Uncertain Biokinetic Parameter Considerations in Stochastic Modeling of the Human Respiratory Tract System in Defense and Consequence Management Applications: Computational and mathematical tools leveraged for an expanded stochastic analysis of biokinetic model parameters

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Purpose: Dose estimation and reconstruction for internalized radionuclides continues to remain a challenge due to inability to directly measure radionuclide body burden from internalized uptakes. Therefore, estimation of radiation dose exposure relies heavily on mathematical models, notably biokinetic models, to determine biodistribution of radionuclides as a function of time post-exposure. For inhaled radionuclides, reference models have been developed, called the human respiratory tract model (HRTM), which have evolved from deterministic quantities given by the International Commission on Radiological Protection in Publication 66 and updated in Publication 130.

For a complete estimation of dose to the lungs, a full description of HRTM, however, deals with several blocks of components such as particle deposition in airways, radioactive decay, systemic biokinetic model, and dose quantification. Where the ICRP employs reference models in the development of biokinetic and dosimetric quantities in the development of dose coefficients, expanded stochastic models are required to encompass the metabolic breadth for dose estimation and reconstruction of inhaled radionuclides. Associated uncertainty and sensitivity analyses are further essential to defense and consequence management applications in which early-phase decisions regarding site-boundary dose estimates and administration of medical countermeasures must be made.

The aim of this works is however to establish the fundamental base-tools required for further expanded stochastic analysis for the updated ICRP HRTM (ICRP 130). Biokinetic model is a component of internal dose estimation methodology which employs mathematical formalisms to model the intake, uptake, retention, and clearance (excretion) of incorporated radionuclide/materials in a biological system. As such, compartmental analysis is employed whereby the biological system under investigation is discretized into several components of organs/tissues to reflect a system of ordinary differential equations (ODEs). The ODEs are then solved using appropriate methods to estimate the radionuclide burden in the body. Several computational toolkits have been developed for solving biokinetic models. However, most of these toolkits are based on routine methodologies and are generic. Updates and customization of these existing codes to reflect realistic exposure and source terms is not trivial and thus lacking the capability for dynamic processing. For an expanded stochastic analysis, python was chosen for its ease and simplicity in serving as a good platform for interoperation of disparate codes, modules, or tools.

Method: In the early phase of this study, efforts were focused on implementation of a robust computational method, in python, for handling the extremely stiff system of ODEs posed by biokinetic models. Several ODE solvers and solving methods, both numerical and algebraic, were investigated subjected to solving sample biokinetics for inhaled fast clearing (type F) ^{131}I (Figure 1). Fast clearing ^{131}I was chosen to test the tolerance level of the solving methods for an extremely stiff problem. The assessment criterion was based on well converged solution methods in a reasonably short period of computational time. Biokinetic solutions for each solver/solving method were compared, and the methods with most converged solutions with less computational time were chosen for which a dose coefficient code, named REDCAL, is constructed.

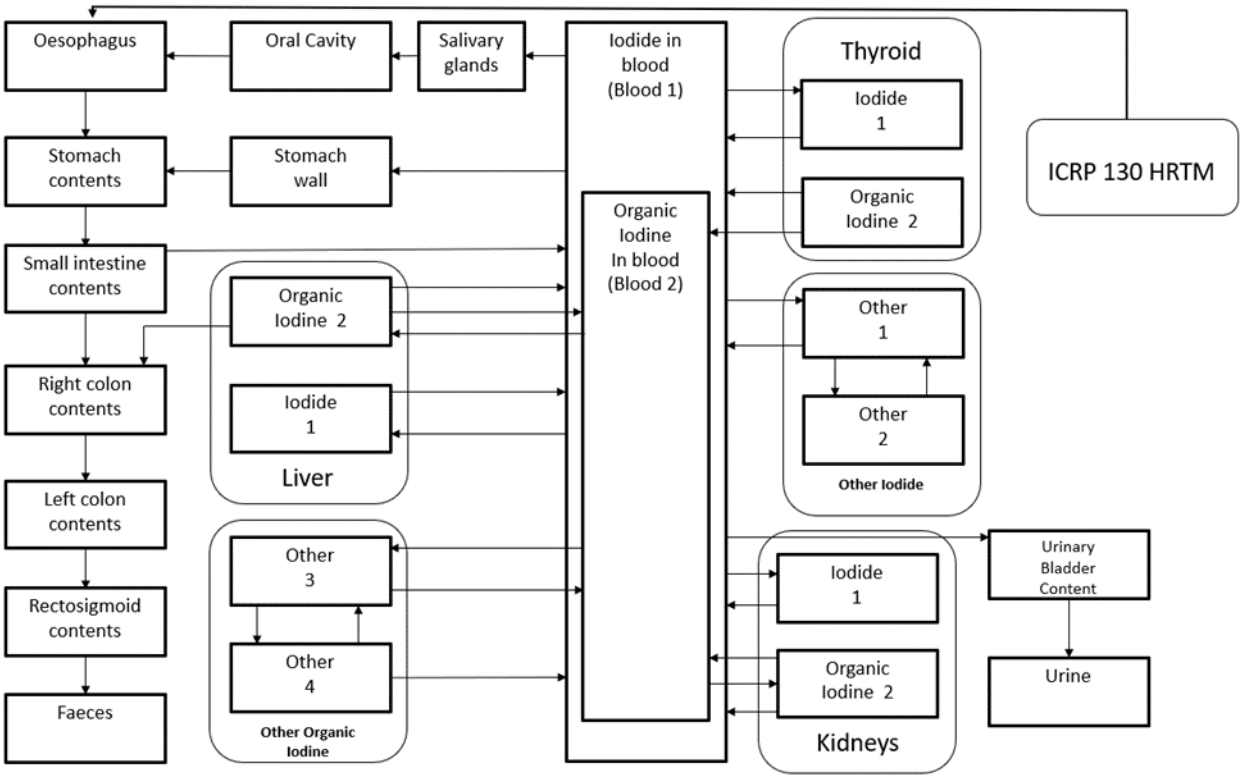

Figure 1: Coupled Inhalation Compartmental Model for iodine (ICRP, 2017).

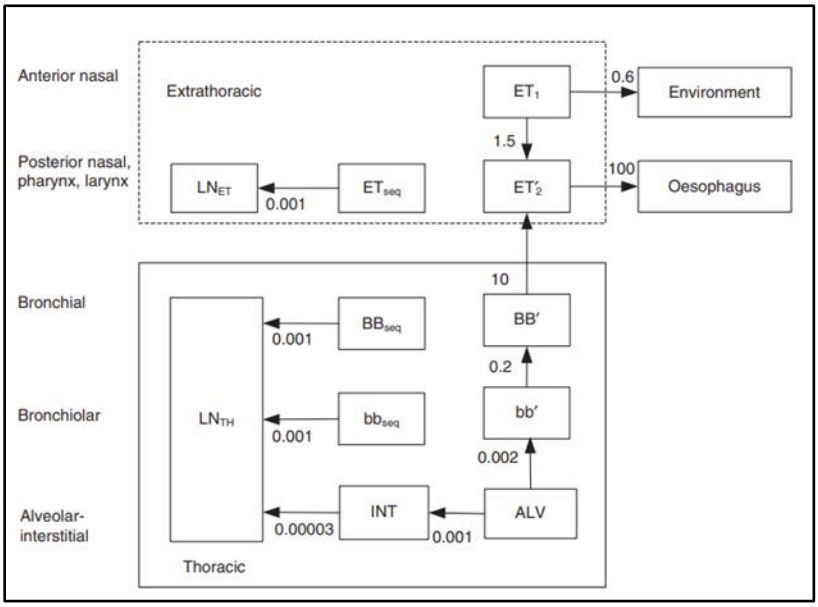

Figure 2: The ICRP revised Human Respiratory Tract compartment model representing time-dependent particle transport of insoluble material (ICRP 130 HRTM) (ICRP, 2015). Arrows in the figure illustrate the mechanical clearance from one compartment to the other alongside values depicting reference transfer coefficients in unit of d^{-1}

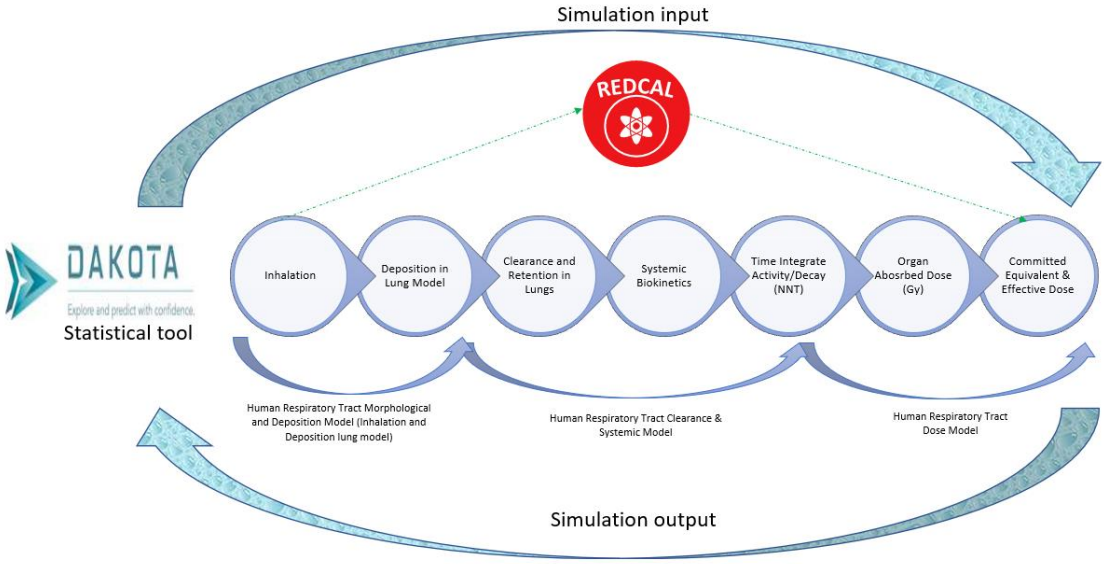

Figure 3: Dose coefficient methodology coupled to statistical sampling module.

Results: Python-based ODE implicit solver from a standard initial value problem evaluation library resulted in converged solutions with very small tolerance level for an optimum local error control (Figure 5). Figure 4 however depicts the divergence observed for the utilization of an explicit ODE solver. Since most internal dose codes uses Fortran based algorithms, the solution obtained was then compared with that obtained with a well-known FORTRAN ODE solver for the same problem set which resulted in a relative difference of 0.26%. Stiff ODE problems are known to be well evaluated using eigen/algebraic methods as opposed to most numerical approaches. To this effect, comparison of the numerical solutions obtained with the implicit method and matrix exponentiation method based on Padé approximation (Figure 6) were conducted which depicted 0% relative difference.

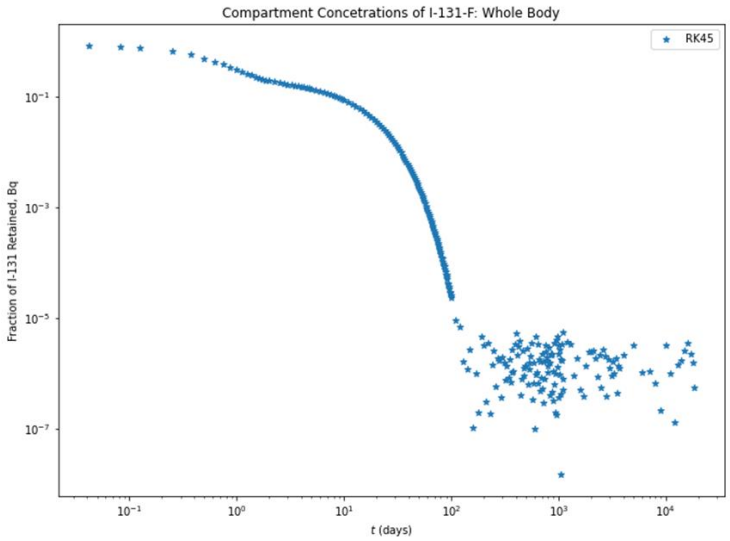

Figure 4: Whole body retention for ^{131}I Type F. Retention solution obtained with python-based Explicit Runge-Kutta method of order 5(4) – RK45. Computationally expensive for the biokinetic problem set and resulted in significantly unstable solution.

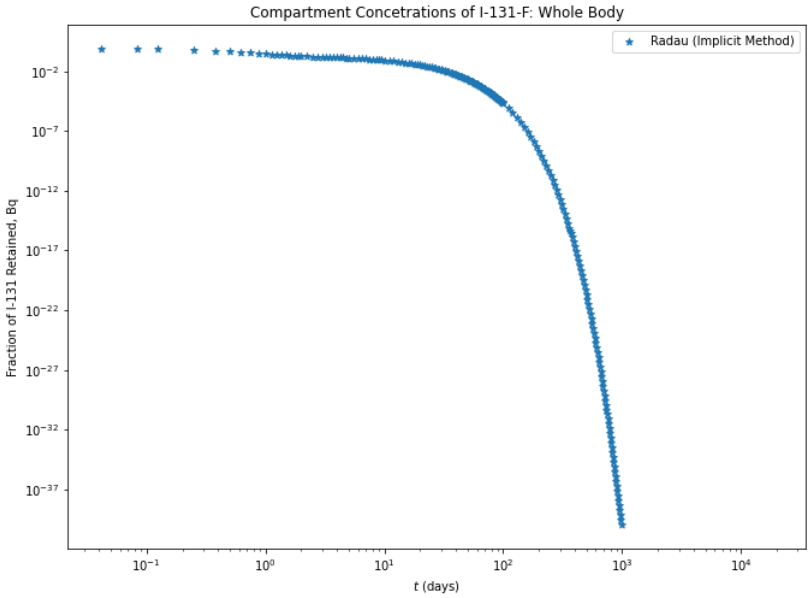

Figure 5: Whole body retention for ^{131}I Type F. Retention solution obtained with python-base Implicit Runge-Kutta method of the Radau IIA family of order 5. Fast calculations for the biokinetic problem set with converged and stable solution – Convergence observed for explicitly controlling the step size for Radau as well as having control over the computation local error.

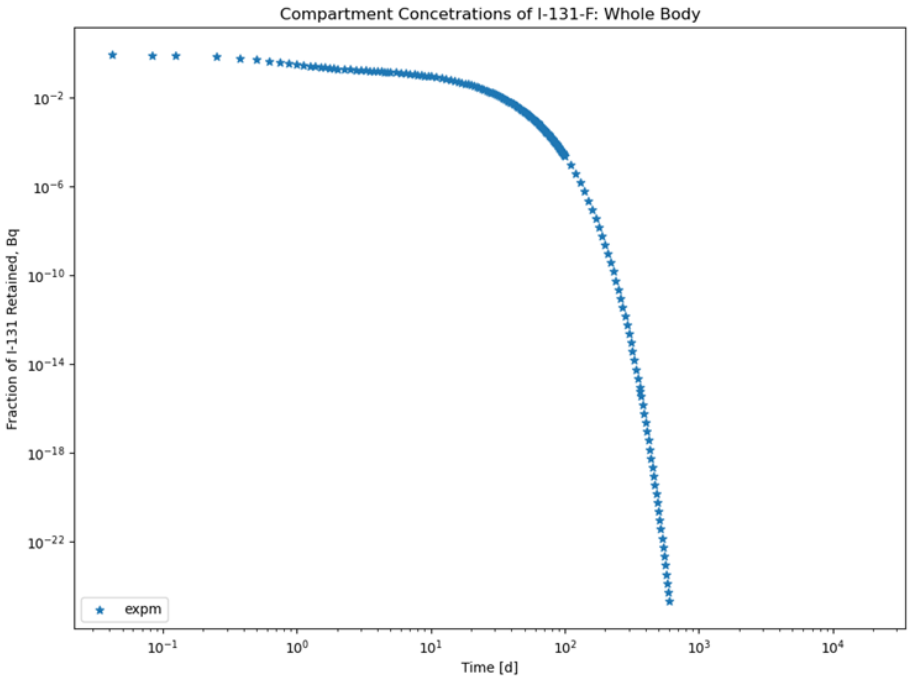

Figure 6: Whole body retention computed using python-based matrix exponential method for ^{131}I Type F. The result depicts stable and converged solutions for extremely stiff system with fast calculation time of approximately 0.4 seconds.

Conclusion: Results obtained depicted that the well-optimized implicit ODE solver and linear algebraic method in python well-converged and robust in solving any extremely stiff system of biokinetic models. The base for further computational reconstruction for stochastic analysis has therefore been laid. Future work is aimed at obtaining fully functioning dose coefficient code allowing for uncertainty analysis, which account for variabilities in individualized monitoring.

Relevance to CIRMS: Expansion of dosimetric estimation to consider variabilities in biokinetic and dosimetry model parameters enhances the delivery of medical countermeasures and effective radiation protection guidelines in consequence management and defense application spaces of interest to the CIRMS community. Drawing upon the community's activities in measurement standardization, such efforts are synergistic in updating existing dosimetry standards, as measurement standards, notably precision and limitations/capabilities, are essential to the development and validation of such models for source term-based dose reconstruction. The first author aims to become an industrious health physicist. He is currently being train as a nuclear and radiological engineer and working with a vibrant team in the Radiological Engineering, Detection, and Dosimetry (RED^2) Laboratory at Georgia Tech.

References:

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