Abstract: Acetate and acetyl-CoA play fundamental roles in all of biology, including anaerobic prokaryotes from the domains Bacteria and Archaea, which compose an estimated quarter of all living protoplasm in Earth’s biosphere. Anaerobes from the domain Archaea contribute to the global carbon cycle by metabolizing acetate as a growth substrate or product. They are components of anaerobic microbial food chains converting complex organic matter to methane, and many fix CO$_2$ into cell material via synthesis of acetyl-CoA. They are found in a diversity of ecological habitats ranging from the digestive tracts of insects to deep-sea hydrothermal vents, and synthesize a plethora of novel enzymes with biotechnological potential. Ecological investigations suggest that still more acetate-metabolizing species with novel properties await discovery.

Keywords: methanogenesis; fermentation; respiration; Methanosarcina; Pyrococcus; carbon monoxide

1. Introduction

Acetate and acetyl-CoA play a prominent role in the metabolism of all three phylogenetic domains of life, including anaerobic prokaryotes from the domains Bacteria and Archaea, which contribute to an estimated quarter of all living protoplasm in Earth’s biosphere [1]. Anaerobes from the domain Archaea play significant roles in the global carbon cycle by metabolizing acetate as a growth substrate or product. Many anaerobes also fix CO$_2$ into cell material via synthesis of acetyl-CoA [2].

In anaerobic environments where terminal electron acceptors (Fe(III), Mn(IV), SO$_4^{2-}$, S$^0$, NO$_3^-$) are absent, anaerobes from both prokaryotic domains convert complex organic matter to CH$_4$ and CO$_2$, providing an essential link in the global carbon cycle (Figure 1). In Step 1, CO$_2$ is incorporated into
biomass driven primarily by photosynthesis. In environments where O\textsubscript{2} is abundant, microbes oxidize the biomass, producing CO\textsubscript{2} that re-enters the carbon cycle (Step 2). A significant portion of the biomass is diverted to an assortment of anaerobic habitats devoid of terminal electron acceptors (Step 3), where anaerobic microbial food chains, comprised of at least three distinct metabolic groups, digest the biomass to CO\textsubscript{2} and CH\textsubscript{4} (Steps 4–7). The fermentative group converts the complex biomass primarily into, acetate along with lesser amounts of volatile fatty acids, H\textsubscript{2}, and CO\textsubscript{2} (Steps 4 and 5). The fatty acids are converted chiefly into acetate plus either formate or H\textsubscript{2} by the acetogenic group (Step 6). Thus, acetate emerges as the principal product of the fermentative and acetogenic groups. The CH\textsubscript{4}-producing (methanogen) group is sub-divided into acetate-utilizing (acetoclastic) and CO\textsubscript{2}-reducing species. Acetoclastic species convert the methyl group of acetate to CH\textsubscript{4} and the carbonyl group to CO\textsubscript{2}. The CO\textsubscript{2}-reducing species reduce CO\textsubscript{2} to CH\textsubscript{4} with electrons derived from H\textsubscript{2} or formate. At least two-thirds of the CH\textsubscript{4} produced derives from acetate, the central intermediary in anaerobic microbial food chains. A portion of the CH\textsubscript{4} is oxidized to CO\textsubscript{2} (Step 8) by associations of anaerobes that utilize sulfate, nitrate, manganese, or iron as terminal electron acceptors [3]. The CO\textsubscript{2} and remaining CH\textsubscript{4} diffuse into aerobic zones (Steps 9 and 10), where O\textsubscript{2}-requiring methanotrophic microbes oxidize the CH\textsubscript{4} to CO\textsubscript{2} (Step 11), completing the carbon cycle. Anaerobes also participate in chemoautotrophic habitats, where they fix carbon dioxide in catabolic and anabolic pathways. Although the fermentative and acetogenic groups are largely populated with characterized isolates from the domain Bacteria, all characterized methanogens are classified in the domain Archaea. Acetate-utilizing anaerobes classified in the domain Archaea also proliferate in environments where terminal electron acceptors are abundant and obtain energy through anaerobic respiration, converting acetate to CO\textsubscript{2}.

Figure 1. The global carbon cycle. Solid lines indicate steps in the cycle (see text) and dotted lines indicate transfer of material between aerobic and anaerobic environments.

This review encompasses the role of acetate, which has the greatest influence on the ecology of environments, in the energy conversion pathways of anaerobes from the domain Archaea; however, acetate and acetyl-CoA also play a prominent role in the biosynthetic pathways of anaerobes from the domain Archaea [2].
2. Acetate Production

2.1. Heterotrophic Energy-Converting Pathways Producing Acetate

Investigations of heterotrophic hyperthermophilic species from the domain *Archaea* have revealed pathways that deviate substantially from pathways in heterotrophic organisms from the domain *Bacteria*. *Pyrococcus furiosus*, for example, grows at 100 °C and ferments carbohydrates to acetate, CO₂, and H₂ by an unusual Emden–Meyerhof pathway involving the novel enzymes ADP-dependent glucokinase, ADP-dependent phosphofructokinase, glyceraldehyde-3-phosphate ferredoxin oxidoreductase (GAPOR), phosphoenolpyruvate synthase, pyruvate: Ferredoxin oxidoreductase (POR), and ADP-forming acetyl-CoA synthetase (Figure 2) [4]. Other heterotrophic acetate-producing hyperthermophiles that utilize one or more of these enzymes include species from the genera *Thermococcus*, *Desulfurococcus*, *Staphylothermus*, and *Archaeoglobus* [5–8]. In the glycolytic pathway exemplified by *P. furiosus* (Figure 2), ferredoxin reduced by GAPOR and POR is re-oxidized by a membrane-bound hydrogenase that generates an ion gradient driving ATP synthesis [4]. GAPOR is an oxygen-sensitive homomonomer with a molecular mass of 63 kDa, and contains a pterin cofactor, one tungsten, and six iron atoms per monomer [9]. Pyruvate is oxidized to acetyl-CoA, catalyzed by pyruvate: Ferredoxin oxidoreductase (POR). The enzyme has a molecular mass of 100 kDa and is comprised of three subunits (45, 31, and 24 kDa), and contains thiamine pyrophosphate (TPP) and two ferredoxin-type [4Fe-4S] clusters [10]. The enzyme requires CoASH but not TPP for pyruvate oxidation activity. The POR also catalyzes the formation of acetaldehyde from pyruvate in a CoA-dependent reaction, although the cofactor plays a structural rather than catalytic role [11]. Acetyl-CoA is converted to acetate by an ADP-forming acetyl-CoA synthetase, which generates ATP by substrate level phosphorylation [12,13]. Conversion of acetyl-CoA to acetate by acetyl-CoA synthetases is characteristic of the domain *Archaea*, in contrast to the domain *Bacteria*, in which phosphotransacetylase and acetate kinase predominate [14]. A reaction mechanism has been proposed for the heterotetrameric (αβ2) enzyme from *P. furiosus* that follows a four-step mechanism including transient phosphorylation of two active site histidine residues (Equations (1)–(4)) [15].

\[
E + \text{acetyl-CoA} + Pi = E\text{-acetyl-P} + \text{CoASH} \quad (1)
\]
\[
E\text{-acetyl-P} = \text{acetate} + E\text{-His}^{257}\alpha\sim P \quad (2)
\]
\[
E\text{-His}^{257}\alpha\sim P = E\text{-His}^{71}\beta\sim P \quad (3)
\]
\[
E\text{-His}^{71}\beta\sim P + \text{ADP} = \text{ATP} + E \quad (4)
\]

*Archaeoglobus fulgidus* is an example of a heterotrophic hyperthermophile from the domain *Archaea* that utilizes terminal electron acceptors in place of reducing protons and producing H₂. A strain of *A. fulgidus* grows with starch as the sole source of carbon and energy by an incomplete oxidation of glucose to acetate and CO₂, utilizing a modified Embden–Meyerhof pathway resembling that of *P. furiosus* [8]. However, in contrast to H₂-producing *P. furiosus*, electrons derived from the oxidation are transferred to sulfate, producing sulfide (Equation (5)):

\[
C_6H_{12}O_6 + H_2SO_4 = 2CO_2 + 2C_2H_4O_2 + H_2S + 2H_2O. \quad (5)
\]
Figure 2. Electron transport and energy conversion during glucose catabolism by *P. furiosus*. G-6-P, glucose 6-phosphate; F-6-P, fructose 6-phosphate; F-1,6-bP, fructose 1,6-bisphosphate; GAP, glyceraldehyde phosphate, GAPOR, GAP: Ferredoxin oxidoreductase; 3-PG, 3-phosphoglycerate; 2-PG, 2-phosphoglycerate; PEP, phosphoenolpyruvate; POR, pyruvate: Ferredoxin oxidoreductase; ACS, acetyl-CoA synthase. Reproduced with permission [4]. Copyright (2006) National Academy of Sciences, USA.

2.2. Chemolithotrophic Energy-Converting Pathways Producing Acetate

Biochemical and quantitative proteomic analyses of *M. acetivorans* revealed a pathway for CO-dependent growth of *M. acetivorans* in which both acetate and CH4 are products [16,17] (Figure 3). In the pathway, electrons derived from the oxidation of CO (Reaction 1a–c) are used to reduce CO2 to a methyl group attached to THSPt (Reactions 2–6), similar to the pathway of obligate H2-utilizing CO2-reducing methanogens, which are the subject of several reviews recommended to the reader [18–21]. The CO dehydrogenase/acetyl-CoA synthetase CODH/ACS is proposed to oxidize CO-reducing ferredoxin, which donates electrons in the first reductive step (Reaction 2). It is possible that ferredoxin also donates electrons to FpoF, catalyzing the reduction of coenzyme F420 to F420H2 (Reaction 1c) that donates electrons to complete the reduction of CO2 to the methyl level (Reactions 5 and 6). Indeed, it was recently shown that the FpoF of *Methanosarcina mazei* catalyzes reaction 1c [22] and a homolog in *M. acetivorans* (encoded by MA3732) is upregulated 11-fold in CO- vs. acetate-grown cells [16]. The methyl group of methyl-THSPt is reduced to CH4 by reactions common to all methanogenic pathways (Reactions 7–9), albeit with two exceptions. First, a membrane-bound complex (FpoA-O) oxidizes F420H2 and transfers electrons to HdrDE mediated by MP, which generates a proton gradient (Reactions
9 and 10) driving ATP synthesis (Reaction 14). Second, transfer of the methyl group of methyl-THSPt to HS-CoM (Reaction 7) is thought to be catalyzed by two enzymes, the membrane-bound Mtr complex coupled to Na⁺ translocation, common to all methanogenic pathways; and a soluble enzyme (CmtA) unique to the CO-dependent CO₂ reduction pathway [23]. Acetate is a prominent product in addition to CH₄. Levels of CODH/ACS, phosphotransacetylase, and acetate kinase are prominent in CO-grown cells [16], supporting a route to acetate wherein CODH/ACS synthesizes acetyl-CoA with the methyl group of methyl-THSPt, CO, and CoA-SH (Reaction 11), which are further converted to acetate by phosphotransacetylase and acetate kinase (Reactions 12 and 13) with the production of ATP. Thus, ATP is synthesized via both substrate level and chemiosmotic mechanisms.

*A. fulgidus* uses essentially the same pathway during CO-dependent growth, employing similar enzymes and electron carriers [24–28], except for conversion of acetyl-CoA to acetate, which is catalyzed by either an AMP- or ADP-forming acetyl-CoA synthetase [29–31]. *A. fulgidus* does not produce methane, and acetate is the sole product in the absence of sulfate.

**Figure 3.** Pathway for conversion of CO to acetate and CH₄ by *M. acetivorans*. See text. Fdₒ, oxidized ferredoxin; Fdᵦ, reduced ferredoxin; F₄₂₀, coenzyme F₄₂₀; MF, methanofuran; THSPt, tetrahydrosarcinapterin; HSCoM, coenzyme M; HSCoB, coenzyme B; Fpo, F₄₂₀H₂ dehydrogenase complex; MP, methanophenazine; Hdr, heterodisulfide reductase. Reproduced from [16] with permission. Copyright (2006) National Academy of Sciences, USA.

### 3. Acetate Utilization

#### 3.1. Acetotrophic Energy-Converting Pathways Producing Methane

Methane-producing species from the genera *Methanosarcina* and *Methanoaeta* are the only known acetoclastic genera in the domain *Archaea*. The majority of studies on the acetoclastic pathway have
involved *Methanosarcina* species, for which *M. acetivorans* is a model (Figure 4). Carbon transfer reactions in the pathway can be divided into two parts: (1) Reactions 1–3: activation to acetyl-CoA and cleaving the C-C bond of the acetyl group, yielding CH$_3$-THSPt and CO$_2$, which are unique to the pathway; and (2) Reactions 4–6: reducing the methyl group of CH$_3$-THSPt to CH$_4$, which is common to all methanogenic pathways. Methanogenesis, and by inference reactions common to all methanogenic pathways, is thought to have evolved soon after the origin of life, approximately 3.75 billion years ago [32,33]. However, evolution of the acetoclastic pathway is proposed to have evolved approximately 250–300 million years ago during the end-Permian carbon cycle that contributed to the mass extinction of that period [34]. Reactions 2 and 3, catalyzed by acetate kinase and CO dehydrogenase/acetyl-CoA synthase CODH/ACS, are thought to be ancient enzymes evolving soon after the origin of life [35,36]. Homologs of acetate kinase and phosphotransacetylase are key enzymes in energy-yielding pathways of fermentative and acetogenic species from the domain *Bacteria*, converting acetyl-CoA to ATP and acetate. These observations are consistent with the evolution of the aceticlastic pathway by horizontal gene transfer of enzymes catalyzing Reactions 1–3 from the domain *Bacteria* and grafting on to Reactions 4–6, common to more ancient methanogenic pathways. Reactions 4 and 5, and the enzymes catalyzing them, are the subject of recent reviews that are recommended to the reader [37,38].

**Figure 4.** Pathway of aceticlastic methanogenesis in *M. acetivorans*. Ack, acetate kinase; Pta, phosphotransacetylase; CoA-SH, coenzyme A; THSPt, tetrahydroinosinapterin; Fdr, reduced ferredoxin; Fdo, oxidized ferredoxin; Cdh, CO dehydrogenase/acetyl-CoA synthase; CoM-SH, coenzyme M; Mtr, methyl-THSPt:CoM-SH methyltransferase; CoB-SH, coenzyme B; MP, methanophenazine; Hdr-DE, heterodisulfide reductase; Rnf, Rnf complex; Mrp, Mrp complex; Atp, ATP synthase. Modified from [39].

The first crystal structure for any acetate kinase was from the acetoclastic methanogen *Methanosarcina thermophila*, which revealed properties suggesting that the enzyme is the founding
member of the Acetate and Sugar Kinase/Hsc70/Actin (ASKHA) superfamily of phosphotransferases [35]. Structural and biochemical investigations established a direct in-line mechanism in which the carboxylate anion attacks the \( \gamma \)-phosphate of ATP enabling transfer of the phosphate group [40–48]. The first crystal structure of any phosphotransacetylase was also from \( M. \) thermophila, the structural and biochemical analyses of which indicate a mechanism that proceeds through base-catalyzed abstraction of the HS-CoA thiol proton and subsequent nucleophilic attack of \( \overset{-}{S} \)-CoA on the carbonyl carbon of acetyl phosphate [49].

The CODH/ACS complex [50–59] cleaves the C-C and C-S bonds of acetyl-CoA, transferring the methyl group to THSPt and oxidizing the carbonyl group to CO₂ with transfer of electrons to ferredoxin [60–62] (Reaction 3). The same enzyme complex functions in reverse to synthesize acetyl-CoA for cell carbon in CO₂-reducing methanogens and oxidizes exogenous CO in the pathway of CO conversion to CH₄, CO₂, and acetate in \( M. \) aceticivorans. Of ancient origin, primitive ancestors of CODH/ACS likely played a central role in the early evolution of life [36,63,64]. Although a two-subunit enzyme has been purified and characterized from an acetate-utilizing species of the genus \( Methanoseta \) [54,57–59], the majority of mechanistic studies have been with the five-subunit (\( \alpha \beta \gamma \delta \epsilon \)) complexes from the acetate-utilizing species \( M. \) thermophila and \( Methanosarcina \) barkeri. The complexes are resolvable into three components containing the \( \alpha \epsilon \), \( \gamma \delta \), or \( \beta \) subunit(s) [65]. The \( \alpha \epsilon \) component catalyzes the oxidation of CO and reduction of ferredoxin [60,66]. The crystal structure from \( M. \) barkeri shows a \( \alpha \beta \varepsilon \) arrangement with the \( \alpha \) subunit containing four 4Fe-4S clusters and a NiFe₃S₄ cluster bridged to an exogenous iron atom called the “C” cluster [67]. Two of the 4Fe-4S clusters are postulated to function in electron transport from the active site “C” cluster to ferredoxin. The structure suggests coupling between CO bound to the nickel and H₂O/OH⁻ bound to the exogenous iron in the C=O bond-forming step leading to the oxidized product CO₂. The structure also shows a gas channel extending from the “C” cluster to the protein surface with the potential to interface with the \( \beta \) component containing the “A” cluster, thus catalyzing acetyl-CoA cleavage and carbonyl group conversion to CO [68–71]. Although the structure is unknown, spectroscopic investigations indicate that the “A” cluster is comprised of a 4Fe-4S center bridged to a binuclear Ni-Ni site [70,72], similar to the homolog from an acetate-producing species from the domain \( Bacteria \) that synthesizes acetyl-CoA [73]. A mechanism is proposed in which transfer of an electron from “C” to “A” maintains the reduced catalytically active Ni(I) redox state of “A” [74]. Both kinetic and EPR approaches support the fact that alterations in the Ni coordination environment of the “A” cluster promote C–C bond cleavage, dependent on changes in the protein conformation from the open to closed state [75,76]. Moreover, CO is proposed to be an inhibitor of C-C bond cleavage; thus, control over C–C bond cleavage in concert with containment of CO in the gas channel explains the requirement for tight coupling of the decarbonylation reaction for efficient transfer of CO to “C” for oxidation [75]. The \( \gamma \delta \) component transfers the methyl group of acetyl-CoA to THSPt, involving a corrinoid cofactor and an iron-sulfur cluster [55,77–79], although it has yet to be determined which of the two subunits interact with THSPt. Spectroscopic EPR analyses indicate that the corrinoid cofactor is maintained in the base-off state with a \( E'_0 \) of −486 mV for the Co²⁺/¹⁺ couple that facilitates reduction of Co³⁺ to Co¹⁺ required for methylation of the corrinoid [77]. The analysis also identified a 4Fe-4S cluster with a midpoint potential close to the Co²⁺/¹⁺ couple, suggesting that the cluster is involved in reducing Co³⁺.
The conversion of acetate to CH₄ and CO₂ provides only a marginal amount of energy available for growth (ΔG°′ = −36 kJ/CH₄) that is spent on the ATP consumed in the activation to acetyl-CoA (Figure 4), which illustrates the importance of cells maximizing thermodynamic efficiency. A theoretical analysis of acetate-grown M. barkeri indicates that transfer of CH₄ and CO₂ into the gaseous phase contributes to the driving force of growth [80]. Thus it has been proposed that a carbonic anhydrase (Cam) from M. thermophila is located outside the cell membrane, where it converts CO₂ to membrane-impermeable HCO₃⁻ (Reaction 10, Figure 4), thereby facilitating removal of CO₂ from the cytoplasm [81]. Cam from M. thermophila is the archetype of an independently evolved class (γ class) of carbonic anhydrases that contains Fe²⁺ in the active site, contrary to all prokaryotic carbonic anhydrases, which contain zinc [82,83]. Structural and biochemical analyses [84] support a two-step ping pong mechanism, shown in Equations (6) and (7), where E represents enzyme residues, M is metal, and B is the buffer.

\[
\begin{align*}
E-\text{Fe}^{2+}\text{-OH}^{-} + \text{CO}_2 & = E-\text{Fe}^{2+}\text{-HCO}_3^{-} \quad (6a) \\
E-\text{Fe}^{2+}\text{-HCO}_3^{-} + \text{H}_2\text{O} & = E-\text{Fe}^{2+}\text{-H}_2\text{O} + \text{HCO}_3^{-} \quad (6b) \\
E-\text{Fe}^{2+}\text{-H}_2\text{O} & = H^{+}\text{-E-Fe}^{2+}\text{-OH}^{-} \quad (7a) \\
H^{+}\text{-E-Fe}^{2+}\text{-OH}^{-} + B & = E-\text{Fe}^{2+}\text{-OH}^{-} + BH^{+} \quad (7b)
\end{align*}
\]

In Step 1 a lone pair of electrons on the metal-bound hydroxide attacks CO₂-producing metal-bound bicarbonate (Equation (6a)), which is subsequently displaced by water (Equation (6b)). In Step 2 a proton is extracted from the metal-bound water (Equation (7a)), and then transferred to the buffer (Equation (7b)).

ATP is synthesized by a chemiosmotic mechanism. Ferredoxin accepts electrons derived from the oxidation of the carbonyl group of acetyl-CoA by CODH/ACS in both H₂-dependent and H₂-independent acetotrophic methanogens. Both types also obtain energy for growth by coupling electron transfer from ferredoxin to the heterodisulfide CoM-S-S-CoB, with translocation of ions generating a gradient that drives ATP synthesis catalyzed by an A₁A₀-type ATP synthase [85–88]. The reduced ferredoxin of H₂-dependent species donates electrons to a membrane-bound hydrogenase (Ech), evolving H₂ and translocating protons [89–91]. It is proposed that a hydrogenase (Vho) reoxidizes H₂ and donates electrons to a quinone-like electron carrier called methanophenazine (MP) [92]. The MP donates electrons to the heterodisulfide reductase HdrDE concomitant with translocation of two protons contributing to the gradient. An additional two protons are translocated by the Vho. However, most acetotrophic methanogens are H₂ independent [93–104] and likely evolved a different strategy for oxidizing ferredoxin and reducing CoM-S-S-CoB typified by M. acetivorans [105,106] (Figure 4). The genome does not encode a functional Ech; instead, acetate-grown cells preferentially synthesize a Rnf complex [87] similar to the six-subunit Rnf complexes in microbes from the domain Bacteria [107–113]. A Δrnf strain is unable to grow with acetate, confirming that the complex is essential [114]. Unlike all other characterized Rnf complexes, the contiguous genes encoding the six-subunit core complex from M. acetivorans are co-transcribed with a gene encoding a multiheme cytochrome c abundant in membranes of acetate-grown cells [87]. A topology model [39] predicts roles for each of the six core subunits and cytochrome c wherein MP mediates electron transfer between cytochrome c and HdrDE, translocating a pair of protons [39]. It has been shown that the Rnf complex translocates Na⁺ (Reaction 7),
joining the Na\(^+\) translocating methyl transfer (Reaction 4) [114]. Thus, both Na\(^+\) and H\(^+\) gradients are generated during growth with acetate. Notably, the A\(_{1}A_{0}\)-type ATP synthase of \textit{M. acetivorans} is dependent on both Na\(^+\) and H\(^+\) gradients [115]. A multisubunit Na\(^+\)/H\(^+\) antiporter (Mrp) is proposed to adjust the Na\(^+\)/H\(^+\) ratio (Reaction 8) optimal for ATP synthesis by the A\(_{1}A_{0}\)-type ATP synthase (Reaction 9) [116].

A genome-wide analysis of \textit{Methanosaeta thermophila} has revealed genes encoding enzymes catalyzing reactions in the pathway of acetate to CH\(_4\) identical to \textit{Methanosarcina} species except for the activation of acetate to acetyl-CoA, which is catalyzed by an AMP- and PPi-forming acetyl-CoA synthetase [117–120]. The synthetase has a several-fold lower \(K_{m}\) for acetate (0.4 mM) than acetate kinase from \textit{M. thermophila} (22 mM) [118,121], a result consistent with \textit{Methanosaeta} species dominating over \textit{Methanosarcina} species in environments where acetate is in low concentrations. Genes encoding Ech and Rnf are absent in the genome of \textit{Methanosaeta}, suggesting an unknown alternative electron transport pathway and mechanism for energy conservation [117].

3.2. Acetotrophic Energy-Converting Pathways Reducing Exogenous Electron Acceptors

Acetate-utilizing prokaryotes from the domain \textit{Archaea} also obtain energy by anaerobic respiration. \textit{Ferroglobus placidus} and \textit{Geoglobus ahangari} are hyperthermophiles growing at 85 °C by oxidizing acetate to CO\(_2\), only with Fe(III) serving as the electron acceptor [122]. \textit{Geoglobus acetivorans} is another hyperthermophile growing optimally at 81 °C and utilizing acetate in addition to formate, pyruvate, fumarate, malate, propionate, butyrate, succinate, glycerol, stearate, palmitate, peptone, and yeast extract as electron donors for Fe(III) reduction. The organism is also able to grow with H\(_2\) as the electron donor and Fe(III) as an electron acceptor without the need for organic substances [123]. Hyperthermophilic \textit{Thermococcus} species have also been implicated in oxidizing acetate and reducing Fe(III) [124].

4. Concluding Remarks

Although heterotrophic acetate-producing hyperthermophiles are abundantly documented, no hyperthermophilic acetoclastic methanogen has been described that presents a disconnect in the ecology of these two metabolic groups for which cognate mesophiles function syntrophically in anaerobic microbial food chains, converting complex biomass to CH\(_4\). One possibility is that hyperthermophilic temperatures are a thermodynamic barrier to the conversion of acetate to CH\(_4\). Additionally, although it appears that heterotrophic organisms from the domain \textit{Archaea} (Thaumarchaea) proliferate in mesothermal anaerobic environments [125], isolates and details of their metabolism are largely unknown. Thus, the finding that anaerobic respiratory acetate-oxidizing species are found in hyperthermophilic environments suggests the possibility that acetate-producing heterotrophs like \textit{P. furiosus} supply acetate in a two-component microbial food chain converting complex organics to CO\(_2\).

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Conflicts of Interest

The author declares no conflict of interest.

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