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Surge Functions and Drug Interactions

Abstract

The objective of this project is to analyze how surge functions work to understand the way drug concentration levels in the bloodstream of a human body vary over time after an initial dose. A surge function increases rapidly at the beginning of the dosage and drops slowly after it reaches its peak. It is important to realize when a certain drug reaches its peak and how long the effects will last on a patient, so a second drug can be administered without risking negative interactions. We explain the calculations used in order to properly understand the curve of a drug's response.

Keywords

surge functions, drug concentration level, bloodstream, drug dose, the curve of a drug's response

Problem statement

Let $C(t)$ = At^4e^{-bt}, where A = 6.2 and b = 0.5, be the function describing the concentration of a medication in the bloodstream (t is in hours, C is in nanograms per milliliter). When does it reach its maximum? What can be said about the rate of increase/decrease of the level of the drug in the organism? Suppose now that the patient has to be treated with a second drug after the effect of the first one wears off. Knowing that the minimum effective concentration of the first drug is 50 ng/ml, when the second treatment can begin.

Motivation

The understating of surge functions is essential for pharmaceutical purposes. It is important for medical staff and pharmacists to understand how long a drug will remain in a patient’s bloodstream. By studying surge functions one can realize how many hours the drug will take to reach its peak concentration and how long this drug will last in the body before it is excreted by the kidneys. Knowing the maximum concentration is important to avoid drug toxicity and not harm the patient. After the levels are below the minimum effective concentration threshold it would be safe to start new treatments with drugs that would ordinarily cause negative interactions so the results obtained here can be used to design a treatment plan.

Mathematical description and solution approach

In mathematics, a function of the following form is used as a surge function:

$$C(t) = At^p e^{-bt}, \tag{1}$$

where p and b are both positive. A surge function is a product of a power function (t^p) and a decaying exponential function (e^{-bt}). The power function causes the surge function to increase rapidly, while the exponential function causes a slow decay after the function reaches its peak. In a surge function, t is typically used to represent time and $C(t)$ represents the dependent variable over time. The graph of this function $C(t) = te^{-t}$, is shown in Figure 1. This is where all constants are equal to 1.

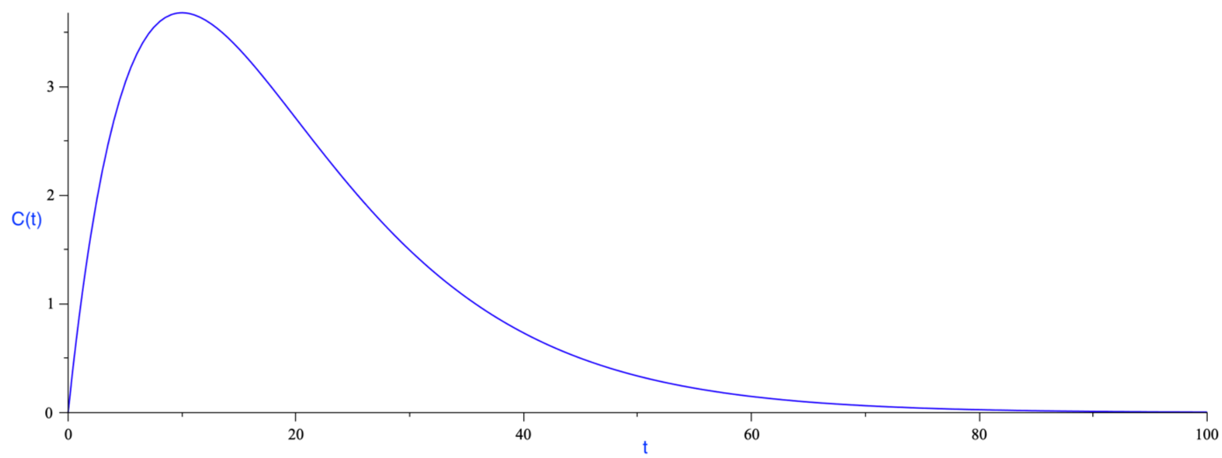

Figure 1. The graph of a surge function.

As seen in the graph above the function has one maximum, it increases rapidly and then falls slowly. This function always starts at the origin as $C(0)$=0. For this application, we set A=6.2, b=0.5 and p=4, resulting in the function:

$$C(t) = 6.2t^4 e^{-0.5t} \tag{2}$$

This will be used to represent the concentration of medication in the bloodstream over time. The graph of the surge function (equation (2)) is displayed below in Figure 2.

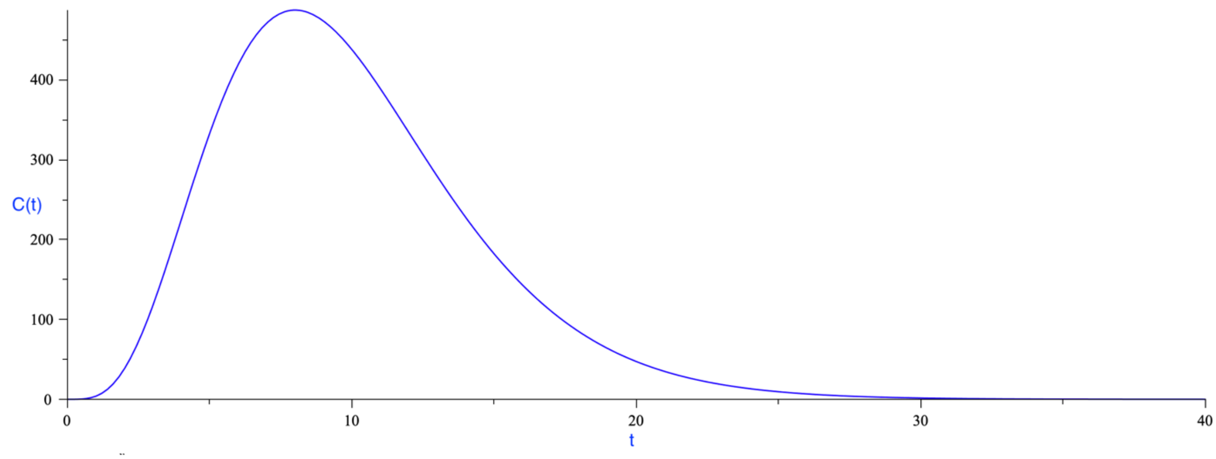

Figure 2. The graph of the surge function being observed.

From this function, the maximum concentration of the medication can be found. The number of hours for the medication to reach its maximum strength can also be calculated. The first step is to find the first derivative of the original function. This is done by using the product rule for derivatives. In this case *f(t)* is $6.2t^4$ and *g(t)* is $e^{-0.5t}$:

$$\frac{d}{dt}[f(t) \cdot g(t)] = \frac{d}{dt}[f(t)] \cdot g(t) + f(t) \cdot \frac{d}{dt}[\,g(t)] \tag{3}$$

$$C'(t) = \frac{d}{dt}[6.2t^4 e^{-0.5t}] \tag{4}$$

$$C'(t) = 24.8t^3 e^{-0.5t} - 3.1t^4 e^{-0.5t} \tag{5}$$

By setting the first derivative equal to zero, the critical points of the function can be found. This is shown in equation (6).

$$24.8t^3 e^{-0.5t} - 3.1t^4 e^{-0.5t} = 0 \tag{6}$$

$$t = 0\,,8 \tag{7}$$

The critical points at *t*=0 and *t*=8 create 2 intervals for this function. The intervals are [0, 8] and [8, ∞). By using the first derivative test we can confirm if *t*=8 is a maximum value. This is done by choosing a test point in the interval and determining the sign of C' for both intervals. If the first derivative of the function changes signs, then the point is considered to be a maximum value. For the interval [0, 8], t=1 can be chosen as a test point:

$$24.8(1)^3e^{-0.5(1)} - 3.10(1)^4e^{-0.5(1)} = 13.16171531 \tag{8}$$

For the interval [8, ∞), t=10 can be chosen as a test point:

$$24.8(10)^3e^{-0.5(10)} - 3.10(10)^4e^{-0.5(10)} = -47.77527139 \tag{9}$$

The sign of the first interval, [0, 8], is a positive value so $C(t)$ is increasing. While the sign of the second interval, [8, ∞), is negative so $C(t)$ is decreasing. C has a maximum when the sign of C' changes from positive to negative. This proves that the critical point t=8 is a maximum value for $C(t)$. At t = 8 the concentration of the drug is approximately 465.13 ng/ml. This is calculated in equation (10) by evaluating at t=8:

$$6.2(8)^4e^{-0.5(8)} = 465.13 \tag{10}$$

The rates of increase and decrease of the function can also be studied. Using the intervals, an average rate of change can be determined from the formula in equation (11). The average rate of change over [0, 8] is calculated below where a=0 and b=8.

$$\left(\frac{1}{b-a}\right)\int_a^b C'(t)\,dt \tag{11}$$

$$\left(\frac{1}{8-0}\right)\int_0^8 (24.8t^3e^{-0.5t} - 3.10t^4e^{-0.5t})dt = 58.11 \tag{12}$$

This shows that the concentration of the drug is increasing at an average rate of approximately 58.11 ng/ml per hour in the [0, 8] interval. The instantaneous rate of change at any time is represented by the derivative of the function $(24.8t^3e^{-0.5t} - 3.10t^4e^{-0.5t})$. The function decreases to 0 for increasing values of t because the exponential function approaches the horizontal asymptote at y = 0. The exponential function decays faster than the polynomial term grows, because $\lim_{t \to \infty} t^4 e^{-bt} = 0$. Thus, the function will continuously get near 0 but it will never reach 0. Medications are administered in dosages and after a number of hours the dosage of the medicine will be so small it is not effective. By finding the time the medication is no longer effective, doctors know when it is safe to begin a second treatment. Since the minimum effectiveness of the drug is known, an interval can be created, and an average rate of decrease can be calculated over the new interval. To estimate the time the concentration loses its effectiveness, we use the given minimum effective concentration that is 50 ng/ml. By substituting the concentration, 50 ng/ml, into the left side of the original function (equation (2)), the value of t can be found. The horizontal line $C(t)$=50 is shown in Figure 3.

$$50 \geq 6.2t^4 e^{-0.5t} \tag{13}$$

$$\mathrm{t} = 2.2257, 19.6494 \tag{14}$$

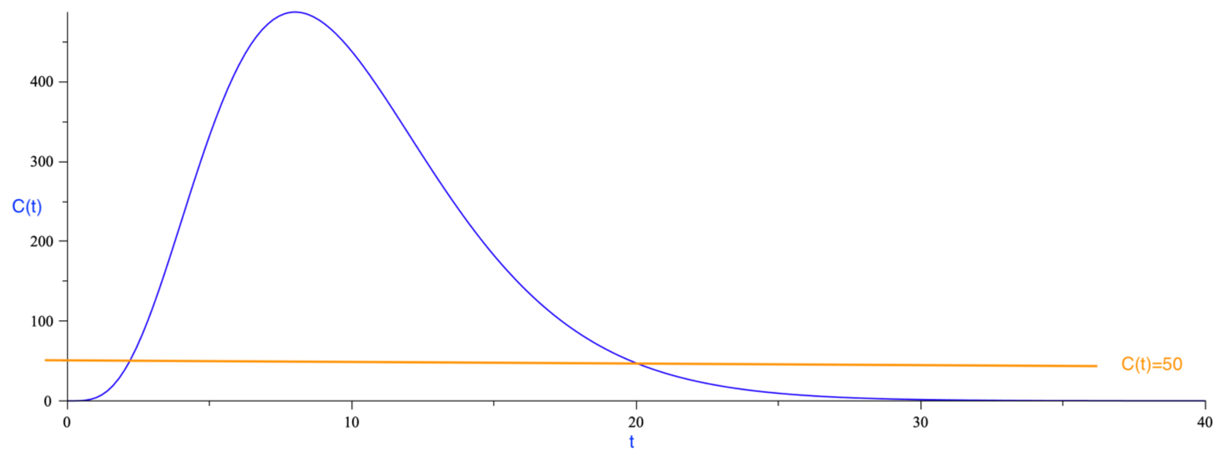

Figure 3. Surge function showing horizontal line.

The values of t in (14) represent the time when the concentration is exactly 50 ng/ml. The solutions give us two intervals [0, 2.2257] and [19.6494, ∞) where the concentration is at most 50 ng/ml. The second interval is chosen because this occurs when $C(t)$ is decreasing. At approximately 19.6 hours a second drug can be administered. Now, the interval is defined, and this specific drug concentration is decreasing over the interval [8, 19.6494]. From this interval an average rate of decrease can be determined by the formula in equation (11) where *a*=8 and *b*=19.6594.

$$\left(\frac{1}{19.6494-8}\right)\int_{8}^{19.6494}(24.8t^{3}e^{-0.5t}-\ 3.10t^{4}e^{-0.5t})\,dt=-35.6352 \tag{15}$$

The average rate of change over the interval [8, 19.6494] is -35.6352 ng/ml per hour. This proves the average rate of decrease is slower than the average rate of increase which is 58.11 ng/ml per hour over the interval [0, 8].

Discussion

The objective of this project is to understand how a surge function represents the drug concentration in the bloodstream. By examining this surge function, we are able to see the maximum concentration the drug will reach and the number of hours it takes to achieve. The values of A and *b* are fitted to specific populations and may need to be computed again for different patient groups so that two people would follow different treatment schedules. This specific drug will reach its maximum concentration of 465.13 ng/ml after approximately 8 hours. The initial concentration of the drug is 0 ng/ml and it starts to increase at an average rate of 58.11 ng/ml per hour over the interval [0, 8]. The minimum effective concentration of the drug is 50 ng/ml which is reached after 19.6 hours. The average rate of change over the interval [8, 19.6494] is -35.6352 ng/ml per hour. Once the drug has reached 19.6 hours a second drug can be administered. The results achieved are anticipated because a surge function increases rapidly from zero to its peak and then decreases slowly after the maximum concentration is achieved.

Conclusions and Recommendations

We observe the way a surge function models the changing concentration of medication in the bloodstream. A surge function is a type of function that starts at the origin and increases rapidly like a power function. After reaching its peak the function decreases slowly like an exponential function. This function accurately represents the way a drug interacts in the bloodstream. Studying this function is essential to doctors and pharmacists because it allows them to administer dosages of medicine correctly.

The specific surge function discussed in this paper allows for a deeper understanding of how drugs interact in the bloodstream. The model for the drug fits perfectly into the original surge function model. It has one maximum value and shows a fast increase but slow decrease. The maximum concentration reached is 465.13 ng/ml after 8 hours. The average rate of increase is 58.11 ng/ml per hour over the interval [0, 8], and it decreases at an average rate of 35.6352 ng/ml per hour over the interval [8, 19.6494]. This proves that there is a significant difference between the rate of increase and the rate of decrease in a surge function. A surge function is also used to estimate the time a drug reaches its minimum effectiveness and a new drug can be given to the patient minimizing the risk of negative interactions. For this drug, the minimum effective concentration is 50 ng/ml and it takes the drug 19.6 hours to reach this level of concentration. From looking at these results we are able to better understand how a surge function models the concentration of a drug and see a direct comparison of the average rates of increase and decrease.

This project is beneficial in helping readers understand how a surge function models real world scenarios. Surge functions are also beneficial outside of biomedical application, as they can be used to represent the delay of radioactive waves or to show results from an advertising campaign. Further research can be conducted on the use of surge functions. The parameters A, b, and p are experimentally determined to fit data for an "average patient." This project could be expanded by repeating the same analysis for different sets of parameters representing different categories of patients and comparing the results.

Nomenclature

C	concentration of medication	ng/ml
t	time	hours

References

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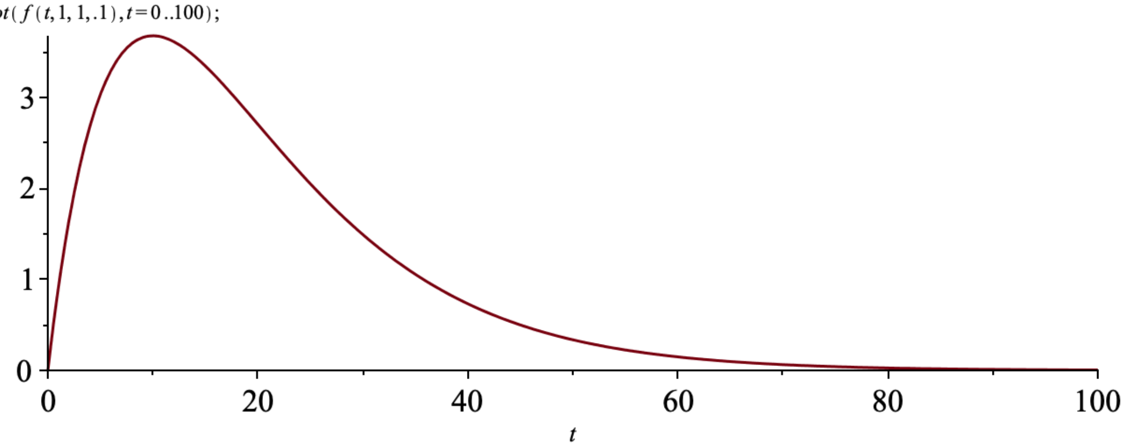
Appendix

Maple 2020, a technical computing software, was used for creating the graphs of the surge functions in this paper.

$f := (t, y, a, b) \rightarrow a * t^y * \exp(-b * t);$

$$f := (t, y, a, b) \mapsto a \cdot t^y \cdot e^{-b \cdot t} \quad \textbf{(1)}$$

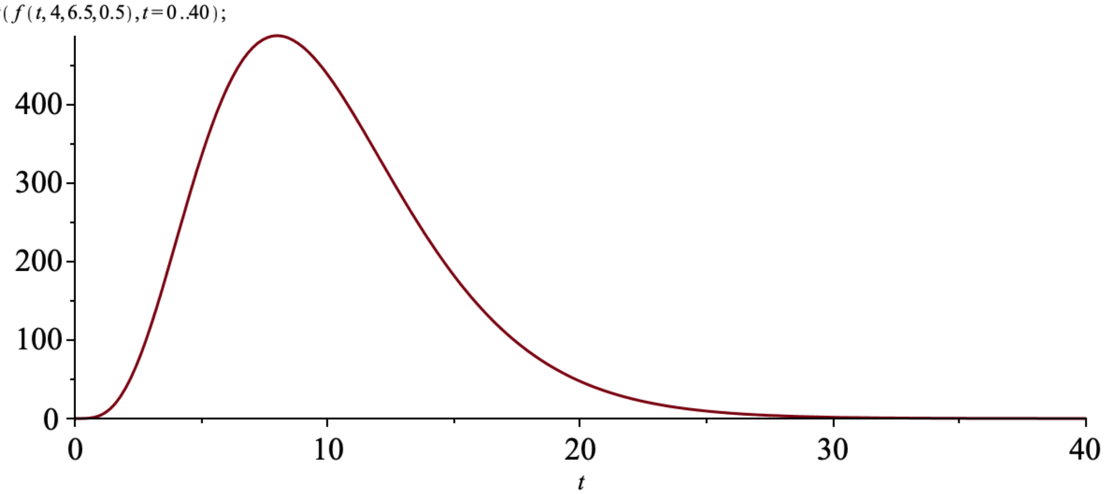
$plot(f(t, 1, 1, .1), t = 0..100);$



$f := (t, y, a, b) \rightarrow a * t^y * \exp(-b * t);$

$$f := (t, y, a, b) \mapsto a \cdot t^y \cdot e^{-b \cdot t} \quad \textbf{(2)}$$

$plot(f(t, 4, 6.5, 0.5), t = 0..40);$



$6.2\, t^4 e^{-0.5\, t} \xrightarrow{\text{differentiate w.r.t. t}} 24.8\, t^3 e^{-0.5\, t} - 3.10\, t^4 e^{-0.5\, t} \xrightarrow{\text{solve for t}} [[t = 0.], [t = 8.]]$