Ingestion of Elemental Mercury Vapor Released from Amalgam Dental Fillings

BEE 4530: Computer-Aided Engineering of Biomedical Processes

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1. Executive Summary

One of the premier medical advancements in dentistry was the development of amalgam as a dental filling. The controversy surrounding the use of amalgam is the mercury content. Mercury is primarily used because of its malleability, which allows dentists to create a flexible compound to mold into the drilled cavity hole. However, mercury is highly toxic when absorbed by the body: high mercury levels in the body have been shown to cause serious health issues, such as neurological disorders, liver failure, and lung damage.

We investigated whether or not the concentration of mercury that diffuses out of amalgam dental fillings can reach toxic levels within the body. The diffusion of mercury from these fillings into the oral cavity was modeled in COMSOL Multiphysics as a 2D semi-ovular structure, with the mercury filling representing the sole source of mercury and the opening of the pharynx as the only exit for mercury from the oral cavity into the body. The respiration cycle (inhalation and exhalation) was assumed to only occur through the nasal cavity, establishing a 'purging' effect at the pharynx opening. The simulation accounted for the total mercury content that diffused from the filling and was ingested via the pharynx over a 24-hour period, which accounted for a wakeful at rest state, sleeping, and eating.

Once establishing the amount of mercury that was ingested for one amalgam filling, the diffusion from the average number of fillings in a patient was simulated. After a 24 hour period, the amount of mercury ingested was found to be 34.61 µg from one amalgam filling and 138.43 µg for the average number of four fillings per patient. The calculated amount ingested was then compared to previously published values to evaluate the safety of such fillings.

The total time it would take for the level of mercury ingested from amalgam dental fillings to reach toxic levels, which was defined as the amount of mercury needed to cause paresthesia, a disorder involving numbness and tingling that is a characteristic trait of mercury poisoning, was also subsequently calculated. Using the threshold of 40 µg mercury, the time it would take to reach toxic levels was determined to be 3.16 years via mercury diffusion from one filling, or 0.792 years via mercury diffusion from the average number of fillings. The toxic levels were previously established by the CDC and were used to further evaluate the safety of the fillings.

By simulating the diffusion of elemental mercury from amalgam dental fillings, we aim to add conclusive evidence to the mercury controversy and to make a definitive conclusion as to the safety of mercury based amalgam fillings and the concern about their toxicity.

2. Introduction

Amalgam has been used as a material for dental filling for more than 150 years, with over 100 million amalgam fillings implanted in patients in the United States annually. Recently, the use of amalgam fillings has declined due to the cosmetic advantages of composite resin fillings. However, in comparison to such resin fillings, amalgam is less expensive, stronger, and more malleable. These characteristics thus define amalgam as a more mechanically appealing material than resin to dentists. Amalgam is composed of 50% metallic mercury (Hg) and 50% alloy, with the alloy components consisting of 35% silver (Ag), 9% tin (Sn), 6% copper (Cu) and a trace of zinc (Zn)[1]. As mercury is a primary component of amalgam, there has been great controversy over the years regarding whether or not the presence of mercury in the oral cavity could ever cause physical harm to the patient.

In the original amalgam reaction, the mercury was bonded to tin via the (unbalanced) equation:

$$Ag_3Sn + Hg \rightarrow Ag_2Hg_3 + Sn_7Hg$$

Because tin can corrode easily, it could degrade almost instantly in the mouth environment. When the tin corroded, the tin-mercury complex became susceptible to disintegration, forming voids that could be filled with mercury vapor. If the vapors escaped and leached into the oral cavity, the patient had an increased risk for mercury poisoning. To prevent such corrosion from occurring, copper and zinc were added to the amalgam mixture, where in the new reaction, copper binds to tin and mercury binds to the silver. As silver is very resistant to corrosion, mercury becomes locked in a silver-mercury matrix, thus creating a more stable amalgam compound where few voids can form and little to no mercury can leach out. Many dentists believe this relatively new composition makes amalgam safer to use.

Nevertheless, recent experiments by Gay *et al.* and Berglund *et al.* have shown that mercury still leaches out of these modified amalgam fillings[2,3]. In two papers regarding the mercury concentration released from dental amalgam, Vimy *et al.* reported that a large percentage of total daily mercury intake was due to such fillings[4]. However, studies by Olsson *et al*., Bergman *et al*., and Mackert *et al*., have independently concluded that experiments such as those conducted by Vimy *et al*. overestimated the amounts of mercury in the oral cavity, as the researchers failed to recognize that mercury vapor release is time-dependent, not constant [5,6,7].

Despite the fact that previous research has examined the diffusion of mercury from amalgam fillings and has evaluated any subsequent toxic effects, the limitations of these past studies have generated more questions about the potentially harmful effects of amalgam fillings and thus warrant an improved methodology for determining the health risks of mercury-based amalgam fillings. Therefore, the purpose of our project was to determine the actual amount of mercury released from such fillings and if the amount ingested by the body ever reaches toxic levels. This was done by to modeling the release of mercury from an amalgam filling as a function of time using COMSOL Multiphysics.

3. Design Objectives

Our ultimate goal was to quantify the amount of elemental mercury vapor ingested via the pharynx following its release from an amalgam dental filling over a 24-hour time period. During this 24-hour period, three scenarios were modeled to simulate normal daily activities: an awake, at rest state (with no labored breathing due to strenuous activity), eating (for a total of two hours a day), and sleeping (for eight hours). The total concentration of mercury released within the 24 hours was then extrapolated to determine the time it would take for mercury released from a single amalgam filling to reach toxic levels within the body. A simulation was also run for an oral cavity with four amalgam fillings, instead of only one, to evaluate the amount of mercury ingested from the average number of fillings. The results obtained can be further utilized to evaluate the safety and efficacy of mercury-based amalgam fillings for use in human dental practices.

3a. Problem Schematic

Although the entire oral cavity is somewhat elliptical in shape, this model solely analyzed the diffusion and consequent ingestion of mercury vapor into the air within the open space of the cavity. Therefore, as shown in Figure 1A, only the non-shaded region of the oral cavity, representing the available open space not occupied by the teeth or tongue, was considered as the solution domain, as depicted by Figure 1B.

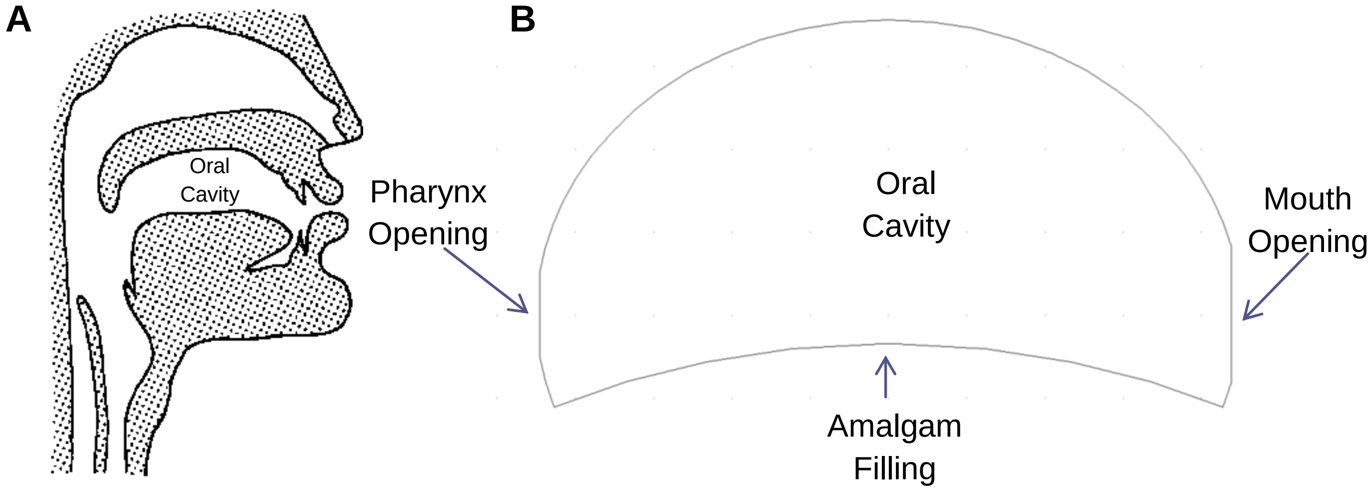

Figure 1: A. Physiological context of the geometry used; a coronal section of the oral cavity containing an amalgam dental filling[8]. B. Overall schematic of the problem geometry, not drawn to scale. The domain analyzed is the open-air region of the oral cavity; the space occupied by the teeth and tongue was not considered.

The oral cavity was modeled as a 2D semi-ovular structure in Cartesian coordinates with the bottom curve (boundary) representing the length of tongue as it normally sits within the mouth and two inlet and outlet holes at opposite ends of the domain, with one serving as the opening of the mouth and the other as the opening of the pharynx. The amalgam filling was modeled as a boundary within the bottom curve of the domain. As the teeth sit at approximately the same level as the tongue within the oral cavity, the amalgam filling boundary can be depicted at this location.

3b. Governing Equation

The release of mercury vapor from an amalgam dental filling was modeled as a 2D problem in Cartesian coordinates with diffusion terms only, using the following equation:

$$\frac{\partial c}{\partial t} = D_{Hg}\left(\frac{\partial^2 c}{\partial x^2} + \frac{\partial^2 c}{\partial y^2}\right)$$

As the conditions describing the sleeping state and the awake, at rest state are identical, the 24-hour simulation was divided into two separate models. The first scenario/simulation included the eight hours of sleep and 14 hours of the awake state, while the remaining scenario modeled two hours of eating. Therefore, different boundary conditions were used to accurately characterize the physical phenomena that occur during each activity. Further descriptions of the above equation and the boundary conditions used can be found in Appendix A.

4. Results

As mentioned above, the model of mercury diffsuion from amalgam dental fillings was simulated in COMSOL for a 24-hour period in two separate iterations. The first scenario simulated was a 22-hour period of a restful awake state and sleep state, followed by a simulation of a two hour period of eating. These results were combined to obtain the final quantity of mercury that was released and ingested from a filling after 24 hours.

In the first simulation, the mercury content from one amalgam filling was modeled, with the normal parameters and conditions implemented, as described in Table 1, Appendix A. Under these conditions, $D_{Hg,\ air} = 1x10^{-5}$ [m^2/s][9]. Upon running the simulation, the following surface plot, Figure 2, was obtained. This figure is a representation of the concentration gradient after 79200 seconds (22 hours), which simulates the average time an individual spends asleep and in an awake, restful state.

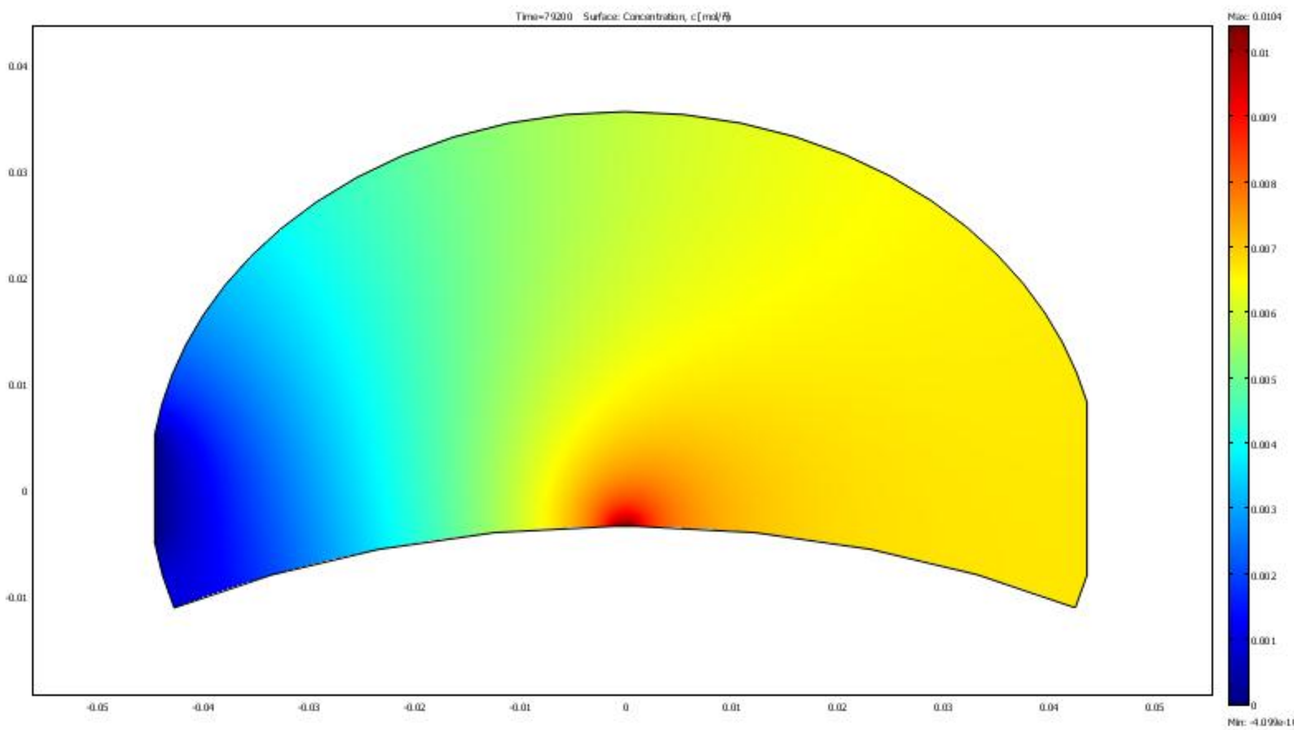

Figure 2: Surface plot of mercury diffusion in the oral cavity at the end of a 22-hour simulation period for an awake, at rest state and sleeping.

In the above solution, the purging phenomenon of mercury at the pharynx boundary can be seen (Figure 2). The concentration of mercury is lowest (blue) at the pharynx and highest at the amalgam filling boundary (red). The mercury diffuses throughout the oral cavity, as noted by the yellow coloring, which indicates a moderate mercury accumulation; yet near the pharynx boundary exit, the mercury concentration decreases to 0.

The simulation also produced a negative concentration shown to be -4.07×10^{-10} g/m^2. Because the time between one inhalation and exhalation is so small (2.5 seconds), the flux of mercury at the boundary does not have enough time to fully go to 0 during exhalation[11]. As a result, a very negligible negative concentration is observed during an exhalation breath at a point during the very beginning phase of the simulation. If the breathing cycle were longer, the flux would have time to reach 0 g/m^{2}s, and the minimum concentration would be a realistic 0 g/m^3. To eliminate and minimize its magnitude, a high mass transfer coefficient (1000 m/s) was used.

The total amount of mercury ingested after 79200 seconds was then found using COMSOL's integration methods. The total amount of mercury [g/m^2] released was plotted against time, as seen in Figure 3.

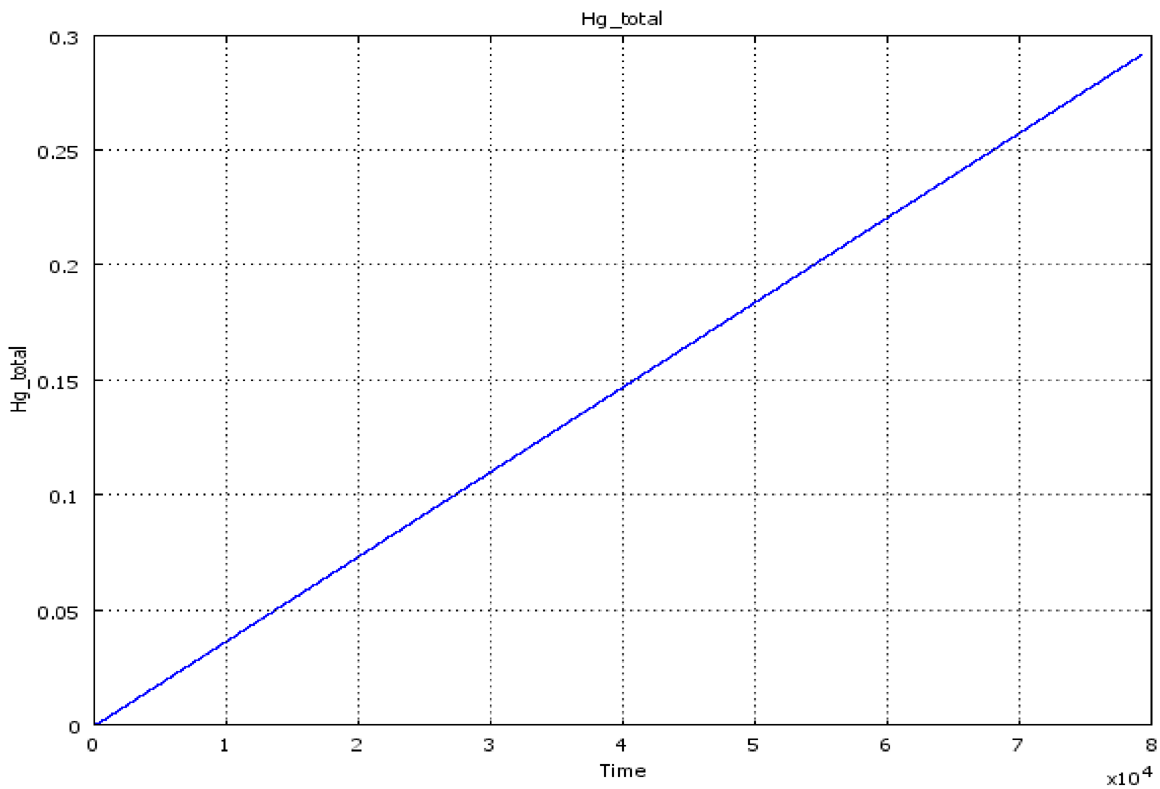

Figure 3: Plot of total amount of mercury [g/m^2] as a function of time for the 22-hour awake and sleeping portion of the simulation.

The concentration of mercury at the end of the simulation (79200 seconds) was obtained from the above graph and calculated to be 0.2914g/m^2. As detailed in the Solution Strategy section of Appendix B, this amount of mercury, in the COMSOL generated units of g/m^2, which was ingested during the 79200 second simulation, was used as the initial concentration for the next simulation involving eating.

The 2-hour period (7200 seconds) representing the average amount of time spent eating was modeled by increasing the diffusivity from 1×10^{-5} m^2/s to 5×10^{-5} m^2/s, to simulate the increase in the release of mercury due to chewing. The results can be seen with the surface plot, which displays the concentration gradient found within the oral cavity at time t=86400 seconds, which is the complete, 24-hour period – the 22 hour simulation and the 2 hour simulation combined (Figure 4).

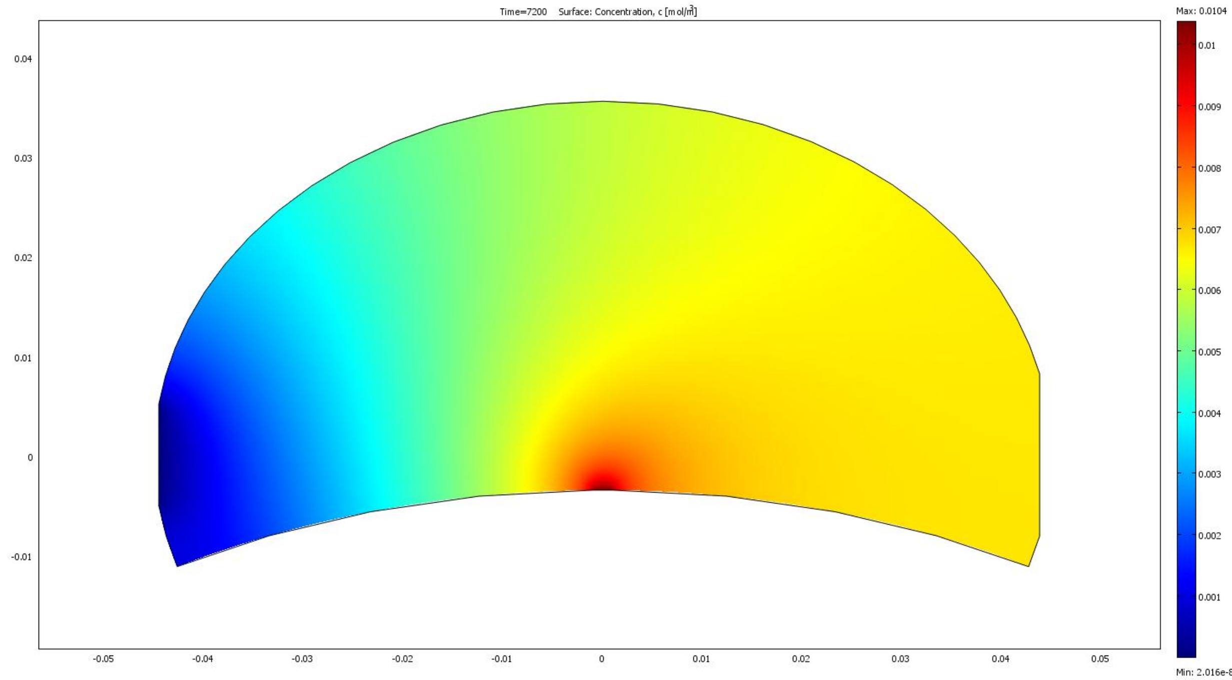

Figure 4: Surface plot of mercury diffusion in the oral cavity at the end of 7200 seconds (2 hours). For eating, the diffusivity was increased to $5x10^{-5}$ m^2/s.

Similar to the 22-hour simulation, the diffusion of mercury throughout the oral cavity can be seen. The highest concentration of mercury that diffused out of the filling is seen directly above the amalgam boundary (red). The concentration of mercury near the pharynx is the lowest (blue), as the result of the purging effect, which is detailed in the Boundary Conditions section of Appendix A. The negative concentration that appears again is a result of the rapid breathing cycle in humans.

In order to obtain the final content of mercury ingested at the end of the 24-hour period, an Hg_total vs. Time plot was again generated (Figure 5). Again, as detailed in Appendix B, the final data point at time t=7200 seconds was used to determine the final mercury content ingested in grams. The plot, as seen in Figure 5**,** shows how the mercury content increases as time progresses, with the initial point beginning at the final point from Figure 3.

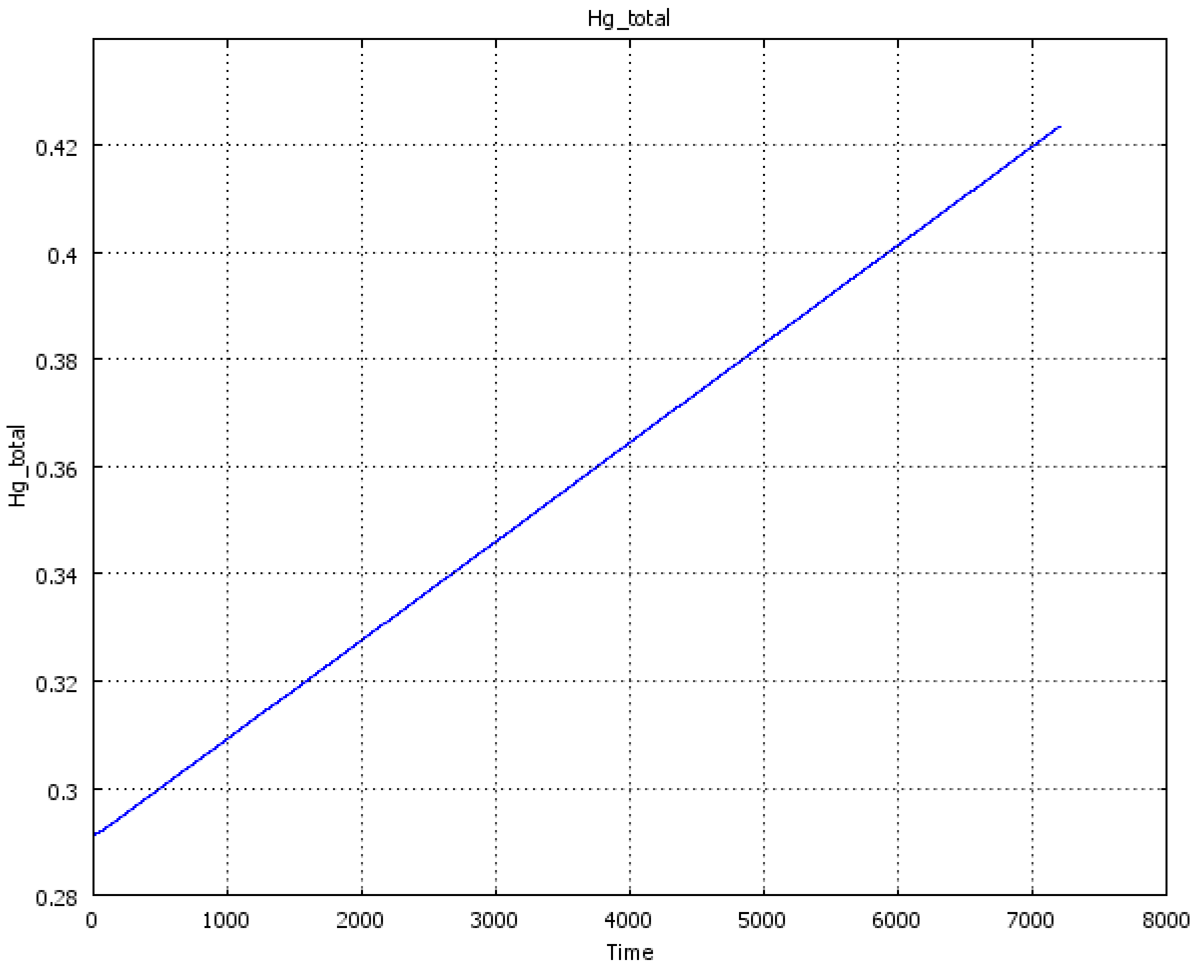

Figure 5: Plot of mercury content [g/m^2] vs. time [s] for the 2-hour eating portion of the simulation.. The amount of mercury ingested after 7200 seconds is 0.42355 g/m.[2]

From Figure 5, the procedure detailed in Appendix B was used to obtain the final quantity of mercury ingested. The final amount of mercury ingested after a 24-hour period was calculated to be 34.61 µg.

After simulating the diffusion of mercury from one amalgam dental filling, the initial concentration of mercury (for details, see Boundary Conditions, Appendix A) was modified to account for the average number of fillings in a patient. As the average person has four dental fillings, the concentration of mercury from one filling was multiplied by four to yield the new concentration[10]. The simulation was run following the previously described protocol for 24 hours. The scenario for the 22 hour sleep/resting state was first run, with the surface plot, Figure 6, generated to show the diffusion of mercury from the filling boundary. Again, the mercury can be seen leaching from the amalgam filling (red) and diffusing throughout the oral cavity. In the same manner, the pharynx boundary condition exhibited a “purging effect,” as seen from the minimum concentration (blue).

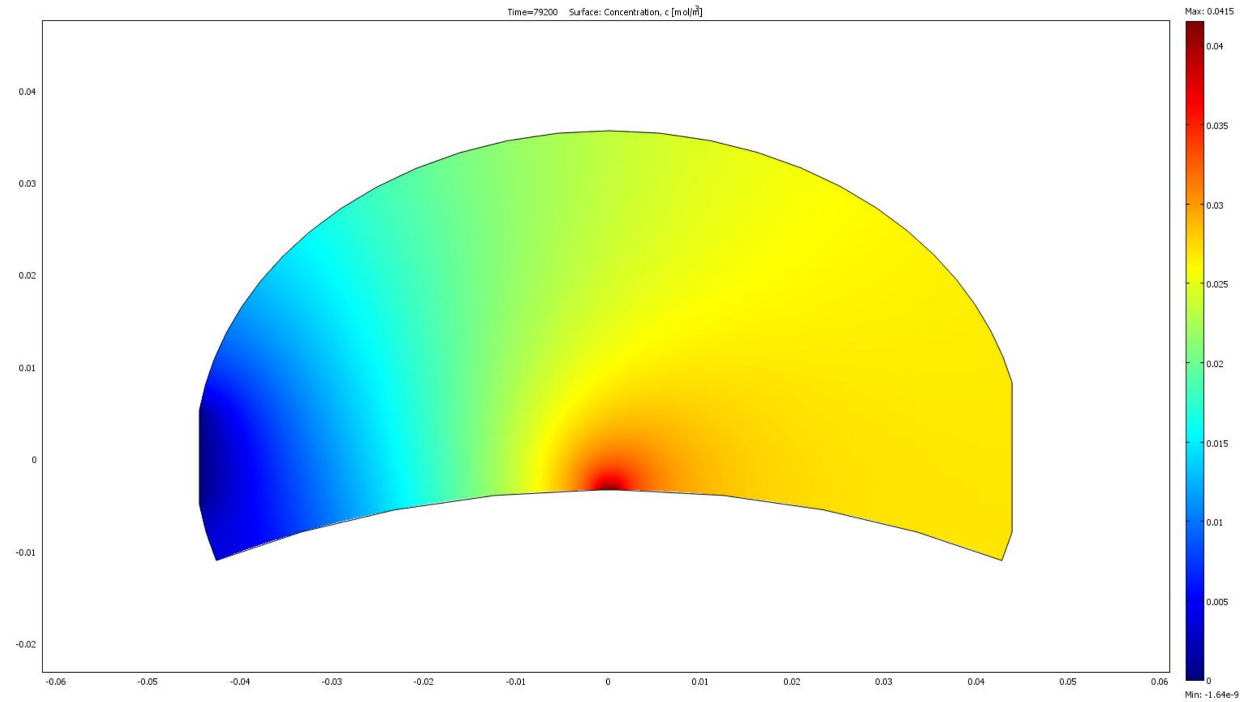

Figure 6: Surface plot of mercury diffusion from four amalgam fillings into the oral cavity after a 22-hour simulation of the awake/sleep states.

As the same boundary conditions were implemented (Appendix A), a plot similar to Figure 2, where only one filling was modeled, was obtained (Figure 6). However, the 22-hour simulation for four fillings yielded a greater maximum mercury concentration, 0.0415 g/m^2, as opposed to the 0.0104 g/m^2observed for one filling after 22 hours.

A similar issue of the small negative concentration had to be addressed in the simulation of the four amalgam fillings. As in the simulation of one filling, the process produced a minimum concentration of $-1.648x10^{-9}$ g/m^2. Again, a high mass transfer coefficient (1000 m/s) was used to decrease the magnitude of this negative value. The short time between an inhalation breath and an exhalation breath creates this negative concentration during a the beginning of the simulation. If the breathing cycle were longer, the flux would have time to reach 0 g/m^2s, and the minimum concentration would be a realistic 0 g/m^3.

After running the simulation for the 22-hour period, the resulting Hg_total vs Time plot was used to obtain the new initial condition for the remaining 2-hour simulation (Figure 7).

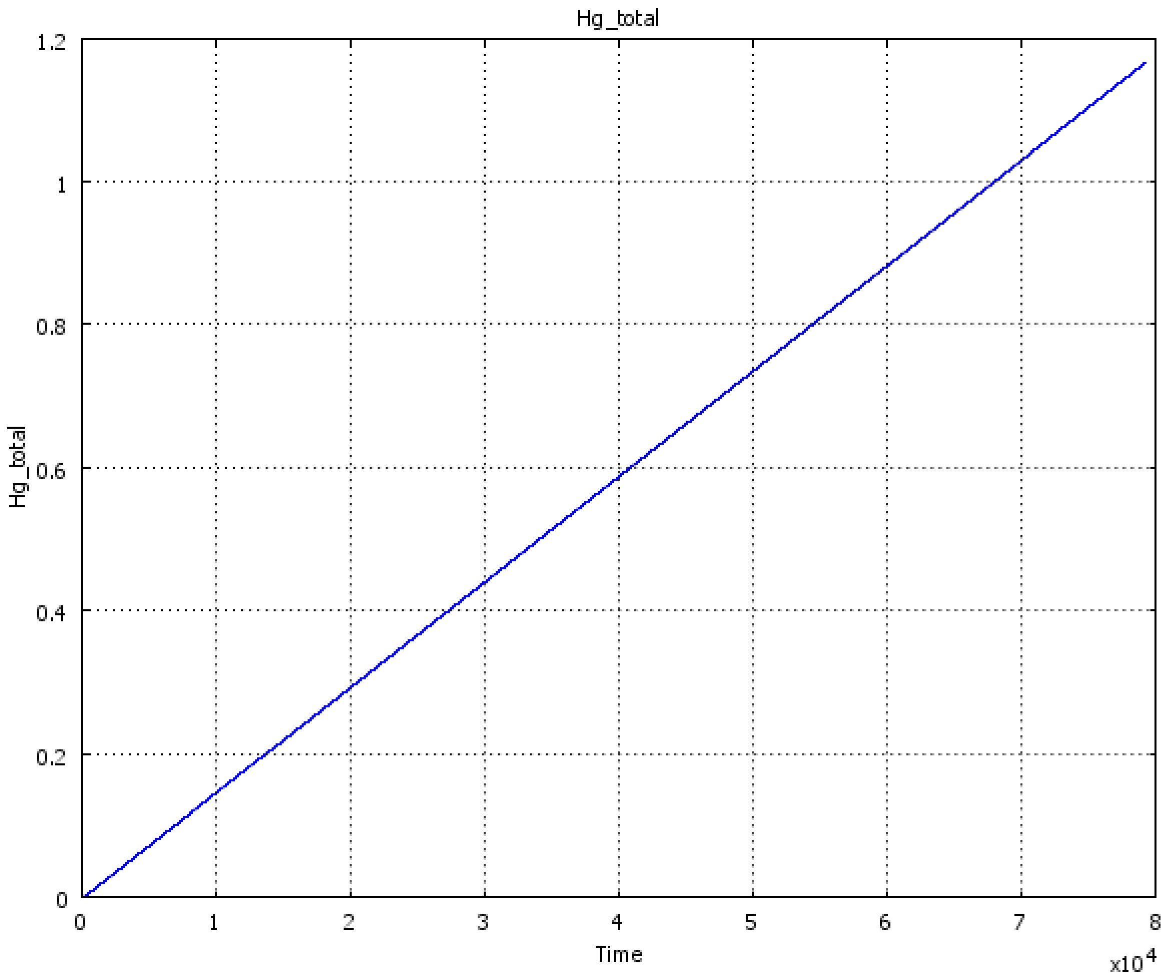

Figure 7: Plot of total amount of mercury [g/m^2] as a function of time for the 22-hour awake and sleeping portion of the simulation for a patient with four amalgam dental fillings.

Once more, the final value of the 22-hour simulation was implemented in COMSOL as the new initial condition for the simulation of two hours of eating (Figure 7). As before, in order to simulate the higher diffusion rates of mercury due to eating, the diffusivity was increased from $1x10^{-5}$ m^2/s to $5x10^{-5}$ m^2/s, and the model was run for 7200 seconds (2 hours). The final concentration gradient shown in Figure 8 after a total of 86400 seconds, or the complete 24 hour period, depicts the effects of mercury diffusion in the oral cavity from four amalgam fillings.

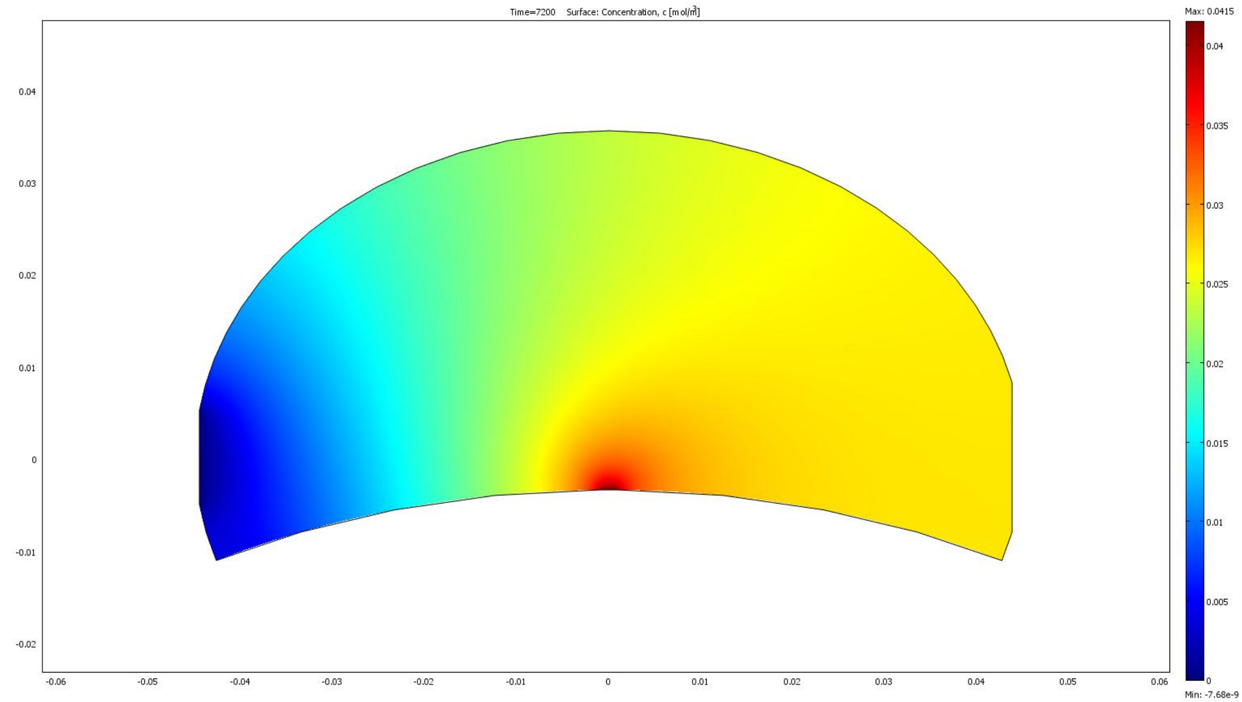

Figure 8: Surface plot of mercury diffusion in the oral cavity at the end of 7200 seconds (2 hours). Diffusivity was increased to $5x10^{-5}$ m^2/s.

As seen above, the mercury concentration is again greatest near the amalgam boundary (red) and lowest near the pharynx opening (blue), again, as a result of the purging effect detailed in the Boundary Conditions section of Appendix A. As a higher initial concentration was used to simulate the effects of four dental fillings, the maximum concentration obtained in this surface plot is 0.0415 g/m^2.

To obtain the final amount of mercury ingested in grams, the Hg_total vs. Time plot, Figure 9, was obtained in the same manner as with the single amalgam filling simulation. The data point at the final time of 79200 seconds was used as the initial condition for the remaining 2-hour simulation of eating (Appendix B).

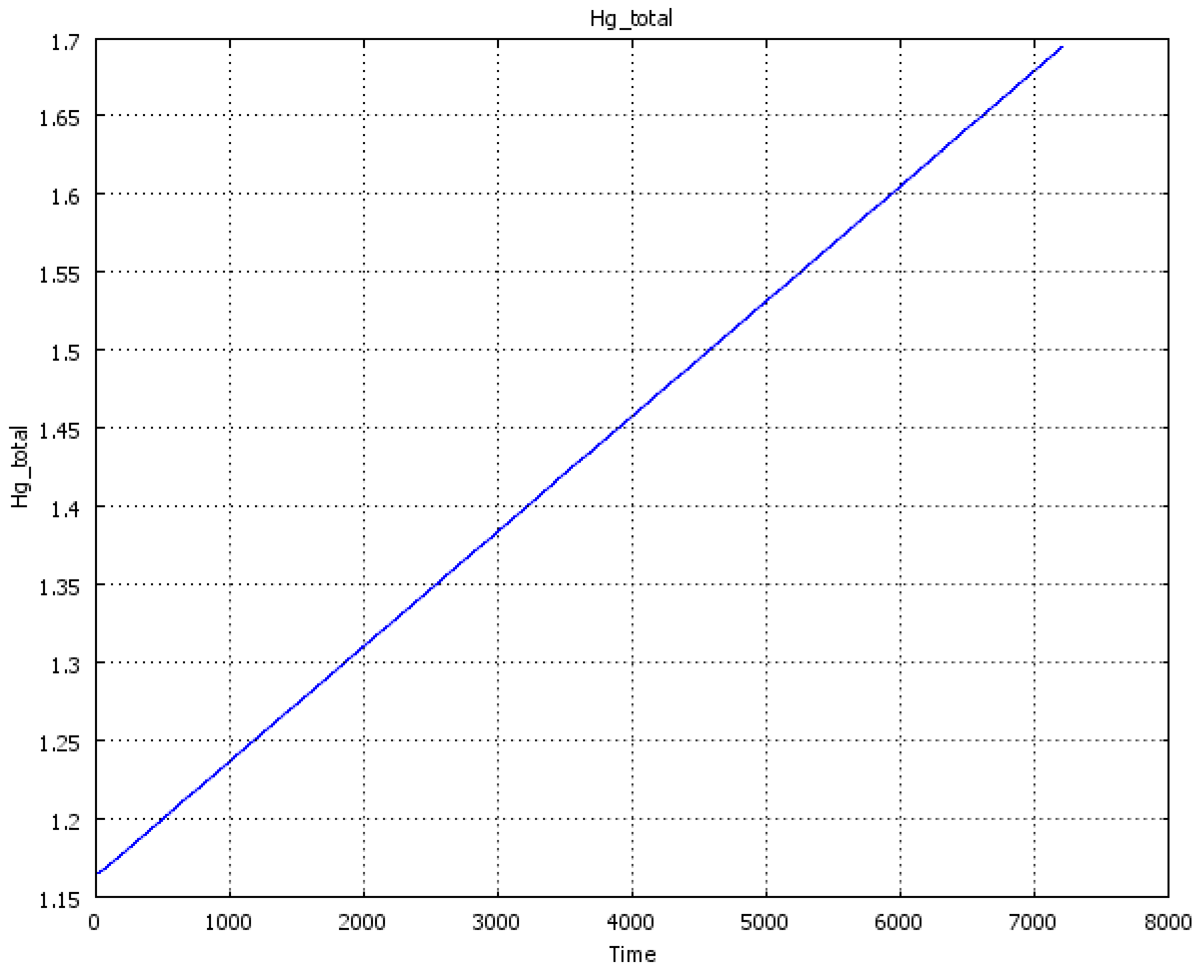

Figure 9: Plot of total amount of mercury [g/m^2] as a function of time for the 2-hour eating portion of the simulation for a patient with four amalgam fillings.

From Figure 9, the amount of mercury ingested from four amalgam fillings after 24 hours was calculated to be 138.43 µg.

To fulfill the second aim of the design objectives, the time for the mercury content to reach toxic levels in the body was determined. These times were extrapolated using the calculated amounts of of mercury that accumulated in the body after 24 hours and the government established toxic levels of mercury. Using the widely accepted threshold value of 40 mg, the amount of ingested mercury that can cause paresthesia, a primary effect of mercury poisoning, it was determined that it would take 27737.65 hours, or 3.16 years, to reach these levels within the body when using the accumulation of mercury from one filling[21]. Alternatively, if the mercury content ingested from the four amalgam filling simulation was used as the foundation for extrapolation, it was found take only 6934.91 hours, or 0.792 years to reach this toxic threshold.

4a. Discussion

This simulation of mercury diffusion from an amalgam dental filling revealed that 34.61 µg of mercury diffuses and is ingested from such a filling within 24-hour period where 22 hours are allotted to sleep and a restful awake state and two hours devoted to eating. When the initial concentration of mercury was increased to account for the average number of fillings per person, a large increase, from 34.61 µg to 138.34 µg, in the amount of mercury ingested, as expected, was calculated.

While the assumptions used to implement the model of mercury diffusion were validated, several aspects of the model lack realistic parameters. For example, in order to simplify the diffusion equations, the diffusion of mercury into the teeth, tongue, and tissues lining the cavity were ignored. An improved model should account for the diffusion into other tissues and the different ways in which the mercury could subsequently be degraded or absorbed. Similarly, the effects of convection from saliva and air-flow were ignored. Other simplifications of the geometry included ignoring the possible escape of mercury vapor through the mouth while talking or eating; this rather unrealistic assumption would likely significantly decrease the obtained quantity of mercury ingested. Moreover, breathing was assumed to occur solely through the nasal cavity, whereas individuals often breathe through both their nasal cavities and mouth. Similarly, alterations in breathing rates due to exercise or exertion were ignored, thus leading to additional inaccuracies. Lastly, as this simulation was performed for only a one-day (24 hour) time span, the long-term effects that saliva, food, and oral hygiene products may have on mercury release were also neglected. Therefore, several aspects of this model could lead to inaccuracies and an over-estimation of mercury accumulation in the body.

While it appears that the toxic levels of mercury are reached within a relatively brief period of time in comparison to the lifespan of a human being, several of the previously described assumptions lead to the conclusion that these are not very accurate numbers. Because the described factors do not account for the degradation of mercury over this longer period of time, nor does the model account for the escape of mercury through the mouth, the calculated values of mercury and the consequent time it takes to reach toxic levels, are considerably exaggerated.

4b. Validation

In order to ensure the accuracy of the model and the parameters implemented, a professional dentist was consulted. Dr. Matthew Ghadami, DDS, described the dimensions of the drills used in treating cavities, which were subsequently used to calculate the volume of an average amalgam filling[12]. The composition of mercury itself was compared to several literature and industry values, but as copyright laws prevent the precise acquisition of these values, general amalgam composition data was utilized[1]. Although content percentages vary slightly, the vast majority of amalgam fillings contain a ratio of 50% mercury to 50% alloy[13].

The parameters used in this study were validated by previous investigations. Literature values for the dimensions of the pharynx opening, mouth opening, and tongue length were implemented into the model, as listed in Table 1, Appendix A. The diffusivity of mercury vapor into air was approximated as the diffusivity of water into air. As the diffusivity of mercury vapor listed in *Biological and Bioenvironmental Heat and Mass Transfer*, by A.K. Datta is 1.3×10^{-5} m^2/s, this was also considered a validated approximation[9].

The increase in diffusivity during the eating portion of the simulations was validated via several assumptions and considerations. It was expected that the additional stresses and compressive forces inherent to the eating process would alter the diffusion rate of mercury into the oral cavity. Because the model did not directly take into account the mechanical effects of chewing via convection, etc., the alterations in mercury release had to be encompassed by an increase in diffusivity. Through trial and error, the fivefold increase is justified: higher values of diffusivity yielded results that were not comparable to previously published values.

To further validate the results of the model, the mercury content ingested in a 24 hour time span was compared to literature values. Previous experiments have shown a large range of values for the average amount of mercury that is released per surface per day. Mackert, et al, conducted an analysis of several previous studies and compared them to their investigation, and demonstrated that diffusion rates per surface per day ranged from 0.73 µg/day to 19.7 µg/day[7]. However, they claimed these large values grossly overestimate mercury diffusion and do not account for the numerous physiological mechanisms that would decrease the value, such as mercury escape through the mouth. They concluded that their rate of 0.4 µg/day was more realistic[7].

Berdouses also reported that the steady state diffusion of mercury from one filling per day was even lower at a rate of 0.03 µg/day[14]. Moreover, other literature values have cited the amount of mercury ingested as 24.81 µg, which is more comparable to the obtained amount of mercury from one dental filling[15]. Therefore, the obtained value of 34.61 µg for the mercury released and ingested in the COMSOL model is on the higher range of literature values for the release rate per surface per day; however, given the highly diversified nature of the investigations of the release rates, our model remains valid.

4c. Sensitivity Analysis

To perform a sensitivity analysis, the diffusivity of mercury into air ($D_{Hg, air}$) and the convective mass transfer coefficient (h) were varied within twenty percent of their original value. The other parameters used in the model are anatomical values that do not change within the one human patient that is being modeled. As a twenty percent variability is often seen in biological properties, the two parameters were varied at 10 and 20 percent above and below the original value (0%).

The sensitivity analysis was performed by varying one parameter, either the diffusivity or the mass transfer coefficient, and maintaining all of the other values constant. The content of mercury ingested in the body at the end of the 24-hour simulation was the quantity used to determine the sensitivity of the model in response to the varied parameters. The sensitivity of the mercury content ingested after the 24-hour simulation is displayed in a bar graph for each of the varied parameters (Figure 10).

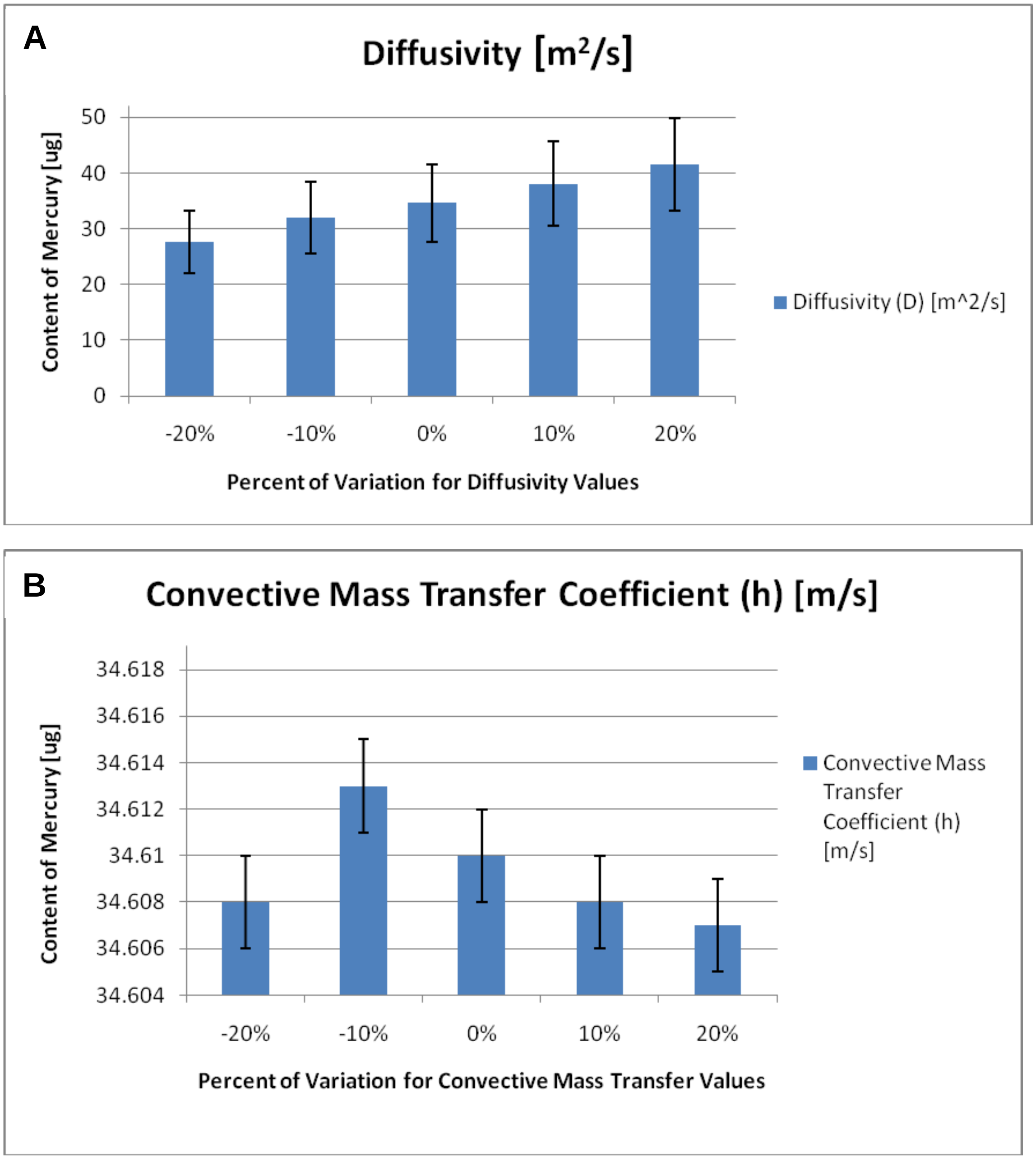

Figure 10: Sensitivity analyses plots for A. the diffusivity of mercury vapor into air, and B. the convective mass transfer coefficient of mercury vapor into air.

The first graph (10A) of the varied diffusivity values demonstrates that the final amount of mercury ingested in the body over a 24-hour period is highly dependent on the value of diffusivity. As the diffusivity value is increased or decreased by a given percentage, the amount of mercury increases or decreases, respectively, by the same ratio. For example, a 10% increase in diffusivity yields an addition of 3.47 µg of mercury ingested, which is 10% of the original quantity ingested. However, varying the heat transfer coefficient (10B) changed the mercury content ingested negligibly. Therefore, the model, and the amount of mercury ingested from amalgam dental fillings, is very sensitive to changes in diffusivity but fairly insensitive to the value of the mass transfer coefficient.

5. Conclusions

In conclusion, the model implemented above can serve as a fundamental tool in both clinical and industrial settings to evaluate both the health risks of a patient with amalgam dental fillings and the safety or toxicity of manufactured amalgam formulas. Our results suggest that approximately 34.61 µg of elemental mercury is ingested by a patient with one amalgam dental filling within a 24-hour time period and that about 138.43 µg is ingested by a patient with 4 fillings. Using the widely accepted data regarding the toxic threshold of mercury within the body (40 mg), it was determined that it would take 3.16 years for the mercury ingested from one filling to reach toxic levels and 0.792 years for mercury from four fillings to do so[21]. These high values and short times can be attributed to the number of assumptions that were implemented throughout the design of the model. However, although these values appear a bit unrealistic, this method of simulating the diffusion of mercury into the oral cavity allows for more control and flexibility than other models and experiments. While previous studies were often limited to complex and variable methods of evaluating mercury content, which sometimes involved the use of invasive probing or measurement techniques on the animals or patients studied, our model's parameters can easily be modified to account for any variation, complex scenario, patient lifestyle, or any other number of considerations.

5a. Design Recommendations

In order to make our model as physiologically relevant as possible, it should be modified to account for the limitations addressed in the Results and Discussion section. That is, the diffusion of mercury into the tissues of the oral cavity, the convection within the oral cavity due to saliva and air-flow, and the effects that certain foods and oral hygiene products may have on the rate of mercury release, should all be examined. Breathing through the mouth, the escape of mercury through the mouth during eating, talking or breathing, and changes in breathing rate due to various activities and the consequent changes in pharynx diameter that occur, should also be taken into consideration. Additionally, in order to study the change in amalgam composition as mercury is continually released from a filling over an extended period of time, and the resulting effects that such changes could have on mercury release rate and ingestion, the filling could be implemented as a separate subdomain within the model geometry, rather than as a simple boundary with a constant concentration. Improvements such as those described should provide a more accurate depiction of mercury diffusion from amalgam fillings and the subsequent accumulation of mercury in the body.

5b. Constraints

Despite the fact that the results obtained from our current model ultimately conclude that amount of the mercury ingested from such fillings can eventually reach toxic levels within the body, these values are still somewhat unrealistic, as our model assumes that all mercury released from the filling(s) is ingested and remains within the body. As mentioned above, the loss of the mercury vapor from talking, eating, and breathing through the mouth is not considered, nor are the mechanisms of how the body filters, detoxifies, and excretes ingested mercury. However, if the suggested design recommendations were implemented and the model was made more physiologically realistic, and the resulting values obtained still reached dangerous levels, the health and safety of the general public and the consequent course of action would have to be evaluated. Physical studies, which are expensive, time consuming, and often yield variable results would have to be conducted. Safe and inexpensive procedures for the removal and replacement of amalgam dental fillings would have to be developed and made readily accessible to all people with such fillings, and/or the possible re-formulation of amalgam compositions would have to be considered. Nevertheless, regardless of the future possible clinical and industrial implications, our current model is an inexpensive and efficient method for analyzing the safety of various amalgam compounds and an invaluable diagnostic tool for determining whether or not someone is at risk for mercury poisoning due to his or her amalgam dental fillings.

Appendix A: Mathematical Statement of the Problem

Governing Equation

$$\frac{\partial c}{\partial t} = D_{Hg}\left(\frac{\partial^2 c}{\partial x^2} + \frac{\partial^2 c}{\partial y^2}\right)$$

A 2D mass transfer equation in Cartesian coordinates solely with diffusion terms was used to solve the model. Because the model was run for only a 24-hour period, no reaction term was included, as the reaction rates of mercury with various foods and oral hygiene products is negligible within such a short time frame. Convection due to air and saliva were ignored, due to low velocities.

In both the above equations and the boundary conditions to follow, c is the concentration of mercury within the oral cavity and/or body and D_{Hg} is the diffusivity of elemental mercury vapor into air. This diffusivity value was increased while modeling the eating portion of the simulation to take into account the increased release of mercury during chewing, as further detailed in the Parameters section.

Initial Condition

$$c_{Hg,mouth} = 0\frac{g}{m^3}$$

Initially, it was assumed that no mercury was present within the oral cavity prior to diffusion.

Boundary Conditions

Because two different scenarios were being considered and modeled, different boundary conditions were implemented at different points within the simulation via the use of Boolean expressions. In all cases, breathing (both inhalation and exhalation) was assumed to occur solely through the nose. During the eating portion of the simulation, it was assumed that swallowing only occurred during inhalation. The boundaries lining the remainder of the oral cavity were insulated.

Mouth opening boundary:

$$Flux_{mouth} = 0$$

Both inhalation and exhalation occurred solely through the nose. It was assumed that no mercury was released during the opening of the mouth while eating, and that no additional mercury entered the oral cavity via the mouth.

Pharynx opening boundary:

$$Flux_{pharynx} = -1000 * c * (\sin(\frac{\pi t}{2.5}) < 0)$$

When air is inhaled through the nose and travels down the airways at a high velocity, a "purging effect" occurs at the opening of the pharynx, as characterized by a convective boundary condition with a high mass transfer value (1000 m/s). This quickly flushes air and any mercury present near the opening of the pharynx out of the oral cavity and into the lungs. Because this "purging effect" only occurs during inhalation, a Boolean expression was used to distinguish between inhalation and exhalation and to assign the appropriate corresponding condition. One complete breath takes approximately 5 seconds, with both inhalation and exhalation lasting about 2.5 seconds each[11]. Because inhalation and exhalation are a continuous, cyclic process, a sine function was implemented in the Boolean expression. During exhalation (sin(πt/2.5) > 0), the boundary condition is $Flux_{pharynx} = 0$; during inhalation (sin(πt/2.5) <0), the convective boundary condition is activated ($Flux_{pharynx} = -h * c$). To allow for mercury accumulation within the oral cavity before being purged, exhalation was simulated first, followed by inhalation.

Amalgam filling boundary:

$$c_{Hg} = 0.01037 \frac{g}{m^3}$$

Because noticeable changes in amalgam composition only occur over extended periods of time, the boundary at the filling surface is defined as a constant concentration, as determined through a series of calculations relating the partial pressure of mercury to concentration. Mole fraction calculations and Raoult's Law were used to obtain this concentration value.

The composition of a standard amalgam filling was found to contain 50% Hg, 34.65% Ag, 8.95% Sn, 5.9% Cu and 0.5% Zn[1]. The average dimensions of a standard amalgam filling are 3mm x 2mm x 2mm[12]. Therefore, the total volume of amalgam used per filling is $12mm^3$. The density of amalgam was found to be 0.0108 g/mm^3. From these values, the mole fraction of mercury in an amalgam filling was calculated as shown below.

The mass of the amalgam filling was first determined from the equation:

$Mass = \rho V$, where ρ is the density of the amalgam and V is the volume of the filling.

$$Mass = 0.0108 \frac{g}{mm^3} * 12mm^3 = 0.1296\ g$$

The mass of the amalgam filling was then used to calculate the moles of each component using the equation below:

$$\frac{Mass * percentage}{MW} = moles\ of\ substance$$

Ag: $\frac{0.1296g * 0.3465}{107.87 \frac{g}{mol}} = 4.163 * 10^{-4} mol\ Ag$

Sn: $\frac{0.1296g * 0.0895}{118.71\ g/mol} = 9.77104 * 10^{-5} mol\ Sn$

Cu: $\frac{0.1296g * 0.059}{63.54\ g/mol} = 1.203399433 * 10^{-4} mol\ Cu$

Zn: $\frac{0.1296g * 0.005}{65.39\frac{g}{mol}} = 9.9097721 * 10^{-6} mol\ Zn$

Hg: $\frac{0.1296g * 0.50}{200.59\ g/mol} = 3.23047 * 10^{-4} mol\ Hg$

After calculating the amount of moles for each element in a filling, the mole fraction, x, defined by the equation below, was then calculated:

$$x = \frac{moles\ Hg}{moles(\ Hg + Zn + Cu + Sn + Ag)} = \frac{3.23047 * 10^{-4}}{6.442612053 * 10^{-4}} = 0.501422$$

Raoult's law, as follows, was then used to calculate the partial pressure of mercury from the saturation pressure of pure mercury multiplied by the above mole fraction. The saturation pressure of mercury was found to be 0.002 mmHg at 300K, which is fairly close to that of body temperature (310 K)[16].

$$P_i = P_{sat} * x = \ 0.002mmHg * 0.50142$$

Therefore, $P_{i,Hg}$= 0.001003mmHg = 0.1337 Pa

The mercury concentration, $c_{surf,Hg}$, was then found using the pressure obtained above (P_i) and the ideal gas law stated below. It was assumed that mercury vapor behaves as an ideal gas.

$$C_{surf,Hg} = \frac{P_i\ MW_{Hg}}{RT} = \frac{0.1337Pa * 200.59\frac{g}{mol}}{8.3145\frac{m^3Pa}{Kmol} * 310K} = 0.01037\ g/m^3$$

Dimensions and Input Parameters

Table 1: Dimensions and input parameters used for the model.

Parameter	Abbreviation	Value
Diameter of pharynx opening[17]	$d_{pharnyx}$	0.0102 [m]
Diameter of mouth opening[17]	d_{mouth}	0.017 [m]
Diameter of amalgam filling[12]	$d_{filling}$	0.002 [m]
Length of tongue[18]	L_{tongue}	0.01 [m]
Height of oral cavity[19]	H_{mouth}	0.071 [m]
Length of oral cavity[20]	L_{mouth}	0.09 [m]
Diffusivity of mercury vapor into air (awake and sleeping)[9]	$D_{Hg, air} \approx D_{water, air}$	10^{-5} [m^2/s]
Diffusivity of mercury vapor into air (eating)	$5*D_{Hg, air} \approx 5*D_{water, air}$	$5x10^{-5}$ [m^2/s]

The diffusivity of mercury vapor into air was approximated as the diffusivity of water vapor into air. This assumption was made because mercury does not regularly exist as a vapor, therefore its diffusivity is difficult to approximate. For the eating portion of the model, the diffusivity of mercury vapor into air utilized was increased to five times the value specified in Table 1. This was to approximate and simulate the increased release of mercury due to chewing. As this model solely focused on the diffusion of mercury vapor into the air within the oral cavity, the possible diffusion of mercury into the teeth, tongue, and tissue lining the cavity was ignored.

Appendix B: COMSOL Implementation and Solution Strategy

Solver

The release of elemental mercury vapor from an amalgam dental filling into the oral cavity and its consequent ingestion via the pharynx was modeled and implemented in COMSOL Multiphysics version 3.5a with the direct linear solver UMFPACK, which utilizes the direct finite element method for calculations.

Tolerance

The tolerance settings used are as follows:
Absolute tolerance: 0.0010
Relative tolerance: 0.01

Time Step

For the 22-hour awake/sleeping portion of the model, the simulation was run for 79200 seconds, with an initial time step of 0.00001 and a maximum time step of 1.25. Under the “Times” Solver Parameter (Solve>>Solver Parameters), the solver was instructed to start at 0 seconds, and save the solution every 5 seconds until the final time of 79200 seconds (0,5,79200).

For the 2-hour eating portion of the model, the simulation was run for 7200 seconds, with an initial time step of 0.00001 and a maximum time step of 1.25. Similarly, under the “Times” Solver Parameter (Solve>>Solver Parameters), the solver was instructed to start at 0 seconds, and save the solution every 5 seconds, until the final time of 7200 seconds (0,5,7200).

Mesh

In order to confirm that the results obtained did not depend on the complexity of the mesh used, convergence analysis was performed to determine the minimum number of mesh elements at which the results achieved mesh-independence and to ensure the greatest efficiency when running the model (Figure 11).

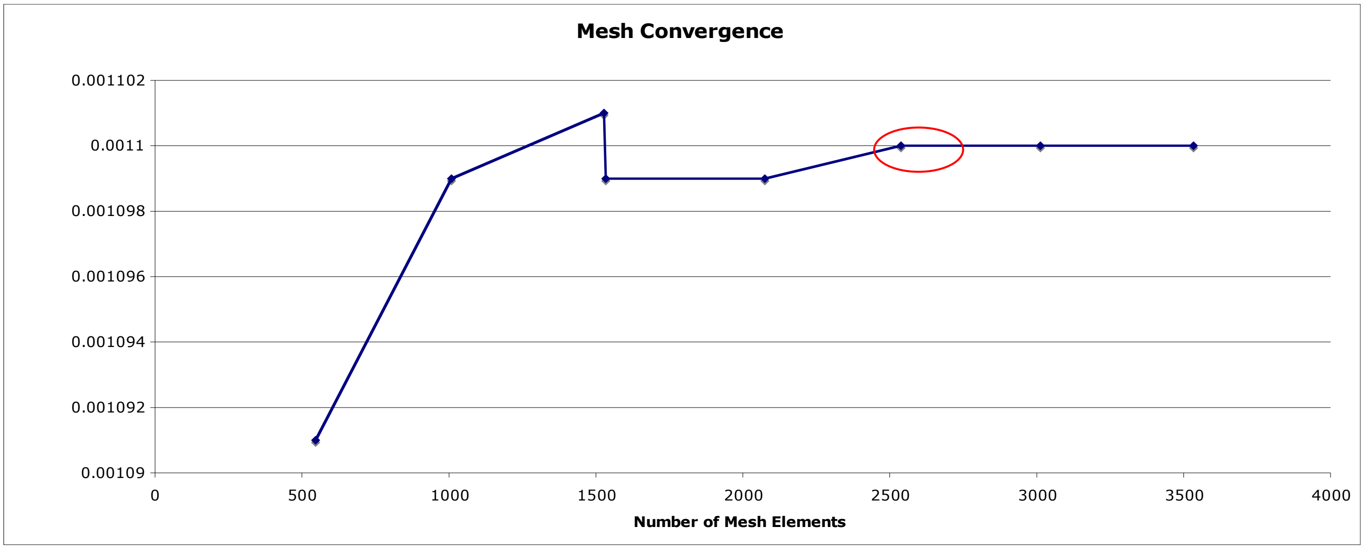

Figure 11: Plot of the average concentration of mercury vapor along the length of the pharynx after 24 hours for varying mesh sizes/complexities. The red circle identifies the mesh ultimately used for the solution of the model.

As the plot in Figure 11 depicts a fairly linear region that eventually levels off to a horizontal asymptote at an average mercury concentration of 0.0011 g/m^3 along the length of the pharynx, it can be concluded that mesh convergence was achieved once the geometry's mesh reached a minimum of 2583 elements. Therefore, this mesh was implemented in the actual solution process of our model (Figure 12).

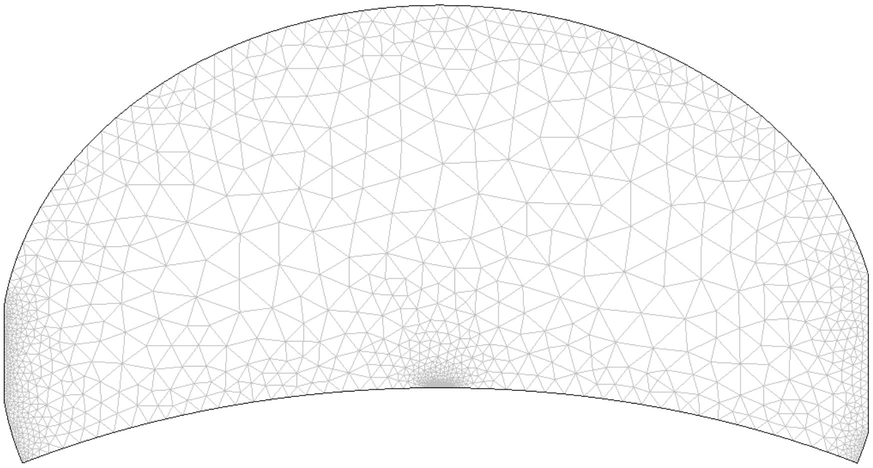

Figure 12: Diagram for the mesh implemented for the solution of the model.

Depicted above above, the final mesh used consisted of 2538 2D triangular elements.

Solution Strategy

The objective of the simulation was to obtain the content of mercury ingested after a 24 hour period of time. As the 22 hour simulation was run first, followed by the two hour simulation of eating, the solver was instructed to use the final solution obtained from the 22 hour simulation as the initial condition for the next stage of simulations.

In order to run the simulation in this manner, expressions for mercury content and flux had to be defined in COMSOL. Using the boundary integration method in COMSOL (Options>> Integration Coupling Variables>> Boundary Integration Variables), the quantity Hg_flux was defined by the expression ntflux_c_cd/0.01m, where nt stands for normal total flux, c stands for concentration and cd stands for the convection diffusion mode. The integration order was 4. This expression yields the flux in g/m^2s.

To determine the total mass of Hg ingested, the flux equation needed to be integrated in COMSOL**.** To obtain this value (Physics>>Global Equations), Hg_total was defined as the total mass of Hg passing through the pharynx. COMSOL solves the differential equation of $\frac{1}{A}\frac{dHg\_total}{dt} = flux = Hg\_flux$. In COMSOL, U=Hg_total; and Ut=dHg_total/dt = Hg_totalt. Therefore, the integration of Hg_flux multiplied by the area of the pharynx from 0-79200sec will give the total amount of mercury in grams. The expression then becomes Ut-flux=0.

The 22 hour simulation of sleep and a restful wake state was then run. After solving the simulation, post processing of the data was performed. Under the expression tab (Post Processing>>Global Plot Parameters>>Expressions), the quantity Hg_total was added to the list of quantities to be plotted, and the plot of Hg_total vs. time was obtained. The solutions at all times (0-79200 sec) were plotted. This gives all the data points of mercury content [g/m^2] for each time point in the simulation. The data set of points from the plot was exported as a text file.

The amount of mercury at time t=79200 seconds was found by multiplying the value by the area of the pharynx. This value was recorded and became the new initial condition for the next two hour (eating) simulation. The final value at the end of the 22hrs simulation was inputted as the initial condition (Physics>>Global Equations>>Initial Condition) for the programmed equation for recording flux. Under the Solver Manager options (Solve>>Solver Manager), the "Initial value expression evaluated using current solution" was selected under the "Initial Value" setting, and the solution at time t=79200 sec was selected. The "Current Solution" option was selected under the "Values of variables not solved for and linearization point" section, with the solution at time t=79200 sec selected. The "Store Solution" tab was selected and the time at t=79200 sec highlighted. This ensures that the two hour simulation uses the values and solutions from the last solution of the 22 hour simulation as the initial setting for beginning the simulation.

The simulation was then run for the two hour eating scenario, with the increased diffusivity value (Table 1, Appendix A), and the mercury content vs time graph obtained in the same aforementioned manner. The data was exported and the final concentration per unit area at the final time t=7200 seconds (and therefore, the quantity at the end of the 24 hour period) recorded. As this value has units of g/m^2, the value was multiplied by the cross sectional area of the pharynx to obtain the content of mercury in grams. Therefore, the final amount of mercury ingested in the body at the end of a 24 hour period was obtained in grams.

Lastly, the simulation results were rerun to determine the mercury ingested after 24 hours based on the average number of fillings in a patient. The initial concentration of mercury that was implemented (Physics>>Boundary Conditions) was changed to $4*c_{Hg}$, as the average number of fillings is four per patient. The aforementioned process was again repeated to obtain the final content of mercury after 24 hours.

Values for the time for the ingested mercury content to reach toxic levels were extrapolated based on the amount reached at the conclusion of the 24 hour simulation. A proportion was used to calculate the time to reach the established threshold of 40 mg mercury. By solving this equation, the time to reach the 40 mg was determined. The time was calculated for both the one amalgam filling simulation as well as the four amalgam filling simulation.

Appendix C: References

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