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APPLICATIONS OF DIFFERENTIAL CALCULUS IN MEDICINE

Igor Costa Santos
https://orcid.org/0000-0002-5637-7750

Adriana Araujo Cintra
https://orcid.org/0000-0002-6856-406X

Nathália Bandeira de Almeida
https://orcid.org/0000-0003-4126-3088

José Alencar Formiga Júnior
https://orcid.org/0000-0002-0155-0341

Hallamark Alvarez Lemos Portella
https://orcid.org/0000-0001-8962-9486

Marília Gabriela Ferreira
https://orcid.org/0000-0002-1993-6242

Luis Fernando Brito
https://orcid.org/0000-0003-2223-4118

Jaqueline Giselle Farias Fernandes
https://orcid.org/0000-0001-8430-0198

Beatriz Lima da Costa
https://orcid.org/0000-0001-7865-4651

Pedro Ricardo Macena Andrade
https://orcid.org/0000-0003-0311-3046

Daniel Machado Moura
https://orcid.org/0000-0001-6140-8809

Tainá Rodrigues Toqueton
https://orcid.org/0000-0002-7568-5572

Abstract: Differential calculus is a branch of mathematics developed from algebra and geometry in which the definition, applications of derivatives and their properties are studied. In this context, this work addressed the main functions of differential calculus through its use in the field of medicine, seeking precisely the best practices for patient prophylaxis and treatment. The current work was developed through the scientific initiation and master's project (PICME), in which weekly meetings were held where doubts were resolved and a new topic was chosen to be studied to present the advances achieved. With this, the theme was selected together with the advisor and later studied the theory of calculus with the choice of exercises being applied in the medical area. It is concluded that the mathematical relationships developed by differential calculus have relevance in understanding the mechanism of body functioning, which leads to the development of innovative possibilities for pharmacological treatment, while at the same time supporting the epidemiological calculations that determine the course of diseases and define measures. health and humanitarian.
Keywords: Mathematics, Design, Prophylaxis, Learning, Treatment, Medicine.

INTRODUCTION

The historical context of the development of integral differential calculus refers to two scientists and mathematicians, Gottfriend Wilhelm Leibniz (1646-1716) and Isaac Newton (1643-1727) in different works. In this set of mathematical knowledge, the graphs, the behavior and the variations of the functions along their trajectory are studied, in addition to the associated geometric analysis (areas and volumes). In other words, it is about a broad and systematized understanding of the functions.

In this sense, it is inferred that this field of knowledge has numerous practical applications, in medical treatments, in the dissemination of diseases, among others.

The present research aims to present the relationship of the exact sciences, specifically with regard to mathematics, with the area of medicine. Although these two fields of knowledge are distinct, both are complementary with regard to the medicinal field as a whole, given that medical practices need numerical accuracy so that it is possible to obtain greater control in the distribution of medicines, in the development of treatments. pharmaceuticals, in performing surgical procedures, among other mechanisms that are limited to health. As an example, the exact sciences have a crucial role in the epidemiological context regarding SARS-CoV-2, since the application of statistical calculations are fundamental for the formulation of theses and probabilities which guide the taking of measures. prophylactic.

Therefore, the study of practical applications of calculus in the context of health was placed as the central point of this project.

METHODOLOGY

The present study is an exploratory and bibliographic experience report about the activities developed in a project originating from the PICME (Scientific Initiation and Master's Program) at the Federal University of Jataí.

PICME is a program that offers university students who have excelled in the Mathematics Olympiads (OBMEP or OBM medalists) the opportunity to undertake advanced studies in Mathematics simultaneously with their degree. The PICME is coordinated at the national level by the Institute of Pure and Applied Mathematics - IMPA and offered by Postgraduate Programs in Mathematics from several universities throughout the country.

From this point of view, the activities were designed with the objective of presenting undergraduate students in health sciences with an introduction to some basic concepts of Integral Differential Calculus with some applied problems, such as, for example, problems with blood circulation, blood pressure, tumor growth and disease spread.

The meetings were held weekly, from January to December 2020. The dynamics were carried out by clarifying doubts, elaborating directed studies on differential calculus, choosing the next theme and presenting the advances obtained. The themes were defined together with the advisor, who first highlighted the theory of calculus for later delimitation of the exercises applied in the health area. This way, the student would be able to understand the relationship between mathematics and medicine.

Regarding the theoretical foundation, the book "Applied Calculus Book: A Modern Course And Its Applications" and the articles "The Physiology of Oxygen Transport by the Cardiovascular System: Evolution of Knowledge", "Physiology, Pulmonary Vascular Resistance", " Barbiturate Toxicity" and "A Mathematical Model of COVID-19 with Vaccination and Treatment". In addition, there was the use of tools such as "Geogebra", a dynamic mathematics software, and "Overleaf", a mathematical cryptography editor (LaTeX).

RESULTS

In this project some mathematical problems that apply differential calculus in the context of medicine were studied. Initially, a mathematical problem involving Poiseuille's Law was studied. The formula described by the French physicist Poiseuille in 1842 innovatively defined the dynamics associated with the determinants of blood flow in arterial tissue and motivated histological and physiological studies focusing on the determination of arterial vasomotor tone (Crystal and Pagel, 2019). Poiseuille's law is simple and can accurately capture the dynamics of blood circulation, but it is limited to the anatomical and histological conditions associated with each arterial tissue.

In exercise number 69 on page 9 of the Applied Calculation Book:

> "Blood Circulation - Biologists have discovered that the velocity of blood in an artery is a function of the distance between the blood and the central axis of the artery. According to Poiseuille's Law, the velocity (in centimeters per second) of blood that is r centimeters from the central axis of an artery is given by the function S(r) = C(R2 − r2), where C is a constant and R is the radius of the artery. Suppose that, for a certain artery, C = 1.76 × 105cm−1s−1e R = 1.2 × 10−2cm.
>
> a) Determine the velocity of the blood along the central axis of the artery.
>
> b) Determine the velocity of the blood midway between the central axis and the artery wall.

A) Solution: when the blood is on the central axis the distance is r=0. Then

$$S(0) = 1,76 \times 10^5((1,2 \times 10^{-2})^2 - 0^2) = 25{,}344$$

So the speed is 25, 344 cm/s.

B) Solution: in this case: $r = \frac{R}{2}$, logo $r = \frac{1{,}2\times10^{-2}}{2}$

So:

$$S(\frac{R}{2}) = C\,[(1{,}2 \times 10^{-2})^2 - (\frac{1{,}2 \times 10^{-2}}{2})^2]$$

Therefore,

$$S(\frac{R}{2}) = \frac{7{,}6032 \times 10}{4} = 19{,}008$$

Therefore, the velocity of the blood will be 19.008 cm/s.

Another topic studied deals with the concentration of a drug in the bloodstream. In the medical context, the dose to be administered intravenously depends both on the toxicity of the drug and on the general condition of the patient. Considering that the threshold between therapeutic dose and toxicity can be narrow, the mathematical quantification of the concentration is essential for adequate treatment.

In exercise number 61 on page 59 of the Applied Calculation Book:

> Concentration of a Drug - The concentration of a drug in the blood of a patient t hours after an injection is C(t) milligrams per milliliter, where
>
> $$C(t) = \frac{0,4}{t^{1,2} + 1} + 0,013$$
>
> a) What is the drug concentration immediately after injection (ie, t = 0)?
>
> b) What is the change in drug concentration during the fifth hour? Does the concentration increase or decrease during this period?
>
> c) What is the residual drug concentration, i.e. the "long-term" concentration (when t → ∞)?

A) Solution: If t = 0 then

$$C(t) = \frac{0,4}{0^{1,2} + 1} + 0,013$$

Therefore,

$$C(t) = 0,413$$

Therefore, the drug concentration is 0.413 mg/ml.

B) Solution: Considering the variation C(5) – C(4). Thus:

$$C(4) = \frac{0,4}{4^{1,2}+1} + 0,013 \text{ e } C(5) = \frac{0,4}{5^{1,2}+1} + 0,013$$

So,

$$C(4) - C(5) = -0,013$$

Therefore, the concentration variation will be 0.013 mg/ml. The concentration decreases.

c) Solution: Considering t → ∞ we have that

$$\lim_{t\to\infty} C(t) = \lim_{t\to\infty} \frac{0,4}{t^{1,2} + 1} + 0,013 = 0,013$$

Therefore, the concentration will be 0.013 mg/ml.

Subsequently, a mathematical model was studied in relation to the mechanism of disease dissemination. Similar to the epidemiological pattern of infection by SARS - Cov - 2 (COVID-19). In the exercise, the data are limited and therefore the results do not take into account associated human factors, while it is a simple model that can demonstrate the initial phase of a pandemic, the plateau of infected and the reduction in the rate of infection. Contagion.

In exercise number 59 on page 183 of the Applied Calculation Book:

> Disease Spread: An epidemiologist determines that a certain disease spreads in such a way that, t weeks after the start of an outbreak, N hundreds of new cases are observed, where
>
> $$N(t) = \frac{5t}{12 + t^{2}}$$
>
> a) Determine N'(t) and N"(t)
>
> b) In which week is the maximum number of cases of the disease? What is this maximum number of cases?
>
> C) Authorities consider the epidemic under control when the rate of increase in the number of new cases is minimal. In which week does this occur and what is the number of cases?

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A) Solution: Using the quotient rule we have

$$N'(t) = \frac{60-5t^2}{(12+t^2)^2} \quad \text{and } N''(t) = \frac{10t^3-360t}{(12+t^2)^3}$$

B) Solution: I need to know how long it will take to reach the maximum. Thus, we will look for the critical point, that is,, N'(t) = 0.

Therefore,

$$60 - 5t^2 = 0.$$

Therefore,

$$t = 2\sqrt{3}$$

Now, we must analyze whether the critical point is maximum or minimum.

As $60\text{-}5t\text{^}2 > 0$, if $t<2\sqrt{3}$ and $60\text{-}5t^2<0$, if $t>2\sqrt{3}$ so it's the maximum point. That is, considering the first derivative we have that the critical point is maximum in approximately 3.5 weeks.

C) Solution: To define the week when the rate of increase is minimum, we need to define where the first derivative N'(t) reaches the minimum point. So we need to analyze where the second derivative vanishes. Soon

$$N''(t) = \frac{10t^3-360t}{(12+t^2)^3}=0$$

Considering that $10t = 0$ or $t^2 - 36 = 0$,, therefore t=0 or t=6 weeks. But what interests us is t=6. As 10t > 0 and $(t^2 +12)^3> 0$ to t > 0 and

$t^2 - 36 < 0$ if $t<6$ and $t^2 - 36 > 0$ if $t>6$

then t=6 is a minimum point. Finally, the rate of increase in the number of new cases is minimal in week 6. Thus, the number of cases considered the inflection point, at which the rate of increase of new cases is minimal, will be given by,

$$N(6) = 0{,}625.$$

Finally, there will be 62.5 cases.

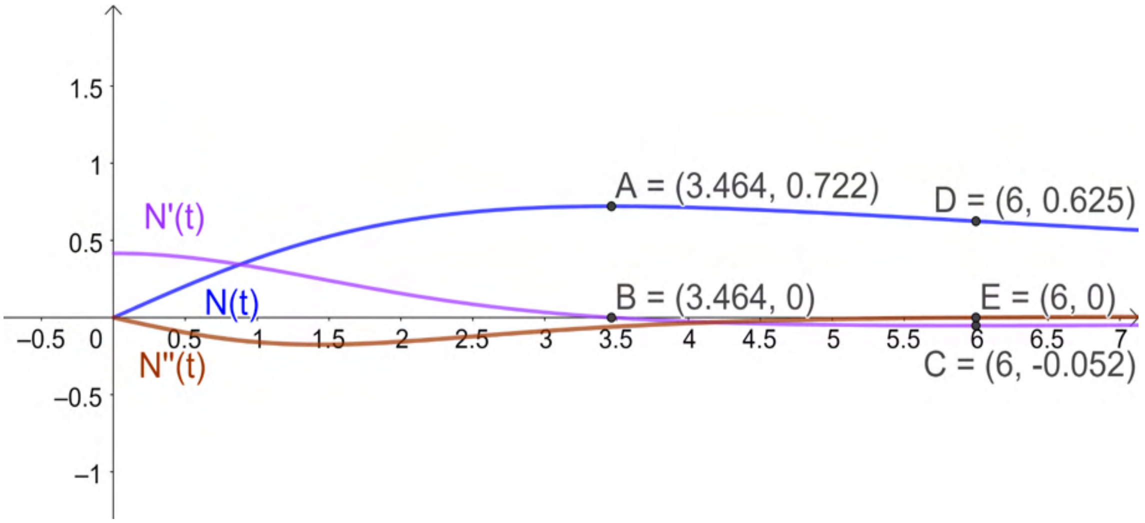
DISCUSSION

The discovery that the radius of the artery is more relevant than its histological features was groundbreaking (Crystal and Pagel, 2019). Poiseuille defined his law based on this principle and sought to quantify the velocity of blood at each point along the diameter of the arterial lumen. Furthermore, the law defined the impact of vasoconstriction or vasodilation on arterial resistance and pulmonary vascular resistance (Widrich and Shetty, 2021). Thus, the use of vasodilators or vasoconstrictors began to be better administered, since the quantification of the reduction in arterial caliber to the detriment of the dynamics of the radius began to be explored by physicians. Thus, Poiseuille's Law brought with it a form of mathematical solution that contributed significantly to the search for better medical precision in the treatment of vascular diseases.

The proper dosage of a drug for intravenous administration is extremely relevant in the medical context. An example of this is the use of sedative-hypnotics, especially barbiturates. They have a low threshold between therapeutic concentration and intoxication, in addition to being used as a drug to cause suicide through overdose (Suddock and Cain, 2021).

In the meantime, it is evident that calculations for adequate concentration are essential for the use of intravenous drugs. As it is a pathway that connects the entire body, a concentration above the ideal can cause systemic effects and thus lead to death.

Mathematical models developed throughout the COVID-19 pandemic have



Graphic 1. The function N(t) presents the course of the spread of a disease according to the exercise formula. The derivative N'(t) shows the rate of increase in the spread of the disease and point A is the maximum moment of infected (3.5 weeks) by the disease in question. The second derivative N"(t) shows the rate of increase in the number of infected by the disease, that is, in the sixth week N"(t) is set to zero, that is, the rate of increase is minimal, which in practice it means a drop in the number of sick cases. Source: The author himself on 05/30/21.

played a crucial role in the development of global health measures. The daily accounting of the increase in the contagion rate continually changed the mathematical formula (Diagne et al, 2021). At the same time that the use of masks, hygiene and especially vaccination acted positively to reduce the curve of infected.

In view of this, the graphs of the spread of COVID-19 became a central focus of government authorities and allowed the population to be made aware of their role in reducing the rate of contamination, through access to pandemic data.

CONCLUSION

Through the study of functions, limits, continuous functions and derivatives of functions, related to the mathematical model that involves drug administration, we understand the importance of Differential Calculus in the context of health. Furthermore, we understand the relevance that the assessment of arterial diameter had in the context of the development of drugs to modulate vasoconstriction and vasodilation of the arteries and in the creation of new methods of controlling blood flow. It was also verified the relationship of the differential calculation with the rates of dissemination of diseases, which imply the importance of addressing this issue in health management and consequently in public authorities.

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