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Heavy metal never tasted so good: A mathematical model of cadmium exposure from dark chocolate consumption

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Abstract

Ingested heavy metals are known to cause adverse health effects, such as reproductive harm and cancer. Unfortunately, many foods consumed today, such as chocolate, baby food, fruit juice, rice, fish, and many more contain trace amounts of heavy metals, including lead, cadmium, and arsenic. Mathematical modeling can simulate how consuming contaminated foods leads to accumulation of harmful compounds in the human body and also provides a tool to determine the impact of consumption changes. As part of the SIMIODE Challenge Using Differential Equations Modeling (SCUDEM) competition, we developed a simple mathematical model to investigate heavy metal accumulation from dark chocolate. Our model included half-life based decay of the metals, a Fourier transform of sales data to account for consumption, and parameters to simulate various concentrations of contaminants present in dark chocolate. The model developed for the competition had inaccuracies, so we began the iterative process of developing a more complex mathematical model. Each iteration showed that, heavy metals-specifically cadmium-accumulate to concerning levels over time and can ultimately contribute to negative health effects. This paper details the evolution of our model, and illustrates the importance of iteratively changing the process in mathematical modeling.

Introduction

Studies over the last decade have increasingly focused on heavy metals in food, with measurable amounts present in foods such as baby food, fruit juice, rice, protein

powder, leafy greens, fish, and dark chocolate [26]. Heavy metals infiltrate food groups primarily through human activities such as industrial production, mining, agriculture and transportation [15]. Heavy metals can also be found in soil and aquatic systems due to sewer networks [15]. While not all heavy metals pose a threat to human health, metals such as lead, cadmium, and arsenic, can have toxic effects on the human body depending on the amount present and length of exposure. Toxic heavy metals can inhibit metabolic pathways, which leads to a wide range of medical issues [3]. Repeated consumption and ingestion of heavy metals has toxic negative health effects, including aging, cancers, and reproductive harm [15] [3].

As a precaution, the California Proposition 65 Act (Proposition 65 Limit) was enacted in November 1986 to warn people about the risks to chemicals that can contribute to cancer risks or reproductive harm and to establish maximum allowable doses deemed safe in food [23]. However, the question remains: How does the consumption of these materials over many years lead to heavy metal accumulation and potential health implications?

The Systemic Initiative for Modeling with Ordinary Differential Equations (SIMIODE), hosts an annual student competition to encourage the use of differential equations in modeling real-world problems [1]. High school or college students from across the world compete in teams of three and create solutions to mathematical problems that deal with potential real-world situations. We created a team at Duquesne University (M.K., M.L., and K.C.) and competed in the 2024 SCUDEM IX (SIMIODE Challenge Using Differential Equations Modeling) challenge. We had three weeks to develop a model to address a situation in one of the following areas: physics/engineering, chemistry/life sciences, or social sciences [1] without assistance from our advisor (K.W.). We selected the life sciences problem, which involved the challenge of modeling the accumulation of heavy metals, such as lead, cadmium, and arsenic, from contaminated dark chocolate. The model developed in this paper received the Outstanding Award for our work, the highest honor granted by SIMIODE.

This competition showed us not only how modeling could be applied outside of a classroom setting but also the importance of understanding how these toxic heavy metals could accumulate in our bodies. In this paper, we discuss the initial model that was developed for the competition, the subsequent revision that we did for a research symposium, the final iteration that adds relevant biological complexity, and possible future directions. We aim to demonstrate the progressive process and share the motivations that drove these revisions. All three versions are simple, well-mixed compartment models, but capture the important characteristics of this problem. We conclude by discussing other features that might be important for future iterations.

1. SIMIODE SCUDEM IX 2024 Challenge

The challenge problem asked teams to address the accumulation of three heavy metals (lead, cadmium, and arsenic) due to ingestion of dark chocolate. Our initial steps in creating the model involved determining simplifying assumptions and finding the foundational data to use within our model. Given the time restrictions of the competition, we decided that a decay model would be the easiest and most straightforward approach. We also had to represent the variation in chocolate consumption throughout the year since that impacts the accumulation of metals compared to constant consumption. As part of the problem statement, we investigated the long-term effects of continuous contaminated dark chocolate consumption, as well as how children might be affected from increased chocolate consumption around birthdays and holidays [1].

1.1. SCUDEM Model Assumptions and Equation Fabrication

For our model we wanted to include the variation in chocolate consumption based on the time of year. We assumed an average healthy American child with no dietary restrictions and a constant cyclic consumption pattern that varied with the holidays. We assumed the same half-lives for adult and children, as there is a lack of literature available for these values in children. Additionally, we assumed no other sources of lead, cadmium, and arsenic, so we were able to analyze the effects on accumulation from chocolate exclusively.

We also assumed that each serving of chocolate had a constant dose of heavy metals. The model of the body was originally conceived as a three-compartment model: the chocolate, the body, and the environment. This was later changed to a single body compartment, with no tracking of accumulation/depletion. With these assumptions and the idea of a one-compartment decay model in mind, we were able to create simple equations for the flow of the heavy metal through the body as follows:

$$\frac{dy_{Pb}}{dt} = S(t) \cdot Pb_{in} \cdot e^{-\lambda_{Pb} t} \tag{1}$$

$$\frac{dy_{Cd}}{dt} = S(t) \cdot Cd_{in} \cdot e^{-\lambda_{Cd} t} \tag{2}$$

$$\frac{dy_{As}}{dt} = S(t) \cdot As_{in} \cdot e^{-\lambda_{As} t} \tag{3}$$

Where y_{Pb}, y_{Cd}, and y_{As} are the concentrations of lead, cadmium, and arsenic, respectively, within the body at a given time (μg); $S(t)$ is the cyclic consumption pattern created to model the variation in chocolate consumption throughout the year (serv-

ings/week); Pb_{in}, Cd_{in}, and As_{in} are the initial amount of contaminant per serving of chocolate (μg /serving); and λ_{Pb}, λ_{Cd}, and λ_{As} are the decay constants based on the half-life of each metal (weeks^{-1}).

We aimed to use equations (1), (2), and (3) to determine how much the contaminants would decay in the body and explored several types of processes to model this contamination. The first option was constant decay within the body, but this did not seem biologically accurate. An exponential decay form was used instead, as it seemed more accurate for how the body filters contaminants. We found the research of M. Rabinowitz while searching for half-live values, and Rabinowitz proposed a compartment model showing the movement of lead in human bone [21]. This study, among others, led us to conclude that metals within the body should typically have a half-life. We used this as our starting point, with the understanding that it is an oversimplification of the actual biological processes of digestion and excretion. We assumed that there would be consistent exponential decay based on contaminant half-lives in adult males. Half-lives were generalized from multiple sources and are as follows: Lead (Pb), 25 years [17]; Cadmium (Cd), 14.2 years [25]; and Arsenic (As), 1.7 weeks [2]. These values were used to calculate the decay constants by integrating the following differential equation:

$$\frac{dx}{dt} = -\lambda x \tag{4}$$

That integration results in the general decay formula:

$$\lambda = \frac{ln(2)}{t_{1/2}} \tag{5}$$

where $t_{1/2}$ is the half-life, in weeks, for each metal, and λ is the decay constant for each metal, in weeks^{-1}.

1.2. **Fourier transform of chocolate sales data**

The SCUDEM problem statement referenced a paper by Hands et al. that provided the concentration per dark chocolate serving of each heavy metal [12]. We utilized the mean, median, the threshold established by the Proposition 65 limit, minimum, and maximum concentrations of each metal found within the samples of dark chocolate as described in that paper (Table 1).

We then needed an accurate way to model the varied consumption of chocolate. We explored creating a sinusoidal function that had multiple peaks at the beginning and end of the year. But, we felt that it might be too simplistic to accurately model this process. While searching for average yearly chocolate consumption data, we found

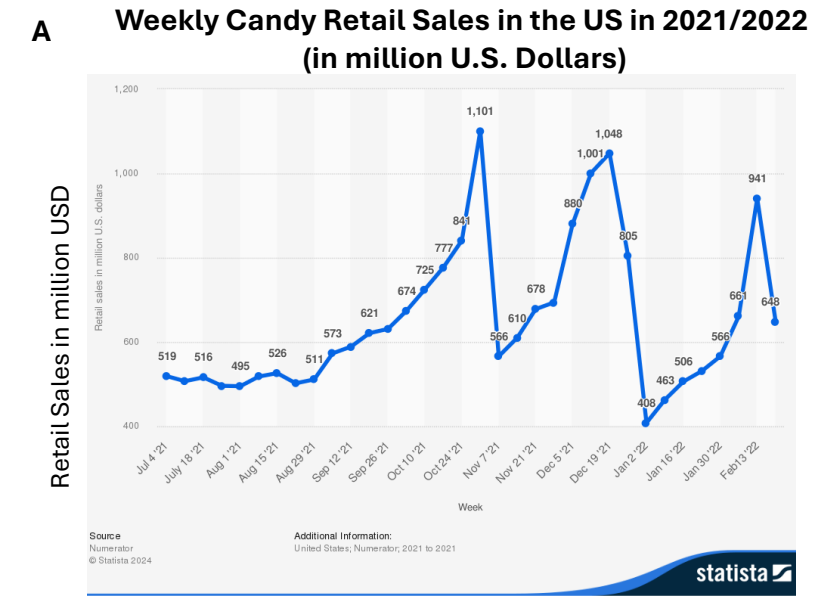
Metal	Mean	Median	CA Proposition 65 Limit	Min	Max
Lead (µg/serving)	0.615	0.375	0.5	0	3.136
Cadmium (µg/serving)	6.986	3.03	4.1	0.1	92.4
Arsenic (µg/serving)	0.931	0.75	10	0.056	2.695

Table 1: Concentrations of heavy metals found in dark chocolate [12].

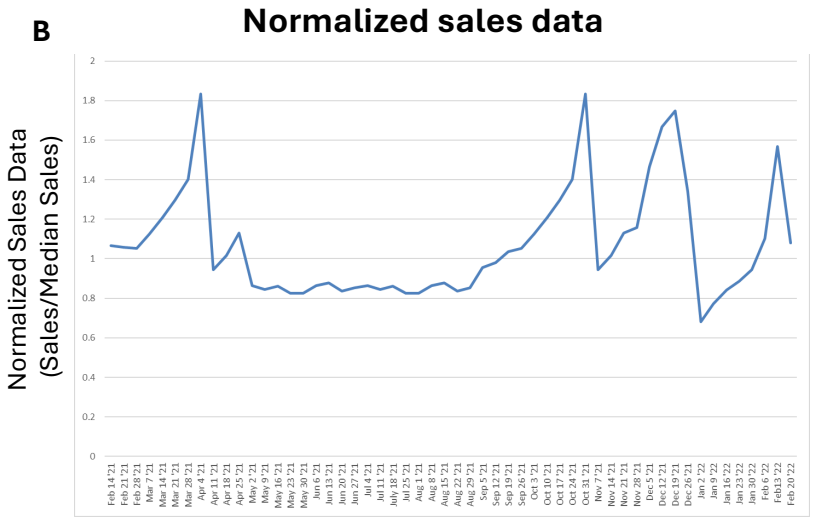
publicly accessible data on weekly candy sales from 2021-2022 on Statista.com [20]. We decided to use this data, and made three assumptions: there is a direct relationship between candy sales and chocolate consumption, dark chocolate sales follow the same pattern as all candy sales, and that children and adults would follow the same consumption pattern. This data showed evidence of sharp increases around major holidays, such as Valentine's Day, Halloween, and Christmas, and provided weekly data points for most of the year.

Although the data was easily downloadable, some issues arose. The first was that the data needed to span a lifetime, rather than just the nine months covered in the dataset we used (Figure 1A). Research suggested that average candy sales during Halloween and Easter are similar [10], thus the data from Halloween was transposed directly into the empty weeks surrounding Easter, giving us a complete and discrete dataset. Although it is possible that chocolate consumption varies with age, we assumed it was constant. The second issue was that it was a discrete data set, and to create a differential equations model, we needed a continuous function. The third issue with this data set was that it was in millions of U.S. dollars. To fix this issue, we normalized the data based on the median sales per week to make this data related to servings over time rather than in monetary units (Figure 1B).

Many options were considered for making this function continuous— the MATLAB curve fitting suite offers a Gaussian, sum of sines, Fourier transform, and interpolant fit system. All of these options were tested, but the Fourier transform worked the best for defining the data. The Fourier transform is a sum of sines and cosines, which makes it ideal for solving differential equations since sine and cosine can easily be integrated. A Fourier transform is a solution to any function or set of data points, and as the number of terms approaches infinity, it should become perfectly accurate and match all the data provided. Although the calculations were not performed by hand, the simplicity and accuracy of the Fourier transform were considered quite desirable, and the fit could be incorporated into our MATLAB code and used with the



Weeks, starting week of July 4, 2021



Weeks, starting week of Feb 14, 2021

Figure 1: Analysis of Sales Data for Chocolate Consumption **A** Sales data collected from Statista.com that served as the source for a cyclical consumption pattern. Peaks in sales occur around Halloween, Christmas, and Valentines Day, with a valley during the summer season. Data spans from July to February. **B** Sales data was extrapolated to span a full year to include Easter Sales and then normalized based on the median sales per week to convert from dollars to a unitless value that could be used for a Fourier Transform.

MATLAB ODE solver.

We used an eight-term Fourier transform resulting in r^2 of 0.77198 (Figure 2). The general form of the equation is:

$$S(t) = 0.389 + \sum_{n=1}^{8}(a_n \cos(0.09897nt) + b_n \sin(0.09897nt)) \tag{6}$$

with a_n and b_n varying with n. Values for a_n and b_n are shown in table 2. MATLAB generated values were easily incorporated into our code.

n	a_n	b_n
1	-0.5008	0.2928
2	-0.3724	0.6198
3	0.04989	0.5317
4	0.3099	0.2726
5	0.3765	0.06025
6	0.2287	-0.1459
7	0.009497	-0.2099
8	-0.06808	-0.104

Table 2: Fourier Transform Coefficients generated from MATLAB's curve fitting suite.

At the time, we believed that this provided an effective modeling of servings consumed throughout the year, and accounted for possible inconsistencies with the average diet. We acknowledge that the fit was not perfect (Figure 2), however, it matched the general trend. At this point we determined how the amount of contaminants and initial concentration can vary in the body, and we ran the model. We utilized MATLAB's ODE solver function, specifically "ode15s", to solve the systems of equations we had created (Equations 1-3). This built-in function allowed us to easily solve and graph the solution of the equations.

1.3. **SCUDEM model results and presentation**

The SCUDEM challenge has teams present their work through a ten-minute video submission. Consistent with the quick pace of the rest of the challenge, ten minutes provided a limited opportunity to fully share the results generated by our model. Therefore, we picked specific cases to include. We explored the variation of initial concentrations [12], and the effect on short-term and long-term accumulation. We examined the impact of varying the initial contaminant concentrations between the

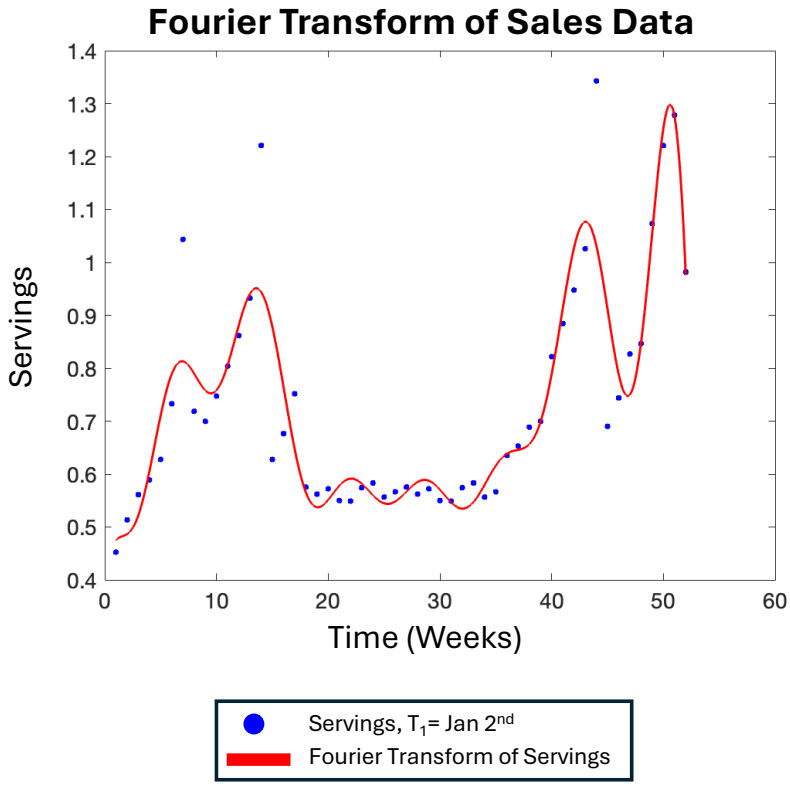


Figure 2: Fourier Transform fit of normalized sales data. Utilizing MATLAB, an eight-term Fourier transform of the normalized sales data was performed. There is a shift in the transform from the sales data since extrapolation was used. While the fit is not perfect ($r^2 = 0.77198$), it matched the general data trend well of sales, and therefore consumption as well. This imperfect fit works for modeling purposes since there can be a delay from purchasing to consumption.

minimum, maximum, median, mean, and Proposition 65 limit [12]. We felt that examining the averages, alongside the extreme cases, would give us the best view of how varying the intake concentrations affected accumulation. Although we saw the same general trends for curves with each starting concentration, specifically with cadmium, there was a range of values where the body concentration curve leveled out over time (Figure 3). The overall results of the model indicated that there would be a large accumulation of cadmium within the body over time, suggesting that cadmium levels could become concerning over time. Lead was also a concern, but not to the same extent as cadmium. Using higher initial concentrations (mean values) led to higher accumulation compared to using intake values in-line with the Proposition 65 limit; the opposite was seen when using the lower median values, indicating the

importance of concentration when considering long-term health effects.

We also examined the effect of birthdays on long-term accumulation. We assumed children increase their chocolate consumption around birthdays, potentially due to gifted chocolate. To examine the effect of birthdays, we assumed a 10% increase in chocolate consumption during the 13-week period in which the birthday fell (Figure 3D). This was done using the mean initial concentrations [12]. We assumed that for a birthday, children might have received more chocolate, yet it is likely that parents would spread the chocolate consumption per week around the birthday, rather than have a large single bolus on that day.

Consistently, we observed that cadmium accumulated to the highest levels, due to its long half-life compared to lead and arsenic (Figure 3). The accumulation over one year (Figure 3A) is minimal for lead and arsenic, while there is a constant and steep rise in the accumulation of cadmium. If the consumption rate was assumed to be consistent over an 80-year lifespan (Figure 3B), negligible amounts of arsenic would accumulate, while lead and cadmium would have a noticeable accumulation. Cadmium levels reached over three milligrams within the body during this period, while lead accumulated to approximately half a milligram.

If the Proposition 65 initial concentrations regarding chocolate are used (Figure 3C); accumulation is significantly less for cadmium but still slightly less than two milligrams of cadmium while lead accumulation reaches approximately 0.4 milligrams. In contrast to Figure 3B, Figure 3C shows a noticeable, though small, accumulation of arsenic over a lifetime, however the level is still significantly lower than predicted for lead or cadmium. Arsenic accumulation is noticeable with the Proposition 65 limit amounts, as the limit is over ten times higher than the median or mean values (Table 1).

The question of to what extent birthdays really impact the data was then examined with respect to children (Figure 3D). Here we focused on cadmium, as our other results showed it accumulated to the highest amounts. The largest accumulation was seen when the birthday fell within the January to mid-March period (weeks 1-13). The second largest level was found when the birthday fell between October and December (weeks 40-52). Both sections saw higher accumulation due to the compound effect of holidays and birthdays. These periods include Halloween, Christmas, New Years, and Valentine's Day, which all see large chocolate sales and consumption [20]. It is conceivable that rather than compounding, birthdays within that period could be off-setting due to "chocolate burnout" from overcompensation or lack on interest but that would simply default to our baseline curves. Additionally, we assumed the consumption pattern for an entire lifetime, which might not be realistic, as children tend to eat more chocolate than adults. However, we wanted to see how this child-like

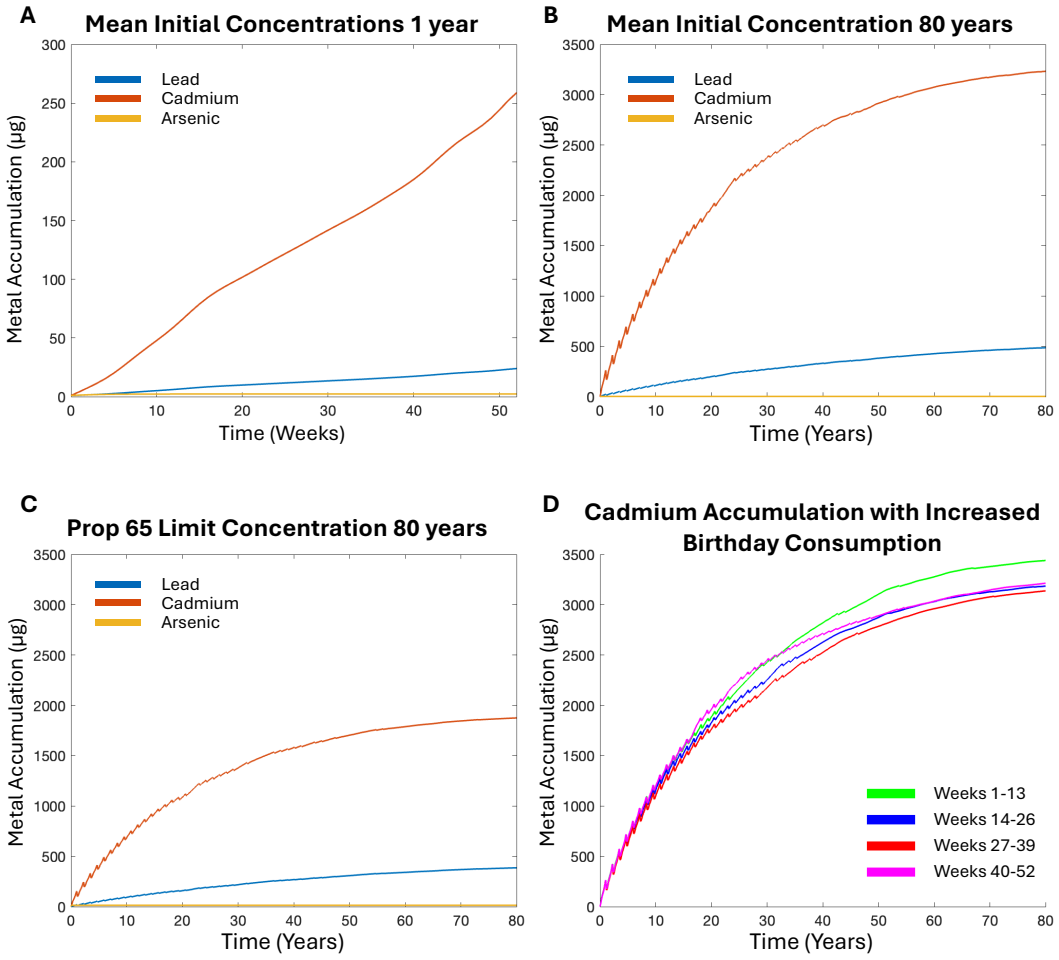


Figure 3: Model results from SCUDEM Challenge displaying short-term and long-term accumulation of heavy metals from contaminated chocolate. Accumulation of lead (blue), cadmium (red), and arsenic (yellow) from contaminated chocolate using: **A** mean initial concentrations over 1 year, **B** mean initial concentrations over 80 years, and **C** Proposition 65 limit initial concentrations over 80 years. The mean initial concentrations resulted in much larger long-term accumulation compared to the Proposition 65 concentrations. **D** 10% increase in chocolate consumption for birthday period. Weeks 1-13 (green) of the year includes New Years and Valentines Day, Weeks 14-26 (blue) encompasses Easter, Weeks 27-39 (red) spans July to September, which does not include any major chocolate consuming holidays, and Weeks 4-52(magenta) includes Halloween and Christmas

consumption pattern would affect accumulation.

One odd thing we had noticed with our results was the "spikes" present within the 80-year graphs. These spikes result from the $S(t)$ function within our code where

it "resets" each year. At the time, we believed the jumps resulted from the drop in chocolate sales that occur at the beginning of each year. We focused more on the overall trends in the lifetime (80 years) rather than the small consumption effects shown with this yearly spikes.

Overall, these results suggest that heavy metal consumption could lead to significant accumulation which may be a significant health risk. However, this initial model did have its shortcomings, and we decided to move forward with correcting the shortcomings post-competition.

2. **Modeling cessation**

2.1. **Addressing limitations from SCUDEM model**

After completing the SCUDEM challenge and receiving the judges' comments, we noticed a few flaws within our initial model. One major flaw we found was that our model failed to account for a cessation in chocolate consumption, perhaps due to a person's aging or simply dietary changes. In our original model, if the concentration of heavy metal was set to zero, a constant body concentration (i.e., flat line) resulted rather than continuous decaying of the remaining contaminants, since the excretion term we were utilizing would be multiplied by zero. When a cessation of consumption occurs, there should still be decay of the heavy metals present in the body. Another limitation of our original model was that it failed to explicitly account for the excretion of metals from the body. To address these issues, we restructured our multiplication term into a subtraction term, leading to the following equations:

$$\frac{dy_{Cd}}{dt} = S(t) \cdot Cd_{in} - y \cdot \lambda_{Cd}. \tag{7}$$

$$\frac{dy_{Pb}}{dt} = S(t) \cdot Pb_{in} - y \cdot \lambda_{Pb}. \tag{8}$$

$$\frac{dy_{As}}{dt} = S(t) \cdot As_{in} - y \cdot \lambda_{As}. \tag{9}$$

where once again, Cd_{in} is the amount of cadmium present per serving (μg/serving), Pb_{in} is the initial amount of lead present per serving (μg/serving), As_{in} is the initial amount of arsenic present per serving (μg/serving), $S(t)$ is the equation for the cyclic consumption pattern (servings/week), y_{Pb}, y_{Cd}, and y_{As} are the concentrations of lead, cadmium, and arsenic respectively within the body at a given time(μg), λ_{Cd} is the half-life of cadmium (weeks^{-1}), λ_{Pb} is the half-life of lead (weeks^{-1}), and λ_{As} is the half-life of arsenic (weeks^{-1}). The half-live values were the same values we utilized in the original model, and the initial concentrations were those provided in

the SCUDEM problem supplemental material [12]. We assumed that the half-life term represented excretion from the body. These updates were presented at Duquesne's Spring 2025 Undergraduate Research and Scholarship Symposium (URSS).

2.2. **Cessation results**

For the URSS, we focused on using the revised model to compare the difference in cumulative accumulation of the heavy metals using the initial median, mean, and Proposition 65 limit metal intake concentrations [12]. Once again, we said the spikes within the accumulation are due to the $S(t)$ function's yearly reset for the long-term accumulation results. Simulating the revised model, we found again that the accumulation of lead and cadmium could become concerning with long term consumption (Figure 4). As in the original model, cadmium accumulates to much higher levels than lead or arsenic, again due to its much higher initial concentration (Table 1). The mean initial value led to the highest accumulation for all three metals (Figure 4A) while using the median initial value led to the smallest accumulation (Figure 4B). Long-term consumption of chocolate with metal levels lower than the Proposition 65 limit led to less accumulation. The inclusion of excretion led to slightly less accumulation compared to our work in the SCUDEM Competition (Figure 3B vs Figure 4A)

One question that arose with these models was whether the accumulation of heavy-metals would diminish if consumption of chocolate stopped. The new model predicted that heavy metal levels in the body would decrease if an individual stopped consuming contaminated chocolate, but that the rate was not particularly rapid (Figure 4D-G). Specifically, we modified our code to allow us to input the length of time we wanted to explore, as well as when we wanted a diet change to begin. We examined short-term consumption over one year (Figure 4D), and more long-term consumption (Figure 4E-G). Interestingly, we found that even after only one year of consumption, metal levels do not approach zero until a significant time has elapsed (Figure 4D). We found that for short-term and long-term accumulation, the rate of decay was about 14.5 years for cadmium. This decay is consistent with the decay constant placed in the model. This illustrates the potential danger from materials that do not quickly clear out of the body, even if consumption is only for a short period of time (Figure 4E-G).

3. **Next step extension**

Both the initial SCUDEM model and the revised URSS model failed to account for how the metals might be distributed throughout the body, which would better

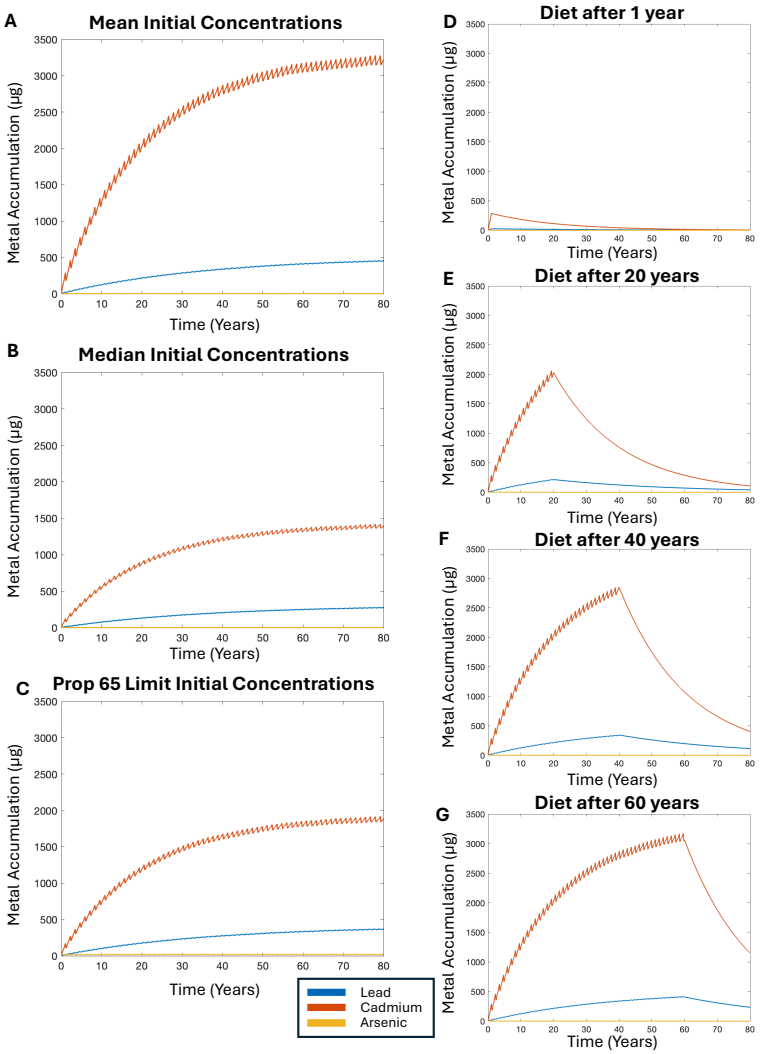


Figure 4: Comparison of dieted vs continuous intake. Accumulation of lead (blue), cadmium (red), and arsenic (yellow) from the URSS model with a constant consumption using: **A** mean, **B** median, **C** Proposition 65 limit initial concentrations. Mean initial concentrations accumulate to nearly double that of the Proposition 65 limit for Cadmium. The median values accumulate to the lowest amounts of metals present. Accumulation with the mean initial concentrations and a variable consumption (i.e., dieting after a specific period and stopping chocolate consumption) with cessation occurring after **D** 1 year, **E** 20 years, **F** 40 years, and **G** 60 years. Cessation in consumption leads to a decrease in metal accumulation, however, it is a very slow decay, especially for cadmium, as the half-life is about 14.5 years

link the model with experimental data and make it more predictive. We decided to

focus on cadmium as it had the most concerning results from our previous models. The literature indicates that cadmium is predominantly distributed between the liver and kidney [6]. Therefore, the next logical step for improving our model was to expand to a multi-compartment model that could track the movement and storage of cadmium in the relevant organs. This simple extension of our work included the three compartments (blood, liver, and kidney) as shown in Figure 5.

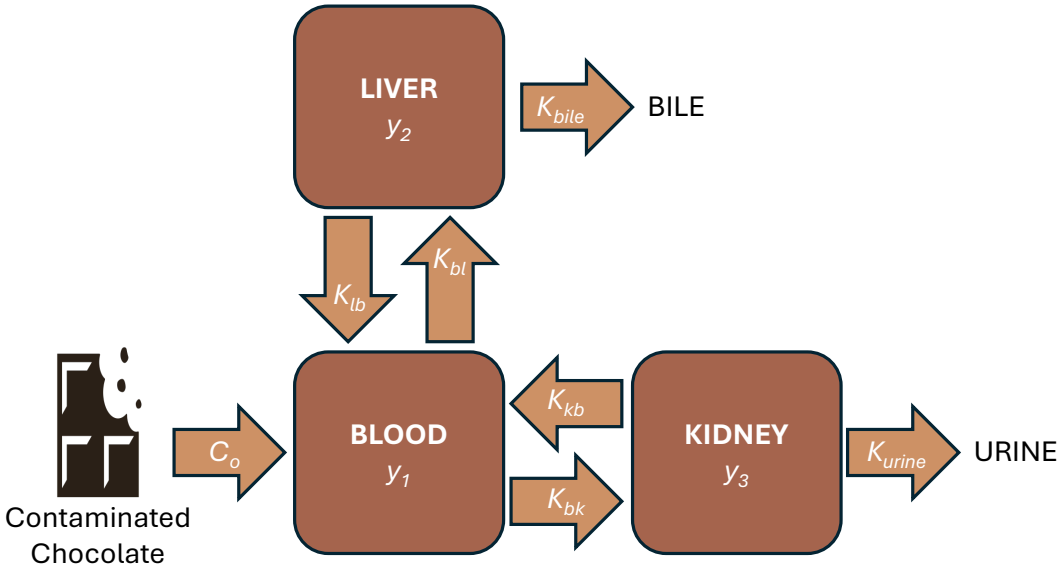


Figure 5: Schematic of the Three Compartment Model.

3.1. **Model set-up**

We maintained our initial approach of modeling the initial concentrations of cadmium [12] and chocolate consumption patterns using the Fourier transform. Like the earlier models, we are considering cadmium only from dark chocolate sources and not any other food sources. The three-compartment model allows us to track how the metal flows through the body and respective organs. Experimental studies indicate that cadmium can bind to a number of proteins in the body with albumin and metallothionein seeming to be the predominant partners [19]. But, for simplicity, we have lumped free cadmium and its bound forms into one species, noting that these alternative states would be logical extensions of the model in the future. The model equations are as follows:

$$\frac{dy_{blood}}{dt} = C_o - K_{bl} \cdot y_1 + K_{lb} \cdot y_2 - K_{bk} \cdot y_1 + K_{kb} \cdot y_3 \tag{10}$$

$$\frac{dy_{liver}}{dt} = K_{bl} \cdot y_1 - y_2 \cdot (K_{lb} + K_{bile}) \tag{11}$$

$$\frac{dy_{kidney}}{dt} = K_{kb} \cdot y_1 - y_3 \cdot (K_{kb} + K_{urine}) \tag{12}$$

$$\frac{dy_{bile}}{dt} = K_{bile} \cdot y_2 \tag{13}$$

$$\frac{dy_{urine}}{dt} = K_{urine} \cdot y_3 \tag{14}$$

with y_1 is the blood cadmium accumulation (μg), y_2 is the liver cadmium accumulation (μg), y_3 is the kidney cadmium accumulation (μg), C_o is initial amount of cadmium entering the blood (μg/weeks), K_{bl} is the rate from the blood to liver (weeks^{-1}), K_{lb} is the rate from the liver to blood (weeks^{-1}), K_{bk} is the rate from blood to kidney (weeks^{-1}), K_{kb} is the rate from kidney to blood (weeks^{-1}), K_{urine} is the rate from the kidney to urine (weeks^{-1}), and K_{bile} is the rate from the liver to bile (weeks^{-1}).

Our compartment model assumes that a constant percentage of the consumed cadmium is transported into the bloodstream. Once in the blood, cadmium can flow anywhere in the body, but the literature suggests that most pit-stops in the liver and then accumulate in the kidney [11]. Cadmium is transported to the liver from the bloodstream, where some cadmium is either excreted through bile (which becomes stool), stays in the liver, or travels back into the bloodstream. Cadmium is also bound by proteins and other molecules [19], which we neglect in this model. Cadmium is also transported from the bloodstream to the kidney, where most long-term storage seems to occur [11]. Short-term studies suggest that the initial cadmium deposition is in the liver prior to kidney delivery, but our model allows simultaneous transfer rather than sequential [11]. Once in the kidney, cadmium can be excreted through urine or returned to the bloodstream to repeat the cycle [11]. Cadmium is excreted primarily through urine and stool [11]. Our model assumes that the cadmium present in bile is directly related to feces excretion with no retention in the body, and, similarly, urine cadmium is unable to reenter the body chambers.

3.2. **Parameter estimation**

One limitation of the new model was the increase in parameter values needed to run simulations. The first step was to determine how much of the consumed chocolate, and therefore how much cadmium entered the bloodstream (Compartment 1). The literature suggests that about 5% of the ingested cadmium is absorbed into the blood through the GI tract [11]. Since we assumed chocolate as the only source of cadmium in this model, 5% of the cadmium present in chocolate is absorbed. To model this, the feed rate of cadmium (C_o) entering the bloodstream, in µg/week, was modeled as

follows:

$$C_o = 0.05 \cdot Cd_{in} \cdot S(t) \tag{15}$$

where Cd_{in} is the initial concentrations of cadmium found in dark chocolate samples [12], $S(t)$ is the equation for the cyclic consumption pattern, and the absorption value 5% serves as a multiplier. There is research that suggests men and women have different intake concentrations, with women having an increased uptake percentage, but we do not consider this asymmetry in the model [19]. Conditions such as iron deficiency can also lead to increased cadmium uptake [11], but for this model we assumed a typical healthy American adult.

To determine transport rates between compartments (blood, liver, kidney), we initially setup the model to have only a bolus of cadmium in the blood, setting the $S(t)$ function to zero and using a non-zero starting concentration in the blood compartment. Using this bolus, we were able to calibrate the rates so that the decay from each location generally matched the biological half-lives within the body. Each transportation rate term has units of weeks^{-1}.

Specifically, the literature suggests that cadmium within the kidney has a half-life between 10 and 30 years [16]. We aimed for the model to demonstrate a half-life of about 20 years (approximately 1040 weeks). To do this, we set the rate of cadmium transport from the blood to the kidney (K_{bk}) equal to that of cadmium from the liver to the kidney(K_{bl}). This was based on the literature that indicates approximately equal amounts (approximately 30%) of cadmium deposited in the liver and kidney [6]. We then set the rate of cadmium from the kidney back to the blood (K_{kb}) to $\frac{K_{bl}}{55}$. The 55 denominator in the K_{kb} term was adjusted to give the desired half-life. We based every other transport term on the blood to liver rate, as the first stop of cadmium in the body is typically the liver [11]. Finally, in regards to the kidney, we set the rate from the kidney to the urine (K_{urine}) to be $\frac{K_{bl}}{400}$ where, again, the denominator of 400 was adjusted so that the decay from the kidney would reflect a half-life of approximately 23 years within our model.

Next, we adjusted the transport rates between the liver and the bloodstream to account for cadmium's half-life in the kidney, liver, and blood. The rate between the blood and liver, K_{bl}, was set to be 0.3 based on about 30% entering the liver [11]. From the liver, we assumed that about 95% of cadmium was returned to the blood, while 5% was excreted through bile based on studies in rats indicating cadmium excretion was primarily urinary with only a small percentage of ingested cadmium being excreted though bile [13] [24]. Initially, we set K_{lb} to be $\frac{K_{bl}}{25}$. But, this led to more of the long-term storage to accumulate in the liver, rather than the kidney. Although the half-life of the liver is still long, with a range of 4 to 19 years [4], it seemed more

biologically correct to have less accumulation in the liver than the kidney. Having set K_{bl}, we were able to establish K_{bile} using ratios. We wanted 95% of cadmium in the liver to return to the blood, as literature suggested very little was found in bile [13]. Assuming a 95 to 5 split, we determined the ratio for biliary excretion to be $\frac{K_{bl}}{475}$. These rates, along with the kidney rates, give the model a half-life value for blood of a few weeks, which is in line with the experimental estimates in blood of 75 to 128 days (approximately four months) [6].

3.3. **Multi-compartment results**

After estimating the rates, we utilized the three-compartment model to assess how continuous consumption of contaminated chocolate impacts the body in both the short and long term. As we started running simulations, we again noticed the "spikey" pattern observed in the earlier models (Figure 6A). In this iteration, we decided to take a deeper look into what was causing these drastic spikes, as it did not seem entirely accurate. As we examined our code, we noticed that the Fourier Transform actually had a point where it went negative outside of the 52-week data, causing the drastic decrease found at the beginning of each new year (Figure 6C). We were able to modify our code to remove this fit anomaly (Figure 6D), and a smoother result was found (Figure 6B) with some very small spikes due to the consumption pattern.

Once the issue with C_o was corrected, we were able to finalize the rest of the parameters used and run the final simulations. The median value for cadmium (Table 1) was utilized for Cd_{in}, and the concentrations are shown for each compartment as well as the total body accumulation, which is the sum of the cadmium present in the blood, liver, and kidney. For a one-year consumption period, the accumulation of cadmium within the liver and kidney follows similar accumulation patterns (Figure 7A), with the blood seeing minimal accumulation as small spikes that correspond to the cyclic consumption pattern. Urinary excretion was slightly higher than bile excretion, but both forms of excretion follow a similar pattern (Figure 7B). The literature suggests that urinary excretion of cadmium is representative of the full body burden [19], and after a simulation time of one-year, cadmium accumulates in sub microgram quantities, suggesting a small burden on the body. If chocolate consumption stopped after one year, the three-compartment model results suggest that cadmium would quickly filter out of the body due to the explicit inclusion of excretion not simply based on half-life. This is a significant difference between our first two models and this compartment version.

Using the model to examine the longer simulation period, we found that there is

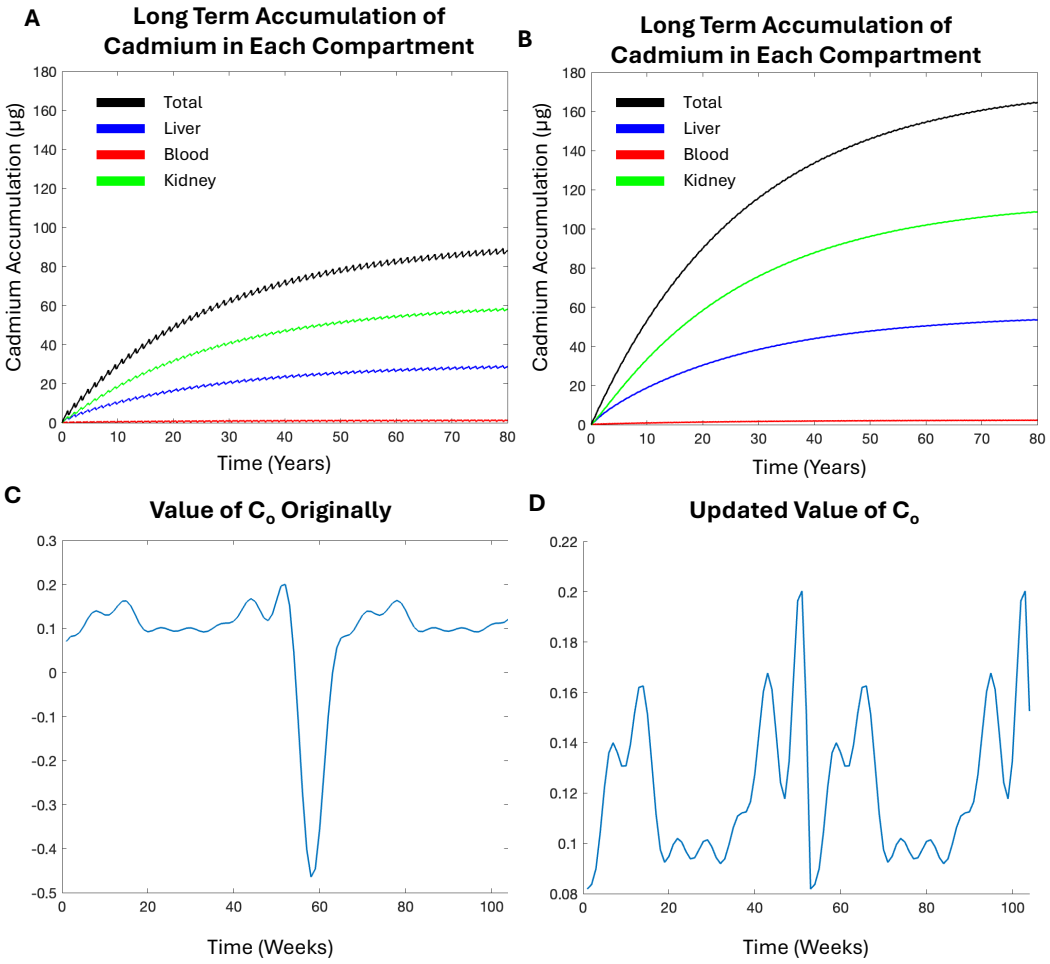


Figure 6: Comparing the total accumulation from the three-compartment model with original and updated C_o values. **A** Long-term accumulation from each compartment with C_o originally where the negative spikes are present. **B** Long-term accumulation from each compartment with modified C_o to remove the negative spike. In both **A** and **B**, the total accumulation of cadmium is in black, liver cadmium accumulation in blue, blood cadmium accumulation in red, and kidney cadmium accumulation in green. Likewise, comparing the shapes of the C_o over two years (**C** vs **D**) where there are no longer negative spikes and a shift at the end of each year.

significant accumulation of cadmium in all compartments (Figure 7C), yet the overall amounts are significantly lower than those found with our simpler models. However, we are not placing significance on the amount accumulated, but on the trends of increased retention with long-term consumption. With this model, we also observed that more than half of the accumulated cadmium would be within the kidney, and

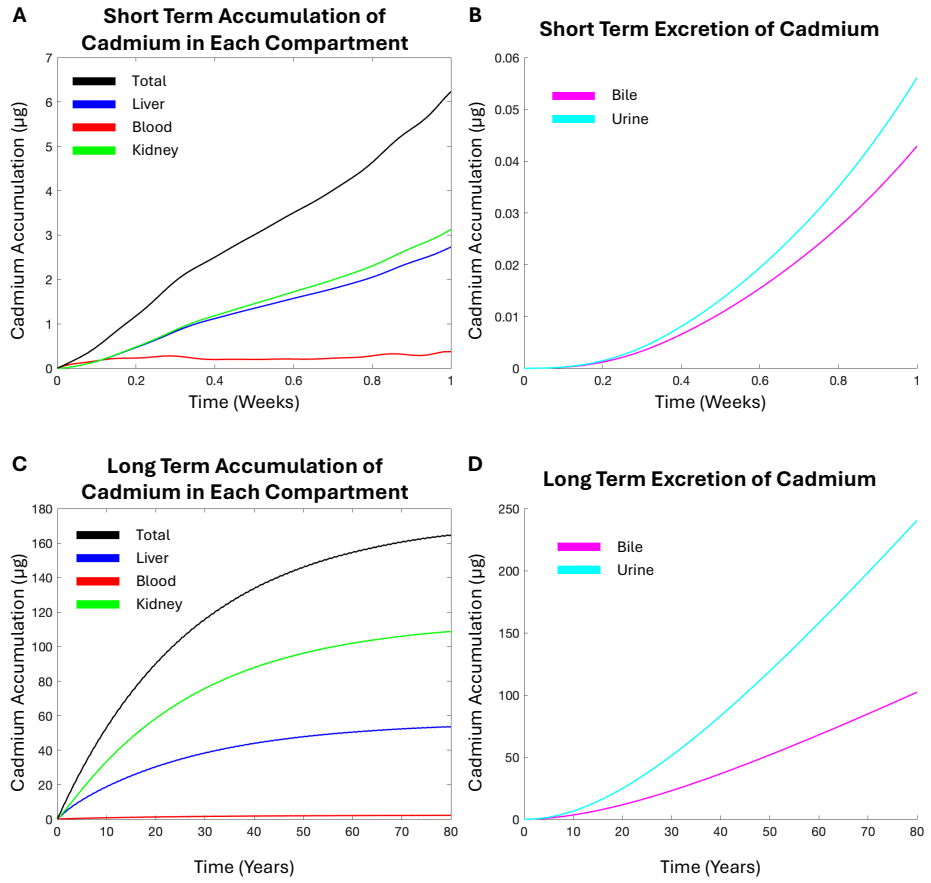


Figure 7: Cadmium accumulation results from three compartment model. **A** Accumulation of cadmium in liver (blue), kidney (green), blood (red), and total body accumulation (black) over 1 year period. Kidney and liver accumulate to similar levels over 1 year, with kidney cadmium accumulation being slightly higher. Blood cadmium exhibits small spikes that correspond with holidays in the consumption pattern. **B** Excretion of cadmium from the body through bile (pink) and urine (light blue) over 1 year period. After 1 year, urine cadmium excretion is slightly more than bile excretion, but for the short-term they both have similar trends upward. **C** Accumulation of cadmium in liver (blue), kidney (green), blood (red), and total body accumulation (black) over lifetime (80 years). Kidney accumulation is nearly double that of liver accumulation, with minimal blood cadmium accumulation with respect to the other two. **D** Excretion of cadmium from the body through bile (pink) and urine (light blue) over lifetime. Urinary excretion of cadmium is the primary excretion method of cadmium expulsion from the body, with urinary output being over double that of bile excretion.

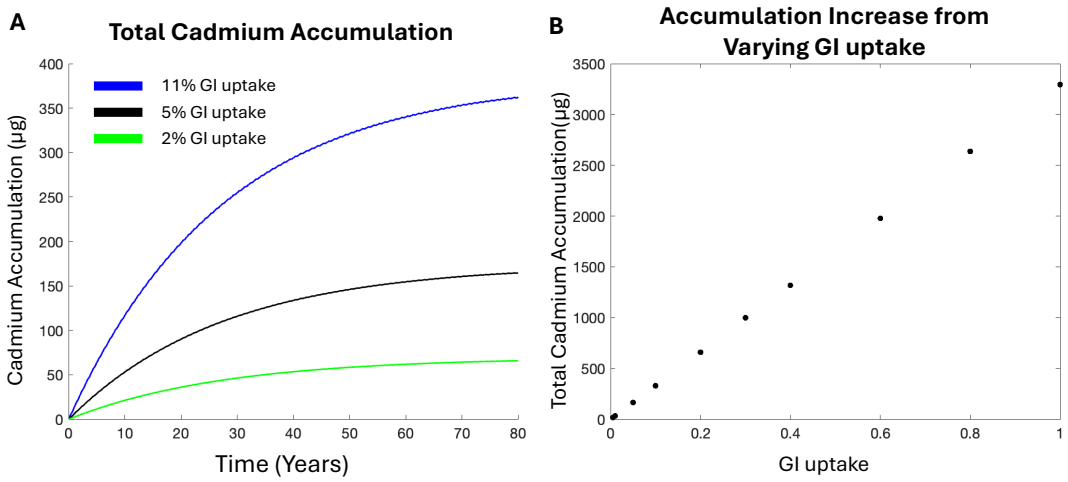


Figure 8: Variation in gastrointestinal intake of cadmium affects long-term accumulation. **A** Effects GI tract uptake has on total accumulation of cadmium. Original 5% is shown in black, 11% GI uptake in blue, and 2% uptake in green. The higher the percentage absorbed into the system, the larger accumulation that occurred over a lifetime. Those affected by medical conditions like iron-deficiency can have over double the accumulation of cadmium in their lifetime. **B** Various GI uptakes and the corresponding total accumulation. Accumulation increases linearly with increased GI uptake.

the majority of the cadmium was excreted through urine (Figure 7D).

Like the URSS model, we were able to examine a cessation of chocolate consumption. The accumulated metal decays when consumption ceases; however, because of the added complexity from the compartments, the half-life of the decay was not simply what was input. We calculated the time for half of the cadmium to decay after consumption stops to be approximately 18.9 years. This longer half-life results from the combination of the compartments. The three-compartment model shows a longer decay time compared to the URSS model, likely because of the inclusion of the liver and kidney as separate long-term storage sites.

We then further looked at how diet changes and medical conditions affect cadmium accumulation. High fiber diets, low vitamin D, or iron deficiency can all lead to an increase in gastrointestinal uptake [11]. Those with iron deficiency can have a 6% increase in cadmium uptake. To model this, we varied C_o through the GI uptake percentage (Figure 8). When we increased the GI uptake to 11% to account for those with iron deficiency, we saw more than double the long-term accumulation of cadmium compared to the baseline. In contrast, when we reduced the uptake percentage to 2%, we saw well more than half the cadmium accumulation compared

to the original (Figure 8A). As the percent of uptake through the GI tract increased, so did accumulation in a linear fashion (Figure 8B).

It is important to recognize that our model is a model and, therefore, does not include all regulatory factors, such as cadmium binding proteins, that might impact distribution and retention. However, this study illustrates how the model can be used to produce hypothetical results. These results should be experimentally investigated and validated to provide impactful insights into heavy metal accumulation.

Conclusions

The literature suggests that heavy metals can accumulate following ingestion of contaminated food and can have negative health effects, including cancer and reproductive harm [15]. Through the SCUDEM 2024 competition, we were introduced to the use of mathematical modeling to investigate these types of phenomenon. All three iterations of our model demonstrated that when heavy metals are consumed, specifically cadmium, arsenic, and lead, they can and will accumulate within the body. Our first model included the very basic idea of accumulation and decay within the body. The second iteration included a form of excretion, which allowed us to look further into how cessation of consumption might be important. Our final model included how cadmium might be distributed through the body using a multi-compartment model. Our project demonstrated the iterative process of modeling. We started with a very simple model, creating the basic premise, and then started challenging our assumptions. As we explored these assumptions, we aimed to create a more realistic model. Our final iteration added limited compartments to simulate some of the complexity inherent in the human body.

Our model was designed to be simple and straightforward to help address a specific question, and compartment modeling appeared to be the most straightforward way to approach it. Although we kept the model simple, there is potential for additional complexity that might allow one to tie predictions to experimental studies. For example, Nordberg and Kjellström developed an eight-compartment model to look at the flow of cadmium through the body based on data from blood, tissue, and urine to address intake through inhalation and consumption [18]. Diamond and coworkers expanded this model by incorporating Monte Carlo techniques to look at the variability of dietary cadmium intake and to provide estimates of health risks [8] [9]. Recently, the eight-compartment model was used to examine the distribution of cadmium from the ingestion of shellfish containing cadmium [7]. It should be noted that studies in 2009 and 2011 suggested that a simplified one compartment model could adequately predict cadmium levels at the population level with its variability for urine and blood

on par with the eight compartment model [5] [14]. It should be noted that pharmacokinetic modeling with heavy metals is not unique to cadmium. For example, a recent report by Rădulescu and Lundgren (2019) used a five-compartment model to look at lead ingestion. The report included that the brain and bone, as well as other soft tissues, and tied the distribution to that of calcium [22]. Similar types of modeling studies could be done with cadmium, including looking at the altered distribution of heavy metals when cadmium binding components such as metallothionein are included [19]. However, these more advanced models are beyond the scope and intent of this paper.

An important part of exploring these model iterations was questioning why our results made sense. For example, we noted accumulation drops and spikes in the first two models, which did not seem reasonable when observed alongside the cessation results. This forced us to look more closely at the way we were using our data fitting model. Challenging the accuracy of modeling results is a large part of modeling research and a key component of the iterative modeling process. Overall, this paper creates a strong foundation for future research regarding the accumulation of toxic heavy metals in the body and emphasizes the importance and power of mathematical modeling.

References

[1] SCUDEM - SIMIODE Challenge using differential equations modeling. https://qubeshub.org/community/groups/scudem. [Accessed 24-06-2025].

[2] Arsenic (total organic and inorganic) - South Tees Hospitals NHS Foundation Trust. https://www.southtees.nhs.uk/services/pathology/tests/arsenic-total-organic-and-inorganic/, 2022. [Accessed 25-06-2025].

[3] Abd Elnabi, M. K., Elkaliny, N. E., Elyazied, M. M., Azab, S. H., Elkhalifa, S. A., Elmasry, S., Mouhamed, M. S., Shalamesh, E. M., Alhorieny, N. A., Abd Elaty, A. E., Elgendy, I. M., Etman, A. E., Saad, K. E., Tsigkou, K., Ali, S. S., Kornaros, M., and Mahmoud, Y. A.-G. Toxicity of heavy metals and recent advances in their removal: A review. *Toxics 11*, 7 (2023).

[4] Agency for Toxic Substances and Disease Registry. Cadmium toxicity: What is the biological fate of cadmium in the body?, 2023.

[5] Amzal, B., Julin, B., Vahter, M., Wolk, A., Johanson, G., and Åkesson, A. Population toxicokinetic modeling of cadmium for health risk assessment. *Environmental Health Perspectives 117* (2009), 1293–1301.

[6] Bernhoft, R. A. Cadmium toxicity and treatment. *TheScientificWorldJournal* (2013), 394652.

[7] Chen, S.-C., Lin, H.-C., and Chen, W.-Y. Risks of consuming cadmium-contaminated shellfish under seawater acidification scenario: Estimates of pbpk and benchmark dose. *Ecotoxicology and Environmental Safety 201* (2020), 110763.

[8] Choudhury, H., Harvey, T., Thayer, W. C., Lockwood, T. F., Stiteler, W. M., Goodrum, P. E., Hassett, J. M., and Diamond, G. L. Urinary cadmium elimination as a biomarker of exposure for evaluating a cadmium dietary exposure-biokinetics model. *Journal of Toxicology and Environmental Health 63* (2001), 321–350.

[9] Diamond, G. L., Thayer, W. C., and Choudhury, H. Pharmacokinetics/pharmacodynamics (pk/ pd) modeling of risks of kidney toxicity from exposure to cadmium: Estimates of dietary risks in the u.s. population. *Journal of Toxicology and Environmental Health 66* (2003), 2141–2164.

[10] Garwood, G. Is easter the MVP of holiday candy sales? - The Food Institute. https://foodinstitute.com/focus/is-easter-the-mvp-of-holiday-candy-sales/, 04 2022. [Accessed 25-06-2025].

[11] Godt, J., Scheidig, F., Grosse-Seistrup, C., Esche, V., Brandenburg, P., Reich, A., and Groneberg, D. A. The toxicity of cadmium and resulting hazards for human health. *Journal of occupational medicine and toxicology 1* (2006), 22.

[12] Hands, J. M., Anderson, M. L., Cooperman, T., Balsky, J. E., and Frame, L. A. A multi-year heavy metal analysis of 72 dark chocolate and cocoa products in the usa. *Frontiers in Nutrition 11* (2024).

[13] Ishihara, N., and Matsushiro, T. Biliary and urinary excretion of metals in humans. *Archives of Environmental Health 41*, 5 (1986), 324–330.

[14] Julin, B., Vahter, M., Amzal, B., Wolk, A., Berglund, M., and Åkesson, A. Relation between dietary cadmium intake and biomarkers of cadmium exposure in premenopausal women accounting for body iron stores. *Environmental Health 10* (2011).

[15] Kamran, S., Shafaqat, A., Samra, H., Sana, A., Samar, F., Muhammad, B., Saima, A., and Tauqeer, H. M. Heavy metals contamination and what are the impacts on living organisms. *Greener Journal of Environmental Management and Public Safety 2* (08 2013), 172–179.

[16] Ma, Y., Ran, D., Shi, X., Zhao, H., and Liu, Z. Cadmium toxicity: A role in bone cell function and teeth development. *Science of The Total Environment 769* (2021), 144646.

[17] Nie, H., Sanchez, B. N., Wilker, E., Weisskopf, M., Schwartz, J., Sparrow, D., and Hu, H. Bone lead and endogenous exposure in an environmentally exposed elderly population: The normative aging study. *Journal of occupational and environmental medicine* (2009), 848–857.

[18] Nordberg, G. F., and Kjellström, T. Metabilic model for cadmium in man. *Environmental Health Perspectives 28* (1979), 211–217.

[19] Nordberg, M., and Nordberg, G. F. Metallothionein and cadmium toxicology—historical review and commentary. *Biomolecules 12*, 3 (2022).

[20] Numerator. Weekly candy retail sales U.S. 2021/2022— Statista. https://www.statista.com/statistics/947149/weekly-candy-retail-sales-us/, 2022.

[21] Rabinowitz, M. Toxicokinetics of bone lead. *Environmental Health Perspect 91* (1991), 33–37.

[22] Rădulescu, A., and Lundgren, S. A pharmacokinetic model of lead absorption and calcium competitive dynamics. *Scientific Reports 9*, 14225 (2019).

[23] State of California. Chemical exposure warnings (proposition 65 warnings). https://www.p65warnings.ca.gov/, 2021. [Accessed 25-06-2025].

[24] Sugawara, N., Lai, Y.-R., Arizono, K., Kitajima, T., and Inoue, H. Lack of biliary excretion of cd linked to an inherent defect of the canalicular isoform of multidrug resistance protein (cmrp) does not abnormally stimulate accumulation of cd in the eisai hyperbilirubinemic (ehb) rat liver. *Archives of toxicology 71*, 5 (1997), 336–339.

[25] Suwazono, Y., Kido, T., Nakagawa, H., Nishijo, M., Honda, R., Kobayashi, E., Dochi, M., and Nogawa, K. Biological half-life of cadmium in the urine of inhabitants after cessation of cadmium exposure. *Biomarkers 14*, 2 (2009), 77–81. PMID: 19330585.

[26] Wong, S. 10 Foods Most Likely to Contain Unsafe Levels of Heavy Metals, Experts Say. https://www.eatthis.com/foods-heavy-metal-contamination/. [Accessed 24-06-2025].

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