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The Kinetics of Lead Transfer in the Human Body

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Abstract

The kinetics of lead in the human body are described by a system of first order differential equations. Parameters are estimated from actual data. The model is applied to specific situations.

1. Introduction

Lead is closely related to human life. Gasoline, paint, and foil contain lead. Lead is contained in the soil in a natural environment [Batschelet]. People ingest lead indirectly through natural foods and water. Human beings have been facing the cumulative effects of lead poisoning for many years. In our society, the lead concentration is extremely high because sophisticated industries pollute the environment with lead. To detect levels of lead in the body, a model of the kinetics of lead transfer is described below.

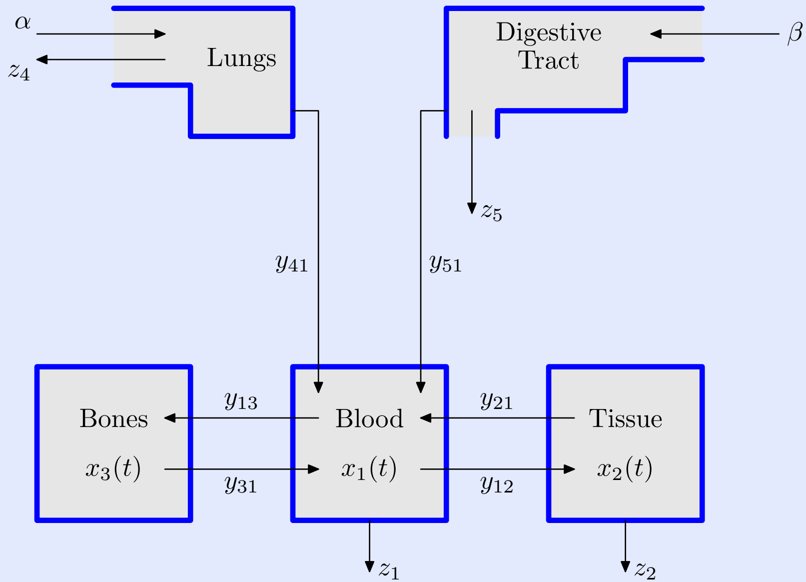

Figure 1: The compartment model for the kinetics of lead.

2. Building the model of the kinetics of lead

We divide the body into three compartments: the blood, the tissue, and the bones (see Figure 1). The lead is transferred from one compartment to another by several blood vessels. We will model this exchange with a system of first order differential equations.

Lead is taken in from outside the body via the lungs and the digestive system. These are the main sources of lead intake. From this point forward, we assume that all lead transfer is measured in micrograms per day (μg/day). Let α be the rate at which lead enters the lungs and let β be the rate at which lead enters the digestive system.

Lead also enters the digestive tract from the tissue compartment (saliva, gastric secretions, bile, etc.). Let Y_{25} be the rate at which this occurs. Of course, a certain amount of lead escapes through the lungs and digestive tract. Let Z_4 be the rate at which lead escapes the lungs through normal breathing. Let Z_5 be the rate at which lead escapes the digestive tract through bowel movements.

Lead from the lungs and digestive tract enters the blood. Let Y_{41} be the rate at which lead enters the blood from the lungs. Let Y_{51} be the rate at which lead enters the blood from the digestive tract.

Next, let's describe the lead exchange between the tissue and blood. Let Y_{12} be the rate at which lead enters the tissue from the blood. Let Y_{21} be the rate at which lead comes back to the blood from the tissue.

Let's describe the lead exchange between the bones and the blood. Let Y_{13} be the rate at which lead enters the bones from the blood. Let Y_{31} be the rate at which lead comes back to the blood from the bones.

Lead can also escape from the body by way of the blood and the tissue. Let

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Z_1 be the rate at which lead escapes the blood as urine. Let Z_2 be the rate at which lead escapes the tissue through the hairs, nails, sweat, etc.

The rate Y_{41} at which lead flows from the lungs to the blood is equal to the rate at which the lungs absorb lead.

$$Y_{41} = \alpha - Z_4 \tag{1}$$

Furthermore, we assume that this rate is proportional to the rate at which lead enters the lungs.

$$Y_{41} = \alpha - Z_4 = p\alpha, \quad \text{where } 0 < p < 1 \tag{2}$$

Next, the rate Y_{51} at which lead flows from the digestive tract to the blood is equal to the rate at which the digestive tract absorbs lead. Remember that the digestive tract absorbs lead from two sources, diet and tissue. If we assume that the rate Y_{51} is proportional to the rate at which lead enters the digestive tract, then we can write

$$Y_{51} = q(\beta + Y_{25}), \quad \text{where } 0 < q < 1. \tag{3}$$

Let $x_1(t)$, $x_2(t)$, $x_3(t)$ represent the amount (μg) of lead in the blood, tissue, and bone compartments, respectively. Then $\dot{x_1}$ represents the rate at which lead enters and escapes the blood compartment. This is equal to the rate at which lead comes into the blood compartment minus the rate at which lead escapes the compartment.

$$\dot{x_1} = -Y_{12} + Y_{21} - Y_{13} + Y_{31} + Y_{41} + Y_{51} - Z_1 \tag{4}$$

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In a similar manner, one can develop rate equations for the tissue and bone compartments.

$$
\begin{aligned}
\dot{x_1} &= -Y_{12} + Y_{21} - Y_{13} + Y_{31} + Y_{41} + Y_{51} - Z_1 \\
\dot{x_2} &= Y_{12} - Y_{21} - Y_{25} - Z_2 \\
\dot{x_3} &= Y_{13} + Y_{31}
\end{aligned} \tag{5}
$$

Assume that the lead flow from the blood compartment to the tissue compartment is proportional to the amount of lead in the blood compartment. In symbols,

$$Y_{12} = a_{12}x_1. \tag{6}$$

In a similar manner,

$$
\begin{aligned}
Y_{21} &= a_{21}x_2 & \qquad Y_{13} &= a_{13}x_1 \\
Y_{31} &= a_{31}x_3 & \qquad Y_{25} &= a_{25}x_2 \\
Z_1 &= bx_1 & \qquad Z_2 &= cx_2
\end{aligned} \tag{7}
$$

Take these proportions and equations (2) and (3) and substitute them in the equations of system (5).

$$
\begin{aligned}
\dot{x_1} &= -a_{12}x_1 + a_{21}x_2 - a_{13}x_1 + a_{31}x_3 + p\alpha + q(\beta + a_{25}x_2) - bx_1 \\
\dot{x_2} &= a_{12}x_1 - a_{21}x_2 - a_{25}x_2 - cx_2 \\
\dot{x_3} &= a_{13}x_1 + a_{31}x_3
\end{aligned} \tag{8}
$$

The $a_{i,k}$, b, c are positive constants. By combining coefficients the equations can be rewritten in the following form.

$$\begin{aligned}
\dot{x}_1 &= A_{11}x_1 - A_{12}x_2 + A_{13}x_3 + D \\
\dot{x}_2 &= A_{21}x_1 + A_{22}x_2 \\
\dot{x}_3 &= A_{31}x_1 + A_{33}x_3
\end{aligned} \tag{9}$$

The three liner nonhomogeneous differential equations are formed. The inhomogeneous term is D, where

$$D = p\alpha + q\beta. \tag{10}$$

3. Identification of the Model

Although the three differential equations are formed in a reasonable way, the coefficients $A_{i,k}$ are not determined. We next consider a real-life study to determine some particular coefficients for our differential equations.

The following data was taken from the Journal of Mathematical Biology in 1979[Batschelet]. The authors used a subject who was healthy 53 year old male, weighing 70 kg, smoking eight cigarettes per day. The subject lived in the southern California. For 104 days, the subject studied was considered to be in a stable state with respect to lead.

$$\begin{aligned}
x_1 &= 1800\,\mu\text{g}, & Y_{12} &= 20\,\mu\text{g/d}, & Z_1 &= 38\,\mu\text{g/d},\\
x_2 &= 700\,\mu\text{g}, & Y_{21} &= 8\,\mu\text{g/d}, & Z_2 &= 4\,\mu\text{g/d},\\
x_3 &= 200000\,\mu\text{g}, & Y_{13} &= Y_{31} = 7\,\mu\text{g/d}, & Z_4 &= 32\,\mu\text{g/d},\\
\alpha &= 49\,\mu\text{g}, & Y_{41} &= 17\,\mu\text{g/d}, & Z_5 &= 38\,\mu\text{g/d},\\
\beta &= 367\,\mu\text{g}, & Y_{51} &= 33\,\mu\text{g/d}, & Y_{25} &= 8\,\mu\text{g/d}.
\end{aligned}$$

Use the data to calculate D.

$$\begin{aligned}
D &= p\alpha + q\beta\\
D &= 49p + 367q
\end{aligned}$$

Use equations (2) and (3) to calculate p and q.

$$\begin{aligned} Y_{41} &= p\alpha \\ p &= \frac{Y_{41}}{\alpha} \\ p &= \frac{17}{49} \end{aligned} \qquad \begin{aligned} Y_{51} &= q(\beta + Y_{25}) \\ q &= \frac{Y_{51}}{(\beta + Y_{25})} \\ q &= \frac{11}{125} \end{aligned}$$

Now that we know the values of p and q, D can be calculated.

$$\begin{aligned} D &= 49p + 367q \\ &= 49(17/49) + 367(11/125) \\ &= 498/25 \\ &\simeq 49.3 \end{aligned} \tag{11}$$

To find the remaining coefficients, we substitute the data from the study into equation (6) and (7).

$$\begin{aligned} Y_{12} &= a_{12} * x_1, \\ a_{12} &= Y_{12}/x_1, \\ a_{12} &= 20/1800, \end{aligned} \qquad \begin{aligned} Y_{21} &= a_{21} * x_2 \\ a_{21} &= Y_{21}/x_2 \\ a_{21} &= 8/700 \end{aligned}$$

$$\begin{aligned} Y_{13} &= a_{13}x_1, \\ a_{13} &= Y_{13}/x_1, \\ a_{13} &= 7/1800, \end{aligned} \qquad \begin{aligned} Y_{31} &= a_{31}x3 \\ a_{31} &= Y_{31}/x_3 \\ a_{21} &= 7/200000 \end{aligned}$$

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$$
\begin{array}{lll}
Y_{25}x_2 = a_{25}, & bx_1 = Z_1, & cx_1 = Z_2 \\
a_{25} = 8/700, & b = 38/1800, & c = 4/700
\end{array}
$$

A comparison of equations (8) and (9) reveals the following relations.

$$
\begin{aligned}
A_{11} &= -(a_{12} + a_{13} + b) & A_{12} &= a_{21} + a_{25}q \\
A_{13} &= a_{31} & A_{21} &= a_{21} \\
A_{22} &= -(a_{21} + a_{25} + c) & A_{31} &= a_{13} \\
A_{33} &= -a_{31}
\end{aligned}
$$

Substituting our calculated coefficients leads to the following $A_{i,k}$.

$$
\begin{aligned}
A_{11} &= -65/1800) & A_{12} &= 1088/87500 \\
A_{13} &= 7/200000 & A_{21} &= 20/1800 \\
A_{22} &= -20/700 & A_{31} &= 7/1800 \\
A_{33} &= -7/1800
\end{aligned}
$$

If we substitute these values into the equations in system (9), we arrive at

$$
\begin{aligned}
\dot{x_1} &= -65/1800x_1 + 1088/87500x_2 + 7/200000x_3 + D \\
\dot{x_2} &= 20/1800x_1 + -20/700x_2 \\
\dot{x_3} &= 7/1800x_1 + -7/200000x_3.
\end{aligned}
\tag{12}
$$

This result is reasonable, but this applies only for the subject tested. However, this will be a good approximation for the real situation.

4. Case Study

Using the first order differential equation (12), several case are applied. First equation (12) is used to construct a graph. Note that the lead in the blood and tissue quickly go to equilibrium levels (see Figure 2). But the lead in the bones continues increasing. This is because the coefficient of x_3 is small. The lead transferred back from the bones to the blood is so small that the lead accumulates in the bones. Even after 1000 days, the lead in the bones is an enormous quantity compared with other two compartments (see Figure 3). To improve the subject's health condition, some further assumptions are applied to the equation (12).

4.1. Non-lead environment

Suppose 400 days later, the subject moves to non-lead environment. The value D in the equation (12) is the total quantity of lead intake per day because from previous equations only D is related to the intake quantity directly from the outside environment. For this case, the value D is arranged be a step function, $49.3\,\mathrm{step}(400-t)$. After 400 days, the lead is gradually taken out of the body because the intake rate goes to zero. The graph 4 shows quick drop of the lead level after 400 days, then reaches to zero in the blood and the tissues. Even the level in the bones changes behavior to horizontal movement, although it does not drop to zero.

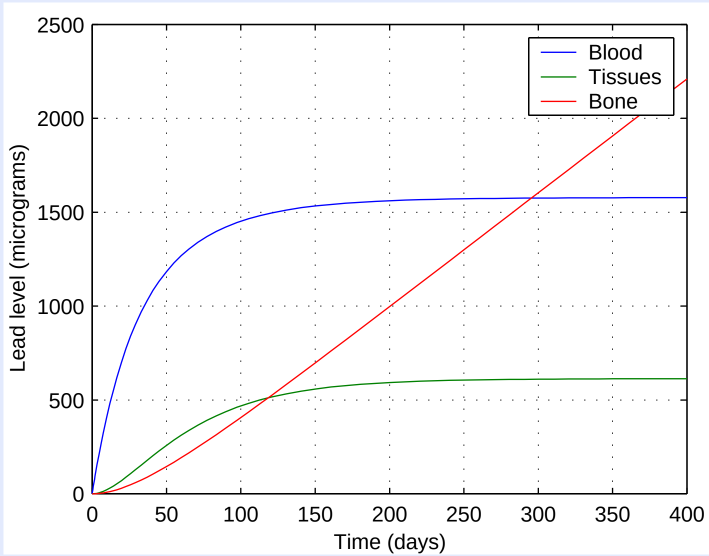

Figure 2: After 400 days, blood and tissue levels go to equilibrium, but bone levels soar.

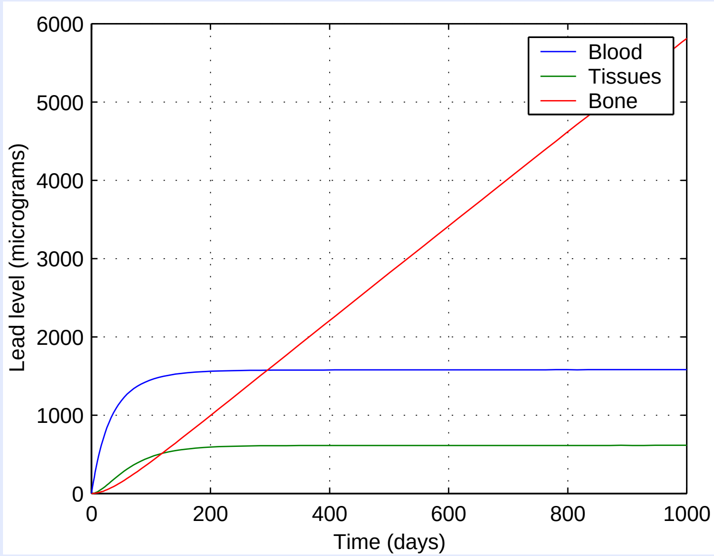

Figure 3: After 1000 days, the lead in the bones continues to increase.

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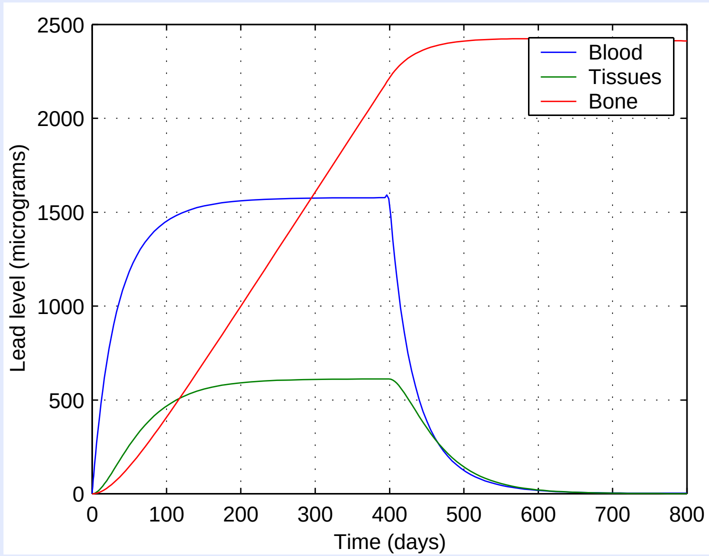

Figure 4: Changing lead intake zeros blood and tissue levels, but not the levels of lead in the bone.

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4.2. Small lead environment

The non-lead environment is not realistic for this industry, so if the lead level is reduced (the subject moves to a rural area or quits smoking after 400 days), what behavior will the differential equations show? For this case, the value D is changed. The lead level of the body is reduced, but some quantity of lead is ingested by the step function. As a reasonable value, the intake rate is reduced from 49.3 to 33 [Borrelli]. D is defined as $D = 49.3\,\mathrm{step}(400-t) + 33\,\mathrm{step}(t-400)$. The graph 5 shows the drop of the lead in the blood and the tissues, but the level in the bones still increases. This tells us that it is difficult to take the lead out of the bones by decreasing the lead intake.

4.3. Massive medication

Suppose that the subject stays in the same area, but he decides to take medication to reduce the lead level in his body. The medication works to remove lead through the urine. This affects the coefficient of Z_1, and indirectly the coefficient value of A_{11} in equation (9). Borrelli and Coleman (see [Borrelli]) define A_{11} as $0.0211\,\mathrm{step}(400-t) + 0.211\,\mathrm{step}(t-400)$. The first of the three differential equations (12) is rewritten as

$$\begin{aligned} \dot{x_1} = {} & (0.0211\,\mathrm{step}(400-t) + 0.211\,\mathrm{step}(t-400))x_1 \\ & + 1088/87500x_2 + 7/200000x_3 + 49.3. \end{aligned} \tag{13}$$

The graph in Figure 6 shows a dramatic drop in lead levels after 400 days, even in the lead level in the bones changes direction significantly. Although this method quickly reduces lead levels, it also kills the subject. So, this medication is not practical in real life.

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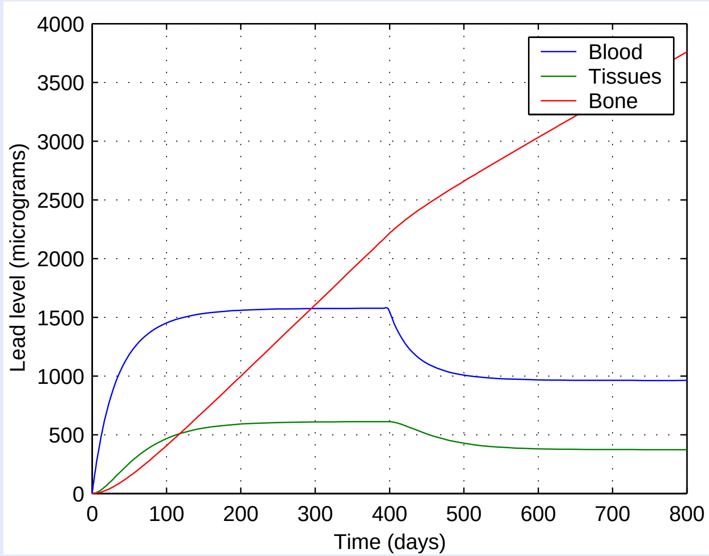

Figure 5: Reduce the lead intake still predicts problems for lead levels in bone.

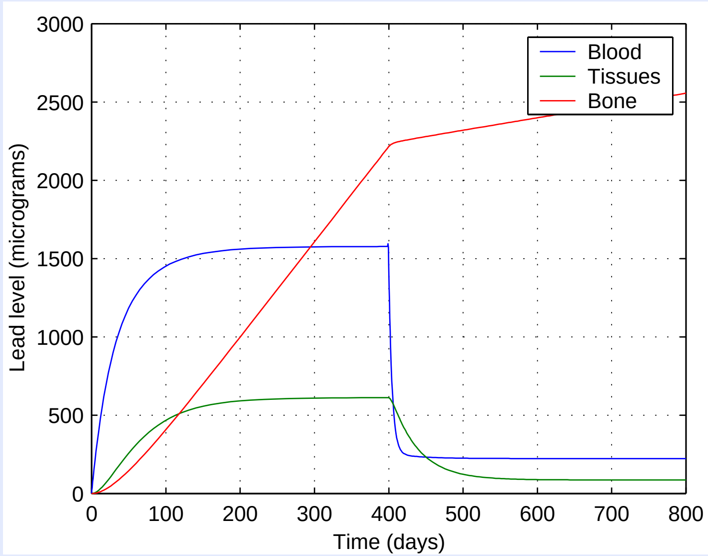

Figure 6: Massive levels of medication slow lead levels.

4.4. Safer Medication

As a safer medication, the effective value of coefficient A_{11} is increased 50% to 0.0316[Borrelli]. The first equation now becomes

$$\begin{aligned}\dot{x_1} = {} & (0.0211\,\mathrm{step}(400-t) + 0.0316\,\mathrm{step}(t-400))x_1 \\ & + 1088/87500x_2 + 7/200000x_3 + 49.3.\end{aligned} \tag{14}$$

This is safer compared with massive doses of medication, and decreases the lead level in the blood and the tissue, but the lead in the bones does not change its drastic behavior (See Figure 7).

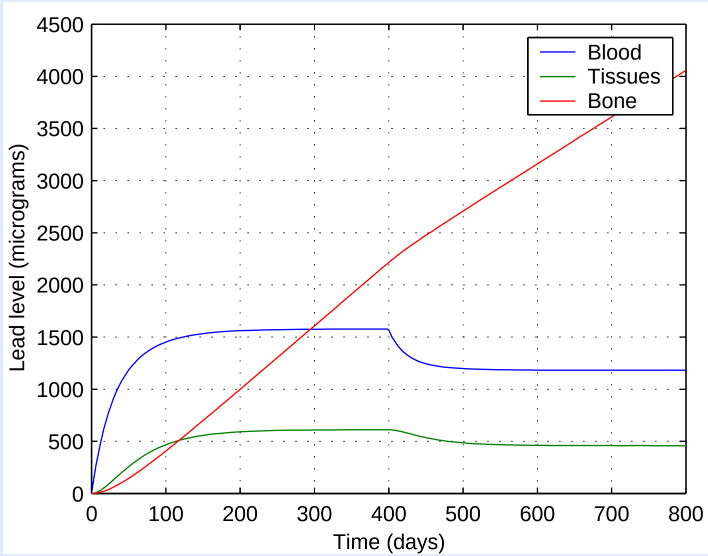

Figure 7: Safe dosages of the medication affect lead levels in the blood and tissue, but the levels in the bone continue to increase.

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5. Conclusion

The intake rate of the lead inside the body is difficult to analyze, but using this system of first order differential equations helps the analysis. Changing the values of the coefficients influences the behavior of the equations.

When I was looking for a subject for this project, many applications of differential equations were for physics or biological materials. However, as I worked on this project, I discovered that a system of differential equations is an effective tool for analyzing data.

References

[Batschelet] Batschelet, E., Brand, L., Steiner, A. *On the Kinetics of Lead in the Human Body*. Journal of Mathematical Biology. 15-23 (1979)

[Borrelli] Borrelli, R., Coleman, C. *Linear Systems of Differential Equations*. Differential Equations.339-344 (1997)