CONCLUDING PERSPECTIVES

Nitrogenase is a fascinating enzyme. It houses not one but two unique iron-sulfur clusters, the FeMo-cofactor and the P-cluster. Neither cluster has been successfully synthesized outside a cellular environment. Due to the complexity of the clusters' structure and their interactions with substrate, electrons, and protons, the mechanism of biological nitrogen fixation has attracted the attention of numerous scientists for the better part of a century but yet remains elusive. Solving the mechanism of biological nitrogen fixation will not only advance the fields of chemistry and biochemistry at a fundamental level and through the invention of new characterization techniques, it also has the potential to significantly impact agriculture by leading to new and cleaner methods of ammonia production for fertilizer.

The work described in this thesis contributes to our understanding of nitrogenase using structural and spectroscopic techniques. Major results include the structural characterization of a 1.08 Å Cp1 structure and its comparison to Av1, analysis of pathways within the MoFe protein, and the characterization of a reversible protonated resting state of the MoFe protein. An underlying principle in all the work described herein is the importance of investigating multiple nitrogenase species that are phylogenetically distinct. While the structure of the cofactors is conserved among all known MoFe proteins, their enzyme activity and structure are not wholly conserved. Understanding the similarities and differences between nitrogenases elucidates the relationship of the structure and function of nitrogenase.

Looking ahead, much work is still needed to achieve a conclusive and complete understanding of the mechanism of biological nitrogen fixation. New technology and creative approaches will undoubtedly get the job done, and I look forward to seeing the results!

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