

Homework Assignment 13: Solutions

In Questions 1-4, you had to:

- Find an antiderivative for the given cortisol concentration function, $m(T)$.
- Determine the limits of integration for the given cortisol curve (that is, the x -values where the area under the curve started and ended).
- Use the antiderivative of $m(T)$ to calculate the area under the cortisol curve.

All of the antiderivatives in this homework assignment could be obtained by using the “short-cut” rules for calculating antiderivatives that you learned about in class on Friday March 15:

Kind of Function	Function $f(x)$	Antiderivative $F(x)$
Constant	$f(x) = m$	$F(x) = m \cdot x + b$
Power function with power Not equal to -1	$f(x) = x^n, n \neq -1$	$F(x) = \frac{x^{n+1}}{n+1} + C$
Power function with power equal to -1	$f(x) = \frac{1}{x}$	$F(x) = \ln(x) + C$
Exponential function	$f(x) = A \cdot B^x$	$F(x) = \frac{A \cdot B^x}{\ln(B)} + C$
Exponential function with Base equal to e	$f(x) = e^x$	$F(x) = e^x + C$

Table 1: Short-cut Rules for Finding Antiderivatives.

1. In this situation (where you will calculate the total cortisol concentration for a long-distance runner immediately after competing in a marathon), the cortisol curve was described by the equation:

$$m(T) = \frac{460}{T + 4}.$$

The function $m(T)$ resembles the function $f(x) = \frac{1}{x}$ from Table 1 the most closely, as it is a fraction with the independent variable (T) in the denominator. The antiderivative, $M(T)$ is therefore:

$$M(T) = 460 \cdot \ln(T + 4) + C$$

where C is a constant.

On the homework assignment, you were asked to use this antiderivative to find the total cortisol concentration (area under curve) for the twenty four hour period following the marathon. The area that you are interested in starts at $T = 0$ and ends at $T = 24$. Using the antiderivative to calculate this area:

$$\begin{aligned} \text{Total cortisol concentration} &= \int_0^{24} m(T) \cdot dT \\ &= M(24) - M(0) \\ &= 460 \cdot \ln(28) + C - [460 \cdot \ln(4) + C] \\ &= 895.1186686 \frac{\mu\text{g} \cdot \text{hour}}{\text{dl}}. \end{aligned}$$

2. In this situation (where you will calculate the total cortisol concentration for a person who has taken the drug “ecstasy”), the cortisol curve was described by the equation:

$$m(T) = 0.3693 \cdot T^4 - 4.0963 \cdot T^3 + 11.63338 \cdot T^2 - 1.4216 \cdot T - 0.0837.$$

This function (a polynomial) is a series of functions that most closely resemble the function $f(x) = x^n$ from Table 1. The antiderivative, $M(T)$ is:

$$M(T) = \frac{0.3693}{5} \cdot T^5 - \frac{4.0963}{4} \cdot T^4 + \frac{11.63338}{3} \cdot T^3 - \frac{1.4216}{2} \cdot T^2 - 0.0837 \cdot T + C.$$

On the homework assignment you were asked to use this antiderivative to find the total cortisol concentration (area under curve) that a person would experience during the six hours immediately after ingesting one 125 mg dose of MDMA. The area that you are interested in starts at $T = 0$ and ends at $T = 6$. Evaluating this area:

$$\begin{aligned} \text{Total cortisol concentration} &= \int_0^6 m(T) \cdot dT \\ &= M(6) - M(0) \end{aligned}$$

$$\begin{aligned}
&= 58.64652 + C - C \\
&= 58.65652 \frac{\mu\text{g} \cdot \text{hour}}{dl}.
\end{aligned}$$

3. In this situation (where you will calculate the total cortisol concentration for a person who suffers from Cushing's Disease), the cortisol curve was described by the equation:

$$m(T) = 48.2699 \cdot (0.9452690908)^T.$$

This function (an exponential function) is a series of functions that most closely resemble the function $f(x) = A \cdot B^x$ from Table 1. The antiderivative, $M(T)$ is:

$$M(T) = \frac{48.2699 \cdot (0.9452690908)^T}{\ln(0.9452690908)} + C.$$

In the homework assignment you were asked to use this antiderivative to find the total cortisol concentration (area under curve) for a person suffering from Cushing's disease over the course of 24 hours. The area that you are looking for starts at $T = 0$ and ends at $T = 24$. Evaluating the area:

$$\begin{aligned}
\text{Total cortisol concentration} &= \int_0^{24} m(T) \cdot dT \\
&= M(24) - M(0) \\
&= \frac{48.2699 \cdot (0.9452690908)^{24}}{\ln(0.9452690908)} + C - \left[\frac{48.2699 \cdot (0.9452690908)^0}{\ln(0.9452690908)} + C \right] \\
&= 635.4568868 \frac{\mu\text{g} \cdot \text{hour}}{dl}.
\end{aligned}$$

4. Finally, in this last situation (where you will calculate the total cortisol concentration for a healthy adult person who lives in a relatively stress-free environment), the cortisol curve was described by the equation:

$$m(T) = -0.00071 \cdot T^4 + 0.02317 \cdot T^3 - 0.1939 \cdot T^2 - 0.3213 \cdot T + 7.7849$$

This function (a polynomial) is a series of functions that most closely resemble the function $f(x) = x^n$ from Table 1. The antiderivative, $M(T)$ is:

$$M(T) = \frac{-0.00071}{5} \cdot T^5 + \frac{0.02317}{4} \cdot T^4 - \frac{0.1939}{3} \cdot T^3 - \frac{0.3213}{2} \cdot T^2 + 7.7849 \cdot T + C.$$

In the homework assignment, you were asked to use this antiderivative to find the total cortisol concentration (area under curve) for a healthy adult during the eighteen hours of the day when they have non-zero levels of cortisol in their body. The area that you are looking for starts at $T = 0$ and ends at $T = 18$. Evaluating this area:

$$\begin{aligned} \text{Total cortisol concentration} &= \int_0^{18} m(T) \cdot dT \\ &= M(18) - M(0) \\ &= 50.8908 + C - C \\ &= 50.8908 \frac{\mu\text{g} \cdot \text{hour}}{\text{dl}}. \end{aligned}$$

5. The introduction to the homework assignment described a number of health and mental problems that had been linked by scientifically studies to elevated levels of cortisol in the body. These problems included:

- Possible permanent damage to the hippocampal formation in the brain¹. (A number of animal studies² have suggested that the hippocampal formation is important in regulating the production of cortisol. If the hippocampus is damaged, then the capacity of the body to regulate subsequent cortisol production may also be impaired.)
- Impairment of memory and learning ability³.
- Mood alteration⁴.
- Depression⁵ and other psychiatric and neurological disorders⁶.
- Psychosomatic disorders (such as chronic fatigue syndrome)⁷.
- Immune system suppression⁸.
- Obesity (in men)⁹.

¹ Source: L. R. Ember. (1998) "Surviving stress." *Chemical and Engineering News*, **76**(21): 1-13.

² For example, see: R. F. McGiven, P. Rittenhouse, F. Aird, L.D. Van der Kar and E. Redei. (1997) "Inhibition of stress-induced neuroendocrine and behavioral responses in the rat by prepro-thyrotropin releasing hormone 178-199." *Journal of Neuroscience*, **17**(12): 4886-4894.

³ Source: J.W. Newcomer, G. Selke, A.K. Melson, T. Hershey, S. Craft, K. Richards and A.L. Alderson. (1999) "Decreased memory performance in healthy humans induced by stress-level cortisol treatment." *Archives of General Psychiatry*, **56**(6):527-533.

⁴ Source: J. Smyth, M.C. Okenfels, L. Porter, C. Kirschbaum, D.H. Hellhammer and A.A. Stone. (1998) "Stressors and mood measured on a momentary basis are associated with salivary cortisol secretion." *Psychoneuroendocrinology*, **23**(4): 353-370.

⁵ Source: B.J. Carroll, G.C. Curtis and j. Mendels. (1976) "Neuroendocrine regulation in depression." *Archives of General Psychiatry*, **33**(11): 1039-1044.

⁶ Source: F. Holsboer, A. Grasser, E. Friess and K. Wiedemann. (1994) "Steroid effects on central neurons and implications for psychiatric and neurological disorders." *Annals of the New York Academy of Sciences*, **746**: 345-359.

⁷ Source: J.C. Pruessner, D.H. Hellhammer and C. Kirschbaum. (1999) "Brunout, perceived stress, and cortisol responses to awakening." *Psychosomatic Medicine*, **61**: 197-204.

⁸ Source: R. Glaser, B. Rabin, M. Chesney, S. Cohen and B. Natelson. (1999) "Stress-induced immunomodulation. Implications for infectious diseases." *Journal of the American Medical Association*, **281**(24): 2268-2270.

⁹ Source: R. Rosmond, M.F. Dallman, P. Bjorntorp. (1998) "Stress-related cortisol secretion in men: Relationships with abdominal obesity and endocrine, metabolic and hemodynamic abnormalities." *Journal of Clinical Endocrinology and Metabolism*, **83**(6): 1853-1859.

In particular, the scientific evidence seems to indicate that anything that significantly elevates your body's levels of cortisol can have potentially dangerous consequences for your health and psychiatric and psychological well-being. The three specific statements that you were asked to examine are given below (together with a discussion of why each could be linked to cortisol).

- **According to DEA statistics¹⁰, employees who test positive for drugs use consume almost twice the medical benefits of employees who do not test positive for drugs.**

In a healthy adult, the total cortisol concentration is about $51 \frac{\mu\text{g}\cdot\text{hour}}{\text{dl}}$. If that adult were to consume 125 mg of 3,4-methylenedioxymethamphetamine, then their total cortisol concentration for the 24 hour period would more than double to $109 \frac{\mu\text{g}\cdot\text{hour}}{\text{dl}}$. As a result of taking the drug, the otherwise healthy person's total cortisol concentration has more than doubled. Scientific studies have linked both psychosomatic illnesses and suppression of the immune system to elevated levels of cortisol. Taking 3,4-methylenedioxymethamphetamine leads to elevated levels of cortisol in the body, and therefore may also lead directly to psychosomatic medical problems, or may indirectly lead to medical problems by leaving the body less able to defend itself against infections. This is of particular concern with 3,4-methylenedioxymethamphetamine, as users frequently expose themselves to sources of infectious agents (through close, prolonged and often intimate physical contact with other drug users) while under the influence of this substance.

- **According to a survey¹¹ of 2311 runners who competed in the Los Angeles marathon, one in seven got a cold within two weeks of competing. About one person in 35 gets a cold every two weeks in the population as a whole.**

Marathon runners are (generally speaking) quite an unusual group of individuals, at least from the point of view of the level of physical fitness that they maintain. Because of this, it is not entirely safe to assume that their "normal" cortisol levels will be comparable to a healthy adult who is not a marathon runner. Nevertheless, the total cortisol concentration for a marathon runner immediately after a race is about eighteen (18) times the normal total cortisol concentration for a healthy adult. Even if a marathon runner's total cortisol concentration is normally higher than a non-runner's, this has to be a much higher total cortisol concentration than normal. Scientific studies have linked elevated cortisol levels and suppression of the body's immune system. Therefore, the highly elevated total cortisol concentration that marathon runners experience after a race

¹⁰ Source: <http://www.usdoj.gov/dea/concern/use.htm>

¹¹ Source: D. Nieman. *The Exercise-Health Connection*. Champaign, IL: Human Kinetics Publishers, 1997.

may suppress their immune systems, making them more vulnerable to disease.

- **A common symptom of Cushing's disease is lack of resistance to common diseases that rarely trouble the population at large.**

The total cortisol concentration of a person who is suffering from Cushing's disease is approximately twelve to thirteen (12-13) times as high as that of a healthy adult. Therefore, people with Cushing's disease have dramatically higher levels of cortisol in their bodies, as compared with healthy adults who do not suffer from this disease. As noted, elevated levels of cortisol have been linked to suppression of the immune system. Therefore, you would expect the immune system of a person with Cushing's disease to be suppressed all of the time, leaving them vulnerable to diseases that would probably not affect a healthy adult who did not have Cushing's disease.