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Economic and sustainable revolution to facilitate one-carbon biomanufacturing

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One-carbon (C1) biomanufacturing serves as a substitute for fossil-based feedstocks, aiming to de-fossilize chemical production and foster a circular carbon economy by recycling waste greenhouse gases. Here, we review the key economic and technical barriers associated with the commercialization of C1 biomanufacturing through case studies. Additionally, a viable roadmap to enhance cost competitiveness is unveiled, underscoring its potential to facilitate carbon neutrality as scalable and sustainable alternatives to traditional chemical production.

The historical development of chemical engineering has been fundamental to industrial advancement. Pioneering chemical engineers significantly advanced the field by founding large-scale chemical facilities. These plants have grown essential in several sectors of society, acting as a foundational element of the industry. They have facilitated the commercial manufacture of a diverse range of chemicals, materials, and products that are vital for modern society[1]. However, the current chemical production processes rely heavily on fossil resources, resulting in a surge of carbon dioxide (CO_2) emissions and resource depletion[2]. The global economy is connected by fossil fuels, operating under a linear model: from extraction to production, followed by consumption, and ultimately disposal (Fig. 1). In light of growing environmental awareness, it is imperative to pursue alternative circular pathways for a smoother transition from traditional petroleum-based processes to renewable and sustainable routes that can yield the same products. A strategic shift towards recycling of wastes, notably one-carbon (C1) feedstocks, can pave the way for bio-based chemical production, supporting the de-fossilization of chemical processes and enhancing production safety[3].

Biomanufacturing utilizes biological systems, including microbes and enzymes, to produce valuable compounds, presenting the potential to substitute fossil-derived chemicals and materials with renewable and drop-in alternatives, while simultaneously sequestering carbon. C1 substrates have emerged as preferred feedstocks in the biomanufacturing sector, gaining attention for their natural abundance, cost-effectiveness, and potential to reduce the impacts of climate change, particularly when accessed as industrial by-products[4]. This shift represents a promising strategy for achieving sustainable and eco-friendly chemical production, as shown in Fig. 1. A sustainable system employing C1 resources can be integrated into circular processes with minimal waste. The formation of a circular bioeconomy reliant on C1 feedstocks requires the development of entirely novel industrial processes. However, the implementation of C1 resource upcycling technologies is currently limited to laboratory or pilot scales, hampered by various techno-economic challenges[5]. Addressing these barriers requires the development of sustainable, cost-effective solutions along with collaboration among key stakeholders[6].

To effectively design a sustainable and economically viable future based on the upcycling of C1 resources, it is essential to focus on two primary objectives (Fig. 1): (1) identifying and addressing the techno-economic driving forces that hinder the industrialization of biomanufacturing from C1 substrates; and (2) developing strategies to mitigate the environmental risks associated with this technological transition.

Feedstock resources

C1 feedstocks, which primarily include CO_2, carbon monoxide (CO), methane (CH_4), and methanol (CH_3OH), play a crucial role as carbon substrates in biomanufacturing[7]. Third-generation (3G) biomanufacturing focuses on converting atmospheric CO_2 and renewable energy sources, such as waste streams and solar power, into valuable products. For example, CH_3OH can be electrochemically produced from CO_2 using renewable energy, while CO can be harvested from syngas derived from waste gases, like those from steel mill. Nature has

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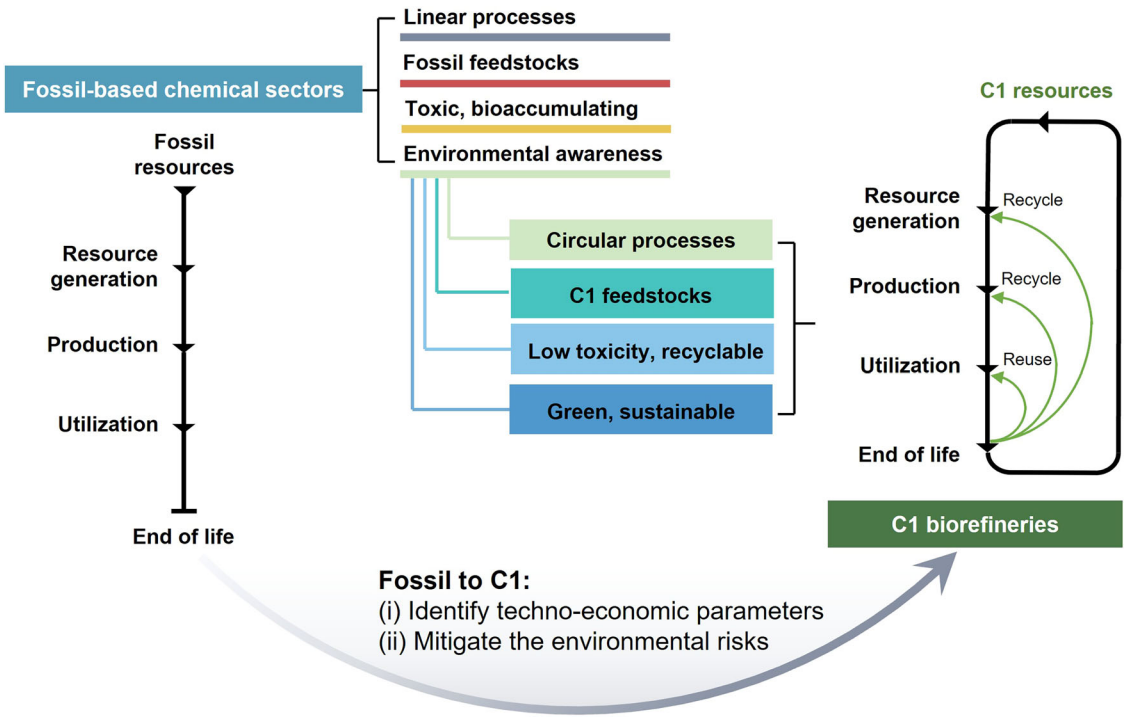

Fig. 1 | Transition from fossil-based chemical routes to circular one-carbon (C1) biomanufacturing. Fossil-based chemical sectors follow a linear path from resources to end of life, marked by fossil feedstocks, toxicity, and environmental awareness. In contrast, circular C1 processes focus on low-toxicity, recyclable, and sustainable practices. The transition to C1 involves identifying economic parameters and reducing environmental risks, as depicted by the shift from linear to circular processes.

evolved numerous complex mechanisms for C1 bio-fixation, with numerous established and proposed pathways[8,9]. C1 biomanufacturing harnesses these feedstocks through the utilization of natural or genetically engineered microorganisms to create valuable chemicals, fuels, and materials. The typical process for C1 biomanufacturing, as illustrated in Fig. 2a, involves various stages including feedstock pretreatment, bioconversion or electro-bio-conversion, product separation, and waste management[10].

Recent advancements in metabolic engineering, synthetic biology, and fermentation technologies are enhancing the feasibility of C1 biomanufacturing on larger scales[11,12]. Efforts have been dedicated to transition these processes from laboratory researches to pilot and ultimately industrial applications[13]. Achieving this goal requires the implementation of techno-economic analysis (TEA) and life cycle assessment (LCA) to evaluate the technical, economic, and environmental aspects associated with the development of novel technologies. As outlined in Fig. 2b, we developed a systematic workflow for synthesizing desired products from C1 feedstocks, integrating advanced analytical tools and computational models. This framework is further validated by robust TEA and LCA case studies, which evaluate the feasibility and environmental impact (Supplementary Methods 1–3). To enable scalable commercialization, C1 biomanufacturing will advance through iterative experimental validation phases. Each phase incorporates TEA and LCA grounded in the n^{th}-plant concept[14], ensuring economic viability and sustainability at industrial scale. This study not only highlights the potential of C1 biomanufacturing but also serves as a framework for guiding future research and commercialization.

Economic barriers to industrialization

To assess and evaluate C1 biomanufacturing for producing platform chemicals and to identify the principal economic obstacles to industrialization, we selected established C1 biomanufacturing case studies and conducted a comprehensive TEA and LCA, as depicted in Fig. 2b. 3-hydroxypropionic acid (3-HP) is a significant building block and platform chemical, functioning as a valuable monomer and precursor for bioplastic synthesis[15,16]. Numerous microbiological strains have exhibited the capacity to synthesis 3-HP[17,18], prompting several corporations to develop pilot facilities for its production; however, commercialization has not yet been realized[15]. The potential cost-effectiveness and environmental benefits of bio-based 3-HP synthesis make its practical implementation highly anticipated. Hence, we propose two sustainable synthesis routes for producing 3-HP from C1 feedstocks (Fig. 3): (1) a two-stage biological system utilizing steel mill off-gas[17], and (2) an integrated hybrid approach combining electrochemical conversion of atmospheric CO_2 to methanol with subsequent microbial conversion to 3-HP[18] (Supplementary Figs. 1–3, Supplementary Tables 1–9, Supplementary Notes 1–2). The latter route employs solar-driven renewable energy to power electricity-generating green hydrogen, a key reactant for transforming CO_2 into methanol. This methanol then serves as the substrate for microbial biosynthesis of 3-HP, establishing a fully renewable pathway[19]. Production parameters for both routes are derived from validated laboratory or pilot-scale data[17–21], with detailed assumptions on yield, energy inputs, and costs provided in Supplementary Tables 1 and 2.

Low carbon yield of C1 utilization

Despite noteworthy advancements in utilizing C1 feedstocks for biomanufacturing via engineered microorganisms or electrocatalyst technologies, the overall carbon conversion rate remains inadequate for meeting the techno-economic requirements essential for industrialization. A number of reviews have thoroughly examined various conversion technologies and provided examples for C1 valorization[22–24]. Our results derived from Aspen Plus, a widely recognized process modelling software, demonstrate that the C1 feedstock-to-chemical conversion efficiency for both bio-cascade and electro-bio-cascade routes remains below 10% (Supplementary Fig. 4 and Supplementary Note 3), relatively lower than the efficiency achieved

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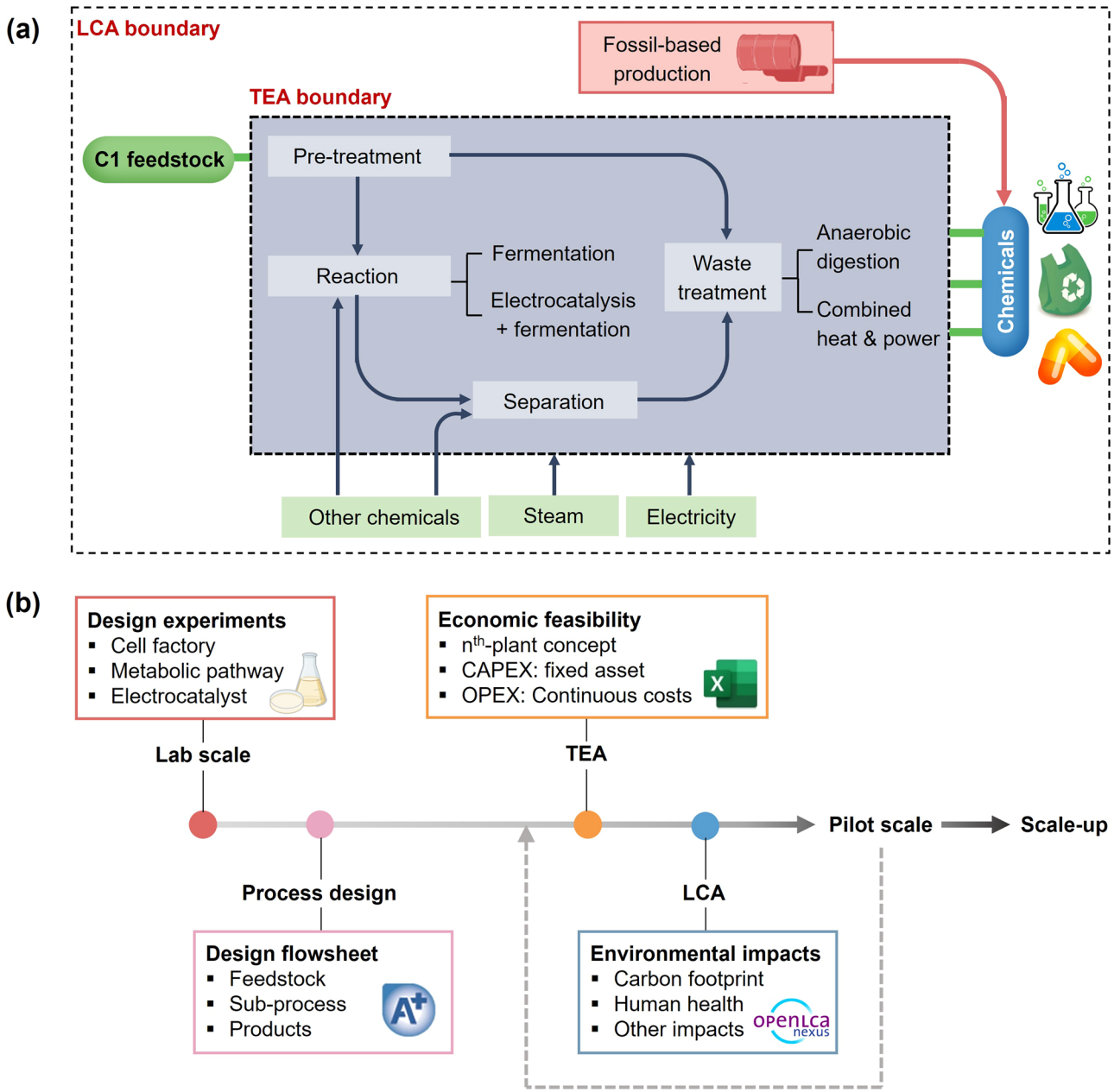

Fig. 2 | One-carbon (C1) industrial biomanufacturing with techno-economic analysis (TEA) and life cycle assessment (LCA). a illustrates the process flow of chemical production within a biomanufacturing setup with different sections of pre-treatment, reaction, separation, and waste treatment, bounded by TEA and LCA. **b** outlines the development stages from lab-scale experiments to commercial scale-up, focusing on process design, economic viability evaluated by TEA, and environmental impacts assessed through LCA. CAPEX capital expenditures, OPEX operating expenditures.

by conventional fossil-derived routes[25]. While C1 utilization offers considerable potential, the challenges of low carbon yields must be addressed for the successful transformation of traditional petroleum refinery systems into 3G biomanufacturing.

From a techno-economic standpoint, the low carbon-to-product yield in C1-to-chemical systems presents a major barrier to economic viability. This issue leads to increased capital expenditures (CAPEX) by requiring larger-scale infrastructure to offset productivity losses as additional (Supplementary Figs. 2 and 3, Supplementary Note 4). For example, the scale of sterilization infrastructure necessary for bioreactors and associated pipelines must expand proportionally to meet the rising demand for increased bioreactor capacity driven by low carbon yield. Moreover, limited carbon yields need a greater supply of C1 raw materials to produce equivalent quantities of chemicals, directly inflating total operating expenditures (OPEX). Economic analyses of converting C1 feedstocks into fuels or chemicals through biological fermentation consistently underscore the need for significant investment in bioreactors[10,26–28], which represent the largest expenditures in equipment and installation. For instance, the fermentation-related equipment in our case study accounted for the highest equipment costs in the production of acrylic acid from CO, more than 92% (Supplementary Figs. 5 and 6, Supplementary Tables 10 and 11, Supplementary Note 5). The expenses associated with fermentation systems are closely tied to the productivity of the target product and the operational fermentation volume required. Optimizing the performance of cell factories to enhance carbon conversion efficiency represents a promising avenue for improving yields and minimizing costs related to bioreactor procurement[26,29].

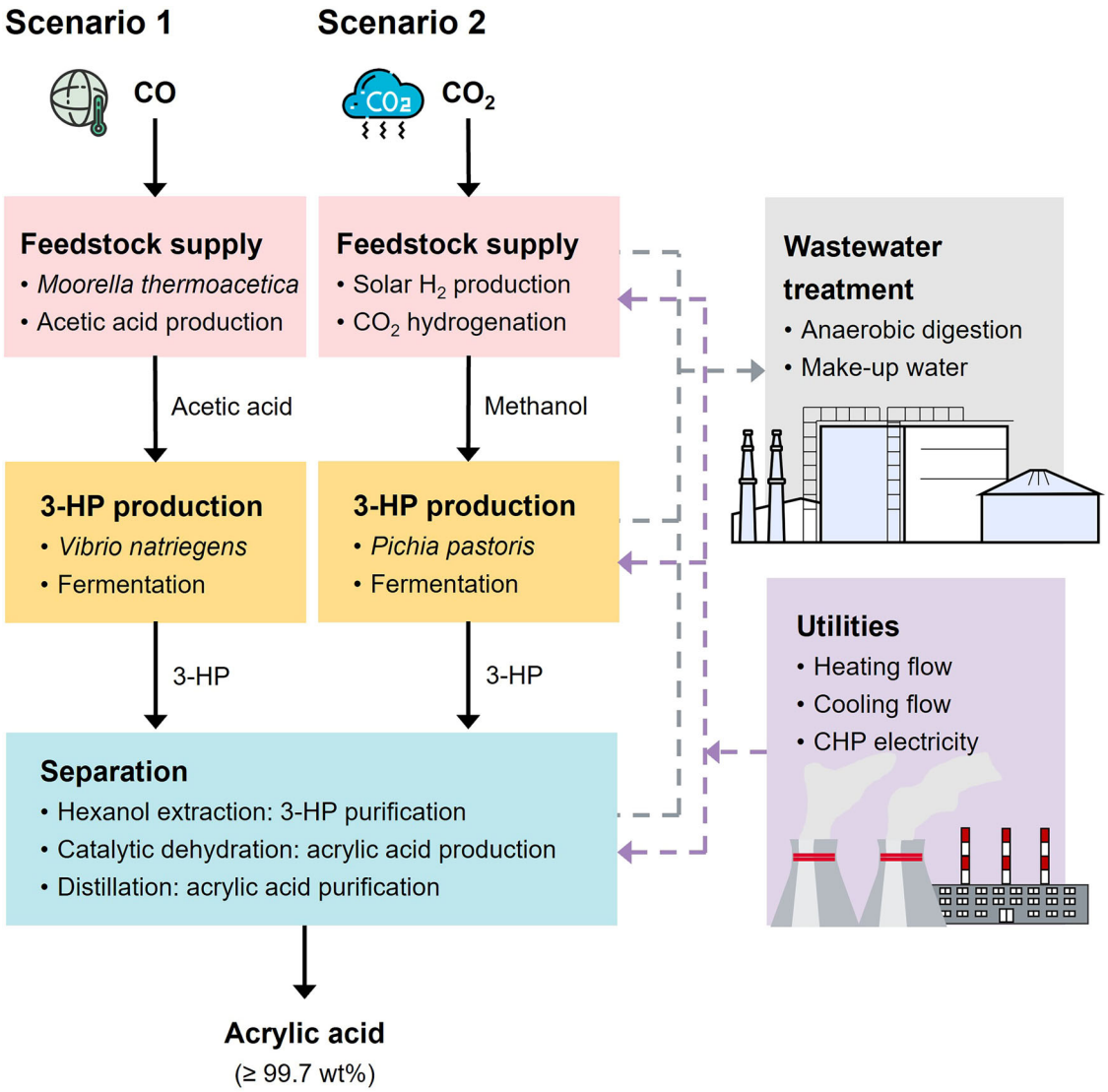

Fig. 3 | Comparative flowchart for producing acrylic acid from different one-carbon (C1) feedstocks. Scenario 1 uses carbon monoxide (CO) to make acetic acid, then producing 3-hydroxypropionic acid (3-HP) via fermentation. Scenario 2 utilizes carbon dioxide (CO_2) and solar hydrogen (H_2) to produce methanol, which is bioconverted to 3-HP. Both employ the same purification process yielding high-purity acrylic acid with considering wastewater treatment and utilities for efficient operation. CHP combined heat and power.

Variable and costly C1 feedstocks

Before advancing with the industrialization of C1 biomanufacturing, it is crucial to assess the availability of feedstocks. In contrast to the established supply chain for crude oil, C1 biomanufacturing encounters challenges due to the decentralized nature of C1 resources. A thorough economic analysis is essential prior to scaling up operations in order to address regional variations in availability and quantity effectively. For instance, the production of stranded CH_4 from various industrial sources in the United States varies significantly, with wastewater treatment plants averaging less than one ton per day and landfills averaging 31 tons per day[10]. The variations result in variable market potentials for the same technology, driven by economies of scale. Larger production capacities tend to be more cost-effective, emphasizing that the variability in availability or composition of C1 feedstocks introduces greater economic risks compared to conventional petrochemical refineries, which benefit from a centralized and continuous supply chain.

In addition, the pricing of chemicals is sensitive to fluctuations in raw material costs, with fossil-based chemicals often following change in the prices of their crude oil-derived precursors[30,31]. In traditional biomanufacturing, the cost of raw materials, including sugar-based feedstocks from the 1st generation and biomass-based feedstocks from the 2nd generation, accounts for around 50% of the total OPEX of a biomanufacturing[32,33]. Likewise, our research finds that the expense of CO and CO_2 feedstocks accounts for the predominant share (exceeding 57%) of OPEX (Supplementary Figs. 5 and 6, Supplementary Tables 12 and 13). The preceding discussion indicates that the advancement of technology enabling the utilization of waste streams as raw materials will enhance the economic viability of C1 biomanufacturing by providing a more cost-effective feedstock source[34], such as food waste[26], municipal solid waste[35,36], and biomass[34,37].

Advancing forwards economic viability

The utilization of C1 feedstocks as carbon substrates for chemical production holds significant potential for improving sustainability. However, current investment priorities continue to favor conventional petroleum refineries, which benefit from superior cost competitiveness, reliable material supply chains, and lower financial risks. Nowadays, chemicals derived from C1 feedstocks currently face a higher minimum selling price than that of fossil-based alternatives

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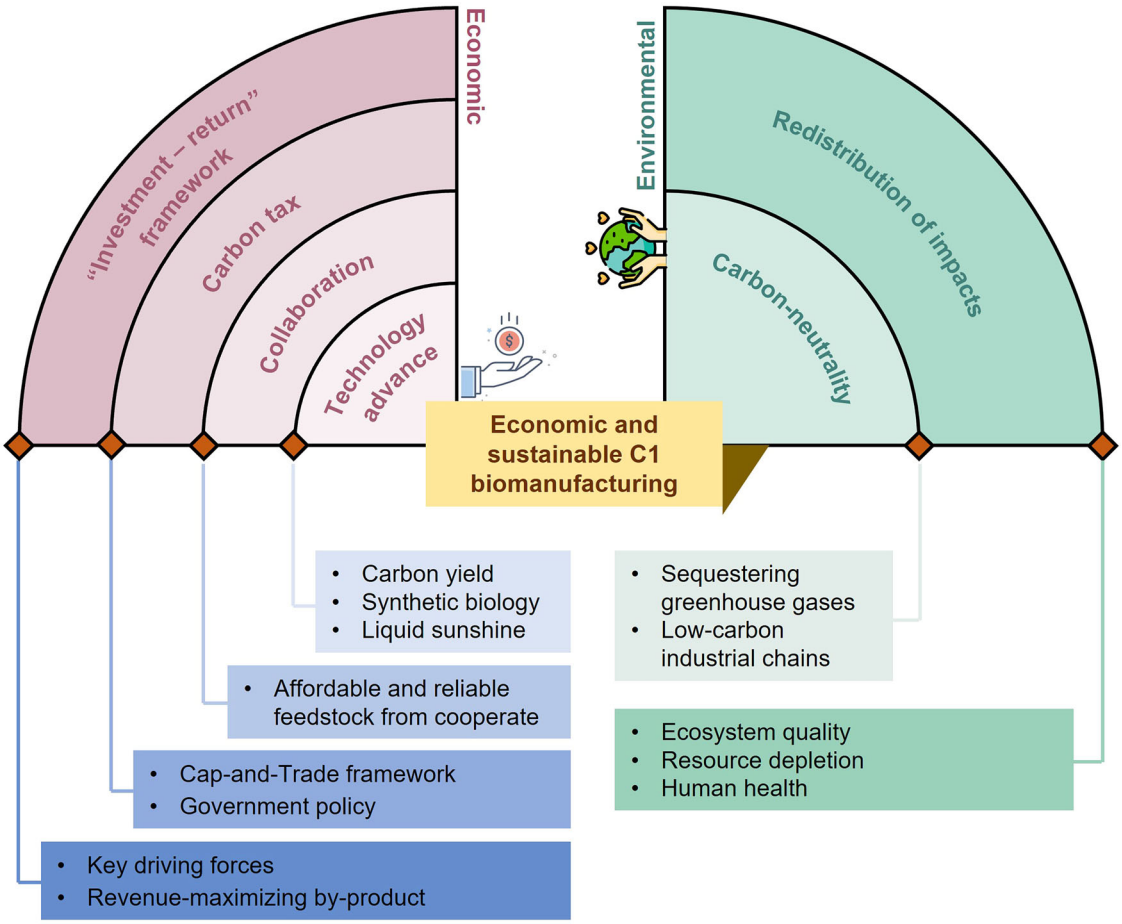

Fig. 4 | Economic and environmental aspects of one-carbon (C1) biomanufacturing. Economic factors, shown in pink, include investment strategies, carbon tax, collaboration, and technological advancements. Environmental considerations, depicted in green, focus on achieving carbon-neutrality, managing the redistribution of environmental impacts, and promoting low-carbon industrial practices. Central to this is the goal of C1 biomanufacturing, which aims to balance and manipulate these economic and environmental driving forces and concerns.

(Supplementary Fig. 7a and Supplementary Note 6). To overcome these obstacles, we propose a roadmap to accelerate the transition from lab-scale innovation to industrial-scale C1 biomanufacturing, which structured around four strategic steps as detailed below (Fig. 4).

Technology advances to accelerate commercialization

Technological advancements aimed at improving carbon conversion efficiency are critical for reducing both equipment and feedstock costs, facilitating an accelerated shift from laboratory study to industrial-scale application. A promising approach involves the development of cell factories with industrial characteristics, concentrating on enhancing the efficiency of metabolic pathways and the robustness of engineered strains as depicted in Supplementary Figs. 7b, c. However, numerous challenges persist in improving carbon conversion rates within synthetic biology. Notably, the effective integration of heterologous C1-utilization pathways into native systems is essential[38,39]. Current limitations, such as inadequate acceptors, cofactors, and enzymes, constrain the efficient use of feedstocks in engineered strains[40–43]. Additionally, managing the tolerance of these strains in the presence of toxic feedstocks and intermediates requires attention[44–46]. Microorganisms should be capable of adapting rapid changes in the environment of large bioreactors, which include elevated levels of toxic products[44]. Besides, integrating the concept of Industry 4.0, including artificial intelligence and machine learning, into C1 biomanufacturing is vital for advancing our understanding of microbial cells and streamlining workflows for predicting optimized strains[47–49].

Building on the "liquid sunshine" concept, coupling electrocatalysis with biocatalysis provides a practical way to enhance carbon utilization efficiency, thereby increasing economic potential[50]. Our TEA shows that electro-biocatalytic cascades could reduce production costs by up to 39% compared to traditional bioprocesses (Supplementary Fig. 7a and Supplementary Note 6). The potential for CO_2-based biomanufacturing is further amplified by advances in direct air capture (DAC) technology. With commercial-scale DAC operations entering the market, the sourcing cost of CO_2 is expected to decline[51–53]. Targeted R&D efforts focused on sorbent optimization, energy demand reduction, and supporting policies will be crucial in driving down costs[51,54–56]. In addition, developing new cathode materials, electrolytes, and modular reactor designs, along with gaining mechanistic insights into reaction mechanisms, remains essential for improving catalyst performance and product selectivity[57,58].

Currently, the efficiency of microbial-based valorization processes does not match the theoretical yields of traditional petroleum-based alternatives[22,59,60]. For instance, in two different tandem systems utilizing CO and electrocatalytically processed CO_2, the production yields of 3-HP are 0.21 $g \cdot g^{-1}$ and 0.23 $g \cdot g^{-1}$, corresponding to 21% and 25% of the theoretical yields, respectively (Supplementary Tables 1 and 2). In contrast, sugar-based processes closely approach their theoretical yields[28,61]. Our single-point sensitivity analysis (Supplementary Fig. 7 and Supplementary Note 6) demonstrates that increasing the CO-derived 3-HP yield from 0.21 $g \cdot g^{-1}$ to 0.35 $g \cdot g^{-1}$ reduces the minimum selling price from \$6.09 kg^{-1} to \$3.66 kg^{-1}. Similarly, elevating CO_2-derived 3-HP yield from 0.23 $g \cdot g^{-1}$ to 0.29 $g \cdot g^{-1}$

decreases minimum selling price by 20%. These findings indicate that higher yields can significantly improve the chances of successful commercialization. Although the technologies explored thus far, along with recent findings, remain a distance from our ideal targets, there is strong optimism that continued advancements can help bridge this gap in the near future.

Cooperate more for C1 feedstock supply stability

To improve the feedstock supply stability of C1 biomanufacturing and overcome existing constraints, a key strategy is to encourage collaboration among stakeholders and research institutions to increase the availability of carbon sources. While advancements in technology have the potential to address issues concerning carbon conversion rates, the inconsistency in the quantity and quality of C1 resources remains a significant barrier to the effective implementation of C1 bioconversion technologies. Gaining direct access to more affordable and reliable carbon sources can help mitigate these challenges. Strengthening partnerships between stakeholders and research institutions requires three key components: feedstock supply, joint technology development, and profit sharing. Industrial partners, particularly raw material suppliers for C1 biomanufacturing, are essential for ensuring feedstock reliability[10]. Academic and R&D institutions should drive innovations in process efficiency and carbon yield to advance industrial scalability. Lastly, transparent profit-sharing mechanisms and non-financial incentives are important to balance common interests. As technology advances and productivity increases, the availability of carbon resources will improve, which will attract more investment and create a positive cycle, thus consequently accelerating the adoption of low-carbon biomanufacturing platforms.

Strategic collaboration between investors and technology innovators is essential for securing C1 feedstocks, such as syngas, mine gas, abandoned petroleum-derived gas, and methane hydrates[62–64]. A practical approach to maximize resource efficiency involves integrating underutilized streams from industry, agriculture, mining, and urban waste management. Localized adaptation of these feedstocks, particularly those discarded or scattered across regions, can stabilize supply chains and improve the reliability of on-site conversion technologies[62–64]. An example of this approach was developed by Lanzatech, which leveraged anaerobic acetogens to transform syngas into jet fuel[65] and collaborated with China Shougang Group Co. Ltd. on a 10,000-ton commercial project in 2024 to biosynthesize ethanol from steel mill gas, demonstrating a scalable model for industrial defossilization. Besides, China's "liquid sunshine" initiative, developed by the Dalian Institute of Chemical Physics (Chinese Academy of Sciences) and industrial partners, employs solar power, water electrolysis, and CO_2-to-methanol catalysis to showcase renewable methanol production, aligning with C1 biomanufacturing goals[21]. These successful commercialization efforts underscore that addressing the sourcing and availability challenges of C1 feedstocks through cooperation with upstream industries can accelerate the industrialization of C1 biomanufacturing.

Leveraging carbon tax policies to raise income

Recent research in synthetic biology and fermentation engineering indicates that C1 biomanufacturing is well-positioned to contribute to carbon capture and sequestration[66–68]. For example, research indicates that the photoautotrophic microbes (such as *Synechococcus elongatus*) may convert CO_2 into useful chemicals via biomanufacturing, resulting in an overall reduction of −17.20 to −1219.03 tons CO_2-equivalent to produce 1 ton of end products[69–71]. Various studies have highlighted the potential positive effects of carbon tax policies on the development of biomanufacturing[72–74]. Under cap-and-trade systems, industries exceeding emissions limits need to purchase allowances, while those operating below thresholds generate tradable credits through carbon utilization initiatives[75,76]. This market-driven mechanism enables cross-sector credit transfers, thereby enhancing the economic viability of carbon-negative C1 biomanufacturing by turning revenue streams for emission reductions.

The European Union's Emission Trading System permits participating facilities to trade in CO_2 allowances, with permit prices escalating from €24 to over €100 per ton of CO_2 between 2020 and 2023[72], and the CO_2 price is expected to rise rapidly in light of the imminent worldwide de-fossilization objectives. The economic benefits of carbon pricing mechanisms are illustrated in Supplementary Fig. 8 and Supplementary Note 7. As carbon credits increase from $0 to $1000 per ton, the break-even price of the final product decreases by more than 22%, signifying considerable positive consequences. Hence, as C1 biomanufacturing improves its carbon conversion efficiency from feedstocks to target products, the transition from laboratory research to large-scale applications will gain momentum due to the prospective revenue from carbon tax policies. This progression underscores the importance of supportive policy frameworks in realizing a sustainable future for biomanufacturing.

Techno-economic analysis to decrease investment risks

In moving toward a viable industrial C1 biomanufacturing, it is necessary to conduct a TEA to identify key factors that affect return on investment. This analysis allows for adjustments to risk elements during the early stages of project development, thereby facilitating the incorporation of new technology into industrial production processes. By pinpointing areas that require optimization or modification of process parameters, TEA plays a crucial role in significantly reducing investment risks[77]. One critical aspect of C1 biomanufacturing is the variability of raw materials, including the supply volume, composition, and cost. TEA can assess the influence of carbon source supply on production investment. Through computational simulations, potential risks can be identified and addressed before practical implementation, enabling more informed decision-making regarding resource management (Supplementary Fig. 7). Additionally, TEA can assist in identifying the revenue-maximizing by-product obtained from the C1 biomanufacturing to reduce economic costs[78–82]. For example, cell mass generated during fermentation can be marketed as single-cell protein or transformed into fertilizer[26]. When determining the most beneficial by-product to pursue, it is essential to consider not just its market value but also the investment required for its treatment and processing. Employing a TEA allows investors to effectively navigate the downstream dimensions of the process and make informed choices that enhance value. By utilizing an "investment-return" framework, stakeholders can better manage the economic variables intrinsic to C1 biomanufacturing operations, leading to more sustainable and profitable practices in the industry.

Following the fundamental "investment-return" framework, the integration of latest methodological advancements can make TEA more precise. For example, integrating uncertainty analysis, such as Monte Carlo methods[77], could enable systematic assessment of parameter sensitivity and variability, thus improving the reliability of TEA outcomes. Additionally, advanced data analysis techniques, like Pareto curve analysis to identify the best balance between different performance goals or targeted process optimization to maximize system efficiency, could yield practical insights[83]. By adopting these tools, the refined framework would elucidate complex relationships in scaling up C1 biomanufacturing, supporting more informed strategic decision-making.

Carbon footprint and environmental insights

C1 biomanufacturing holds promise for achieving carbon neutrality and potentially becoming carbon-negative. Numerous prospective chassis for chemical production from C1 feedstocks have been developed as viable options for carbon-neutral or even carbon-negative biomanufacturing, such as *Pichia pastoris* (*Komagataella phaffii*)[68],

Cupriavidus necator[84], *Methylotuvimicrobium buryatense*[85], and *Moorella thermoacetica*[86]. By permanently incorporating C1 feedstocks into products, this approach could address global warming while creating economic benefits through carbon tax policies. Techniques such as gas fermentation and bio-electro conversion offer avenues for sequestering anthropogenic carbon by capturing greenhouse gases (GHG) and transforming them into valuable products, hence diminishing the overall carbon footprint[87]. Our estimations also suggest that acrylic acid production using C1 feedstocks could lead to a reduction of up to 3.09 tons of GHG emissions for every ton of acrylic acid produced, compared to traditional fossil-based methods (Supplementary Figs. 9 and 10, Supplementary Table 14, and Supplementary Note 8). Overall, carbon-negative C1 biomanufacturing can reduce carbon emissions by utilizing C1 raw materials for chemical production, hence facilitating the transition of established industries to low-carbon industrial chains.

The shift from traditional fossil-based production methods to innovative recycling technologies that utilize waste C1 gases can lead to a complex redistribution of environmental impacts. While this transition may reduce risks in some areas, it could simultaneously intensify challenges in others (Supplementary Table 14)[88]. LCA comparing C1-based products to their fossil-based counterparts provides a substantial opportunity to mitigate carbon emissions. Nevertheless, these assessments also reveal that some environmental effects may surpass those associated with fossil alternatives. Therefore, it is essential to carefully evaluate the sustainability of specific bio-based chemicals during their development.

Conducting comprehensive LCA prior to the implementation of novel technology is crucial for ensuring their safety, along with considering the entire value chain. For example, our analysis of DAC units revealed that their reliance on natural gas significantly contributes to fossil fuel depletion and emissions[89,90]. In light of these insights, there is considerable promise in developing platform chemicals from CO_2 using alternative, renewable energy sources. Harnessing solar, wind, and geothermal energy could help mitigate environmental impacts, potentially replacing or reducing the reliance on DAC units. This alignment of innovative production methods with sustainable energy sources presents an opportunity for a greener and more economically viable future in chemical production.

Outlook and perspectives

C1 biomanufacturing represents a revolutionary approach to sustainable chemical production. However, its commercial viability is currently hindered by ongoing technical, economic, and environmental challenges. Continuous innovation in synthetic biology and electrocatalysis will be crucial for addressing the current limitation of low carbon conversion efficiency. Developing efficient cell factories and improving electro-biocatalytic systems requires a comprehensive investigation of metabolic pathways, enzyme engineering, and reaction mechanisms. Furthermore, the establishment of stable C1 feedstock supply chains through cooperation between industries, academia, and research institutions needs to break through geographical and resource limitations. This requires not only the development of new technologies for feedstock utilization but also the establishment of effective communication and cooperation mechanisms to ensure the stable supply of feedstocks and the sharing of innovation benefits.

Moreover, the integration of C1 biomanufacturing into existing industrial systems will bring new opportunities for industrial upgrading and transformation, promoting the development of the circular economy. The ongoing enhancement of carbon tax policies and the creation of more favorable regulatory frameworks will be pivotal in advancing C1 biomanufacturing. It is highly important to enhance international collaboration in policy formulation, promote the advancement and implementation of low-carbon and carbon-negative technologies, and establish a more conducive market environment for C1 biomanufacturing. By aligning technical advancements with policy incentives and circular economy principles, stakeholders can accelerate the shift from laboratory innovation to industrial application. These combined efforts will pave the way for a sustainable chemical industry, balancing environmental responsibility with economic needs.

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Data availability

Data supporting the findings of this work are included within the paper and its Supplementary Information files. A reporting summary for this Article is available as a Supplementary Information file.

References

1. Mitchell, S., Martín, A. J. & Pérez-Ramírez, J. Transcending scales in catalysis for sustainable development. *Nat. Chem. Eng.* **1**, 13–15 (2024).
2. Mou, J. H. et al. Key techno-economic barriers in the valorization of organic solid wastes for chemical production. *One Earth* **7**, 742–746 (2024).
3. Guillén-Gosálbez, G. & Francisco dos Santos, L. Integrating industrial sectors in the transition to more sustainable chemicals. *Nat. Chem. Eng.* **1**, 336–337 (2024).
4. Ali, Z., Ma, J. & Sun, R.-C. Scaling-up clean production of biomass-derived organic acids a step towards the realization of dual carbon goals: a review. *Green Chem.* **26**, 11061–11082 (2024).
5. Li, J. et al. Upcycling C1 gas-derived resources in future food system. *Resour. Conserv. Recycling* **210**, 107827 (2024).
6. Hermens, J. G., Jensma, A. & Feringa, B. L. Highly efficient biobased synthesis of acrylic acid. *Angew. Chem. Int. Ed.* **61**, e202112618 (2022).
7. Jiang, W. et al. Metabolic engineering strategies to enable microbial utilization of C1 feedstocks. *Nat. Chem. Biol.* **17**, 845–855 (2021).
8. Montaño López, J., Duran, L. & Avalos, J. L. Physiological limitations and opportunities in microbial metabolic engineering. *Nat. Rev. Microbiol.* **20**, 35–48 (2022).
9. Schulz-Mirbach, H. et al. New-to-nature CO_2-dependent acetyl-CoA assimilation enabled by an engineered B12-dependent acyl-CoA mutase. *Nat. Commun.* **15**, 10235 (2024).
10. El Abbadi, S. H., Sherwin, E. D., Brandt, A. R., Luby, S. P. & Criddle, C. S. Displacing fishmeal with protein derived from stranded methane. *Nat. Sustain.* **5**, 47–56 (2022).
11. Devi, N. B., Pugazhenthi, G. & Pakshirajan, K. Synthetic biology approaches and bioseparations in syngas fermentation. *Trends Biotechnol.* **43**, 111–130 (2024).
12. Gao, Z. et al. A novel nutritional induction strategy flexibly switching the biosynthesis of food-like products from methane by a methanotrophic bacterium. *Green. Chem.* **26**, 7048–7058 (2024).
13. Yilmaz, S., Nyerges, A., van der Oost, J., Church, G. M. & Claassens, N. J. Towards next-generation cell factories by rational genome-scale engineering. *Nat. Catal.* **5**, 751–765 (2022).
14. Hossain, T. et al. The nth-plant scenario for blended feedstock conversion and preprocessing nationwide: Biorefineries and depots. *Appl. Energy* **294**, 116946 (2021).
15. Choi, S. Y. et al. Sustainable production and degradation of plastics using microbes. *Nat. Microbiol.* **8**, 2253–2276 (2023).

16. Gao, J. et al. Engineering co-utilization of glucose and xylose for chemical overproduction from lignocellulose. *Nat. Chem. Biol.* **19**, 1524–1531 (2023).
17. Xu, M. et al. Production of 3-hydroxypropionic acid from syngas-derived acetic acid by engineered Vibrio natriegens combined with adaptive laboratory evolution. *ACS Sustain. Chem. Eng.* **11**, 4125–4132 (2023).
18. Wu, X. et al. Efficient bioproduction of 3-hydroxypropionic acid from methanol by a synthetic yeast cell factory. *ACS Sustain. Chem. Eng.* **11**, 6445–6453 (2023).
19. Wang, J. et al. A highly selective and stable ZnO-ZrO_2 solid solution catalyst for CO_2 hydrogenation to methanol. *Sci. Adv.* **3**, e1701290 (2017).
20. Hu, P., Rismani-Yazdi, H. & Stephanopoulos, G. Anaerobic CO2 fixation by the acetogenic bacterium Moorella thermoacetica. *AICHE J.* **59**, 3176–3183 (2013).
21. Wang, J. et al. Liquid sunshine methanol. *Chem. Ind. Eng. Prog.* **41**, 1309–1317 (2022).
22. Aggarwal, N. et al. Microbial engineering strategies to utilize waste feedstock for sustainable bioproduction. *Nat. Rev. Bioeng.* **2**, 155–174 (2024).
23. Bachleitner, S., Ata, Ö & Mattanovich, D. The potential of CO_2-based production cycles in biotechnology to fight the climate crisis. *Nat. Commun.* **14**, 6978 (2023).
24. Orsi, E., Nikel, P. I., Nielsen, L. K. & Donati, S. Synergistic investigation of natural and synthetic C1-trophic microorganisms to foster a circular carbon economy. *Nat. Commun.* **14**, 6673 (2023).
25. Sandid, A., Esteban, J., D'Agostino, C. & Spallina, V. Process assessment of renewable-based acrylic acid production from glycerol valorisation. *J. Clean. Prod.* **418**, 138127 (2023).
26. Zhang, C. et al. An upcycling bioprocess for sustainable aviation fuel production from food waste-derived greenhouse gases: life cycle assessment and techno-economic analysis. *Chem. Eng. J.* **486**, 150242 (2024).
27. Xu, J. et al. Embracing a low-carbon future by the production and marketing of C1 gas protein. *Biotechnol. Adv.* **63**, 108096 (2023).
28. Yan, X. et al. Paradigm of engineering recalcitrant non-model microorganism with dominant metabolic pathway as a biorefinery chassis. *Nat. Commun.* **15**, 10441 (2024).
29. Kim, J., Hwang, S. & Lee, S.-M. Metabolic engineering for the utilization of carbohydrate portions of lignocellulosic biomass. *Metab. Eng.* **71**, 2–12 (2022).
30. Al-Breiki, M. & Bicer, Y. Techno-economic evaluation of a power-to-methane plant: levelized cost of methane, financial performance metrics, and sensitivity analysis. *Chem. Eng. J.* **471**, 144725 (2023).
31. Bhagwat, S. S. et al. Sustainable production of acrylic acid via 3-hydroxypropionic acid from lignocellulosic biomass. *ACS Sustain. Chem. Eng.* **9**, 16659–16669 (2021).
32. Louw, J., Dogbe, E. S., Yang, B. & Görgens, J. F. Prioritisation of biomass-derived products for biorefineries based on economic feasibility: a review on the comparability of techno-economic assessment results. *Renew. Sustain. Energy Rev.* **188**, 113840 (2023).
33. Lima, E. A. D. et al. Development of an economically competitive Trichoderma-based platform for enzyme production: bioprocess optimization, pilot plant scale-up, techno-economic analysis and life cycle assessment. *Bioresour. Technol.* **364**, 128019 (2022).
34. Lee, S. Y. Fungible and non-fungible technologies in biomanufacturing scale-up. *Nat. Chem. Eng.* **1**, 442–443 (2024).
35. Li, J. et al. Microwave-assisted pyrolysis of solid waste for production of high-value liquid oil, syngas, and carbon solids: a review. *Renew. Sustain. Energy Rev.* **189**, 113979 (2024).
36. Ali, A. M. et al. Conversion of municipals waste into syngas and methanol via steam gasification using CaO as sorbent: an Aspen Plus modelling. *Fuel* **349**, 128640 (2023).
37. Katla-Milewska, D., Nazir, S. M. & Skorek-Osikowska, A. Synthetic natural gas (SNG) production with higher carbon recovery from biomass: techno-economic assessment. *Energy Convers. Manag.* **300**, 117895 (2024).
38. Lv, X. et al. C1-based biomanufacturing: advances, challenges and perspectives. *Biores. Technol.* **367**, 128259 (2023).
39. Satanowski, A. et al. Awakening a latent carbon fixation cycle in Escherichia coli. *Nat. Commun.* **11**, 5812 (2020).
40. Mao, J. et al. Relieving metabolic burden to improve robustness and bioproduction by industrial microorganisms. *Biotechnol. Adv.* **74**, 108401 (2024).
41. Dai, K. et al. Cofactor engineering in Thermoanaerobacterium aotearoense SCUT27 for maximizing ethanol yield and revealing an enzyme complex with high ferredoxin-NAD+ reductase activity. *Bioresour. Technol.* **402**, 130784 (2024).
42. Tang, R., Yuan, X. & Yang, J. Problems and corresponding strategies for converting CO_2 into value-added products in Cupriavidus necator H16 cell factories. *Biotechnol. Adv.* **67**, 108183 (2023).
43. Lu, L. et al. A bacterial platform for producing aromatic esters from glycerol. *Nat. Chem. Eng.* **1**, 751–764 (2024).
44. Blombach, B., Grünberger, A., Centler, F., Wierckx, N. & Schmid, J. Exploiting unconventional prokaryotic hosts for industrial biotechnology. *Trends Biotechnol.* **40**, 385–397 (2022).
45. Gao, J., Li, Y., Yu, W. & Zhou, Y. J. Rescuing yeast from cell death enables overproduction of fatty acids from sole methanol. *Nat. Metab.* **4**, 932–943 (2022).
46. Yi, X., Khey, J., Kazlauskas, R. J. & Travisano, M. Plasmid hypermutation using a targeted artificial DNA replisome. *Sci. Adv.* **7**, eabg8712 (2021).
47. Gurdo, N., Volke, D. C. & Nikel, P. I. Merging automation and fundamental discovery into the design–build–test–learn cycle of non-traditional microbes. *Trends Biotechnol.* **40**, 1148–1159 (2022).
48. Orsi, E., Schada von Borzyskowski, L., Noack, S., Nikel, P. I. & Lindner, S. N. Automated in vivo enzyme engineering accelerates biocatalyst optimization. *Nat. Commun.* **15**, 3447 (2024).
49. Oruganti, R. K. et al. Artificial intelligence and machine learning tools for high-performance microalgal wastewater treatment and algal biorefinery: a critical review. *Sci. Total Environ.* **876**, 162797 (2023).
50. Guo, S. et al. Scalable electro-biosynthesis of ectoine from greenhouse gases. *Angew. Chem. Int. Edn.* **64**, e202415445 (2024).
51. Erans, M. et al. Direct air capture: process technology, techno-economic and socio-political challenges. *Energy Environ. Sci.* **15**, 1360–1405 (2022).
52. Liu, J., Zhang, H., Xu, Y., Meng, H. & Zeng, A.-P. Turn air-captured CO2 with methanol into amino acid and pyruvate in an ATP/NAD(P)H-free chemoenzymatic system. *Nat. Commun.* **14**, 2772 (2023).
53. Kar, S. et al. Direct air capture of CO2 for solar fuel production in flow. *Nat. Energy* **10**, 448–459(2025).
54. Holmes, H. E. et al. Tuning sorbent properties to reduce the cost of direct air capture. *Energy Environ. Sci.* **17**, 4544–4559 (2024).
55. Olabi, A. G. et al. Assessment of the pre-combustion carbon capture contribution into Sustainable Development Goals SDGs using novel indicators. *Renew. Sustain. Energy Rev.* **153**, 111710 (2022).
56. Young, J., McIlwaine, F., Smit, B., Garcia, S. & van der Spek, M. Process-informed adsorbent design guidelines for direct air capture. *Chem. Eng. J.* **456**, 141035 (2023).
57. Hussain, I., Alasiri, H., Ullah Khan, W. & Alhooshani, K. Advanced electrocatalytic technologies for conversion of carbon dioxide into

methanol by electrochemical reduction: Recent progress and future perspectives. *Coord. Chem. Rev.* **482**, 215081 (2023).
58. Liu, Y. et al. Strategies for achieving carbon neutrality: dual-atom catalysts in focus. *Small* **21**, 2407313 (2024).
59. Nielsen, J., Tillegreen, C. B. & Petranovic, D. Innovation trends in industrial biotechnology. *Trends Biotechnol.* **40**, 1160–1172 (2022).
60. Clomburg, J. M., Crumbley, A. M. & Gonzalez, R. Industrial biomanufacturing: the future of chemical production. *Science* **355**, aag0804 (2017).
61. Jain, S. & Kumar, S. A comprehensive review of bioethanol production from diverse feedstocks: current advancements and economic perspectives. *Energy* **296**, 131130 (2024).
62. Choe, C., Cheon, S., Kim, H. & Lim, H. Mitigating climate change for negative CO_2 emission via syngas methanation: techno-economic and life-cycle assessments of renewable methane production. *Renew. Sustain. Energy Rev.* **185**, 113628 (2023).
63. Silva, J., Gonçalves, J. C., Rocha, C., Vilaça, J. & Madeira, L. M. Biomethane production from biogas obtained in wastewater treatment plants: process optimization and economic analysis. *Renew. Energy* **220**, 119469 (2024).
64. Pérez, V., Moltó, J. L., Lebrero, R. & Muñoz, R. Ectoine production from biogas: a sensitivity analysis. Effect of local commodity prices, economy of scale, market trends and biotechnological limitations. *J. Clean. Prod.* **369**, 133440 (2022).
65. Waltz, E. Microbe-made jet fuel. *Nat. Biotechnol.* **42**, 163–166 (2024).
66. Zhu, P. & Chen, X. Carbon-negative biomanufacturing of chemicals from waste gases. *Chem* **8**, 1178–1180 (2022).
67. Scown, C. D. Prospects for carbon-negative biomanufacturing. *Trends Biotechnol.* **40**, 1415–1424 (2022).
68. Guo, F., Qiao, Y., Xin, F., Zhang, W. & Jiang, M. Bioconversion of C1 feedstocks for chemical production using Pichia pastoris. *Trends Biotechnol.* **41**, 1066–1079 (2023).
69. Li, C., Yin, L., Wang, J., Zheng, H. & Ni, J. Light-driven biosynthesis of volatile, unstable and photosensitive chemicals from CO2. *Nat. Synth.* **2**, 960–971 (2023).
70. Li, C. et al. A highly compatible phototrophic community for carbon-negative biosynthesis. *Angew. Chem. Int. Ed.* **62**, e202215013 (2023).
71. Wang, W. et al. Bioupcycling methane into triacylglycerol for the production of sustainable aviation fuel by methanotrophic bacteria. *Chem. Eng. J.* **501**, 157639 (2024).
72. Vasilakou, K., Nimmegeers, P., Billen, P. & Van Passel, S. Geospatial environmental techno-economic assessment of pretreatment technologies for bioethanol production. *Renew. Sustain. Energy Rev.* **187**, 113743 (2023).
73. Velvizhi, G. et al. Carbon credit reduction: a techno-economic analysis of "drop-in" fuel production. *Environ. Pollut.* **316**, 120507 (2023).
74. Wang, W., Zeng, C. & Tsubaki, N. Recent advancements and perspectives of the CO2 hydrogenation reaction. Green. *Carbon* **1**, 133–145 (2023).
75. Cheng, P., Ji, G., Zhang, G. & Shi, Y. A closed-loop supply chain network considering consumer's low carbon preference and carbon tax under the cap-and-trade regulation. *Sustain. Prod. Consum.* **29**, 614–635 (2022).
76. Xu, S., Govindan, K., Wang, W. & Yang, W. Supply chain management under cap-and-trade regulation: a literature review and research opportunities. *Int. J. Prod. Econ.* **271**, 109199 (2024).
77. Zhou, R. et al. Techno-economic analysis and network design for CO_2 conversion to jet fuels in the United States. *Renew. Sustain. Energy Rev.* **210**, 115191 (2025).
78. Park, S., Mun, H., Park, J. & Lee, I. Cost optimization methodology based on carbon-techno-economic analysis: an application to post-combustion carbon capture process. *J. Clean. Prod.* **434**, 139887 (2024).
79. Castro, J. et al. Life cycle assessment and techno-economic analysis for biofuel and biofertilizer recovery as by-products from microalgae. *Renew. Sustain. Energy Rev.* **187**, 113781 (2023).
80. Tian, H. et al. Techno-economic analysis of developing miscanthus biorefinery for the production of platform chemicals and renewable resins. *J. Clean. Prod.* **427**, 139172 (2023).
81. Ebrahimpourboura, Z. et al. Comparative techno-economic and life cycle assessment of electrocatalytic processes for lignin valorization. *Green. Chem.* **26**, 11303–11315 (2024).
82. Pratschner, S., Radosits, F., Ajanovic, A. & Winter, F. Techno-economic assessment of a power-to-green methanol plant. *J. CO2 Utilization* **75**, 102563 (2023).
83. Ranga, M. & Sinha, S. Mechanism and techno-economic analysis of the electrochemical process. *ChemBioEng Rev.* **10**, 336–362 (2023).
84. Panich, J., Fong, B. & Singer, S. W. Metabolic engineering of Cupriavidus necator H16 for sustainable biofuels from CO2. *Trends Biotechnol.* **39**, 412–CO424 (2021).
85. Jiao, Z. et al. A de novo auto-activated solar-driven biohybrid system for hydrogen production in methanotrophic cells. *Angew. Chem. Int. Ed.* **64**, e202419973 (2025).
86. Fei, P. et al. Carbon-negative bio-production of short-chain carboxylic acids (SCCAs) from syngas via the sequential two-stage bioprocess by Moorella thermoacetica and metabolically engineered Escherichia coli. *Bioresour. Technol.* **416**, 131714 (2025).
87. Symons, J. et al. Engineering biology and climate change mitigation: policy considerations. *Nat. Commun.* **15**, 2669 (2024).
88. Liu, F. et al. Regionalized life-cycle monetization can support the transition to sustainable rural food waste management in China. *Nat. Food* **4**, 797–809 (2023).
89. Qiu, Y. et al. Environmental trade-offs of direct air capture technologies in climate change mitigation toward 2100. *Nat. Commun.* **13**, 3635 (2022).
90. Madhu, K., Pauliuk, S., Dhathri, S. & Creutzig, F. Understanding environmental trade-offs and resource demand of direct air capture technologies through comparative life-cycle assessment. *Nat. Energy* **6**, 1035–1044 (2021).

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Author contributions

C.Z. and Q.F. conducted the techno-economic analysis and life cycle assessment. R.F. conducted an analysis and interpretation of research data regarding techno-economic analysis and life cycle assessment. L.M. provided syngas production and bioconversion data. Y.J.Z. Supplied experimental data for methanol bioconversion. Q.F., L.M., and T.T. coordinated the writing process, ensuring coherence across sections and managing author feedback. C.Z. and Q.F. drafted the original manuscript. R.F., Y.J.Z., and T.T. conducted a thorough review of the manuscript, contributing critical revisions to improve clarity and scientific rigor. L.M. and Q.F. are responsible for the funding acquire. Q.F. and T.T. conceived and designed the study. All authors read, revised, and approved the final version of the manuscript.

Competing interests

The authors declare no competing interests.

Additional information

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