The Fourth-Annual Christopher S. Foote Lecture
with Professor Joan S. Valentine

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“Oxygen, Manganese, and Early Life on Earth”

Abstract. Superoxide, \( \text{O}_2^- \), is formed in all living organisms that come in contact with air and, depending upon its biological context, it may act as a signaling agent, a toxic species, or a harmless intermediate that decomposes spontaneously. Although superoxide has long been an important factor in evolution, it was not so when life first emerged on Earth at least 3.5 billion years ago. At that time, the early biosphere was highly reducing and lacking in any significant concentrations of dioxygen (\( \text{O}_2 \)), very different from what it is today. Instead, the history of biological \( \text{O}_2 \) probably commences somewhere around 2.4 billion years ago, when the biosphere started to experience what has been termed the Great Oxidation Event, a transformation driven by the increase in \( \text{O}_2 \) levels, formed by cyanobacteria as a product of oxygenic photosynthesis. The rise of \( \text{O}_2 \) on Earth led to the formation of the so-called reactive oxygen species (ROS), e.g., superoxide, hydrogen peroxide, and hydroxyl radical, and to a need for antioxidant enzymes and other antioxidant systems to protect against the growing levels of oxidative damage to living systems.

The first superoxide dismutase (SOD) enzyme to be identified was originally isolated in 1939 on the basis of its blue-green color and named hemocuprein, a copper protein of unknown function. Three decades later, Irwin Fridovich published his historic discovery of the SOD activity of this protein, and he proposed that this antioxidant activity represented its biological function.

Now we know that SOD enzymes evolved independently at least three times and that each contains redox-active metal ions at its active sites. The importance of the SOD enzymes is indicated by their near ubiquitous distribution in the natural world. Over the years since they were each discovered, we have come to appreciate that each of the SOD metalloenzymes has been designed exquisitely by evolution so that its active site metal ion has the proper degree of reactivity with superoxide to enable it to be an excellent catalyst of superoxide disproportionation.

But there remain several puzzles in the story of the superoxide dismutases, particularly in the case where the redox-active metal is manganese. The first of these is to explain the surprising observation that simple inorganic manganous ion, \( \text{Mn}^{2+} \), without any protein at all, can functionally replace SOD enzymes in living cells. This phenomenon seems to contradict the above statement that a highly evolved metalloprotein active site is required for high SOD activity. These and other puzzles related to manganese and superoxide, which have been the subject of recent research in our laboratory, will be described, as well as our new hypothesis that simple complexes of \( \text{Mn}^{2+} \) were the primordial antioxidants and that they protected and preserved life in the early oceans during the Great Oxidation Event.

Thursday, February 20, 2014
4:00 PM Reception – Weinstein Café Commons, 3037 Young Hall
5:00 PM Foote Lecture – CS24 Young Hall

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