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A pharmacokinetic model of lead absorption and calcium competitive dynamics

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Lead is a naturally-occurring element. It has been known to man for a long time, and it is one of the longest established poisons. The current consensus is that no level of lead exposure should be deemed "safe." New evidence regarding the blood levels at which morbidities occur has prompted the CDC to reduce the screening guideline of 10 μg/dl to 2 μg/dl. Measurable cognitive decline (reduced IQ, academic deficits) have been found to occur at levels below 10mg/dl.

Knowledge of lead pharmacology allows us to better understand its absorption and metabolization, mechanisms that produce its medical consequences. Based upon an original and very simplified compartmental model of Rabinowitz (1973) with only three major compartments (blood, bone and soft tissue), extensive biophysical models sprouted over the following two decades. However, none of these models have been specifically designed to use new knowledge of lead molecular dynamics to understand its deleterious effects on the brain. We build and analyze a compartmental model of lead pharmacokinetics, focused specifically on addressing neurotoxicity. We use traditional phase space methods, parameter sensitivity analysis and bifurcation theory to study the transitions in the system's behavior in response to various physiological parameters.

We conclude that modeling the complex interaction of lead and calcium along their dynamic trajectory may successfully explain counter-intuitive effects on systemic function and neural behavior which could not be addressed by existing linear models. Our results encourage further efforts towards using nonlinear phenomenology in conjunction with empirically driven system parameters, to obtain a biophysical model able to provide clinical assessments and predictions.