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Izadi, Paniz; Harnisch, Falk. «Microbial | electrochemical CO₂ reduction : To integrate or not to integrate?». *Joule*, Vol. 6, Issue 5 (May 2022), p. 935-940.
DOI 10.1016/j.joule.2022.04.005

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Microbial | Electrochemical CO₂-reduction - to integrate or not to integrate?!

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Calling for technology platforms to turn carbon dioxide into feedstock

Carbon dioxide (CO₂) has to turn from waste to feedstock for establishing a circular economy. Albeit there is consensus that chemicals and fuels for consumer goods will be based on the carbon that was recently CO₂, one can only surmise the technology platform(s) to reach such an industrial transformation. Certainly, the current petro-based industries will not be simply replaced by one technology. Rather a broad portfolio of platforms comprising physical, chemical and biological technologies can be expected to allow development towards a true circularity of (bio)chemical synthesis. Among these are platforms based on interweaving microbial and electrochemical synthesis¹. Microbial synthesis based on the immediate utilization of CO₂ as a feedstock in gas fermentation, for instance, suffers from low solubility of gaseous compounds in liquid phase. It limits the accessibility of CO₂ and/or H₂ for microbial cells and therefore conversion efficiency². Electrochemistry allows using electric and not chemical energy to exploit CO₂ for synthesis. Yet, the electrochemical CO₂-reduction reaction (CO₂RR) is characterized by its low product portfolio that is commonly limited to C₁- or C₂-compounds³, but possesses high kinetics, particularly when compared to biological CO₂-reduction⁴.

Therefore, combining or *integrating* microbial conversions with CO₂RR for synthesis seems very appealing. Integration may allow harnessing the best of both and hence using nothing but electric energy and CO₂ for creating a broad portfolio of products.

Microbial electrochemical synthesis from carbon dioxide

Microbial electrochemical synthesis (MES) is based on interfacing of electrochemical and microbial transformations to allow the purposeful transformation of a feedstock into a desired product¹. MES can be based on the activity of autotrophic microorganisms that reduce CO₂ using cathodic electrons or hydrogen. Despite a first hype and significant research on MES from CO₂, its development stagnates and seems to face insurmountable hurdles. The main obstacles are limited electron transfer rates and hence reaction rates, limited product portfolio, insufficient yields as well as long time required for developing a cathodic microbial electrocatalyst and hence production start-up⁵.

Synthesis from CO₂ can also be based on less immediate interfacing of microbial and electrochemical reactions. Through CO₂RR, first CO₂ is electrochemically reduced to yield formate (HCOOH) or other C₁-compounds, which are already established feedstocks for microbial syntheses. Hence, one can foresee that in addition to using formatotrophs (formate consuming microorganisms) for synthesis, strain engineering will make formate an excellent feedstock for several production hosts, including yeasts⁶. Integration of CO₂RR *to formate* with microbial synthesis *from formate* was first reported by Li et al⁷. Since then a significant development took place that concerned electrochemical and microbial engineering of components as well as process engineering.

There is more than one way to integrate

When integrating CO₂RR and microbial synthesis, different approaches are feasible. The integration can occur *in situ* that is in one compartment (Figure 1a). CO₂ is converted to formate by CO₂RR proceeding at the cathode and linked to synthesis by microorganisms. Here the synchronisation of the CO₂RR and microbial synthesis rates is a challenge. To avoid disturbing CO₂RR at the electrode, microorganisms that form no biofilm thereon are favourable. The microorganisms submerged are also more appealing in terms of volumetric production rates and yields, especially when exploiting co-cultures of different microorganisms, which allows creating food webs for gaining complex products. It is noteworthy that often the main or only electrochemical side-product is H₂ that is an ideal energy source for many microbial catalysts.

Alternatively, CO₂RR to formate proceeds spatially separated from the microbial synthesis (Figure 1b and 1c). The solution composition can be critical, as it needs to balance the requirements of both process steps and thus provide (optimal) conditions for CO₂RR and microbial synthesis. A challenge can be inhibition of CO₂RR by bio-products. Using two separate reactors (Figure 1b) including inline separation of the microbial products and reusing the solution for CO₂RR can overcome this. Solution design can be especially challenging as some compounds vital for microbial growth or a pH required for microbial growth and activity can hamper CO₂RR⁴. In this line the purity of the gaseous CO₂-feed is also of relevance, for instance when assuming an industrial feed of flue gas containing impurities (e.g. traces of O₂ or sulphur compounds).

As well as chemical compounds, biomass can be detrimental for CO₂RR when present at the electrode and be affected by the electrochemical reaction. Thus, biomass removal, e.g. filtering, is advantageous when integrating separate reactors. In addition, a small share of impurities (e.g. O₂) in the feed gas can be tolerated by CO₂RR. We are confident that engineering allows to balance the operational conditions for CO₂RR and microbial synthesis as required, albeit controlling operational conditions such as pH for integrated processes remains challenging. Alternatively, the electrochemical and biological reactions can be fully separated (Figure 1c). This separation allows decoupling two process steps in space and time. As CO₂RR and microbial synthesis are fully independent, they do not affect each other and the solutions can be optimized for the respective process step. Further, it allows concentration as well as amendment, for instance with trace elements, of the solution containing CO₂RR products before supplying to a bioreactor.

The rate of CO₂RR and microbial synthesis can be disconnected in time when both are spatially fully separated (Figure 1c), whereas only a spatial separation requires synchronization to some extent (Figure 1b) and particularly full synchronization is required when operating in one compartment (Figure 1a). At the first glance, separated processes may be further advantageous by allowing precise control of the feed of formate to the bioreactor. This is in particular advantageous, as high formate concentration can be toxic as well as high concentration of the bio-products. The latter can be removed using downstream processing (DSP). Although the toxicity threshold of formate is different (ranging from <100 mM for weak (e.g. *E.coli*) to >100 mM for those with strong (e.g. yeasts) formate dehydrogenases), higher concentration than the threshold causes decline of biosynthesis⁶. However, when using locally separated process steps (Figure 1b, 1c), concentration gradients in the bioreactor do already limit the microbial synthesis. This requires improved mass transfer such as increased energy consuming agitation or implementation of baffles⁸. We argue that this limitation can be elegantly and economically overcome by using an appropriate electrode and reactor design for *in situ* integration, e.g. implementation of three-dimensional electrodes as discussed below.

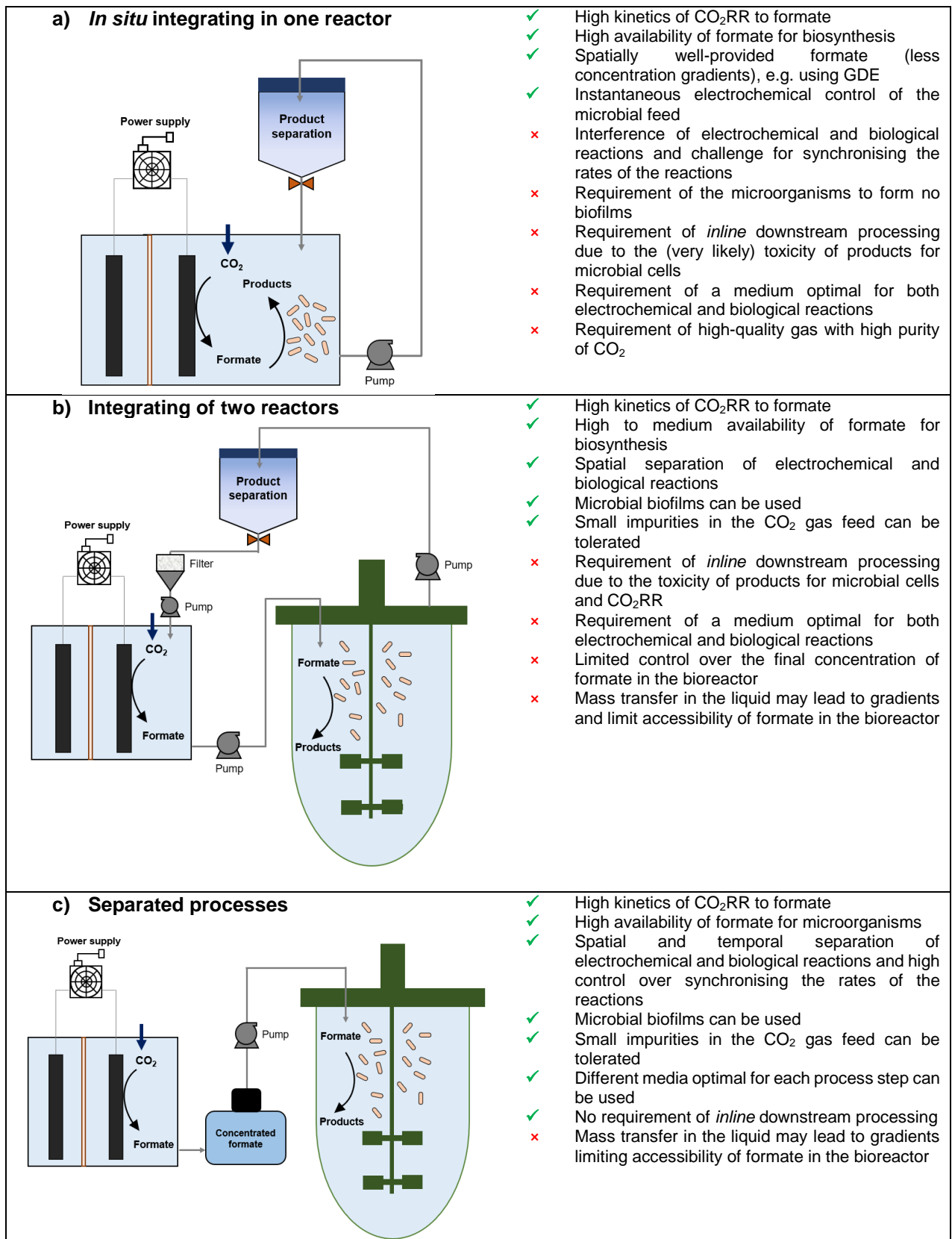


Figure 1. Schematic of the potential reactor designs for CO₂-reduction reaction (CO₂RR) and further microbial synthesis to value-added products a) integrated in one reactor (*in situ*) including product recovery, in which CO₂RR and microbial synthesis occur in the cathodic compartment of an electrochemical reactor, b) integrated in two reactors including product recovery in which CO₂RR and microbial synthesis occurring spatially separated in a cathodic compartment and a bioreactor, and c)

separated processes, in which CO₂RR and microbial synthesis occurring spatially as well as temporarily separated in a cathodic compartment and a bioreactor, linked with the concentrated formate stage.

It seems a long way down, but worth it!

We are confident that the above illustrated integration can become economically competitive, with their main assets being the kinetics of CO₂RR leading to a low ratio of the needed active electrode surface area to reactor volume and the product diversity of microbial synthesis. The main competitor will be gas fermentation from syngas (from CO/H₂O or CO₂/H₂). However, the solubility of gaseous feedstock is limited (e.g. 28mg L⁻¹ CO, 1.6mg L⁻¹ H₂ and 1.7g L⁻¹ CO₂, 293K and 1atm⁸), and hence is setting boundaries to bio-production, especially in a large scale. Here we foresee a clear advantage for the *in situ* integration (Figure 1a) in case high surface three-dimensional electrodes are used. Among these three-dimensional electrodes, gas diffusion electrodes (GDEs) seem most promising to us due to their role in not only enhancing the CO₂ mass transfer in aqueous media, but also decreasing the internal resistance by removing the bubbles covering the active surface areas of the electrodes when feeding CO₂ directly in the aqueous media⁹. In GDE, CO₂ feed is transported through the gas diffusion layer⁹ (Figure 2) allowing permanent availability of CO₂ directly at the electrochemical reaction sites. The higher solubility of formate than CO₂ in aqueous solution in turn assures the increased availability of feed for microbial synthesis. Further, the energetic efficiency of bioconversion using formate is higher compared to H₂/CO₂ (e.g. +80-90% compared to +60-80% in anaerobic acetogens)¹⁰. In addition to formate, production of other C₁-compounds such as methanol from CO₂RR can be achieved. Methanol is more energy-rich than formate and has been known as an established feedstock for microbial syntheses¹⁰. The selectivity of the products from CO₂RR strongly depends on the electrode materials. For instance, while indium (In) or tin (Sn) (also Hg, Cd, etc.) are known for catalysing CO₂RR to formate, oxidation state of copper (Cu₂O) or addition of other metals to copper (e.g. Cu₃Pt or Cu₃Pd) can form methanol (although at different potentials).

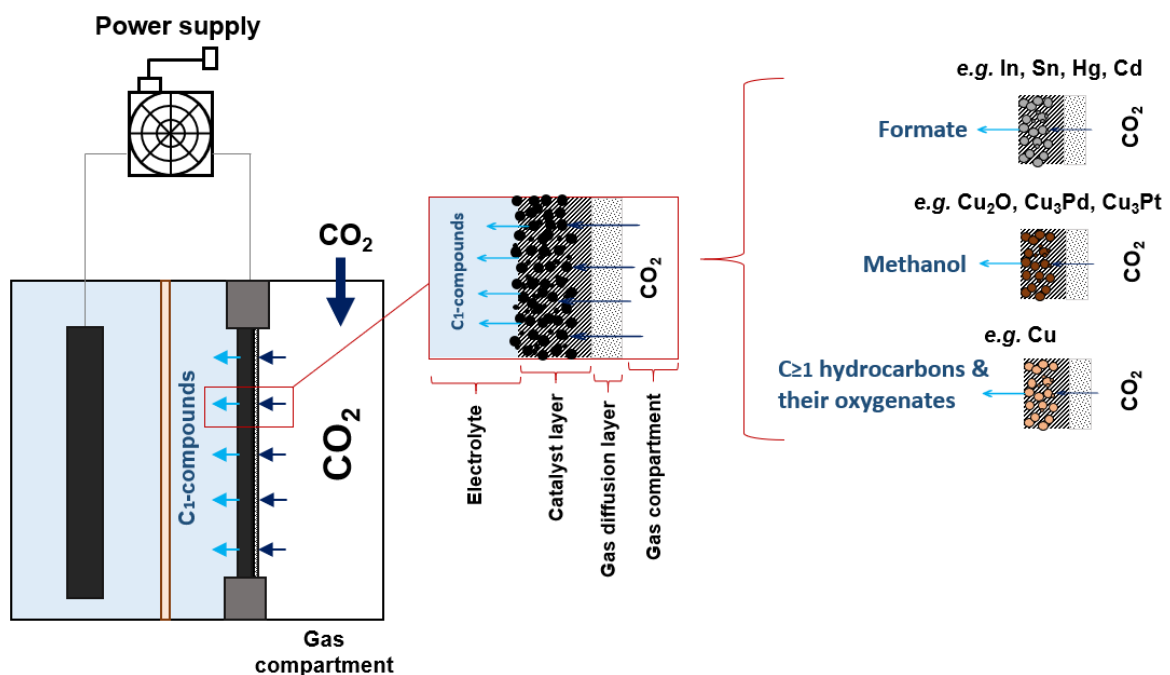


Figure 2. Schematic of CO₂-reduction reaction to C₁-compounds in an electrochemical reactor using a gas diffusion electrode (GDE) and different electrocatalysts.

There are a number of external costs that needs to be considered when developing processes for a bio-based and circular economy from lab-bench to industrial reality. Product recovery through DSP such as extraction is required in any presented process design for turning CO₂ and electric power to chemical products or fuels. Yet, it is of special importance for the designs with solution recirculation due to the potentially toxic effect of bio-products (Figure 1a and 1b). For instance, high concentration of microbial produced carboxylic acids and their effect on the pH can have damaging effects on the cell membrane resulting in growth inhibition. Production of longer chain carbon products than C₁-compounds such as terpenes, drugs or even proteins not only increases the economic and energetic value but also makes the separation of the products more convenient. In addition to DSP, the quality of the gas feed is important particularly in the designs based on interfacing electrochemical and biological reactions (Fig. 1a and 1b). Even when the electrochemical reactor is separated from the bioreactor (Figure 1c), impurities such as high percentage of oxygen can affect the CO₂RR⁴. The flue gas from cement industries, for instance, includes sulphur oxides (SO_x) and nitrogen dioxides (NO_x) in addition to dust and oxygen¹¹ which could disturb the electrochemical and microbial reactions and hence decrease the overall efficiency. In this case, an extra gas-purification is required leading to increase in operational costs. CO₂ purification and compression from flue gas of cement industry through three different methods were calculated to require 256 – 466 kJ kg_{clinker}⁻¹ energy¹¹.

As of today, ethanol and butanol produced by bio-based technologies are considered as a potential alternative to fossil-based transportation fuels. Syngas fermentation in an industrial scale is developed and pursued by some companies such as LanzaTech and its joint partner of Shougang group (Chinese Steel company), Genomatica, Kiverdi, IneosBio and Coskata^{12,13}, in particular for ethanol production (although IneosBio and Coskata stopped operation due to the operational and financial difficulties¹³). To make syngas fermentation even more economically and operationally feasible for industry, remarkable efforts were taken resulting in significant achievements over the past years. Different designs such as multi-stage fermentation or gas-liquid enhanced bioreactor for ethanol production have been patented¹³. Although COVID-19 pandemic decreased the ethanol production in 2020, ethanol biorefineries are remaining major drivers in clean ethanol production in U.S.A., Brazil, and certain parts in Asia and Europe¹⁴. Despite the pandemic, 2.7 million tons of CO₂ were captured in 2021 for ethanol biorefineries which was used for further applications such as bottling and food processing. Production of other compounds than ethanol from syngas fermentation, such as acetate, isoprene or 3-hydroxypropionate using genetically modified microorganisms were also patented¹³. In spite of the growing progress observed in such biological syntheses, organic electrochemical syntheses on industrial scales seem not as mature. Thus far, electrochemical synthesis of valuable chemicals such as adiponitrile (a key-intermediate for production of nylon-6,6) is established since decades and used in industrial scales for instance in Japan (Asahi Chemical in Nobeoka)¹⁵. Electrochemical organic synthesis has the advantages of high product selectivity and purity, simple integration with renewable energies as well as with biosynthesis due to the ambient temperature and pressure required for its operation, low number of reaction steps and few polluting side-products. However, its limited application in industry especially without a known integration with developed biological synthesis in large scales can be seen as the consequence of several limits being in place up to now. These limits comprise missing suitable resources and manufacturing technologies, considered excessive costs for capital expenditures, especially for changing and implementing in existing production lines, lack of scientists and engineers being educated for integrating microbiology and electrochemistry, and lack of the collaboration between research and governmental sectors. To benefit from the electrochemical routes for production of diverse value-added organic compounds from CO₂ using renewable energies, strong partnerships between universities and research institutes, as well as industry and government are required. We are confident these partnerships on the long run will create values for society as well as shareholders.

ACKNOWLEDGEMENT

The authors acknowledge the support of the VIVALDI project that has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement N°101000441. This work was supported by the Helmholtz Association in the frame of the Integration Platform "Tapping nature's potential for sustainable production and a healthy environment" at the UFZ.

AUTHOR CONTRIBUTIONS

The idea of this article and the manuscript were conceived and written by P.I. and F.H.

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Falk Harnisch holds a Full Professorship at Leipzig University for Electrobiotechnology and is a group leader at the Helmholtz-Centre for Environmental Research – UFZ, Germany. He received his PhD from Greifswald University, Germany in 2009 as well as several fellowships and awards and is currently serving as a President of the International Society for Microbial Electrochemistry and Technology (ISMET). His research ranges from fundamentals of microbial electrochemistry via electroorganic synthesis to engineering of microbial electrochemical technologies.