Hydrogenases spill the beans: Key catalytic moves revealed

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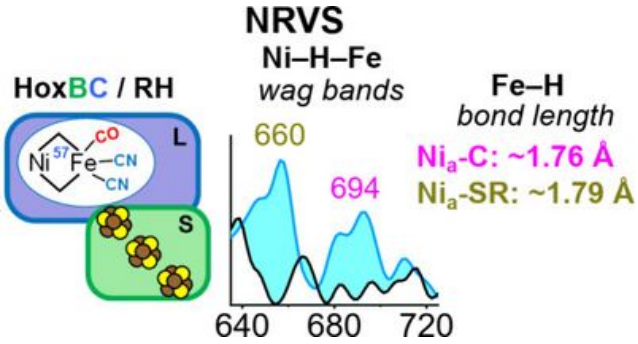

Catalytic Cycle of [NiFe]-Hydrogenases: Identification of Two Key Bridging Hydride Intermediates

A recent UniSysCat study has shed light on how [NiFe]-hydrogenases—nature's remarkably efficient hydrogen-processing enzymes—perform their catalytic work. These metalloenzymes oxidize and produce molecular hydrogen (H_2), making them extremely attractive for future biotechnological and energy applications. Yet even after decades of research, important steps in their reaction mechanism remained elusive.

The research teams led by Oliver Lenz and Ingo Zebger collaborated with researchers at the **DESY synchrotron** in Hamburg to track down elusive catalytic intermediates. By selectively labeling the active-site iron of an H_2-sensing [NiFe]-hydrogenase with the Mössbauer isotope ^{57}**Fe**, they were able to probe the enzyme using **nuclear resonance vibrational spectroscopy (NRVS)**—a powerful synchrotron-based method capable of detecting metal–hydride vibrations with exceptional sensitivity.

This strategy enabled the direct observation of the **two key bridging hydride species** in the catalytic cycle and revealed their distinct binding environments at the metal center. In addition, the researchers uncovered a unifying feature: the **[NiFe]-active site remains structurally rigid in all catalytically relevant states**. This rigidity appears to be crucial for the rapid electron and proton transfers required for efficient H_2 activation.

The findings not only deepen our understanding of hydrogenase function, but also provide valuable design principles for next-generation biomimetic catalysts. They show that only the precise balance between a rigid scaffold of the active site and finely tuned hydride coordination can replicate the remarkable efficiency of natural [NiFe]-hydrogenases.

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The study has been published in the *Journal of the American Chemical Society*:
G. Caserta et al., *J. Am. Chem. Soc.* 2025, 147, 45, 41216–41220.
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