Elucidating mechanistic principles of complex metalloenzymes through protein-based models

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Abstract:

Nature has evolved diverse systems to carry out energy conversion reactions. Metalloenzymes such as hydrogenase, carbon monoxide dehydrogenase (CODH), acetyl coenzyme A synthase (ACS), and methyl coenzyme M reductase use earth-abundant transition metals such as nickel and iron to generate and oxidize small-molecule fuels such as hydrogen, carbon monoxide, acetate, and methane. These reactions are highly valuable in the context of the impending global energy and climate crisis. However, due to substantial challenges associated with studies of these native enzymes, much remains unknown about the basic catalytic mechanisms, hindering efforts to harness this chemistry for anthropogenic purposes. To address these limitations and develop a molecular-level understanding of these systems, we have developed robust, protein-derived models as structural, functional, and mechanistic mimics of hydrogenase, CODH and ACS. In this presentation, our recent efforts to install and modulate novel reactivity in rubredoxin, ferredoxin, and azurin scaffolds will be discussed. along with findings from multiple complementary spectroscopic techniques used to probe the catalytic mechanisms. These engineered metalloenzymes provide direct insight into the fundamental chemical principles driving the natural systems.

Bio:

Hannah received her B.S. in Chemistry from the California Institute of Technology (Caltech) in 2006, where she performed research on spectroscopic endospore viability assays with [Adrian Ponce](http://ponce.caltech.edu/Home.html) (NASA Jet Propulsion Laboratory) and [Harry Gray](http://www.bilrc.caltech.edu/webpage/22). She received her Ph.D. in Physical Chemistry from the University of California, San Diego (UCSD) in 2011, under the direction of Professor [Judy Kim](http://galileo.ucsd.edu/index.html), as an NSF Graduate Research Fellow and a National Defense Science and Engineering Graduate Fellow. During her graduate research, she used many different types of spectroscopy to study the structure and dynamics of amino acid radical intermediates in biological electron transfer reactions. After earning her Ph.D., Hannah moved across the ocean to Germany to study hydrogenase and oxidase enzymes and learn advanced EPR techniques as a Humboldt Foundation Postdoctoral Fellow working under Director [Wolfgang Lubitz](https://www.mpg.de/339774/chemische_energiekonversion_wissM) at the Max Planck Institute for Chemical Energy Conversion. Since starting her independent career, Hannah has received the NSF CAREER award in 2015 to support work on hydrogenase mimics, and in 2017, she was awarded the DOE Early Career award to support the group’s research on one-carbon activation in model nickel metalloenzymes. Recently, the group has received support for their research on heterobimetallic Mn/Fe cofactors through the NIH R35 MIRA program for New and Early Stage Investigators. Hannah was also awarded the 2018 Sloan Research Fellowship.

