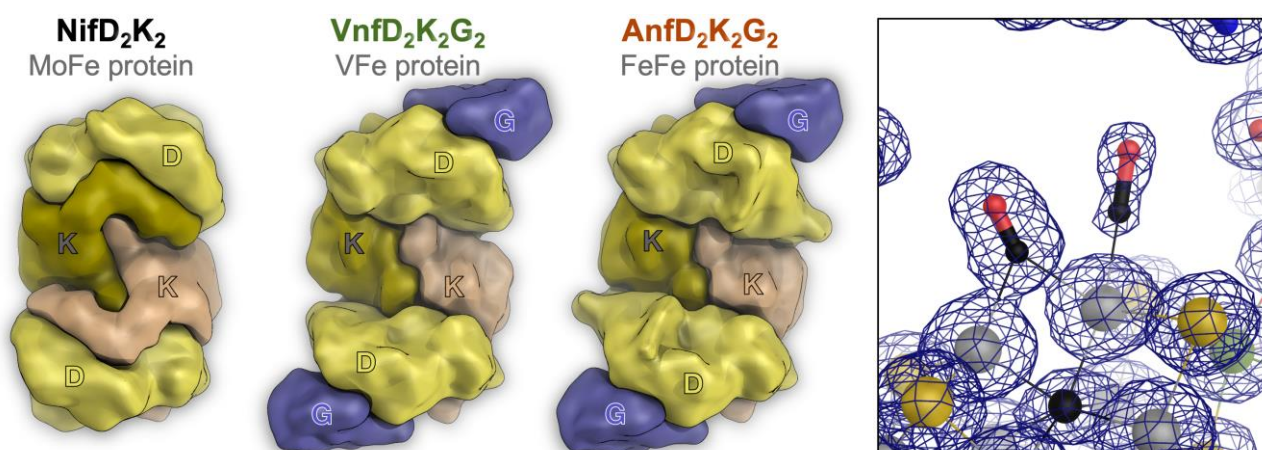


Towards a Unified Concept of Nitrogenase Catalysis

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Nitrogenases catalyze the reduction of atmospheric N₂ to bioavailable NH₄⁺ as the only known agents of biological nitrogen fixation^{1,2}. They exist in three different, but structurally and mechanistically closely related classes distinguished by the inclusion of an apical heterometal in their active site iron-sulfur cofactor that is either Mo, V or another Fe. With the most recent analysis of Fe-nitrogenase, all components of the three systems are structurally characterized, and kinetic analyses and HD exchange experiments have underlined that the fundamental mechanistic principles of these isoenzymes are retained. However, their catalytic competence towards physiological N₂ reduction and the ability of some to reduce CO, CO₂, acetylene, cyanide, nitrite and many other small substrates including protons differs strongly, and while often the products are fully reduced ammonium or methane, CO reduction predominantly yields ethylene and therefore involves C-C coupling.



Understanding nitrogenases has been a multidisciplinary effort for decades, and while a conclusion has not yet been reached, the integration of available data allows for increasingly detailed mechanistic models. Based on our analysis of a turnover state,³ and of CO binding to the CO-converting V-nitrogenase^{4,5} a model of cofactor activation and substrate reduction is discussed that breaks down the elementary steps of nitrogenase catalysis and leads to a core mechanism that is at play in any of the diverse reactions mediated by this family of metalloenzymes.

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³ D. Sippel *et al.* *Science*, **2018**, *359*, 1484-1498.

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⁵ M. Rohde, K. Laun, I. Zebger, S. Stripp, O. Einsle *Science Adv.*, **2021**, *7*, eabg4474.