



PROBABILISTIC MODELING OF THE RENAL STONE FORMATION MODULE

*Integrated Medical Model
Exploration Medicine Capabilities Project*

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Outline



- Overview of IMM
- Renal Stone Risk Module
- Probabilistic Wrapper – Front End
- Biochemistry Model
- Probabilistic Wrapper – Back End



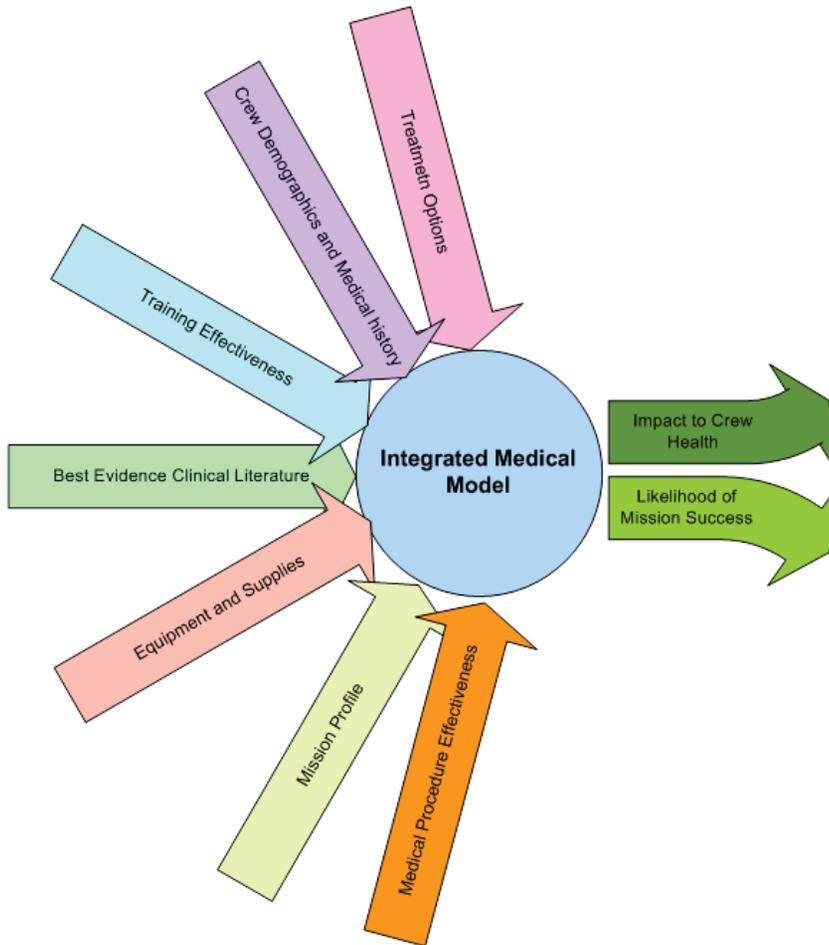
Integrated Medical Model (IMM)

- IMM is a probabilistic tool – quantifies the probability and consequences of medical risks
- Identifies medical resources necessary to optimize health and mission success

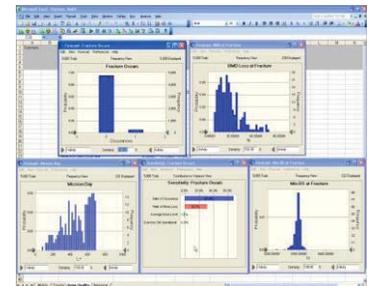
Potential Medical Condition



Evaluate with IMM



Likelihood of occurrence, probable severity of occurrence, and optimization of treatment and resources

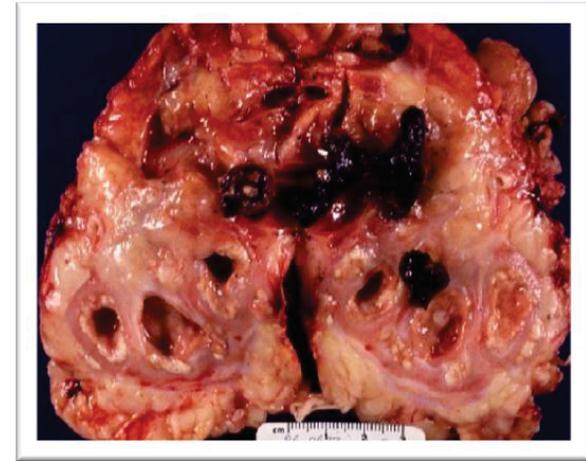




Renal Stone Risk Module



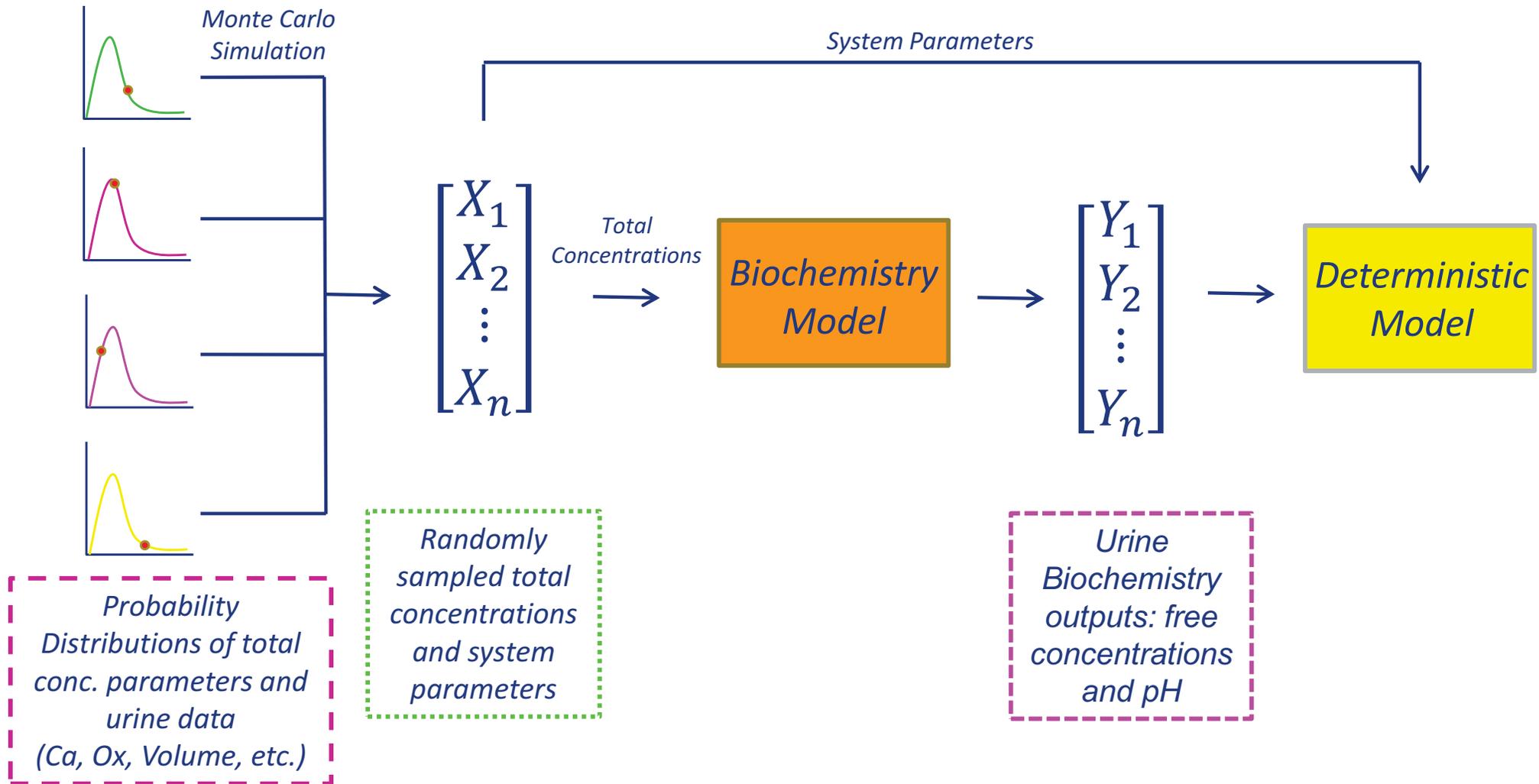
- Astronaut urine samples have exhibited characteristics associated with renal stone formation, demonstrating an increased risk that clinically significant renal stones could form in flight
- External module to IMM
 - Adds higher fidelity to model where little data is available
- Deterministic Model (*Kassemi et. al*)
 - integrates physics and physiology into formation of renal stone based on probabilistic input
- Probabilistic Wrapper – feeds needed information into deterministic model and transforms output into a useful distribution of risk of renal stones





Probabilistic Wrapper: Front-End

Through Monte Carlo methods, randomly samples array of probability distributions to compile a set of random inputs into biochemistry and deterministic model





Monte Carlo Sampling



- Lognormal probability distributions formed from \bar{x} and σ and number of desired MC samples (N) in MATLAB
 - Truncated to the 95th CI
 - Example:

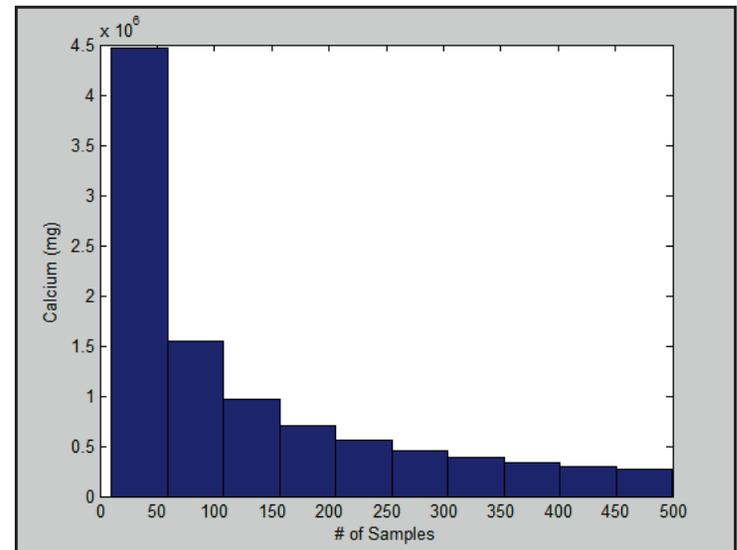
$$P_{Ca} = \begin{bmatrix} X_{Ca_1} \\ X_{Ca_2} \\ \vdots \\ X_{Ca_N} \end{bmatrix}$$

- Parameters randomly sampled and placed into matrix
- Parameter matrix is divided by randomly sampled volume to create total concentrations (mol/L)

$$[M] = \frac{[P_{Ca} \quad P_{Ox} \quad \dots \quad P_{Creat}]}{V}$$

Parameters:

- Calcium
- Oxalate
- Uric Acid
- Citrate
- Sulfate
- Phosphate
- Magnesium
- Sodium
- Potassium
- Ammonium
- Creatinine (Creatine)



Example histogram of Calcium (truncated)



Biochemistry Model



- JESS Biochemistry model – compiles 100+ applicable urine chemistry reactions and computes outputs based on system parameters and thermodynamics
- Transforms total concentration matrix, M , via system of equations into free ion concentrations (c_i) based on urine chemistry reactions
- Free ion must be converted to activity (a_i) for deterministic model:

$$a_i = \frac{\gamma_i c_i}{c^\ominus}, \gamma_i = \text{species activity coefficient}$$

$c^\ominus = \text{standard concentration}$



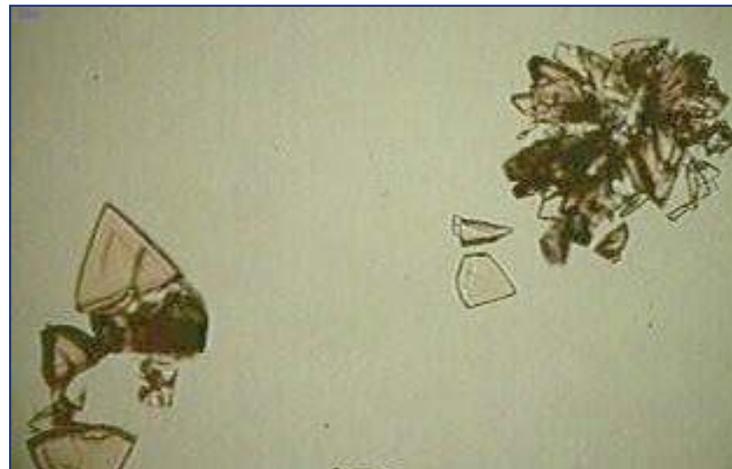


Biochemistry Model

- Relative Supersaturation calcium oxalate (RS_{CaOx})
 - More of the dissolved material than could be dissolved by the solvent
 - RS: Metric that represents the ability of spontaneous crystallization of the solution

$$RS = [C_{Ca}C_{Ox}\gamma_{CaOx}]^{1/2}$$

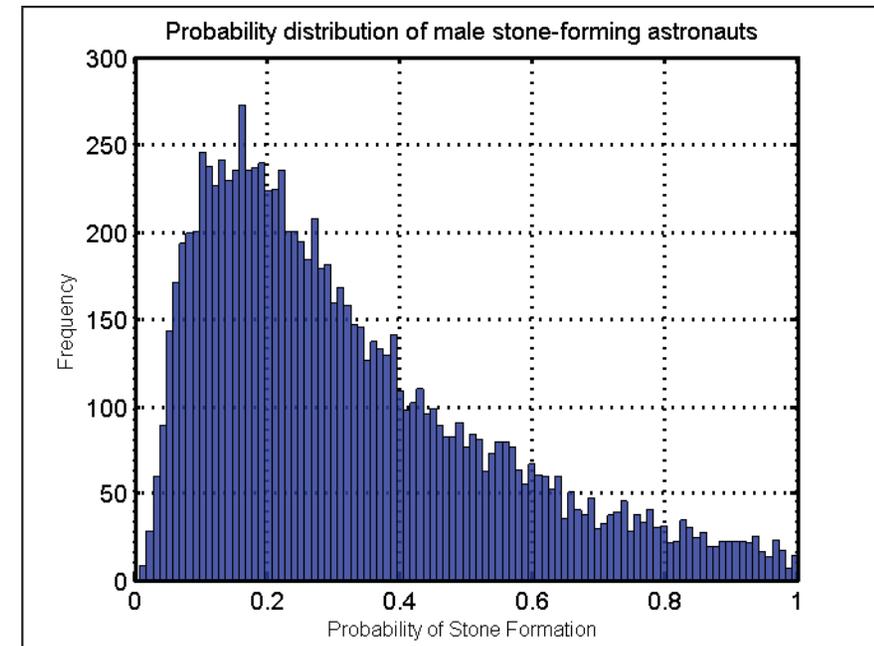
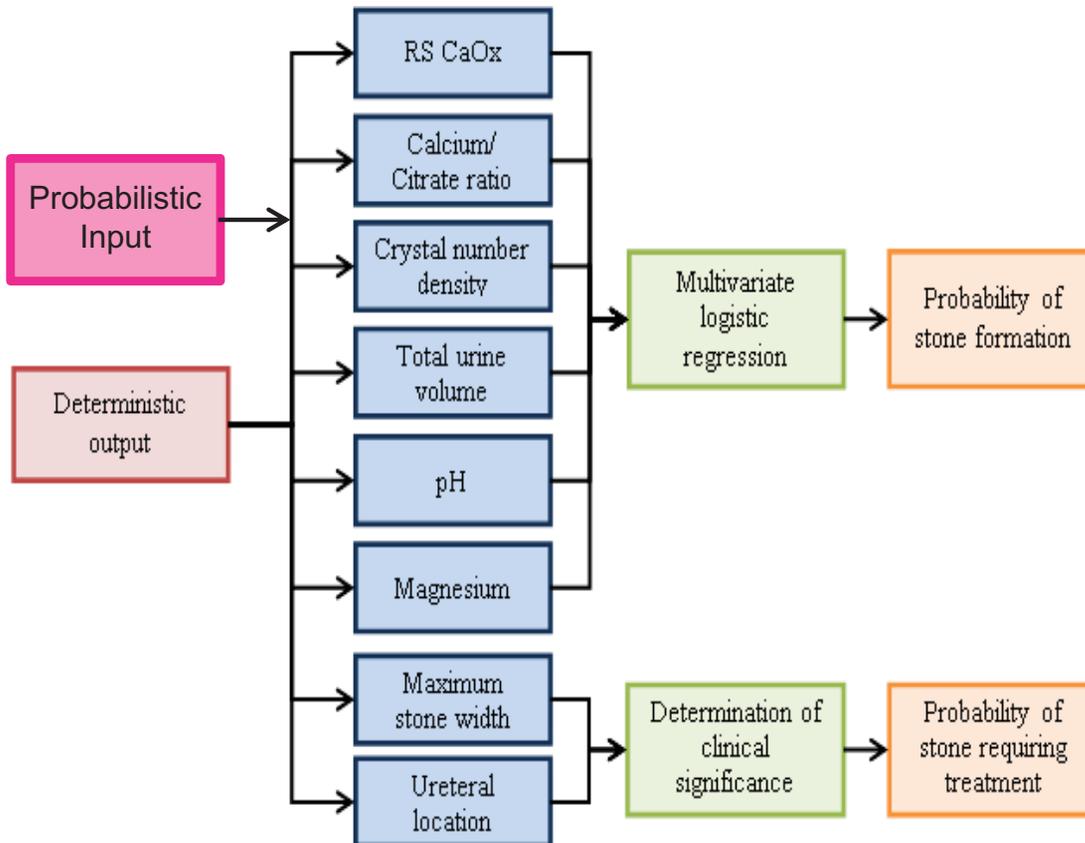
- Necessary outputs to deterministic model: activity (indirect), pH, temperature, pressure, RS_{CaOx}





Probabilistic Wrapper: Back-End

- Couples deterministic model output and randomly sampled input parameters to quantify the risk of stone formation and treatment
- Utilizes two major sections: (Initially design by Mike McRae and Travis Jackson)
 1. Probability of stone formation
 2. Probability that a stone passes spontaneously (without treatment)





Back-End Continued...

- *Stone Formation:*

- Determined by Multivariate logistic regression equation below via MATLAB statistical functions
- Additional parameters can be added with additional β factors

$$P(SF) = \frac{1}{1 + e^{-(\alpha + \beta_1[RS] + \beta_2\left[\frac{Cit}{Ca}\right] + \beta_3[TV] + \beta_4[pH] + \beta_5[Mg])}}$$

- *Stone Passage:*

- Determined via spontaneous passage rates related to renal stone width and ureter stone location
- Treatment determined by the probability of stone passage:

$$P(Treatment) = 1 - P(Passage)$$



Acknowledgements



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