Modeling Cholesterol Levels in Humans

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Abstract

Differential equations provide a means for modeling an individual's cholesterol level as a function of physiology and lifestyle.

1 Introduction

Cholesterol is a fatty lipid found in the bloodstream and cells of all humans. The presence of cholesterol is normal, and indeed necessary, because it is used to form cell membranes and is used in the synthesis of Vitamin D3, various steroid hormones, and some sex hormones. Though it is a necessary component of the body, it can become dangerous when present in too high quantities. High cholesterol level, or hypercholesterolemia, is a major risk factor for coronary heart disease, which leads to heart attack, and can also contribute to having a stroke.

Cholesterol can be introduced into the body in two ways. First of all, cholesterol is naturally produced biosynthetically in the liver for use in the aforementioned biological processes. Secondly, cholesterol is added to the body through foods that come from animals, which also naturally produce cholesterol. The cholesterol from animals is passed on to humans through consumption of such foods. Other cholesterol-free foods high in trans-fats and saturated fats can also cause the body to make more cholesterol when eaten often.

2 The Model

Because cholesterol is naturally produced in the body in addition to being absorbed from consumption of certain foods, a model for the cholesterol level of an individual must take into account an individual's physiology and lifestyle. The model that I will study predicts cholesterol level as a function of an individual's natural cholesterol level, daily cholesterol intake, and biological metabolism of cholesterol. In the textbook "Differential Equations," the authors, Paul Blanchard, Robert L. Devaney, and Glen R. Hall, propose a mathematical model for predicting the cholesterol level of an individual. Their proposed model is the differential equation

$$\frac{dC}{dt} = k_1(L - C) + k_2 E \qquad (1)$$

where t, $C(t)$, L, E, k_1, and k_2 represent the following quantities:

t	time measured in days
$C(t)$	individual's cholesterol level at time t measured in mg/dl
L	individual's natural cholesterol level that would result from a diet excluding products containing cholesterol or that induce higher levels of cholesterol production in the body
E	individual's cholesterol intake, measured in mg/day
k_1	parameter that measures how rapidly an individual's body responds to changes in cholesterol level from the natural level
k_2	parameter that measures the rate at which an individual's body produces cholesterol from foods that have been ingested

3 Analyzing the Model

In order to study and analyze this model for cholesterol level, I apply it to a set of hypothetical identical twin brothers, Bubba and Biff. Using a set of identical twins to study this model is very effective, because twins boast the same physiology (natural cholesterol level and absorption and consumption parameters), but may differ in their eating habits, and thus their individual cholesterol intake. Since we can control for physiological features, we can isolate and study the effect of lifestyle changes (change in eating habits, exercise, etc.) on an individual's cholesterol level.

In this hypothetical scenario, Bubba and Biff have the same natural cholesterol level of $L = 140$ mg/dl, and the same production and absorption parameters of $k_1 = 0.1$ and $k_2 = 0.05$. Initially, Bubba and Biff are 22 years old, and since they have both been living at home together and eating the same meals prepared by their mother, they both have a daily cholesterol intake of $E = 80$ mg/day. Eventually, though, Bubba decides to move away from home into his own place, where he is forced to make his own nutritional decisions.

3.1 Bubba

On his own for the first time, Bubba does not consider forming healthy eating habits a high priority. Instead of cooking healthy meals for himself, Bubba finds it much more convenient to come home from work and patronize the local fast food restaurant next door. He becomes settled into a nightly routine of dinner at this fast food restaurant, and thus his daily cholesterol intake rises significantly to $E = 250$ mg/day. According to model (1), Bubba's cholesterol level can be modeled by

$$\frac{dC}{dt} = 0.1(140 - C) + 0.05(250)$$

which simplifies to

$$\frac{dC}{dt} = -0.1C + 26.5.$$

By factoring out 0.1, this differential equation can also be easily written as

$$\frac{dC}{dt} = 0.1(265 - C). \qquad (2)$$

Assuming that $t_0 = 0$ is the time at which Bubba first started eating at the fast food restaurant and that Bubba's cholesterol level at this time was $C_0 = 180$ mg/dl, then Bubba's cholesterol level can be modeled by the following initial value problem

$$\begin{aligned} \frac{dC}{dt} &= 0.1(265 - C), \\ C(0) &= 180. \end{aligned} \qquad (3)$$

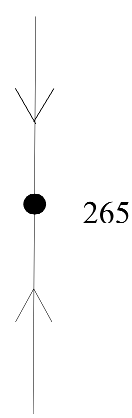
Because the right-hand side of the differential equation is independent of t, it is an autonomous equation, whose slope field can instead be represented by a phase line. To create the phase line, we set the right-hand side of (2) equal to 0 in order to find the equilibrium point(s).

$$\begin{aligned} 0 &= 0.1(265 - C) \\ 0.1C &= 26.5 \\ C &= 265 \end{aligned}$$

This differential equation only has one equilibrium point, which occurs at $C = 265$. In order to classify this equilibrium point, we can apply the Linearization Theorem and calculate the second derivative of (2), which is

$$\frac{d^2C}{dt^2} = -0.1.$$

Since the derivative of the differential equation is less than 0, by the Linearization Theorem we can conclude that $C = 265$ is a sink, and thus the phase line of (2) is



With a general idea of the solution of (2) obtained from the analysis of the phase line, which shows $C = 265$ as a sink, we can also look to the direction field to analyze the behavior of different solutions of the differential equation.

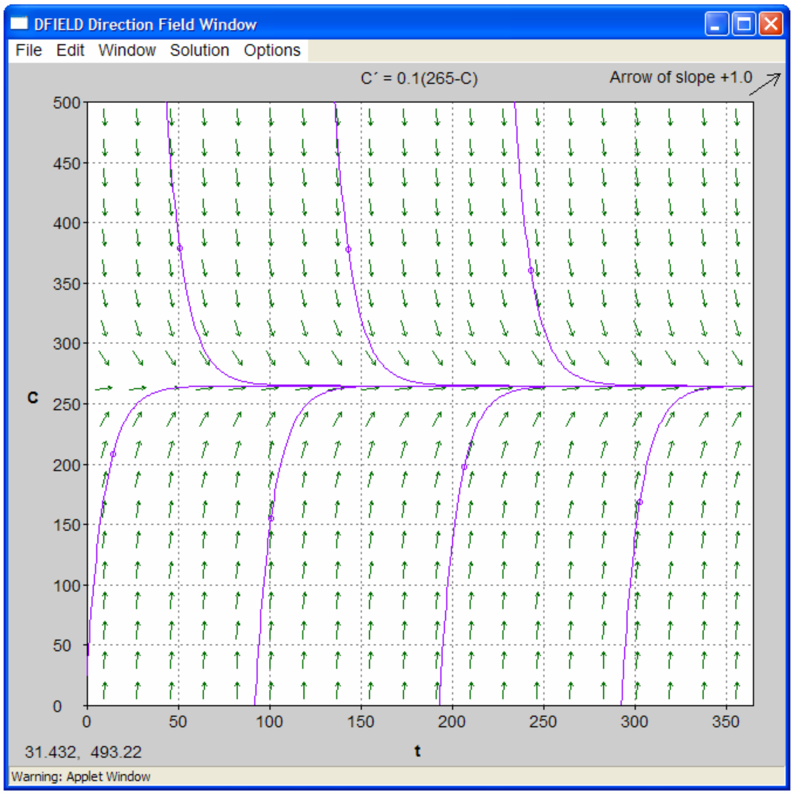


Figure 1: Direction Field of $\frac{dC}{dt} = 0.1(265 - C)$

The direction field of (2) confirms the phase line analysis that $C = 265$ is a sink. Solutions with initial values greater than 265 will exponentially decrease until they reach the equilibrium cholesterol level of 265, and similarly solutions with initial values less than 265 will increase exponentially until they reach the equilibrium cholesterol value of 265.

Because (2) is autonomous, in addition to being analyzed qualitatively, it can also easily be solved analytically by using separation of variables, as shown below

$$\frac{dC}{dt} = 0.1(265 - C)$$

$$\frac{dC}{(265 - C)} = 0.1dt$$

$$\int \frac{dC}{(265 - C)} = \int 0.1dt$$

$$-\ln|265 - C| = 0.1t + \alpha$$

$$\ln|265 - C| = -0.1t + \alpha$$

$$e^{\ln|265 - C|} = e^{-0.1t + \alpha}$$

$$265 - C = \alpha e^{-0.1t}$$

$$C = 265 - \alpha e^{-0.1t}.$$

Solving this general solution for the particular solution of the initial value-problem (3) with $C(0) = 180$ yields

$$
\begin{aligned}
180 &= 265 - \alpha e^{-0.1*0} \\
180 &= 265 - \alpha \\
\alpha &= 85 \\
C(t) &= 265 - 85e^{-0.1t}.
\end{aligned}
$$

If Bubba were to maintain his high cholesterol diet for a very long time, his approximate cholesterol level would be 265, which is determined by taking the limit of $C(t)$ as $t \to \infty$:

$$\lim_{t \to \infty} 265 - 85e^{-0.1t} = 265 - 85e^{-0.1*\infty} = 265 - 0 = 265.$$

This result is consistent with the phase portrait discussed above. The long-term behavior of the model of Bubba's cholesterol level shows an equilibrium cholesterol level of 265, confirmed qualitatively and analytically. If Bubba continues on his present diet, eventually his cholesterol level will increase to 265 and level off.

3.2 Biff

Unlike his brother Bubba, Biff chooses to continue living at home, eating his mother's cooking. Again, Biff's natural cholesterol level is $L = 140$ mg/dl, and he has the production and absorption parameters of $k_1 = 0.1$ and $k_2 = 0.05$. Biff's daily cholesterol intake remains at $E = 80$ mg/day. According to model (1), Biff's cholesterol level can be modeled by

$$\frac{dC}{dt} = 0.1(140 - C) + 0.05(80)$$

which simplifies to

$$\frac{dC}{dt} = -0.1C + 18.$$

By factoring out 0.1, this differential equation can easily be written as

$$\frac{dC}{dt} = 0.1(180 - C). \qquad (4)$$

Assuming that at $t_0 = 0$ Biff's cholesterol level is $C_0 = 180$ mg/dl, then Biff's cholesterol level can be modeled by the following initial-value problem

$$\frac{dC}{dt} = 0.1(180 - C), \qquad (5)$$
$$C(0) = 180.$$

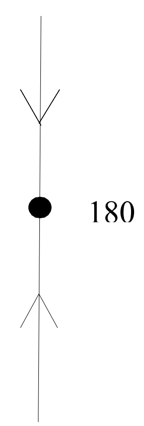
Because the right-hand side (4) is independent of *t*, it is an autonomous equation whose slope field can simply be represented by a phase line. To create the phase line, we set the right-hand side of (4) equal to 0 in order to find the equilibrium point(s).

$$0 = 0.1(180 - C)$$
$$0.1C = 18$$
$$C = 180$$

This differential equation has only one equilibrium point, which occurs at $C = 180$. In order to classify this equilibrium point, we can apply the Linearization Theorem and calculate the second derivative of (4), which is

$$\frac{d^2C}{dt^2} = -0.1.$$

Because the derivative of the differential equation is less than 0, by the Linearization Theorem we can conclude that $C = 180$ is a sink, and thus the phase line of (4) is



The phase line of (4) gives us a general idea of the behavior of the differential equation. We can also look at the direction field to find a more detailed picture of the solutions of the differential equation.

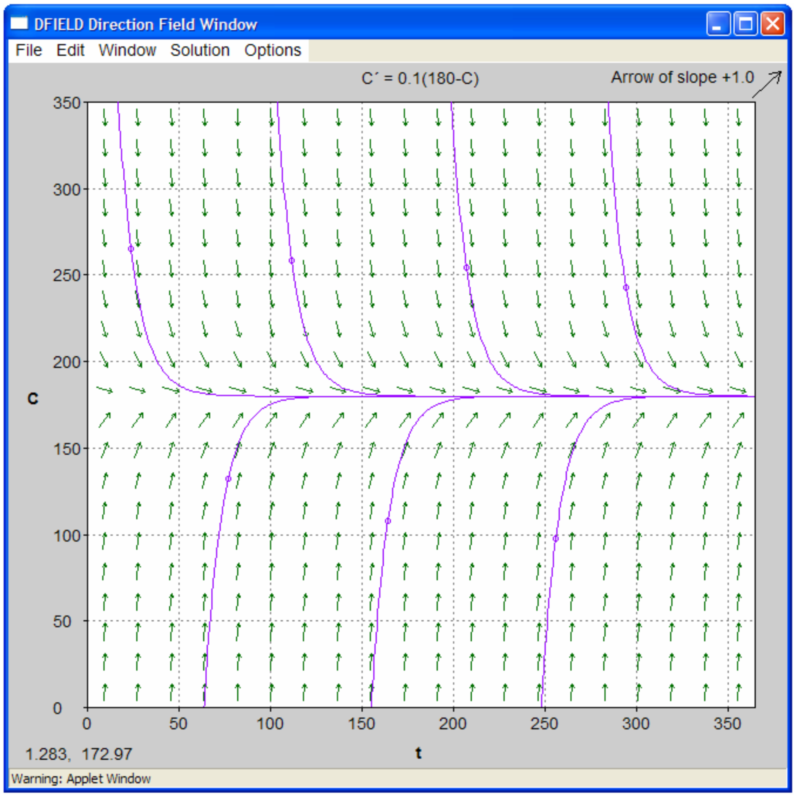


Figure 2: Direction field of $\frac{dC}{dt} = 0.1(180 - C)$

The direction field of (4) reiterates the phase line analysis that $C = 180$ is a sink equilibrium point. Solutions of (4) with initial values greater than 180 will decrease exponentially until they reach the equilibrium cholesterol level of $C = 180$, and solutions with initial values less than 180 will increase exponentially until they attain the equilibrium cholesterol level of $C = 180$.

Because (4) is autonomous, in addition to being analyzed qualitatively, it can also easily be solved analytically by using separation of variables. Because Biff's model only differs from Bubba's model by one number, I will not reproduce the details for solving Biff's model as it is identical in method to Bubba's solution, with a slightly different end result. The general solution for Biff's cholesterol level is

$$C = 180 - \alpha e^{-0.1t}.$$

Solving this general solution for the particular solution of the initial-value problem (5) with $C(0) = 180$ yields

$$180 = 180 - \alpha e^{-0.1*0}$$
$$180 = 180 - \alpha$$
$$\alpha = 0$$
$$C(t) = 180$$

Biff's particular solution is quite different from Bubba's. Unlike Bubba, at time $t = 0$ with $C(0) = 180$, Biff has already reach his equilibrium cholesterol level. The long-term behavior of this particular solution of (4) is merely a horizontal line through $C = 180$. If Biff's physiological and lifestyle conditions remain constant, his cholesterol level will not change. This long-term behavior can be seen graphically through the solution of the direction field at $t = 0$ with $C(0) = 180$:

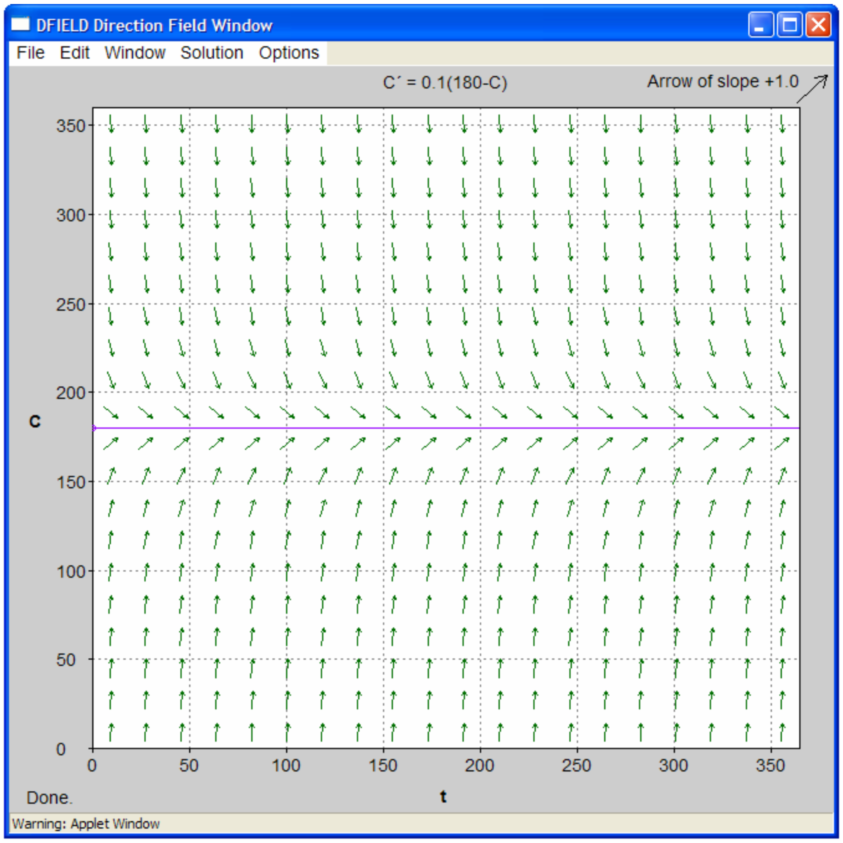


Figure 3: $\frac{dC}{dt} = 0.1(180 - C)$ with initial condition C(0) = 180

This long-term behavior of Biff's cholesterol level can also be solved algebraically by taking the limit of $C(t)$, which easily works out to 180

$$\lim_{t \to \infty} 180 = 180.$$

3.3 General Analysis of the Model

In applying the cholesterol model to Bubba and Biff, a pattern arose for the form of the differential equation. The general form of the initial value problem that models an individual's cholesterol level appears to be

$$\frac{dC}{dt} = k_1(M - C),$$
$$C(t_0) = C_0. \qquad (6)$$

The parameter M in (6) can be written in terms of L, E, k_1, and k_2. M can be derived by the following simple procedure:

$$\frac{dC}{dt} = k_1(L - C) + k_2 E$$
$$\frac{dC}{dt} = k_1 L - k_1 C + k_2 E$$
$$\frac{dC}{dt} = k_1\left(L + \frac{k_2}{k_1}E - C\right)$$
$$\therefore M = L + \left(\frac{k_2}{k_1}\right)E$$

All of the parameters of M (L, k_1, k_2, and E) are assumed to be positive numbers (except for E, which could potentially equal 0) because they have biological meanings that would not be meaningful if they were negative. Because all of the elements of M are positive, and because there is only addition involved (and not subtraction), M must always be positive. Even if E happened to be 0, L is still positive, and thus M would be positive. In the previous examples, Bubba had a value of $M = 265$, and Biff had a value of $M = 180$. The initial-value problem (6) can be solved with a separation of variables as in the previous examples, while maintaining M as an undetermined parameter.

$$\frac{dC}{dt} = k_1(M - C)$$
$$\frac{dC}{(M - C)} = k_1 dt$$
$$\int \frac{dC}{(M - C)} = \int k_1 dt$$
$$-\ln|M - C| = k_1 t + \alpha$$
$$\ln|M - C| = -k_1 t + \alpha$$
$$e^{\ln|M - C|} = e^{-k_1 t + \alpha}$$
$$M - C = \alpha e^{-k_1 t}$$
$$C = M - \alpha e^{-k_1 t}$$

Solving this general solution for the particular solution of the initial-value problem (6) with $C(t_0) = C_0$ yields

$$C_0 = M - \alpha e^{-k_1 t_0}$$
$$\alpha e^{-k_1 t_0} = M - C_0$$
$$\alpha = \left(\frac{M - C_0}{e^{-k_1 t_0}} \right)$$
$$\therefore C(t) = M - \left(\frac{M - C_0}{e^{-k_1 t_0}} \right) e^{-k_1 t}.$$

The long-term behavior of this solution for a general model of an individual's cholesterol level can be determined by taking the limit of $C(t)$, which generates

$$\lim_{t \to \infty} C(t) = M - \left(\frac{M - C_0}{e^{-k_1 t_0}} \right) e^{-k_1 t} = M - 0 = M.$$

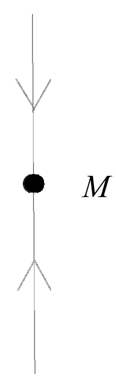
This shows that the long-term behavior of the general cholesterol model reaches an equilibrium cholesterol level at M for every individual, which is consistent with the results obtained from analyzing the identical twins Bubba and Biff. The general behavior for the cholesterol model (6) can also be studied qualitatively through the use of a phase line. The equilibrium point(s) of (6) can be found by setting the right-hand side of the differential equation equal to 0.

$$\frac{dC}{dt} = k_1 (M - C)$$
$$0 = k_1 (M - C)$$
$$0 = (M - C)$$
$$C = M$$

Thus, the only equilibrium point of the general cholesterol model is equal to M. The behavior of solutions close to the equilibrium point can be determined by again applying the Linearization Theorem:

$$\frac{d^2 C}{dt^2} = -k_1.$$

Because the derivative of (6) is negative, the equilibrium point M is a sink, and has the following phase line:



4 Varying the Model Parameters

The cholesterol model assumed above predicts a person's cholesterol level as a function of an individual's physiology and lifestyle habits. In the previous examples, it has been assumed that these parameters all remain constant throughout an individual's lifetime. But, this is not always the case, because the parameters may change as a result of lifestyle changes by the individual. An individual may change eating habits throughout his/her lifetime, and thus the parameter E would not stay the same, and would be sensitive to these changes.

For example, let $k_1 = 0.8$, $k_2 = 0.2$, and $L = 150$. The model for an individual's cholesterol level in this situation becomes

$$\frac{dC}{dt} = 0.8\left(150 + \left(\frac{0.2}{0.8}\right)E - C\right)$$
$$\frac{dC}{dt} = 0.8(150 + .25E - C). \qquad (7)$$

By comparing the phase portraits for values of E as it is slowly decreased to zero, we will be able to see how the long-term predicted cholesterol level of an individual changes in response to changing eating habits.

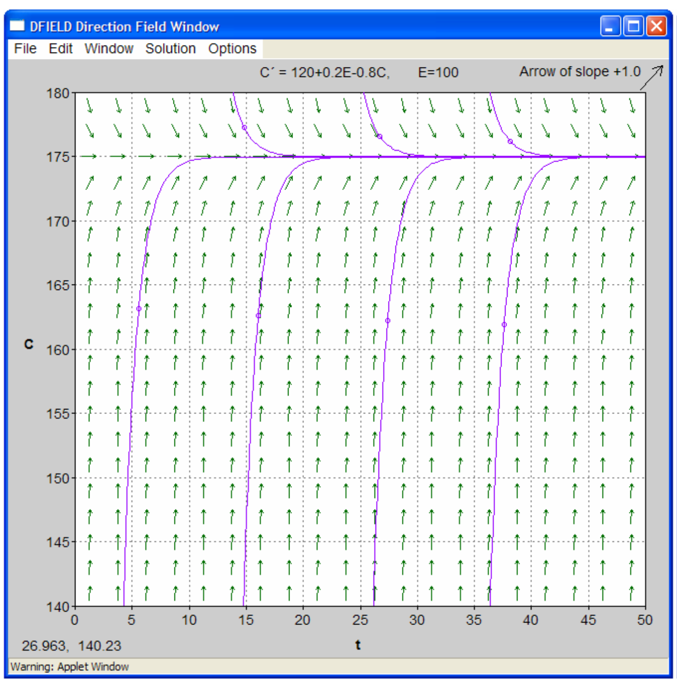


Figure 4: $\frac{dC}{dt} = 0.8(175 - C), E = 100$

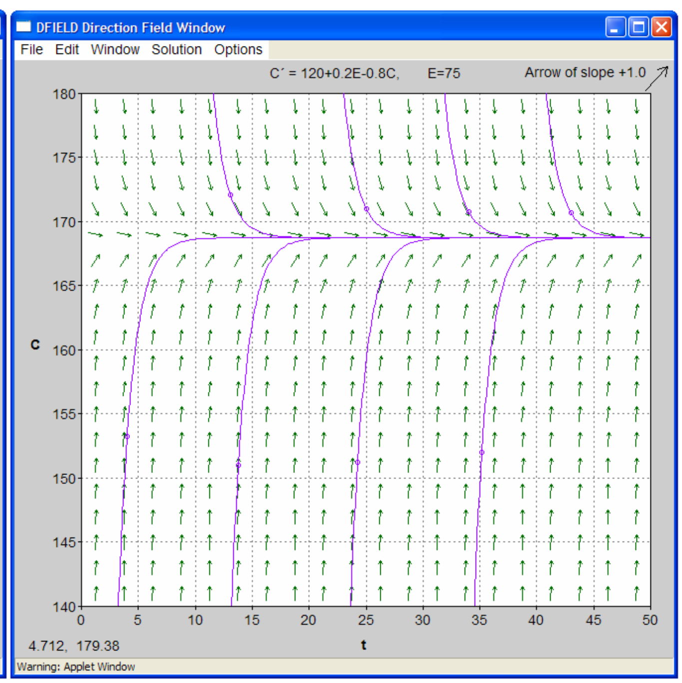


Figure 5: $\frac{dC}{dt} = 0.8(168.75 - C), E = 75$

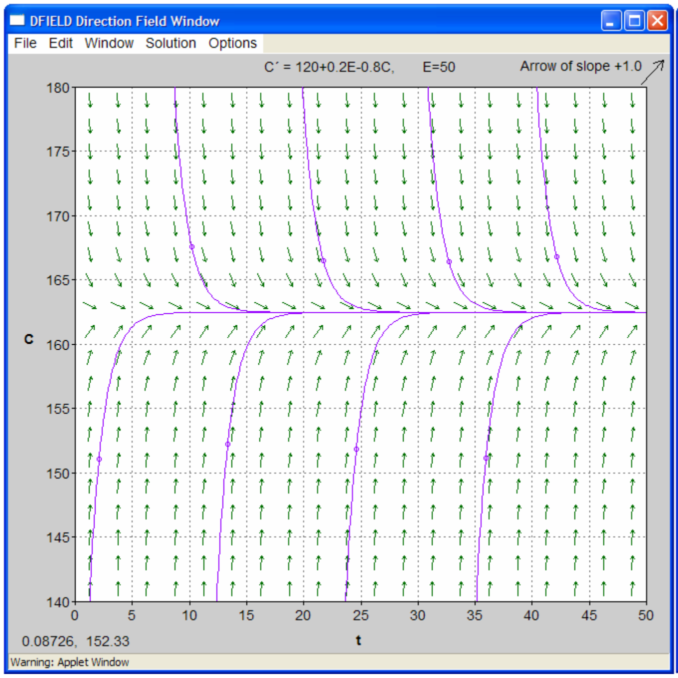


Figure 6: $\frac{dC}{dt} = 0.8(162.5 - C), E = 50$

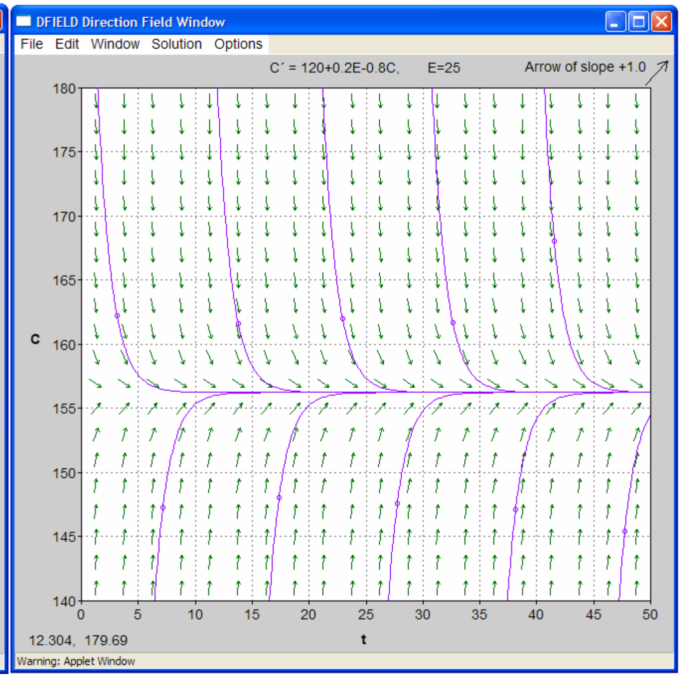


Figure 7: $\frac{dC}{dt} = 0.8(156.25 - C), E = 25$

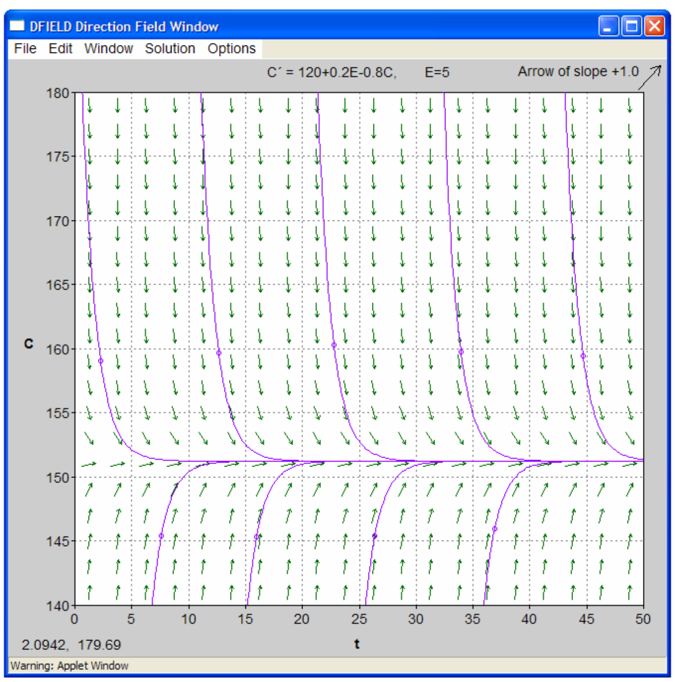


Figure 8: $\frac{dC}{dt} = 0.8(151.25 - C), E = 5$

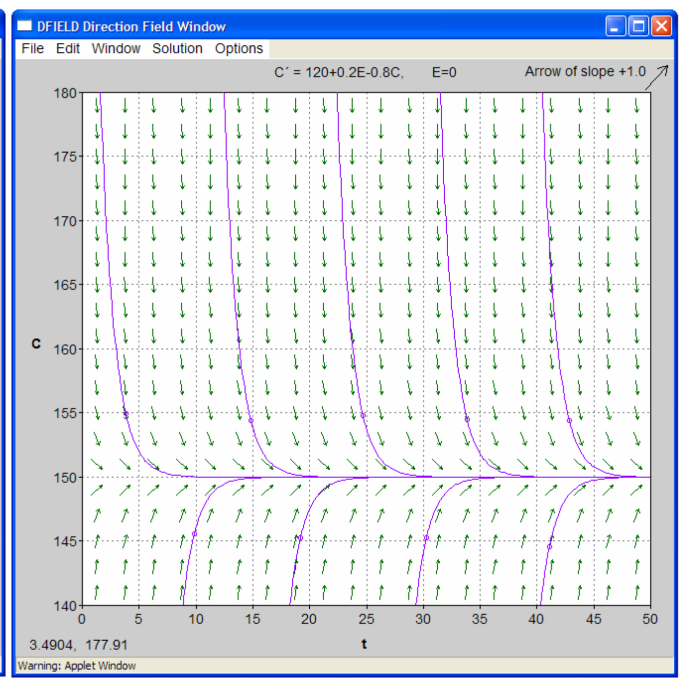


Figure 8: $\frac{dC}{dt} = 0.8(150 - C), E = 0$

These phase portraits illustrate how changing one's eating habits can have a significant impact on the long-term behavior of one's predicted cholesterol level. Decreasing the intake of foods high in cholesterol, or foods that signal the body to create more cholesterol, decreases the predicted cholesterol level of an individual, but not forever. As E is decreased closer and closer to 0, its rate of decreasing slows. Once a value of $E = 0$ is obtained, the individual returns to maintaining the original natural cholesterol level, which in this case was $L = 150$.

5 Conclusion

Using a model to predict an individual's cholesterol level in the future can be very useful, especially in cases where an individual may have certain lifestyle habits that could prove dangerous. By being able to model and predict the long-term behavior of an individual's cholesterol level, measures can be taken to help someone's chances of survival, from altering one's diet or exercise to taking medicine to lower cholesterol.

The Bubba and Biff example perfectly illustrated the difference that eating habits make on one's cholesterol level. Since they were identical twins, they had the same biological makeup, so there was no way that anything physiological could interfere with their predicted cholesterol levels. The only difference was their change in eating habits that occurred when they were 22, when Bubba moved out and starting eating poorly, while Biff remained at home eating healthily. While Biff was able to maintain his already healthy cholesterol level, Bubba's predicted cholesterol level equilibrium became 85 mg/dl higher than his brother's cholesterol level and even his own original cholesterol level. Their example showed how eating habits alone can radically change the predicted fate of one's cholesterol level.

This change in cholesterol level due to eating habits was also demonstrated by varying the model parameters. By looking at the phase portraits of the hypothetical individual at various levels of cholesterol consumption, it was evident that decreasing the intake of food high in cholesterol or food that increases cholesterol consumption in the body could have an impact on one's future cholesterol level. By lowering the value of E gradually from 100 to 0, there was a 25 mg/dl decrease in cholesterol level in that particular example, showing that an individual can alter his/her future cholesterol level by making personal, non-biological lifestyle changes.

6 Sources

About Cholesterol. American Heart Association. 22 November 2003 <http://www.americanheart.org/presenter.jhtml?identifier=512>.

Ellermeyer, S. F. Cholesterol Level in Humans – Differential Equations. 6 October 2003 <http://science.kennesaw.edu/~sellerme/moduleshtml/science/choleste/decholesterol.html>.