

*Lab Assignment 2*

**Bioaccumulation of Methyl Mercury**

*Written by*

Prof. Erin N. Bodine

*Prepared for*

Math 214: Discrete Math Modeling

Rhodes College

Last Edited: September 9, 2018

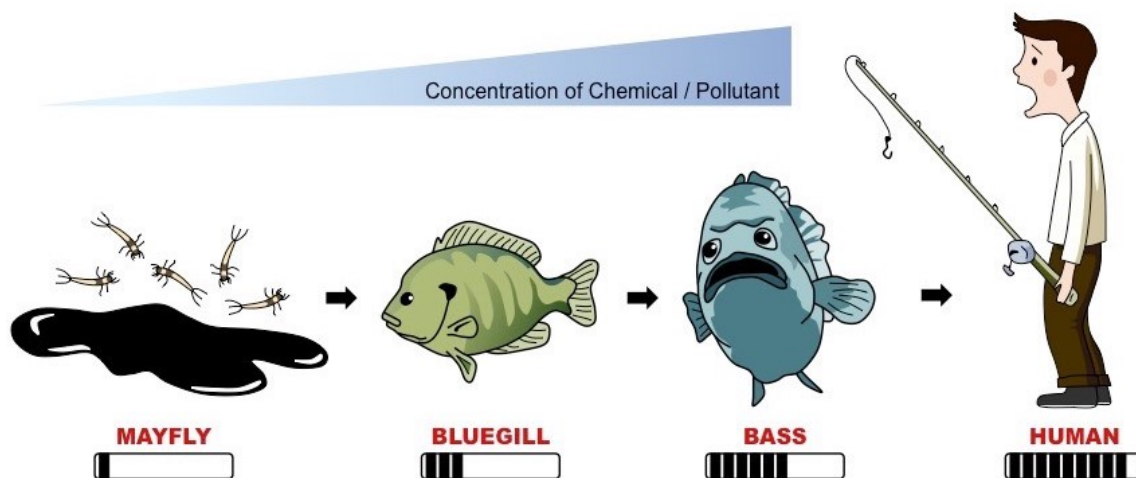
Scientists have known about the adverse effects of mercury on the health of humans for more than a century. The term “mad as a hatter” stems from the nineteenth-century use of mercuric nitrate in the making of felt hats. Human activities are responsible for most mercury emitted into the environment. For example, mercury is released from smokestack emissions of old, coal-fired power plants in the Midwest and South. Particles containing mercury rise in smokestack plumes and then disperse on prevailing winds which often blow towards the northeast. Eventually, the particles drop to earth in the form of acid rain. Once in the ecosystem, microorganisms in the soil and in reservoir/lake sediment break down the mercury and produce a toxic chemical known as methyl mercury.

Methyl mercury undergoes a process known as bioaccumulation. This occurs when organisms take in contaminants more rapidly than their bodies can eliminate them. Therefore, the amount of methyl mercury in their bodies accumulates over time. Biological organisms eliminate the amount of methyl mercury in their system at a rate proportional to the amount remaining (i.e. the amount decays exponentially). In humans, the half-life of methyl mercury is 65 to 75 days. If humans consume food containing methyl mercury at a rate faster than they are eliminating it, methyl mercury will accumulate in their body. Methyl mercury becomes lethal in humans when the concentration exceeds 30 mg/kg, but there can be detrimental effects to the fetuses of pregnant women if the concentration exceeds 0.02 mg/kg in the mother (referred to as *fetal methyl mercury poisoning*).

Officials in the town of Nowhere have collected and tested 2,425 samples of largemouth bass from nearby reservoirs and found that all fish were contaminated with methyl mercury. The mean concentration of methyl mercury in the fish samples was  $0.43 \mu\text{g}$  (micrograms) per gram of fish mass. The average mass of the sampled largemouth bass was 0.817 kg. Assuming the average adult person in Nowhere is 70 kg and regularly consumes largemouth bass, what public health policy recommendation would you make to the people of Nowhere concerning the consumption of largemouth bass caught in local reservoirs?

The goals of this lab assignment are to:

- Construct a difference equation model of the amount of methyl mercury in an average adult resident in the town of Nowhere.
- Utilize your model to make a public health policy recommendation for the residents of Nowhere.



**Figure 1:** The equilibrium amount of a contaminant, like methyl mercury, that an organism can accumulate over time increases from prey to predator along the food chain. This increase up the food chain is known as biomagnification.

## MATLAB Skills

There are a couple of new MATLAB skills you will need in order to complete this lab. **Note, all example files are posted on Moodle.**

### While-Loops

In Lab 1 we introduced the concept of loops. Recall that there are two types of loops: *for-loops* and *while-loops*. A ***for-loop*** executes a block of code a specified number of times. Specifically, a for-loop in MATLAB iterates through the an array of values. A ***while-loop***, on the other hand, executes a block of code until a logical condition is met which is triggered by an event in the loop. Most importantly, there is not array of values to iterate through, because that would pre-determine the number of iterations through the loop.

In Lab 1 we used for-loops because we knew how many times we needed to repeat a certain operation (i.e. calculating ratios or generating a certain number of terms in a sequence). However, in this lab we will need to use while-loops so that we can generate terms in a sequence until the most recently generated value in the sequence meets a certain criteria.

**Caffeine Example** · The half-life of caffeine in the human body is about 6 hours. Suppose you drink one cup (8 oz) of coffee every morning at 8 am; one cup of coffee has approximately 100 mg of caffeine. We can model the amount of caffeine in your body right after you drink your coffee each morning with the difference equation

$$x_{n+1} = ax_n + b, \quad x_0 = b, \quad (1)$$

where  $a = 0.5^4$ ,  $b = 100$ , and one time step represents one day. The closed form solution of this equation is

$$x_n = a^n (x_0 - x^*) + x^*,$$

where  $x^* = b/(1 - a) = 106.667$  mg. Since  $a < 1$ , we can see that  $x_n \rightarrow x^*$  as  $n \rightarrow \infty$ . Suppose we want to know the first day by which the amount of caffeine within our body will be within 0.01 mg of  $x^*$ . In lecture, we would solve the inequality

$$x_n > x^* - 0.01 \quad (2)$$

for  $n$  to answer this question. In this lab, we will use a *while-loop* to answer this question.

**General Structure of a For-Loop** · Recall the general structure of a for-loop in MATLAB is

```
for <variable> = <array of values>
    <commands>
end
```

where we have been referring to <variable> as the *index* of the for-loop. In a for-loop each iteration through the loop uses the next array value of <variable>.

**General Structure of a While-Loop** · A while-loop in MATLAB uses the structure

```
while <condition>
    <commands>
end
```

where each iteration through the loop checks to see if the `<condition>` evaluates to true; if `<condition> = true` then the `<commands>` inside the loop will be executed, if `<condition> = false` then MATLAB will exit the loop. Notice the while-loop structure does not require a loop index. Thus, if we want to keep track of the number of times we execute the while loop, we must create such an index ourselves, and increment the index in each iteration of the loop.

**Writing a While-Loop for the Caffeine Example** · To generate a while-loop which would generate terms of the sequence generated by Equation (1) with  $a = 0.5^4$  and  $b = 100$  until Inequality (2) is true could use `Lab02Ex01.m`.

```

L02Ex01.m
1  % Lab 2 Example 1 by Prof Bodine
2
3  % Model parameters
4  a=0.5^4; b=100;
5
6  % Model equilibrium
7  xstar = b/(1-a);
8
9  % Generate terms of sequence until x(n) > x* - 0.01
10 x(1) = b; n = 1;
11 while x(n) <= xstar - 0.01
12     x(n+1) = a*x(n) + b;
13     n = n + 1;
14 end
15
16 % Print the information we want to know to the Command Window
17 fprintf('The first day the amount of caffeine is within 0.01 of %.3f mg is day %d\n',...
18     xstar,n);
```

1. Create `L02Ex01.m` or download it from Moodle. Now, let us take a moment to understand everything within this script.

- (a) Lines 1, 3, 6, and 9 provide comments and help us understand what each portion of code is designed to do.
- (b) Line 4 defines the parameter values  $a$  and  $b$  that we will use later in the code. If you are going to use

certain values multiple times, it is a good idea to save them as a variable near the top of the code.

- (c) Line 7 uses the variable values to calculate the model equilibrium  $x^*$ .
- (d) Lines 10–14 set up and execute the while-loop.
- i. Line 10 creates the first term in our sequence ( $x_0 = b$ ), and creates a loop index and initializes its value to 1. We will need our loop index to increase by one for each iteration through the loop.
  - ii. Line 11 is the beginning of the while loop. The condition for iterating through the loop is `x(n) <= xstar - 0.01`. Written in mathematical notation, this is the condition  $x_n \leq x^* - 0.01$ , which is the negation (i.e. the opposite) of Inequality (2). In the first iteration of the loop  $n = 1$  and `x(1)=100` which is less than  $x^* - 0.01 = 106.6567$ , thus the commands inside the loop will be executed.
  - iii. Lines 12 and 13 are the commands inside the loop that will be executed with each iteration of the loop. Line 12 creates the next term in the sequence, and line 13 increases the loop index `n` by 1. During the first iteration through the loop `n=1`, thus line 12 generates the `x(2)` term in the `x` array (this corresponds to the  $x_1$  term in the sequence), and then line 13 increases the value of `n` to 2.
  - iv. Line 14 bookends the while-loop structure. Once lines 12 and 13 have been executed during the first iteration of the loop, line 14 indicates to go back to the start of the loop. At the start of the loop the `<condition>` is checked again to see if the loop should iterate again. If the condition is not met, then the loop is exited and MATLAB will move on to executing line 17.
- (e) Lines 17-18 contain a single command, specifically an `fprintf` command. However, since this command is particularly long, it is broken up over two lines. Note, the `...` at the end of line 17 indicates that the command continues onto the next line.

The `fprintf` command will print out the information we were trying to find by creating the while-loop. There are two placeholders for formatted numbers. The first placeholder is a floating-point value that will print the value of `xstar` to the nearest 0.001, and the second placeholder is an integer value that will print the value of `n`. Recall that the value of `n` was increased by 1 through each iteration of the while-loop and will correspond to the length of the array `x`.

- (f) Take another moment to review the code. **Do you understand what each line of the code is doing?** If not, now is the time to stop and ask?

This completes the Matlab Skills section. You will review these skills in the group discussion, and put these skills to use in the Lab Assignment.

## Lab Group Discussion

**Week 1:** Suppose a patient with heart disease is being treated with digoxin (see Exercise 3 and Example 5 in reference readings). The patient takes a 0.1 mg dose every day, and the half-life of the drug is 1.868 days.

1. Given the half-life of digoxin, what is the decay rate of digoxin?
2. Construct a difference equation of the form  $x_{t+1} = e^{-k\tau} x_t + b$ .
  - (a) What is  $k$ ? What does it represent?

- (b) What is  $\tau$ ? What does it represent?
  - (c) What is  $b$ ? What does it represent?
3. What is the equilibrium point,  $x^*$ , of the difference equation you constructed in #2?
  4. Is the equilibrium point stable or unstable? Explain.
  5. What does the equilibrium point represent biologically?
  6. Find the closed form solution of the difference equation you constructed in #2.
  7. Construct a while-loop which determines the number of doses until the amount of digoxin in the patient is within 0.01 of  $x^*$ .
  8. Change the while-loop to determine the number of doses until the amount of digoxin in the patient is within 0.001 of  $x^*$ .

**Week 2:** All of the questions for this week's discussion relate to the bioaccumulation of methyl mercury described in the introduction. For each calculation you must complete, **pay careful attention to the units** and make unit conversions when necessary.

1. The introduction states that methyl mercury becomes lethal in humans when the concentration exceeds 30 mg/kg. What do these units mean?
2. What is the conversion rate between mg and  $\mu\text{g}$ ? *It is okay if you need to look this up; you are not expected to know this off the top of your head.*
3. The average citizen of Nowhere has a mass of 70 kg. What is the weight in pounds of the average citizen of Nowhere?
4. Officials in the town of Nowhere have collected and tested 2,425 samples of largemouth bass from nearby reservoirs and found that all fish were contaminated with methyl mercury. The mean concentration of methyl mercury in the fish samples was  $0.43 \mu\text{g}$  (micrograms) per gram of fish mass. The average mass of the sampled largemouth bass was 0.817 kg. Calculate the amount of methyl mercury in an average size largemouth bass. Report this value in both mg and  $\mu\text{g}$ .
5. A range of 65–75 days is given for the half-life of methyl mercury in humans. If we want to use the half-life to calculate the decay rate, what half-life value should we use? What is the impact of using a smaller half-life versus a large half-life?
6. Given the half-life of methyl mercury in humans, calculate the decay rate of methyl mercury in humans. That is, find the value of  $k$  in the equation  $x(t) = x(0)e^{-kt}$ , where  $x(t)$  is the amount of methyl mercury (measured in mg) in a human at time  $t$  (measured in days), and  $k$  is the decay rate.
7. Assume the average adult citizen of Nowhere consumes one largemouth bass per day (they must really like to eat fish!). Construct a difference equation which models the amount of methyl mercury in an average adult over time, where the time step is one day.
8. Using the model you constructed in the previous question, determine the maximum amount of methyl mercury (in mg) that will accumulate in an adult citizen of Nowhere over their lifetime. For an average adult citizen of

Nowhere with a mass of 70 kg, what is the concentration of methyl mercury (in mg/kg) in their body if they have accumulated up to the maximum amount of methyl mercury?

## Checkpoint Exercise

Recall the scenario from the Week 1 discussion: Suppose a patient with heart disease is being treated with digoxin (see Exercise 3 and Example 5 in reference readings). The patient takes a 0.1 mg dose every day, and the half-life of the drug is 1.868 days.

1. Write a script file which does the following:
  - Clear all variables currently in the workspace.
  - Define and set the model parameters:  $k$ ,  $\tau$ ,  $b$ ,  $a$ .
  - Calculate the value of the equilibrium point  $x^*$  and use an `fprintf` statement to report the value to the Command Window.
  - Calculate the minimum value of  $n$  (call this `minn`) such that  $x^* - x_n < 0.0001$  and use an `fprintf` statement to report the value to the Command Window. *Hint: Don't do this calculation by hand, use Matlab to do the heavy lifting by constructing the inequality in terms of  $x^*$ ,  $x_0$ , and  $a$ .*
  - Create an array `x` containing the terms of the sequence generated by the difference equation model. The array should start with the  $x_0$  term and contain all subsequent terms up to  $x_{\text{minn}+5}$ .
2. **CHECKPOINT:** Verify that your computed values for  $x^*$  and `minn`, and your generated plot are correct.

## Lab Assignment

The lab assignment uses the bioaccumulation of methyl mercury model you have developed during the Week 2 discussion.

1. Write a script file (saved as `Lab02_YourLastName.m`) which does the following:
  - Clear all variables currently in the workspace.
  - Define and set the model parameters:  $k$ ,  $\tau$ ,  $b$ ,  $a$ .
  - Calculate the value of the equilibrium point  $x^*$  and use an `fprintf` statement to report  $x^*$  and the concentration of methyl mercury in a 70 kg citizen to which it corresponds to the Command Window.
  - Use a while-loop to calculate the minimum value of  $n$  (call this `minn`) such that  $x^* - x_n < 0.0001$  and use an `fprintf` statement to report the value to the Command Window. The while-loop should create an array `x` containing the terms of the sequence generated by the difference equation model. Plot the array `x` with appropriate axes labels.
2. Run your script file. Save the graph produced as `Lab02a_YourLastName.jpg`.
3. **CHECKPOINT:** Verify that your computed values for  $x^*$  and `minn`, and your generated plot are correct.

4. Add a while-loop to your m-file `Lab02_YourLastName.m` to determine the minimum number of fish an average citizen of Nowhere would have to eat each day such that the maximum accumulated amount of methyl mercury in their body (i.e., the value of  $x^*$ ) would exceed 30 mg/kg. Do this by considering multiples of the dose size  $b$ . If the loop has an index of  $n$ , then each iteration of the loop would calculate the value of  $x^*$  using  $n*b$  instead of  $b$ . *Note:  $x^*$  is a measure of mg of total methyl mercury in the body, and 30 mg/kg is a concentration of methyl mercury in the body.*

Use an `fprintf` statement to print out the number of fish an average citizen of Nowhere would have to eat in order to eventually exceed 30 mg/kg of accumulated methyl mercury.

5. Add a while-loop to your m-file `Lab02_YourLastName.m` to determine how often a pregnant woman in Nowhere should eat one largemouth bass such that the maximum accumulated amount of methyl mercury in her body (i.e., the value of  $x^*$ ) would not exceed 0.02 mg/kg. Do this by indexing the loop over increasing values of  $\tau$ . For example, if a pregnant woman eats one largemouth bass a day, then  $\tau = 1$ , but if she eats one largemouth bass every 3 days then  $\tau = 3$ . Note, that when  $\tau = 1$ , the one time step represents 1 day, but when  $\tau = 3$  one time step represents 3 days. Thus, at  $t = 2$ , 6 days would have passed.

Use an `fprintf` statement to print out how often a pregnant woman in Nowhere should eat largemouth bass so that she does not run the risk of fetal methyl mercury poisoning.

6. **Submit:** Place the following files into a folder titled `Lab02_YourLastName` and submit to Box.
  - 1 script file (`Lab02_YourLastName.m`)
  - 1 word document (`Lab02_YourLastName.docx`); Use the template provided on Moodle. Your image file will be included in this Word document and should not be submitted separately.

**Print & Bring to Class:** One printed copy of `Lab02_YourLastName.docx`. If there are multiple pages, please staple them together (or print double-sided). *Make sure your name is on the printed copy.*