**Figure S1: The reductive acetyl-CoA pathway for autotrophic $CO_2$ fixation in bacteria (purple) and archaea (cyan).** The topology of the pathway in bacteria and archaea is conserved. However, bacteria use tetrahydrofolate (FH4) as $C_1$-carrier, whereas archaea make us of methyltetrahydropterin (MPT). Note that in the reductive acetyl-CoA pathway two molecules of $CO_2$ are reduced onto the level of formate/carbon monoxide for fixation. Thus, these $CO_2$ fixation reactions are not carboxylations in *strictu senso*. The only actual carboxylation reaction in the reductive acetyl-CoA pathway place is the carboxylation of acetyl-CoA into pyruvate via pyruvate:ferredoxin oxidoreductase (①).

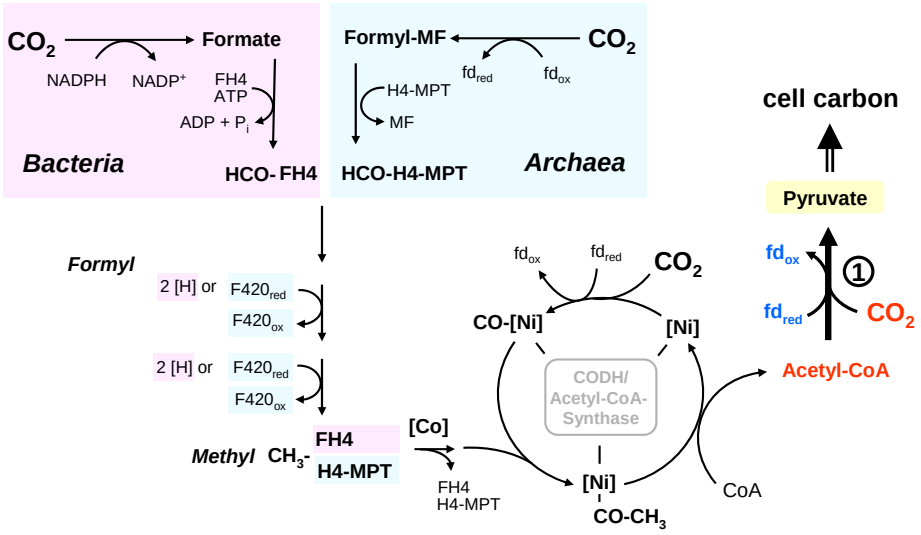


**Figure S2: The reductive citric acid (rTCA) cycle for autotrophic $CO_2$ fixation.** The rTCA makes use of most of the citric acid cycle reactions in the "reverse" direction, including isocitrate dehydrogenase (②). However, some of the TCA cycle reactions are essentially not reversible and are replaced in the rTCA. This includes the key carboxylases of the rTCA cycle, α-ketoglutarate:ferredoxin oxidoreductase (①) and pyruvate:ferredoxin oxidoreductase (③). Note that all carboxylases in the rTCA are reductive carboxylases.

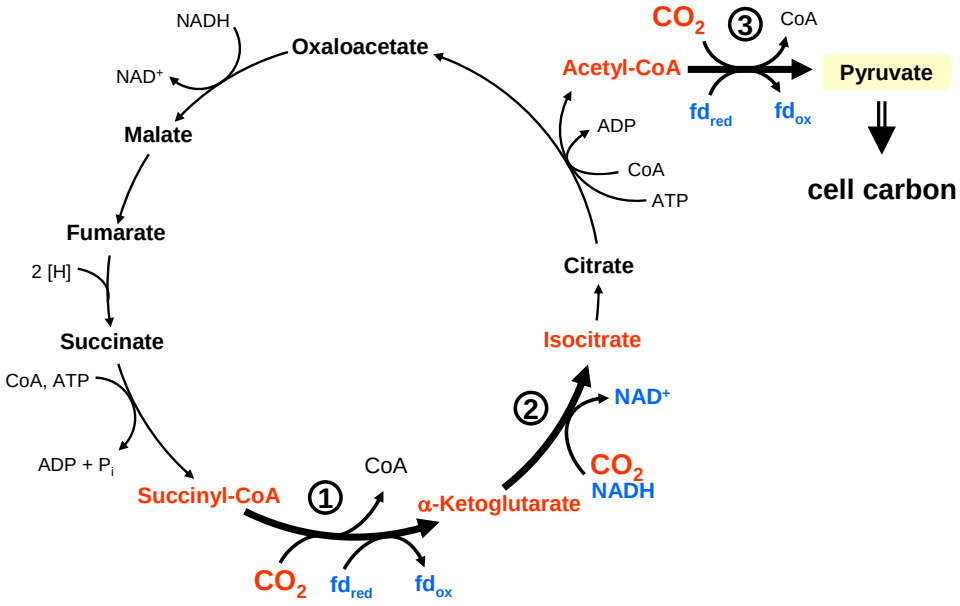

**Figure S3: The Calvin-Benson-Bassham (CBB) cycle for autotrophic $CO_2$ fixation.** The carboxylase of the CBB cycle is Ribulose-1,5-bisphoshate (RubisCO, ①). Note that RubisCO is a non-reductive carboxylase. Reduction of the $CO_2$ group fixed is carried out by a separate enzyme and requires activation of the substrate by ATP hydrolysis.

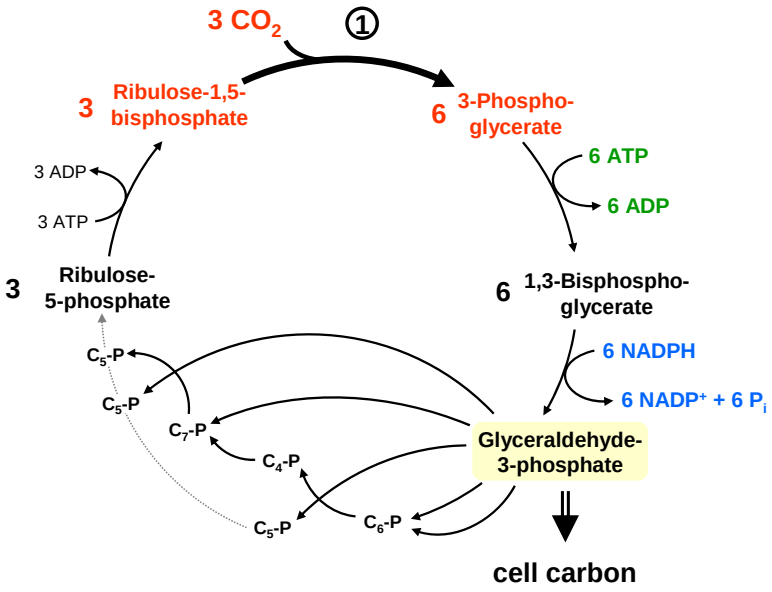


**Figure S4: The Fuchs-Holo bicycle (3HP bicycle).** The 3HP bicycle uses biotin-dependent acetyl-CoA/propionyl-CoA carboxylase (①) for $CO_2$ fixation. Acetyl-CoA/propionyl-CoA carboxylase is presumably bifunctional. Note that these biotin-dependent carboxylations require ATP hydrolysis. Moreover, acetyl-CoA/propionyl-CoA carboxylase catalyzes a non-reductive carboxylation reaction. Although the 3HP bicycle and the hydroxybutyrate/hydroxypropionate cycle both share the $CO_2$ fixation sequence, they differ in the acetyl-CoA regeneration cycle.

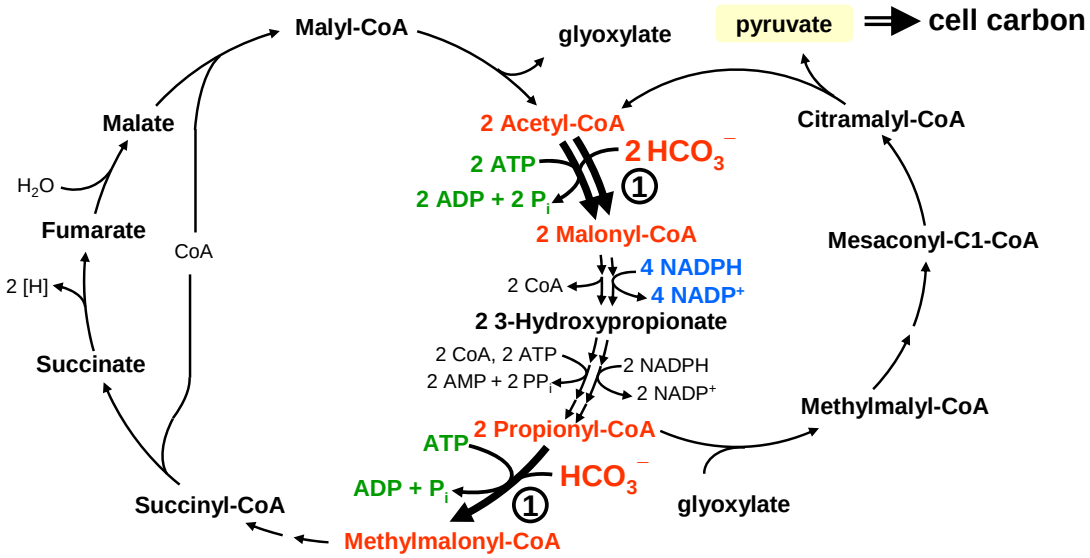

**Figure S5: The Hydroxypropionate/hydroxybutyrate (HP/HB) cycle.** The HP/HB cycle uses the same reactions as the Fuchs-Holo bicycle for $CO_2$ fixation (including biotin-dependent acetyl-CoA/propionyl-CoA carboxylase, ①). However, the regeneration of acetyl-CoA from succinyl-CoA differs from the former one. The regeneration of acetyl-CoA that proceeds *via* HB is actually shared with the dicarboxylate/hydroxybutyrate cycle (see below).

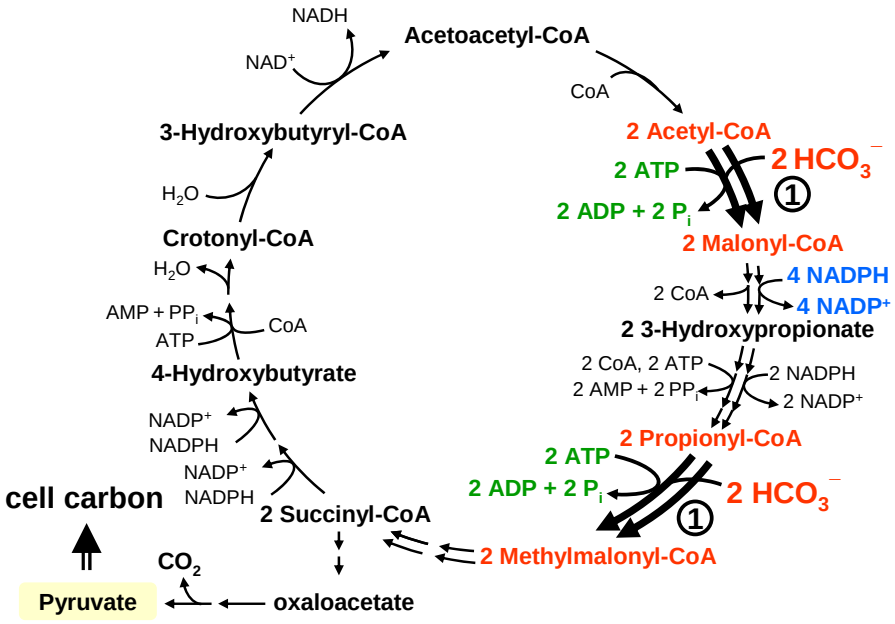


**Figure S6: The dicarboxylate/hydroxybutyrate (DC/ HB, fig. S6) cycle.** The DC/HB cycle uses the same reaction sequence for regeneration of the acceptor molecule acetyl-CoA as the HP/HB cycle, which proceeds in both pathways *via* HB. However, the CO2 fixation reactions differ essentially. In contrast to the HP/HB cycle, the DC/HB cycle makes use of reductive carboxylations *via* pyruvate:ferredoxin oxidoreductase (①), and non-reductive carboxylation *via* phosphoenolpyruvate carboxylase (②).

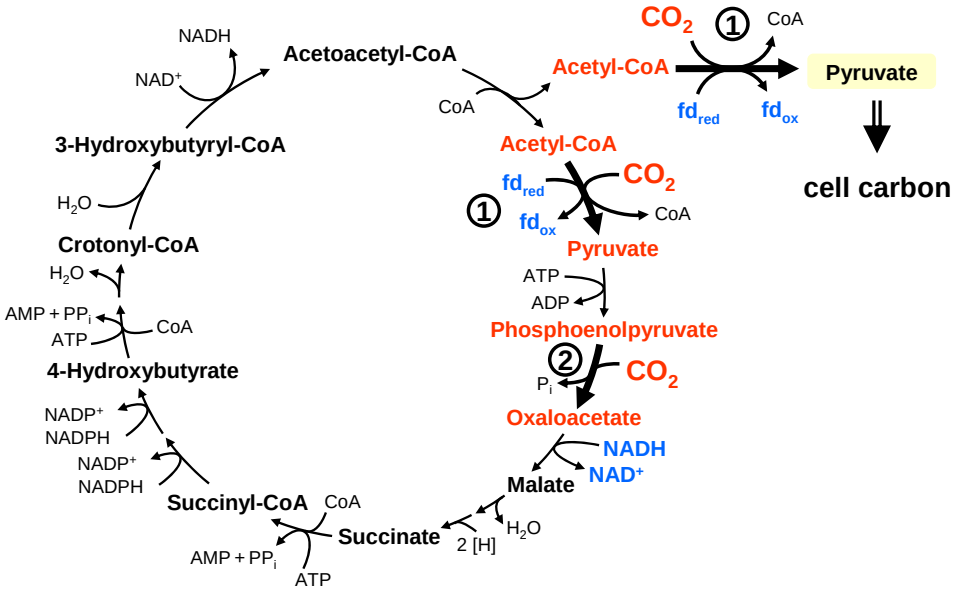

**Figure S7: Acetate assimilation pathways.** Four different acetate assimilation pathways have been described so far that all start from acetyl-CoA. **A Glyoxylate cycle:** The glyoxylate cycle is a modified citric acid cycle that is carboxylation-independent. **B Ethylmalonyl-CoA pathway:** Assimilation *via* the Ethylmalonyl-CoA pathway requires two carboxylation reactions that are catalyzed by crotonyl-CoA carboxylase/reductase (①) and biotin-dependent propionyl-CoA carboxylase (②). **C Methylaspartate cycle:** Acetate assimilation *via* the methylaspartate cycle shares some reactions with both the citric acid cycle and the ethylmalonyl-CoA pathway, and requires similar to the latter one also propionyl-CoA carboxylase (②). **D "Pyruvate:ferredoxin oxidoreductase pathway in anaerobes":** Many strictly anaerobes make use of pyruvate:ferredoxin oxidoreductase (③) for the assimilation of acetate. Then, pyruvate is converted into citric acid cycle intermediates *via* anaplerotic carboxylations involving pyruvate carboxylase or phosphoenolpyruvate carboxylase (see text).

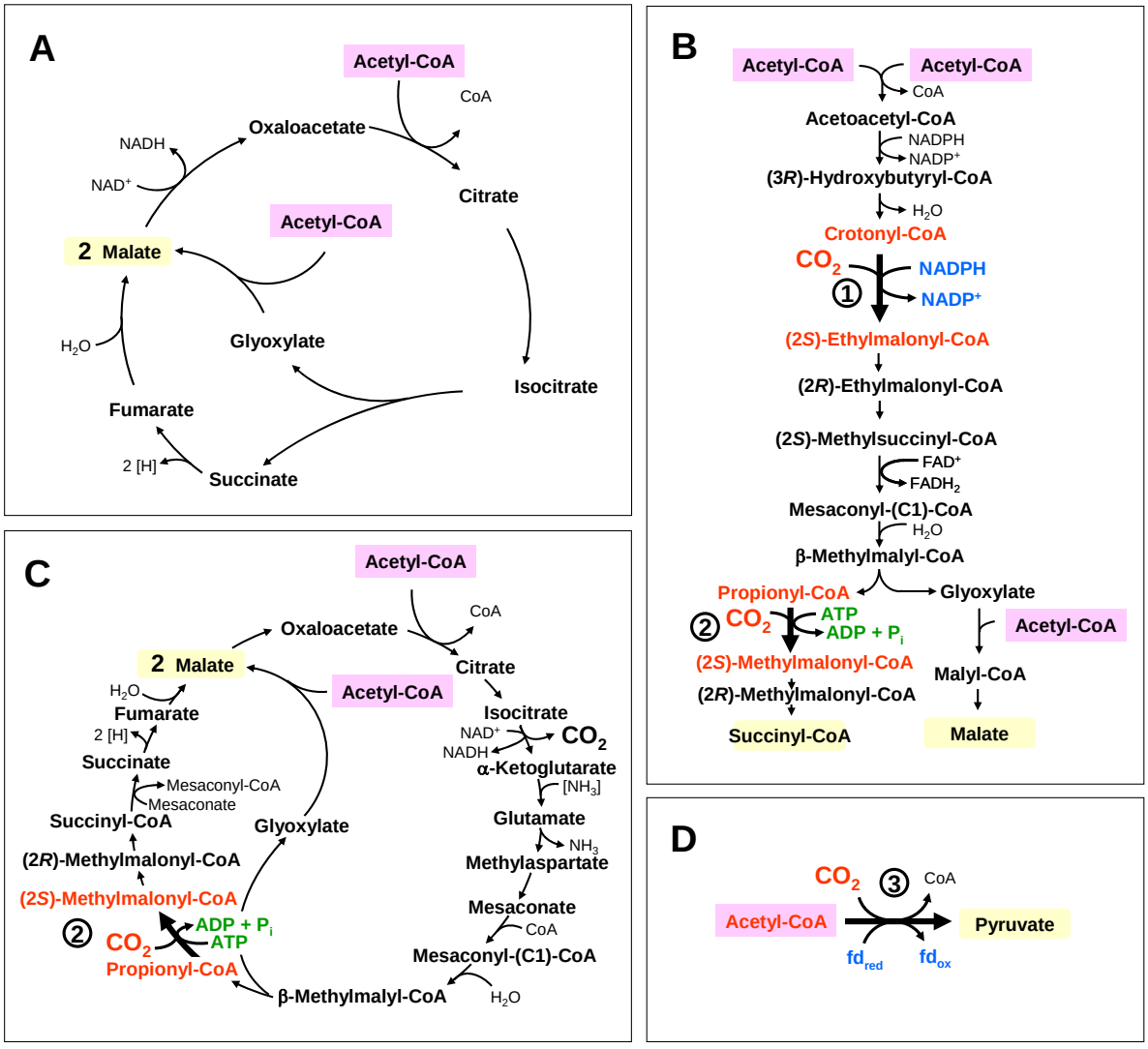

**Figure S8: Biosynthetic Carboxylation reactions.** In fatty acid and polyketide biosynthesis, carboxylation reactions are used for the supply of extender units that are added to the growing carbon chain. Carboxylation of the respective CoA esters yields α-carboxylic CoA esters that are transferred onto the "synthase-module (or domain)". Here, the α-carboxyl group is eliminated to yield a reactive enolate intermediate. This enolate then reacts with the nascent fatty acid/polyketide chain in a Claisen condensation-like reaction. Note that the carboxylation is pure catalytic nature and only used to activate the extender unit for the Claisen reaction.