Interdisciplinary methodologies for high precision isotopic characterization of biological processes

Dr Fiona Larner[1,2], Professor Alex N Halliday[1]

1. Department of Earth Sciences, University of Oxford
2. Department of Oncology, Weatherall Institute of Molecular Medicine, University of Oxford

Abstract

Trace metals are essential to biological function, and the fine line between metal deficiency and metal toxicity in an organism must be walked to ensure a healthy status is maintained. Trace metal isotopic compositions have been a useful tool to investigate metal pathways in geochemical applications and provide a way to interrogate the behavior of metals in biological systems.

Biological interactions have been shown to induce fractionation of metal isotopes between different reservoirs in healthy subjects, as well as produce changes in the isotopic compositions of these reservoirs due to disease. High precision isotopic composition analyses continue to be employed in clinical studies and animal models to both understand the processes responsible for the observed fractionation and how this fractionation may be used to provide mechanistic and diagnostic probes.

The fundamental interactions behind such isotopic signatures are, however, largely unknown. Laboratory-based studies to understand the basic metal-protein interactions, and what governs isotopic selectivity in biological scenarios, are needed. However, the resolution required to distinguish natural variations in metal isotopic signatures is not naturally compatible with many techniques originating in biology or biochemistry, due to high background metal concentrations and procedures that can induce experimental fractionation. Here we present a range of approaches to address the lack of fundamental metal-protein isotopic data, the major pitfalls in these methodologies, ways to overcome them, and the variety of data their application can yield.