

Unifying Mechanism in NiFe Hydrogenase Using Advanced Spectroscopic Techniques

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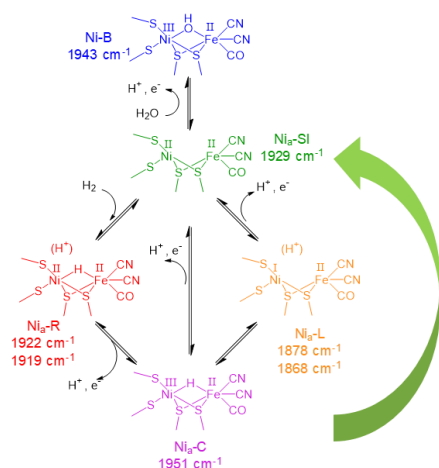
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Hydrogenases remain a source of great curiosity to chemists and biochemists alike: their bimetallic catalytic core is similar to small molecule metal carbonyl complexes known to inorganic chemists for decades, but their catalytic rates far exceed those of any known mimetic catalysts.¹ Different classes of NiFe hydrogenase share a common active site structure, but possess a range of catalytic bias towards H₂ production or oxidation, turnover frequency, and tolerance to inhibitors such as O₂.² Molecular hydrogen activation is the simplest of all proton-coupled electron transfer reactions. Despite this, key open questions remain about NiFe hydrogenase mechanism, in particular concerning how intimately proton and electron transfer are coupled throughout the catalytic cycle, and whether proton and electron transfers are concerted or sequential.³ Indeed, it is unclear whether a universal mechanism operates for all classes of NiFe hydrogenase. Using a unique combination of electrochemical control with steady-state, transient, and single crystal infrared spectroscopy, we have identified catalytic ‘bottle necks’,^{4,5} and now begin to reveal hidden short-lived intermediates that unify our mechanistic understanding of NiFe hydrogenases.



Concerted vs stepwise PCET?

Universal mechanism?

How is H₂ heterolytically cleaved?

Importance of conserved amino acids?

¹ S.L. Behnke *et al. Comments Inorg. Chem.*, **2016**, *36*, 123-140.

² W. Lubitz *et al. Chem. Rev.*, **2014**, *114*, 4081-4148.

³ P.A Ash *et al. ACS Catal.*, **2017**, *7*, 2471-2485.

⁴ P.A Ash *et al. Acc. Chem. Res.*, **2019**, *52*, 3120-3131.

⁵ P.A Ash *et al. Chem. Sci.*, **2021**, *12*, 12959-12970.