Proceeding Series of the Brazilian Society of Computational and Applied Mathematics, v. 11, n. 1, 2025.

Trabalho apresentado no XLIII CNMAC, Centro de Convenções do Armação Resort - Porto de Galinhas - PE, 2024

Proceeding Series of the Brazilian Society of Computational and Applied Mathematics

Fractional Model in Dengue with Real Data

Micaeli M. Theodoro[1], Guilherme Rodrigues[2]
Graduate Program in Biometrics, IBB-Unesp, Botucatu, SP
Fernando L. P. Santos[3], Rubens F. Camargo[4]
Institute of Biosciences, Unesp, Botucatu, SP

Abstract. The aim of this study is to bring forward a fractional model for Dengue, incorporating the effects of temperature and rainfall variations throughout the year. In addition, real data from Dengue cases in the city of Bauru, state of São Paulo, Brazil, were used to estimate the case curve with the fractional model using the Intraclass Correlation Coefficient (ICC) to measure the estimation accuracy. The results showed that the parameter estimation of the fractional model has a higher ICC than the numerical simulations of the classical model, demonstrating greater accuracy of the fractional model. Furthermore, a sensitivity analysis of the $\mathcal{R}_0$ parameters was carried out using the Partial Rank Correlation Coefficients (PRCC) method to evaluate which parameters have the greatest influence on the increase or decrease in the basic reproduction number. According to the sensitivity analysis carried out, we can conclude that the most effective control to reduce $\mathcal{R}_0$ are the efforts directed to the vector.

Keywords. Fractional modeling, Sensitivity Analysis, Parameter Estimation, Real data

1 Introduction

Dengue is a viral disease caused by a virus belonging to the *Flaviviridae* family and *Flavivirus* genus. The dengue virus has four distinct serotypes: DENV1, DENV2, DENV3, and DENV4. Transmission to humans occurs through vectors, specifically mosquitoes of the *Aedes aegypti* and *Aedes albopictus* species. In Brazil, the spread of the disease primarily occurs through the *Aedes aegypti* mosquito, which is predominantly found in urban areas.

Female *Aedes* mosquitoes deposit their eggs in stagnant water, preferably in containers such as cans, empty bottles, tires, gutters, and uncovered water tanks. The incubation period for the eggs, known as embryogenesis, lasts approximately three days, followed by hatching, which is influenced by environmental factors such as temperature and air humidity. The resulting larvae feed on organic material in the environment, with the duration of the larval stage varying depending on the availability of this substrate. The pupal stage, averaging around two days, precedes metamorphosis, leading to the emergence of adult mosquitoes. Their diet is based on carbohydrates from sap, fruits, and flowers, with only females being hematophagous and feeding on blood to supplement specific nutrients.

In the context of infectious diseases, mathematical modeling plays a crucial role, significantly contributing to the understanding of both cellular dynamics and the spread of diseases in the population. Specifically, in the case of dengue, numerous mathematicians, epidemiologists, and

[1]micaeli.theodoro@unesp.br
[2]g.rodrigues2@unesp.br
[3]fernando.pio@unesp.br
[4]rubens.camargo@unesp.br

researchers worldwide have dedicated themselves to utilizing real data, curve fitting, and predicting the evolution of disease transmission in various locations [10, 13].

Despite remarkable advances in understanding the dynamics of dengue transmission through Ordinary Differential Equation (ODE) models, especially for outlining control strategies, the increasing complexity of ODE models required to refine the viral dynamics description poses challenges in obtaining analytical solutions [10]. This can be a significant limitation to the progress of knowledge about the disease.

In this context, Non-Integer Order Calculus, commonly known as Fractional Calculus (FC), emerges as a fundamentally important element, characterized by the study of integrals and derivatives of non-integer order [2]. Despite the lack of direct physical and geometric interpretations for fractional derivatives and integrals, fractional differential equations are inherently related to systems with memory, given the non-local nature of fractional derivatives [12]. The presence of memory processes in biological systems and the ability of fractional differential equations to reduce errors arising from neglected parameters in real-life phenomena modeling highlight its relevance.

In this article, we propose a fractional generalization of a classic dengue transmission model, accompanied by a sensitivity analysis of parameters, aiming to outline control strategies.

2 Fractional Model in Dengue with Aquatic Phase

The proposed compartmental mathematical model presents the interactions between humans and mosquitoes and also the aquatic phase of the mosquito that includes egg, larva, and pupa stages. Humans are subdivided into three compartments: susceptible (H_S), infected (H_I) and recovered (H_R), with constant $H = H_S + H_I + H_R$. The *Aedes* mosquito population will be divided into an aquatic phase (A) and an adult phase (M), which is subdivided into susceptible (M_S) and infected (M_I) mosquitoes, with $M = M_S + M_I$. The subsequent ODE model, presented by Costa [5], is herein extended to encompass a non-integer order model denoted by the parameter γ, along with the inclusion of a dimensional tuning parameter denoted as τ. The generalization[1] for the Fractional Differential Equation (FDE) is given by

$$
\begin{cases}
\dfrac{d^\gamma H_S}{dt^\gamma} = \tau^{1-\gamma}\left[\mu_H\left(H - H_S\right) - \dfrac{b\beta_H H_S M_I}{H}\right], \\
\dfrac{d^\gamma H_I}{dt^\gamma} = \tau^{1-\gamma}\left[\dfrac{b\beta_H H_S M_I}{H} - \left(\mu_H + \sigma\right) H_I\right], \\
\dfrac{d^\gamma H_R}{dt^\gamma} = \tau^{1-\gamma}(\sigma H_I - \mu_H H_R), \\
\dfrac{d^\gamma M_S}{dt^\gamma} = \tau^{1-\gamma}\left(\alpha A - \dfrac{b\beta_M M_S H_I}{H} - \mu_M M_S\right), \\
\dfrac{d^\gamma M_I}{dt^\gamma} = \tau^{1-\gamma}\left(\dfrac{b\beta_M M_S H_I}{H} - \mu_M M_I\right), \\
\dfrac{d^\gamma A}{dt^\gamma} = \tau^{1-\gamma}\left[k\delta\left(1 - \dfrac{A}{C}\right)\left(M_S + M_I\right) - \left(\mu_A + \alpha\right) A\right].
\end{cases}
\tag{1}
$$

The biological parameters of the model are described in [5] with the addition of the parameter μ'_M which is additional vector mortality rate.

In the present work, we seek to use the ODE model (1) proposed by Costa [5], carry out its fractional generalization with numerical simulations and sensitivity analysis of the parameters of R_0, the basic reproduction number.

[1] The interested reader is directed to consult the fractional generalization method outlined in Theodoro [15] for further elucidation on the proposed extension

3 Model Incorporating the Effects of Temperature and Rainfall Variations

During the year, temperature and rainfall are not constant. Therefore, in accordance with the findings of Costa [5] we can incorporate the effects of temperature and rainfall variations in the parameters. Furthermore, as suggested by Huber *et al.* [8] we can represent temperature and rainfall throughout the year through the following functions:

$$T(t) = \left(\frac{T_{\max} - T_{\min}}{2}\right)\cos\left(\frac{2\pi}{365}t\right) + T_{\text{med}}, \text{ and } \omega(t) = \left(\frac{\omega_{\max}}{2}\right)\cos\left(\frac{2\pi}{365}t\right) + \left(\frac{\omega_{\max}}{2}\right), \quad (2)$$

where $T_{\max}$ is the average of maximum temperatures, $T_{\min}$ is the average of minimum temperatures, T_{med} is the average of the year's average temperatures, and $\omega_{\max}$ is the annual maximum daily precipitation in millimeters.

Therefore, we have parameters dependent on temperature and rainfall:

$$\begin{aligned}
&\delta(T) = -15.837 + 1.2897\,T - 0.0163\,T^2,\\
&b(T) = 0.056\,\delta(T),\\
&\beta_M(T) = 0.033\,T - 0.41,\\
&\beta_H(T) = 0.023\,T + 0.122,\\
&\mu_M(T) = 0.8962 - 0.159\,T + 1.116\times10^{-2}\,T^2 - 3.408\times10^{-4}\,T^3 + 3.809\times10^{-6}\,T^4,\\
&\mu_A(T) = \frac{2.13 - 0.3797\,T + 2.457\times10^{-2}\,T^2 - 6.778\times10^{-4}\,T^3 + 6.794\times10^{-6}\,T^4}{7},\\
&\alpha(T) = (0.131 - 5.723\times10^{-2}\,T + 1.164\times10^{-2}\,T^2 - 1.341\times10^{-3}\,T^3 + 8.723\times10^{-5}\,T^4\\
&-3.017\times10^{-6}\,T^5 + 5.153\times10^{-8}\,T^6 + 3.42\times10^{-10}\,T^7)/7,\\
&C(\omega) = C_{\max}\left(\frac{\omega}{\omega_{\max}}\right),
\end{aligned} \quad (3)$$

in which, T is the temperature in degrees Celsius, $C_{\max}$ is the maximum carrying capacity of the aquatic phase (fixed in the classical model simulation and estimated in the fractional model), ω is the precipitation and $\omega_{\max}$ is the maximum precipitation in millimeters.

We set the parameters $\mu_H = 3.46417\times10^{-5}$, birth rate and death rate per capita, $\sigma = 1/7$, human recovery rate, $k = 0.8$, ratio of male to female mosquitoes [6, 7, 11].

4 Numerical Simulations and Estimation of Fractional Model Parameters

To analyze the accuracy of each simulation, we use the Intraclass Correlation Coefficient (ICC). In this work, the ICC was calculated using a function implemented in MatLab and available at [14] for free download. The categorization of ICC values is based on guidelines presented by Cicchetti [4] is as follows: "Not acceptable" designates ICC values below 0.7; "Weak" corresponds to ICC values ranging from 0.7 to 0.79; "Good" encompasses ICC values between 0.8 and 0.89; and "Excellent" denotes ICC values falling within the range of 0.90 to 1. This classification serves as a reference for interpreting the reliability of the simulations, where higher ICC values indicate a more accurate and reliable performance.

In Figure 1 we can see the comparison of the simulated curve with real data from Dengue cases available in [16]. In this simulation, we set $C_{\max} = 1 \times 10^3$ and $\mu'_M = 0.03$. The ICC obtained by this simulation was 0.6718, considered not acceptable. We can also observe that there is an acceleration in the simulated case curve, in addition to a slightly higher peak than compared to the real data.

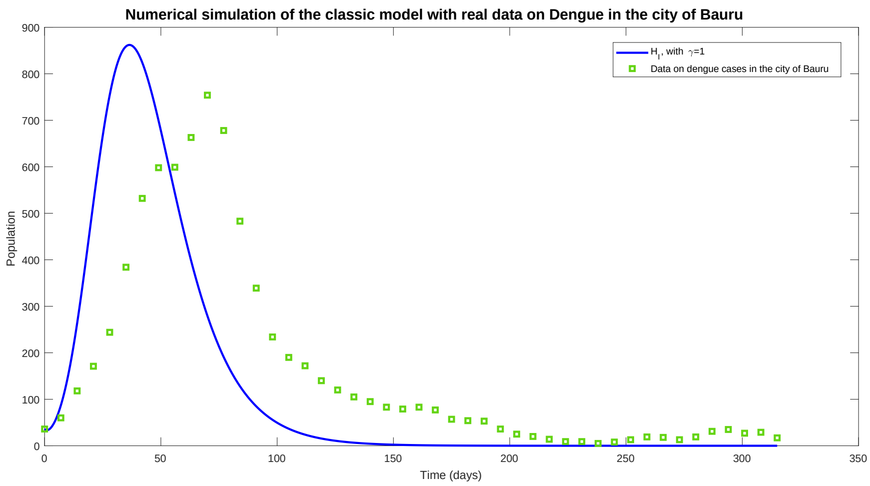

Figure 1: Numerical simulation of the classical model, i.e., $\gamma = 1$ and considering $C_{\max} = 1 \times 10^3$ $\mu'_M = 0.03$. Source: By the authors.

In the fractional model (1), our primary outcome is centered around the estimation of important parameters. Specifically, we have determined the non-integer order of the derivative, denoted as γ, to be 0.9760. Additionally, the parameter τ, which governs the redimensionalization of FDE, was estimated at 6.185×10^{-9}. The maximum support capacity of the aquatic environment, denoted as $C_{\max}$, was established as 1.371×10^3, and the parameter μ'_M, signifying additional mortality in infected and susceptible mosquitoes, was estimated to be 0.0397. It is noteworthy that the ICC value obtained in this estimation process is 0.9731, a classification deemed excellent in accordance with the criteria outlined by Cicchetti (1994) [4]. The Figure 2 hows the estimated curve of the fractional model.

In Figure 2 we can see that the peak of the estimated curve does not coincide with the peak of the real case data, this is because when observing the temperature and rainfall data for the year 2022 it is noted that 14 days before the dengue peak there were temperatures above 30°C [1] in an unexpected period (between the months of April and May) which contributed to an increase in cases not predicted by the estimations made.

5 Sensitivity Analysis

The parameters in the proposed model are biologically interpretable but are also subject to notable uncertainties, allowing for a diverse set of values. Consequently, a thorough investigation of these uncertainties via Sensitivity Analysis (SA) techniques is necessary to discern how these input parameters may influence the model's responses. Specifically, the focus is on understanding

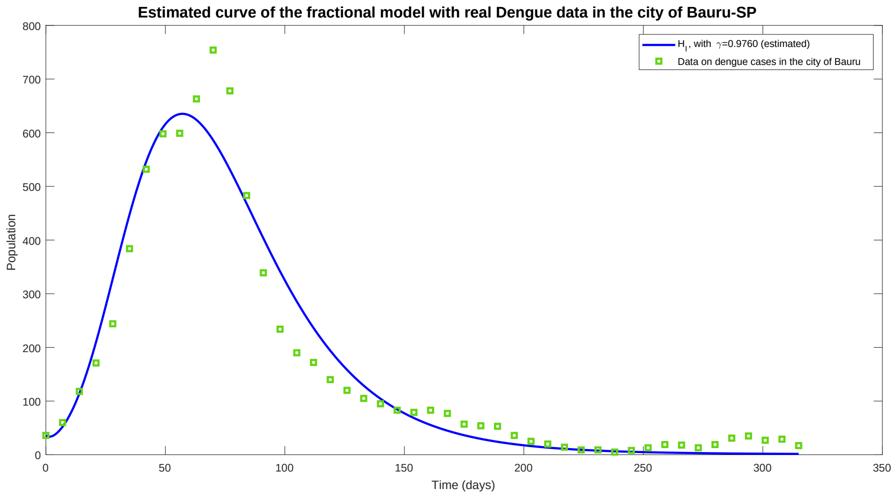

Figure 2: Estimated curve of the fractional model, with $\gamma = 0.9760$, $C_{\max} = 1.371 \times 10^3$ $\mu'_M = 0.0397$. Source: By the authors.

how the parameters related to the basic reproductive number, $\mathcal{R}_0$, which measures disease spread, can contribute to either the propagation or elimination of the disease. The $\mathcal{R}_0$ equation associated to model (1) is given by

$$\mathcal{R}_0 = \sqrt{\left(\frac{b^2\beta_M\beta_H\alpha C}{H(\mu_M+\mu'_M)^2(\mu_H+\sigma)}\right)\left(1-\frac{1}{Q_0}\right)}, \text{ where } Q_0 = \frac{k\delta\alpha}{(\mu_M+\mu'_M)(\alpha+\mu_A)}. \quad (4)$$

We conducted a SA considering the terms $b\beta_M$, $b\beta_H$, $\mu_M+\mu'_M$, μ_A, α, C, σ, and Q_0 to assess their impact on the $\mathcal{R}_0$ function. We employed the Latin Hypercube Sampling (LHS) technique for parameter sampling, which involves subdividing the intervals of each input variable into N equally spaced subintervals and belongs to the class of Monte Carlo sampling methods [9]. For parameter sampling, we utilized $N = 5000$ sets of sampled parameters $X_i = (b\beta_M, b\beta_H, \mu_M + \mu'_M, \mu_A, \alpha, C, \sigma, Q_0)$, evaluating the resulting $Y_i = \mathcal{R}_0$. The PRCC [9], covering all sampled values, were employed to provide a comprehensive assessment of the overall impact of the parameters. The results of both analyses are depicted in Figure 3.

Figure 3 displays the results of the SA, where the findings reveal that the daily production of humans infected by a mosquito, daily production of mosquitoes infected by a human, and aquatic phase maturation rate play significant roles in increasing disease spread, leading to an increase in $\mathcal{R}_0$ and these findings are biologically coherent. On the other hand, both vector population mortality and additional mortality contribute to the reduction in disease spread. Remarkably, it is observed that mortality in the aquatic phase, carrying capacity of mosquitoes in the aquatic phase, and human recovery rate exhibit a weak correlation with the model outcome. This observation suggests that these factors have a relatively small or insignificant contribution to the variation in $\mathcal{R}_0$.

6 Conclusions

Fractional modeling emerges as an essential tool in the generalization of integer models, offering not only an extension of them, but also the ability to make more accurate predictions in certain

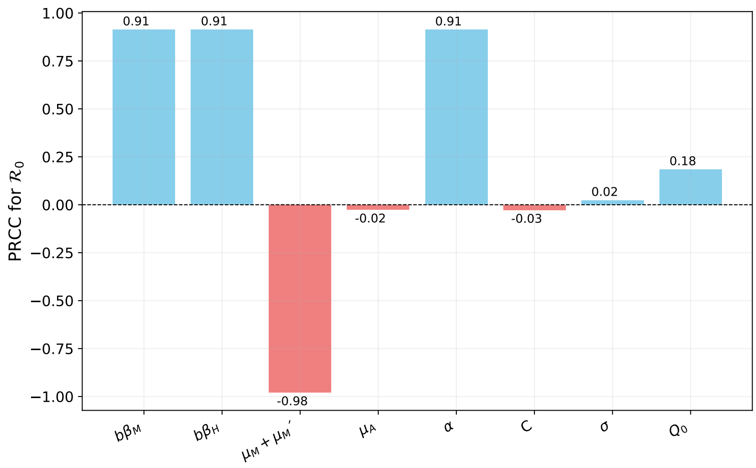

Figure 3: PRCC sensitivity analysis in the $\mathcal{R}_0$. Source: By the authors.

contexts, overcoming the limits of the classical model [3].

In this study, through numerical simulations and parameter estimation, we observed that the fractional model (1) demonstrated superior accuracy compared to the classical model when analyzing data on Dengue cases in the city of Bauru in 2022 [16]. Accuracy was assessed by the ICC, in which values closer to 1.0 indicate better adherence to the observed data. The results revealed an ICC of 0.9731 for the non-integer order model, contrasting with the ICC of 0.6718 for the classical model, suggesting greater accuracy in the fractional version.

The sensitivity analysis of the parameters related to $\mathcal{R}_0$ showed that the factors that significantly contribute to the increase in this basic reproduction number are $b\,\beta_H$, $b\,\beta_M$ and α, which represent, respectively, the number of infected humans produced by a single infected mosquito, the number of infected mosquitoes generated by a single infected human, and the maturation rate of the aquatic phase. On the other hand, the parameters $\mu_M + \mu_M'$, which represent the natural mortality of mosquitoes throughout the year plus additional vector mortality (control), play a crucial role in reducing $\mathcal{R}_0$.

Therefore, we concluded that, according to the proposed model (1), the most effective control of the disease would be vector-directed. This conclusion highlights the importance of control strategies aimed at the mosquito population as a fundamental approach in combating the spread of Dengue.

Acknowledgment

This study was financed by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES) (MMT 88887.809595/2023-00 and GR 88887.826921/2023-00)

References

[1] **Agritempo: Sistema de monitoramento agrometeorológico (2002–2024)**. Avalible at `https://www.agritempo.gov.br/agritempo/index.jsp`. Acessed: 10 oct. 2023.

[2] R. F. Camargo, R. Charnet, and E. C. Oliveira. "On some fractional Green's functions". In: **Journal of Mathematical Physics** 50.4 (2009), p. 043514.

[3] L. C. Cardoso, F. L. P. Dos Santos, and R. F. Camargo. "Analysis of fractional-order models for hepatitis B". In: **Computational and Applied Mathematics** 37.4 (2018), pp. 4570–4586.

[4] D. V. Cicchetti. "Guidelines, criteria, and rules of thumb for evaluating normed and standardized assessment instruments in psychology." In: **Psychological assessment** 6.4 (1994), p. 284.

[5] M. M. Costa. "Investigação dos efeitos da sazonalidade e da mobilidade humana na dinâmica de transmissão da dengue em *patches*". PhD thesis. 2022.

[6] G. Cruz-Pacheco, L. Esteva, and C. P. Ferreira. "A mathematical analysis of zika virus epidemic in Rio de Janeiro as a vector-borne and sexually transmitted disease". In: **Journal of Biological Systems** 27.01 (2019), pp. 83–105.

[7] L. Esteva and H. M. Yang. "Assessing the effects of temperature and dengue virus load on dengue transmission". In: **Journal of Biological Systems** 23.04 (2015), p. 1550027.

[8] J. H. Huber, M. L. Childs, J. M. Caldwell, and E. A. Mordecai. "Seasonal temperature variation influences climate suitability for dengue, chikungunya, and Zika transmission". In: **PLoS neglected tropical diseases** 12.5 (2018), e0006451.

[9] S. Marino, I. B. Hogue, C. J. Ray, and D. E. Kirschner. "A methodology for performing global uncertainty and sensitivity analysis in systems biology". In: **Journal of theoretical biology** 254.1 (2008), pp. 178–196. DOI: 10.1016/j.jtbi.2008.04.011.

[10] M. Martcheva. **An introduction to mathematical epidemiology**. Vol. 61. Springer, 2015.

[11] H. Nishiura et al. "Mathematical and statistical analyses of the spread of Dengue." In: (2006).

[12] R. Pakhira, U. Ghosh, and S. Sarkar. "Study of memory effects in an inventory model using fractional calculus". In: **Applied Mathematical Sciences** 12.17 (2018), pp. 797–824.

[13] P. Rohani and M. Keeling. **Modeling Infectious Diseases in Humans and Animals**. Princeton, New Jersey: Princeton University Press, 2008.

[14] A. Salarian. **Intraclass Correlation Coefficient (ICC)**. https://www.mathworks.com/matlabcentral/fileexchange/22099-intraclass-correlation-coefficient-icc. 2022.

[15] M. M. Theodoro. "Modelagem Fracionária da dinâmica da COVID-19". In: (2022).

[16] Centro de Vigilância Epidemiológica "Prof. Alexandre Vranjac". **Dados estatísticos em Dengue - Distribuição dos casos notificados e confirmados**. Available at https://www.saude.sp.gov.br/cve-centro-de-vigilancia-epidemiologica-prof.-alexandre-vranjac/areas-de-vigilancia/doencas-de-transmissao-por-vetores-e-zoonoses/arboviroses-urbanas/dengue/dados-estatisticos. Acessed: 11 dec. 2023. 2023.

