# In the active center of carbon dioxide conversion

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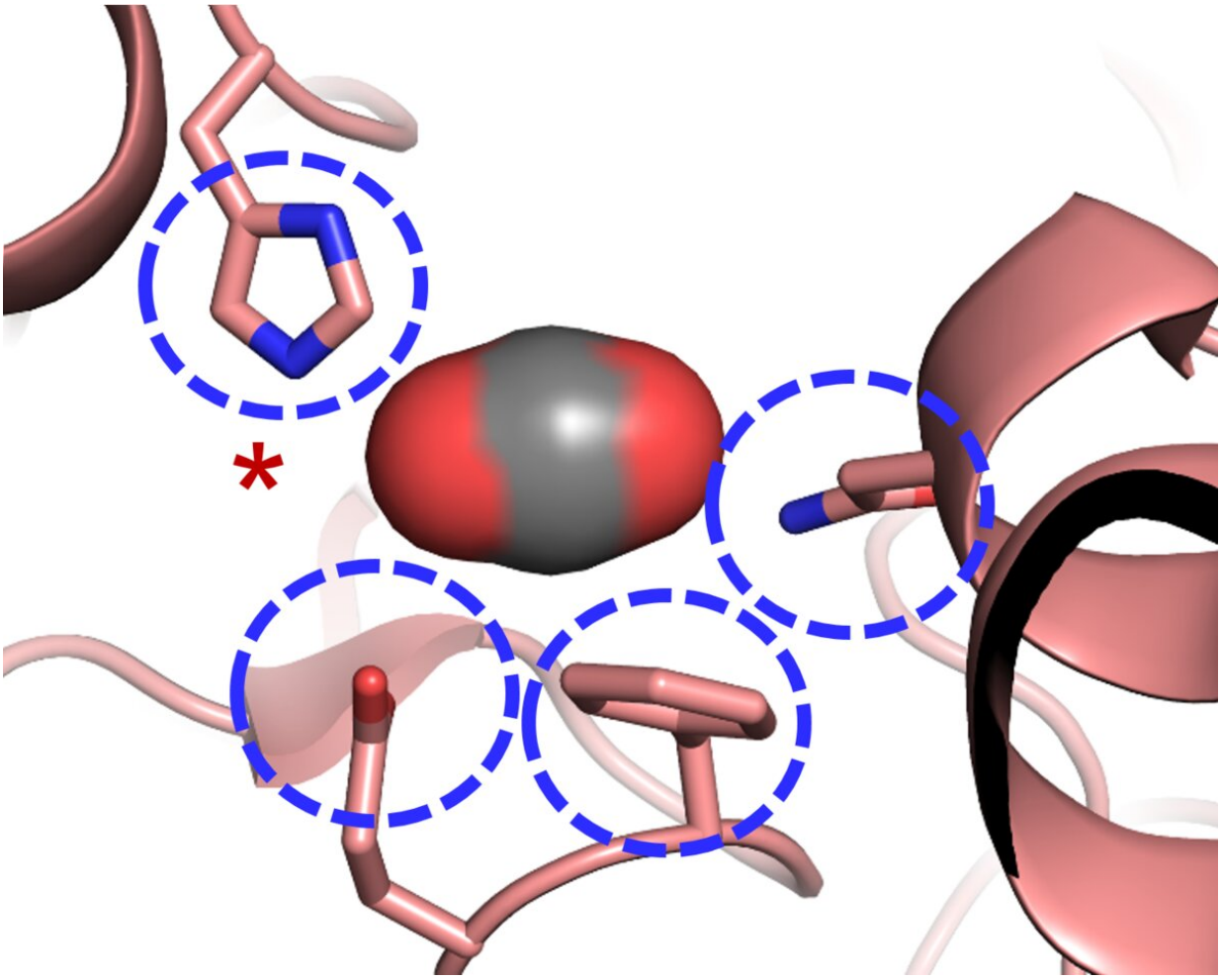


The Carboxylase active site: Four amino acids are important for CO2 binding in highly efficient CO2 fixing enzymes. Credit: Max-Planck-Institute for Terrestrial Microbiology/Erb

In order to overcome the climate crisis, two measures are required: The reduction of carbon dioxide ($CO_2$) emissions, and removal of $CO_2$ from the earth atmosphere. The latter is the goal of Tobias Erb's research group at the Max Planck Institute for Terrestrial Microbiology in Marburg. Their approaches not only aim to benefit climate protection, but also to secure sustainability in the long term: to filter $CO_2$ from the air and make it usable for technology.

In order to overcome the climate crisis, two measures are required: reduction of $CO_2$ emissions and active removal of $CO_2$ from the Earth's atmosphere. The latter is the goal of Tobias Erb and his department "Biochemistry and Synthetic Metabolism" at the Max Planck Institute for Terrestrial Microbiology in Marburg. Their approach aims to benefit climate protection, but also to secure sustainability in the long term: filtering $CO_2$ from the air and making it usable for technology.

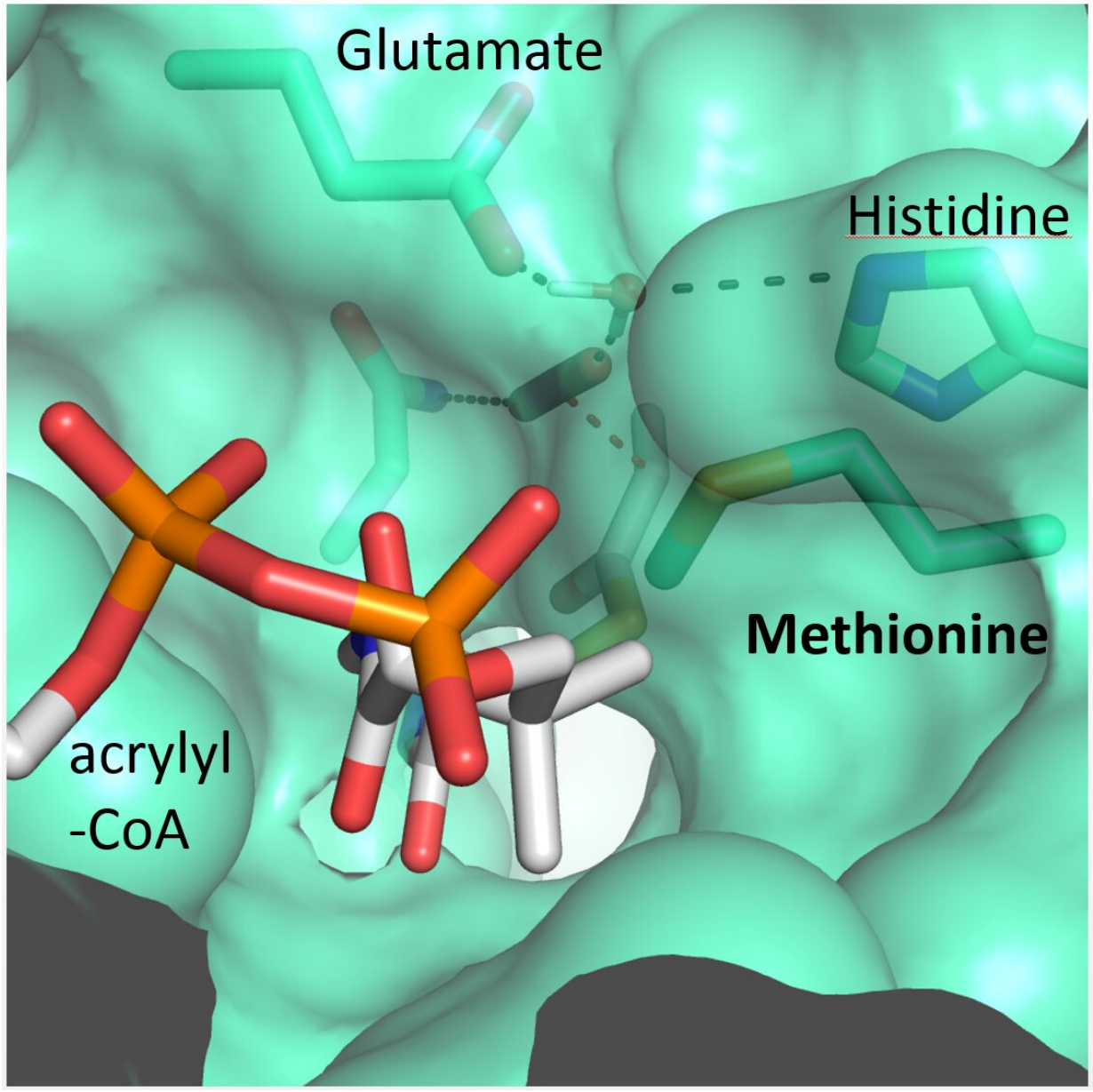
Filtering $CO_2$ efficiently from the air—nature can do this through photosynthesis, converting $CO_2$ into biomass. Unlike industrial technologies which can only use the gas in a highly concentrated form (which in turn consumes fossil energy), photosynthesis works directly with ambient air containing only 0.4% gaseous carbon dioxide. Its secret lies in the enzymes, proteins that act as catalysts to mediate specific chemical reactions, such as the fixation of $CO_2$. In photosynthesis, this reaction is driven by the enzyme RubisCO. However, the efficiency of natural photosynthesis is not very high: in more than a fourth of all cases, RubisCO metabolizes oxygen from the air, which is a strong competitor of $CO_2$ in this reaction.

## ECR enzymes are faster and more precise than RubisCo

Therefore, the Max Planck researchers in Marburg have decided on alternatives to RubisCO. Enoyl-CoA Carboxylase/Reductase enzymes (ECRs) are much more efficient than RubisCO and do not make

mistakes with oxygen. After many years of scientific work in order to understand this capacity, the scientists have succeeded in building a functioning process in the test tube that fixes $CO_2$ better than nature itself. Robustness and energy efficiency are the qualities that the team would like to bestow to their artificial photosynthesis. "Learn from the best" is the motto: nature itself serves as a model for molecular biology.

What is the reason for the high efficiency of ECRs? What is the magic spell to create a turbo $CO_2$ fixator? Max Planck junior researchers Gabriele Stoffel and Iria Bernhardsgrütter pursued this question together with colleagues from Chile and the U.S.. They analyzed the ECR from the bacterium Kitasatospora setae, currently the fastest known carboxylase. Using a combined approach of structural biology, biochemistry and computer simulations, they were able to understand for the first time how the enzyme binds and converts $CO_2$.




A methionine residue shields the active site from the competing water molecules. Credit: Max-Planck-Institute for Terrestrial Microbiology/Erb

## Teamwork in the active centre

"We were surprised to learn that only four amino acids are sufficient to

provide control over the $CO_2$ molecule," explains Gabriele Stoffel, postdoctoral fellow in the Erb department and first author of the study. "Three amino acids—one asparagine, glutamate and a histidine—hold the $CO_2$ in place from two sides. Another amino acid, a phenylalanine, shields the bound $CO_2$ from water, which would inhibit the reaction," says Stoffel.

These findings open up new paths for researchers. "We wanted to transfer the capability of binding $CO_2$ to other enzymes. This would offer us much greater possibilities for optimizing photosynthesis," says Iria Bernhardsgrütter, Ph.D. student in the research group. In another study, Bernhardsgrütter focused on two candidates for the protein scaffold: Propionyl-CoA synthase (PCS) and Archaeal Enoyl-CoA reductase (AER).

**Enhancing $CO_2$ fixation capacity**

Both enzymes were already able to use $CO_2$, but only with an efficiency of about five percent and with concentrated $CO_2$. Computational models revealed that those enzymes only possessed some of the four amino acids required and those were also misaligned. Iria Bernhardsgrütter succeeded by exchanging amino acids to correct the "miscasts" in PCS. Immediately, the efficiency of $CO_2$ increased to around 20 percent. Now the second aspect was targeted, namely shielding the binding site from water. Iria Bernhardsgrütter was also able to solve this problem: another amino acid replacement blocked the water's access to the binding site. The combination of both changes led to a carboxylation rate of almost 95%. Similar experiments with AER increased $CO_2$-conversion efficiencies to almost 90%.

This knowledge of the exact requirements of $CO_2$-fixing enzymes and its successful application has brought research a decisive step closer to its high goals: on the one hand, being able to filter $CO_2$ efficiently from the

atmosphere, on the other hand, integrating $CO_2$ into sustainable use—towards the recycling of valuable substances following nature's example.

**More information:** Gabriele M. M. Stoffel et al. Four amino acids define the CO2 binding pocket of enoyl-CoA carboxylases/reductases, *Proceedings of the National Academy of Sciences* (2019). DOI: 10.1073/pnas.1901471116

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