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Introduction to the spotlight collection on bioinorganic chemistry

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Bioinorganic chemists broadly explore the roles of metal ions in various life processes, applying this knowledge to develop impactful applications, such as metallodrugs, sensors, and catalysts. The fundamental questions driving this field have led to the advancement of numerous synthetic, spectroscopic, analytical and theoretical methods, which have benefitted not only bioinorganic chemists, but also the broader scientific community and industry. Not surprisingly, bioinorganic chemistry has long attracted scientists from diverse backgrounds across the globe, making it one of the most inter-disciplinary and collaborative areas of research. The spotlight collection on "Bioinorganic chemistry", featuring articles from Chemical Science and Dalton Transactions, highlights the remarkable diversity inherent in this field.

Metalloenzyme biochemistry

A central focus of bioinorganic chemistry lies in understanding the biochemistry and biophysical chemistry of metalloenzymes in nature. Behera and co-workers investigate the role of nanoconfinement in feractivity involved in iron biomineralization within bacterioferritins (https://doi.org/10.1039/D4SC07021F). a related study, Behera reports enhanced stability of chitosa-functionalized ferritin for iron delivery with minimal cage degradation and leakage (https://doi.org/

10.1039/D4DT01839G). Fujii contributes to our understanding of the electronic structure of blue copper proteins through L₃-edge XANES to reveal that azurin has a more covalent Cu-S bond than (https://doi.org/10.1039/ amicyanin D4DT02891K). Elliott examines reactivity of bacterial cytochrome c peroxidase using a combination of spectroscopic techniques to demonstrate that the oxidant produced by the reaction of H₂O₂ with the diferric resting state is compound I and not the Fe(IV)Fe(IV)=O species proposed for MauG (https:// doi.org/10.1039/D4SC07339H). employs hybrid QM/MM calculations, MD simulations, and DFT calculations to investigate the mechanism of the C-C bond formation of arylomycin by an engineered cytochrome P450 (https:// doi.org/10.1039/D4DT02197E). Ghosh Dev

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Abhishek Dey

Abhishek Dey has a background in electronic structure in inorganic chemistry. His research aims at emulating the reactivity of enzyme active sites in synthetic analogues using the geometric and electronic structure function relationships present in natural systems. His current area of interest includes multiproton and multi-electron transformations that are key for clean energy and environment and development of new analytical techniques for interrogation and intuition driven innovations in electrocatalysis. He is a Professor of Chemistry at the Indian Association for the Cultivation of Science (IACS) and an Associate Editor of ACS Catalysis.

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identifies a ferric peroxide (compound 0) intermediate in the peroxidic oxidation of neurotransmitters by heme-bound AB peptides relevant to the pathology of Alzheimer's disease (https://doi.org/10.1039/ D5DT00234F). Dev uses a combination of self-assembly and in situ Raman spectroscopy naturally-occurring hemes and their artificial analogues to illustrate the interplay between electron withdrawing groups and hydrophobicity in determining spin states and reduction potentials of heme active sites (https:// doi.org/10.1039/D5DT00028A).

Metal-based tools and therapies

Metal-based diagnostic tools and therapeutics are crucial in the detection and treatment of a variety of diseases. Nitric oxide, a key signalling molecule in biology, is the focus of a review by Cho and coworkers, who outline NO donors that can be photo-triggered to release NO on demand under physiological conditions (https://doi.org/10.1039/D4SC06820C).

Babak, Ang and co-workers review metalbased inducers of immunogenic cell death and their potential for advancing cancer immunotherapy (https://doi.org/ 10.1039/D4SC08495K). Zhang Rahman report that platinum complexes of piperidine-functionalized hydrazone inhibit EZH2-dependent tumorigenesis pancreatic ductal in adenocarcinoma, showing synergistic effects with PARP inhibitors (https:// doi.org/10.1039/D4DT01243G). Sasmal biotinylated Pt(IV)-SAHA presents a

conjugate for the treatment of cutaneous T-cell lymphoma, designed to enhance the of cisplatin (https://doi.org/ Hartinger 10.1039/D4DT01571A). describes biotin-functionalized hydroquinoline $Os(\pi)/Rh(\pi)/Ir(\pi)$ complexes, identifying a Rh complex with high anti-proliferative activity (https:// doi.org/10.1039/D4DT02296C). Gasser and Batista introduce two new phosphine-mercapto complexes with promising anti-cancer activity (https:// doi.org/10.1039/D4DT01191K). Liu, Wu and Chao report a cyclometalated Ir(III)tetrazine complex which can generate singlet oxygen in cells via two-photon excitation (https://doi.org/10.1039/ Rudd D4DT01665C). and Donnelly develop a theranostic strategy for breast cancer by conjugating either β^- or β^+



Mi Hee Lim

Dr Mi Hee Lim is the Director of the Center for MetalloNeuroProteinoChemistry in the Department of Chemistry at the Korea Advanced Institute of Science and Technology (KAIST). She earned her B.S. in Chemistry from Ewha Womans University in Seoul, Korea, in 1999, and her M.Sc. in 2001 under the mentorship of Professor Wonwoo Nam. In 2002, she began her Ph.D. at MIT under the supervision of Professor Stephen J. Lippard. Following her doctoral studies, she conducted postdoctoral research in the laboratory of Professor Jacqueline K. Barton at Caltech. In 2008, she launched her independent career as an Assistant Professor of Chemistry and Research Assistant Professor in the Life Sciences Institute at the University of Michigan, Ann Arbor. In 2013, she joined the Ulsan National Institute of Science and Technology (UNIST) in Ulsan, Korea, as a tenured Associate Professor. Since 2018, she has been a Professor in the Department of Chemistry at KAIST in Daejeon, Korea. Her research focuses on bioinorganic chemistry and chemical neuroscience, particularly on elucidating the roles of metal-involved biological networks in neurodegenerative diseases, such as Alzheimer's and Parkinson's, and on developing chemical tools, diagnostics, and therapeutics for these conditions. She serves as an Associate Editor for Dalton Transactions.



Serena DeBeer

Serena DeBeer is a Professor and Director at the Max Planck Institute for Chemical Energy Conversion in Mülheim an der Ruhr, Germany. She is also an Adjunct Professor in the Department of Chemistry and Chemical Biology at Cornell University, an honorary faculty member at both Ruhr University in Bochum and University of Duisburg Essen, and the group leader of the PINK Beamline at the Energy Materials In-Situ Laboratory at Helmholtz Zentrum in Berlin. She received her B.S. in Chemistry at Southwestern University in 1995 and her Ph.D. from Stanford University in 2002. From 2002–2009, she was a staff scientist at the Stanford Synchrotron Radiation Laboratory, before moving to her faculty position at Cornell. She is the recipient of a European Research Council Synergy Award (2019), the American Chemical Society Inorganic Chemistry Lectureship Award (2016), the Society of Biological Inorganic Chemistry Early Career Award (2015), a European Research Council Consolidator Award (2013), a Kavli Fellowship (2012), and an Alfred P. Sloan Research Fellowship (2011). Recently, she received the Seaborg Lectureship Award from UC Berkeley (2023), the R. J. P. Williams lectureship from Oxford (2022) and the Michael Lappert lectureship from the Royal Society of Chemistry (2024). She served as an Associate Editor for the Royal Society of Chemistry flagship journal Chemical Science from (2018–2024) and recently moved to the American Chemical Society as an Associate Editor for Journal of the American Chemical Society (2024–

present). Research in the DeBeer group is focused on the development and application of advanced X-ray spectroscopic tools for understanding key mechanisms in biological and chemical catalysis.

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emitting isotopes, like ⁶⁷Cu or ⁶⁴Cu, to HER2-targeted sarcophaginetrastuzumab construct (https://doi.org/ 10.1039/D4SC06969B). For imaging applications, Wilson and co-workers report two pyridine-containing chelators that demonstrate excellent 111 In binding and delivery in a mouse model (https:// doi.org/10.1039/D4DT02146K). Finally, Codd expands the repertoire of metalbinding ligands by designing multimeric linear and macrocyclic hydroxamic acid chelators, which were screened against Ga(III) or Zr(IV) (https://doi.org/10.1039/ D4SC04888A).

Biomimetic and bioinspired chemistry

Biomimetic and bio-inspired chemistry is another pillar of bioinorganic chemistry, where researchers strive to replicate the elegant and powerful chemistry of enzymatic active sites using smaller analogues. These analogues can be entirely artificial, as illustrated by Yoo, Choi and Lee's review of nickel-based models of NiCODH (https:// doi.org/10.1039/D4SC06957A). Kojima and co-workers develop structurally distinct molecules inspired by CODH electrochemically reduce CO2 to CO (https://doi.org/10.1039/D4DT02922D). Bo, Gil-Sepulcre, Llobet and Shalom report the heterogenization of a molecular ruthenium-based catalyst onto a polymeric carbon nitride photoanode, resulting in a highly efficient water oxidation catalyst (https://doi.org/10.1039/ Alternatively, naturally-D4SC04678A). occurring peptides can be harnessed for

novel reactivity, as shown by Bren and coworkers, who use a cobalt porphyrin minienzyme to reduce CO2 (https://doi.org/ 10.1039/D4SC07026G). Zhang, Chen and Zhang report the oxidation of aromatic rings to phenols using H2O2 and a binuclear copper catalyst with an asymmetric ligand that mimics the reactivity of tyrosinases (https://doi.org/ 10.1039/D4DT02872D). Morimoto, Itoh and co-workers explore a series of copper complexes that activate small molecules, such as NO, CO and O2, finding that complexes with more positive reduction potentials preferentially bind NO over O2 and CO, which emphasizes the importance of ligand design in tuning (https://doi.org/10.1039/ selectivity D4DT03001J). Jarjayes, Thomas, Storr and co-workers resonate with this principle in their use of a tetradentate bis-carbene bisphenolate ligand to stabilize unusual metal nitrides, which undergo M-C reactions (https://doi.org/ insertion 10.1039/D4DT01765J). The ligand's redox activity aids in lowering the transitionstate barrier. Ligand redox chemistry also plays a major role in nickel complexes Ivanović-Burmazović, reported by Goldsmith and co-workers, where a pendant quinol group in the outer coordination sphere enables a nonpeptide complex to exhibit promising (https://doi.org/10.1039/ activity D4DT03331K). Protein environments also critically influence active site reactivity. Follmer, Borovik and co-workers use a biotin-streptavidin platform to mimic the active sites and reactivity of natural

copper metalloenzymes, demonstrating

aromatic residues within the secondary coordination sphere, designed to oxidize substrates with H2O2, may instead undergo self-oxidation, suggesting a potential deactivation pathway in natural copper enzymes (https://doi.org/ 10.1039/D4SC06667G). The role of the secondary coordination sphere is further examined by Chen, Rath and co-workers, who use paramagnetic NMR spectroscopy to study substrate binding in synthetic iron porphyrins (https://doi.org/10.1039/ D4SC05432F). Berben and co-workers report that including an amine group in the secondary sphere enhances both the selectivity and rate of catalytic hydride transfer reactions. The amine group stabilizes the metal hydride intermediate via hydrogen bonding, thereby preventing undesired hydride transfer to CO2 and avoiding formate production (https:// doi.org/10.1039/D4SC07359B). Similarly. Kovacs shows that hydrogen bonding slows O2 binding in a thiolate-bound nonheme iron complex, offering vital insights into how electronic structure controls function in enzymes, such as CDO and (https://doi.org/10.1039/ **IPNS** D4SC02787F).

As bioinorganic chemistry continues to grow in scope, more and more researchers are joining in with new expertise to address unanswered questions that still perplex us. New techniques under development herald the promising future of this community. We look forward to these with excitement. We enjoyed editing this spotlight collection and we hope that the readers enjoy reading these articles too.