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# Editorial overview: Emergent lessons from the elements of life

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Kyle M. Lancaster was born in sunny Fullerton, CA (USA). Following undergraduate study majoring in molecular biology at Pomona College (Claremont, CA), Kyle found his love for metalloproteins and spectroscopy at Caltech (Pasadena, CA) where he carried out his dissertation research with Harry B. Gray. He then traded the sunshine of Southern California for the pastoral beauty of 'gorges' Ithaca, NY where he carried out postdoctoral research with Serena DeBeer at Cornell University. Now an Associate Professor in the Cornell Department of Chemistry and Chemical Biology, Kyle applies the 'bioinorganic toolbox' to study synthetic base metal catalysis and biological ammonia oxidation, among other topics.

Biogeochemical cycles have furnished fertile grounds for inquiry to bioinorganic chemists since the advent of our field. The chemical reactions underlying the interconversions of biologically relevant forms of carbon, nitrogen, sulfur, and phosphorus continue to be actively explored, and the insights gleaned from decades of study have impacted diverse disciplines including energy research and chemical synthesis. Discovery of new bioinorganic chemistry continues apace, spurred by researchers in complementary fields such as microbiology actively filling 'black boxes' in nutrient fluxes through identification of new metabolic 'lifestyles' via environmental sampling, modern cell culturing/enrichment methodologies, and emergent omics approaches. This section of *Current Opinion in Chemical Biology* has been curated to showcase new developments in biochemistry germane to the C, N, S, and P cycles. I have purposefully expanded the scope of contributors beyond card-carrying bioinorganic chemists, inviting microbiologists, a plant biologist, and a geochemist to guide readers toward exciting new avenues of inquiry and to introduce alternative perspectives on topics in our vibrant field.

This section features two articles pertaining to reactions within the carbon cycle, although perhaps their more salient points concern perspectives on the roles of metals in biology. [Huub op den Camp and Nunzia Picone](#) summarize the recent exciting expansion of the 'bioinorganic periodic table' to include early lanthanides that are now recognized as essential micronutrients for the growth of some methanotrophic microbes. Since this discovery, bioinorganic chemists of both 'synthetic' and 'biochemical' stripes have seized upon the opportunity to explore new model complexes [1] and to explore design criteria for lanthanide-binding metalloproteins [2]. [Arnold Bloom's](#) contribution focuses on how metal substitution influences reactivity. Swapping metals in active sites *in vitro* has historically afforded tremendous insight into metalloprotein electronic/geometric structure and function—Bloom's perspective considers such substitutions *in vivo* as a means to tune reaction outcomes. His key focus is on whether manganese versus magnesium uptake by proteins such as Rubisco is a means by which Nature allows photorespiration—considered a 'waste' pathway in C<sub>3</sub> carbon fixation—to function as a vital source of reducing equivalents for nitrate assimilation [3].

Two articles concern biological ammonia oxidation—in one, [Lisa Stein](#) summarizes the state of the field of aerobic ammonia oxidation (nitrification) by both bacteria and archaea. While recent progress has been made in understanding the mechanisms of some nitrification enzymes, many gaps persist [4]. The enzyme that initiates nitrification—ammonia

monooxygenase (AMO)—has never been purified in an active form. AMO and related proteins such as particulate methane monooxygenase present major challenges to bioinorganic chemists, but their ability to selectively hydroxylate some of the strongest C–H and N–H bonds makes them vital targets of inquiry. Stein also highlights key absences in the nitrification enzymological catalogue—namely, it is not understood how archaea oxidize hydroxylamine, nor is it understood how nitrifying bacteria and archaea oxidize nitric oxide to nitrite. Thus, nitrification remains a major ‘frontier’ for our community.

The article from [Laura van Niftrik and Stijn Peeters](#) concerns *anaerobic* ammonia oxidation (anammox). This metabolism offers microbes another alternative to a carbon-fueled lifestyle, but the underlying metallobiochemistry is largely unknown. For example, the unique hydrazine-forming reaction catalyzed by hydrazine synthase remains mysterious due to the absence of a purification protocol that affords active enzyme. Biological N–N bond formation is emerging as a hot area in natural product biosynthesis [5,6] and the potential roles of nitric oxide in this area are highlighted in [Jonathan Caranto’s](#) contribution to this issue. Elucidating the mechanism by which the prototypical N–N bond of N<sub>2</sub>H<sub>4</sub> is formed by anammox bacteria is certain to inspire new synthetic avenues to this important functional group and will add to the recognized natural toolbox for biosynthesis of important pharmaceutical targets.

[EJ Crane’s](#) contribution highlights key enzymatic players in the biogeochemical sulfur cycle. However, rather than elaborating on advances in mechanistic understanding, this article offers a challenge to the community: how do we assemble metabolic/bioenergetic networks when many of the known enzyme players are capable of reversible operation? How do we identify the directionality of an enzyme from the gene, and how are reaction outcomes defined by the cell and its environment? Meanwhile, [Michael Pluth and Nathanael Lau](#) survey recent advances concerning the roles of reactive sulfur species, with emphasis on new chemical tools available to probe biological sulfur signaling and reactivity.

Finally, this section features an article by [Matthew Pasek](#) discussing hypotheses concerning the role of reduced intermediates such as phosphonate in the biogeochemical phosphorus cycle. The phosphorus cycle is rarely discussed in bioinorganic chemistry. It is unique in its lack of gaseous/volatile intermediates, and the incorporation of phosphorus into biomolecules remains enigmatic given the relatively inert nature of phosphate. Pasek points out key observations that have been made that suggest life may be able to form and employ species as reduced as phosphine (PH<sub>3</sub>). While some chemical progress has been made in terms of recovering phosphorus and using inorganic phosphate as feedstock [7], additional biochemical inquiry is merited not only to solve key origin of life questions, but also to inspire novel phosphorus management strategies.

In summary, this section presents perspectives on the state of the art concerning cycles of the ‘elements of life’, while also offering viewpoints on broader challenges in biochemical research. Many open-ended questions are scattered throughout this section, affording ample directions to ensure the vitality of the bioinorganic discipline.

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