



## Article/Artigo

# Dynamic behavior of sylvatic yellow fever in Brazil (1954-2008)

Comportamento dinâmico da febre amarela silvestre no Brasil (1954-2008)

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### ABSTRACT

**Introduction:** Sylvatic yellow fever (SYF) is enzootic in Brazil, causing periodic outbreaks in humans living near forest borders or in rural areas. In this study, the cycling patterns of this arbovirose were analyzed. **Methods:** Spectral Fourier analysis was used to capture the periodicity patterns of SYF in time series. **Results:** SYF outbreaks have not increased in frequency, only in the number of cases. There are two dominant cycles in SYF outbreaks, a seven year cycle for the central-western region and a 14 year cycle for the northern region. Most of the variance was concentrated in the central-western region and dominated the entire endemic region. **Conclusions:** The seven year cycle is predominant in the endemic region of the disease due the greater contribution of variance in the central-western region; however, it was possible identify a 14 cycle that governs SYF outbreaks in the northern region. No periodicities were identified for the remaining geographical regions.

**Keywords:** Sylvatic yellow fever. Periodicity. Spectral analysis. Epidemiology.

### RESUMO

**Introdução:** A febre amarela silvestre (FAS) é enzoótica no Brasil, causando surtos periódicos em humanos que vivem próximos às áreas florestais ou em áreas rurais. Neste estudo, foram analisados os padrões de periodicidade desta arbovirose. **Métodos:** Utilizamos a análise espectral de *Fourier* para capturar os padrões de periodicidades da FAS em séries temporais. **Resultados:** Os surtos de FAS aparentemente não aumentaram em frequência, mas em número de casos. Há dois ciclos dominantes na FAS, um de sete anos predominando na região centro-oeste, e um de 14 anos predominando na região norte. A maior parte da variância concentrou-se na região centro-oeste e dominava toda região endêmica. **Conclusões:** O ciclo de sete anos é predominante para a região endêmica da doença devido a maior contribuição da variância do centro-oeste. No entanto, foi possível identificar um ciclo de 14 que rege a FAS na região norte. Não foram detectadas periodicidades nas demais regiões geográficas.

**Palavras-chaves:** Febre amarela silvestre. Periodicidade. Análise espectral. Epidemiologia.VV

### INTRODUCTION

Urban yellow fever has been eradicated in Brazil since 1942<sup>1</sup>; however, the zoonotic form of this arbovirose, sylvatic yellow fever (SYF), remains active in the forest regions and their borders, causing sporadic human cases and small outbreaks. The resurgence of the mosquito *Aedes aegypti* (*Ae. aegypti*) in Brazilian urban areas about 40 years ago<sup>2</sup> brought back dengue fever virus to Brazil<sup>3</sup> and has been an important matter of concern regarding the possibility of the re-urbanization of yellow fever in the country<sup>1,4</sup>. Historically, this mosquito has been the urban vector of YF virus in Brazil.

In the Brazilian rain forest, the yellow fever virus is maintained by the sylvatic mosquito vectors *Haemagogus* sp. and *Sabethes* sp., in a enzootic cycle involving primates<sup>1</sup>. Sporadic human cases of SYF have been reported since 1954, with a total of 964 cases between 1954 and 2008<sup>5,6</sup> and a mortality rate around 50%. The endemic region for SYF is composed by the northern and central-western regions and the State of Maranhão, in the northeastern region<sup>7</sup>, which forms about 68% of the Brazilian territory. Some states from the southeastern, northeastern (State of Bahia) and southern regions have reported sporadic cases imported from the endemic region.

In this paper, the periodic behavior of SYF in Brazil from 1954 to 2008 was analyzed.

### METHODS

#### Areas studied

Brazil is divided in 5 geographical regions: south, southeast, central-west, north and northeast. The southeastern region is the most populated (demographic density about 78 inhabitants/km<sup>2</sup>) and the northern region is the least populated (about 3 inhabitants/km<sup>2</sup>). The endemic area for SYF in Brazil comprises the northern and central-western regions and part of the State of Maranhão (northeastern region), corresponding to about 68% of Brazilian territory. A part of the State of Maranhão has ecological landscapes similar to the northern region.

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## Data

Sylvatic yellow fever annual case data was obtained from the National Health Foundation (*Fundação Nacional de Saúde*)<sup>5</sup> and the Secretariat of Health Surveillance of the Brazilian Ministry of Health (*Secretaria de Vigilância em Saúde, Ministério da Saúde do Brasil*)<sup>6</sup>.

### Spectral Fourier analysis

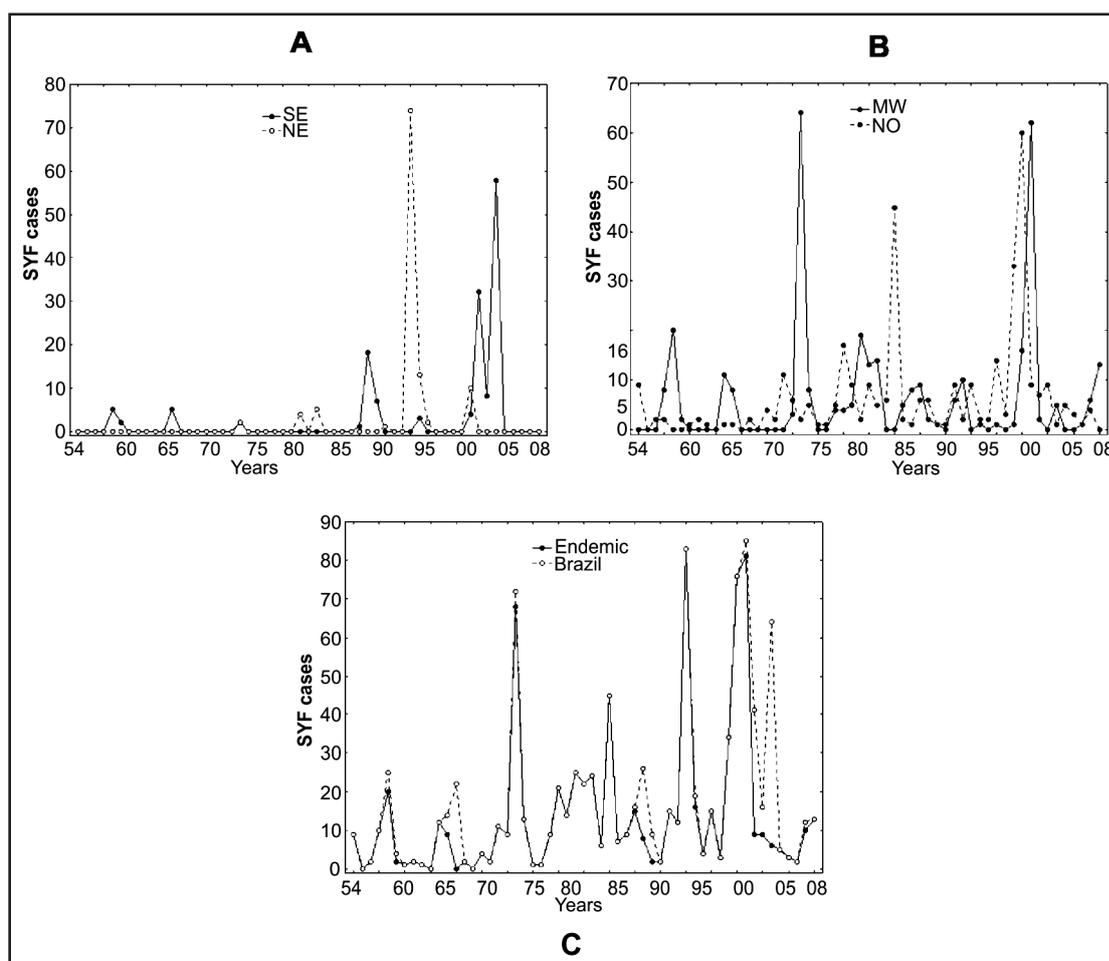
Normal data series and log transformed data series were analyzed using the Statistica 7.0 software package. Spectral analysis was performed after data was subtracted from the mean and detrended before analysis. Spectral analysis was performed by smoothing the series using the Hamming method (a weighted moving averages technique) to obtain the frequencies that significantly contribute to the cyclical behavior of the series. In order to improve the precision of analysis, window width was adjusted to sets of three data.

## RESULTS

**Figure 1** shows the time series for SYF cases from 1954 to 2008 for each geographical region of the country; the southern region was not represented because cases were rare and sporadic during

this period. Analysis of **Figure 1A** confirmed that the number of SYF cases increased significantly after 1980 in the southeastern region (State of Minas Gerais) and northeastern region (States of Maranhão and Bahia); however, the difference between number of outbreaks before and after 1980 for these regions was not statistically significant. Analysis of **Figure 1B** revealed that the central-western and northern regions concentrated significantly more outbreaks than the southeastern and northeastern regions (Chi square,  $p=0.015$ ). Analysis of **Figure 1C** presents comparisons between SYF cases in the endemic region and in the entire country. Analysis confirmed that outbreaks in both areas are connected; however, an outbreak occurred in the southeastern region in 2003 that was apparently not connected to endemic cases.

**Figure 2**, on the left, shows the spectral densities for the central-western and northern regions. In **Figure 2**, on the right, the central-western region showed a dominant cycle of approximately 7 years, while the northern region displayed a dominant cycle of approximately 14 years, followed by a minor cycle of 3 years. The southwest and northeast showed no cyclic behavior, because outbreaks in these areas are sporadically and probably imported from the endemic region.



**FIGURE 1 - (A) and (B)** show the number of SYF cases in the southeastern/ northeastern regions and in the central-western/ northern regions, respectively. **(C)** Number of SYF cases in the endemic region and in Brazil as a whole (all registered cases). Legends are shown in the figures.

SYF: sylvatic yellow fever, SE: south eastern, NE: north eastern, MN: midwest region, NO: northern.

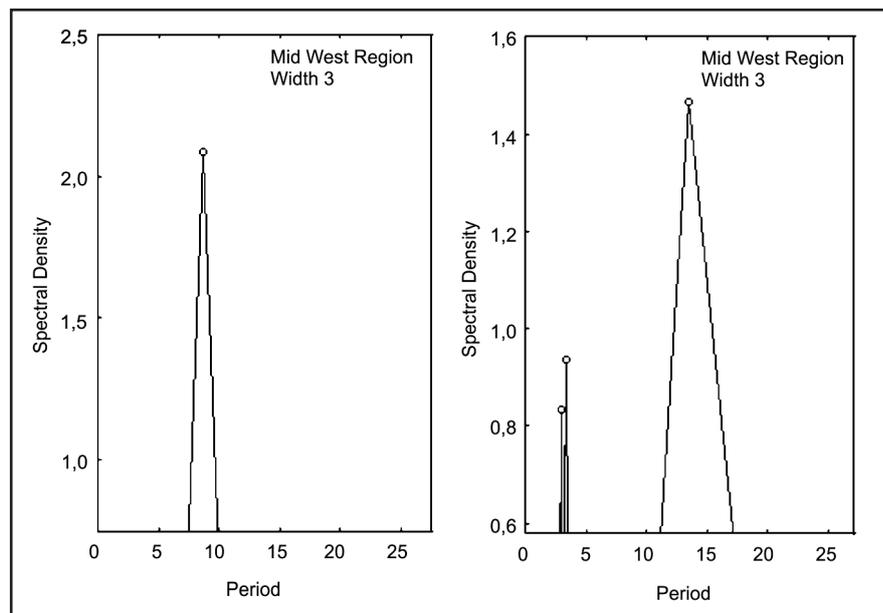


FIGURE 2 - A dominant cycle of 7 years occurs in the central-western region (left), and a dominant cycle of 14 years occurs in the northern region (right). Minor cycles of approximately 3 years were verified in both regions and a minor cycle of 7 years was also verified in the northern region. Legends are shown in the figures.

## DISCUSSION

Although the number of cases of SYF increased after 1980, the frequency of outbreaks had not changed significantly in the southeastern and northeastern regions. However, the frequency of outbreaks inside the endemic region remains high. The increase in magnitude of outbreaks in the southeastern (State of Minas Gerais) and northeastern (State of Bahia) regions may reflect an increase in human traffic between these places and the endemic region. This suggests active pressures for the expansion of yellow fever outside of the endemic region, where most of the urban communities of the country lives. Although *Ae. aegypti* and *Ae. albopictus* are present in these places, no sustained transmission of yellow fever was detected in these areas.

The dynamic of SYF in the central-western region is characterized by a stable dominant cycle of seven years. The northern region showed a dominant cycle of approximately 14 years, twice the length of the central-western dominant cycle, and a minor cycle of 3 years (Figure 2).

Several researchers have empirically suggested a cycle of seven years for SYF; however, this has not previously been confirmed, and the 14 years cycle has never been mentioned. The spectral analysis of time series confirmed a major cycle of seven years for the central-western region, while also revealing a dominant cycle of 14 years for the northern region. This suggests different epidemiological cycles for both regions; however, when analyzing the entire endemic region, the cycle of seven years stands out as dominant. This suggests that the majority of cases of yellow fever outbreaks spread from the central-west.

In conclusion, the seven years cycle is prevalent for the endemic region due to the greater contribution of variance in the central-western region; however, it was possible identify a 14 year cycle governing sylvatic yellow fever outbreaks in the northern region. This suggests two ecological peculiarities under the epidemiological mechanism of sylvatic yellow fever.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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