

Review

Technological Innovation in Syngas Fermentation and Prospects for Industrial Application

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ABSTRACT: In the context of the global carbon neutrality strategy, syngas fermentation technology has emerged as a research hotspot in biomanufacturing because it can recover and convert industrial exhaust gas. Relying on the Wood-Ljungdahl pathway in acetogens, this technology converts gaseous substrates, such as CO and CO₂, into high-value-added chemicals. However, bottlenecks including low gas-liquid mass-transfer efficiency and challenges with scale-up, severely limit its industrialization. The review focuses on core research-level topics, including the key enzymatic mechanisms of acetogens, metabolic regulation strategies, and high-throughput strain construction technologies; systematically analyzes the feed gas pretreatment process, design principles of large-scale reactors, fermentation process optimization, efficient product separation and purification technologies, and full-process integration at the process level; and summarizes techno-economic analysis and global policy support for industrial application. Finally, it thoroughly analyzes the core challenges of this technology across core mechanisms, engineering operations, economic markets, and industrial chain coordination, and outlines the future development direction of the technology. By systematically collating the syngas fermentation technology system and its industrialization bottlenecks, this review provides references for its industrialization. It is positioned to boost the economic viability and industrial appeal of the CCUS system, acting as a pivotal engine for advancing deep industrial decarbonization and fostering emerging green industries.

Keywords: Carbon neutrality; Syngas fermentation; Acetogens; Wood-Ljungdahl pathway; Scale-up

1. Introduction

Global climate change is a significant challenge facing humanity, driven primarily by greenhouse gas emissions from human activities. Among these, CO₂ accounts for 76.7% of total global greenhouse gas emissions, making it the most dominant greenhouse gas. CO₂ is not only a major contributor to global climate change but also poses a serious threat to ecosystem stability and human sustainable development [1,2]. The CO₂ concentration in 2024 reached 422.3 ppm, continuing the upward trend and setting another all-time high [3]. In addition, CO is also an important component of industrial exhaust gas. Incomplete combustion of fossil fuels, steelmaking, and other industrial processes emits large amounts of CO, CO₂,

and H₂ [4–6]. Traditional combustion for power generation generates substantial pollutants and has low energy utilization efficiency.

In response to the challenges, the Paris Agreement explicitly sets the goal of limiting global temperature rise to well below 2 °C above pre-industrial levels, and the United Nations further advocates that all countries achieve carbon neutrality by 2050 [7]. Achieving this goal requires transitioning to a bio-based economy and renewable energy to reduce emissions from sources, and it also relies on breakthroughs in key technologies such as carbon capture, utilization, and storage (CCUS) [8–11]. CCUS technology captures CO₂ from industrial emissions for geological sequestration or resource utilization, while bio-CCUS technology sequesters CO₂ using microorganisms, plants, and algae [12,13]. Despite its broad prospects, CCUS technology still faces challenges, including potential leakage risks from geological sequestration (annual leakage rates of 0.00001–1%) and high costs [14,15].

Among numerous technologies for reducing carbon emissions and improving resource utilization, syngas fermentation has attracted widespread attention [5,16]. Syngas is a mixed gas containing CO, CO₂, and H₂, and syngas fermentation converts gaseous feedstock into high-value-added chemicals and biofuels in a single step through microbial fermentation [17–20]. Using syngas as the carbon and energy source, this technology employs acetogens to convert CO₂ and CO into acetyl-CoA via the Wood-Ljungdahl pathway, which is then converted into various high-value chemicals and biofuels, such as ethanol, acetic acid, butanol, 2,3-butanediol, and butyric acid [21–27]. Compared with traditional chemical conversion technologies, syngas fermentation offers distinct advantages, including operation at low temperature and pressure and the ability to handle flexible gas compositions. It is particularly suitable for the resource utilization of industrial exhaust gas from steel plants and other industrial facilities [28–33]. However, this technology still faces bottlenecks, such as limited gas-liquid mass transfer efficiency and difficulty in scale-up, which restrict its large-scale industrial application [31].

In summary, syngas fermentation technology has significant strategic value for carbon neutrality and the utilization of industrial exhaust gas resources. However, numerous challenges remain, including the in-depth exploration of breakthroughs in key technologies and the implementation of industrialization. Existing studies have not yet formed a systematic technical system or industrialization solutions. Based on this, this review focuses on strain construction, technology optimization, process integration, and breakthroughs in bottlenecks, systematically analyzing and discussing core technologies, key process technologies, full-process integration, and industrialization challenges. It aims to provide comprehensive theoretical and technical support for the sustainable development of syngas fermentation technology, facilitating its greater role in energy transition practices.

2. Syngas Fermentation Strains

Syngas fermentation is a highly promising biotechnological route that relies on acetogens to convert syngas into biofuels and bio-based chemicals. Industrial strains directly determine the range of feedstocks that can be used, the types of target products, and industrial production costs. Acetogens possess the most extensive and flexible substrate utilization system among known microorganisms; they can not only utilize simple C1 compounds such as CO and CO₂ but also metabolize complex carbohydrates [34–37].

2.1. Key Enzymes of Acetogens

Acetogens are strictly anaerobic, Gram-positive bacteria, with typical representatives including *Clostridium autoethanogenum*, *Clostridium ljungdahlii*, *Acetobacterium woodii*, and *Moorella thermoacetica* [24,38]. As shown in Figure 1, the Wood-Ljungdahl pathway (WLP) is the core pathway for acetogens to metabolize syngas, in which Acetyl-CoA is generated through the synergistic cooperation of the methyl and carbonyl branches [39]. In the methyl branch, CO₂ is reduced by a sequence of

metalloenzymes using tetrahydrofolate as the cofactor, namely formate dehydrogenase (FDH), formyltetrahydrofolate synthetase (FHS), methenyltetrahydrofolate cyclohydrolase/dehydrogenase (FCH/MDH), methylenetetrahydrofolate reductase (MTHFR), and methyltransferase (MT). Ultimately, the methylcobamide iron-sulfur protein (Methyl-CoFeS) serves as the methyl donor. In the carbonyl branch, the carbon monoxide dehydrogenase/acetyl-CoA synthase (CODH/ACS) complex catalyzes the reduction of another molecule of CO₂ to CO [40]. Subsequently, the methyl donor, coenzyme A, and CO generated from the carbonyl branch condense, mediated by CODH/ACS, to form acetyl-CoA [40–42]. If CO is present in the substrate, it can be directly utilized by the CODH/ACS complex.

WLP cannot generate net ATP via substrate-level phosphorylation, and insufficient energy supply is a core bottleneck in its metabolism. In response to this bottleneck, acetogens have evolved two key energy conservation mechanisms: first, establishing a proton-motive force via membrane-bound ferredoxin: NAD⁺ oxidoreductase (Rnf) or energy-converting hydrogenase complexes to drive ATP synthesis through chemiosmotic phosphorylation; second, enhancing energy utilization efficiency by coupling exergonic reactions with endergonic reactions through the flavin-based electron bifurcation mechanism [43,44].

In *Clostridium autoethanogenum*, there are three carbon monoxide dehydrogenase (CODH) isozymes, namely AcsA, CooS1, and CooS2. Among them, AcsA is the CODH subunit of the CODH/ACS complex, which converts CO₂ to CO as its core function. It provides the critical CO precursor for the complex to synthesize acetyl-CoA, and the CO generated by AcsA is transferred to the ACS active site through a molecular tunnel to participate in the condensation reaction [45]. Inactivation of this enzyme results in the inability of the strain to grow under CO conditions, making it an indispensable core unit of the WLP. Additionally, CooS1 and CooS2 are monofunctional CODHs that primarily catalyze the reversible conversion between CO₂ and CO, thereby exhibiting functional redundancy. CooS1 oxidizes CO for energy production and provides electrons for hydrogen production (reaction: $\text{CO} + \text{H}_2\text{O} \rightarrow \text{CO}_2 + 2\text{H}^+ + 2\text{e}^-$), and is responsible for extracting and transferring electrons from CO [46]. Similarly, CooS2 is a monofunctional CODH that usually coexists with CooS1, and its function is more biased toward CO₂ reduction under anaerobic conditions (reaction: $\text{CO} + \text{H}_2\text{O} \rightleftharpoons \text{CO}_2 + 2\text{H}^+ + 2\text{e}^-$), providing CO precursors and reducing power [46]. In *C. autoethanogenum*, *acsA* is indispensable for autotrophic growth, while deletion of *cooS1* and *cooS2* exerts only a minor impact [47].

During CO conversion in *Carboxydotherrmus hydrogenoformans*, carbon monoxide dehydrogenase (CODH) serves as the core catalytic component, and ChCODH-II is a key functional unit of this pathway by virtue of its high catalytic activity [48]. However, ChCODH-II exhibits extreme sensitivity to oxygen and is prone to conformational disruption of the active site, leading to catalytic inactivation. This inherent characteristic severely restricts its large-scale application in complex industrial gas environments. To address this bottleneck, Kim adopted a comparative structural biology approach to systematically elucidate the structural differences between the oxygen-sensitive ChCODH-II and its oxygen-tolerant homolog, ChCODH-IV, ultimately identifying the key amino acid residue A559 in the substrate channel [48]. The research team then conducted site-directed mutagenesis on ChCODH-II, which significantly reduced its sensitivity to oxygen while retaining almost all of its original high CO conversion activity.

Hydrogenases and formate dehydrogenases (FDHs) also play crucial roles in electron transfer and carbon fixation, and their functional efficiency determines the syngas utilization rate and product yield. In autotrophic growth, hydrogenases primarily provide reducing power and energy to cells by oxidizing H₂ and transferring electrons to carriers, such as ferredoxins, to drive energy-consuming reactions, including CO₂ reduction. Based on the metals in their active sites, hydrogenases are classified into [NiFe]-, [FeFe]-, and [Fe]-types. These types differ in catalytic activity and oxygen sensitivity, and most acetogens contain multiple hydrogenases to meet diverse metabolic demands [49]. Formate dehydrogenases, on the other hand, are responsible for CO₂ fixation in the methyl branch of the WLP, catalyzing the conversion of CO₂ to formate and fixing the carbon atoms of the methyl group into acetyl-CoA.

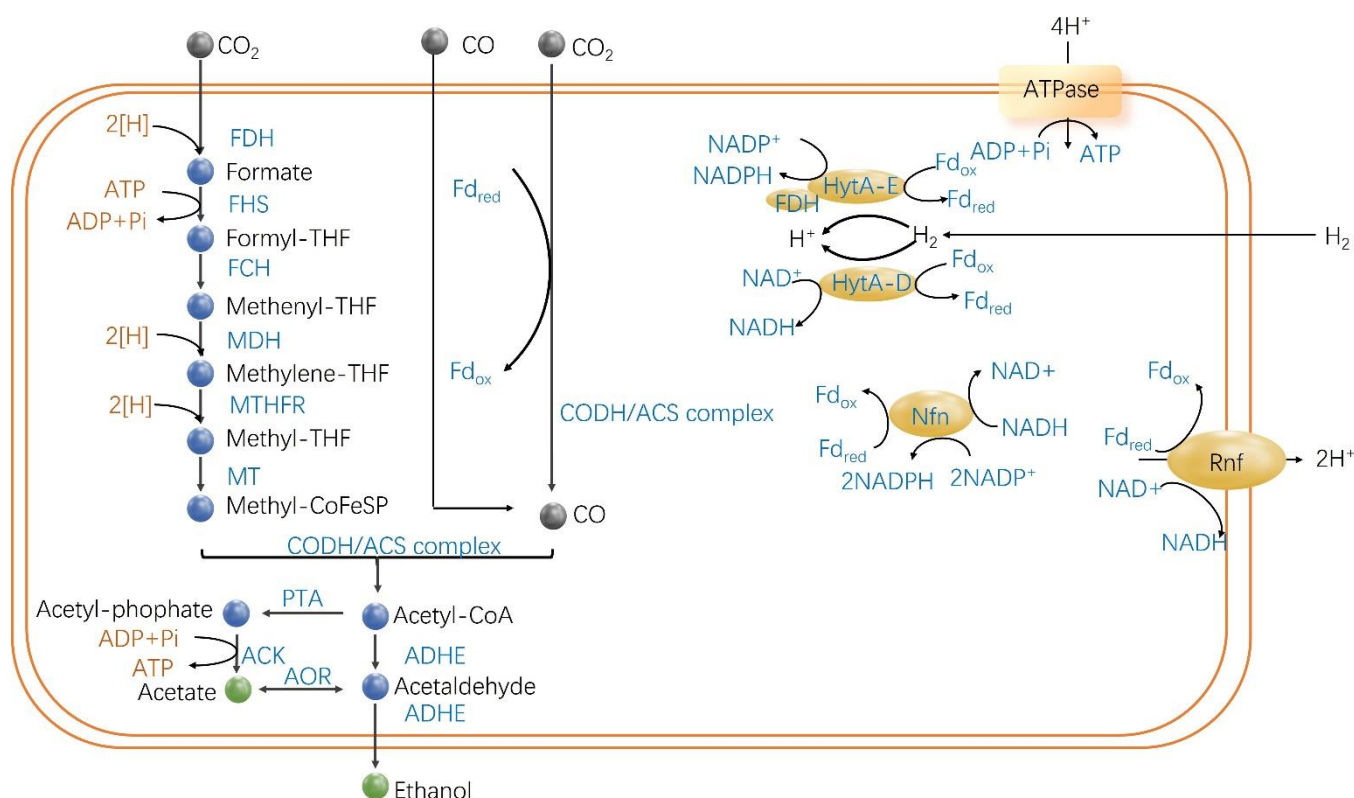


Figure 1. Key metabolic pathways and key enzymes of acetogens [50]. Adapted from reference [50]. THF: Tetrahydrofolate; FDH: Formate dehydrogenase; FHS: Formyl-tetrahydrofolate synthase; FCH: Formyl-cyclohydrolase; MDH: Methylene-tetrahydrofolate dehydrogenase; MTHFR: Methylene-tetrahydrofolate reductase; MT: Methyltransferase; CoFeSP: Corrinoid iron-sulfur protein; CODH: CO dehydrogenase; ACS: Acetyl-CoA synthase; PTA: Phosphotransacetylase; ACK: Acetate kinase; Fd_{ox}: Oxidized ferredoxin; Fd_{red}: Reduced ferredoxin.

The synthesis of ethanol from acetyl-CoA as the precursor is tightly regulated in *C. autoethanogenum*, relying primarily on two core metabolic pathways: the AOR (aldehyde: ferredoxin oxidoreductase) pathway, which first reduces acetate to acetaldehyde and then reduces acetaldehyde to ethanol via alcohol dehydrogenase (Adh); and the ADHE (bifunctional aldehyde/alcohol dehydrogenase) pathway, in which AdhE directly reduces acetyl-CoA to ethanol. The genome of *C. autoethanogenum* encodes two AOR isoenzymes (Aor1 and Aor2) and two AdhE isoenzymes (AdhE1 and AdhE2). When using syngas, the AOR pathway exhibits tighter coupling with ATP metabolism, thereby conferring a competitive advantage in energy-limited environments. Furthermore, previous studies have shown that *aor2* knockout enhances ethanol synthesis, suggesting functional differences between Aor1 and Aor2; *aor2* deletion likely reduces metabolic flux diversion or substrate competition. Similarly, knockout of *adhE1* or *adhE2* also increases ethanol production, presumably by blocking the AdhE-mediated reversible reaction that oxidizes ethanol back to acetate, thereby diverting more reducing power and carbon flux toward the AOR pathway [51]. In addition, both the AOR and ADHE pathways possess bidirectional catalytic activity: they not only reduce acetate to ethanol during the exponential growth phase of the strain but also oxidize ethanol to acetate during the stationary growth phase or under specific conditions.

2.2. Metabolic Regulation Strategies of Acetogens

The construction and optimization of strains represent a core step in enhancing the commercial feasibility of syngas fermentation processes. Adaptive laboratory evolution (ALE) has been successfully applied to the performance improvement of acetogens. For instance, the *C. autoethanogenum* strain *LAbrini*, obtained via ALE, exhibits superior growth performance, product synthesis efficiency, and environmental

robustness compared to the wild-type strain [52]. The development of specialized molecular tools is the fundamental basis for the engineering application of acetogens [53]. Given that most acetogens are strictly anaerobic Gram-positive bacteria, researchers have established shuttle plasmid systems that can be stably replicated and expressed in hosts. These systems provide a platform for the efficient expression of heterologous genes and genetic manipulation. Gene editing technologies have evolved from early traditional methods based on homologous recombination to efficient editing strategies based on the CRISPR-Cas system, enabling precision manipulations such as gene knockout, knock-in, and base editing. This advancement provides critical technical support for precise, multi-site genome modifications [54–57]. In recent years, three anaerobically compatible fluorescent systems—FAST (fluorescent-activating and absorption-shifting tag), HaloTag, and SNAP-tag—have been reported, laying the foundation for high-sensitivity, fluorescent-based, high-throughput, rapid screening of acetogens [58,59].

In terms of high-value and diversified product modification, the expansion and regulation of product profiles have been successfully achieved through strategies such as gene deletion, modification, and heterologous pathway expression: knockout of the bifunctional aldehyde/alcohol dehydrogenase in *C. ljungdahlii* can regulate the yield ratio of acetate to ethanol [60,61]; heterologous expression of acetone and butanol synthesis pathways, as well as construction of non-natural product synthesis pathways, have enabled the synthesis of various high-value target products including acetone, butanol, biodiesel precursors, and polyhydroxybutyrate (PHB), thereby enhancing the industrial value of syngas fermentation [25,62–64]. In addition, researchers have further improved the fermentation performance of strains through auxiliary engineering strategies: by regulating factors related to extracellular polysaccharide synthesis and biofilm formation, combined with the development of hollow fiber membrane bioreactors, the reaction stability of strains has been improved [65]; by precisely regulating the expression of Spo0A, a key regulatory factor for sporulation, or targeting downstream regulators to construct asporogenous strains, the negative impact of sporulation on fermentation efficiency has been reduced [66].

2.3. High-Throughput Construction of Syngas-Fermenting Strains

High-throughput construction of syngas-fermenting strains is a key step toward overcoming the inherent drawbacks of acetogens and promoting their industrial application. Relying on gene editing, automation, and screening technologies, it enables rapid, large-scale construction and screening of genetically modified strains, thereby optimizing gas utilization efficiency, product yield, tolerance, and strain robustness. Compatible with automated strain construction, high-throughput screening technologies have developed rapidly, enabling rapid screening of mutants with application value from genetically diverse strain libraries and enhancing the industrial application capacity of the strains [67–69].

Currently, microplate, microdroplet, and single-cell screening are widely used high-throughput screening systems [70]. For the high-throughput screening under anaerobic conditions, there are presently successful cases focusing on key areas such as strain viability detection and metabolite screening. For metabolite screening, researchers have developed a high-throughput spectrophotometric detection method based on the alcohol dehydrogenase of the thermophilic anaerobic bacterium *Thermotoga hypogea*. Using microplates, this method can quickly and efficiently screen high-butanol-producing mutant libraries under anaerobic conditions [71]. In evaluating the growth characteristics of anaerobic production strains, researchers have combined high-throughput anaerobic growth curve determination technology with a systematic data analysis framework, and this strategy has been successfully applied to screening research on *Clostridium kluyveri* [72]. This integrated technology can simultaneously detect and analyze the concentrations of multiple substrates and products, providing strong technical support for bioprocess modeling and optimization as well as the screening of high-efficiency strains. The core design concept of anaerobic high-throughput screening platforms is to adapt and integrate high-throughput detection and culture systems for use in an anaerobic environment.

However, reports on high-throughput screening systems targeting syngas-fermenting microorganisms are relatively rare. The toxicity, flammability, and explosiveness of CO and H₂ in syngas have led to a lag in the research and development of high-throughput screening technologies for strictly anaerobic acetogens, and there is a lack of mature commercial solutions. In addition, the system requires extensive customization to ensure stable operation, further increasing the use cost [73]. In 2019, LanzaTech established the world's first fully automated, high-throughput *Clostridium* workstation, achieving whole anaerobic operation in a toxic, flammable gaseous environment [74]. The construction and screening of thousands of strains were completed based on microplate fermentation technology, providing a paradigm for technological breakthroughs in this field. Regarding the workstation-specific design principles and operational mechanisms, no detailed elaboration has been provided in the relevant reports. Nevertheless, this microplate platform has drawbacks, including limited gas-liquid mass transfer, inability to fully simulate the real fermentation environment, cumbersome isolation and purification of dominant strains, and limited iterative throughput. Therefore, there is an urgent need to develop high-throughput screening systems with smaller systems and higher mass transfer efficiency. Microdroplet culture systems have advantages such as microliter-scale culture, efficient gas-liquid mass transfer, online culture, and in-situ detection and sorting [75]. No relevant research reports on the application of microdroplet systems in syngas fermentation have been published so far. Although this strategy has significant application potential, syngas fermentation strains generally grow slowly and require long-term incubation. Therefore, two key issues urgently need to be addressed for the engineering application of this technology. One is maintaining the physical and chemical stability of microdroplets for several days; the other is efficiently recovering strain cells from target droplets after screening to support downstream culture and sequencing analysis [75].

Currently, the high-throughput construction and screening of syngas-fermenting strains remain challenging. At the host level, the low transformation efficiency and homologous recombination efficiency of some acetogens limit the construction of large-scale libraries. Moreover, wild-type strains exhibit slow growth and poor tolerance, requiring optimization of chassis cells through adaptive evolution or rational design, which is a time-consuming process. At the screening technology level, high-throughput methods for gas fermentation-related phenotypes remain immature. The most essential traits require verification in small-scale bioreactors, which is time-consuming and labor-intensive. At the automation level, it is necessary to address challenges such as equipment stability and reliability, the balance between standardization and flexibility, and the development and compatibility of information automation protocols [76,77]. Furthermore, due to workflow variability, customized solutions need to be designed for different scenarios [76].

3. Scale-Up of Syngas Fermentation

The large-scale production of syngas fermentation is a highly integrated biomanufacturing platform. The full release of its industrial potential relies on the collaborative optimization and in-depth coupling of the upstream, midstream, and downstream integrated industrial chain technology systems. Upstream technology focuses on syngas purification as the core; its technical level directly determines the purity, composition stability, and supply cost of the feed gas, thereby affecting the microbial activity and product selectivity in the subsequent fermentation process. Midstream technology focuses on the construction and regulation of the fermentation system, which determines product yield, production efficiency, and process stability. Downstream technology involves the separation and purification of target products, the utilization of by-products as resources, and heat recovery. The application of efficient separation technology can significantly reduce energy consumption in product purification, while recycling fermentation wastewater can achieve the dual goals of efficient resource utilization and environmental friendliness.

3.1. Feed Gas Pretreatment

Feed gas pretreatment is a critical link to ensuring stable fermentation operation. Its main objectives are to remove or reduce toxic impurities harmful to fermentative microorganisms, while adjusting the physicochemical parameters of the gas to better match fermentation conditions. Syngas is mainly derived from coal or biomass gasification or from industrial exhaust gas, and it contains various impurities, such as particulates, ash, tar, sulfides, and nitrides [64]. As shown in Table 1, particulates and ash can cause equipment abrasion and pipeline blockages; tar can cover microbial cell surfaces, hinder mass transfer, or damage membrane integrity; sulfides and other substances can destroy enzyme activity and inhibit metabolism. Untreated syngas severely inhibits cell growth and can even terminate fermentation, whereas appropriately pretreated syngas can significantly promote the synthesis of target products, such as ethanol [39,78–80]. As shown in Figure 2, as a multi-step integrated system, the core processes of pretreatment include: first, cooling and particulate removal, which removes particulates and ash from high-temperature gasification gas (>800 °C) through equipment such as cyclone separators and ceramic filters [81]; second, tar removal, which can adopt technologies such as scrubbing, catalytic cracking and adsorption; third, desulfurization treatment, which achieves deep removal of sulfides through amine absorption or adsorption by zinc oxide and activated carbon [82,83]; fourth, gas conditioning, which adjusts the gas composition ratio by pressure swing adsorption (PSA) or membrane separation, combined with compression regulation to match fermentation requirements [84]. The pretreated feed gas must meet the cleanliness requirement, with impurity content below the microbial tolerance threshold, and have an appropriate composition that meets the metabolic needs of the strains.

Table 1. Common impurities in syngas.

Impurity Categories	Typical Representatives	Main Sources	Tolerance Threshold
Particulates and Ash	Dust, carbon particles	Entrained by gasification feedstock, generated during reactions [64]	No mentioned
Tar and Aromatic Hydrocarbons	Benzene, toluene, naphthalene, phenols	Incomplete pyrolysis products of biomass/coal [78]	Benzene, toluene, and xylenes (BTX) < 0.19mM [85]
Sulfides	Carbonyl sulfide (COS)	Converted from sulfur elements in the feedstock during gasification [80]	No mentioned
Nitrides	Hydrogen cyanide (HCN)	Converted from nitrogen elements in feedstock [79]	<0.1 mM [86]
Other Impurities	O ₂ , acetylene	Feedstock impurities or incomplete reactions [79]	<1900 ppm O ₂

In practical applications, multiple factors need to be considered when selecting purification technologies. The pretreatment process of feed gas is a core challenge for its industrial application. This process is not merely a collection of purification steps, but a dynamic, integrated systems engineering approach that must cope with upstream gas-source fluctuations and connect to downstream bioconversion [79]. Its implementation approaches can be divided into the following aspects. At the process design level, flexible modular configuration, multi-stage enhanced purification combination, online monitoring with adaptive control, and reliability design are adopted. These measures enable the system to adapt to fluctuations in the composition, impurity content, and flow rate of complex industrial gas sources, ensuring that the outlet gas quality remains within the safe tolerance range for microorganisms. Among them, the adoption of high-efficiency technologies, such as catalytic cracking, further expands the scope of treatable gas sources. At the strain level, targeted measures are implemented to enhance strain resistance to residual impurities: exploring the intrinsic tolerance of industrial strains and reinforcing their detoxification mechanisms via metabolic engineering modification. This not only relaxes the requirements for pretreatment depth to cut costs, but also serves as an essential supplementary approach for improving the

overall tolerance of the system [84,87]. Economy is the core inspection criterion for the pretreatment process, and a balance must be achieved between purification depth and investment-energy consumption. Through energy integration strategies such as heat and pressure energy recovery and a long-term, stable operation design that ensures catalyst lifespan and adsorbent regeneration efficiency, life-cycle cost optimization is realized.



Figure 2. Feed gas pretreatment [88]. Created with AI tool Doubao.

3.2. Syngas Fermentation

3.2.1. Large-Scale Reactors

Gases supply both the carbon source and energy for syngas fermentation. Among them, the low solubility of CO and H₂ impairs mass transfer efficiency, thereby limiting the metabolic rate of strains [89–91]. Gas-liquid mass transfer refers to the process of mass exchange between the gas and liquid phases. It occurs as gas molecules diffuse across the interfacial boundary layer at the phase interface, thereby accomplishing the transfer from the gas phase into the liquid phase. A three-phase system consisting of a mixture of gaseous substrates, a liquid nutrient solution, and cells suspended in the broth is present in the reactor. For gases with poor solubility, the primary mass transfer resistance lies in the liquid film at the gas-liquid interface [92]. The volumetric mass transfer coefficient, K_{La} , is commonly used to evaluate the mass transfer characteristics of the reaction system. K_{La} is specific to each system and depends on various parameters, such as agitation speed, gas flow rate, bubble size, liquid circulation rate, reactor geometry, internal structure, or packing material [93,94]. Gas-liquid mass transfer is a vital reactor characteristic that can be improved by selecting appropriate parameters or designs. Since systems with efficient gas-liquid mass transfer usually require increased energy consumption, which reduces efficiency, the K_{La} value must be correlated with the required volumetric power input (P/V) for a more reliable comparison [95,96]. While increasing power input enhances mass transfer, the optimization objective is to minimize energy consumption while meeting process requirements. This necessitates a careful consideration of reactor geometry, operating conditions, and biological system characteristics. In gas fermentation, this balance is critical, as it directly affects the economic feasibility of the process. Therefore, optimizing bioreactor design is crucial for improving cell growth and unit productivity in gas fermentation [31,97,98].

Currently, improvements in K_{La} are primarily accomplished by increasing the gas-liquid contact area, reducing mass transfer resistance, and enhancing the mass transfer driving force. Hollow fiber membrane reactors (HFMRs) utilize a unique membrane structure in which micropores in the membrane wall serve as gas-distribution units. HFMRs leverage the high specific surface area of membrane materials to intensify gas-liquid mass transfer. The membrane also serves as a carrier for microbial biofilm attachment [99,100]. As shown in Table 2, Yasin constructed a membrane reactor using hydrophobic polyvinylidene fluoride (PVDF) material, achieving a K_{La} of 155.16 h⁻¹ [99]. In the membrane reaction system established by Shen

et al., the K_{La} for CO reached a peak of 1096.2 h^{-1} , and efficient mass transfer was maintained even at low gas flow rates [101,102].

Table 2. Reactors applied to syngas fermentation and their fermentation performance.

Reactor Configuration	Microorganisms	Gas Composition	$K_{La} \text{ (h}^{-1}\text{)}$	Product	Productivity/Titer	P/V
CSTR	<i>C. ljungdahlii</i>	Syngas consisted of 70% CO	135	Ethanol, acetate	Total concentration 11 g/L [103]	Not mentioned
Airlift reactor	<i>C. carboxidivorans</i>	CO, CO ₂	23.8–153.6 (CO) 19.0–122.2 (H ₂)	Acetate	Acetate 7.2 mmol/L, Ethanol 32.3 mmol/L,	3–23 W/m ³ [104]
HFMBR	<i>Eubacterium limosum</i>	CO	63.72–135.72 (CO)	Acetate	20.92 mmol/L [99]	Not mentioned
HFMBR	<i>C. carboxidivorans</i>	CO, CO ₂ , H ₂	400–1096.2 (CO)	Ethanol	3.12 mmol/L/h [101]	Not mentioned
Trickle bed	Not applied	Air	421 [105]	Not applied	Not applied	Not mentioned
Trickle bed	<i>Clostridium ragsdalei</i>	CO, N ₂ , CO ₂ and H ₂	Not mentioned	Ethanol	3.43 mmol/L/h [106]	Not mentioned

Airlift reactors drive liquid circulation relying on density differences, eliminating the need for mechanical agitation. When optimized with microporous spargers, the maximum K_{La} can reach 91.1 h^{-1} , featuring uniform flow fields and mild shear stress [107]. Biofilm-packed trickle bed reactors form thin liquid-film structures within the packing materials, which shorten the substrate diffusion path; their mass transfer rates are significantly higher than those of traditional continuous stirred-tank reactors (CSTRs) [105,108,109]. CSTRs can improve flow field distribution and intensify bubble breakup by optimizing the agitation structure, thereby further enhancing K_{La} [110]. The bulk-gas-to-atomized-liquid (BGAL) contactors disperse liquids into micron-scale droplets via atomization, reconstructing the gas-liquid contact interface. When oxygen is used as the model gas, the K_{La} can reach approximately 8208 h^{-1} , and the mass transfer efficiency is improved by more than one order of magnitude compared with traditional reactors [88,107].

Gas distributors can enhance K_{La} by regulating the initial bubble size and distribution; their performance determines the initial level of gas-liquid contact area [111]. Optimizing the structure, pore size, and material can achieve bubble miniaturization and homogenization, thereby significantly improving mass transfer efficiency. Among them, microbubble dispersers are the most widely used and effective, capable of generating microbubbles with diameters less than $100 \mu\text{m}$. Compared with traditional large bubbles, these microbubbles have a much larger specific surface area, a slower rising speed, and a longer liquid-phase residence time, which can significantly increase gas-liquid contact opportunities and reduce liquid film thickness [111].

Without changing the reactor hardware configuration and components, optimizing operating conditions and process parameters is the preferred approach to improving mass transfer efficiency of existing devices. According to Henry's law, increasing the reactor operating pressure can directly increase the solubility of gaseous substrates in the fermentation broth, enhance the mass transfer driving force, and thus improve K_{La} ; increasing gas and liquid flow rates can promote bubble breakup and dispersion, strengthen liquid phase turbulence, and reduce liquid film thickness and boundary layer thickness. Shen et al. have confirmed that increasing gas-liquid flow rates in hollow fiber membrane reactors can significantly improve the K_{La} for CO, and higher liquid flow rates can also avoid bubble coalescence and maintain the renewal frequency of the gas-liquid interface; for stirred-tank reactors, agitation speed is a key control parameter [101,102]. Increasing the rotation speed can enhance impeller shear force, refine bubble size, and improve the uniformity of liquid-phase mixing. However, excessively high rotation speed may damage microbial cells and inhibit metabolic activity, and this balance needs to be considered in combination with strain characteristics.

The design objective of commercial reactors is to enhance feed gas conversion efficiency with low energy consumption, thereby improving the yield of target products. Therefore, this objective should serve as a benchmark for balancing the relationships among various operating parameters. Airlift reactors offer advantages such as no mechanical agitation required, low maintenance costs, energy conservation, low shear forces, and a simple mechanical structure. They can improve gas conversion efficiency by extending gas residence time [104,112,113]. As shown in Figure 3, the reactor consists of two interconnected compartments: a riser section for receiving gas flow and a downcomer section for liquid reflux. The density difference between the riser and downcomer sections drives liquid circulation [108]. In addition, due to their unique design, airlift reactors offer advantages for handling high-viscosity or high-density liquids, thereby effectively enhancing gas-liquid mass transfer and promoting microbial growth. Peter conducted syngas fermentation using *Clostridium carboxidivorans* in an airlift reactor and a CSTR, with product concentrations of 1.5 g/L ethanol and 0.7 g/L butanol, and 1.2 g/L ethanol and 0.4 g/L butanol, respectively [104]. Under the same operating conditions, compared with CSTRs, the volumetric power input, mass transfer coefficient, and mixing time of the airlift bioreactor are 0.05%, 5%, and up to 2806% of those of the CSTRs, respectively [104]. Therefore, compared with CSTRs, airlift reactors have lower operating costs.

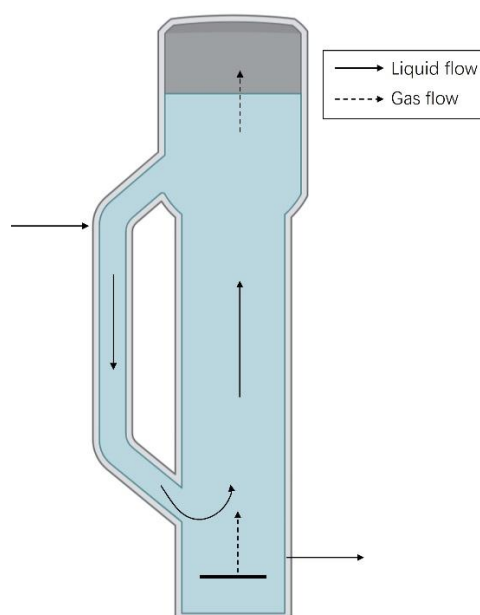


Figure 3. Airlift reactor. Created with BioRender.com.

For syngas fermentation to achieve economic feasibility on a commercial scale, it must rely on a simplified process design and cost control as prerequisites [114]. During scale-up, if productivity increases solely by replicating the number of reactors, production costs will increase linearly. According to the estimates by Takors et al., the volume of a single bioreactor for syngas fermentation must exceed 500 m³, and the specific power consumption must be within 0.3 kW/m³ for the entire process to be economically viable [115].

The economics of reactor selection and scale-up are a crucial factor limiting the commercialization of syngas fermentation. Although CSTRs are widely used in laboratory research, they face high operating costs during scale-up. The gas-liquid mass transfer limitation in the syngas fermentation process must be overcome by high-speed agitation, but this high volumetric agitation power results in a drastic increase in energy consumption. In addition, although membrane reactors have the advantage of a large specific surface area for improving mass transfer efficiency, they also face prominent economic bottlenecks in scale-up: on one hand, membrane reactors have inherent problems such as membrane fouling and high investment costs,

with membrane modules accounting for up to 73% of the equipment procurement cost; on the other hand, the modular nature of membrane systems determines that capacity expansion relies on increasing membrane area or adding module quantities, and scale economies cannot be achieved by increasing the size of a single unit [5]. This results in investment costs that are difficult to decrease linearly with scale expansion, constituting a significant barrier to scale-up. The economic limitations of the above two types of reactors fully indicate that the scale-up of syngas fermentation must overcome the problem of economic adaptability at the reactor level, which is supported by commercial cases represented by Shougang LanzaTech, which have selected airlift reactors, a type of reactor that achieves a better balance between mass transfer efficiency and operating costs.

3.2.2. Fermentation Strategy

Single-stage fermentation is a process completed in a single reactor, in which syngas is directly converted into target products. Its advantages lie in a simple process flow and low equipment requirements. At the same time, its disadvantages include the potential for microbial strains to be subject to product inhibition, leading to reduced product yield. Consequently, single-stage fermentation is suitable for simple, rapid production, but its efficiency and yield may be constrained. In single-stage syngas fermentation, ethanol inhibits microbial metabolic activity, limits ethanol concentration in the fermentation broth, and thereby affects product yield [107].

Two-stage fermentation divides the syngas fermentation process into two stages for treatment. In the first stage, syngas is converted into intermediate products, and in the second stage, these intermediates are further transformed into the final target products. Different operating conditions or microorganisms can be adopted in each stage to optimize fermentation efficiency [116]. *Butyrivibrio methylotrophicus* converts syngas into acetic acid and butyric acid, and then *Clostridium acetobutylicum* is used to convert the products of the first stage into ethanol and butanol [117]. By separating the growth and production stages and optimizing the process parameters for each, the production efficiency of syngas fermentation can be further improved. *C. ljungdahlii* conducts syngas fermentation, which is divided into growth and production stages through different reactors and operating conditions. The operating conditions of both stages are optimized to adapt to their respective objectives, and the final ethanol production rate can reach 0.37 g/L/h [118]. Meanwhile, this system recovers and reuses the incompletely converted gas to improve substrate conversion rate and reduce production costs. Multi-stage fermentation can not only increase product yield but also enhance product diversity. *C. carboxidivorans* is first used to convert syngas into acetic acid and butyric acid, and then *Yarrowia lipolytica* utilizes acetic acid and butyric acid to synthesize β -carotene [119].

The feed gas for syngas fermentation is mainly derived from industrial off-gases, suggesting that a continuous fermentation process is suitable. Upstream industrial processes, such as blast furnace ironmaking and coal gasification, operate continuously 24 h a day, and off-gases are continuously produced [88]. The CO-containing feed gas is toxic, flammable, and has a low energy density. Large-scale storage is not only technically complex and costly but also poses significant safety hazards; the optimal approach is on-site production and immediate use. Continuous fermentation can stably and continuously consume the continuously supplied gas source, matching the upstream production [120]. They avoid the shutdown issues caused by batch switching, equipment preparation, and sterilization in batch fermentation, thereby preventing resource waste and carbon emissions resulting from feed gas venting [121]. Dynamic balance is achieved through continuous material flow, improving the material utilization rate [122]. From an operational perspective, because the growth of syngas-fermenting microorganisms is slower than in batch fermentation, continuous fermentation reduces batch intervals, shortens the fermentation cycle, improves equipment utilization, and lowers operating costs.

3.2.3. Fermentation Process Control

In the process control of syngas fermentation, in addition to routine monitoring of temperature, pH, ORP (oxidation-reduction potential), cell density, and other parameters, gas composition analysis is also essential. Mass spectrometry can detect almost all gases and enable simultaneous multi-component analysis in a single measurement, making it suitable for the accurate detection of complex gas mixtures [123].

During syngas fermentation, real-time monitoring of dissolved CO, CO₂, and H₂ concentrations in the fermentation broth is crucial for process control. However, commercial electrodes capable of directly detecting these dissolved gases have not yet been developed. Current technologies mostly rely on offline analysis methods, which still have limitations in practical applications [124]. Although the CO-myoglobin optical absorption method can detect dissolved CO, it is complex to operate, and the protein has a limited lifespan, making long-term online monitoring difficult [124]. The low solubility of CO and H₂ results in extremely low concentrations in the liquid phase, requiring sensors with extremely high sensitivity [39]. Complex components in the fermentation broth may interfere with sensor signals, so it is necessary to develop anti-contamination materials or specific recognition technologies [124]. In industrial-scale reactors, the concentration of dissolved gases fluctuates on a second-by-second scale, requiring sensors with a response time of less than 1 s, which is far beyond current technical capabilities [125].

3.2.4. Process Simulation and Reactor Scale-Up Design

Modeling of the syngas fermentation process can be classified into three closely related systems, ranging from microscale to macroscale, based on the research methods and scales used. Cell-scale metabolic and kinetic modeling focuses on intracellular metabolism and quantifies the kinetic behaviors of microbial growth, substrate consumption, and product synthesis. Based on analyses of the metabolic pathways of specific acetogens, it uses classical kinetic equations, such as the Monod and Haldane equations, or genome-scale metabolic network models to clarify growth rates, substrate inhibition effects, and product distribution rules. It serves as the foundation for revealing the intrinsic mechanisms of biotransformation and optimizing strain performance [126,127]. Interphase mass transfer modeling targets the rate-limiting step in the three-phase gas-liquid-solid system of syngas fermentation, describing the transfer of gas from bubbles to the liquid phase and then to the cell surface [112]. By calculating the K_{La} and constructing mass transfer equations based on the two-film theory, it quantifies the limiting effect of mass transfer rate on the overall reaction rate, linking gas-phase substrate supply with cellular metabolism. Hydrodynamic and system modeling at the reactor scale enables the coupling of microscale kinetics, mass transfer processes, and macroscale reactor behavior, and is primarily applied to process scale-up design and optimization. Specifically, this modeling method establishes mass and momentum balance equations for different reactor types. It also simulates the flow field, bubble distribution, and concentration field inside the reactor by integrating computational fluid dynamics (CFD) techniques [128].

In addition, the core bottleneck in the industrial-scale up of syngas fermentation lies in the heterogeneity of large-scale reactors. In laboratory-scale small-volume reactor systems, approximate ideal mixing conditions can be achieved through intensified stirring, thereby maintaining uniformity in key reaction parameters such as substrate concentration, pH, and pressure, providing a stable environment for microbial metabolism. However, fundamental changes occur in the hydrodynamic characteristics of the system as the reactor scale is scaled up from several liters to hundreds of cubic meters, and these changes trigger a series of chain reactions. On the one hand, macro mixing and circulation time are prolonged, with the time required for the liquid to complete a full cycle in the reactor increasing significantly [129]. On the other hand, the characteristic time constants (e.g., microbial substrate consumption rate and gaseous substrate dissolution rate) may be shorter than the fluid circulation time. This further results in the formation of significant gradients in concentration, pressure, and gas composition along the fluid flow direction inside

the reactor [130]. During fluid circulation, microorganisms experience periodic drastic environmental fluctuations between “nutrient-rich zones” and “nutrient-depleted zones”, which directly affect their metabolic activity and stability [131].

To address heterogeneity challenges in large-scale reactors, optimizing reactor structures and operational modes is essential. Airlift reactors, driven by bubble ascent, offer lower energy consumption and larger gas-liquid contact areas, making them the preferred option for large-scale production [127]. Meanwhile, mass transfer efficiency can be enhanced and concentration gradients mitigated through gas recirculation (recovering unreacted off-gas) and microbubble generation [108]. Furthermore, mixing performance can be optimized by adjusting circulation parameters and gas delivery strategies, thereby reducing reactor heterogeneity [132].

In addition, the CRD-CFD coupled model can facilitate the accurate design and regulation of industrial scale-up [133]. CFD is employed to simulate the flow field, mixing time, shear stress, and concentration fields of key substances within the reactor, identifying dead zones and gradient regions [134]. The fluid environment information is then coupled with the CRD cell metabolism and growth model, and the Euler-Lagrange method is used to track virtual cell trajectories, predicting their physiological responses and differences in population metabolic activity [133]. To reduce computational costs, the CFD flow field can be divided into several perfectly mixed flow regions; flow rates derived from CFD are used to connect these regions, and the CRD model is run within each region, balancing computational efficiency with spatial heterogeneity. Based on scale-down model experiments, reaction kinetic parameters and microbial environmental response characteristics are determined. The CFD-CRD coupled model is established and calibrated using these parameters to achieve an integrated simulation of flow, mass transfer, and reaction. The model is iteratively calibrated using pilot-scale data, and the validated model serves as a “digital twin” tool for virtual screening of optimal configurations and operational parameters for industrial reactors, minimizing scale-up risks [132,135,136].

The CFD-CRD coupled model also faces several challenges. Full-scale, long-term, high-resolution simulations entail high computational costs; therefore, intelligent coupling strategies, such as surrogate modeling or machine learning, are used to improve computational efficiency while ensuring accuracy. Existing CRD models are relatively simplistic and fail to adequately reflect dynamic cellular stress responses. It is necessary to couple dynamic Metabolic Flux Analysis (dMFA) with CFD, and integrate real-time calibration using online sensor data to enhance prediction reliability [137]. Cells in the reactor exhibit heterogeneity in physiological states and other aspects; thus, population balance models (PBM) or individual-based models (IBM) should be incorporated into the CFD-CRD framework to comprehensively simulate changes in the distribution of cell population characteristics induced by environmental gradients and evaluate process stability [138,139].

Industrial pilot-scale studies have been conducted to tackle the heterogeneity challenge. For example, during syngas fermentation for acetone and isopropanol production at scales exceeding 120,000 L, LanzaTech achieved stable microbial production under fluctuating concentration conditions by deepening understanding of microbial metabolic robustness and optimizing gas delivery and mixing strategies [132]. In conclusion, addressing heterogeneity in large-scale syngas fermentation reactors is a systematic engineering task that requires integrating innovative reactor design, an optimized operational plan, and advanced simulation tools.

3.3. Separation and Purification of Products

In syngas fermentation, downstream product separation and purification are complex processes that aim to remove impurities and recover high-purity target products [16]. The concentration of products in the broth directly affects the cost and energy consumption of separation and extraction, and determines the economic benefits of the entire process. In the practical operation of syngas fermentation, the concentration

of target products is typically low, leading to high energy consumption during extraction. In addition, the target products contain numerous impurities, including microbial cell debris and metabolic by-products. The presence of these impurities further complicates separation and extraction. Ethanol is currently the main commercial product of syngas fermentation, which is mainly recovered by distillation. In the ethanol industry, distillation has emerged as the preferred option, as it delivers high ethanol recovery rates and can be paired with professional software to enable process simulation [140]. However, it still has shortcomings in practical applications: it requires additional separation steps to handle azeotropes, consumes high energy, and high-temperature operation may inactivate microorganisms and proteins [141].

Pervaporation is a membrane separation technology in which liquid permeates (such as ethanol) are vaporized downstream of the membrane under vacuum conditions and then recovered through condensation [16]. Pervaporation performance depends on the separation membrane characteristics, but in practice, membrane fouling and scaling require frequent cleaning, which, in turn, affects production efficiency. Previous studies have shown that combining membrane separation, extraction, and vacuum distillation can achieve efficient ethanol separation [142].

Given that each separation technology has its unique advantages and limitations, integrating multiple separation unit modules and implementing stage-wise separation would be an effective strategy to improve efficiency and compensate for the shortcomings of each method. However, many separation technologies are still in the early stages of development, and further studies are needed to confirm their industrial applicability. The future development of downstream separation in syngas fermentation will focus on the application of in situ product-removal technology. This technology can simultaneously separate products during fermentation, effectively reducing product inhibition and increasing cell density and yield. Meanwhile, the co-development of by-products into high-value products such as chemical raw materials or bio-feed can expand diversified revenue channels to improve process economics.

In the industrial field of syngas fermentation, distillation is a validated and widely adopted separation technology (exemplified by Shougang LanzaTech). Although technologies such as pervaporation offer significant energy-saving potential, they have not yet become mainstream industrial options, and their application remains at the pilot-scale-up or evaluation phase for specific projects.

3.4. Process Integration

In discussions of the stability and efficiency of syngas fermentation technology, the efficient treatment of upstream feed gas and the separation and recovery of downstream products are undeniably crucial. Meanwhile, the stable operation of auxiliary systems, such as water circulation and heat recovery, also significantly affects them. To utilize these feedstocks efficiently and sustainably, stable auxiliary facilities for water, electricity, gas, heat, and other resources must be equipped. The high integration of these links is a key factor in ensuring continuous, stable fermentation product output and high-efficiency production. Shougang LanzaTech has integrated six sections—raw gas pretreatment, biological fermentation, distillation dehydration, protein separation, waste heat recovery, and sewage treatment—into an integrated process technology. The high-temperature steam generated during the fermentation process can be used as a heat source for the process. Through waste heat recovery technology, it not only improves energy utilization efficiency but also reduces carbon emissions. By-products produced during fermentation need to be effectively separated and recovered; otherwise, they will adversely affect the stable operation of the system. Through protein separation, microbial proteins are removed from the fermentation broth, thereby avoiding interference with system operation and enabling further utilization of these resources. This highly integrated process design not only improves resource utilization efficiency but also reduces production costs and environmental impacts.

4. Economics and Policy Support of Syngas Fermentation

The main products derived from syngas fermentation are bulk chemicals, which exhibit significant price volatility and low profit margins. Although this technology features high resource utilization efficiency and environmental friendliness, its economics and profitability are constrained by multiple factors, requiring a comprehensive techno-economic analysis of specific projects. The construction of syngas fermentation facilities entails substantial capital expenditure (Capex), including reactors, gas pretreatment systems, sewage treatment systems, and other equipment. Operating expenditure (OpEx) is equally essential and covers feedstock costs, energy consumption, equipment maintenance, and more. Syngas can be derived from diverse sources, such as biomass gasification, coal gasification, and iron and steel plant off-gases. Syngas from different sources exhibits significant cost differences: the costs of syngas derived from natural gas and corn stover are 1724 USD/ton and 2878 USD/ton, respectively [143]. Many studies on the techno-economic analysis of syngas fermentation for fuel ethanol and microbial protein production overlook these factors, focusing primarily on environmental impacts [144]. Vlaeminck developed a comprehensive model covering the fermentation process of acetic acid and microbial protein production via gas fermentation, as well as gas pretreatment and downstream processing technologies. Techno-economic analysis using this model demonstrated the economic feasibility of the process. The study showed that increasing the acetic acid concentration to 45 g/L and the productivity to 4 g/L/h could reduce the cost from 4.15 USD/kg to 2.78 USD/kg. However, this model also overlooked many other details; the impact of ambient temperature on reactor temperature control cannot be ignored. In cost-sensitive regions, the accumulation of these secondary factors can also affect the final profit margin.

The feedstock price for syngas fermentation is subject to fluctuations in the coal or biomass markets; for instance, rising coal prices may drive up syngas costs. Meanwhile, process energy consumption accounts for 20–30% of total costs, and fluctuations in energy prices directly affect ethanol costs [145,146]. Fuel ethanol projects are price-sensitive and highly influenced by ethanol selling prices, which directly determine their economic viability. The price of fuel ethanol is closely correlated with that of gasoline. Changes in government subsidy can also lead to periodic price fluctuations [147]. Issues such as regional supply disruptions or demand changes in international trade and supply chains may disrupt the balance of the global ethanol market, thereby affecting ethanol prices [148]. Currently, only a small number of demonstration projects for syngas fermentation have achieved commercialization, and the scale effect and economic benefits have not yet been fully realized. Due to the dynamic changes and interconnections among the aforementioned factors, short-term operational data from a small number of projects cannot fully reflect the complex situation across the entire industry, nor can a clear conclusion be drawn about the economic benefits of syngas fermentation.

The United States regards bioconversion technology as an essential technical support for achieving carbon neutrality goals, with multi-departmental collaboration in conducting research and development (R&D) and industrial layout. Strategic documents issued by the United States, such as *Biomanufacturing to Advance the Bioeconomy*, released in 2022, and *Bold Goals for U.S. Biotechnology and Biomanufacturing*, issued in 2023, explicitly identify the conversion of renewable feedstocks, the development of low-carbon product preparation pathways, and the circular utilization of carbon sources such as CO₂ as core R&D directions. In October 2024, the U.S. Bioindustrial Manufacturing and Design Ecosystem (BioMADE) explicitly identified gas fermentation as a key technical pathway for producing fuels and chemicals using waste carbon sources such as industrial exhaust gas and syngas. The annual tender theme and the project scale determine the project funding amount. In January 2025, the Bioenergy Technologies Office (BETO) of the U.S. Department of Energy (DOE) and the Environmental Protection Agency (EPA) jointly announced the provision of a total of 6 million US dollars in funding for three biofuel promotion projects to support the leading position in energy and emission innovation. Among them, Air

Company Holdings, based in Brooklyn, New York, received 2 million US dollars in funding for its project “Conversion of Biobased Carbon Dioxide to Sustainable Aviation Fuel”. On 16 January 2025, the U.S. Department of Energy (DOE) announced an investment of approximately 13.7 million US dollars in four carbon conversion technology R&D projects, aiming to promote the conversion of carbon dioxide into environmentally friendly, high-value-added products and ensure U.S. energy and critical mineral security. Among them, the project “Large-Scale Electrolysis of Carbon Dioxide to Produce Carbon Monoxide and Chemicals” received approximately 5.9397 million US dollars in funding; another project converts carbon dioxide generated from starch fermentation in biorefining into carbon monoxide through electrocatalysis, which is then transported to a gas fermenter to produce ethanol.

The European Union (EU) takes the development of the circular bioeconomy and the transition to industrial decarbonization as its core orientation. By formulating a series of strategic plans and providing exceptional funding support, it promotes the innovative development of bioconversion technologies. Policy documents such as the *2023 Strategic Research and Innovation Agenda for Bioenergy* identify CO₂ bioconversion and synthetic fuel production as key technical directions, among which the PyroCO₂ innovation project focuses on industrial CO₂ conversion. The Industrial Carbon Management Strategy clearly defines phased goals for CCUS from 2030 to 2040. In 2021, the European Union (EU) invested 44 million euros to launch the PyroCO₂ innovation project, focusing on converting industrial carbon dioxide into chemical building blocks via biotechnology, and constructing facilities capable of capturing 10,000 tons of industrial carbon dioxide annually. On 16 November 2021, the EU announced an investment of 1.1 billion euros in 7 large-scale cross-border innovation projects across multiple European countries under the “Innovation Fund” framework, aimed at promoting the commercialization of breakthrough decarbonization technologies for energy-intensive industries. This funding covers technologies such as hydrogen energy, CCUS, and so on. In 2022, under the “Innovation Fund” framework, the EU launched a 150-million-euro large-scale climate transition innovation project to construct the first large-scale commercial bioenergy with carbon capture and storage (BECCS) facility.

Other developed countries have also deployed targeted policy frameworks to promote the development of relevant technologies based on their respective energy and environmental strategic needs. The United Kingdom has identified technologies such as bioenergy with carbon capture and storage (BECCS) and CO₂ conversion for sustainable aviation fuel production as core supporting technologies for achieving net-zero carbon emission goals, through measures including annual special funding and project carriers such as the “Direct Air Capture Technology Competition”. Within the framework of the Green Growth Strategy for Carbon Neutrality 2050, Japan focuses on supporting core technical areas, such as the development of CO₂-fixing microbial platforms and CO/CO₂ feedstock-oriented manufacturing technologies.

China’s goals for carbon neutrality provide strategic guidance for the biomanufacturing industry, and a series of policy documents have established a multi-level policy support system covering technological R&D, industrial application, and financial incentives. Policy documents, such as the 14th Five-Year Plan for Bioeconomy Development, explicitly identify biomanufacturing, CCUS, and non-grain-based biobased materials as key development areas. The *Guiding Opinions on Accelerating the Green Development of Manufacturing Industry* further focus on key technical fields such as industrial process coupling with CCUS and CO₂ bioconversion and utilization. The technology of producing ethanol from industrial off-gases has been successively included in the list of green and low-carbon technology demonstration projects and the *Fifth Batch of National Key Promoted Low-Carbon Technology Catalog*. *C. autoethanogenum* protein has been selected into the list of landmark biomanufacturing products, forming a full-chain policy incentive system covering technological R&D, pilot-scale amplification, and industrial application.

Overall, the United States emphasizes overall bioeconomy competitiveness, the European Union focuses on climate goals and circular economy, while China prioritizes integration with industrial system upgrading and comprehensive resource utilization. However, their commonality lies in providing extensive

support for cutting-edge green technologies from technological breakthroughs to market introduction through systematic policy design, thus accelerating their progression from the laboratory to industrialization.

Global policies universally endorse low-carbon technologies, yet specific provisions, including fiscal and tax incentives and integration with carbon markets that target syngas fermentation, have not been clarified. The primary barriers to the current promotion of syngas fermentation are the lack of detailed policy guidelines, high technological costs, and inadequate collaboration along the industrial chain. To address these challenges, efforts should focus on special incentives, standard formulation, demonstration projects, and international cooperation.

5. Challenges and Outlook

Although syngas fermentation technology offers advantages across multiple areas, such as carbon neutrality and process stability, it still needs breakthroughs in the following areas to support its commercialization.

The future development of industrial strains will center on the in-depth integration of the Design-Build-Test-Learn (DBTL) cycle: genome-scale metabolic models and machine learning are leveraged to predict design targets, with automated platforms combined to enable rapid construction of strain libraries; microreactor arrays coupled with gas consumption and product generation detection are developed to realize high-throughput phenotypic screening under actual fermentation conditions; and multi-omics analyses including transcriptomics, proteomics and metabolomics are applied to analyze microbial physiological responses, thereby guiding the next round of precise strain design. With the maturation of high-throughput screening technology for gaseous substrates, the automation and standardization of strain construction and testing will be gradually realized, thereby generating high-quality and large-scale datasets. These datasets support complex experimental design, facilitate close, iterative feedback between machine learning models and strain testing, and accelerate the research and development of syngas fermentation strains.

At the core technical level, low gas mass transfer efficiency constitutes a technical bottleneck that severely restricts production intensity. There is an urgent need to develop novel and high-efficiency reactors while reducing energy consumption associated with agitation, mixing, and other processes. Additionally, the issues of feed gas quality and high purification costs cannot be overlooked. Syngas derived from industrial exhaust gas or biomass gasification exhibits significant compositional fluctuations and contains impurities. Although deep purification can mitigate this issue, it substantially increases capital and operating costs. In the future, priority should be given to developing more tolerant engineered strains to reduce gas-purity requirements, while optimizing low-cost, high-efficiency online gas purification technologies to lower energy consumption and pretreatment costs.

In terms of engineering and operations, high energy consumption in downstream separation is a core challenge. The ethanol concentration in fermentation broth is usually low, resulting in high energy consumption during product separation, concentration, and purification. The development of in-situ product separation technology to continuously remove ethanol during fermentation can not only alleviate product inhibition but also reduce downstream separation load. Furthermore, the difficulties in scale-up and integration optimization urgently need to be addressed. Moreover, integrating and matching the energy requirements of multiple units, including purification, fermentation, and separation, is complex. It is necessary to develop more accurate scale-up models and process simulation tools, and to promote modular, standardized plant design to reduce investment risks and shorten the construction cycle.

In the economic and market domain, weak cost competitiveness constitutes the primary obstacle to commercialization. The large initial investment scale and persistently high operating costs render syngas-to-ethanol less competitive under the current price structure for fossil fuels and traditional bioethanol. It is imperative to reduce whole-process costs through technological breakthroughs while exploring business models for the co-production of high-value products, such as long-chain alcohols and microbial proteins, to enhance overall economic viability. Additionally, inadequate policy and market mechanisms restrict

industrial development, and the carbon-emission-reduction value of syngas-based ethanol has not been fully realized through carbon markets. There is a need to establish a carbon credit mechanism to monetize environmental benefits.

At the industrial chain and infrastructure construction level, the instability of the raw material supply chain is particularly prominent. Reliance on steel plant exhaust gas is constrained by geography and industry cycles, while biomass raw materials face high collection, transportation, and storage costs, as well as scattered supply. In the future, it is necessary to develop small- to medium-sized, modular production models adapted to distributed raw materials such as agricultural waste and municipal solid waste, while establishing long-term, stable cooperative relationships with large-scale industrial emission sources.

Under the guidance of the “dual carbon” goals, carbon capture and utilization technology serves as a core pillar for building a low-carbon energy and material system. Syngas fermentation, as a unique biocatalytic pathway, acts as a “flexible and efficient carbon molecular hub”. It forms strong complementary relationships with diverse carbon utilization technologies, jointly building a resilient carbon-neutrality solution.

Syngas fermentation exhibits significant complementary and synergistic relationships with other CCUS carbon utilization technologies. Traditional CCUS focuses on CO₂ geological storage and emission reduction. Syngas fermentation can share its capture and transportation infrastructure, create value through carbon utilization, and reduce storage costs, forming economic complementarity. CO₂ thermocatalytic/electrocatalytic conversion requires harsh conditions and has high reaction rates but limited product types. It complements syngas fermentation in technical routes, as the latter offers mild conditions, strong impurity tolerance, and a diverse product range. Biomethanation specifically produces CH₄ suitable for natural gas pipelines. It can flexibly adjust the output of energy and chemical products through syngas fermentation to meet end-user needs, thereby achieving product-matrix complementarity. Microalgal carbon sequestration relies on light, covers large areas, and has a long growth cycle. It complements syngas fermentation in terms of temporal and spatial efficiency, as syngas fermentation enables all-weather industrial production with higher volumetric productivity and adapts to different application scenarios.

Syngas fermentation is not intended to replace other carbon utilization pathways; instead, it serves as a key, flexible node in the carbon cycle network. Leveraging its bioconversion advantages, it converts waste carbon sources into green products. It forms a synergistic pattern in which storage secures the bottom line, and utilization generates economic value with storage, thermocatalysis, and other technologies. Its core positioning lies in enhancing the economic viability and industrial attractiveness of the CCUS system, serving as an essential engine for deep industrial decarbonization and the cultivation of emerging green industries.

Statement of the Use of Generative AI and AI-Assisted Technologies in the Writing Process

During the preparation of this manuscript, the authors used DeepSeek to improve the grammar and syntax. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

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As this article is a review paper, no original research data were generated. All information and data cited in this study were obtained from the published literature.

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