Goldschmidt 2026 Abstract
https://doi.org/10.46427/gold2026.37174

From qualitative biomarkers to predictive clinical tools: the need for Systemic Homeostasis Models in Isotope Metallomics

THEO TACAIL AND FRANÇOIS L.H. TISSOT
California Institute of Technology

Stable isotope measurements of bio-essential metals now routinely achieve sub-permil precision, creating unprecedented opportunities to interrogate elemental cycling across environmental and biological systems. In human physiology, these advances have catalyzed the emergence of isotope metallomics - the use of naturally occurring metal isotope variations to probe metabolism, exposure, and disease [1]. Yet a structural gap persists between analytical performance and interpretive rigor. High-precision datasets are frequently interpreted within simplified compartmental frameworks that inadequately represent organism-scale regulation, thereby constraining mechanistic resolution and limiting translational impact.

Here, we advocate for a transition from descriptive tracer applications toward quantitatively constrained, physiology-explicit modeling. Using calcium (Ca) as a case study, we present a systemic isotope mass-balance framework that integrates the principal regulated fluxes of Ca homeostasis, including intestinal absorption, renal reabsorption and excretion, endogenous secretion, and skeletal exchange. Rather than attributing isotopic variability to a single compartment, this approach formalizes the dynamic coupling among organs and feedback mechanisms that govern both elemental and isotopic steady states and disequilibria.

Such a model enables rigorous exploration of how isotopic signatures emerge from homeostatic cycles, how inter-individual baseline variability reflects differences in physiological set points, and how perturbations to specific pathophysiological processes propagate through measurable reservoirs such as plasma or urine. Critically, it also provides a framework to define and optimize isotopically informed quantitative metrics derived from models (rather than empirical correlation), and to clarify how these metrics can be constrained using non-isotopic clinical parameters.

Although illustrated here with Ca, the principles are broadly applicable to other bioessential metals. We argue that the next phase of isotope metallomics will depend on integrating high-precision analytics with systemic numerical models and on sustained dialogue with clinicians and experimental physiologists. Embedding isotopic measurements within mechanistically explicit frameworks will allow the field to progress from qualitative biomarker discovery toward predictive, quantitatively interpretable tools that bridge geochemical processes and human health.

[1] Albarède F. 2015 Metal stable isotopes in the human Body: A tribute of geochemistry to medicine. *Elements* **11**, 265–269. (doi:10.2113/gselements.11.4.265)