Nature routinely uses metalloenzyme catalysts comprised of Earth-abundant base metals like iron, manganese, cobalt, and copper to perform remarkable chemical transformations, many that have no parallel in chemical synthesis. The economic and environmental advantages of developing such base-metal catalysts for chemical synthesis are clear: iron, manganese, nickel, copper are significantly more abundant and less toxic than noble metals like rhodium, iridium, palladium (for example, manganese and iron are six orders of magnitude more abundant than rhodium). The lack of long-term sustainability and the toxicity of many noble metals has propelled important research in developing base-metal catalysts that may replace them by paralleling their reactivity scope. Much of the catalyst design is focused on developing ligands and reaction conditions to suppress the one-electron reaction pathways common to base-metals in favor of two-electron pathways for bond breaking and making processes. These efforts and others have resulted in remarkable reactions such as iron- and cobalt-catalyzed hydrogenations and cross-couplings.

A complementary approach taken by our group is to embrace and unleash the potential for base metals to operate via distinct mechanisms and achieve reactivity and selectivity that has not been accessed with precious metals. In 2007, 2010, and 2013 our group reported two iron catalysts Fe(PDP) and Fe(CF₃PDP) that are capable of preparative, site-selective C–H hydroxylations of aliphatic methylene (2°) and tertiary (3°) C–H bonds without directing groups. Aliphatic C–H hydroxylations are well-precedented with iron oxidation catalysts found in nature, however, there are no analogous reactions known with noble metal catalysts. In 2015, we reported a manganese catalyst Mn(t-BuPc) that is capable of effecting intramolecular C–H aminations of every type of C(sp³)–H bond, including very strong primary aliphatic bonds, while leaving more reactive π-functionality (that is olefins and alkynes) untouched.

This combination of high reactivity and high selectivity is unprecedented with the noble metal rhodium catalysts canonically used to promote such C–H aminations. Both of these reactions are thought to occur via a biomimetic mechanism involving a high-valent metal oxidant (such as a metal oxo or nitrene) where both the C–H abstraction step and the functionalization steps proceed via single electron pathways that are closely regulated at the metal center. This enables stereospecificity and tunable catalyst-controlled selectivity based on subtle electronic, steric and stereoelectronic interactions between the catalysts and substrates, without the requirement for a protein binding pocket.

A biomimetic mechanism is certainly not requisite for achieving unique and highly selective processes via base-metal catalysis. Reactions are emerging that proceed via organometallic intermediates (that is carbon–metal intermediates) such as copper-catalyzed olefin hydroamination reactions and asymmetric nickel-catalyzed cross-couplings. Such reactions proceed with scope and stereoselectivities that are unprecedented for noble metal catalysts to furnish valuable optically enriched products. In asymmetric nickel-catalyzed cross-couplings, it is by virtue of the single-electron reaction mechanism for bond breaking in racemic electrophiles (ablating stereochemistry) that catalyst-controlled asymmetric induction is achieved.
Base metals have been relatively unexplored in modern catalysis, primarily because of the widely held notion that they are “wild ones”, whose reactivity must be “tamed” in order to achieve preparatively useful selectivities. With the emergence of base metal-catalyzed reactions that expand access to reactivity and selectivity not normally possible with noble metal catalysis, this perception will undoubtedly be supplanted by the recognition that there is vast opportunity in exploring and embracing the wild side.

References