The size and 3D shape of the BDI* ligand hits the sweet spot when it comes to stabilizing the magnesium(0) compound. The authors report that the compound consists of a central core of magnesium and sodium atoms – $[Mg_2Na_2]^{2+}$ – arranged in a ring and enveloped by two BDI* ligands (Fig. 1). Computational analyses reveal that the magnesium atoms have the same number of electrons as magnesium metal, which means that the compound could be viewed as a soluble form of the metal. There is, however, some sharing of electrons between the magnesium and sodium atoms. This doesn't detract from the assignment of the oxidation state of the magnesium atoms as zero, and the observation of a magnesium–sodium 'bond' in the compound is itself another first.

Given that the magnesium atoms are in the zero oxidation state, the compound should display a level of reactivity similar to that of the elemental metal. In fact, Rösch and co-workers' preliminary experiments show that it is even more reactive than that. For example, it can readily activate (break or weaken) very strong bonds, such as hydrogen–hydrogen and carbon–fluorine bonds, at room temperature. Many other compounds that contain main-group elements in low oxidation states can do the same[8]. A true demonstration of the exceptional reducing ability of the magnesium(0) compound would be the activation of even more staunchly inert molecules, such as dinitrogen (N_2). This seems achievable, given the recent demonstration that dinitrogen can be activated by a transiently formed calcium(I) compound[9].

A more surprising aspect of the reactivity of Rösch and colleagues' compound is that its magnesium(0) atoms can transfer electrons to its sodium atoms, reducing them back to sodium metal. This seems counter-intuitive, because the reverse process – the reduction of magnesium(II) to magnesium(0) by sodium metal – was used to make the magnesium(0) compound in the first place. The authors' experimental evidence backs up the observation that the sodium atoms are reduced, but more work is required to examine the processes by which this operates.

Rösch and co-workers' stable magnesium(0) compound is a landmark in the chemistry of the *s*-block elements. It will fundamentally change chemists' views about what can be synthesized using these elements. Moreover, it will help to advance our understanding of – and raise questions about – the unusual 'non-classical' bonding in low-oxidation-state main-group compounds. The development of highly reducing magnesium(0) compounds might also pave the way to their use in chemical reactions that, at present, cannot normally be carried out with *s*-block metals. The future is surely bright for magnesium now that it has hit zero.

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Microbiology

Life in a carbon dioxide world

Martina Preiner & William F. Martin

Microorganisms living in hydrothermal vents that emit carbon dioxide gas provide a striking example of metabolic finesse. This pathway sheds light on microbial ecology in extreme environments and offers clues to early life on Earth. **See p.784**

Few chemicals have hit the headlines so widely that everyone knows their formula, but carbon dioxide is an exception. It is so crucial for understanding climate change that we recognize its shorthand name of CO_2 as a threat to our future. For most microbes, however, CO_2 looks more like a feast than a threat. Microbes have tools at their disposal – CO_2-fixation pathways – that enable them to incorporate CO_2 into their cell mass. These pathways are essential for life because all ecosystems on Earth ultimately depend on cells that make organic material from CO_2. On page 784, Steffens *et al.*[1] uncover key details about an ingenious pathway that enables bacteria to thrive in a hydrothermal environment surrounded by gases consisting mainly of CO_2.

Steffens and colleagues studied *Hippea maritima* bacteria. These microorganisms shun oxygen, love temperatures near 60 °C, and obtain energy from the reaction of hydrogen gas (H_2) with sulfur to make hydrogen sulfide (H_2S). As with all life forms, they need a carbon source to grow. And, like many, they can choose this source depending on what is available in their environment. If a rich diet of protein is on offer, *H. maritima* incorporate this as a building block into their metabolic pathways for growth.

But if *H. maritima* grow in the presence of CO_2 concentrations of 40% (1,000 times higher than atmospheric CO_2 levels), they do some 'chemical engineering', using a pathway called the reversed oxidative tricarboxylic acid cycle. That might sound complicated, but it is connected to something familiar – human nutrition. After the food we eat is broken down in the gut, our cells convert the sugars, fats and proteins contained in the food into energy and CO_2 using a pathway called the tricarboxylic acid (TCA) cycle. This is also called the Krebs cycle, after the scientist who discovered it[2]. The TCA cycle is used by nearly all life forms, but it can run backwards in some bacteria[3]: this change of direction, to give the reversed oxidative TCA cycle (Fig. 1), invests energy that converts CO_2 into amino acids, sugars and lipids.

What enables the TCA cycle to run in reverse under specific growth conditions has been a mystery, until now. Steffens *et al.* show that *H. maritima*'s secret trick is to adjust levels of a crucial enzyme in an unexpected way, so as to be ready to assimilate high concentrations of CO_2 before they are encountered. This generates an elegant harmony between the microbe's environment and its metabolism.

H. maritima uses the reversed oxidative TCA cycle when high levels of CO_2 are present, and this is where the technical brilliance of Steffens and colleagues' investigation becomes evident. The authors fed the bacteria amino acids and CO_2 labelled with the ^{13}C isotope of carbon. Both of these food sources were channelled into the reversed oxidative TCA cycle. Tracking ^{13}C accumulation in the intermediate molecules of this pathway in growing cells enabled the authors to uncover which carbon source the cells used down which route of the pathway. It also enabled them to determine how many full 'turns' of the reversed oxidative TCA cycle occur as carbon is assimilated.

This revealed that *H. maritima* preferentially uses CO_2 as its carbon source, but only when CO_2 is in abundant supply. To enable the TCA cycle to run backwards in response to high levels of CO_2, the cells harbour huge amounts of the enzyme citrate synthase. A high level of citrate synthase makes it easier to generate acetyl coenzyme A (acetyl-CoA) molecules,

which exit the reversed oxidative TCA cycle by forming pyruvate, which is converted to lipids, sugars and amino acids (Fig. 1). This in turn, invites CO_2 to enter the cycle. In this way, high environmental CO_2 levels push the cycle in the direction of converting CO_2 to acetyl-CoA.

This would cause a logjam at the acetyl-CoA stage of the cycle were it not for the high levels of CO_2. The main connection between the reversed oxidative TCA cycle and other metabolic pathways is the molecule pyruvate, which is made by a reaction involving CO_2 and acetyl-CoA. That reaction, like the two other reactions that incorporate CO_2 in this cycle, is reversible and can run in either direction. A high CO_2 concentration – typically expressed as high partial pressure relative to the total pressure of all the gases present – pushes all three of these reactions forwards. The whole pathway is thereby pushed in the direction of pyruvate production, as long as there is no bottleneck at the reaction catalysed by citrate synthase. High amounts of that enzyme avert this potential bottleneck, and keep cells poised to exploit high levels of CO_2 if the environment provides them.

Ecosystems with high CO_2 harbour many environments in which resident microbes have genes that encode enzymes of the reversed oxidative TCA cycle, as metagenomics analysis (genome sequencing of microbial communities) has indicated[4]. However, the presence of genes alone cannot reveal in which direction cells are using a pathway because the environment can dictate the flow of substrates, as this exquisitely detailed example of *H. maritima* underscores.

Hippea maritima is not the only known example of a bacterium with reversible metabolism. Another example is the bacterium *Thermacetogenium phaeum*, which grows under conditions similar to those that support *H. maritima* (high CO_2 and an absence of oxygen), but in industrial cellulose-processing reactors[5]. If the environment offers abundant H_2 and CO_2, *T. phaeum* grows using these to make the molecule acetate. However, if those gases become scarce and acetate is abundant, the microbe's main metabolic reaction runs backwards[5], and it survives on the conversion of acetate to H_2 and CO_2. How it achieves this is unknown. Looking at the genes that microbes use in a given environment can reveal important clues to the secrets of life in microbial communities[6]. But to really understand the chemical reactions that support microbial life, there is no substitute for studies such as those by Steffens and colleagues, which show us, carbon atom by carbon atom, what cells are doing with the substrates that their environment presents.

Individual microbes, such as *H. maritima*, and even whole ecosystems, can thrive on the energy supplied by the reaction of H_2 with CO_2. This not only offers examples of fascinating microbial ecology, but also provides a window into the ancient past, by presenting strategies for growth in conditions thought to be similar to those that the first microbes on Earth encountered[3]. Those pioneering microbes had to be able to survive on a diet of CO_2 because it was the carbon source that the early Earth had available[7].

Yet CO_2 is only half of the story. To convert CO_2 into organic compounds, microbes need a source of energy and electrons. For the first ecosystems on Earth, and for *H. maritima* today, the source of chemical energy and electrons for CO_2 fixation is H_2. For four billion years, microbes have been living from the energy provided by the vast amounts of H_2 that Earth's crust constantly generates[8]. Given the effort that *H. maritima* invests in making pyruvate from H_2 and CO_2, it seems almost unimaginable that the very first biochemical pathways could have got going before there were enzymes to assist the carbon-fixing reactions. Yet, surprisingly, H_2 and CO_2 can form pyruvate overnight without any enzyme involvement if simple metal catalysts, of the kinds found in the oceanic crust, are provided[9]. This suggests that early metabolism on Earth was built around the naturally occurring chemistry between CO_2 and H_2 in mineral-rich environments[10].

The chemical reactions that underpin the lifestyle of *H. maritima* thus hark back to a time when the first cells lived in a world of carbon dioxide. By investigating cells that still inhabit such realms today, we can discover some clues about the life and times of the most ancient microbial ancestors.

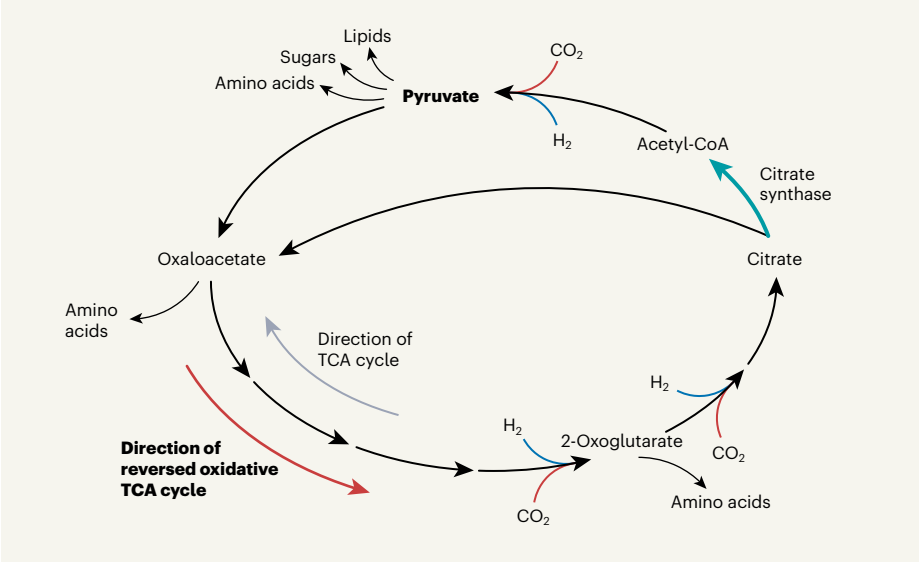

Figure 1 | The reversed oxidative tricarboxylic acid (TCA) cycle. Almost all life forms use the TCA cycle to convert molecules such as amino acids, sugars and lipids into energy and carbon dioxide by means of a pathway that involves molecules such as pyruvate, oxaloacetate, 2-oxoglutarate, citrate and acetyl coenzyme A (acetyl-CoA). Some bacteria can run this cycle in the reverse direction (it's then called the reversed oxidative TCA cycle), incorporating CO_2 and hydrogen (H_2) to form molecules such as amino acids, sugars and lipids. Steffens *et al.*[1] used approaches such as tracking labelled carbon atoms to reveal the mechanism that enables the bacterium *Hippea maritima* to run the TCA cycle backwards. The authors report that a high level of the enzyme citrate synthase is key to pathway reversal.

"The presence of genes alone cannot reveal in which direction cells are using a pathway because the environment can dictate the flow of substrates."

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