A Mathematical Approach to the Transfer of Lead in the Human Body

by

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I dedicate my thesis to my
beloved grandmother and childhood guardian, the late
Mrs. Dorothy Margaret Antonio Thompson
whose Christian values and words of wisdom will always
remain indelibly planted within my heart.

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ABSTRACT

The inherent interaction between mathematics and physiology is demonstrated by describing a physiological phenomenon in terms of first order differential equations. Specifically, this thesis discusses the kinetics of lead transfer in the human body by using a system of first order differential equations. The parameters involved are estimated from actual data obtained from a clinical study, and the mathematical model is then applied to specific cases, once solutions to the model are calculated.

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INTRODUCTION

The field of applied mathematics has made a considerable impact in understanding and modeling numerous biological phenomena, and it is rapidly becoming apparent that applied mathematics and physiology have a great deal to offer one another. Mathematics may be used to give insight into physiological questions, and physiological questions can, in turn, lead to new mathematical problems. Thus, it is in this sense, that mathematical science is inherently interdisciplinary.

To gain a deeper insight into biological models, it is necessary to have a knowledge of differential equations. With the knowledge of differential equations, scientists are in a position to begin an analysis of such physiological processes as the heart beat, nerve impulse transmission, and chemical reactions at the cellular level.

The physiology of lead in humans is currently a subject of considerable interest, primarily because of the potential toxicity of lead. This paper discusses the kinetics of lead, detailing how this chemical is transferred from the lungs and digestive tract through the blood and to the bones and tissues. The kinetics of lead in the human body is described by a system of first order differential equations, and parameters are then estimated from actual data. Finally, once solutions to the mathematical model are calculated, the model is applied to various cases.

In writing this thesis, it is the author's hope to show that the bridge between applied mathematics and biological science can be traveled, thereby demonstrating the inherent interaction between mathematics and physiology.

Chapter 1

OVERVIEW

Lead (Pb) is a chemical that is closely related to human life. Such products as gasoline, paints, PVC (vinyl) plastic, pipes, and ceramic glazes once contained lead, and nowadays, this heavy metal continues to be used in the production of batteries, ammunition, devices that shield X-rays, and computer monitors that block radiation (Children's Health Environmental Coalition, 2002). Lead is also found naturally in the soil environment (Children's Health Environmental Coalition, 2002). Unfortunately, this chemical is one of the most insidious environmental toxins that can have devastating consequences to the human body, especially in children (Kuhlman *et al.*, 1997).

High levels of lead intake have been known to cause various illnesses in humans. The observations of Hippocrates (380 BC) and Pliny the Elder (AD 23-79) have been documented by Hunter (1957). In later times, Bernardino Ramazzini (1714) and Sir George Baker (1941) described lead poisoning from various sources in people with differing occupations and habits (Barry, 1975). Further, a study conducted on the samples of President Andrew Jackson's hair from 1815 suggests that the former US President suffered from symptoms compatible with mercury and lead poisoning, as a result of his harboring two lead bullets and his frequent intake of mercurous chloride and sugar of lead prescriptions (Deppisch *et al.*, 1999).

The nervous system is the primary target of low level lead exposure which has the potential to inhibit oxygen and calcium transport, thereby altering nerve transmission in the brain (Natural Resources Defense Council, 2000). Lead accumulates in and damages mitochondria, the organelles mediating cellular energy metabolism (Lidsky *et al.*, 2003). Furthermore, a study conducted by White *et al.* found cognitive, attentional, and affective deficits in adults nearly fifty years later since childhood lead poisoning (1993).

Most lead intake occurs when people ingest lead chips, drink polluted water containing lead particles, or inhale lead dust produced by industrial waste and automobile exhaust (Natural Resources Defense Council, 2000). Foods such as fruits, vegetables, grains, seafood, and soft drinks may contain a significant amount of lead, and the second-hand smoke from certain cigarettes may also contain small amounts of lead (Natural Resources Defense Council, 2000). Once lead enters the gastrointestinal tract or the lungs, it is taken up by the red blood cells and rapidly distributed throughout the body (Borrelli and Coleman, 1987). The lead is gradually absorbed by such soft tissues as the liver, kidneys, bone marrow, and brain, and high concentrations can slowly accumulate in the bones (Natural Resources Defense Council, 2000). Although the slowest uptake occurs by the bones, it is reported that "in the steady state the skeleton carries 90% or more of the body burden of lead" (Castellino and Aloj, 1964). Gwiazda *et al.* further notes that over 70% of the lead burden in children is contained within the skeleton (2005). Such a consequence is due to the fact that lead is a biological analog to calcium, a natural chemical that the body needs for bone growth (Gwiazda *et al.*, 2005). Minute

concentrations of lead may be excreted from the body via the urinary system and through hair, nails, and sweat (Borrelli and Coleman, 1987).

Furthermore, lead absorption rates can very. For instance, the gastrointestinal tracts of adults typically absorb nearly 15 percent of ingested lead, while those of children and pregnant women can absorb as high as 50 percent (Natural Resources Defense Council, 2000). This high absorption rate of lead in pregnant woman is attributed to the fact that lead readily binds to fetal hemoglobin (Children's Health Environmental Coalition, 2002). Consequently, pregnant women exposed to dangerous levels of lead often experience miscarriages and subtle abortions, as well as babies born with low-birth weight (Natural Resources Defense Council, 2000).

Although the United States government decreased the allowable levels of lead in certain products to negligible amounts in the late 1970s, lead still possess a threat to growing children, particularly since low levels of lead can accumulate overtime, thereby causing irreparable damage (Schwemberger, J.G. *et al.*, 2005). In fact, current research indicates that no amount of lead is safe for children (Mushak *et al.*, 1989; Natural Resources Defense Council, 2000). Nevertheless, according to the Centers for Disease Control and Prevention, nearly one million children in the U.S. under the age of six have elevated levels of lead in their blood system (Centers for Disease Control and Prevention). Eliminating blood lead levels (BLLs) $\geq$ 10 μg/dL (micrograms per deciliter) in children by the year 2010 is one of the national health objectives (Schwemberger, J.G. *et al.*, 2005).

Chapter 2

DEVELOPING THE MATHEMATICAL MODEL

The mathematical model for the kinetics of lead transfer in the human body is based on the fundamental conservation principle:

Net rate of change of a substance	=	*rate in (input)*	–	*rate out in each compartment (output)*

(Borrelli and Coleman, 1987).

In developing this model, the human body is divided into five compartments: blood (**1**), tissue (**2**), bones (**3**), lungs (**4**) and gastrointestinal (digestive) tract (**5**) (see **Figure 1**). However, the model primarily focuses on compartments **1**, **2**, and **3**, since compartments **2** and **3** exchanges lead continuously with compartment **1** by the process of diffusion. Further, the lead is transferred from one compartment to another by blood vessels, and the rate of lead input, output and exchange is measured in micrograms per day (μg/day).

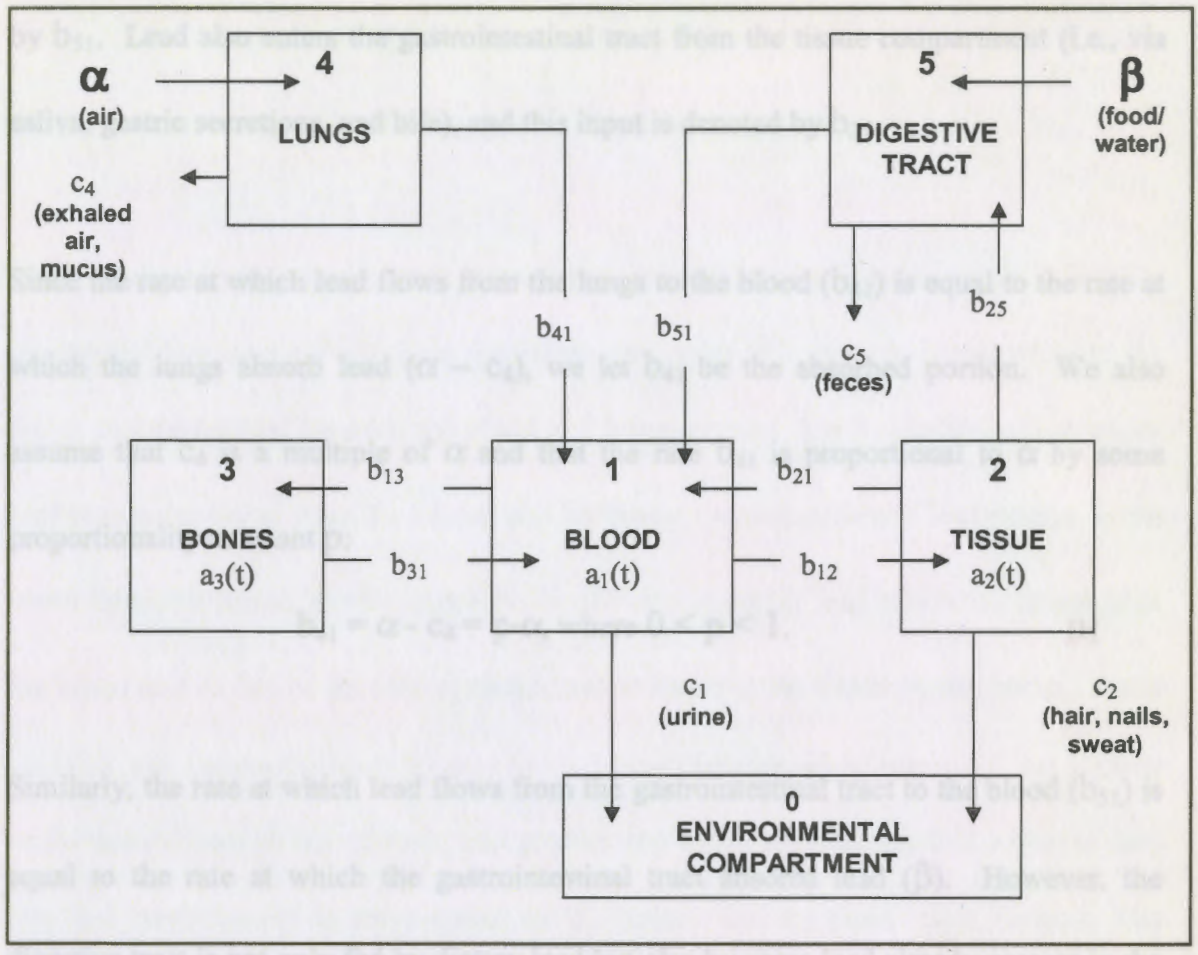

FIGURE 1. Compartment model for the kinetics of lead illustrating lead ingestion, digestion, and excretion in the human body. All quantities are measured in μg.

The primary sources of lead intake are via the respiratory tract (i.e., breathing in lead dusts) and via the gastrointestinal tract (i.e., eating and drinking lead particles). Let α denote the amount (μg) of lead which enters the lungs, and let β be the amount (μg) which enters the gastrointestinal tract. The lungs do not absorb the total amount of lead, since some of the dust particles are partly exhaled or excreted by mucous, and a certain amount of lead escapes the gastrointestinal tract through bowel movements. These lead output are denoted by c_4 and c_5, respectively. However, the lead input that is absorbed by the lungs is denoted by b_{41}, and that absorbed by the gastrointestinal tract is denoted

by b_{51}. Lead also enters the gastrointestinal tract from the tissue compartment (i.e., via saliva, gastric secretions, and bile), and this input is denoted by b_{25}.

Since the rate at which lead flows from the lungs to the blood (b_{41}) is equal to the rate at which the lungs absorb lead ($\alpha - c_4$), we let b_{41} be the absorbed portion. We also assume that c_4 is a multiple of α and that the rate b_{41} is proportional to α by some proportionality constant p:

$$b_{41} = \alpha - c_4 = p \cdot \alpha, \text{ where } 0 < p < 1. \qquad [1]$$

Similarly, the rate at which lead flows from the gastrointestinal tract to the blood (b_{51}) is equal to the rate at which the gastrointestinal tract absorbs lead (β). However, the digestive tract is not only fed by dietary lead but also by some lead already present in the tissues (denoted by b_{25}). The guts will not absorb all of this lead; rather, part of it is excreted by the feces (c_5). We let b_{51} be the absorbed portion of lead. So, based on the fundamental conservation principle:

$$b_{51} + c_5 = \beta + b_{25} \quad \Rightarrow \quad b_{51} = \beta + b_{25} - c_5.$$

However, since we are not interested in the quantity of lead expelled outside of the body, but rather we are concerned about the amount of lead that enters and is present within the body (specifically within the three compartments), we exclude c_5 from the above equation. If we assume that the rate b_{51} is proportional to $\beta + b_{25}$ by some proportionality constant q, then:

$$b_{51} = q\cdot(\beta + b_{25}), \text{ where } 0 < q < 1. \quad [2]$$

Thus, the total amount of daily absorption of lead that enters the blood is $b_{41} + b_{51}$.

Once lead from the lungs and gastrointestinal tract enters the blood, it is readily transported throughout the body to the tissues and bones, where an exchange between the blood and tissues and between the blood and bones occurs. Let b_{12} be the rate at which lead enters the tissue from the blood, and let b_{21} be the rate at which lead returns to the blood from the tissue. Similarly, let b_{13} be the rate at which lead enters the bones from the blood and let b_{31} be the rate at which lead is return to the blood by the bones. Since lead can also escape the body by way of the blood (through urine excretion) and by way of the tissue (through hair growth, nail growth, and sweat production), this output of lead into the environment is represented by c_1 (urine) and c_2 (hair, nails, sweat). The environmental component is not significant in the model since it does not send the lead back into the system.

Using t as the time variable (measured in days), the amount of lead (μg) stored in compartments 1, 2, and 3 is denoted by $a_1(t)$, $a_2(t)$ and $a_3(t)$, respectively. Letting $\frac{da_1(t)}{dt}$ be the rate at which lead enters and escapes the blood, we have:

$$\frac{da_1(t)}{dt} = b_{41} + b_{51} + b_{21} - b_{12} + b_{31} - b_{13} - c_1. \quad [3]$$

Substituting equations [1] and [2] into equation [3] yields:

$$\frac{da_1(t)}{dt} = p\alpha + q\cdot(\beta + b_{25}) + b_{21} - b_{12} + b_{31} - b_{13} - c_1. \quad [4]$$

In a similar manner, we obtain the following differential equations for the rates at which lead enters and leaves compartments **2** and **3**:

$$\frac{da_2(t)}{dt} = b_{12} - b_{21} - b_{25} - c_2 \quad [5]$$

$$\frac{da_3(t)}{dt} = b_{13} - b_{31}. \quad [6]$$

Now, assuming that the lead flow from compartment **1** to compartment **2** and vice versa is proportional to the amount of lead in compartment 1, we have

$$b_{12} = k_{12} \cdot a_1, \text{ where } 0 < k_{12} < 1 \quad [7]$$

$$b_{21} = k_{21} \cdot a_2, \text{ where } 0 < k_{21} < 1. \quad [8]$$

In a similar manner, if we assume that the lead flow from compartment **1** to another compartment and vice versa is proportional to the amount of lead in compartment **1**, as well as the flow of lead from one compartment to another is proportional, then the following equations are produced:

$$b_{13} = k_{13} \cdot a_1, \text{ where } 0 < k_{13} < 1 \quad [9]$$

$$b_{31} = k_{31} \cdot a_3, \text{ where } 0 < k_{31} < 1 \quad [10]$$

$$b_{25} = k_{25} \cdot a_2, \text{ where } 0 < k_{25} < 1 \quad [11]$$

$$c_1 = m \cdot a_1, \text{ where } 0 < m < 1 \quad [12]$$

$$c_2 = n \cdot a_2, \text{ where } 0 < n < 1. \quad [13]$$

Substituting equations [9], [10], [11], [12], and [13] into equations [4], [5], and [6] yields the following system of equations:

$$\frac{da_1(t)}{dt} = p\cdot\alpha + q\cdot(\beta + k_{25}\cdot a_2) + k_{21}\cdot a_2 - k_{12}\cdot a_1 + k_{31}\cdot a_3 - k_{13}\cdot a_1 - m\cdot a_1 \quad [14]$$

$$\frac{da_2(t)}{dt} = k_{12}\cdot a_1 - k_{21}\cdot a_2 - k_{25}\cdot a_2 - n\cdot a_2 \quad [15]$$

$$\frac{da_3(t)}{dt} = k_{13}\cdot a_1 - k_{31}\cdot a_3. \quad [16]$$

Finally, by combining the coefficients, the system of equations above becomes the following nonhomogenous differential equations:

$$\frac{da_1(t)}{dt} = K_{11}\cdot a_1 + K_{12}\cdot a_2 + K_{13}\cdot a_3 + L, \quad [17]$$

$$\frac{da_2(t)}{dt} = K_{21}\cdot a_1 + K_{22}\cdot a_2, \quad [18]$$

$$\frac{da_3(t)}{dt} = K_{31}a_1 + K_{33}a_3, \quad [19]$$

where $L = p\cdot\alpha + q\cdot\beta$ [20]

$K_{11} = -k_{12} - k_{13} - m$ [21]

$K_{12} = q\cdot k_{25} + k_{21}$ [22]

$K_{13} = -K_{33} = k_{31}$ [23]

$K_{21} = k_{12}$ [24]

$K_{22} = -k_{21} - k_{25} - n$ [25]

$K_{31} = k_{13}$. [26]

Chapter 3

CONSTRUCTING THE MATHEMATICAL MODEL FROM A CLINICAL STUDY

Using the results from a real-life study, we are able to calculate the coefficients of a_1, a_2, and a_3 and, thereby, test the model. We consider the steady state defined by $\frac{da_1(t)}{dt} = \frac{da_2(t)}{dt} = \frac{da_3(t)}{dt} = 0$ for all values of t. The following data was taken from *Science*, where Rabinowitz *et al.*, used a healthy, 53 year-old male subject, weighing 70 kg, to study lead metabolism in the human body (1973). The subject was a resident of California who smoked eight cigarettes per day. His regular diet contained an average of 367 μg/day of lead; however, for 104 days, part of his lead intake was replaced by the stable lead isotope ^{204}Pb and for 10 days by ^{207}Pb. For the next 46 days, the patient received a diet low in lead. Prior to the last experiment, his body was considered to be in a metabolic steady state with respect to lead. From the data provided for the experiment conducted by Rabinowitz *et al.*, we obtain the following information summarized in **Table 1** below:

Table 1. Summary of results obtained by Rabinowitz *et al* in their study of lead metabolism in a 53 year-old male subject .

Lead Transfer	Amount of lead
α (lead inhaled)	49 µg/day
β (lead ingested)	367 µg/day
a_1 (blood compartment)	1.8 mg (1800 µg)
a_2 (tissue compartment)	0.7 mg (700 µg)
a_3 (bone compartment)	200 mg (200000 µg)
b_{12} (lead from blood to tissue)	20 µg/day
b_{21} (lead from tissue to blood)	8 µg/day
b_{13} (lead from blood to bone)	7 µg/day
b_{31} (lead from bone to blood)	7 µg/day
b_{41} (lead from lungs to blood)	17 µg/day
b_{51} (lead from digestive tract to blood)	33 µg/day
b_{25} (lead from tissue to digestive tract)	8 µg/day
c_1 (lead from blood to urine)	38 µg/day
c_2 (lead from tissue to hair, nails, and sweat)	4 µg/day
c_4 (lead exhaled)	32 µg/day
c_5 (lead from expelled through feces)	342 µg/day

Using the data provided in **Table 1**, it follows that

$$L = 49p + 367q. \qquad [27]$$

Using equation [1] and [2], we are able to calculate the values of p and q:

$$b_{41} = \alpha - c_4 = p\cdot\alpha \quad \Rightarrow \quad 49\ \mu g/day - 32\ \mu g/day = p\cdot(49\ \mu g/day) \quad \Rightarrow \quad p = 17/49$$

$$b_{51} = q\cdot(\beta + b_{25}) \quad \Rightarrow \quad 33\ \mu g/day = q\cdot(367\ \mu g/day + 8\ \mu g/day) \quad \Rightarrow \quad q = 11/125.$$

Substituting the above values for p and q into [27] gives

$$\begin{aligned} L &= 49\cdot(17/49) + 367\cdot(11/125) \\ &= 6162/125 \\ &= 49.296\ \mu g/day. \end{aligned}$$

To find the remaining coefficients of k_{12}, k_{21}, k_{13}, k_{31}, k_{25}, m and n, we substitute the data from the study into equations [7] - [13]:

$b_{12} = k_{12}a_1 \Rightarrow 20 = k_{12}\cdot 1800 \Rightarrow k_{12} = 20/1800 \Rightarrow k_{12} = 1/90$

$b_{21} = k_{21}a_2 \Rightarrow 8 = k_{21}\cdot 700 \Rightarrow k_{21} = 8/700 \Rightarrow k_{21} = 2/175$

$b_{13} = k_{13}a_1 \Rightarrow 7 = k_{13}\cdot 1800 \Rightarrow k_{13} = 7/1800 \Rightarrow k_{13} = 7/1800$

$b_{31} = k_{31}a_3 \Rightarrow 7 = k_{31}\cdot 200000 \Rightarrow k_{31} = 7/200000 \Rightarrow k_{31} = 7/200000$

$b_{25} = k_{25}a_2 \Rightarrow 8 = k_{25}\cdot 700 \Rightarrow k_{25} = 8/700 \Rightarrow k_{25} = 2/175$

$c_1 = ma_1 \Rightarrow 38 = m\cdot 1800 \Rightarrow m = 38/1800 \Rightarrow m = 19/900$

$c_2 = na_2 \Rightarrow 4 = n\cdot 700 \Rightarrow n = 4/700 \Rightarrow n = 1/175.$

Now substituting the above coefficients into equations [21] - [26] lead to the following $K_{i,j}$:

$K_{11} = -k_{12} - k_{13} - m \Rightarrow K_{11} = -1/90 - 7/1800 - 19/900 \Rightarrow K_{11} = -13/360$

$K_{12} = q\cdot k_{25} + k_{21} \Rightarrow K_{12} = (11/125)\cdot(2/175) + 2/175 \Rightarrow K_{12} = 272/21875$

$K_{13} = -K_{33} = k_{31} \Rightarrow K_{13} = -K_{33} = 7/200000 \Rightarrow K_{33} = -7/200000$

$K_{21} = k_{12} \Rightarrow K_{21} = 1/90$

$K_{22} = -k_{21} - k_{25} - n \Rightarrow K_{22} = -2/175 - 2/175 - 1/175 \Rightarrow K_{22} = -1/35$

$K_{31} = k_{13} \Rightarrow K_{31} = 7/1800.$

Finally, if we substitute these values into equations [17] - [19], then we obtain the following equations:

$$\frac{da_1(t)}{dt} = -13/360 \cdot a_1(t) + 272/21875 \cdot a_2(t) + 7/200000 \cdot a_3(t) + 6162/125 \qquad [28]$$

$$\frac{da_2(t)}{dt} = 1/90 \cdot a_1(t) - 1/35 \cdot a_2(t) \qquad [29]$$

$$\frac{da_3(t)}{dt} = 7/1800 \cdot a_1(t) - 7/200000 \cdot a_3(t). \qquad [30]$$

From the above system, we note that lead is somewhat slow to enter the bones and very slow to leave them. Further, the above system of equations is based on the male subject studied in the experiment conducted by Rabinowitz *et al.*, and therefore, we are aware that the above coefficients might vary with different individuals. Nevertheless, the system is reasonable and will serve as a good approximation for real life situations involving male adults with a similar background to that of the subject studied.

However, the system would be inappropriate for children for five main reasons. First, children have relatively smaller body masses. Second, the nervous systems of children are still developing. Third, children have rapid growth and differentiation of cells (Vander *et al.*, 2001). Fourth, children have a higher basal metabolic rate, which affects the absorption and metabolism of toxicants (Vander *et al.*, 2001). Finally, children have a different breathing zone than most adults in that they are closer to the ground or floor where lead may be deposited. Thus, because of these reasons, we would expect the coefficients given in equations [28] - [30] to be significantly different for children.

Chapter 4

CALCULATING THE SOLUTIONS TO THE MATHEMATICAL MODEL

Using Maple 10 software, we determine solutions to the mathematical model (see **Appendix A**). The compartment model illustrated in **Figure 1** leads to a vector differential equation of the form:

$$\mathbf{x}'(t) = \mathbf{E}\cdot\mathbf{x}(t) + \mathbf{b},$$

where $\mathbf{E}$ is the matrix of the system, and $\mathbf{b}$ is the matrix of the nonhomogeneous term written in the form $\mathbf{b} = \begin{bmatrix} constant \\ 0 \\ 0 \end{bmatrix}$.

The system rewritten in matrix form (5 significant figures) is as follows:

$$E := \begin{bmatrix} -0.036111 & 0.012434 & 0.000035000 \\ 0.011111 & -0.028571 & 0 \\ 0.0038889 & 0 & -0.000035000 \end{bmatrix} \cdot \quad [31]$$

The eigenvalues and respective eigenvectors of the matrix system $\mathbf{E}$ are calculated to be:

$\lambda_1 = -0.020000$ days^{-1}; eigenvectors $\mathbf{v}_1 = \{[-0.61118, -0.79227, 0.11905]\}$

$\lambda_2 = -0.000030643$ days^{-1}; eigenvectors $\mathbf{v}_2 = \{[0.011212, 0.0043649, 10.007]\}$

$\lambda_3 = -0.044687$ days^{-1} ; eigenvectors $\mathbf{v}_3 = \{[-0.82322, 0.56757, 0.071698]\}$.

We observe that since all three eigenvalues are negative, it means that the system is stable in the sense that it tends asymptotically to an equilibrium state whenever $L = 49 \cdot p + 367 \cdot q$ takes on a new value.

Furthermore, we let $\mathbf{a}(t) = \begin{bmatrix} a_1(t) \\ a_2(t) \\ a_3(t) \end{bmatrix} = \mathbf{a}_h(t) + \mathbf{a}_p(t)$, where $\mathbf{a}_h(t)$ is the general solution of the corresponding homogeneous system and $\mathbf{a}_p(t)$ is an equilibrium solution of the model nonhomogeneous system. Specifically, the general solution to the homogeneous equation is written as

$$\mathbf{a}_h(t) = \begin{bmatrix} a_1^h(t) \\ a_2^h(t) \\ a_3^h(t) \end{bmatrix} = f_1 \cdot e^{\lambda_1 t} \cdot \mathbf{v}_1 + f_2 \cdot e^{\lambda_2 t} \cdot \mathbf{v}_2 + f_3 \cdot e^{\lambda_3 t} \cdot \mathbf{v}_3, \quad [32]$$

where f_1, f_2, and f_3 are coefficients; the equilibrium solution is a particular solution of the nonhomogeneous equation written as

$$\mathbf{a}_p(t) = \begin{bmatrix} a_1^p(t) \\ a_2^p(t) \\ a_3^p(t) \end{bmatrix} = \begin{bmatrix} d_1 \\ d_2 \\ d_3 \end{bmatrix}. \quad [33]$$

To determine $\mathbf{a}_p(t)$, we use $\mathbf{a}_p'(t)$, where $\mathbf{a}_p'(t) = \mathbf{E} \cdot \mathbf{a}_p(t) + \mathbf{b}$. [34]

Since $\mathbf{a}_p(t) = \begin{bmatrix} d_1 \\ d_2 \\ d_3 \end{bmatrix}$, then $\mathbf{a}_p'(t) = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix} = \mathbf{E} \cdot \begin{bmatrix} d_1 \\ d_2 \\ d_3 \end{bmatrix} + \begin{bmatrix} constant \\ 0 \\ 0 \end{bmatrix}$. [35]

Once we solve for $\begin{bmatrix} d_1 \\ d_2 \\ d_3 \end{bmatrix}$, we are able to calculate $\begin{bmatrix} f_1 \\ f_2 \\ f_3 \end{bmatrix}$ by specifying the initial conditions.

If the initial conditions are $\mathbf{x}(t_o) = \begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix}$, then we are able to solve for $\begin{bmatrix} f_1 \\ f_2 \\ f_3 \end{bmatrix}$ using the following system:

$$\begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix} = [e^{\lambda_1 t_o} \cdot \mathbf{v}_1,\ e^{\lambda_2 t_o} \cdot \mathbf{v}_2,\ e^{\lambda_3 t_o} \cdot \mathbf{v}_3] \begin{bmatrix} f_1 \\ f_2 \\ f_3 \end{bmatrix} + \begin{bmatrix} d_1 \\ d_2 \\ d_3 \end{bmatrix}. \quad [36]$$

Now, assuming the experimental subject inhales 49 µg/day and ingests 367 µg/day and using the matrix system $\mathbf{E}$ and the value of $L = 49.296$ µg/day obtained from the study, we employ the above setup to solve the nonhomogeneous system. So, using [35] we see that

$$\begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix} = \mathbf{E} \cdot \begin{bmatrix} d_1 \\ d_2 \\ d_3 \end{bmatrix} + \begin{bmatrix} 49.296 \\ 0 \\ 0 \end{bmatrix} \Rightarrow \begin{bmatrix} d_1 \\ d_2 \\ d_3 \end{bmatrix} = \begin{bmatrix} 1800.0 \\ 700.00 \\ 200001 \end{bmatrix} \quad [37].$$

We determine the values of $\begin{bmatrix} f_1 \\ f_2 \\ f_3 \end{bmatrix}$ by letting the initial conditions be such that when $t = 0$, then $\mathbf{a}(t) = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix}$.

So, therefore,

$$\begin{bmatrix} a_1(0) \\ a_2(0) \\ a_3(0) \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix} = \begin{bmatrix} -.61118 & 0.011212 & -.82322 \\ -.79227 & 0.0043649 & 0.56757 \\ 0.11905 & 10.007 & 0.071698 \end{bmatrix} \cdot \begin{bmatrix} f_1 \\ f_2 \\ f_3 \end{bmatrix} + \begin{bmatrix} \mathbf{1800.0} \\ \mathbf{700.00} \\ \mathbf{200001} \end{bmatrix} \quad [38]$$

$$\Rightarrow \quad \begin{bmatrix} f_1 \\ f_2 \\ f_3 \end{bmatrix} = \begin{bmatrix} \mathbf{1399.9} \\ \mathbf{-20009} \\ \mathbf{874.69} \end{bmatrix}.$$

Finally, we obtain the desired solution to the mathematical model for the original case:

$$\mathbf{a}(t) = \begin{bmatrix} a_1(t) \\ a_2(t) \\ a_3(t) \end{bmatrix} = 1399.9 \cdot e^{-0.020000 \cdot (t)} \cdot \begin{bmatrix} -.61118 \\ -.79227 \\ 0.11905 \end{bmatrix} +$$

$$- 20009 \cdot e^{-0.000030643 \cdot (t)} \begin{bmatrix} 0.011212 \\ 0.0043649 \\ 10.007 \end{bmatrix} +$$

$$874.69 \cdot e^{-0.044687 \cdot (t)} \cdot \begin{bmatrix} -.82322 \\ 0.56757 \\ 0.071698 \end{bmatrix} + \begin{bmatrix} \mathbf{1800.0} \\ \mathbf{700.00} \\ \mathbf{200001} \end{bmatrix}. \quad [39]$$

Appendix A provides the codes used in Maple 10 to obtain the above solution to our mathematical model.

Chapter 5

Graphical Illustrations of Subject's Blood, Tissue, and Bone Lead-Levels for Various Cases

Case 0: Using the solutions derived for the mathematical model [39], we are able to produce graphs that will enable us to observe the blood, tissue, and bone lead levels in the experimental subject at various times. Within the first 100 days, we observe that the lead levels in the blood, tissue, and bone compartments begin to rise considerably, with the lead level being highest in the blood and lowest in the bones (see **Figure 2**).

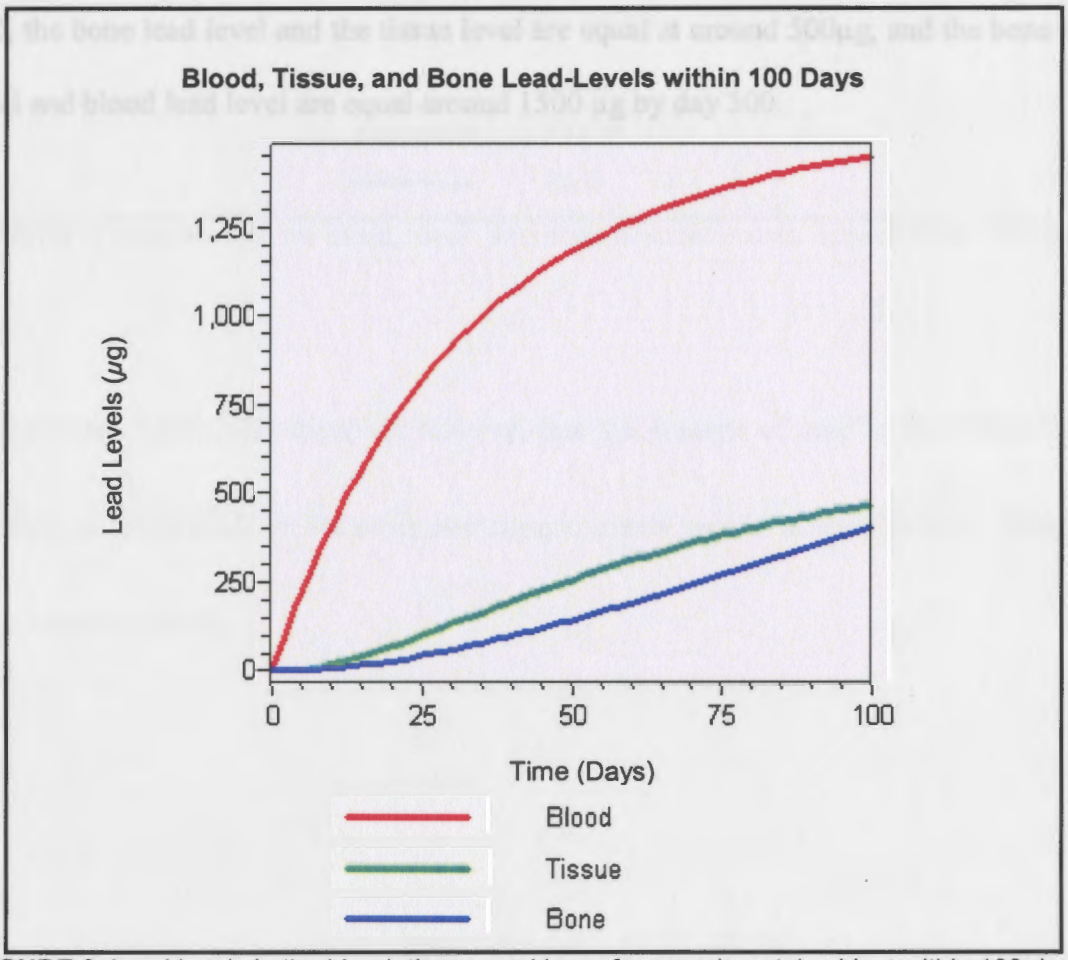

FIGURE 2. Lead levels in the blood, tissue, and bone for experimental subject within 100 days.

Within the next 400 days (500 days in total), we observe that the lead in the blood and tissue quickly go to equilibrium levels (see **Figure 3**). However, the lead level in the bone continues to increase. This observation is expected given that the coefficient of a_3 in equations [28] and [30] is extremely small. Subsequently, since the quantity of lead that is transferred from the bones to the blood is so minute compared to that entering the bones from the blood, the lead accumulates in the bones. On the other hand, the lead levels in the blood and tissue reach equilibrium at a faster rate (between days 100 – 180) given that the amount of lead transferred out of these compartments is relatively high (compared to that transferred out of the bone), as well as the fact that both the blood and tissue compartments have more avenues for the lead to exit. Finally, we note that by day 120, the bone lead level and the tissue level are equal at around 500μg, and the bone lead level and blood lead level are equal around 1500 μg by day 300.

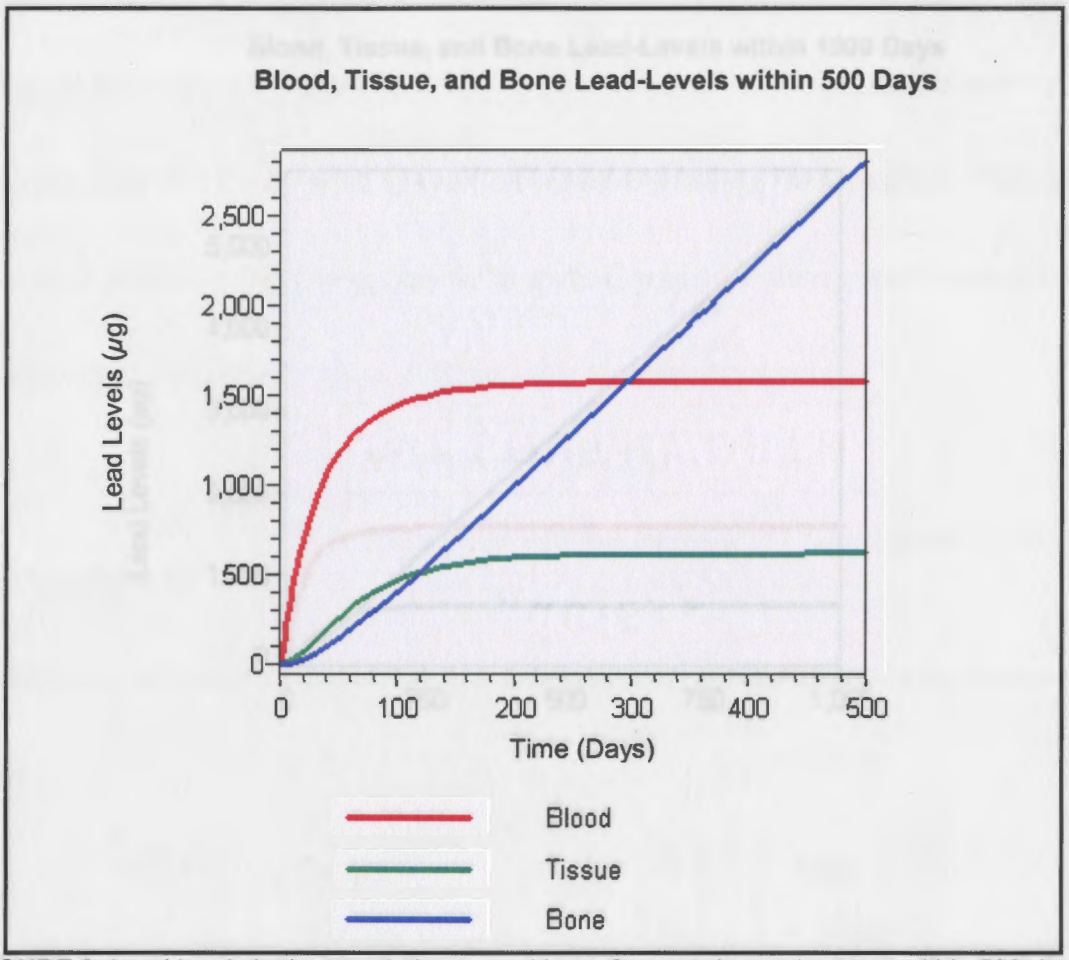

FIGURE 3. Lead levels in the blood, tissue, and bone for experimental subject within 500 days.

Furthermore, after 1000 days, we observe that the amount of lead in the bones soars drastically, while those in the other two compartments remain at equilibrium. **Figure 4** illustrates this graph.

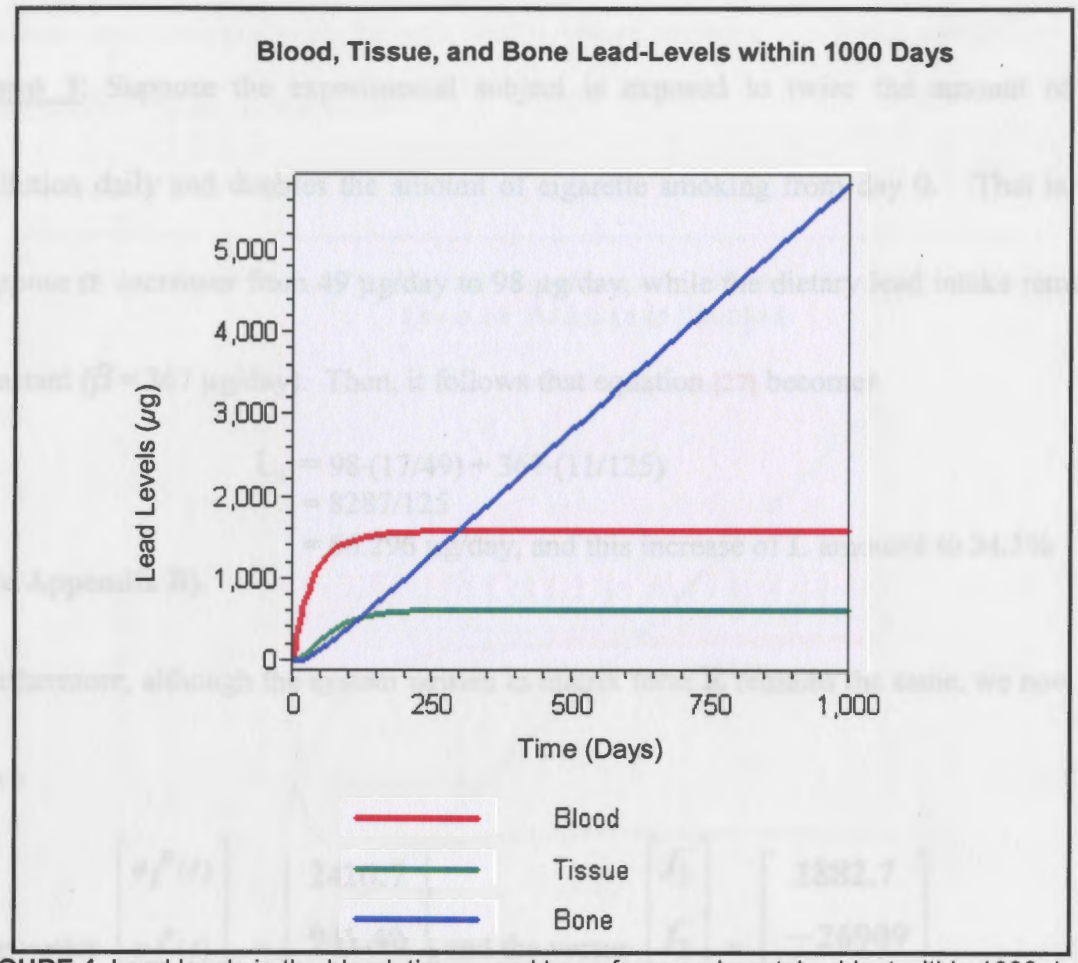

FIGURE 4. Lead levels in the blood, tissue, and bone for experimental subject within 1000 days.

We now apply different cases to determine how the graph for our experimental subject would differ from those given in **Figures 2 – 4**.

Case 1: Suppose the experimental subject is exposed to twice the amount of air pollution daily and doubles the amount of cigarette smoking from day 0. That is, we suppose α increases from 49 μg/day to 98 μg/day, while the dietary lead intake remains constant ($\beta = 367$ μg/day). Then, it follows that equation [27] becomes

$$\begin{aligned} L_1 &= 98\cdot(17/49) + 367\cdot(11/125) \\ &= 8287/125 \\ &= 66.296 \text{ μg/day, and this increase of } L \text{ amounts to } 34.5\% \end{aligned}$$

(see **Appendix B**).

Furthermore, although the system written in matrix form **E** remains the same, we now have

$$\text{the vector } \begin{bmatrix} a_1^p(t) \\ a_2^p(t) \\ a_3^p(t) \end{bmatrix} = \begin{bmatrix} 2420.7 \\ 941.40 \\ 268972 \end{bmatrix}, \text{ and the vector } \begin{bmatrix} f_1 \\ f_2 \\ f_3 \end{bmatrix} = \begin{bmatrix} 1882.7 \\ -26909 \\ 1176.3 \end{bmatrix}.$$

Figure 5 illustrates the graph for this case, where we consider the time from 0 to 500 days. In comparing this graph with that shown in **Figure 3**, we notice some differences, as well as similarities. First, we see that the blood lead level in **Figure 5** is higher, and this level reaches equilibrium near the 2200 μg mark versus the 1500 μg mark as seen in **Figure 3**. In addition, we notice that the tissue lead level in **Figure 5** proceeds to equilibrium near day 120 at around 800 μg, whereas the tissue lead level shown in the initial graph reaches equilibrium around 500 μg near day 120. Finally, we observe that

the bone lead level is similar for both graphs, where the bone lead levels continue to soar without approaching equilibrium.

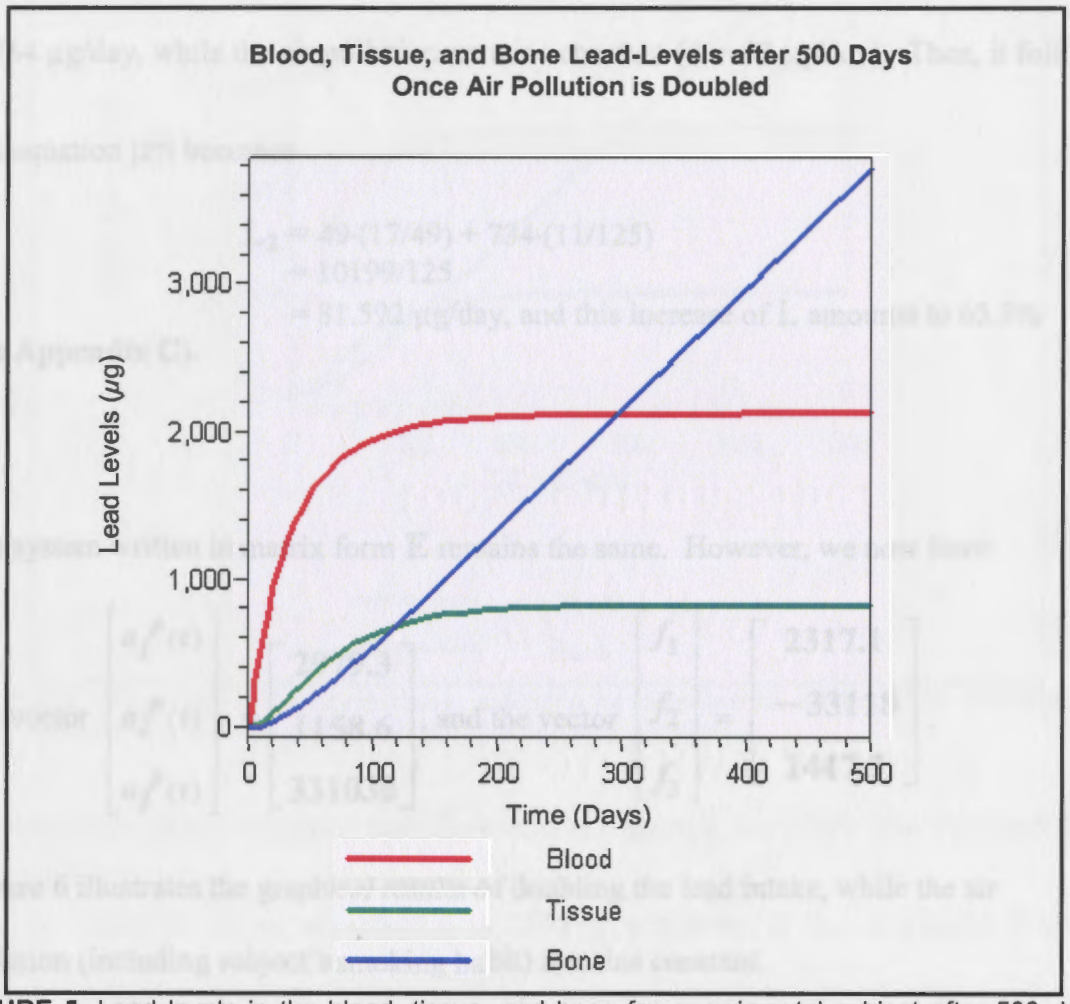

FIGURE 5. Lead levels in the blood, tissue, and bone for experimental subject after 500 days once air pollution is doubled and lead intake remains constant.

Case 2: Suppose the experimental subject ingests daily twice the amount of lead compared to before beginning at day 0. That is, we suppose β increases from 367 μg/day to 734 μg/day, while the air pollution remains constant ($\alpha = 49$ μg/day). Then, it follows that equation [27] becomes

$$\begin{aligned} L_2 &= 49\cdot(17/49) + 734\cdot(11/125) \\ &= 10199/125 \\ &= 81.592 \text{ μg/day, and this increase of } L \text{ amounts to } 65.5\% \end{aligned}$$

(see **Appendix C**).

The system written in matrix form **E** remains the same. However, we now have

$$\text{the vector } \begin{bmatrix} a_1^P(t) \\ a_2^P(t) \\ a_3^P(t) \end{bmatrix} = \begin{bmatrix} 2979.3 \\ 1158.6 \\ 331030 \end{bmatrix}, \text{ and the vector } \begin{bmatrix} f_1 \\ f_2 \\ f_3 \end{bmatrix} = \begin{bmatrix} 2317.1 \\ -33118 \\ 1447.7 \end{bmatrix}.$$

Figure 6 illustrates the graphical results of doubling the lead intake, while the air pollution (including subject's smoking habit) remains constant.

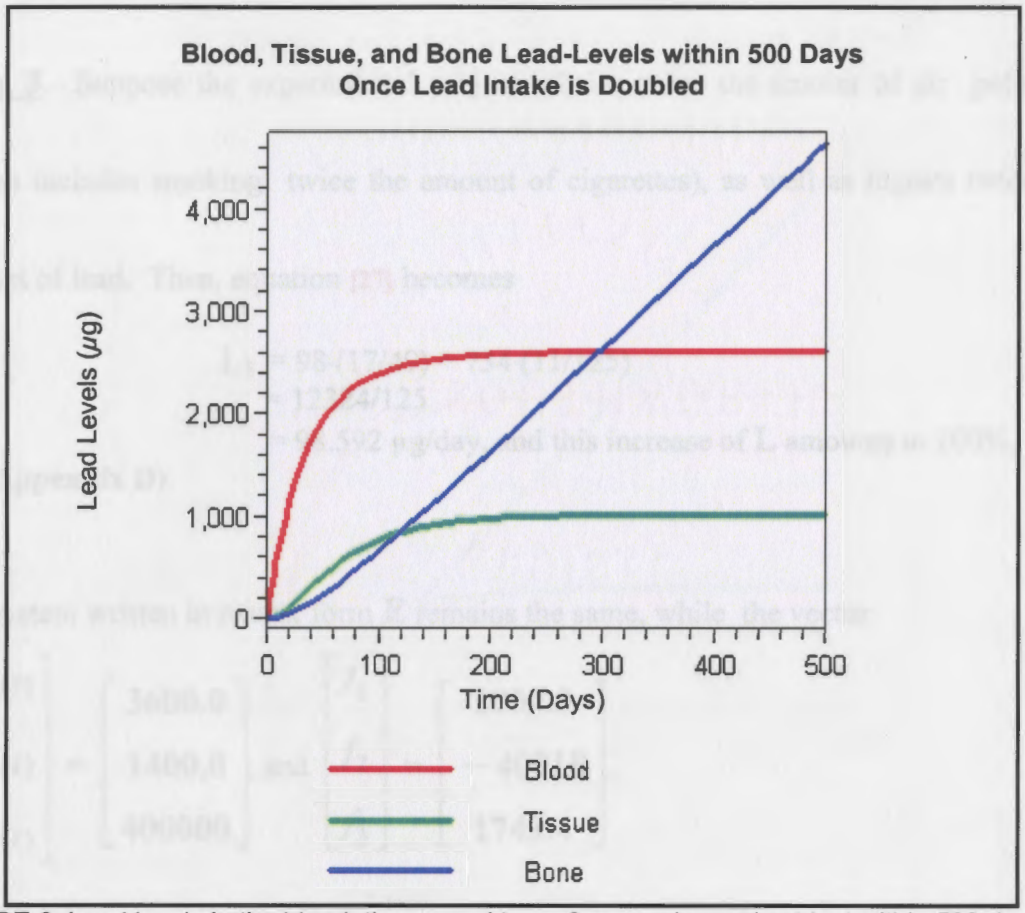

FIGURE 6. Lead levels in the blood, tissue, and bone for experimental subject within 500 days once lead intake is doubled and the air pollution remains constant.

In comparison to our original graph illustrated in **Figure 3**, we notice that the blood lead level in **Figure 6** reaches equilibrium at 2600 μg compared to that in **Figure 3** which reaches equilibrium at 1500 μg. The bone and tissue lead levels follow a similar pattern as those seen in the original graph, except that the tissue lead level in **Figure 6** reaches equilibrium at a higher level of around 900 μg compared to 500 μg in our original graph.

Case 3. Suppose the experimental subject inhales twice the amoint of air pollution (which includes smoking twice the amount of cigarettes), as well as ingests twice the amount of lead. Then, equation [27] becomes

$$\begin{aligned} L_3 &= 98\cdot(17/49) + 734\cdot(11/125) \\ &= 12324/125 \\ &= 98.592\ \mu g/day, \text{ and this increase of } L \text{ amounts to } 100\% \end{aligned}$$

(see **Appendix D**).

The system written in matrix form $\mathbf{E}$ remains the same, while the vector

$$\begin{bmatrix} a_1^P(t) \\ a_2^P(t) \\ a_3^P(t) \end{bmatrix} = \begin{bmatrix} 3600.0 \\ 1400.0 \\ 400000 \end{bmatrix}, \text{ and } \begin{bmatrix} f_1 \\ f_2 \\ f_3 \end{bmatrix} = \begin{bmatrix} 2800.0 \\ -40018 \\ 1749.4 \end{bmatrix}.$$

Figure 7 presents the graph for this case.

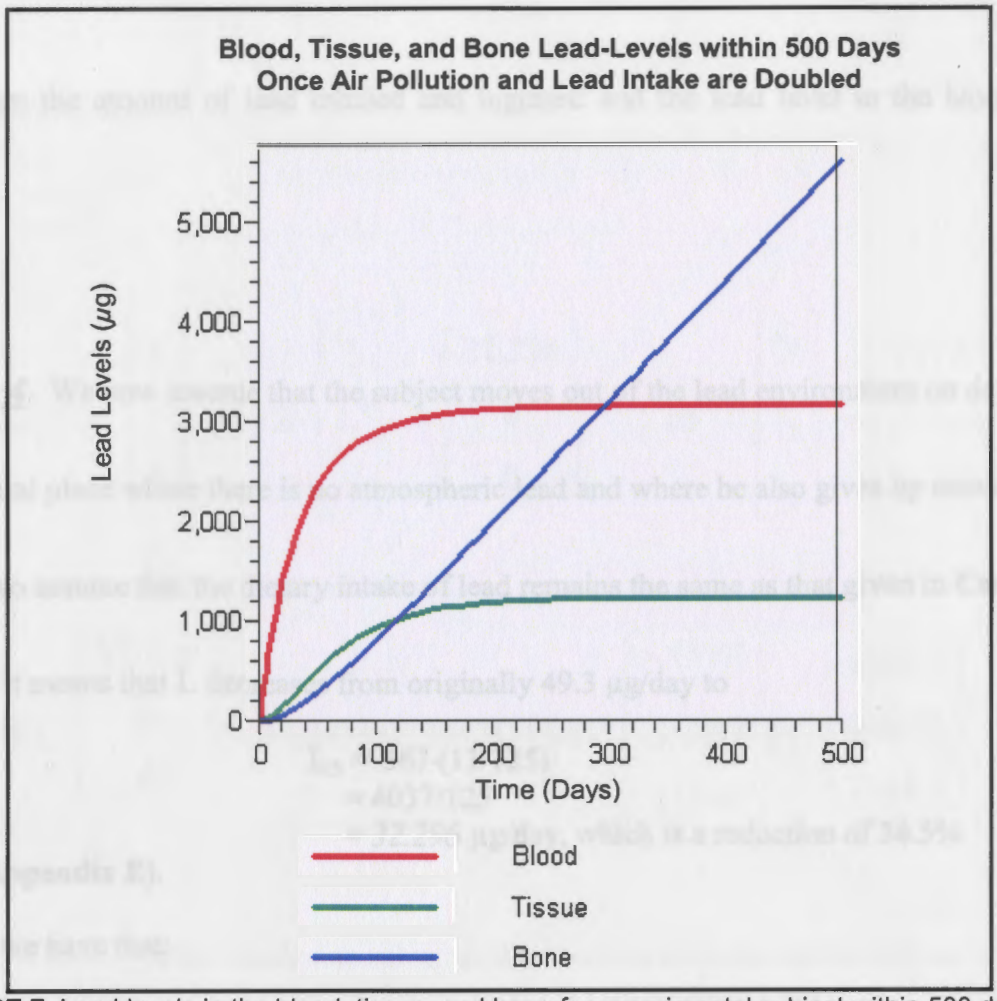

FIGURE 7. Lead levels in the blood, tissue, and bone for experimental subject within 500 days once air pollution and lead intake are doubled.

As suspected, a similar pattern for all three lead levels is observed as those seen in **Figure 6**, where the blood and tissue lead levels reach equilibrium at higher amounts and the bone lead level continues to rise. For this case, however, the blood lead level illustrated in **Figure 7** reaches equilibrium near 3200 μg. In addition, the tissue lead level increases to 1200 μg, before proceeding to equilibrium. The bone lead level soars as illustrated in the previous cases. Thus, it appears that there is a positive correlation

between the amount of lead inhaled and ingested and the lead level in the blood and tissue.

Case 4. We now assume that the subject moves out of the lead environment on day 500 to a rural place where there is no atmospheric lead and where he also gives up smoking. We also assume that the dietary intake of lead remains the same as that given in **Case 0**.

Then, it means that L decreases from originally 49.3 μg/day to

$$\begin{aligned} L_5 &= 367\cdot(11/125) \\ &= 4037/125 \\ &= 32.296 \text{ μg/day, which is a reduction of 34.5\%} \end{aligned}$$

(see **Appendix E**).

Now, we have that:

$$\mathbf{x}(t) = \begin{bmatrix} x_1(t) \\ x_2(t) \\ x_3(t) \end{bmatrix} = \mathbf{a}(t) + \mathbf{a}_p(t), \text{ and } \mathbf{x}'(t) - \mathbf{E}\cdot\mathbf{x}(t) = \mathbf{b}.$$

Given that $\mathbf{b} = \begin{bmatrix} 32.296 \\ 0 \\ 0 \end{bmatrix}$ and t = 500, it means that

$$\mathbf{x}(500) = \begin{bmatrix} x_1(500) \\ x_2(500) \\ x_3(500) \end{bmatrix} = f_1 e^{(\lambda_1 \cdot 500)}\cdot\mathbf{v}_1 + f_2 e^{(\lambda_2 \cdot 500)}\cdot\mathbf{v}_2 + f_3 e^{(\lambda_3 \cdot 500)}\cdot\mathbf{v}_3 + \begin{bmatrix} a_1^P(t) \\ a_2^P(t) \\ a_3^P(t) \end{bmatrix}, \quad [40]$$

where we let $\mathbf{a}_p(t) = \begin{bmatrix} l_1 \\ l_2 \\ l_3 \end{bmatrix}$.

So, $\mathbf{a}_p'(t) = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix} = \mathbf{E} \cdot \begin{bmatrix} l_1 \\ l_2 \\ l_3 \end{bmatrix} + \begin{bmatrix} 32.296 \\ 0 \\ 0 \end{bmatrix} \Rightarrow \begin{bmatrix} l_1 \\ l_2 \\ l_3 \end{bmatrix} = \begin{bmatrix} 1179.3 \\ 458.60 \\ 131030 \end{bmatrix}$.

When $\mathbf{b} = \begin{bmatrix} 32.296 \\ 0 \\ 0 \end{bmatrix}$, we determine that $\mathbf{x}(500) = \begin{bmatrix} x_1(500) \\ x_2(500) \\ x_3(500) \end{bmatrix} = \begin{bmatrix} 1034.5 \\ 402.22 \\ 1844.3 \end{bmatrix}$.

The new linear system required to calculate the coefficients in the solution of the new initial value problem is

$$G := \begin{bmatrix} -0.000027748 & 0.011042 & -1.628800000\ 10^{-10} \\ -0.000035969 & 0.0042985 & 1.123000000\ 10^{-10} \\ 0.0000054049 & 9.8548 & 1.418600000\ 10^{-11} \end{bmatrix}. \quad [41]$$

Thus, the new coefficients in the solution become $\begin{bmatrix} f_1 \\ f_2 \\ f_3 \end{bmatrix} = \begin{bmatrix} 833.69 \\ -13109 \\ -2.8215 \cdot 10^7 \end{bmatrix}$.

Substituting these values into [40] allows us to produce the following graph provided in **Figure 8**, where we allow the time to extend to day 3,000.

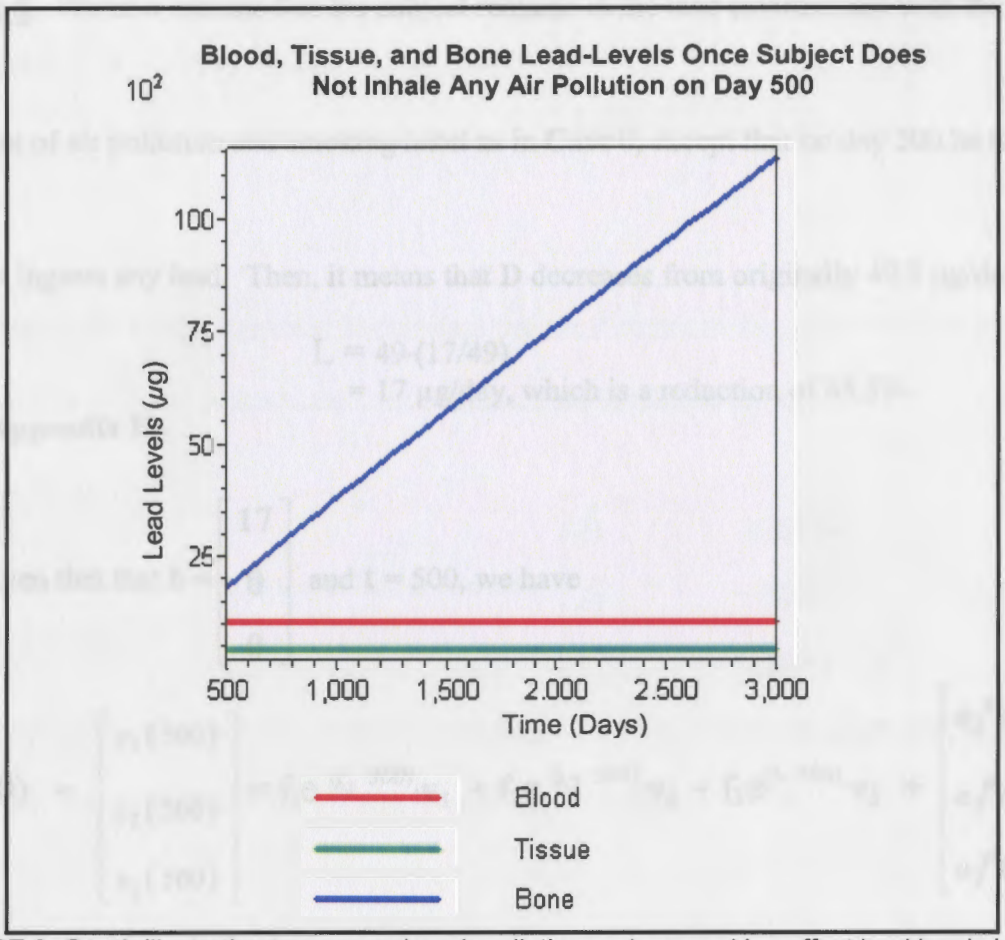

FIGURE 8. Graph illustrating how removing air pollution and no smoking affect lead levels in the blood, tissue, and bone of experimental subject at day 500, with lead consumption remaining constant.

From **Figure 8**, we observe that the lead levels in the tissue and blood remain at equilibrium as the time increase, while the bone lead level continues to soar. We also note that the blood lead level is higher with an equilibrium lead level of approximately 1000 μg compared to that of the tissue lead level which maintains an equilibrium level at approximately 400 μg. We further note that these equilibrium levels are slightly lower compared to those illustrated in **Figure 3**. Thus, it appears that removing air pollution from our subject while keeping the consumption of lead has no effect on the bone lead level.

Case 5. We now assume that the subject remains in the lead environment with the same amount of air pollution and smoking habit as in **Case 0**, except that on day 500 he no longer ingests any lead. Then, it means that **D** decreases from originally 49.3 μg/day to

$$L = 49\cdot(17/49)$$
$$= 17 \text{ μg/day, which is a reduction of 65.5\%}$$

(see **Appendix F**).

So, given that that $\mathbf{b} = \begin{bmatrix} 17 \\ 0 \\ 0 \end{bmatrix}$ and t = 500, we have

$$\mathbf{x}(500) = \begin{bmatrix} x_1(500) \\ x_2(500) \\ x_3(500) \end{bmatrix} = f_1 e^{\lambda_1 \cdot 500)} \cdot \mathbf{v_1} + f_2 e^{\lambda_2 \cdot 500)} \cdot \mathbf{v_2} + f_3 e^{(\lambda_3 \cdot 500)} \cdot \mathbf{v_3} + \begin{bmatrix} a_1^p(t) \\ a_2^p(t) \\ a_3^p(t) \end{bmatrix}, \quad [42]$$

where we let $\mathbf{a}_p(t) = \begin{bmatrix} e_1 \\ e_2 \\ e_3 \end{bmatrix}$.

$$\text{So, } \mathbf{a}^{p'}(t) = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix} = \mathbf{E}_2 \cdot \begin{bmatrix} e_1 \\ e_2 \\ e_3 \end{bmatrix} + \begin{bmatrix} 17 \\ 0 \\ 0 \end{bmatrix} \Rightarrow \begin{bmatrix} e_1 \\ e_2 \\ e_3 \end{bmatrix} = \begin{bmatrix} 620.74 \\ 241.40 \\ 68971 \end{bmatrix}.$$

When $\mathbf{b} = \begin{bmatrix} 17 \\ 0 \\ 0 \end{bmatrix}$, we determine that $\mathbf{x}(500) = \begin{bmatrix} x_1(500) \\ x_2(500) \\ x_3(500) \end{bmatrix} = \begin{bmatrix} 544.54 \\ 211.72 \\ 970.80 \end{bmatrix}$.

The new linear system required to calculate the coefficients in the solution of the new initial value problem is the same as that determined in **Case 4** (matrix [41]).

So, the new coefficients in the solution become $\begin{bmatrix} f_1 \\ f_2 \\ f_3 \end{bmatrix} = \begin{bmatrix} 438.84 \\ -6900.3 \\ -1.4852 \cdot 10^7 \end{bmatrix}$.

Substituting these values into [42] allows us to produce the following graph provided in **Figure 9**, where we allow the time to extend to day 3,000.

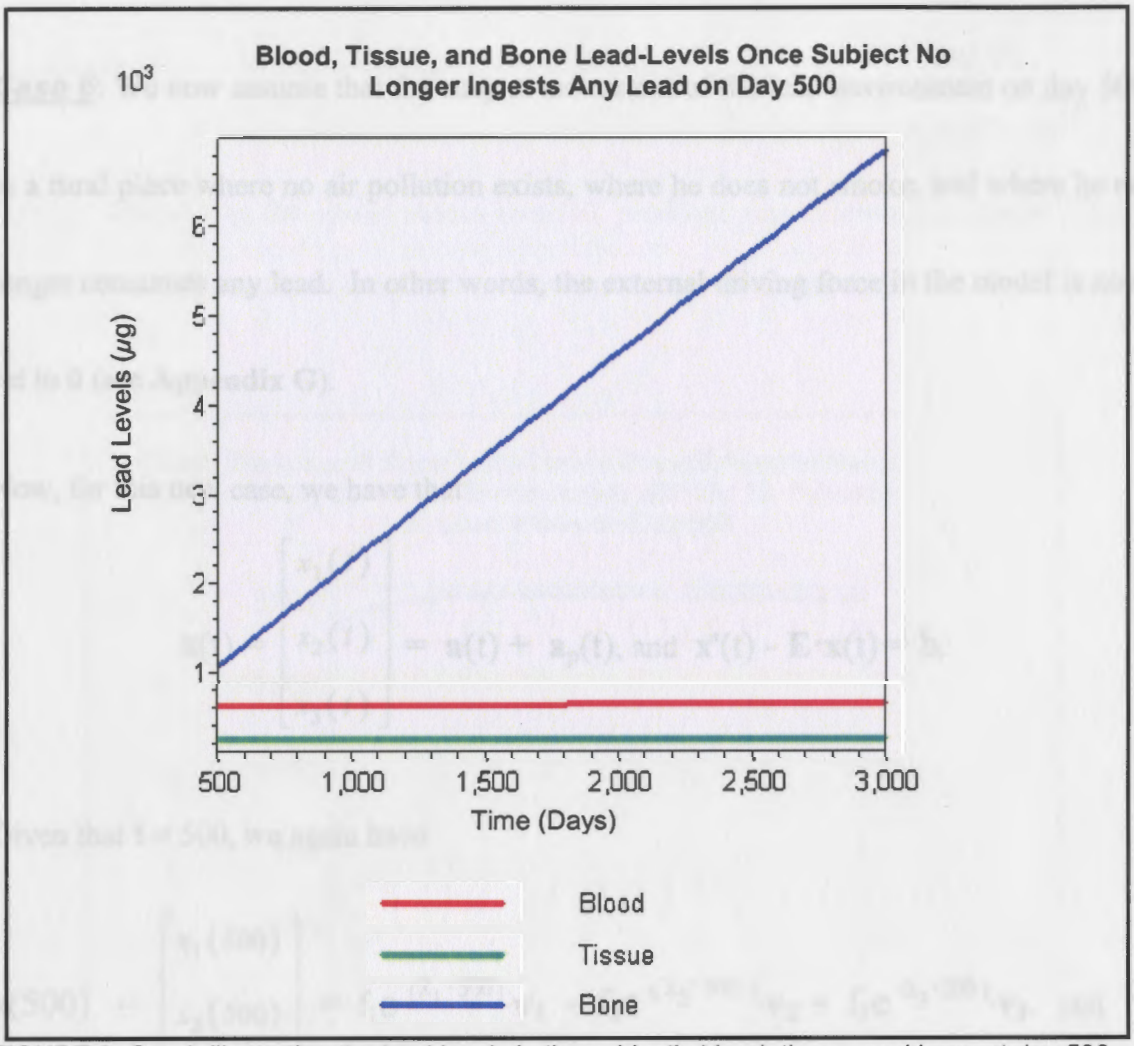

FIGURE 9. Graph illustrating the lead levels in the subject's blood, tissue, and bone at day 500 when lead consumption is removed (with air pollution and smoking habit remaining constant).

Based on **Figure 9**, we observe a similar pattern in lead levels as that seen in **Figure 8**. The only major difference between the two figures is that the tissue and blood lead equilibrium levels are lower in **Figure 9** with respective values of 200 μg and 600 μg, compared to 500 μg and 2000 μg as illustrated in **Figure 8**. Such a difference is attributed to the fact that for this case our subject's intake of lead at day 500 and beyond is much lower (17 μg/day) compared to that for **Case 4** (32.3 μg/day)

Case 6: We now assume that the subject moves out of the lead environment on day 500 to a rural place where no air pollution exists, where he does not smoke, and where he no longer consumes any lead. In other words, the external driving force in the model is now set to **0** (see **Appendix G**).

Now, for this new case, we have that

$$\mathbf{x}(t) = \begin{bmatrix} x_1(t) \\ x_2(t) \\ x_3(t) \end{bmatrix} = \mathbf{a}(t) + \mathbf{a}_p(t), \text{ and } \mathbf{x}'(t) - \mathbf{E}\cdot\mathbf{x}(t) = \mathbf{b}.$$

Given that t = 500, we again have

$$\mathbf{x}(500) = \begin{bmatrix} x_1(500) \\ x_2(500) \\ x_3(500) \end{bmatrix} = f_1 e^{(\lambda_1 \cdot 500)}\cdot\mathbf{v}_1 + f_2 e^{(\lambda_2 \cdot 500)}\cdot\mathbf{v}_2 + f_3 e^{(\lambda_3 \cdot 500)}\cdot\mathbf{v}_3. \quad [43]$$

We determine $\mathbf{x}(500) = \begin{bmatrix} x_1(500) \\ x_2(500) \\ x_3(500) \end{bmatrix} = \begin{bmatrix} \mathbf{1579.0} \\ \mathbf{613.94} \\ \mathbf{2915.1} \end{bmatrix}$, and the new linear system required to calculate the coefficients in the solution of the new initial value problem is the same as that given in matrix [41].

Consequently, we determine the new coefficients to be $\begin{bmatrix} f_1 \\ f_2 \\ f_3 \end{bmatrix} = \begin{bmatrix} -3.0834 \cdot 10^7 \\ 308.93 \\ -4.4207 \cdot 10^{12} \end{bmatrix}$.

Finally, substituting the above values into [43] produces the following graphical results illustrated in **Figure 10**, where we allow the time to extend to day 1000.

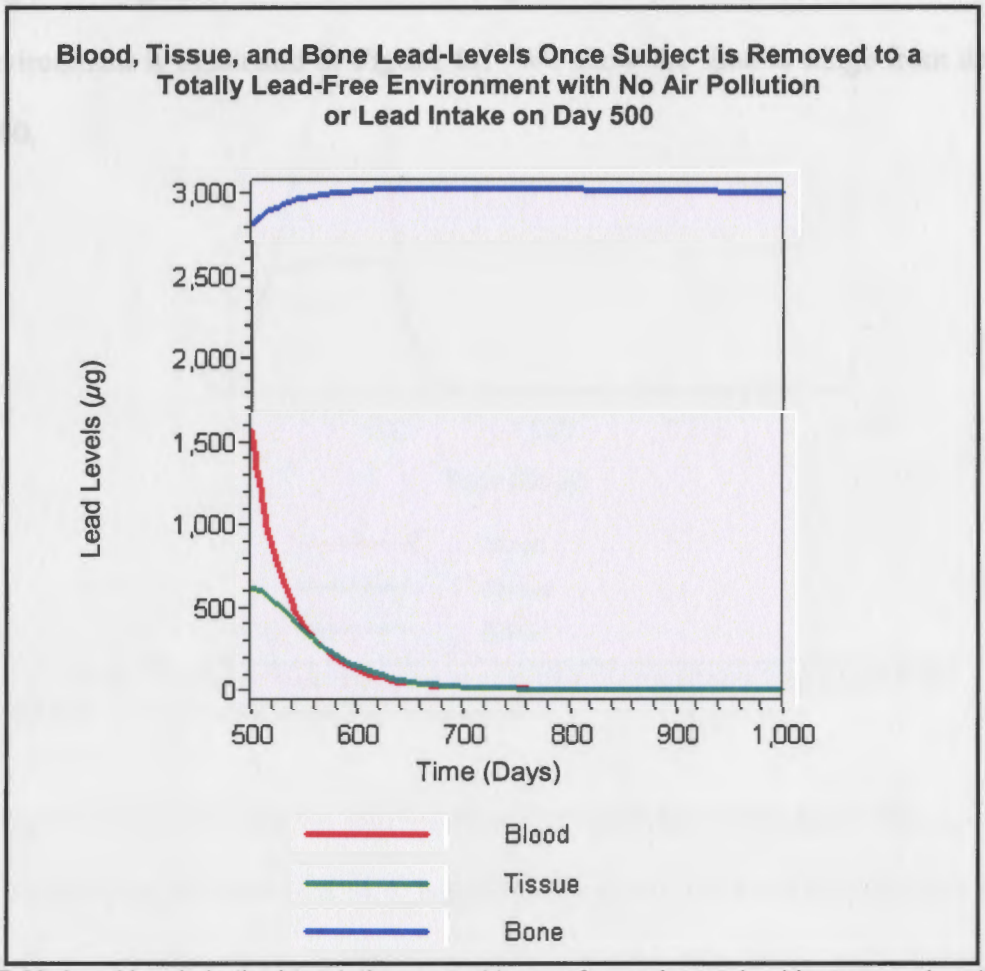

FIGURE 10. Lead levels in the blood, tissue, and bone of experimental subject once air pollution and lead intake are removed at day 500.

For this case, we observe a quick drop in the blood and tissue lead levels, which both eventually approach 0 μg by day 680. We also observe a dramatic change in the bone

lead level. Although the bone lead level does not drop to zero, it appears to reach equilibrium by day 620 at nearly 3000 μg.

To see the complete picture of removing the subject from the original lead environment to a lead-free environment on day 500, we combine **Figures 3** and **10**. This new graph showing the change in lead levels from the original lead environment to those in the lead-free environment is illustrated in **Figure 11**. We allow the time to range from day 0 to day 2000.

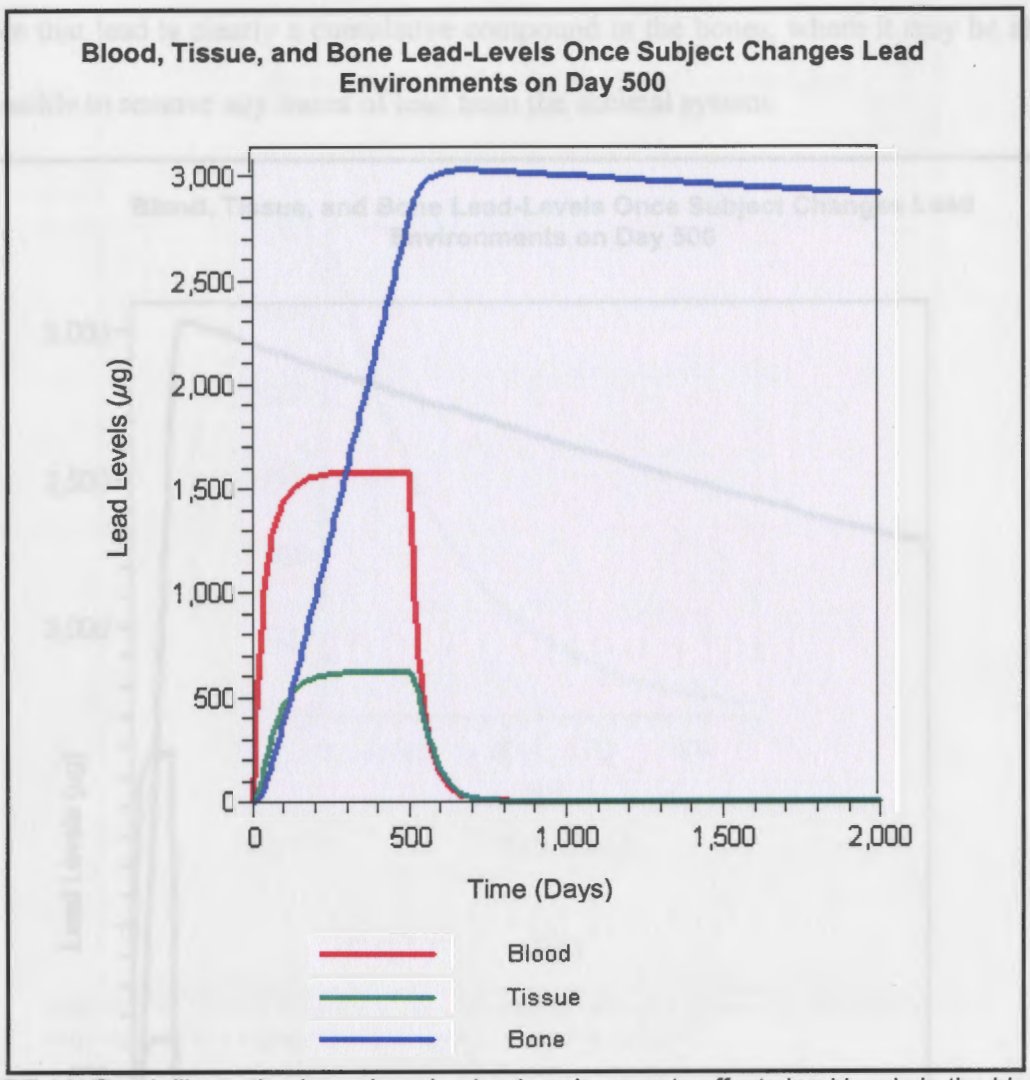

FIGURE 11. Graph illustrating how changing lead environments affects lead levels in the blood, tissue, and bone of experimental subject at day 500.

From **Figure 11** we note that the lead levels of the blood and tissue are at zero μg by day 700. In addition, the bone lead level begins to decrease; however, the decrease in bone lead levels is extremely slow compared to the lead levels of the other two compartments. Even if we allow the time to extend to day 10,000 as much as 2,300 μg of lead still remains in the bone (**Figure 12**). It is only by day 120,000 (approximately 328 years) when we see that the bone lead level approaches 0 μg (**Figure 13**). From these graphs,

we see that lead is clearly a cumulative compound in the bones, where it may be almost impossible to remove any traces of lead from the skeletal system.

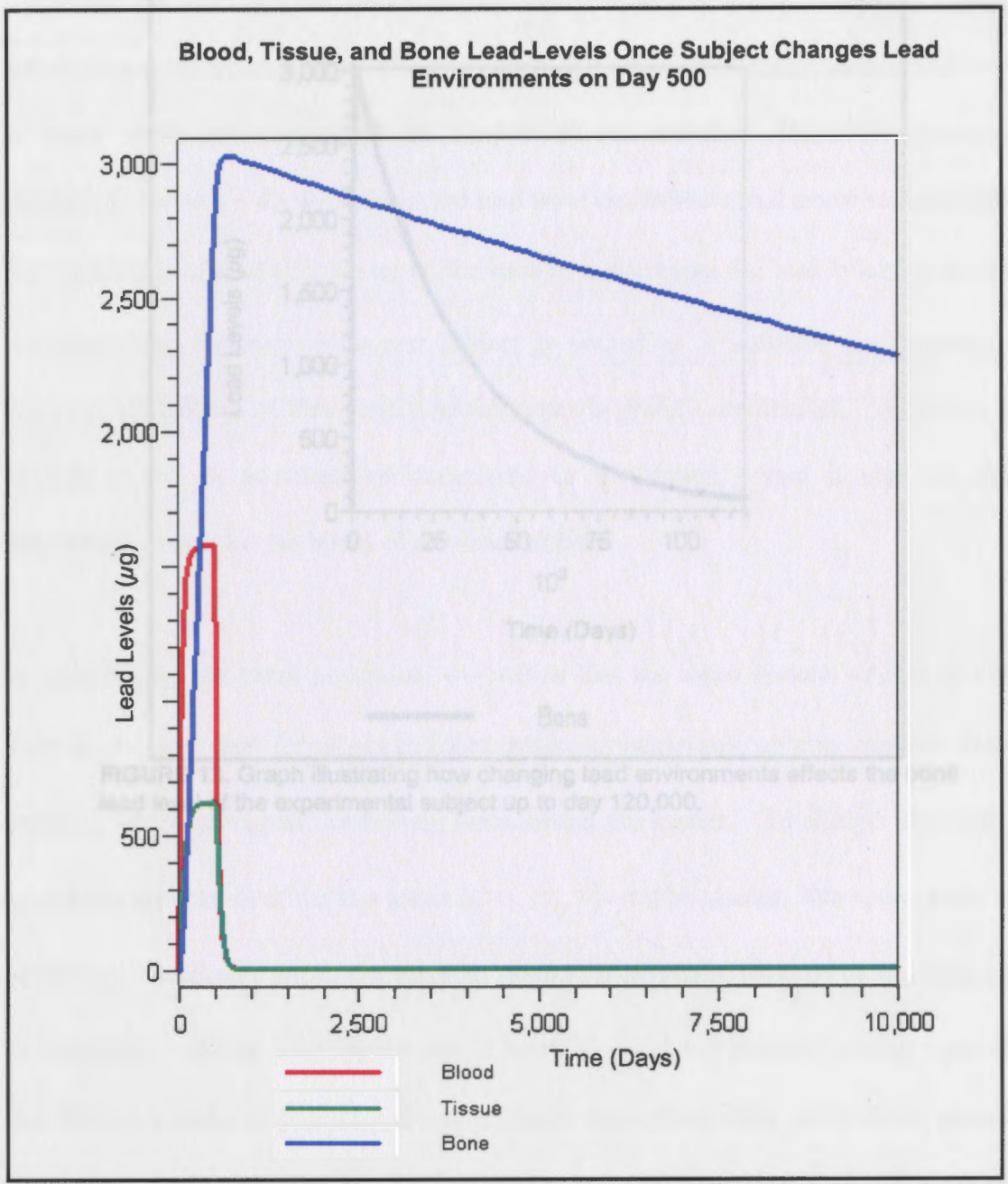

FIGURE 12. Graph illustrating how changing lead environments affects lead levels in the blood, tissue, and bone of experimental subject up to day 10,000.

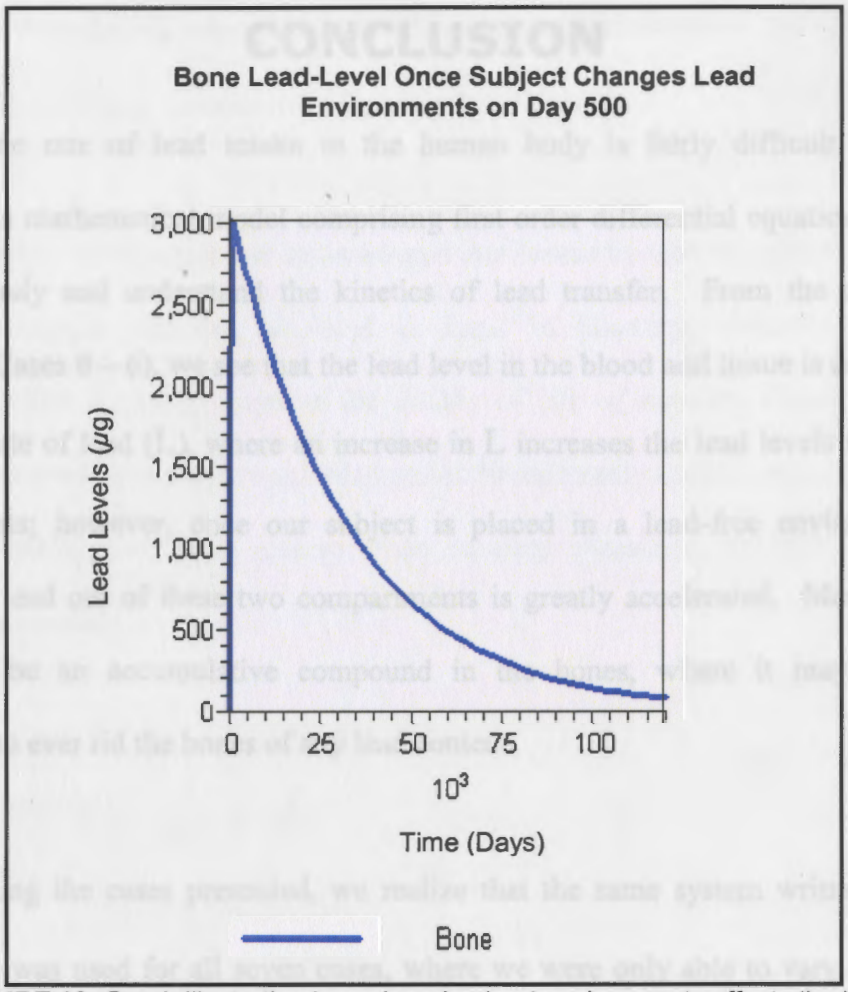

FIGURE 13. Graph illustrating how changing lead environments affects the bone lead level of the experimental subject up to day 120,000.

CONCLUSION

Although the rate of lead intake in the human body is fairly difficult to analyze, developing a mathematical model comprising first order differential equations allows us to better study and understand the kinetics of lead transfer. From the case studies presented (**Cases 0 – 6**), we see that the lead level in the blood and tissue is dependent on the intake rate of lead (L), where an increase in L increases the lead levels in these two compartments; however, once our subject is placed in a lead-free environment, the removal of lead out of these two compartments is greatly accelerated. Moreover, lead appears to be an accumulative compound in the bones, where it may be almost impossible to ever rid the bones of any lead content.

In establishing the cases presented, we realize that the same system written in matrix form **E** [31] was used for all seven cases, where we were only able to vary the external input L, which served as the driving force within the system. To change the matrix **E** would require that all of the b_{ij}s given in [1], [2], [7]- [11] be altered. We suspect that each of the b_{ij}s would vary from individual to individual primarily because of the differences in biological makeup. Ideally, we would have liked to have obtained a large number of b_{ij}s from a variety of individuals and examine how these rates differ from person to person. Unfortunately, acquiring the necessary data is simply not feasible. Therefore, in addition to determining the kinetics of lead transfer in children, future work based on this thesis would include analyzing how taking appropriate medication would change each of

the b_{ij}s, and determining what dosage is sufficiently safe to decrease the lead content in the three compartments, especially in the bones.

Nonetheless, this manuscript has demonstrated one means by which applied mathematics and the biological sciences go hand in hand in allowing medical doctors and environmentalists to better improve the quality of life of humans. Constructing such mathematical models as the one provided would be extremely useful, especially since the model developed gives us an idea as to the inherent interaction between lead and the three compartments.

APPENDIX A

Maple code for Case 0:

```
> with(linalg): with(plots):
```

Enter the matrix E and the vector b:

```
> E := matrix(3,3,[K11, K12, K13, K21, K22, 0, K31, 0,
K33]);
> b := [L, 0, 0];
```

$$E := \begin{bmatrix} K11 & K12 & K13 \\ K21 & K22 & 0 \\ K31 & 0 & K33 \end{bmatrix}$$

$$b := [L, 0, 0]$$

Enter the transfer coefficients and environmental lead burden from the study (5 significant figures):

```
> K11:=-0.036111; K12:=0.012434; K13:=0.000035000;
K21:=0.011111; K22:=-0.028571; K31:=0.0038889; K33:=-
0.000035000; L:= 49.296;
```

$$K11 := -0.036111$$

$$K12 := 0.012434$$

$$K13 := 0.000035000$$

$$K21 := 0.011111$$

$$K22 := -0.028571$$

$$K31 := 0.0038889$$

$$K33 := -0.000035000$$

$$L := 49.296$$

Redefine E and b with numerical values:

```
> E := matrix(3,3,[K11, K12, K13, K21, K22, 0, K31, 0,
K33]);
> b := [L, 0, 0];
```

$$E := \begin{bmatrix} -0.036111 & 0.012434 & 0.000035000 \\ 0.011111 & -0.028571 & 0 \\ 0.0038889 & 0 & -0.000035000 \end{bmatrix}$$

$$b := [49.296, 0, 0]$$

Compute a_p with numerical values:

```
> ap := evalm(-(inverse(E)&*b));
```

$$ap := [1800.002319 \quad 700.0044018 \quad 2.000008291\ 10^5]$$

Compute the eigenvalues and eigenvectors of E:

```
> eigenvects(E);
```

$$[-0.01999966145, 1, \{[-.6111800578 \quad -.7922708414 \quad 0.1190512600]\}]$$
$$[-0.00003064299534, 1, \{[0.01121188255 \quad 0.00436487979 \quad 10.00730884]\}]$$
$$[-0.04468669551, 1, \{[-.8232245684 \quad 0.5675738998 \quad 0.07169801700]\}]$$

Assign eigenvalues to a vector λ and construct eigenvectors v_1, v_2, and v_3 (5 significant figures):

```
> lambda:=[-0.020000,-0.000030643, -0.044687];
> v1:=[-0.61118, -0.79227, 0.11905];
v2:=[0.011212, 0.0043649, 10.007];
v3:=[-0.82322, 0.56757, 0.071698];
```

$$\lambda := [-0.020000, -0.000030643, -0.044687]$$

$$v1 := [-.61118, -.79227, 0.11905]$$

$$v2 := [0.011212, 0.0043649, 10.007]$$

$$v3 := [-.82322, 0.56757, 0.071698]$$

Construct the matrix of eigenvectors:

```
> P:=augment(v1,v2,v3);
```

$$P := \begin{bmatrix} -.61118 & 0.011212 & -.82322 \\ -.79227 & 0.0043649 & 0.56757 \\ 0.11905 & 10.007 & 0.071698 \end{bmatrix}$$

Solve for the coefficients in the solution of the initial value problem, $\frac{dx}{dt} = Ex + b$, $x(0) = 0$:

```
> f:= evalm(-(inverse(P)&*ap));
```

$$f := [1399.917839 \quad -20009.01395 \quad 874.6865592]$$

Define the blood lead function x_1, the tissue lead level x_2, and the bone lead level x_3 :

```
> x1 := t-> f[1]*P[1, 1]*exp(λ[1]*t)
    + f[2]*P[1, 2]*exp(λ[2]*t)
    + f[3]*P[1, 3]*exp(λ[3]*t)+ ap[1];
```

$$x1 := t \rightarrow f_1 P_{1,1} e^{(\lambda_1 t)} + f_2 P_{1,2} e^{(\lambda_2 t)} + f_3 P_{1,3} e^{(\lambda_3 t)} + ap_1$$

```
> x2 := t-> f[1]*P[2, 1]*exp(λ[1]*t)
    + f[2]*P[2, 2]*exp(λ[2]*t)
    + f[3]*P[2, 3]*exp(λ[3]*t)+ ap[2];
```

$$x2 := t \rightarrow f_1 P_{2,1} e^{(\lambda_1 t)} + f_2 P_{2,2} e^{(\lambda_2 t)} + f_3 P_{2,3} e^{(\lambda_3 t)} + ap_2$$

```
> x3 := t-> f[1]*P[3, 1]*exp(λ[1]*t)
    + f[2]*P[3, 2]*exp(λ[2]*t)
    + f[3]*P[3, 3]*exp(λ[3]*t)+ ap[3];
```

$$x3 := t \rightarrow f_1 P_{3,1} e^{(\lambda_1 t)} + f_2 P_{3,2} e^{(\lambda_2 t)} + f_3 P_{3,3} e^{(\lambda_3 t)} + ap_3$$

Plot the blood, tissue, and bone functions together for function x:

```
> plot1:=plot([x1(t), x2(t), x3(t)], t=0..500, color=[red,
green, blue], thickness=2):%;
```

APPENDIX B

Maple code for Case 1:

```
> with(linalg): with(plots):
```

Enter the matrix E and the vector b:

```
> E := matrix(3,3,[K11, K12, K13, K21, K22, 0, K31, 0,
K33]);
> b := [L, 0, 0];
```

$$E := \begin{bmatrix} K11 & K12 & K13 \\ K21 & K22 & 0 \\ K31 & 0 & K33 \end{bmatrix}$$

$$b := [L, 0, 0]$$

Enter the transfer coefficients and environmental lead burden from the study(5 significant figures):

```
> K11:=-0.036111; K12:=0.012434; K13:=0.000035000;
K21:=0.011111; K22:=-0.028571; K31:=0.0038889; K33:=-
0.000035000; L:= 66.296;
```

$$K11 := -0.036111$$

$$K12 := 0.012434$$

$$K13 := 0.000035000$$

$$K21 := 0.011111$$

$$K22 := -0.028571$$

$$K31 := 0.0038889$$

$$K33 := -0.000035000$$

$$L := 66.296$$

Redefine the matrix E and the vector b:

```
> E := matrix(3,3,[K11, K12, K13, K21, K22, 0, K31, 0,
K33]);
> b := [L, 0, 0];
```

$$E := \begin{bmatrix} -0.036111 & 0.012434 & 0.000035000 \\ 0.011111 & -0.028571 & 0 \\ 0.0038889 & 0 & -0.000035000 \end{bmatrix}$$

$$b := [66.296, 0, 0]$$

Compute a_p with numerical values:

```
> ap := evalm(-(inverse(E)&*b));
```

$$ap := [2420.743139 \quad 941.4048163 \quad 2.689722284\,10^{5}]$$

Compute the eigenvalues and eigenvectors of E:

```
> eigenvects(E);
```

```
[-0.01999966145, 1
  , {[-.6111800578  -.7922708414  0.1190512600]} ]
  , [
  -0.00003064299534, 1
  , {[0.01121188255  0.00436487979  10.00730884]} ]
  , [
  -0.04468669551, 1
  , {[-.8232245684  0.5675738998  0.07169801700]} ]
```

Assign eigenvalues to a vector λ and construct eigenvectors v_1, v_2, and v_3 (5 significant figures):

```
> lambda:=[-0.020000,-0.000030643, -0.044687];
> v1:=[-0.61118, -0.79227, 0.11905];
v2:=[0.011212, 0.0043649, 10.007];
v3:=[-0.82322, 0.56757, 0.071698];
```

$$\lambda := [-0.020000, -0.000030643, -0.044687]$$

$$v1 := [-.61118, -.79227, 0.11905]$$

$$v2 := [0.011212, 0.0043649, 10.007]$$

$$v3 := [-.82322, 0.56757, 0.071698]$$

Construct the matrix of eigenvectors:

```
> P:=augment(v1,v2,v3);
```

$$P := \begin{bmatrix} -.61118 & 0.011212 & -.82322 \\ -.79227 & 0.0043649 & 0.56757 \\ 0.11905 & 10.007 & 0.071698 \end{bmatrix}$$

Solve for the coefficients in the solution of the initial value problem, $\frac{dx}{dt} = Ex + b$, $x(0) = 0$:

```
> f:= evalm(-(inverse(P)&*ap));
```

$$f := [1882.687300 \quad -26909.23380 \quad 1176.327089]$$

Define the blood lead function x_1, the tissue lead level x_2, and the bone lead level x_3 :

```
> x1 := t-> f[1]*P[1, 1]*exp(λ[1]*t)
  + f[2]*P[1, 2]*exp(λ[2]*t)
  + f[3]*P[1, 3]*exp(λ[3]*t)+ ap[1];
```

$$x1 := t \rightarrow f_1 P_{1,1} e^{(\lambda_1 t)} + f_2 P_{1,2} e^{(\lambda_2 t)} + f_3 P_{1,3} e^{(\lambda_3 t)} + ap_1$$

```
> x2 := t-> f[1]*P[2, 1]*exp(λ[1]*t)
  + f[2]*P[2, 2]*exp(λ[2]*t)
  + f[3]*P[2, 3]*exp(λ[3]*t)+ ap[2];
```

$$x2 := t \rightarrow f_1 P_{2,1} e^{(\lambda_1 t)} + f_2 P_{2,2} e^{(\lambda_2 t)} + f_3 P_{2,3} e^{(\lambda_3 t)} + ap_2$$

```
> x3 := t-> f[1]*P[3, 1]*exp(λ[1]*t)
  + f[2]*P[3, 2]*exp(λ[2]*t)
  + f[3]*P[3, 3]*exp(λ[3]*t)+ ap[3];
```

$$x3 := t \rightarrow f_1 P_{3,1} e^{(\lambda_1 t)} + f_2 P_{3,2} e^{(\lambda_2 t)} + f_3 P_{3,3} e^{(\lambda_3 t)} + ap_3$$

Plot the blood, tissue, and bone functions together for function x:

```
> plot2 := plot([x1(t), x2(t), x3(t)]
  , t = 0..500, color=[red, green, blue], thickness = 2)
  :%;
```

APPENDIX C

Maple code for Case 2:

```
> with(linalg): with(plots):
```

Enter the matrix E and the vector b:

```
> E := matrix(3,3,[K11, K12, K13, K21, K22, 0, K31, 0,
K33]);
> b := [L, 0, 0];
```

$$E := \begin{bmatrix} K11 & K12 & K13 \\ K21 & K22 & 0 \\ K31 & 0 & K33 \end{bmatrix}$$

$$b := [L, 0, 0]$$

Enter the transfer coefficients and environmental lead burden from the study (5 significant figures):

```
> K11:=-0.036111; K12:=0.012434; K13:=0.000035000;
K21:=0.011111; K22:=-0.028571; K31:=0.0038889; K33:=-
0.000035000; L:= 49.296;
```

$$K11 := -0.036111$$

$$K12 := 0.012434$$

$$K13 := 0.000035000$$

$$K21 := 0.011111$$

$$K22 := -0.028571$$

$$K31 := 0.0038889$$

$$K33 := -0.000035000$$

$$L := 81.592$$

Redefine the matrix E and the vector b:

```
> E := matrix(3,3,[K11, K12, K13, K21, K22, 0, K31, 0,
K33]);
> b := [L, 0, 0];
```

$$E := \begin{bmatrix} -0.036111 & 0.012434 & 0.000035000 \\ 0.011111 & -0.028571 & 0 \\ 0.0038889 & 0 & -0.000035000 \end{bmatrix}$$

$$b := [81.592, 0, 0]$$

Compute a_p with numerical values:

```
> p := evalm(-(inverse(E)&*b));
```

$$ap := [2979.263819 \quad 1158.608389 \quad 3.310302591\ 10^5]$$

Compute the eigenvalues and eigenvectors of E:

```
> eigenvects(E);
```

$$[-0.01999966145,\ 1,\ \{[-.6111800578 \quad -.7922708414 \quad 0.1190512600]\}],\ [-0.00003064299534,\ 1,\ \{[0.01121188255 \quad 0.00436487979 \quad 10.00730884]\}],\ [-0.04468669551,\ 1,\ \{[-.8232245684 \quad 0.5675738998 \quad 0.07169801700]\}]$$

Assign eigenvalues to a vector λ and construct eigenvectors v_1, v_2, and v_3 (5 significant figures):

```
> lambda:=[-0.020000,-0.000030643, -0.044687];
> v1:=[-0.61118, -0.79227, 0.11905];
> v2:=[0.011212, 0.0043649, 10.007];
> v3:=[-0.82322, 0.56757, 0.071698];
```

$$\lambda := [-0.020000, \ -0.000030643, \ -0.044687]$$

$$v1 := [-.61118, \ -.79227, \ 0.11905]$$

$$v2 := [0.011212, \ 0.0043649, \ 10.007]$$

$$v3 := [-.82322, \ 0.56757, \ 0.071698]$$

Construct the matrix of eigenvectors:

```
> Q:=augment(v1,v2,v3);
```

$$Q := \begin{bmatrix} -.61118 & 0.011212 & -.82322 \\ -.79227 & 0.0043649 & 0.56757 \\ 0.11905 & 10.007 & 0.071698 \end{bmatrix}$$

Solve for the coefficients in the solution of the initial value problem, $\frac{dx}{dt} = Ex + b$, $x(0) = 0$:

```
> f:= evalm(-(inverse(P)&*ap));
>
```

$$f := [2317.066220 \quad -33117.80807 \quad 1447.732589]$$

Define the blood lead function x_1, *the tissue lead level* x_2, *and the bone lead level* x_3 :

```
> x1 := t-> f[1]*P[1, 1]*exp(λ[1]*t)
    + f[2]*P[1, 2]*exp(λ[2]*t)
    + f[3]*P[1, 3]*exp(λ[3]*t)+ ap[1];
```

$$x1 := t \to f_1 P_{1,1} e^{(\lambda_1 t)} + f_2 P_{1,2} e^{(\lambda_2 t)} + f_3 P_{1,3} e^{(\lambda_3 t)} + ap_1$$

```
> x2 := t-> f[1]*P[2, 1]*exp(λ[1]*t)
    + f[2]*P[2, 2]*exp(λ[2]*t)
    + f[3]*P[2, 3]*exp(λ[3]*t)+ ap[2];
```

$$x2 := t \to f_1 P_{2,1} e^{(\lambda_1 t)} + f_2 P_{2,2} e^{(\lambda_2 t)} + f_3 P_{2,3} e^{(\lambda_3 t)} + ap_2$$

```
> x3 := t-> f[1]*P[3, 1]*exp(λ[1]*t)
    + f[2]*P[3, 2]*exp(λ[2]*t)
    + f[3]*P[3, 3]*exp(λ[3]*t)+ ap[3];
```

$$x3 := t \to f_1 P_{3,1} e^{(\lambda_1 t)} + f_2 P_{3,2} e^{(\lambda_2 t)} + f_3 P_{3,3} e^{(\lambda_3 t)} + ap_3$$

Plot the blood, tissue, and bone functions together for function z:

```
> plot3:=plot([s1(t), s2(t), s3(t)], t=0..500,
  color=[red, green, blue], thickness=2):%
```

APPENDIX D

Maple code for Case 3:

```
> with(linalg): with(plots):
```

Enter the matrix E_2 and the vector b:

```
> E := matrix(3,3,[K11, K12, K13, K21, K22, 0, K31, 0,
K33]);
> b := [L, 0, 0];
```

$$E := \begin{bmatrix} K11 & K12 & K13 \\ K21 & K22 & 0 \\ K31 & 0 & K33 \end{bmatrix}$$

$$b := [L, 0, 0]$$

Enter the transfer coefficients and environmental lead burden from the study(5 significant figures):

```
> K11:=-0.036111; K12:=0.012434; K13:=0.000035000;
K21:=0.011111; K22:=-0.028571; K31:=0.0038889; K33:=-
0.000035000; L:= 98.592;
```

$$K11 := -0.036111$$

$$K12 := 0.012434$$

$$K13 := 0.000035000$$

$$K21 := 0.011111$$

$$K22 := -0.028571$$

$$K31 := 0.0038889$$

$$K33 := -0.000035000$$

$$L := 98.592$$

Redefine the matrix E_2 and the vector b:

```
> E := matrix(3,3,[K11, K12, K13, K21, K22, 0, K31, 0,
K33]);
> b := [L, 0, 0];
```

$$E := \begin{bmatrix} -0.036111 & 0.012434 & 0.000035000 \\ 0.011111 & -0.028571 & 0 \\ 0.0038889 & 0 & -0.000035000 \end{bmatrix}$$

$$b := [98.592, 0, 0]$$

Compute a_p with numerical values:

```
> ap := evalm(-(inverse(E)&*b));
```

$$ap := [3600.004638 \quad 1400.008804 \quad 4.000016583\ 10^5]$$

Compute the eigenvalues and eigenvectors of E:

```
> eigenvects(E);
```

$$[-0.01999966145, 1, \{[-.6111800578 \quad -.7922708414 \quad 0.1190512600]\}], [-0.00003064299534, 1, \{[0.01121188255 \quad 0.00436487979 \quad 10.00730884]\}], [-0.04468669551, 1, \{[-.8232245684 \quad 0.5675738998 \quad 0.07169801700]\}]$$

Assign eigenvalues to a vector λ and construct eigenvectors v_1, v_2, and v_3 (5 significant figures):

```
> lambda:=[-0.020000,-0.000030643, -0.044687];
> v1:=[-0.61118, -0.79227, 0.11905];
> v2:=[0.011212, 0.0043649, 10.007];
> v3:=[-0.82322, 0.56757, 0.071698];
```

$$\lambda := [-0.020000, -0.000030643, -0.044687]$$

$$v1 := [-.61118, -.79227, 0.11905]$$

$$v2 := [0.011212, 0.0043649, 10.007]$$

$$v3 := [-.82322, 0.56757, 0.071698]$$

Construct the matrix of eigenvectors:

```
> P:=augment(v1,v2,v3);
```

$$P := \begin{bmatrix} -.61118 & 0.011212 & -.82322 \\ -.79227 & 0.0043649 & 0.56757 \\ 0.11905 & 10.007 & 0.071698 \end{bmatrix}$$

Solve for the coefficients in the solution of the initial value problem, $\frac{dx}{dt} = E_2x +$ ***b,*** $x(0) = 0$***:***

```
> f:= evalm(-(inverse(P)&*ap));
```

$$f := [2799.835680 \quad -40018.02792 \quad 1749.373118]$$

Define the blood lead function x_1***, the tissue lead level*** x_2***, and the bone lead level*** x_3***:***

```
> x1 := t -> f[1]*P[1, 1]*exp(λ[1]*t)
  + f[2]*P[1, 2]*exp(λ[2]*t)
  + f[3]*P[1, 3]*exp(λ[3]*t)+ ap[1];
```

$$x1 := t \rightarrow f_1 P_{1,1} e^{(\lambda_1 t)} + f_2 P_{1,2} e^{(\lambda_2 t)} + f_3 P_{1,3} e^{(\lambda_3 t)} + ap_1$$

```
> x2 := t -> f[1]*P[2, 1]*exp(λ[1]*t)
  + f[2]*P[2, 2]*exp(λ[2]*t)
  + f[3]*P[2, 3]*exp(λ[3]*t)+ ap[2];
```

$$x2 := t \rightarrow f_1 P_{2,1} e^{(\lambda_1 t)} + f_2 P_{2,2} e^{(\lambda_2 t)} + f_3 P_{2,3} e^{(\lambda_3 t)} + ap_2$$

```
> x3 := t -> f[1]*P[3, 1]*exp(λ[1]*t)
  + f[2]*P[3, 2]*exp(λ[2]*t)
  + f[3]*P[3, 3]*exp(λ[3]*t)+ ap[3];
```

$$x3 := t \rightarrow f_1 P_{3,1} e^{(\lambda_1 t)} + f_2 P_{3,2} e^{(\lambda_2 t)} + f_3 P_{3,3} e^{(\lambda_3 t)} + ap_3$$

Plot the blood, tissue, and bone functions together for function z:

```
> plot4:=plot([x1(t), x2(t), x3(t)], t=0..500,
      color=[red, green, blue], thickness=2):%;
```

APPENDIX E

Maple code for Case 4:

```
> with(linalg): with(plots):
```

Enter the matrix E and the vector b:

```
> E := matrix(3,3,[K11, K12, K13, K21, K22, 0, K31, 0,
K33]);
> b := [L, 0, 0];
```

$$E := \begin{bmatrix} K11 & K12 & K13 \\ K21 & K22 & 0 \\ K31 & 0 & K33 \end{bmatrix}$$

$$b := [L, 0, 0]$$

Enter the transfer coefficients and environmental lead burden from the study (5 significant figures):

```
> K11:=-0.036111; K12:=0.012434; K13:=0.000035000;
K21:=0.011111; K22:=-0.028571; K31:=0.0038889; K33:=-
0.000035000; L:= 98.592;
```

$$K11 := -0.036111$$

$$K12 := 0.012434$$

$$K13 := 0.000035000$$

$$K21 := 0.011111$$

$$K22 := -0.028571$$

$$K31 := 0.0038889$$

$$K33 := -0.000035000$$

$$L := 32.296$$

Redefine the matrix E_2 and the vector b:

```
> E := matrix(3,3,[K11, K12, K13, K21, K22, 0, K31, 0,
K33]);
> b := [L, 0, 0];
```

$$E := \begin{bmatrix} -0.036111 & 0.012434 & 0.000035000 \\ 0.011111 & -0.028571 & 0 \\ 0.0038889 & 0 & -0.000035000 \end{bmatrix}$$

$$b := [32.296, 0, 0]$$

Compute a_p with numerical values:

```
> ap := evalm(-(inverse(E)&*b));
```

$$ap := [1179.261500 \quad 458.6039874 \quad 1.310294299\,10^{5}]$$

Compute the eigenvalues and eigenvectors of E:

```
> eigenvects(E);
```

$$[-0.01999966145, 1, \{[-.6111800578 \quad -.7922708414 \quad 0.1190512600]\}]$$
$$, [-0.00003064299534, 1, \{[0.01121188255 \quad 0.00436487979 \quad 10.00730884]\}]$$
$$, [-0.04468669551, 1, \{[-.8232245684 \quad 0.5675738998 \quad 0.07169801700]\}]$$

Assign eigenvalues to a vector λ and construct eigenvectors v_1, v_2, and v_3 (5 significant figures):

```
> lambda:=[-0.020000,-0.000030643, -0.044687];
> v1:=[-0.61118, -0.79227, 0.11905];
v2:=[0.011212, 0.0043649, 10.007];
v3:=[-0.82322, 0.56757, 0.071698];
```

$$\lambda := [-0.020000, -0.000030643, -0.044687]$$

$$v1 := [-.61118, -.79227, 0.11905]$$

$$v2 := [0.011212, 0.0043649, 10.007]$$

$$v3 := [-.82322, 0.56757, 0.071698]$$

Construct the matrix of eigenvectors:

```
> P:=augment(v1,v2,v3);
```

$$P := \begin{bmatrix} -.61118 & 0.011212 & -.82322 \\ -.79227 & 0.0043649 & 0.56757 \\ 0.11905 & 10.007 & 0.071698 \end{bmatrix}$$

Solve for the coefficients in the solution of the initial value problem, $\frac{dx}{dt} = A\,x + b$, $x(0) = 0$:

```
> j:= evalm(-(inverse(P)&*ap));
```

$$j := [917.1483803 \quad -13108.79412 \quad 573.0460305]$$

Define the blood lead function x_1, the tissue lead level x_2, and the bone lead level x_3 :

```
> x1 := t-> j[1]*P[1, 1]*exp(λ[1]*t)
  + j[2]*P[1, 2]*exp(λ[2]*t)+ j[3]*P[1, 3]*exp(λ[3]*t)
  + ap[1];
```

$$x1 := t \to j_1 P_{1,1} e^{(\lambda_1 t)} + j_2 P_{1,2} e^{(\lambda_2 t)} + j_3 P_{1,3} e^{(\lambda_3 t)} + ap_1$$

```
> x2 := t-> j[1]*P[2, 1]*exp(λ[1]*t)
  + j[2]*P[2, 2]*exp(λ[2]*t)+ j[3]*P[2, 3]*exp(λ[3]*t)
  + ap[2];
```

$$x2 := t \to j_1 P_{2,1} e^{(\lambda_1 t)} + j_2 P_{2,2} e^{(\lambda_2 t)} + j_3 P_{2,3} e^{(\lambda_3 t)} + ap_2$$

```
> x3 := t-> j[1]*P[3, 1]*exp(λ[1]*t)
  + j[2]*P[3, 2]*exp(λ[2]*t)+ j[3]*P[3, 3]*exp(λ[3]*t)
  + ap[3];
```

$$x3 := t \to j_1 P_{3,1} e^{(\lambda_1 t)} + j_2 P_{3,2} e^{(\lambda_2 t)} + j_3 P_{3,3} e^{(\lambda_3 t)} + ap_3$$

Set up the linear system that determines the coefficients in the solution of the new initial value problem:

```
> G:=matrix(3,3,[-0.000027748, 0.011042, -1.6288*10^(-10),
-0.000035969, 0.0042985, 1.1230*10^(-10), 0.0000054049,
9.8548, 1.4186*10^(-11)]);
```

$$G := \begin{bmatrix} -0.000027748 & 0.011042 & -1.628800000\,10^{-10} \\ -0.000035969 & 0.0042985 & 1.123000000\,10^{-10} \\ 0.0000054049 & 9.8548 & 1.418600000\,10^{-11} \end{bmatrix}$$

Define the vector of constants for the new initial conditions:

```
> r:=[x1(500), x2(500), x3(500)];
```

$$r := [1034.494978,\ 402.2224157,\ 1844.2831]$$

```
> s := evalm(r - (ap));
```

$$s := [-144.766522\ \ -56.3815717\ \ -1.291851468\,10^{5}]$$

```
> f := evalm((inverse(G) &·s));
```

$$f := [833.691\ \ -13108.85568\ \ -2.82149\,10^{7}]$$

Change the name of the dependent (vector) variable to y to avoid conflict with the functions already defined; leave the time scale untouched so that the x and y functions can be plotted together

```
> y1 := t -> f[1]*P[1, 1]*exp(λ[1]*t)
    + f[2]*P[1, 2]*exp(λ[2]*t)
    + f[3]*P[1, 3]*exp(λ[3]*t)+ ap[1];
```

$$y1 := t \rightarrow f_1 P_{1,1} e^{(\lambda_1 t)} + f_2 P_{1,2} e^{(\lambda_2 t)} + f_3 P_{1,3} e^{(\lambda_3 t)} + ap_1$$

```
> y2 := t -> f[1]*P[2, 1]*exp(λ[1]*t)
    + f[2]*P[2, 2]*exp(λ[2]*t)
    + f[3]*P[2, 3]*exp(λ[3]*t)+ ap[2];
```

$$y2 := t \rightarrow f_1 P_{2,1} e^{(\lambda_1 t)} + f_2 P_{2,2} e^{(\lambda_2 t)} + f_3 P_{2,3} e^{(\lambda_3 t)} + ap_2$$

```
> y3 := t -> f[1]*P[3, 1]*exp(λ[1]*t)
    + f[2]*P[3, 2]*exp(λ[2]*t)
    + f[3]*P[3, 3]*exp(λ[3]*t)+ ap[3];
```

$$y3 := t \rightarrow f_1 P_{3,1} e^{(\lambda_1 t)} + f_2 P_{3,2} e^{(\lambda_2 t)} + f_3 P_{3,3} e^{(\lambda_3 t)} + ap_3$$

Plot the blood, tissue, and bone functions together for function y:

```
> plot5 := plot( [y1(t), y2(t), y3(t)], t = 500..3000, color
      = [red, green, blue], thickness = 2) : %
```

APPENDIX F

Maple code for Case 5:

```
> with(linalg): with(plots):
```

Enter the matrix E and the vector b:

```
> E := matrix(3,3,[K11, K12, K13, K21, K22, 0, K31, 0,
K33]);
> b := [L, 0, 0];
```

$$E := \begin{bmatrix} K11 & K12 & K13 \\ K21 & K22 & 0 \\ K31 & 0 & K33 \end{bmatrix}$$

$$b := [L, 0, 0]$$

Enter the transfer coefficients and environmental lead burden from the study (5 significant figures):

```
> K11:=-0.036111; K12:=0.022857; K13:=0.000035000;
K21:=0.011111; K22:=-0.028571; K31:=0.0038889; K33:=-
0.000035000; L:= 17;
```

$$K11 := -0.036111$$

$$K12 := 0.022857$$

$$K13 := 0.000035000$$

$$K21 := 0.011111$$

$$K22 := -0.028571$$

$$K31 := 0.0038889$$

$$K33 := -0.000035000$$

$$L := 17$$

Redefine E and b with numerical values:

```
> E := matrix(3,3,[K11, K12, K13, K21, K22, 0, K31, 0,
K33]);
> b := [L, 0, 0];
```

$$E := \begin{bmatrix} -0.036111 & 0.012434 & 0.000035000 \\ 0.011111 & -0.028571 & 0 \\ 0.0038889 & 0 & -0.000035000 \end{bmatrix}$$

$$b := [17, 0, 0]$$

Compute a_p with numerical values:

```
> ap := evalm(-(inverse(E)&*b));
```

$$ap := [620.7408193 \quad 241.4004145 \quad 68971.39921]$$

Compute the eigenvalues and eigenvectors of E:

```
> eigenvects(E);
```

$$[-0.01999966145, 1, \{[-.6111800578 \quad -.7922708414 \quad 0.1190512600]\}], [-0.00003064299534, 1, \{[0.01121188255 \quad 0.00436487979 \quad 10.00730884]\}], [-0.04468669551, 1, \{[-.8232245684 \quad 0.5675738998 \quad 0.07169801700]\}]$$

Assign eigenvalues to a vector λ and construct eigenvectors v_1, v_2, and v_3 (5 significant figures):

```
> lambda:=[-0.020000,-0.000030643, -0.044687];
> v1:=[-0.61118, -0.79227, 0.11905];
> v2:=[0.011212, 0.0043649, 10.007];
> v3:=[-0.82322, 0.56757, 0.071698];
```

$$\lambda := [-0.020000, -0.000030643, -0.044687]$$

$$v1 := [-.61118, -.79227, 0.11905]$$

$$v2 := [0.011212, 0.0043649, 10.007]$$

$$v3 := [-.82322, 0.56757, 0.071698]$$

Construct the matrix of eigenvectors:

```
> P:=augment(v1,v2,v3);
```

$$P := \begin{bmatrix} -.61118 & 0.011212 & -.82322 \\ -.79227 & 0.0043649 & 0.56757 \\ 0.11905 & 10.007 & 0.071698 \end{bmatrix}$$

Solve for the coefficients in the solution of the initial value problem, $\frac{dx}{dt} = Ex + b$, $x(0) = 0$:

```
> j:= evalm(-(inverse(P)&*ap));
>
```

$$j := [482.7694596 \quad -6900.219840 \quad 301.6405287]$$

Define the blood lead function x_1, the tissue lead level x_2, and the bone lead level x_3 :

```
> x1 := t-> j[1]*P[1, 1]*exp(λ[1]*t)
  + j[2]*P[1, 2]*exp(λ[2]*t)+ j[3]*P[1, 3]*exp(λ[3]*t)
  + ap[1];
```

$$x1 := t \rightarrow j_1 P_{1,1} e^{(\lambda_1 t)} + j_2 P_{1,2} e^{(\lambda_2 t)} + j_3 P_{1,3} e^{(\lambda_3 t)} + ap_1$$

```
> x2 := t-> j[1]*P[2, 1]*exp(λ[1]*t)
  + j[2]*P[2, 2]*exp(λ[2]*t)+ j[3]*P[2, 3]*exp(λ[3]*t)
  + ap[2];
```

$$x2 := t \rightarrow j_1 P_{2,1} e^{(\lambda_1 t)} + j_2 P_{2,2} e^{(\lambda_2 t)} + j_3 P_{2,3} e^{(\lambda_3 t)} + ap_2$$

```
> x3 := t-> j[1]*P[3, 1]*exp(λ[1]*t)
  + j[2]*P[3, 2]*exp(λ[2]*t)+ j[3]*P[3, 3]*exp(λ[3]*t)
  + ap[3];
```

$$x3 := t \rightarrow j_1 P_{3,1} e^{(\lambda_1 t)} + j_2 P_{3,2} e^{(\lambda_2 t)} + j_3 P_{3,3} e^{(\lambda_3 t)} + ap_3$$

Set up the linear system that determines the coefficients in the solution of the new initial value problem:

```
> evalm(P);
> mulcol(P,1,exp(lambda[1]*500));
```

$$\begin{bmatrix} -.61118 & 0.011212 & -.82322 \\ -.79227 & 0.0043649 & 0.56757 \\ 0.11905 & 10.007 & 0.071698 \end{bmatrix}$$

$$\begin{bmatrix} -0.00002774752907 & 0.011212 & -.82322 \\ -0.00003596900235 & 0.0043649 & 0.56757 \\ 0.000005404861638 & 10.007 & 0.071698 \end{bmatrix}$$

```
> mulcol(P, 2, exp(λ[2]*500));
```

$$\begin{bmatrix} -.61118 & 0.01104152465 & -.82322 \\ -.79227 & 0.004298532905 & 0.56757 \\ 0.11905 & 9.854846337 & 0.071698 \end{bmatrix}$$

```
> mulcol(P, 3, exp(λ[3]*500));
```

$$\begin{bmatrix} -.61118 & 0.011212 & -1.628760230\ 10^{-10} \\ -.79227 & 0.0043649 & 1.122950662\ 10^{-10} \\ 0.11905 & 10.007 & 1.418561879\ 10^{-11} \end{bmatrix}$$

```
> G := matrix(3, 3,[-0.000027748, 0.011042, -1.6288*10^(
    -10), -0.000035969, 0.0042985, 1.1230*10^(
    -10), 0.0000054049, 9.8548, 1.4186*10^(-11)]);
```

$$G := \begin{bmatrix} -0.000027748 & 0.011042 & -1.628800000\ 10^{-10} \\ -0.000035969 & 0.0042985 & 1.123000000\ 10^{-10} \\ 0.0000054049 & 9.8548 & 1.418600000\ 10^{-11} \end{bmatrix}$$

Define the vector of constants for the new initial conditions:

```
> r:=[x1(500), x2(500), x3(500)];
```

$$r := [544.5384762,\ 211.7222278,\ 970.79560]$$

```
> s :=evalm(r- (ap));
```

$$s := [-76.2023431 \quad -29.6781867 \quad -68000.60361]$$

```
> f :=evalm( (inverse(G) &·s));
```

$$f := [438.839 \quad -6900.252243 \quad -1.48517\ 10^{7}]$$

Change the name of the dependent (vector) variable to y to avoid conflict with the functions already defined; leave the time scale untouched so that the x and y functions can be plotted together

```
> y1 := t -> f[1]*P[1, 1]*exp(λ[1]*t)
    + f[2]*P[1, 2]*exp(λ[2]*t)
    + f[3]*P[1, 3]*exp(λ[3]*t)+ ap[1];
```

$$y1 := t \rightarrow f_1 P_{1,1} e^{(\lambda_1 t)} + f_2 P_{1,2} e^{(\lambda_2 t)} + f_3 P_{1,3} e^{(\lambda_3 t)} + ap_1$$

```
> y2 := t -> f[1]*P[2, 1]*exp(λ[1]*t)
    + f[2]*P[2, 2]*exp(λ[2]*t)
    + f[3]*P[2, 3]*exp(λ[3]*t)+ ap[2];
```

$$y2 := t \rightarrow f_1 P_{2,1} e^{(\lambda_1 t)} + f_2 P_{2,2} e^{(\lambda_2 t)} + f_3 P_{2,3} e^{(\lambda_3 t)} + ap_2$$

```
> y3 := t -> f[1]*P[3, 1]*exp(λ[1]*t)
    + f[2]*P[3, 2]*exp(λ[2]*t)
    + f[3]*P[3, 3]*exp(λ[3]*t)+ ap[3];
```

$$y3 := t \rightarrow f_1 P_{3,1} e^{(\lambda_1 t)} + f_2 P_{3,2} e^{(\lambda_2 t)} + f_3 P_{3,3} e^{(\lambda_3 t)} + ap_3$$

Plot the blood, tissue, and bone functions together for function y:

```
> plot6 := plot( [y1(t), y2(t), y3(t)], t = 500..3000, color
    = [red, green, blue], thickness = 2) : %;
```

APPENDIX G

Maple code for Case 6:

```
> with(linalg): with(plots):
```

Enter the matrix E and the vector b:

```
> E := matrix(3,3,[K11, K12, K13, K21, K22, 0, K31, 0,
K33]);
> b := [L, 0, 0];
```

$$E := \begin{bmatrix} -0.036111 & 0.012434 & 0.000035000 \\ 0.011111 & -0.028571 & 0 \\ 0.0038889 & 0 & -0.000035000 \end{bmatrix}$$

$$b := [49.296, 0, 0]$$

Compute a_p with numerical values:

```
> ap := evalm(-(inverse(E)&*b));
```

$$ap := [1800.002319 \quad 700.0044018 \quad 2.000008291\ 10^5]$$

Compute the eigenvalues and eigenvectors of E:

```
> eigenvects(E);
```

```
[-0.01999966145, 1
  , {[-.6111800578  -.7922708414  0.1190512600]} ]
  , [
  -0.00003064299534, 1
  , {[0.01121188255  0.00436487979  10.00730884]} ]
  , [
  -0.04468669551, 1
  , {[-.8232245684  0.5675738998  0.07169801700]} ]
```

Assign eigenvalues to a vector λ and construct eigenvectors v_1, v_2, and v_3 (5 significant figures):

```
> lambda:=[-0.020000,-0.000030643, -0.044687];
> v1:=[-0.61118, -0.79227, 0.11905];
v2:=[0.011212, 0.0043649, 10.007];
v3:=[-0.82322, 0.56757, 0.071698];
```

$$\lambda := [-0.020000,\ -0.000030643,\ -0.044687]$$

$$v1 := [-.61118,\ -.79227,\ 0.11905]$$

$$v2 := [0.011212,\ 0.0043649,\ 10.007]$$

$$v3 := [-.82322,\ 0.56757,\ 0.071698]$$

Construct the matrix of eigenvectors:

```
> P:=augment(v1,v2,v3);
```

$$P := \begin{bmatrix} -.61118 & 0.011212 & -.82322 \\ -.79227 & 0.0043649 & 0.56757 \\ 0.11905 & 10.007 & 0.071698 \end{bmatrix}$$

Solve for the coefficients in the solution of the initial value problem, $\frac{dx}{dt} = Ex + b$, $x(0) = 0$:

```
> j:= evalm(-(inverse(P)&*ap));
```

$$j := [1399.917839\ \ -20009.01395\ \ 874.6865592]$$

Define the blood lead function x_1, the tissue lead level x_2, and the bone lead level x_3 :

```
> x1 := t-> j[1]*P[1, 1]*exp(λ[1]*t)
  + j[2]*P[1, 2]*exp(λ[2]*t)+ j[3]*P[1, 3]*exp(λ[3]*t)
  + ap[1];
```

$$x1 := t \rightarrow j_1 P_{1,1} e^{(\lambda_1 t)} + j_2 P_{1,2} e^{(\lambda_2 t)} + j_3 P_{1,3} e^{(\lambda_3 t)} + ap_1$$

```
> x2 := t-> j[1]*P[2, 1]*exp(λ[1]*t)
  + j[2]*P[2, 2]*exp(λ[2]*t)+ j[3]*P[2, 3]*exp(λ[3]*t)
  + ap[2];
```

$$x2 := t \rightarrow j_1 P_{2,1} e^{(\lambda_1 t)} + j_2 P_{2,2} e^{(\lambda_2 t)} + j_3 P_{2,3} e^{(\lambda_3 t)} + ap_2$$

```
> x3 := t-> j[1]*P[3, 1]*exp(λ[1]*t)
  + j[2]*P[3, 2]*exp(λ[2]*t)+ j[3]*P[3, 3]*exp(λ[3]*t)
  + ap[3];
```

$$x3 := t \rightarrow j_1 P_{3,1} e^{(\lambda_1 t)} + j_2 P_{3,2} e^{(\lambda_2 t)} + j_3 P_{3,3} e^{(\lambda_3 t)} + ap_3$$

Plot the blood, tissue, and bone functions together for function x:

```
> plot7:=plot([x1(t), x2(t), x3(t)], t=0..500,
>       color=[red, green, blue], thickness=2):%;
```

Calculate and set up the linear system that determines the coefficients in the solution of the new initial value problem:

```
> evalm(P);
> mulcol(P,1,exp(lambda[1]*500));
```

$$\begin{bmatrix} -.61118 & 0.011212 & -.82322 \\ -.79227 & 0.0043649 & 0.56757 \\ 0.11905 & 10.007 & 0.071698 \end{bmatrix}$$

$$\begin{bmatrix} -0.00002774752907 & 0.011212 & -.82322 \\ -0.00003596900235 & 0.0043649 & 0.56757 \\ 0.000005404861638 & 10.007 & 0.071698 \end{bmatrix}$$

```
> mulcol(P, 2, exp(lambda[2]*500));
```

$$\begin{bmatrix} -.61118 & 0.01104152465 & -.82322 \\ -.79227 & 0.004298532905 & 0.56757 \\ 0.11905 & 9.854846337 & 0.071698 \end{bmatrix}$$

```
> mulcol(P, 3, exp(lambda[3]*500));
```

$$\begin{bmatrix} -.61118 & 0.011212 & -1.628760230\ 10^{-10} \\ -.79227 & 0.0043649 & 1.122950662\ 10^{-10} \\ 0.11905 & 10.007 & 1.418561879\ 10^{-11} \end{bmatrix}$$

```
> G := matrix(3, 3
   , [ − 0.000027748, 0.011042, −1.6288 10^-10,
    − 0.000035969,
   0.0042985, 1.1230· 10^− 10, 0.0000054049, 9.8548, 1.4186
   · 10^− 11 ]);
```

$$G := \begin{bmatrix} -0.000027748 & 0.011042 & -1.628800000\ 10^{-10} \\ -0.000035969 & 0.0042985 & 1.123000000\ 10^{-10} \\ 0.0000054049 & 9.8548 & 1.418600000\ 10^{-11} \end{bmatrix}$$

Define the vector of constants for the new initial conditions:

```
> r :=[x1(500), x2(500), x3(500)];
```

$$r := [1579.033454,\ 613.9446434,\ 2815.0789]$$

Calculate coefficients for new conditions (at t = 500):

```
> f := evalm((inverse(G)&*p));
```

$$f := [-3.083383602 \cdot 10^{7} \quad 308.9301527 \quad -4.42078285 \cdot 10^{12}]$$

Change the name of the dependent (vector) variable to y to avoid conflict with the functions already defined; leave the time scale untouched so that the x and y functions can be plotted together:

```
> y1 := t -> f[1]*P[1, 1]*exp(λ[1]*t)
    + f[2]*P[1, 2]*exp(λ[2]*t)
    + f[3]*P[1, 3]*exp(λ[3]*t)+ ap[1];
```

$$y1 := t \rightarrow f_1 P_{1,1} e^{(\lambda_1 t)} + f_2 P_{1,2} e^{(\lambda_2 t)} + f_3 P_{1,3} e^{(\lambda_3 t)} + ap_1$$

```
> y2 := t -> f[1]*P[2, 1]*exp(λ[1]*t)
    + f[2]*P[2, 2]*exp(λ[2]*t)
    + f[3]*P[2, 3]*exp(λ[3]*t)+ ap[2];
```

$$y2 := t \rightarrow f_1 P_{2,1} e^{(\lambda_1 t)} + f_2 P_{2,2} e^{(\lambda_2 t)} + f_3 P_{2,3} e^{(\lambda_3 t)} + ap_2$$

```
> y3 := t -> f[1]*P[3, 1]*exp(λ[1]*t)
    + f[2]*P[3, 2]*exp(λ[2]*t)
    + f[3]*P[3, 3]*exp(λ[3]*t)+ ap[3];
```

$$y3 := t \rightarrow f_1 P_{3,1} e^{(\lambda_1 t)} + f_2 P_{3,2} e^{(\lambda_2 t)} + f_3 P_{3,3} e^{(\lambda_3 t)} + ap_3$$

Plot the blood, tissue, and bone functions together for function y:

```
> plot8:=plot([y1(t), y2(t), y3(t)], t=0..500,
    color=[red, green, blue], thickness=2):%;
```

Combine plots7 and 8:

```
> display(plot7, plot8);
```

Plots to observe time when bone lead level approaches zero:

```
> plot9:=plot([x1(t), x2(t), x3(t)], t=0..500,
    color=[red, green, blue], thickness=2):%;

> plot10:=plot([y1(t), y2(t), y3(t)], t=0..500,
    color=[red, green, blue], thickness=2):%;

> display(plot9, plot10);
```

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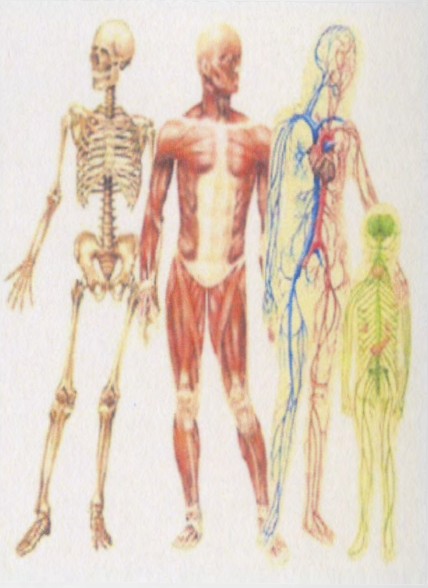
A Mathematical Approach to the Transfer of Lead in the Human Body

By

Sean Leonardo Knowles



The kinetics of lead transfer in the human body is described by a system of first order differential equations . . .

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