate/short chain fatty acids (SCFA) which can be further upgraded to longer chain carboxylates, biofuels, bioplastics, polysaccharides and protein with multi-step bioconversions (Chu et al., 2019). For example, CH4 produced in MES can be used as a feedstock in syngas platform to produce methanol, formaldehyde, and ethylene (Verbeeck et al., 2018). In case of acetate production in MES along with other SCFAs, further upgrading has been reported mainly via chain elongation platform to produce butyrate and caproate as mentioned above (Jourdin et al., 2018). In other approaches of further conversion of SCFAs, production of poly-hydroxyalkanoates and single-cell proteins (SCPs) has been reported (Alloul et al., 2018; Molitor et al., 2019).

6. Integrating renewable energy and chain-elongation platform to reduce energy consumption in MES

The economics of bioelectrochemical CO2 reduction to different products (formic acid, acetic acid and oxalic acid) in terms of cost-

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Fig. 3. (a) A scheme of direct CO2 delivery through the pores on hollow fiber membrane electrode for the generation of diverse bioproducts from CO2 with different microbes. (b) The prospect of producing high-value products in MES from CO2 by further bioprocessing of primary products. (PHB: Poly-hydroxybutyrate, PHA: Poly-hydroxyalkanoates) (c) MES platform for biochemical/biofuel production and methane upgrading through integration with other bioprocesses.
effectiveness, energy and raw material costs has recently been analyzed (ElMekawy et al., 2016). Since acetate is the main product of current MES studies, the discussion on economic analysis is focused mainly on acetate production. In summary, if CO2 is converted to acetate at a rate of 10 g m−2 h−1, one MES stack with a cathode surface area of 45 m2 could reduce 3.94 tons of CO2 and generate 5.37 tons of acetic acid annually. Considering the electricity cost of 406 EUR/ton of acetic acid generated with 30% electrical efficiency (ElMekawy et al., 2016), the total electricity cost for one MES stack is around 2180 EUR/year, which is close to the cost for the annual replacement of electrodes and membrane materials (50 EUR/m2). It is worthwhile to mention that the energy cost does not include the energy-intensive processes for acetic acid extraction. To make MES economically viable technology for scale-up, it is necessary to significantly lower the energy consumption required for MES operation and product separation/extraction.

As mentioned above, microbial CO2 reduction at the cathode could be achieved by applying a low cathode potential (< ~0.4 V vs SHE). Also, cost-effective OER catalysts or photo/bio-assisted anode could be utilized to drive efficient electron generation at the anode surface and significantly reduce the energy consumption. Apart from these strategies for reducing energy consumption for MES operation, utilizing renewable energy to replace the traditional electricity input could be another option for future MES scale-up and sustain artificial photosynthesis (Zhang et al., 2013). The increasing abundance and reduced cost of renewable electricity for solar (US$0.04–0.06 kWh−1) approaching parity with fossil fuels, make CO2 transformation via MES attractive. To make MES economically viable technology for scale-up, it is necessary to significantly lower the energy consumption required for MES operation and product separation/extraction.

### Table 3
Materials and energy input for VFA extraction via (bio)-electrochemical systems.

<table>
<thead>
<tr>
<th>Cathode</th>
<th>Membrane</th>
<th>Product</th>
<th>Energy input for extractiona (kWh kg−1)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon felt</td>
<td>CEM &amp; AEM</td>
<td>Acetate</td>
<td>19</td>
<td>(Gildemyn et al., 2015)</td>
</tr>
<tr>
<td>Carbon felt</td>
<td>CEM &amp; AEM</td>
<td>Acetate</td>
<td>26.5</td>
<td>(Gildemyn et al., 2017)</td>
</tr>
<tr>
<td>Carbon felt</td>
<td>CEM</td>
<td>Acetate</td>
<td>44.3</td>
<td></td>
</tr>
<tr>
<td>Carbon felt</td>
<td>BPM</td>
<td>Acetate</td>
<td>30.7</td>
<td></td>
</tr>
<tr>
<td>Graphite felt</td>
<td>AEM</td>
<td>Acetate</td>
<td>–20.5</td>
<td>(Back et al., 2018)</td>
</tr>
<tr>
<td>316 SS</td>
<td>10 bipolar</td>
<td>Acetate</td>
<td>6.3</td>
<td>(Prochaska et al., 2018)</td>
</tr>
<tr>
<td>10 AEM</td>
<td>1 CEM</td>
<td>Acetate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>316L SS</td>
<td>AEM</td>
<td>C2-C6</td>
<td>2</td>
<td>(Andersen et al., 2015)</td>
</tr>
<tr>
<td>Ti mesh</td>
<td>AEM &amp; CEM</td>
<td>Acetate, Butyrate Propionate</td>
<td>5.43</td>
<td>(Pan et al., 2018)</td>
</tr>
<tr>
<td>Pt coated Ti plate</td>
<td>10 AEM &amp; CEM</td>
<td>VFAs</td>
<td>0.395</td>
<td>(Bak et al., 2019)</td>
</tr>
<tr>
<td>SS felt</td>
<td>AEM</td>
<td>Caproic acid</td>
<td>2</td>
<td>(Khor et al., 2017)</td>
</tr>
<tr>
<td>SS mesh</td>
<td>AEM</td>
<td>n-Capric/caprylic acid</td>
<td>4.08 ± 0.66</td>
<td>(Xu et al., 2015)</td>
</tr>
</tbody>
</table>

a Calculated based on the energy consumption per kg of the product extracted from bioreactors. CEM - cation exchange membrane, AEM - anion exchange membrane, AC - activated carbon, BPM - bipolar membrane.
and butyric acid (> $3.5/kg) (Baroi et al., 2017), and lower water solubility than acetate. Extraction of medium-chain fatty acids is preferable, since it requires much less energy input (< 2 kWh/m3) compared to acetate extraction (Table 3). The chain-elongation from acetate could be conducted either in MES reactors (Battle-Vilanova et al., 2017; Vassilev et al., 2018) or in separate fermentation reactors after microfiltration of MES effluent. Membrane liquid–liquid extraction unit using hollow fiber membranes pretreated with 6% dodecanol has been recently applied for butyrate extraction from MES reactor (Battle-Vilanova et al., 2017). Acetate was chain elongated to butyrate, with ethanol serving as electron donors in the MES reactor. An excellent butyrate selectivity (16.4) over acetate was achieved, demonstrating the potential application of chain-elongation technology in MES to reduce the energy cost for VFA extraction. A minimum power consumption of 4.08 ± 0.66 kW h kg⁻¹ product extracted was achieved for the separation of medium-chain carboxylic acids after chain elongation using membrane electrolysis, which was far lower compared to the energy input for acetate extraction using the same technique (Xu et al., 2015). Khor et al. (2017) further lowered the energy consumption for caproic acid extraction (2 kWh kg⁻¹ carboxylic acid extracted) using membrane electrolysis in a fermentation system for the electricity-assisted production of caproic acid from grass. All the results above clearly exhibited the sharp decrease in energy consumption for bioproduct extraction after chain elongation. Hence, such production and extraction system developed out of MES would be relevant in supporting circular bioeconomy. Even though the caproate production rate in MES is yet slower than that in AD through chain-elongation (Journin et al., 2018), MES could serve as a complementary technology to AD in the future, if it fully utilizes its anode compartment for wastewater treatment and increases its profitability (Reddy et al., 2018).

### 7. Future perspectives

Transition from the linear model of material and energy production and consumption to a circular bioeconomy is a key aspect in maintaining environmental sustainability for the future. The MES platform could incorporate the use of renewable electricity for CO₂ recycling and commodity production, showing a promising prospect for electricity-driven bioproduction of short and medium chain fatty acids from CO₂ employing acetogenic bacteria as biocatalysts. MES can further play a complementary role in attaining circular CO₂/bio-based economy (Fig. 3c), if we can overcome some limiting factors to its application such as high operating costs and low product specificity as discussed recently by Prévôteau et al. (2020).

To bring MES to the level of industrial application, the CO₂ conversion rates have to be significantly improved, which could be achieved in three aspects as follows:

1. Ensuring sufficient CO₂ availability and electron donors will enhance the enrichment of chemolithoautotrophs. Development of porous membrane electrodes and gas diffusion electrodes in MES systems has been shown to be effective for CO₂ delivery to the biofilm (Alqahtani et al., 2018; Bian et al., 2018a). Higher CO₂ concentration and smaller CO₂ bubbles have been proven to achieve higher mass transfer coefficient, which improved the CO₂ utilization efficiency and bacterial growth (Ryu et al., 2009). Therefore, electrically conductive and catalytic porous membrane and gas diffusion electrodes could be utilized to bring MES technology closer to commercialization. However, several operation conditions, such as gaseous CO₂ flow rates, bubble size and gas diffusion at the cathode-microbe-media interface, that are believed to greatly enhance the MES performance, should be optimized before introducing this type of cathode architecture into large-scale industrial application.

2. Gaining a better understanding of electron transfer mechanisms from the cathode to chemolithoautotrophs is required to develop better strategies for enhancing VFA production rates from CO₂ reduction. Direct electron transfer (DET) from the electrode to chemolithoautotrophs appears to be thermodynamically more favorable than indirect electron transfer via the electrochemically evolved hydrogen. However, the coexistence of both electron transfer mechanisms is highly probable in mixed culture biocathodes. Therefore, a clear understanding of the dominant mechanism (i.e., direct versus H₂-mediated electron transfer) in MES is important for the rational design of cathode. For example, if direct electron transfer is dominant, then biocompatible cathodes with high specific surface area are needed for bacterial attachment, whereas for H₂-mediated electron transfer, the cathode design can be modified by introducing more active sites for better HER.

3. The selection of highly-efficient chemolithoautotrophs is of high priority. Genetic engineering of appropriate microbes could be one good option. For example, the acetogen *Clostridium ljungdahlii* was metabolically engineered for the production of more valuable bio-commodities (such as butyrate) from H₂:CO₂ (Ueki et al., 2014). Microorganisms present in saline habitats such as mangrove and salt marsh are excellent habitats for CO₂ fixing species and are playing an important role in carbon cycling (Alqahtani et al., 2019). Thus, saline environments could potentially become an ideal location to discover novel and efficient CO₂ fixing communities that can potentially produce useful products with diversity in metabolism.

The energy cost for MES operation may pose another challenge for scaling-up MES. Several strategies could be adopted to reduce energy input, such as the integration of renewable energy sources to MES, reduction of anodic OER overpotential using low-cost and effective catalyst, utilization of saline electrolyte to reduce ionic losses, and chain elongation of SCFA to medium chain fatty acids (MCFAs) for easy extraction. Further research on electricity-driven microbial chain elongation is required to develop MCFAs production process with high efficiency, reliability and controllability. However, a comprehensive energy analysis should be conducted to identify energy consumption from the different components in MES.

Future aspects of improvement in MES from CO₂ also include the use of hybrid systems, comprising of autotrophs for CO₂ reduction and heterotrophs for further conversion of products after CO₂ reduction (Fig. 3b). Similarly, hybrids of autotrophs at the biocathode with heterotrophs at the bioanode can be used to achieve energy saving with simultaneous treatment of organic waste streams. Integration of MES with established biotechnologies, such as AD and fermentation, is a promising alternative for future development (Jiang et al., 2019).

### 8. Conclusion

This report summarized the recent development of MES platform for the synthesis of bioproducts from CO₂. To lower the energy consumption, comprehensive strategies were proposed for efficient anodic electron generation and bioproduct extraction. Apart from the common requirements of high surface area and excellent bacterial adhesion, MES cathodes with direct CO₂ delivery and highly-efficient chemolithoautotrophs were developed to improve the bioproduct formation. The application of MES systems is suggested in the scenario of joint development with renewable energy, wastewater treatment, anaerobic digestion and fermentation, so that a circular bioeconomy of CO₂ reduction and diverse chemical production could be achieved.

**CRediT authorship contribution statement**

Bin Bian: Visualization, Writing - original draft. Suman Bajracharya: Visualization, Writing - original draft. Jiajie Xu: Writing - original draft. Deepak Pant: Writing - review & editing. Pascal Salkal: Conceptualization, Supervision, Writing - review & editing.
Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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