Goldschmidt 2025 Abstract
https://doi.org/10.7185/gold2025.31790

Systemic modelling of calcium isotope dyshomeostasis in human

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

Calcium (Ca) isotopes have emerged as valuable tracers of Ca metabolism, with potential applications in diagnosing mineral imbalances and pathological bone loss. The early recognition that bone is enriched in lighter Ca isotopes led to the development of isotopic box-models aimed at quantifying bone mineral balance using $\delta^{44/42}$Ca values in blood plasma or urine [e.g., 1–3]. Existing Ca homeostasis isotopic models primarily focus on bone mineral balance, particularly bone loss, while oversimplifying key homeostatic fluxes and fractionation processes. These limitations restrict the ability to model the interactions among homeostasis effectors at the scale of the whole organism, thereby limiting the accurate interpretation, prediction, and quantification of Ca dyshomeostasis beyond bone loss.

Here, we model the isotopic response of the organism to major dyshomeostasis affecting key physiological functions, including bone metabolism, renal function, and absorption, in a simulated population of individuals with variable nutritional and physiological baselines.

To achieve this, we build on a systemic Ca homeostasis isotopic model (Tacail et al., in prep.), which incorporates all major regulated and unregulated effectors of Ca homeostasis, including bone remodeling, intestinal absorption, endogenous losses, renal excretion, and integumentary losses. Simulations were conducted using the isobxr R package [4], enabling exploration of parameter space under both steady-state and disequilibrium conditions.

Through systematic parameter exploration and model validation, we investigate the isotopic response of the organism to various dysregulations (e.g., bone loss, bone excess, ectopic mineralization, renal disorders) in relation to baseline nutritional and physiological factors. This approach allows us to assess the predictive performance of Ca isotopes across multiple reservoirs as quantitative biomarkers of dysregulation. By exploring clinical strategies—such as cross-sectional and self-referencing methods—we discuss how to optimize isotopic techniques for diagnosing Ca-related disorders, ultimately providing a more comprehensive framework for understanding Ca homeostasis and advancing the development of isotopic biomarkers.

[1] Skulan & DePaolo (1999) *PNAS* **96**, 13709–13713
[2] Eisenhauer et al. (2019) *Bone Rep* **10**, 100200
[3] Shroff et al. (2021) *Adults. J Bone Miner Res* **36**:133–42
[4] Tacail (2021) **isobxr**, *CRAN*, DOI: 10.32614/CRAN.package.isobxr