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Mathematical modeling of dengue transmission dynamics in *Wolbachia*-infected mosquitoes

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2026

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**Mathematical modeling of dengue
transmission dynamics in
Wolbachia-infected mosquitoes**

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Resumo

A dengue, doença causada pelo vírus da dengue (DENV), é endêmica nas Américas e constitui a arbovirose de maior prevalência mundial, apresentando índices crescentes de morbidade e mortalidade. Trata-se de uma doença sistêmica, sazonal, infecciosa, de caráter agudo e febril, transmitida à população humana pela picada de fêmeas do mosquito *Aedes aegypti* ou *Aedes albopictus* infectadas pelo DENV. A ineficiência dos métodos usuais de controle, químicos e mecânicos, a expansão do mosquito para novas áreas e o impacto dessa arbovirose sobre o sistema de saúde tornam urgente a busca por novas estratégias de controle. Nesse contexto, a liberação de mosquitos infectados com *Wolbachia*, uma bactéria intracelular capaz de inibir a replicação do vírus no organismo do vetor, tem sido utilizada em larga escala. Adicionalmente, a vacinação da população — atualmente em curso — pode atuar como uma peça-chave na redução e eventual supressão dos casos de infecção por dengue. Neste trabalho, propõe-se um modelo de equações diferenciais ordinárias para descrever a interação entre as populações de vetores infectados e não infectados por *Wolbachia*, a população humana e o vírus da dengue. Considera-se ainda a vacinação da população humana. Os resultados mostram como o efeito combinado da vacinação e da redução da capacidade vetorial altera a prevalência da doença, destacando regiões no espaço de parâmetros nas quais uma ou ambas as medidas de controle podem alcançar reduções substanciais ou até a eliminação completa da transmissão da dengue.

Palavras-chave: controle biológico; vacinação; equações diferenciais ordinárias; limiares.

Abstract

Dengue, a disease caused by the dengue virus (DENV), is endemic in the Americas and constitutes the most prevalent arboviral disease worldwide, with increasing rates of morbidity and mortality. It is a systemic, seasonal, acute febrile infectious disease transmitted to the human population through the bite of female *Aedes aegypti* or *Aedes albopictus* mosquitoes infected with DENV. The inefficiency of conventional chemical and mechanical control methods, the expansion of the mosquito into new areas, and the impact of this arboviral disease on public health systems make the search for new control strategies urgent. In this context, the release of *Wolbachia*-infected mosquitoes—harboring an intracellular bacterium capable of inhibiting viral replication within the vector—has been implemented on a large scale. Additionally, vaccination of the population, which is currently underway, may play a key role in reducing and potentially suppressing dengue cases. In this work, we propose a system of ordinary differential equations to describe the interaction between *Wolbachia*-infected and uninfected vector populations, the human population, and the dengue virus. Vaccination of the human population is also incorporated into the model. The results illustrate how the combined effects of vaccination and reduced vectorial capacity modify disease prevalence, highlighting regions of parameter space in which one or both control measures can achieve substantial reductions or even complete elimination of dengue transmission.

Key-words: biological control; vaccination; ordinary differential equations; thresholds.

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1 Introduction

Dengue is currently the most prevalent arboviral disease worldwide, being reported in more than 100 tropical and subtropical countries. The dengue virus (DENV) is an arbovirus belonging to the *Flaviviridae* family and the *Flavivirus* genus, and it comprises four distinct serotypes (DENV-1, DENV-2, DENV-3, and DENV-4), with DENV-2 being the most prevalent serotype in Brazil (MENEZES et al., 2021). Transmission occurs through the bite of the mosquito *Aedes aegypti* Linnaeus, 1762 (Diptera: Culicidae), which is considered the primary vector of the disease in Brazil. It is known that *A. aegypti* prefers tropical, warm, and humid environments, which also characterizes dengue as a seasonal disease. These mosquitoes typically breed in stagnant water habitats (BIASSOTI; ORTIZ, 2017).

In 2023, a total of 1.408.684 dengue cases were confirmed in Brazil, of which 1.179 were fatal. In 2024, dengue virus infection in Brazil reached a historical record, with 5.973.343 reported cases nationwide - an increase of 324.04% compared to 2023 - and 6.321 deaths attributed to the disease. In 2025, 1.469.018 dengue cases had been confirmed in Brazil, representing a 75.41% decrease relative to the previous year, with 1.776 deaths caused by the virus. In the same year, 877.795 dengue cases were confirmed in the State of São Paulo, including 1.480 cases in the city of Botucatu (Governo Federal, 2025).

Currently, the main methods for controlling the disease include public education and prophylaxis (reducing sites with standing water, where the vector lays its eggs), mosquito population control (with insecticides and larvicides), and medical intervention after infection (mainly hydration and symptomatic relief). During outbreaks, the most direct and effective approach to ensure vector population control is the use of insecticides; however, this is not a sustainable method, since *A. aegypti* has developed resistance to insecticides, and their continuous use can cause severe environmental damage (BALDACCHINO et al., 2015). Thus, the search for alternative control strategies, such as biological control, has become increasingly urgent.

Wolbachia is an intracellular symbiotic bacterium found in more than half of all insect species worldwide, and its application in biological control has attracted considerable attention in recent years. It has been demonstrated that the use of *Wolbachia* can inhibit dengue virus replication in *A. aegypti* (HOFFMANN et al., 2011; WALKER et al., 2011). Different *Wolbachia* strains, such as *wMel*, *wAlbA*, *wAlbB*, *wAu*, and *wMelPop*, produce distinct effects on the mosquito, including a reduction in the vector's lifespan, preventing the dengue virus from becoming

infectious within its lifetime (WALKER et al., 2011), or the deformation of the proboscis (mouth-part structure), rendering the vector ineffective (ITURBE-ORMAETXE; WALKER; O'NEILL, 2011). Another well-documented effect is the reduction of dengue virus particles present in the mosquito's saliva (TURLEY et al., 2009). One of the most significant effects induced by *Wolbachia* is the phenomenon known as Cytoplasmic Incompatibility (CI), which occurs between the gametes of infected males and the eggs of uninfected females, leading to embryo death. In contrast, females infected with *Wolbachia* produce viable infected offspring when mating with either infected or uninfected males through maternal transmission, resulting in a reproductive advantage over uninfected females (WALKER et al., 2011). These factors demonstrate that the use of this bacterium is indeed effective as a biological control strategy.

In Brazil, the *Wolbachia* Method, patented by the World Mosquito Program (WMP), is implemented by the Oswaldo Cruz Foundation (Fiocruz) with funding from the Brazilian Ministry of Health. The project aims to promote the release of *Aedes aegypti* mosquitoes infected with *Wolbachia* as a strategy for vector control and for the suppression or interruption of the transmission of arboviruses such as Dengue, Zika, and Chikungunya. The first field trials began in 2014 in the State of Rio de Janeiro, in Tubiacanga, a neighborhood located on Ilha do Governador Island. In Niterói, Rio de Janeiro, the release of *Wolbachia*-infected mosquitoes started as a pilot project in the Jurujuba neighborhood in 2015. In 2017, the program was expanded for the first time within the municipality, and by 2021 the method already covered 75% of the city. Currently, Niterói is the first city in Brazil to be protected by the method; the 158 confirmed dengue cases reported in the year of project implementation decreased to 67 in 2023, representing a reduction of approximately 64%. Data demonstrating the effectiveness of the protection provided by the *Wolbachia* Method were released by WMP Brazil. In addition to the decrease in dengue cases, these data also indicate a 60% reduction in Chikungunya and a 40% reduction in Zika in the areas where the entomological intervention was carried out. The *Wolbachia* Method is also being applied in Belo Horizonte, state of Minas Gerais. Its implementation in the state capital took place in stages. The first stage, in the Venda Nova region, was completed in January 2021. In 2022, a new expansion phase began, and the releases were concluded in 2023. Currently, a randomized controlled clinical trial, of great epidemiological importance, is underway to assess the method's efficacy and its impact in terms of population protection. Belo Horizonte is also home to the *Wolbachia* Biofactory, responsible for maintaining the complete life cycle of *A. aegypti* mosquitoes infected with *Wolbachia* (Wolbitos), from egg production to adult mosquitoes, as well as the distribution of these biological materials and administrative coordination. The facility is expected to reach a weekly production capacity of approximately two million mosquitoes (Fundação Oswaldo Cruz, 2024).

In the municipality of Joinville, in the State of Santa Catarina, the program began in December 2023. In 2024, the community engagement phase was initiated, consisting of outreach activities to promote the *Wolbachia* Method. These actions involved public and state schools, including teacher training, as well as the participation of teams engaged in the process. This

was the final phase before the release of mosquitoes, which started in August 2024. For the first release phase, 20 weeks of mosquito releases and 70 routes were planned, meaning that the releases continued until January 2025 (DIVESC, 2024). For the second release phase, technical teams established 3.844 release points distributed across 84 routes. The strategy provides for 26 weeks of field releases through early 2026. The selection of neighborhoods considered criteria such as the number of breeding sites and confirmed cases. The selected neighborhoods comprise approximately 75% of Joinville's population (Prefeitura de Joinville, 2024). In Joinville, at the beginning of 2025, a 98% reduction in dengue infection cases was observed compared to the previous year. According to the Joinville Department of Health, 58.322 cases and 66 deaths from the disease were recorded in the first four months of 2024. During the same period in 2025, 622 cases and no deaths were confirmed (G1 Santa Catarina, 2025).

Other Brazilian cities where the technology is being applied include Campo Grande (MS) and Petrolina (PE). Community engagement activities are also planned to be carried out in Uberlândia (MG), Presidente Prudente (SP), and Natal (RN) (FIOTEC, 2024).

Developed by the Butantan Institute in Brazil, the tetravalent dengue vaccine Butantan-DV has been formally approved by the National Health Surveillance Agency (Anvisa), on 26 November 2025, for use in the Brazilian population aged 12 to 59 years and represents the first single-dose dengue vaccine in the world protecting against all four dengue virus serotypes. Clinical trials conducted with over 16 000 volunteers demonstrated an overall efficacy of approximately 74% against symptomatic dengue, more than 91% effectiveness against severe disease, and 100% protection against hospitalization due to dengue, with robust safety profiles in both previously exposed and previously unexposed individuals (Instituto Butantan, 2026). Following the regulatory approval, a first batch of doses has already been manufactured and delivered for early deployment through the Brazilian Unified Health System (SUS). The national vaccination strategy launched in January 2026 includes a pilot mass vaccination campaign in Botucatu (São Paulo), where the immunization program targets eligible residents aged 15 to 59 years in order to evaluate the real-world impact of vaccination on dengue transmission and disease burden (Ministério da Saúde, 2026). The federal Ministry of Health and Instituto Butantan plan to scale production and distribution throughout 2026 and beyond, in coordination with the National Immunization Program (PNI), with the aim of progressively expanding coverage and integrating Butantan-DV into routine public health vaccination schedules (Presidência da República – Casa Civil, 2025; Agência Brasil, 2025).

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