

# CO<sub>x</sub> Fixation to Elementary Building Blocks: Anaerobic Syngas Fermentation vs. Chemical Catalysis

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Supporting Information  
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Heterogeneous catalysis and anaerobic syngas fermentation represent two different approaches for the conversion of synthesis gas into chemicals and fuels. This review provides a unique comparison of different reaction paths for the fixation of CO<sub>2</sub>, CO and H<sub>2</sub> into elementary building blocks such as methanol, acetic acid and ethanol. Operating conditions, reactor engineering, influence of gas impurities, yields, conversion efficiencies as well as downstream product recovery are compared. It was found that mass-specific productivity ranges in the same order of magnitude for both technologies, while space-time yield of heterogeneous catalysis is up to three orders of magnitude higher.

**Keywords:** Acetogenic C<sub>1</sub> conversion, Biofuels, Carbon utilization, Heterogeneous catalysis, Reaction networks

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## 1 Introduction

A modern, stable civilization needs secure, affordable and sustainable energy sources. Our current dependency towards limited fossil resources leads via the inevitable liberation of carbon dioxide to major problems, which are currently perceived as “climate change” [1].

Two strategies can be outlined to lessen the impact of anthropogenic CO<sub>2</sub> emissions: an utilization as it is without prior modification stored in natural reservoirs [2] or its conversion into high added-value products. CO<sub>2</sub> is either being harvested from the atmosphere via concentration processes or directly used from stationary industrial point sources after appropriate purification [3].

The thermodynamic stability of CO<sub>2</sub> clearly hinders a direct utilization as alternative renewable carbon feedstock. However, the increasing share of sustainable energy production methods leads via water electrolysis to a seemingly inexhaustible hydrogen gas source. The combined utilization of green hydrogen and carbon dioxide opens the way to a range of exciting sustainable applications, opening the way to neutral-balanced productions and strongly contributing to a modern circular economy [4].

Synthesis gas (syngas) is one of the keystones of the current carbon-based chemistry and one of the solutions to circumvent the problematic carbon dioxide stability. Water-gas shift reaction (WGS) and its reversed variant

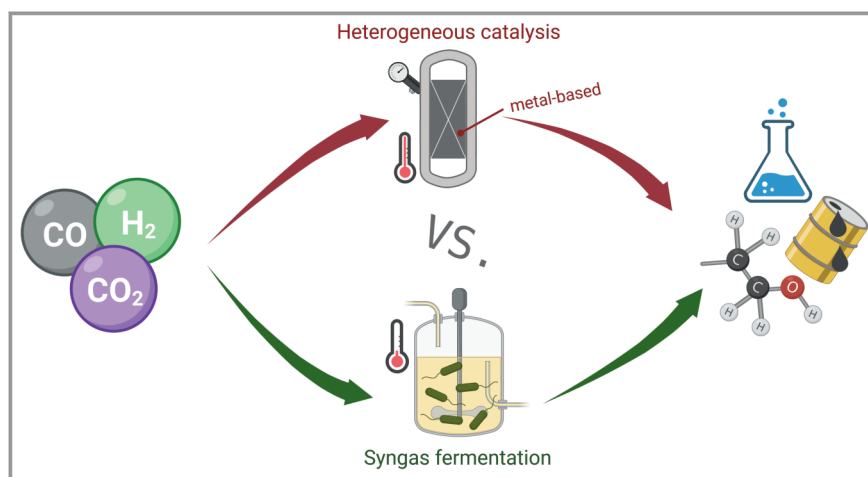
(RWGS) play a preponderant role in this context, allowing both activation of CO<sub>2</sub> and an adjustment of the required CO/H<sub>2</sub> gas compositions [5]. Tunable syngas compositions come in handy in relevant chemical processes such as the Fischer-Tropsch (FT) reaction or the production of methanol [6, 7]. Methanol plays a central role in new models for a sustainable economy via its extended portfolio of derivatives and its well investigated chemistry [8]. Alongside pure chemical processes, biochemical pathways using syngas relying either on natural or tailor-made enzymes [9] or even on whole cells [10] (e.g., bacteria) are in the focus of a growing interest. Owing to mild operating conditions, simple (bio)catalyst cultivation and the possibility to reach a complete conversion of the feed gas without necessary expensive loop management, biocatalytic conversion processes represent a promising contribution to a sustainable circular economy.

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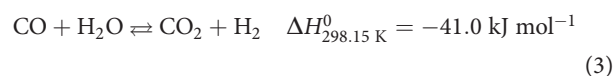
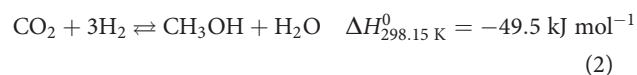
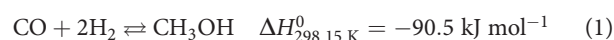
**Figure 1.** Conversion of CO<sub>2</sub>-rich syngas to fuels and chemicals via heterogeneous catalysis vs. syngas fermentation (created with BioRender.com).

In this contribution, we present an overview focusing particularly on C<sub>1</sub> and C<sub>2</sub> molecules (principally methanol (MeOH), ethanol (EtOH), dimethylether (DME) and acetic acid (AcOH)) directly obtained from CO<sub>2</sub>-rich synthesis gas (Fig. 1). Since MeOH is one of the most known process in the heterogeneous catalysis, it was chosen for a comparison with EtOH and AcOH through biocatalytic processes. The prevalent generation of MeOH from syngas using standard heterogeneous catalysis pathways is shortly presented in the first part, followed by an overview of the biosynthesis of C<sub>2</sub> building blocks based on syngas fermentation. This part focuses more on the mechanistic aspects and the connected process development. The tuning of the biocatalysts as well as the operating conditions are also documented allowing a broad comparison with the common chemical synthetic way. Having presented generalities on chemical and biochemical paths to C<sub>1</sub> and C<sub>2</sub> molecules, the third section of this review takes aim at some specific topics like stability of the catalyst, optimal temperature and pressure regions as well as yields encountered along the chemical and biochemical synthetic routes. Efficiency of the catalysts in terms of gas conversion and product range will be also discussed, as well as the connected downstream processes, important for the industrial relevance of the chosen synthetic way.

## 2 Heterogeneous Catalysis of C<sub>1</sub> and C<sub>2</sub> Building Blocks

Methanol is a key intermediate in the chemical industry, being a feedstock in the production of chemicals (e.g., formaldehyde, methyl tert-butyl ether, olefins, DME) and liquid fuels (e.g., gasoline, diesel, jet fuel) [11–14]. Besides, it is a suitable chemical energy storage, which can be used as fuel in spark-initiation compression engines, in fuel cells and in traditional fired heaters [15]. Worldwide, there is a combined methanol production capacity of ca. 164 Mt a<sup>-1</sup> with 10 % annual increase projected for the next decade [16].

In the methanol synthesis, the main reactions are CO hydrogenation (Eq. (1)), CO<sub>2</sub> hydrogenation (Eq. (2)) and WGS (Eq. (3)):



The most used catalyst in the methanol synthesis is the Cu/ZnO/Al<sub>2</sub>O<sub>3</sub> (CZA). The high activity of this catalyst comes from a Cu/Zn synergy as Zn increases binding to oxygen-bound species [10, 11, 17], while Al<sub>2</sub>O<sub>3</sub> contributes to a more uniform Cu distribution and improves stability [18–20]. Cu/Zn-based catalysts supported by zirconium oxide (Cu/ZnO/ZrO<sub>2</sub>, CZZ) have also proven to be highly active for the methanol synthesis, including for CO<sub>2</sub>-rich syngas [21–23].

Since its commercial production, Cu/Zn-based catalysts have been subjected to studies and continuous improvements, as the catalytic activity strongly depends on the catalyst properties (e.g., porosities, metal dispersion, surface area), which are influenced by synthesis protocols [18, 24]. Therefore, high efforts are put in the optimization of the catalyst preparation methods, further increasing the activity and stability of the catalysts [19, 25–28].

Despite the high activity and selectivity presented by the Cu-based catalyst, unfavorable effects related to the ZnO mobility also take place, particularly when water is formed via the reverse WGS. Therefore, numerous catalytic materials with unique compositions have been studied as possible alternatives to the Cu-based catalysts, aiming to increase the selectivity to methanol and stability to sintering during the reaction, especially at high CO<sub>2</sub> rich feeds [29]. Supported Pd and Pt alloys [30–32], In<sub>2</sub>O<sub>3</sub> and Ga-based catalysts

[32,33] as well as metal-organic frameworks (MOFs) [31,32,34] have been reported as efficient materials with high catalytic activity and stability for methanol formation.

In the methanol synthesis on Cu/Zn-based catalysts, the dominant reaction pathway is CO<sub>2</sub> hydrogenation to methanol on the Cu/Zn site via the formate intermediate (HCOO\*), even for a CO-rich syngas [35,36]. The produced water reacts with CO on both active sites (Cu and Cu/Zn) via the WGSR, closing the CO<sub>2</sub> cycle [35,37]. Direct CO hydrogenation could occur at moderate rates on the Cu active site, but is severely inhibited by formate, which accumulates on both active site types (Cu and Cu/Zn) in the presence of CO<sub>2</sub> [35,36]. In Fig. 2, the reaction mechanism is presented, and the main reaction pathway for a CO-rich syngas is highlighted. For a CO<sub>2</sub>-rich syngas, RWGSR acts as a side reaction, resulting in water accumulation in the reactor [35].

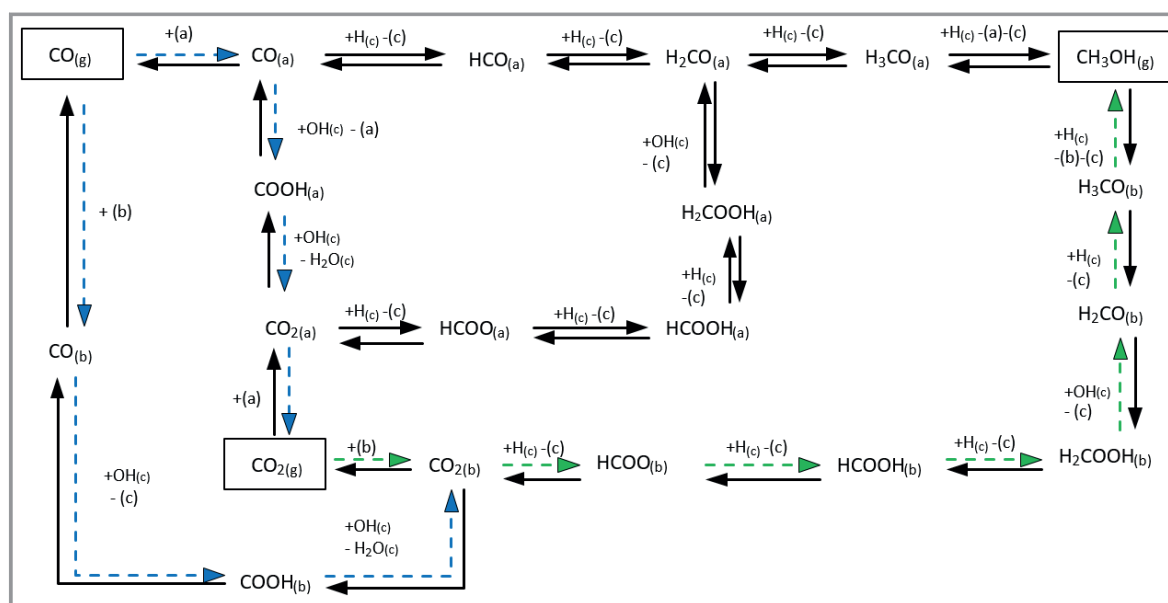
In Cu/Zn-based catalysts, the composition of zinc on the active surface is dependent on the concentration of reducing (H<sub>2</sub>, CO) and oxidizing agents (H<sub>2</sub>O, CO<sub>2</sub>) [38,39]. In the presence of H<sub>2</sub> or CO, ZnO is (partially) reduced and migrates to the surface, with its true nature being still under debate (either Zn<sup>0</sup>, Zn<sup>δ+</sup>, or ZnO<sub>x</sub>) [40]. The reduced Zn state is stabilized on the catalyst surface [41]. The reduction process is equilibrated with the concentration of CO<sub>2</sub> and water, causing dynamic changes in catalyst structure when syngas composition is varied [38,41]. Therefore, although direct CO hydrogenation is not significant in the methanol synthesis, CO enhances methanol production not only by consuming water via the WGSR, but also by promoting the quantity of Cu/Zn active sites [35].

Typically, methanol is synthesized from syngas (H<sub>2</sub>/CO) with low CO<sub>2</sub> content in gas phase reactors, which are operated at elevated pressures (50–100 bar) and temperatures (200–300 °C) [11].

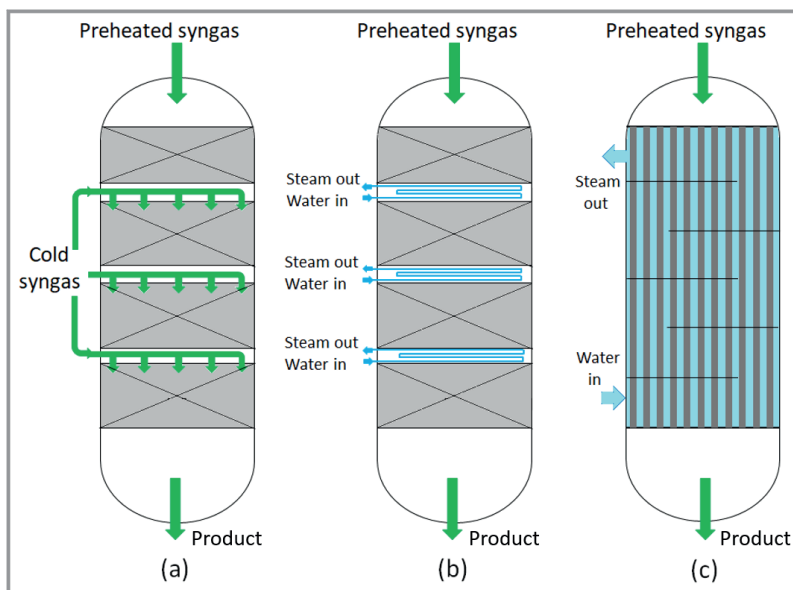
Because of the exothermic nature of the reactions (Eqs. (1)–(3)), the generated heat must be removed from the reacting system in order to control the temperature. In so-called quench reactors (see Fig. 3a), several catalyst beds are placed in series in adiabatic operation, and intermediate cooling is provided by the addition of cold syngas (e.g., ICI & Casale partnership, Haldor Topsoe process) [12]. Alternatively, boiling water inside inner tubes can also perform the intermediate cooling (see. Fig. 3b; e.g., Toyo Engineering reactor) [42].

A different approach is the so-called isothermal reactor, in which the catalyst bed is placed inside inner tubes and boiling water flows on the shell side, so that continuous cooling is provided to the reacting system (see. Fig. 3c; e.g. Lurgi methanol reactor, Linde isothermal reactor) [11,43]. While the quench reactor is simpler to operate, easier for changing the catalyst and less expensive, the isothermal reactor provides better temperature control, which increases catalyst activity, enables higher single-pass conversion, reduces catalyst deactivation and reduces by-product formation [12]. Novel reactor concepts such as microstructured [44,45] and membrane reactors [46–48] have been also proposed to optimize the process efficiency and product purity.

The MeOH synthesis in combination with its dehydration to produce DME (Eq. (4)) [49] is a particular example of combining two processes in a single reactor to enhance the CO<sub>x</sub> equilibrium conversion (see Fig. 4), hence, reduc-

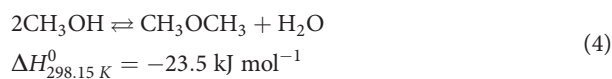


**Figure 2.** Reaction mechanism of the methanol synthesis on CZA. The colored arrows show the dominant pathway for a CO-rich syngas. a) Cu active site, b) Cu/Zn active site, c) Cu and Cu/Zn active sites available only for H<sub>2</sub> and H<sub>2</sub>O. Adapted from Campos et al. [35] with permission from the Royal Chemistry Society.

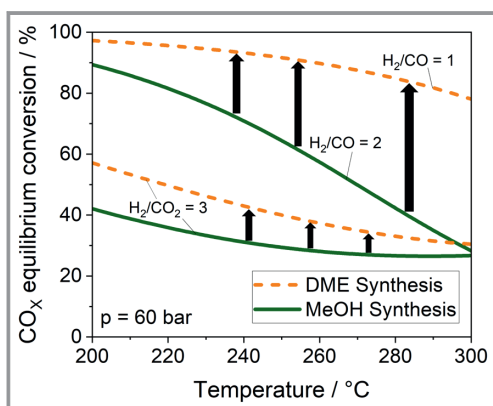
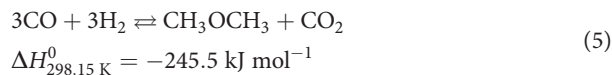


**Figure 3.** Basic types of a methanol reactor. a) Quench reactor, b) adiabatic reactor with intermediate heat exchange, c) isothermal reactor.

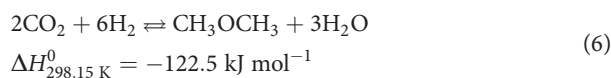
ing the number of reactors and the need for large downstream processes [25]. The dehydration reaction is given as follows:



Merging the methanol synthesis reactions (Eqs. (1)–(3)) with the dehydration reaction (Eq. (4)), the stoichiometric ratio is 1:1 for a  $\text{H}_2$ :CO feed (Eq. (5)) and 3:1 for a  $\text{H}_2$ : $\text{CO}_2$  feed (Eq. (6)):



**Figure 4.**  $\text{CO}_x$  equilibrium conversion of the methanol (solid lines  $\text{H}_2/\text{CO} = 2$  and  $\text{H}_2/\text{CO}_2 = 3$ , Eqs. (1)–(2)) and the direct DME synthesis (dashed lines  $\text{H}_2/\text{CO} = 1$  and  $\text{H}_2/\text{CO}_2 = 3$ , Eqs. (5)–(6)) at stoichiometric conditions and different temperatures. Data generated with Aspen Plus V10.

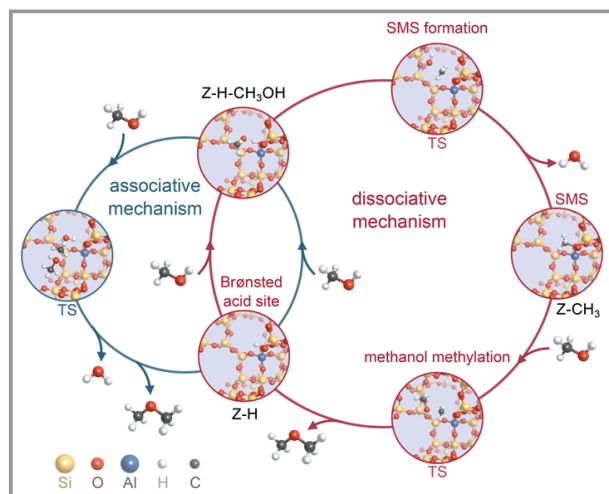


DME is a synthetic fuel that can substitute or blend into the liquefied petroleum gas (LPG) without modifications in the existing storage and handling infrastructure [50–52]. It is also a promising fuel for the transportation section due to its considerable energy density, its high cetane number (CN) and the absence of C-C bonds, resulting in lower emissions of particulate matter (PM), soot, hydrocarbons and CO, when comparing to diesel [53, 54]. DME is also a feedstock for different processes such as DME-to-Gasoline, DTG [55, 56], aromatic free olefins ( $\text{C}_4$  to  $\text{C}_7$  range) [57] and oxymethylene ethers (OMEs) [58].

In the direct DME synthesis from syngas, both catalysts are mixed in a single reactor (or a bifunctional catalyst is used), enabling both the methanol production from syngas and its further conversion to DME [59]. Besides, since the dehydration catalyst is significantly more active than the methanol synthesis catalyst, only 3–10 % m/m of the dehydration component is necessary to sufficiently convert methanol to DME [21, 60].

The selective dehydration of methanol to DME is catalyzed by a moderate acid catalyst, such as modified  $\gamma\text{-Al}_2\text{O}_3$  [61, 62], zeolites (e.g., MFI-type [63–65], FER-type [22, 66]), heteropoly acids (HPAs) [67, 68], silicoaluminophosphates (SAPOs) [69]. Ion exchange resins [70] have been studied as promising materials with high activity and selectivity to DME [71].

The methanol dehydration can occur either via the associative or the dissociative pathways (see Fig. 5). According to theoretical calculations from Arvidsson et al. [72] for different zeolites, the associative pathway is dominant at lower temperatures ( $< 300^\circ\text{C}$ ), while the dissociative pathway is preferred at higher temperatures.



**Figure 5.** Associative and dissociative mechanisms of the methanol dehydration to DME on a zeolite. Reproduced with permission from [72]. Copyright 2020 American Chemical Society.

### 3 Anaerobic Syngas Fermentation of C<sub>2</sub> Building Blocks

#### 3.1 Process Parameters and Microorganisms as Biocatalyst

The main difference between heterogeneous catalysis and syngas fermentation is that all fermentation processes take

place in aqueous solutions. A redox reaction delivers the energy for the bacteria to grow, that means to synthesize more bacteria. In opposite to traditional fermentation processes that are based on starch feedstocks [73, 74], synthesis gas fermentation uses gaseous C<sub>1</sub>-substrates and offers great flexibility regarding the feedstock. The fermentation reaction is catalyzed by a chemolithoautotrophic microorganism, and the products could be fuels, chemicals, fats, and proteins [75]. Knallgas bacteria, carboxydrotrophs, methanotrophs and methanogens could be used as chemolithoautotrophic platforms for gas fermentation [75–81]. Beyond that, anaerobic acetogens represent another possibility for gas fermentation. They are well investigated and already successfully in use at industrial pilot scale and commercial plants for anaerobic syngas fermentation [75, 82]. Therefore, they are discussed in more detail here.

Acetogens are found in 23 genera, and they are distributed all over the world with many possible habitats, among which: different types of sediment, soil, sewage, or manure [83]. Tab. 1 contains a list of well investigated mesophilic and thermophilic acetogenic microorganisms. They can use either CO or CO<sub>2</sub> and H<sub>2</sub> or all three gases as substrate gas and convert these to acetic acid, ethanol, 2,3-butanediol and other alcohols and organic acids as products. Metabolic engineering enables the conversion of substrate gas to higher added-value compounds like butanol and isoprene. Optimal growth for mesophilic acetogenic microorganisms is between 25–40 °C and up to 65 °C for thermophilics [84]. Further details on both optimal and possible temperature operating ranges of acetogenic bacteria can be found elsewhere [78, 85, 86].

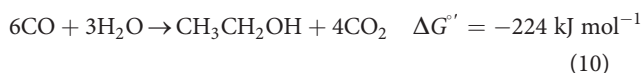
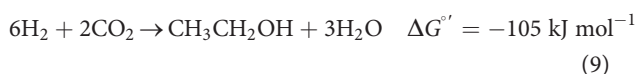
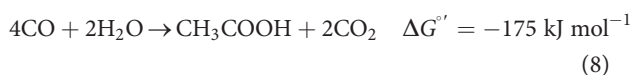
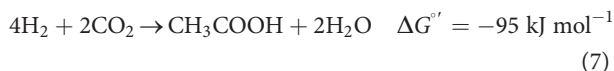
**Table 1.** Acetogenic microorganisms: a selection of key organisms of different genus.

Microorganism	Substrate gas	Products	Products of metabolic engineered strains	References
<i>Clostridium autoethanogenum</i>	Syngas, CO <sub>2</sub> /H <sub>2</sub> , CO	Acetic acid, ethanol, 2,3-butanediol, lactic acid	Butanol, acetone, isopropanol, fatty acid ethyl ester, fatty acid butyl ester, 3-Hydroxypropionate, 2-butanol, MEK, meso-2,3-butanediol, butanoic acid butyl ester, mevalonate, isoprene, franesene, ethylene glycol, poly-3-hydroxybutyrate	[86–98]
<i>Clostridium ljungdahlii</i>	Syngas, CO <sub>2</sub> /H <sub>2</sub> , CO/H <sub>2</sub> , CO	Acetic acid, ethanol, 2,3-butanediol, 2-oxo-butyrate, formic acid	Butanol, butyrate, isoprene, lactate, acetone, mevalonate, isopropanol, hexanol,	[85, 87, 91, 96, 99–106]
<i>Clostridium carboxidivorans</i>	CO <sub>2</sub> /H <sub>2</sub> , CO	Butanol, butyrate, acetic acid, ethanol, lactate, 2,3-butanediol, hexanol, hexanoic acid, caproate	Propanal, propan-1-ol	[85, 86, 95, 107, 108]
<i>Clostridium acetivum</i>	CO <sub>2</sub> /H <sub>2</sub> , CO	Acetic acid, ethanol, 2-oxobutyrate	Acetone	[83, 86, 102, 109, 110]
<i>Blautia productus</i>	CO <sub>2</sub> /H <sub>2</sub> , CO	Acetic acid	1-butanol	[87, 111–113]
<i>Acetobacterium woodii</i>	CO <sub>2</sub> /H <sub>2</sub> , CO	Acetic acid, ethanol	Acetone, 1-butanol	[87, 114–118]
<i>Moorella thermoacetica</i>	CO <sub>2</sub> /H <sub>2</sub> , CO	Acetic acid	Acetone	[113, 119]



### 3.2 Reaction Mechanism

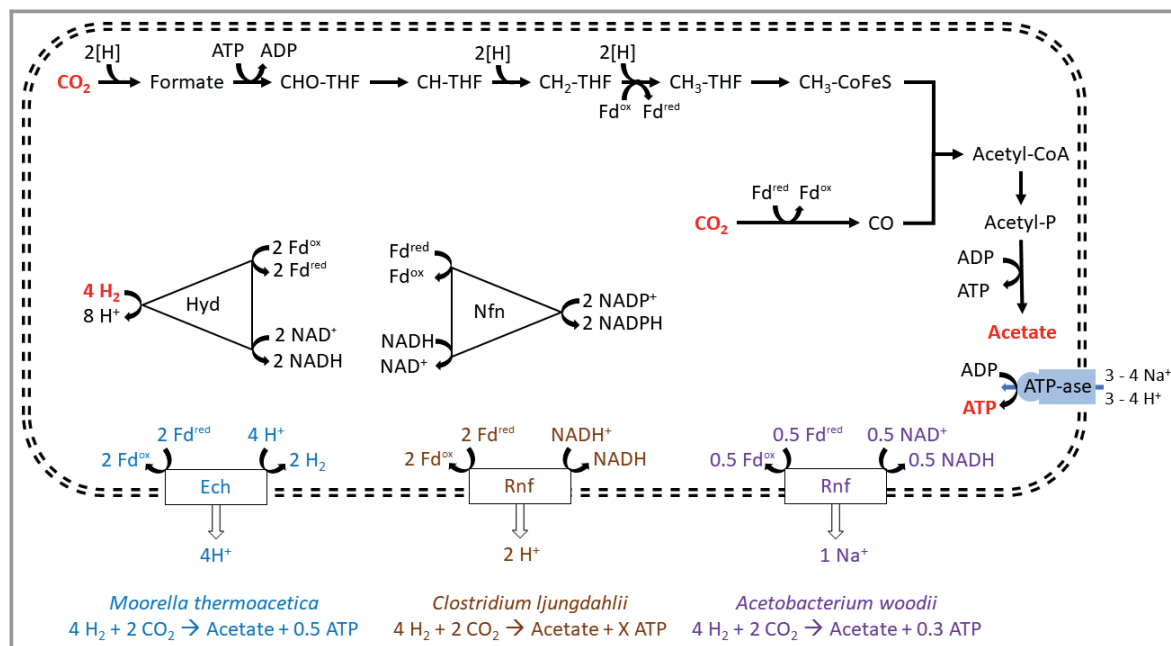
Anaerobic acetogens are able to produce acetate or ethanol through the fixation of CO<sub>2</sub> via the so-called Wood-Ljungdahl pathway (WLP, Fig. 6). The free energy of the production of acetate and ethanol from either H<sub>2</sub>/CO<sub>2</sub> or CO is given in Eqs. (7)–(10) where  $\Delta G^{\circ'}$  is the free energy change calculated under standard conditions (1 M concentrations of substrates and products, partial pressure of gases 1 bar, pH 7):



Due to the mechanistic constraints the energy of these reactions can only partially be harvested by the bacteria. This is a result of the reactions and interactions of the WLP, the bifurcating hydrogenase (Hyd) and electron-bifurcating transhydrogenase (Nfn) and either the energy-converting

hydrogenase complex (Ech) or the *Rhodobacter* nitrogen fixation complex (Rnf) [82, 120].

In the methyl-branch (upper branch) of the WLP, CO<sub>2</sub> is reduced to formate. In an ATP dependent reaction formate is activated and bond to tetrahydrofolate (THF). In two reducing steps, it is further reduced to a THF-bound methyl group. This methyl group is transferred via a corrinoid-iron-sulfur protein to the central CO-dehydrogenase/acetyl-CoA-synthase enzyme complex (CODH/AcCoA-S). This enzyme also binds and reduces one CO<sub>2</sub> to CO with reduced ferredoxin (Fd<sup>red</sup>) as electron donor in the carbonyl branch. Finally, the methyl-CoA and the bond CO are fused to yield one acetyl-CoA [83, 121, 122]. Acetyl-CoA is converted by the phosphotransacetylase and acetate kinase to yield one acetate and the ATP needed for the activation of formate. Hydrogen enters the reaction through Hyd delivering Fd<sup>red</sup>. Nfn supplies NADPH [82]. Depending on the microorganism, either the membrane bound Ech or the Rnf complex reoxidizes Fd<sup>red</sup> whilst transferring H<sup>+</sup> (or Na<sup>+</sup>) across the membrane. An overview of the presence of Ech or Rnf and H<sup>+</sup> or Na<sup>+</sup> as protons is given by Rosenbaum and Müller [120]. For every 3 to 4 (3.66 in *C. ljungdahlii*) protons reentering the cell through the ATP-ase one ATP is generated. The NADH produced in this final step by the Rnf complex is reoxidized in the methyl branch. The ATP gain per one mole of acetate synthesized depends on the nature of the reducing equivalents (2[H]) used in those three reducing reactions in the methyl branch of the WLP. For *M. thermoacetica* this results in the formation of 0.5 ATP [82], whereas for *C. ljungdahlii* from -0.14 [123]



**Figure 6.** Overview of the Wood-Ljungdahl pathway and a model for chemiosmotic energy conservation in Ech and Rnf acetogens. THF: Tetrahydrofolate; CoFeS: corrinoid/iron sulfur protein; CoA: coenzyme A; Fd<sup>red</sup>: reduced ferredoxin; Fd<sup>ox</sup>: oxidized ferredoxin; [H]: reducing equivalent (= 1e<sup>-</sup> + 1H<sup>+</sup>); Hyd: bifurcating hydrogenase; Nfn: electron-bifurcating transhydrogenase; Ech: energy-converting hydrogenase; Rnf: *Rhodobacter* nitrogen fixation; adapted from Schuchmann and Müller [82] and Rosenbaum and Müller [120].

up to 0.63 [82] ATP per mole acetate have been proposed. CO can also be used directly in the carbonyl branch and saves one  $Fd^{red}$  leading to higher ATP yield [124].

The second main product of syngas fermentation is ethanol. It can be either produced from acetyl-CoA via acetaldehyde or via reduction of non-activated acetate by an aldehyde oxidoreductase (AOR) and the reduction of the formed acetaldehyde to ethanol via an alcohol dehydrogenase reaction with  $Fd^{red}$  as electron donor. It is assumed that all commercially used acetogens produce ethanol via this AOR pathway as it is more energy efficient (first formation of ATP by acetate production, then formation of acetaldehyde and ethanol) [125]. Products other than acetate and ethanol are thermodynamically very difficult, since for mechanistic and thermodynamic reasons only less than 1 ATP can be formed per organic acid produced [126].

### 3.3 Process Development

Due to WLP as reaction mechanism space-time yield in syngas fermentation is limited by the availability of the substrate. This could be optimized by the reactor design and pressure. The “concentration” of the catalyst, the biomass, could be enhanced by cell retention and optimization of media and fermentation conditions. To synthesize other products like butanol or acetone the cell internal flux of acetyl-CoA and the balance of redox equivalents could be influenced by metabolic engineering. Therefore, the main research topics can be classified in three categories: hardware, metabolic engineering and modeling as well as operating conditions (see Fig. 7).

#### 3.3.1 Hardware

The reactor design has strong influence on the mass transfer rate and, therefore, it has to be optimized in order to overcome a low gas-liquid mass transfer, since  $H_2$  and CO have a low solubility in water [127]. Reactor types for syngas fermentation processes could be agitated reactor systems, like stirred vessels, and non-agitated ones, such as

bubble columns, gas lift reactors, loop reactors, trickle bed reactors, membrane and biofilm reactors [128–130]. Stirred vessels, e.g., continuously stirred-tank reactors (CSTR), enable high gas-liquid mass transfer rates by mechanical agitation. However, the specific energy input for agitation is typically ca.  $1 \text{ kW m}^{-3}$  [131], which is too high for the commercialization of syngas fermentation processes at industrial scale, as it should not surpass  $0.3 \text{ kW m}^{-3}$  [132]. Trickle bed reactors have a thin liquid film contacting the gas phase and, therefore, a low liquid resistance to mass transfer [133]. Membrane reactors could reach a maximum  $k_L a$  of  $1096 \text{ h}^{-1}$  at laboratory scale, which is three times higher than that of industrially used bubble columns [134]. However, due to the high membrane costs, they are less suitable for the production of bulk chemicals like ethanol [134]. Another possibility to achieve high mass transfer rates but with low operational and maintenance costs are bubble and gas-lift reactors. LanzaTech developed a modified, improved loop reactor by adding a secondary loop to a forced-circulation loop reactor [135]. Furthermore, a serial adding of reactors in a row, called multistage fermentation, could enable optimized conditions in each reactor system [85] leading to enhanced growth and productivity [136–139]. Further improvements and patents of reactor engineering are summarized in Takors et al. [140].

The low productivity of fermentation processes is, among others, caused by low cell densities. Cell recycling via separation and retention could be implemented through the use of centrifuges, membranous filtration techniques (e.g., hollow fibers, ceramic filter systems) or other solid/liquid separator systems [137]. Medeiros et al. [141] has observed a 3.6 times higher cell density and an increased ethanol productivity of 30 % with cell retention. Further investigations on the influence of cell retention can be found elsewhere [136, 138, 142–148].

#### 3.3.2 Metabolic Engineering and Modeling

Metabolic engineering and modeling have the goal of expanding product spectrum, increasing productivity and better understanding the microbial process steps. Adaptive

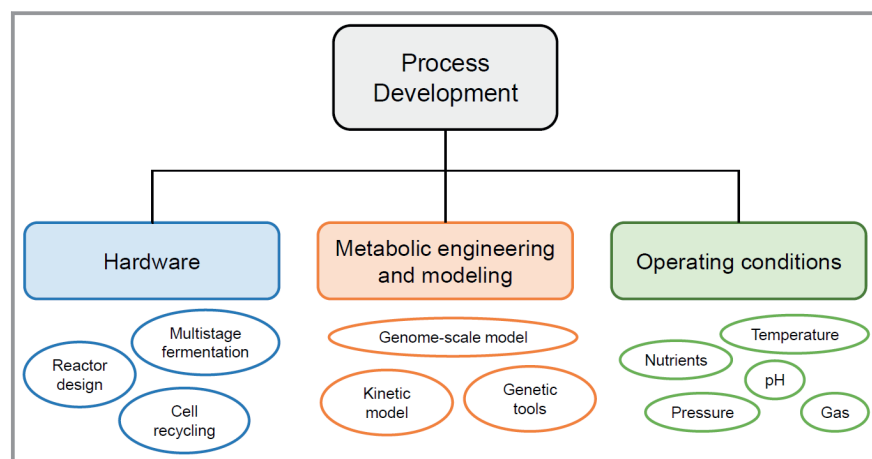


Figure 7. Components of process development for acetogenic syngas fermentation.

laboratory evolution, DNA transfer and knock-down of target genes are among others very successful tools to expand product spectrum and increase productivity [86, 99, 149]. Overexpressing of THF-dependent enzymes in WLP has led to an increase in volumetric acetate productivity [150]. Furthermore, production of butanol as well as acetone and isopropanol under autotrophic growth on syngas has been successfully demonstrated as a result of genetically modified *Clostridia* [87, 151]. More information on genetic tools for manipulating microorganisms can be found in Liew et al. [151] and Fackler et al. [75].

For metabolic engineering, a particularly deep understanding of the metabolic network is necessary. There are two different modeling approaches: a constraint-based model (CBM) and a kinetic model. CBMs are able to predict flux distribution, growth rate, knockouts and theoretical yields [152]. Nagarajan et al. [103] developed the first genome-scale model for the acetogen *Clostridium ljungdahlii*, which included 637 genes, 785 reactions and 698 metabolites. This model gives insight into the genetic and energetic metabolic constraints. Marcelling et al. [90] compared heterotrophic growth on fructose with autotrophic growth on syngas, in order to investigate the Rnf and Nfn complex. Liu et al. [153] developed the first macromolecular synthesis model (ME-model) of a gram-positive bacterium and used it to investigate the influence of protein allocation and media composition on metabolic pathway and energy conservation. With a reduced stoichiometric metabolic model (rSMM), Hermann et al. [124] found out that the consumption of CO led to a higher energy availability than the use of H<sub>2</sub> as electron source. Foster et al. [154] investigated the influence of cell fusion on growth phenotype and panel of metabolites with a co-culture of *Clostridium acetobutylicum* and *Clostridium ljungdahlii*. For further information on genome-scale models, see Veas et al. [147] and Fackler et al. [75].

However, since a relationship between the prediction of flux distribution, growth rate and theoretical yields cannot be built in a constraint-based model, a kinetic model approach should be used in this case. With a kinetic model, metabolic states and rate-limiting steps can be predicted. Medeiros et al. [141] optimized CO conversion and ethanol productivity by using a differential equation system with kinetic parameters as well as with experimental data from operating conditions. By combining a genome-scale model with thermodynamics via implementing a Gibbs free energy constraint, Greene et al. [155] accurately predicted intracellular metabolite concentrations and engineering strategies for improved ethanol production.

### 3.3.3 Operating Conditions

The gas-liquid mass transfer is known to be a bottleneck in syngas fermentation. Due to Henry's law, an increase in gas pressure leads to higher gas solubility and increased gas-liquid mass transfer. Kantzow and Weuster-Botz [156]

found that an increased hydrogen partial pressure from 0.4 bar to 2.1 bar led to both significant reduction in acetate and significant increase in formate concentration. Bertsch and Müller [157] stated that the hydrogen partial pressure has strong dependence on the energy-conserving enzyme *Ech*. Younesi et al. [158] have seen that a slight increase in syngas pressure of up to 1.8 bar promotes ethanol productivity, while acetate concentration stays almost constant. Hurst et al. [159] observed that acetate concentration decreases when CO partial pressure is above 1 bar. High pressures up to 6 bar and 8 bar in a continuous operating mode were investigated for the first time by Gaddy et al. [137] and Stoll [160], respectively. For both investigations, the highest ethanol concentrations of 25 g L<sup>-1</sup> and 4.8 g L<sup>-1</sup> occur at 6 bar. The highest overall efficiency of C<sub>2</sub>-compounds as well as highest cell density can be detected at 2 bar [160].

Another important operating parameter is the gas composition. Different CO<sub>x</sub>/H<sub>2</sub> ratios have a significant influence on the fermentation performance. If CO is supplied together with H<sub>2</sub>, ethanol concentration will be enhanced [161]. However, Jack et al. [162] observed an increase in acetate to ethanol ratio when the amount of hydrogen in the headspace is raised in a range of 0.5–2 (initial hydrogen to carbon monoxide headspace concentration ratio). High H<sub>2</sub> ratios together with low amounts of CO<sub>2</sub> direct the cell metabolism towards ethanol synthesis [163]. Furthermore, CO and H<sub>2</sub> can both serve as electron donors [161, 164], while CO is preferred due to a higher available Gibbs free energy [162]. Besides the gas composition, the gas rate also has strong influence on the fermentation process. Substrate inhibition can occur if too much gas is transferred into the liquid phase [137, 162, 164–168]. Syngas impurities also influence the fermentation process [163, 169–171] (see Sect. 4.1).

Experimental results have shown that lowering the pH shifts the products from acidogenic phase (growth and mainly acetate formation occurs) to solventogenic phase (growth rate is lower and more reduced products like ethanol are built) [108, 136, 144, 165, 172–181].

A moderate lowering of temperature to 32 °C with *Clostridium ragsdalei* leads to higher ethanol concentration [181, 182]. Lowering the temperature to 25 °C with *Clostridium carboxidivorans* (optimal growth temperature 37–40 °C) favors alcohol production and carbon chain elongation [183–185].

Furthermore, nutrients like salts, trace elements, vitamins and reducing agents have high impact on microbial growth and product formation. Reviews on the influence of medium composition and medium costs as well as further experimental studies can be found elsewhere [85, 86, 165, 173, 180, 181, 184, 186–193].



## 4 A Comparative Perspective between Syngas Fermentation and Catalytic MeOH Synthesis

In this chapter chemical and biological catalysis for the conversion of syngas into chemicals are compared, taking into account the process parameters and the syngas nature used as feed gas. A brief overview of the main characteristics from both approaches is presented in Tab.2. For chemical catalysis heterogeneous methanol synthesis is chosen, while for biological catalysis EtOH and AcOH by syngas fermentation are considered.

### 4.1 Tolerance of the Catalyst to Syngas Impurities

Depending on the feedstock and the process route for the synthesis gas production, the type of impurities present may vary, e.g., particulate matter, condensable hydrocarbons, sulfur compounds, nitrogen compounds like nitric oxides, alkali metals, reactive oxygen species as well as hydrogen chloride [75, 86, 149, 178–180, 194, 195]. In comparison to wood or wheat straw, synthesis gas based on the gasification of coal has the highest impurity content for sulfur, ash, ammonia and hydrogen cyanide [178]. Gasification of biomass leads to higher concentration of alkali than the gasification of coal [181]. Natural gas may contain 1–5000 ppmv sulfur, which would be a problem for nickel- and copper-based catalysts [182]. Composition and purity of the synthesis gas are fundamental in processes such as the heterogeneous catalyzed methanol synthesis, especially regarding to operation and investment costs [196]. Specific purity requirements for methanol synthesis in terms of particulates, tars, sulfur, nitrogen and alkali halides are summarized by Woolcock et al. [197]. Information on purification technology of synthesis gas can be found elsewhere [178, 180, 182, 183, 195, 198].

In the following section, the effects of relevant syngas impurities on chemical (focus on CZA-based catalysts) and

biological catalysis (focus on acetogenic microorganisms) are compared (see Tab.3). Both syngas fermentation and MeOH synthesis rely on metal-containing catalysts such as transition metal-based catalysts or metalloenzymes to convert C<sub>1</sub>-gases to products. In the case of syngas fermentation, metalloenzymes are responsible for the conversion. However, the risk of biocatalyst poisoning is lower than that of chemical catalyst poisoning, as the microorganisms acting as the biocatalyst are continuously regenerated [75].

A key difference between fermentation and chemical catalysis is the tolerance to sulfur compounds in the substrate gas. Sulfur is an important nutrient to stimulate growth of microorganisms, as reported by Mohammadi et al. [165] and Phillips et al. [127]. In contrast, CZA-based catalysts are strongly deactivated by H<sub>2</sub>S, which blocks part of the Cu active sites, hence reducing the surface area and therefore leading to a significant decrease of carbon conversion. The extent of the activity loss is proportional to the sulfur molar concentration accumulated on the catalyst [178, 179, 199]. An impurity level of H<sub>2</sub>S should be lower than 0.1 ppm in order to avoid catalyst poisoning [180].

On the other hand, the chemical catalyst has a much higher tolerance to HCN than the microorganisms. There is no catalyst deactivation even at HCN concentrations of up to 101.5 ppmv [200], while HCN is very toxic for microorganisms as it binds to the key enzyme CODH [86]. HCN concentrations lower than 1 ppm are required for industrial syngas fermentation [201], but a laboratory study concluded that the microorganisms are able to adapt to HCN concentrations lower than 2.7 ppm [202].

For syngas fermentation, the removal of polycyclic aromatics is necessary, although adaptation to tar after prolonged exposure is possible [86, 169, 203]. For CZA-based catalysts, hydrocarbons seem to act as inert spectators with no effect on catalytic activity, selectivity and process stability during methanol synthesis [204].

Studies on the influence of oxygen on syngas fermentation do not come to a clear conclusion: while O<sub>2</sub> is particularly critical during inoculation [86], tolerance in certain

**Table 2.** Characteristics of pure chemical catalysts versus biochemical catalysts for the production of synthetic carbon-neutral and oxygenated hydrocarbons.

	Heterogeneous catalyst	Biocatalyst
Catalyst	Solid metal-based; simple inorganic molecules as reactants	Living cells; simple inorganic molecules as reactants
Synthesis/Cultivation	Multi step syntheses; metal loss via leaching issues; high temperature needed	Cultivation under mild conditions; narrow optimal window
Reaction media	Solid-Gas / Solution-Gas / Solution-Solid	Water and solutions
Operating conditions	High temperature and pressure	Mild temperature and pressure, close to ambient conditions
Selectivity	Fair-to-high	High
Space-Time-Yield	Generally high	Low-to-fair
Waste	Potentially dangerous for the environment; cost intensive regeneration and disposal	Low environmental footprint; easy disposal

conditions [205] and even detoxification and enhancement of ethanol formation is possible [206]. For CZA-based catalysts, O<sub>2</sub> deactivates Cu and Zn active sites by oxidation. This is reversed by syngas reducing agents (H<sub>2</sub>, CO), but O<sub>2</sub> concentration should not surpass 300 ppm, otherwise this oxidation-reduction cycle is fast enough to accelerate irreversible sintering [207, 208].

Ammonia directly leads to a significant decrease of the productivity in case of methanol synthesis. However, after ammonia removal full generation of catalyst takes place [204]. The formation of the by-product trimethylamine is triggered when ammonia is present in syngas. For syngas fermentation, one study concludes that ammonia reduces cell growth and inhibits hydrogenase [169], while increased cell growth and ethanol formation are observed in another study [170].

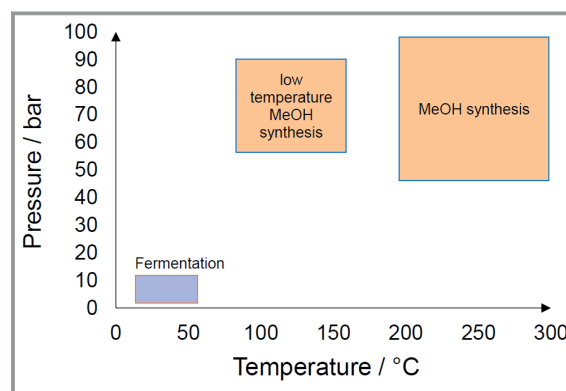
Another syngas contaminant, HCl, accelerates sintering of CZA-based catalysts due to the formation of low-melting CuCl [200]. There is literature that even mentions concentration limits for HCl as low as 1 ppb [209]. In contrast, microorganisms are less susceptible to poisoning by chlorine [165].

Microorganisms are sensitive to NO, as hydrogenase activity is inhibited [203]. A concentration for nitric oxide lower than 40 ppm could be tolerated by the biocatalyst without a loss in enzyme activity and growth [210]. To our knowledge, no studies on the influence of NO on CZA-based catalysts are known.

## 4.2 Process Parameters

### 4.2.1 Temperature and Pressure

Anaerobic syngas fermentation and methanol synthesis show significant differences in operating conditions for pressure and temperature (see Fig. 8). While syngas fermentation with acetogens is operated at low temperature and pressure, MeOH synthesis requires high temperature and pressure conditions. Due to enzyme activities, acetogens



**Figure 8.** Operating windows for anaerobic syngas fermentation and MeOH synthesis. Data taken from [11, 84, 137, 160, 211–215].

have a narrow operating temperature window. Cultivation, growth and productivity is possible between 15–65 °C [84, 211]. An increase in temperature above that limit would not lead to an enhanced productivity, but instead irreversibly destroy the microorganisms. Fermentation typically takes place at atmospheric pressure conditions with the highest process pressure of 8 bar at continuous operating mode being reported by Stoll [160]. In contrast to fermentation, the heterogeneous catalysis for MeOH synthesis needs higher temperatures of 200–300 °C [11]. Typical process pressures range between 50–100 bar [11]. Methanol synthesis can be also operated at lower temperatures (80–150 °C) by using alternative catalysts (Ru, Mn, Fe, Co) in a liquid phase [212–214], although this process is currently not commercially available. A TOF of 458 h<sup>-1</sup> with a Ru(tdpccy)(TMM) catalyst at 90 bar H<sub>2</sub>, 30 bar CO<sub>2</sub> and 120 °C was reported by Schieweck et al. [215]. A further reduction of temperature and pressure with current catalysts materials would directly lead to a significantly reduced reaction rate and a productivity close to zero. As a result, activity of microorganisms used for anaerobic syngas fermentation is significant higher compared to heterogeneous catalysts at low temperature and pressure conditions.

The much milder conditions of syngas fermentation present an interesting advantage in comparison to heterogeneous catalysis. The required high pressures of the latter, significant investment costs are related to the compressors, while considerable operating costs are related to their power input [208, 216]. Besides, the wall thickness of the equipment must be thicker to handle high pressures, at least doubling the price in relation to operating at atmospheric pressure (see Supporting Information). Finally, to achieve the required high temperatures in the catalytic process, it is necessary to build

**Table 3.** Most common syngas impurities and their influence on process performance in comparison for fermentation and MeOH synthesis (–: negative impact; +: positive impact; o: neutral, no impact).

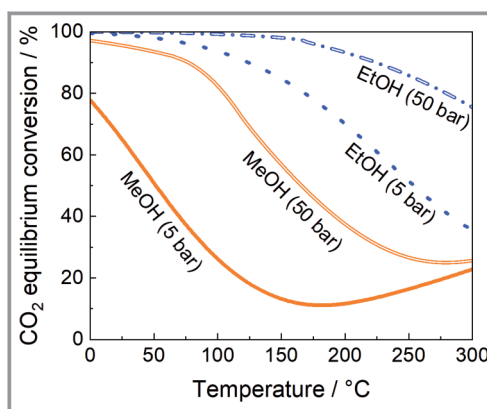
Impurity component	Fermentation	MeOH synthesis	References
Sulfur compounds	+	–	[127, 190, 199, 204]
Tar	o / –	o	[86, 169, 203, 204]
HCN	o / –	o	[200–202]
HCl	o	–	[165, 200, 209]
Particulates	–	–	[86]
O <sub>2</sub>	+ / o / –	–	[86, 204–208]
NO <sub>x</sub>	o / –	–	[169, 170, 203, 210]
NH <sub>3</sub> /NH <sub>4</sub> <sup>+</sup>	+ / –	–	[169, 170, 199, 204]

preheating and cooling units, as well as to implement strategies to control the reactor temperature (as discussed in Sect. 2), which also have an impact on the investment and operating costs. However, heat of reaction can be used directly for generating steam and heating the distillation columns for downstream product recovery. Temperature control of syngas fermentation is also necessary, but at a lower level and therefore the heat of reaction cannot be directly used for heat integration.

#### 4.2.2 Gas Conversion and Product Ratio

Fig. 9 shows the theoretical thermodynamic equilibrium for CO<sub>2</sub> conversion to MeOH and EtOH at two different pressures. At typical syngas fermentation conditions (e.g.,  $p = 5$  bar,  $T < 65$  °C) CO<sub>2</sub> conversion of more than 95 % is possible. In this temperature range, there is no significant influence of the pressure on the equilibrium conversion. However, at typical catalytic methanol synthesis conditions (e.g.,  $p = 50$  bar,  $T > 200$  °C) CO<sub>2</sub> conversion is lower and ranges between 30–40 %. Even at low temperatures (< 100 °C) regardless of the pressure, CO<sub>2</sub> conversion during MeOH synthesis is lower than during EtOH synthesis. Furthermore, Fig. 9 shows according to Le Chatelier's principle a strong influence of pressure and temperature on CO<sub>2</sub> conversion: the lower the temperature and the higher the pressure, the higher the conversion rate. However, CO<sub>2</sub> conversion during methanol synthesis at 5 bar increases for temperatures higher than 175 °C. This is due to the endothermic RWGSR, which is more present at high temperatures, converting CO<sub>2</sub> to CO resulting in an increased CO<sub>2</sub> equilibrium conversion. In addition, Fig. 9 makes clear that CO<sub>2</sub> conversion during EtOH synthesis is higher at any operating condition compared to MeOH synthesis.

During methanol synthesis, gas composition also influences CO<sub>x</sub> equilibrium conversion (see Fig. 4 in Sect. 2) as CO<sub>x</sub> equilibrium conversion is lower for CO<sub>2</sub>-rich syngas compositions in comparison to CO/H<sub>2</sub>-rich gas. In case of syngas fermentation, this means, that if gas-to-liquid mass transfer is high enough, then complete gas conversion and simultaneous usage of CO and CO<sub>2</sub> are possible. Many experimental studies revealed CO or CO<sub>2</sub> conversion of more than 90 % [137, 143, 160, 180, 217]. Furthermore, anaerobic syngas fermentation is flexible in terms of CO<sub>x</sub>/H<sub>2</sub> ratio [131, 218]. A significant advantage of syngas fermentation is the theoretical ability to produce organic molecules even with a pure CO feed (see also Eq. (8) and (10)), as the reaction medium contains enough water for the WGSR. In case of heterogeneous catalysis, if the H<sub>2</sub>/CO<sub>x</sub> ratio is too low, addition of water, conversion of CO and H<sub>2</sub>O to CO<sub>2</sub> and H<sub>2</sub> and removal of excess CO<sub>2</sub> via absorption are necessary steps to adjust gas composition. However,



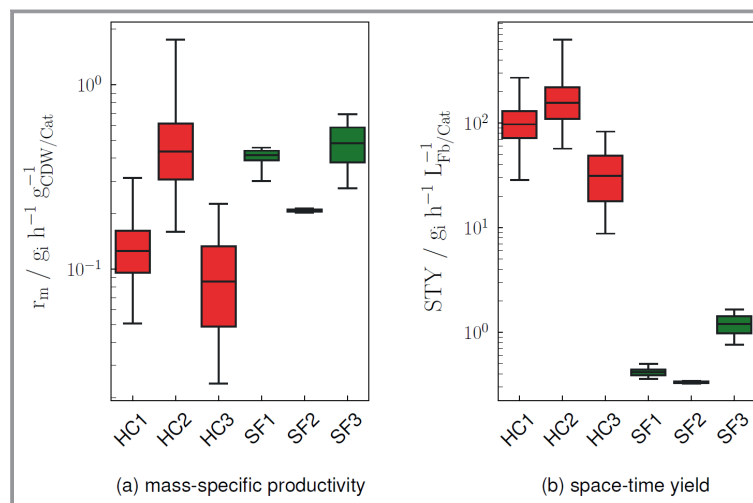
**Figure 9.** Theoretical CO<sub>2</sub> equilibrium conversion of methanol synthesis (Eq. (2)) and ethanol synthesis (Eq. (9)) at stoichiometric conditions (H<sub>2</sub>/CO<sub>2</sub>: 3/1), different temperatures and two different pressures (5 bar, 50 bar). The WGSR is considered in both cases. Data generated with Aspen Plus V10 with UNIF-DMD as property methods.

the CO<sub>x</sub>/H<sub>2</sub> ratio of substrate gas can be used to influence product ratio of fermentation (see Sect. 3.3.3).

#### 4.2.3 Productivity

Fig. 10a shows the mass-specific productivity  $r_m$ , where  $r$  is the productivity in g<sub>i</sub> h<sup>-1</sup> of product  $i$  and  $m_{CDW/Cat}$  is the mass of the cell-dry weight of the biomass in g<sub>CDW</sub> or the mass of the heterogeneous catalyst in g<sub>Cat</sub>:

$$r_m = \frac{r}{m_{CDW/Cat}} \left[ \frac{g_i}{h} \right] \quad (11)$$



**Figure 10.** A comparative perspective of productivities between heterogeneous catalysis (HC) and syngas fermentation (SF) for a) mass-specific productivity  $r_m$  and b) space-time yield  $STY$ . The boxes show the quartiles of the productivity values, the whiskers extend to show the rest of the distribution. HC1 (syngas):  $\Sigma$ MeOH + DME, Wild et al. [22]; HC2 (syngas): MeOH, Campos et al. [35]; HC3 (CO<sub>2</sub>, H<sub>2</sub>): MeOH, Slotboom et al. [219]; SF1 (syngas):  $\Sigma$ AcOH+EtOH, Stoll [160], SF2 (syngas):  $\Sigma$ AcOH + EtOH, Acharya et al. [220]; SF3 (CO<sub>2</sub>, H<sub>2</sub>): AcOH, Kantzow et al. [148].

The data shown in Fig. 10a are taken from experiments at continuous operating mode. C<sub>2</sub> compounds (acetic acid and ethanol) via syngas fermentation (SF) and methanol and DME via heterogeneous catalysis (HC) are presented. The mass-specific productivity of methanol is between 0.02–2 g<sub>MeOH</sub> g<sub>Cat</sub><sup>-1</sup> h<sup>-1</sup> with 0.08 g<sub>MeOH</sub> g<sub>Cat</sub><sup>-1</sup> h<sup>-1</sup> as the lowest quartile for MeOH formation reported by Slotboom et al. [219] and 0.45 g<sub>MeOH</sub> g<sub>Cat</sub><sup>-1</sup> h<sup>-1</sup> as the highest quartile reported by Campos et al. [35]. A narrow range of mass-specific productivities compared to heterogeneous catalysis can be observed for syngas fermentation (0.2–0.7 g<sub>C<sub>2</sub></sub> g<sub>CDW</sub><sup>-1</sup> h<sup>-1</sup>). The quartiles are comparable to that of Campos et al. [35] and almost an order of magnitude higher compared to Slotboom et al. [219], thus indicating that the mass-specific productivities of syngas fermentation are of the same order of magnitude and even of one order higher compared to heterogeneous catalysis.

Apart from the mass-specific productivity, the volumetric productivity is of particular importance for operation and profitability of a process. Fig. 10b shows the volumetric productivity  $r_v$ , also known as space-time yield (STY), where  $r$  is the productivity in g<sub>i</sub> h<sup>-1</sup> of product  $i$  and  $V_{Fb/Cat}$  the volume of fermentation broth (Fb) or solid catalyst (Cat):

$$STY = r_v = \frac{r}{V_{Fb/Cat}} \left[ \frac{\frac{g_i}{h}}{L_{Fb/Cat}} \right] \quad (12)$$

The data in Fig. 10b are taken from the same source as in Fig. 10a and the mass-specific productivities have been converted to volumetric productivities. Volumetric productivities of methanol synthesis range from 9–650 g<sub>MeOH</sub> L<sub>Cat</sub><sup>-1</sup> h<sup>-1</sup>, while for acetic acid and ethanol formation via fermentation volumetric productivities are lower and range from 0.3–1.7 g<sub>C<sub>2</sub></sub> L<sub>Fb</sub><sup>-1</sup> h<sup>-1</sup>. This difference between fermentation and catalysis is in the range of two to three orders of magnitude and points out a significant disadvantage of syngas fermentation: due to low cell densities of the biomass in the fermenter, volumetric productivity is low. Therefore, there is still need for research to increase the cell density in the reactor (see Sect. 3.3.1 for cell recycling).

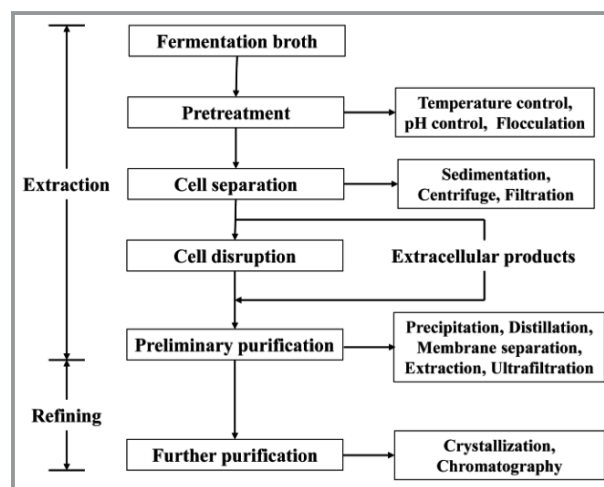
#### 4.2.4 Intermediates and By-products

The number of intermediates and by-products is low for both fermentation and catalysis. An overview of the reaction mechanisms is described in Sect. 2 and 3. For fermentation, formate is an intermediate product in the methyl branch of WLP. Besides formate, acetyl-CoA is another important intermediate, as biomass, acetate and ethanol could be built by further conversion of acetyl-CoA. In some cases, acetate is also treated as an intermediate, as acetate could be converted to ethanol via AOR [221]. Formate is an important intermediate for methanol synthesis as well, as it is converted to methanol via CO<sub>2</sub> hydrogenation. However, formate accumulates and is an inhibitor of direct CO hydrogenation. The occurrence of water as a by-product of

catalytic methanol synthesis depends, among other things, on the substrate gas. When working with CO<sub>2</sub>-rich syngas, water is formed via both methanol synthesis and reverse WGS, leading to reduced productivities [199, 218]. Further by-products occur at hot reactor zones [12]. Compared to methanol synthesis, there are no by-products worth mentioning during fermentation. The high product selectivity of syngas fermentation leads to fewer and less toxic by-products [131].

#### 4.3 Downstream

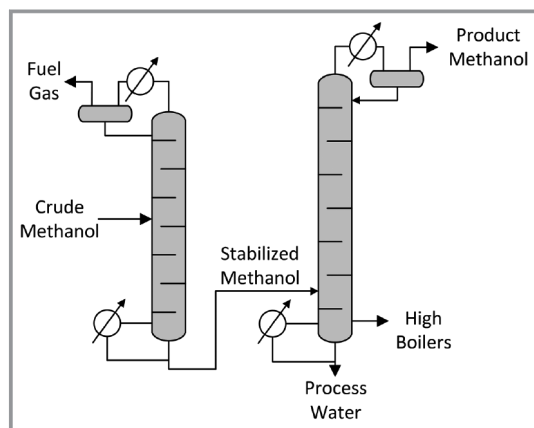
For product recovery of MeOH, EtOH and AcOH, different separation techniques are necessary. Fig. 11 and 12 portray the product recovery process for fermentation and MeOH synthesis. In the methanol synthesis, distillation costs for methanol recovery can represent up to 10 % of the plant's investment costs [222]. Costs of separation processes for syngas fermentation can account for over 60 % of the production costs [223].



**Figure 11.** Process scheme of product separation for fermentation broth recovery. Figure copyright: The Korean Society for Microbiology and Biotechnology [223].

In a LanzaTech process for ethanol production via syngas fermentation, a distillation-based separation system is used for product and co-product recovery. However, distillation for low titer products represents an energy-intensive and therefore cost-intensive separation technique. 2.0–2.5 t of steam per ton of ethanol are necessary for product separation [225]. Biomass, other organics and waste liquids from the fermenter are separated by a filter and are finally treated on-site in an anaerobic digestion unit [225]. The successful usage of microbial biomass waste as animal feed due to its similar amino acid profile to that of fishmeal was investigated by Chen et al. [226]. Electro-membrane processes as well as liquid-liquid extraction represents promising separation techniques to remove organic acids like acetic acid at





**Figure 12.** Two-column methanol distillation for product recovery with permission from the Royal Society of Chemistry [224].

reduced separation costs [86, 227, 228]. Further information on separation techniques can be found in Li et al. [223].

Since distillation columns are cost intensive due to the necessary phase change, it is less advisable to already separate after the production step for  $C_2$ -compounds when using syngas fermentation (as shown in Fig. 11). Rather there is the possibility of using co-cultures or serially adding further fermentation stages without the need for intermediate treatment and separation in order to synthesize higher-value products such as fats, lipids and long-chain alcohols and carboxylic acids [86]. Hu et al. [229], Oswald et al. [191], Lagoa-Costa et al. [230], Tran and Simpson [231] and Molitor et al. [232] are using different microorganisms in their multistage fermentation systems to convert syngas in several steps to lipids, malic acids, polyhydroxybutyrate (PHB) and single-cell proteins. By using these further process steps for chain elongation, product separation can be processed using less energy-intensive extraction, crystallization and precipitation compared to distillation columns.

For methanol purification, a unit distillation system is used to remove undesirable by-products and the water generated during methanol synthesis. For fuel grade methanol process a single distillation column is sufficient to meet commercial specifications [224]. However, for chemical grade methanol several extraction and distillation steps are necessary [233].

In contrast to the biocatalyst used for syngas fermentation, the chemical catalyst cannot regenerate by itself. Deactivation due to poisoning and sintering takes place over time and therefore a catalyst's lifetime is commonly limited to 2–6 years for industrial use [224]. Therefore, the disposal and recycling of the chemical catalyst represent an extra cost factor and disadvantage compared to the biocatalyst.

## 5 Conclusion

In this review article, two different approaches for the conversion of  $CO_x$  into chemicals and fuels have been com-

pared. The MeOH synthesis was taken as an example for heterogeneous catalyzed reactions, where metal-based catalysts are used, while the formation of ethanol and acetic acid via syngas fermentation is applied with an acetogenic microorganism as the biocatalyst.

This review highlights the operating parameters for chemical and biological catalysis, which differ significantly. Syngas fermentation takes place at mild conditions with pressures lower than 10 bar and temperatures lower than  $65^\circ C$ , while methanol synthesis is operated at 50–100 bar and  $200\text{--}300^\circ C$ . Due to the low temperature in syngas fermentation, an almost complete gas conversion is possible, whereas at temperatures above  $200^\circ C$  only partial conversions of  $CO_x/H_2$  can be achieved in methanol synthesis. As a result, a cost-intensive high-pressure separation of the gas from the liquid is necessary with subsequent recompression of the recycled gas in order to achieve a circular process for methanol synthesis. However, due to high temperatures during MeOH synthesis, the resulting heat of the reaction can be directly integrated in the process of downstream product recovery. The catalyst mass-based productivities are in the same order of magnitude for both chemical and biological catalysis. However, the space-time yield for chemical catalysis is two to three orders of magnitude higher than that for biological catalysis. Low cell densities as well as low gas-liquid mass transfer rates are mentioned as important bottlenecks for syngas fermentation resulting in low volumetric productivities.

Sulfur compounds commonly present in synthesis gas directly lead to deactivation of CZA-based catalysts, while sulfur could be used as a nutrient for syngas fermentation. However, while even low concentrations of HCN can poison microorganisms, the tolerance of CZA-based catalysts to HCN is much higher.

Variable  $CO_x$  sources and the fluctuating availability of  $H_2$  lead to new challenges for chemicals production technologies, as they commonly operate at steady state conditions. Under fluctuating conditions, syngas fermentation is considered to be of advantage to MeOH synthesis due to its flexibility in terms of gas composition. In case of methanol synthesis,  $CO_2$ -rich gases lead to the formation of water as a by-product, which can lead to catalyst deactivation. An important disadvantage of syngas fermentation is the low product titer resulting in an energy- and cost-intensive product recovery. However, as the non-toxic biocatalyst could regenerate itself, a periodical replacement of the catalyst unit is not necessary. The biocatalyst in the product stream could be even used as food for the animal industry and thus makes a positive contribution to the value chain.

This study has shown that syngas fermentation is an interesting alternative to the traditional catalytic methanol synthesis. While there are still bottlenecks to overcome, e.g., low cell density and low gas-liquid mass transfer, equilibrium conditions of gas conversion is remarkably better for syngas fermentation. Further studies should address the development of mechanistic studies as well as coupling

chemical with biological catalysis for the production of long-chain hydrocarbons in order to overcome difficult activation of C-OH bonds and low space-time yield.

## Supporting Information

Supporting Information for this article can be found under DOI: <https://doi.org/10.1002/cite.202200153>. This section includes additional references to primary literature relevant for this research [234, 235].

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### Symbols used

$c_1, c_2$	[mm]	allowance
$D_o$	[m]	outer diameter
$\Delta G^{\circ}$	[kJ mol <sup>-1</sup> ]	standard free energy change
$\Delta H_{298.15\text{ K}}^{\circ}$	[kJ mol <sup>-1</sup> ]	standard enthalpy
$K$	[N m <sup>-2</sup> ]	strength parameter
$k_1 a$	[s <sup>-1</sup> ]	volumetric mass transfer coefficient
$m$	[kg]	mass
$p$	[bar]	pressure
$r$	[g h <sup>-1</sup> ]	production rate
$r_m$	[g h <sup>-1</sup> g <sub>CDW</sub> <sup>-1</sup> Cat <sup>-1</sup> ]	mass-specific productivity
$r_v$	[g h <sup>-1</sup> L <sup>-1</sup> ]	volumetric productivity
$S$	[-]	safety factor
$s$	[mm]	wall thickness
$STY$	[g h <sup>-1</sup> L <sup>-1</sup> ]	space time yield
$TOF$	[h <sup>-1</sup> ]	turnover frequency
$v$	[-]	weld factor
$V$	[m <sup>3</sup> ]	volume

### Abbreviation

AcOH	acetic acid
AOR	aldehyde oxidoreductase
Cat	catalyst
CBM	constraint-based model
CDW	cell dry weight
CN	cetane number
CoA	Coenzyme A
CODH	carbon monoxide dehydrogenase
CODH/AcCoA-S	CO-Dehydrogenase/Acetyl-CoA-Synthase
CoFeS	Corrinoid/Iron Sulfur protein

CSTR	continuous stirred-tank reactor
CZA	Cu/ZnO/Al <sub>2</sub> O <sub>3</sub>
CZZ	Cu/ZnO/ZrO <sub>2</sub>
DME	dimethyl ether
DTG	DME-to-Gasoline
Ech	Energy-converting hydrogenase
EtOH	ethanol
Fb	fermentation broth
Fd	ferredoxin
FT	Fischer-Tropsch
HC	heterogeneous catalysis
HCl	hydrogen chloride
HCN	hydrogen cyanide
Hyd	bifurcating hydrogenase
LNG	liquefied natural gas
LPG	liquefied petroleum gas
MeOH	methanol
MOF	metal-organic framework
MTG	Methanol-to-Gasoline
NADP	nicotinamide adenine dinucleotide phosphate
Nfn	electron-bifurcating transhydrogenase
NG	natural gas
OME	oxymethylene ether
PHB	polyhydroxybutyrate
PM	particulate matter
PtG	Power to gas
PtH	Power to heat
PtL	Power to liquid
rSMM	reduced stoichiometric metabolic model
Rnf	<i>Rhodobacter</i> Nitrogen fixation
RWGSr	reverse water-gas shift reaction
SF	syngas fermentation
THF	tetrahydrofolate
WGSr	water-gas shift reaction
WLP	Wood-Ljungdahl pathway

### Sub- and Superscripts

Cat	catalyst
CDW	cell dry weight
m	mass-specific
o	outer
ox	oxidized
R	reactor
red	reduced
v	volumetric

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