Trends in Chemistry

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Forum

Electrifying biosynthesis for CO_2 upcycling

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The integration of electrochemical and microbial processes offers a promising and sustainable approach for upcycling CO_2 into valuable long-chain chemicals using renewable energy sources. This Forum highlights some of the remarkable progress and emerging strategies in projecting electrobiochemical systems and examines their prospects to realize the electricity-driven manufacturing industry.

Why electrocatalysis + biosynthesis?

Fossil fuels are central to modern industrial society, but meanwhile the emissions of greenhouse gases such as carbon dioxide (CO_2) from burning fossil fuels have overdrawn the future of humankind by warming the climate. Towards achieving a circular carbon economy and weaning industry from dependence on fossil carbons, CO_2 upcycling goes mainstream, with the ultimate goal of sustainable production of advanced chemicals, pharmaceuticals, and food [1]. The rapidly growing availability of cheap electricity from renewable sources has given electrocatalysis unprecedented potential to produce valuable chemicals via upcycling of CO_2 and to compete with traditional processes that mostly rely on fossil fuels. However, the extensive utility of electrocatalysis is substantially impeded – it hardly achieves carbon–carbon chain propagation – giving rise to a limited product spectrum confined to C_1–C_3 species [2]. By comparison, biological carbon utilization technologies, taking advantage of metabolic rewiring, can selectively produce long-chain compounds, but with slow production rates and narrow substrate scope [3,4]. To expand the product portfolio and improve production rates, a hybrid system that combines scalable electrocatalysis and biological upgrading shows promise [5,6]. The electrobiochemical system (Figure 1), which amalgamates the superior features of the respective functions and takes advantage of both electrochemistry and synthetic biology, affords a pliable platform to upcycle CO_2 into products that are both virtuous and profitable.

Electrobiochemical systems have evolved over the past years following several generic strategies, and they can be categorized based on how electrochemical and biological processes are integrated [7]. Directly attaching the microbes to the electrode allows either direct electron transfer to the attached microbes or *in situ* consumption of the electrogenerated compounds. Alternatively, the electrochemical and biological processes are spatially decoupled, wherein the mediator compounds are first produced from electrolysis and then consumed by the microorganisms for carbon chain growth. To establish a competitive process to produce current fossil-fuel-derived commodities, it is important to understand the fundamentals of electro/biochemistry, to evaluate the most promising integration method, and to identify the bottlenecks of electrobiochemical production at a realistic scale.

Direct microbial electrosynthesis

Electricity-driven microbial conversion is usually referred to as microbial electrosynthesis, where the microbes are directly attached to the electrode [8]. Such microorganisms can take up electrons from electrodes and use them in their metabolism to convert CO_2, excreting a reduced chemical as an electron sink. Generally, microbial electrosynthesis for carbon fixation can be categorized into two electron-transfer pathways: microbes utilize electrical power through either direct electron transfer from the electrode or mediated electron transfer by *in situ* consumption of reduced species (e.g., H_2) [7]. Direct attachment of microbes to the electrode enables feasible electron transfer, thus favoring a high energy efficiency of up to 90% [9]. Still, the mechanism of electron transfer between electro/biochemical interfaces remains elusive. Over the past decades, several microbial electrosynthesis systems have been developed that demonstrate prominent capability for the conversion of CO_2 into acetate, isobutanol, and 3-methyl-1-butanol, to name a few [6,7]. Nevertheless, this approach is restricted in the selection of electroactive microorganisms, most of which are anaerobic microbes undertaking the reductive acetyl-CoA pathway [9], resulting in a limited product spectrum. Moreover, microbial electrosynthesis often suffers from disparities in operating conditions and rates between electrochemical and biological components, resulting in a lower current density in the range 1–20 mA cm^{-2} [10]. A simple back-of-the-envelope calculation by Bar-Even and coworkers suggested that this constraint would be almost impossible to overcome [7], highlighting the importance of developing spatially decoupled electrochemical and microbial processes.

Decoupling electrochemical and microbial processes

In a decoupled electrobiosystem, electrochemical and microbial processes are independently operated, whereby the intermediate products produced by electrocatalysis are fed to the microbes cultured in a separate space. The production rates and energy conversion efficiencies of the two processes can be individually optimized and then coupled. Besides the disparity in operation mode, microbial growth via organic substrates or electrical current as reducing power also appears to differ from a metabolic standpoint. Generally, microbes feeding

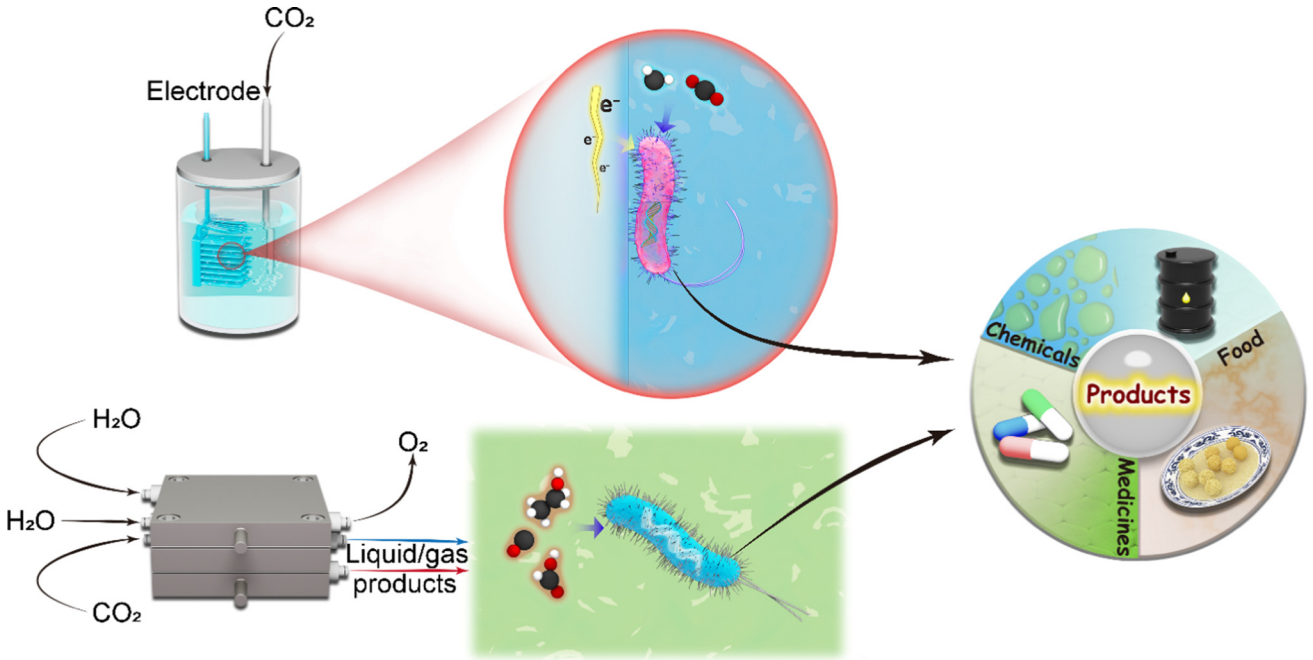

Figure 1. Schematic illustration of CO_2 upcycling via the hybrid electrobiochemical system to produce valuable products such as advanced chemicals, pharmaceuticals, and food. Electrobiochemical systems can be categorized into two integration modes: directly attach the microbes to the electrodes; or spatially decouple the electro/biochemical processes. These electrobiochemical systems, with further technological advances, open a tantalizing possibility of electricity-driven manufacturing industry.

on organic substrates allow the simultaneous production of reducing equivalents NADH and NADPH as well as ATP via well-known biochemical pathways [11]. For electricity-energized microbes, issues may arise concerning the formation of NADPH and ATP, depending on whether the metabolism is lithoautotrophic or heterotrophic [11]. Because the compatibility issue is no longer considered for microbial growth in a decoupled system, it offers more flexibility for the engineering of cell factories, which greatly expands the product spectrum.

Electron carriers

As the nexus between electrochemical and microbial processes, intermediate products, also termed electron carriers, are highly critical to the feasibility and overall efficiency of a decoupled system. Therefore, it requires the cooperation of the two fields to identify the most appropriate electron carriers that make both processes feasible and practical. Attempts have been made by Schmid and coworkers using syngas from the CO_2 electrolyzer as the electron carrier, which was converted to a butanol/hexanol mixture in a fermentation module (Figure 2A) [12]. However, the insolubility of gaseous CO/H_2 limits mass transfer and constrains productivity. In this regard, soluble electron carriers are much more favorable. We thus suggest that formate or methanol may represent a more promising electron carrier, although their fermentation is limited in some cases due to the formation of formaldehyde, a toxic intermediate that is detrimental to biological metabolism [9].

Acetate is a soluble electron carrier that can be electrochemically produced from CO_2 and is more readily metabolized by a wide array of microorganisms. In light of this, Xia and coworkers previously showcased a tandem system combining a two-step CO_2 electrolysis with yeast fermentation, where the resulting acetic acid from the CO_2 electrolyzer is directly fed to the yeast, generating glucose or free fatty acids (Figure 2B) [13]. In this case, by virtue of the solid-electrolyte reactor, the out-coming aqueous acetic acid is pure and concentrated, enabling an exemption from separation from the electrolyte salts that would otherwise deactivate cell growth. Likewise, Jiao and colleagues proposed a two-step CO_2 electrolyzer to produce a highly concentrated acetate stream, allowing its direct use for the heterotrophic cultivation of yeast, fungus, and green alga in the dark [14]. Despite this progress, the diffusion of acetate or formate in protonated acid across the cell membrane will lead to undesirable dissipation. The same problem should be alleviated in the case of alcohol. Nevertheless, high-purity and concentrated alcohols are not yet available from CO_2 electroreduction due to the low Faradic efficiency and stability, as well as the unavoidable mixing of electrolyte salts.

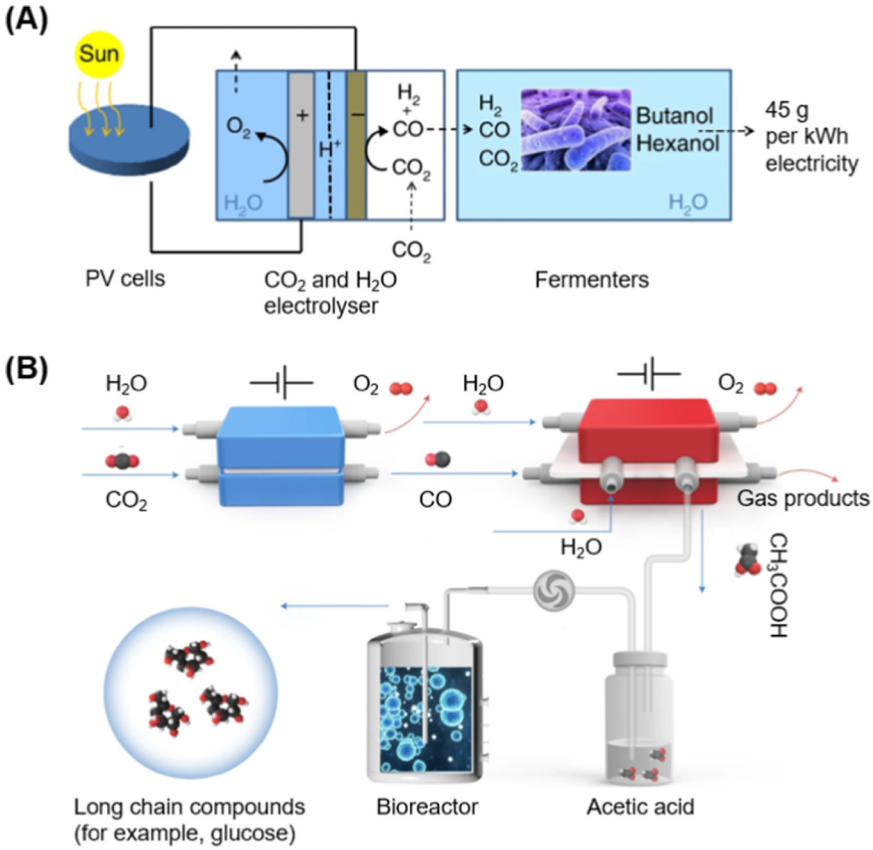

Figure 2. Schematic illustration of the decoupled electrobiosystem with gas or liquid electron carriers. (A) Sketch of the modules used in technical photosynthesis of 1-butanol and 1-hexanol from CO_2 and H_2O. Syngas was first produced by solar-powered electrochemical reduction of CO_2 and H_2O and then fermented to butanol and hexanol [12]. Reproduced, with permission, from [12]. (B) Sketch of the *in vitro* artificial sugar synthesis system from CO_2 and H_2O. CO_2 was first converted to pure and aqueous acetic acid through two-step electrolysis, which was then directly fed for microorganism fermentation in a bioreactor to produce long-chain compounds; for example, glucose [13]. Reproduced, with permission, from [13].

Concluding remarks and perspectives

Although significant progress has been made in understanding the fundamental principles of the integration of electrochemical and biochemical processes, most of the research remains limited to laboratory-scale and proof-of-concept studies. To scale these technologies, there is still a long way to go. Nevertheless, the pilot success of biological fermentation, as in the case of LanzaTech [15], imparts confidence in the pursuit of developing a practical and cost-efficient electrobiochemical system. From the perspective of large-scale production, the direct attachment of microbes to electrodes suffers from various constraints that would be almost impossible to conquer. However, their studies remain vital to leverage understanding of microbial metabolism. As things stand, decoupling of the electrochemical and biological units seems the most viable option for practical use. A gratifying point, we believe, is that it broadens the boundaries of this field, to invite more valuable inputs from talents beyond electrochemists who understand biology or biologists who excel in electrochemistry.

The projection of a robust and profitable decoupled system is nontrivial and will require comprehensive considerations from a variety of disciplines. We argue that CO_2 electrolysis should be operated in a technoeconomically feasible manner. On the other hand, the electrogenerated carbon feedstock is expected to be very pure, concentrated, and nontoxic, such that microbes can directly feed on it at a high consumption rate. Through ongoing technological advances in the design of highly efficient catalysts and scalable reactors, opportunities are granted for the electrofixation of CO_2 into carbon substrates at the rates and concentrations needed. The engineering of microbial fermentation at a practical scale appears to be another tough challenge. Efforts are necessary for metabolic rewiring to increase microbial tolerance to harsh environments (e.g., pH, temperature, salt). Moreover, expansion of the growing genetic toolbox of microorganisms or the use of multiple parallel electron carriers as feedstock is anticipated to improve energy efficiency and widen the scope of products [7]. Furthermore, rationally devising fermentation reactors for continuous cultivation is crucial to dictate the overall cost-effectiveness and sustainability of bioproduction [10]. We believe that with continued refining and scaling of electrobiochemical platforms, the vision of electricity-driven agriculture and industry will be translated into reality in the near future.

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Declaration of interests

The authors have no interests to declare.

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