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Statistical Modeling of the Effect of Meteorological Variables on Dengue Transmission

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Abstract

This study investigates the effects of climate variables and previous cases of dengue on current cases of dengue. The meteorological variables, average, maximum and minimum temperature, relative humidity, total precipitation, and previous cases are identified with a time interval as input parameters for artificial neural network (ANN) RNA. Specific parameters and time intervals are defined by a correlation analysis between each variable with the current dengue cases. In short, the ANN is developed as a result of this research in order to predict dengue outbreaks in the municipality of Campo Grande, with a promisng accuracy rate.
Keywords: Dengue; Time series; Neural networks.

1. Introduction

Dengue is a public health problem and considered as one of the most important arbovirus that affects humans. It is caused by the vector Aedes Aegyp, whose proliferation is related to climate variables, with the summer being the period of the greatest transmission. The endemic regions for this disease are the tropical and subtropical countries, where environmental conditions favor the life cycle of the vector.

Climatic variations affect the health-disease process directly, causing positive and negative impacts on the population's quality of life and health. The theme health and environment should be the object of study, aiming to understand the importance of understanding that the behavior of environmental factors directly interferes in this process, considering that health encompasses the environment as one of its determinants.

In this interface between health and environment, climate variables such as temperature, relative air humidity and rainfall should be studied and associated with the health issues, including dengue. As a reemerging infectious disease, it has been increasing its incidence of reported cases, indicating a concern for managers in public health.

Modeling dengue in endemic areas is important for mitigating and improving control of vector-borne diseases to reduce outbreaks.

Disease occurrence models can be based on linear and nonlinear approaches that simulate complex relationships between short- and long-term environmental variables (climate) and dengue incidence [1-3]. Linear models are often unable to simulate complex interactions between these factors, and the powers tend to be smaller [4]. Nonlinear approaches generally demonstrate greater power than linear models [5]. For example, Husin, *et al.* [6] predicted dengue in Malaysia using a nonlinear model to help the government fight the disease. A similar study in Singapore used genetic algorithms and support vector machines to predict the number of dengue cases [7]. Studies in Thailand, Singapore, and Malaysia have also used artificial neural network (RNA) models to predict dengue cases, reaching greater than 80% accuracy [8-10]. A similar study in Sri Lanka with RNA showed lower accuracy (ie 60%) [11]. RNAs considerad attractive because they usually reach a higher ability than other types of models [12].

Abdiel, *et al.* [13], applied artificial neural networks (ANNs) to predict occurrences of dengue outbreaks in San Juan, Puerto Rico (USA) and various coastal municipalities in the state of Yucatan, Mexico, based on specific boundaries. The models were trained with 19 years of dengue data in Puerto Rico and six years in Mexico. Environmental and demographic data included in the predictive models were sea surface temperature (SST), precipitation, air temperature (ie minimum, maximum and mean), humidity, previous dengue cases and population size. Two models were applied for each study area. One predicted dengue incidence rates based on population at risk (ie number of people under 24) and the other on the size of vulnerable population (ie number of people under five and over 65 years). Predictive power was above 70% for all four runs of the model. ANNs were able to successfully model the occurrence of dengue outbreaks in both areas. The variables with the most influential in predicting dengue outbreak occurrences in San Juan, Puerto Rico included population size, previous dengue cases, maximum air

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temperature, and date. In Yucatan, Mexico, the most important variables were population size, previous cases of dengue, minimum air temperature, and database.

Artificial neural networks use combinations of predictor variables (eg environmental factors) to simulate relationships with target variables (eg occurrences of dengue outbreaks). These models can be adapted to assimilate data, and this helps to improve the functional relationships between climate factors and dengue outbreaks. In our study, we applied Multilayer Perceptron (MLP) which is a popular neural network type to predict dengue outbreaks in Campo Grande. We identified important environmental factors in the conduct of dengue outbreaks. The candidate variables were air surface temperature, humidity, precipitation, previous cases of dengue. Previous cases of dengue are defined as those cases that occurred days / months / months before an outbreak [12]. Artificial neural networks are an alternative to traditional methods for solving time series prediction problems. This technique allows multiple variables in the input and output layers. Thus, it is possible to use distinct climate variables in modeling dengue case prediction, thereby increasing the effectiveness of the predictor model.

Prediction models using this technique have presented low error results in several types of application, including dengue prediction, as can be observed in Aburas, *et al.* [8]; Munyque and Daniel [14]. The main contribution of this work is developing an accurate prediction model for dengue cases using ANNs for Guarulhos municipality. The main goal is to model the approach to a study area with a higher incidence of the disease which hasa greater need to perform an accurate prediction.

1.1. Artificial Neural Networks (ANNs)

An ANN can be defined as a parallel distributed processor consisting of simple processing units (also known as artificial neurons), which have the ability to store experimental knowledge and make it available for prediction. Haykin [15]. One of the most important characteristics of ANNs is their ability to learn from previous examples. The learning stage consists of an iterative process of adjusting the synaptic weights, which at the end of the process store the knowledge that the network has acquired from the external environment [16].

1.2. Multilayer Perceptron Networks

Multilayer Perceptron Networks (MLP) belong to the neural architecture known as multilayer feedforward, being characterized by the presence of at least one intermediate (hidden) layer of neurons, situated between the input layer and the output layer [17].

Signals are presented to the network at its input layer. The intermediate layers extract most of the information regarding their behavior and encode it through the synaptic weights and thresholds of their neurons [17]. The processing performed by each neuron of a given input is defined by the combination of the processing performed by the anterior layer that are connected to it Braga, *et al.* [18]. The output layer receives the stimuli from the last intermediate layer , producing a response pattern that will be the output that made by the network.

The MLP network training process is usually performed with the backpropagation algorithm, which uses input and output pairs to adjust the network weights and thresholds through an error correction mechanism [18].

The use of the conventional backpropagation algorithm in practice tends to converge too slowly, thus requiring a high computational effort. Some of the alternatives to make the network convergence process more efficient are: the insertion of the momentum term; or the use of backpropagation variants such as the Levenberg-Marquardt algorithm and Bayesian Regularization [17].

Given the above, this study aimed to analyze the relationship of climate variables with dengue cases in Campo Grande, MS, from 2008 to 2018, using the **ANNs.**

2. Materials and Methods

2.1. Data Collection

Geographically, the municipality of Campo Grande is located near the Brazilian border with Paraguay and Bolivia. It is located at latitude 20º26'34 "south and longitude 54°38'47" west. Campo Grande's climate is classified as tropical with a dry season (Aw, according to the Köppen-Geiger climate classification), indicating the coldest months (June and July) with an average compensated temperature of 18.6°C. transition between the tropical monsoon (Am according to Köppen), the tropical dry season and the humid subtropical (Cfa according to Köppen). The thermal amplitude is relatively high due to the great influence of continentality, Campo Grande has quite variable temperatures during the year, with two very well defined seasons: hot and humid in summer and less rainy and mild in winter. In winter months, the temperature can drop considerably with sporadic and light frosts, sometimes the thermal sensation can reach below 0 ° C.

Data were collected from a secondary source, related to the series and number of dengue cases reported in the Notified Disease Information System (SINAN) (CID-10 codes A90-A91).

Monthly data on average, minimum and maximum temperature, relative humidity and precipitation were provided by the Mato Grosso do Sul State Water Resources Monitoring Center (CEMTEC-MS).

Before using the data, data normalization was performed. This process aims to scale the data samples to the dynamic range of hidden layer activation functions to avoid neuronal saturation [17].

Also a random subsampling cross-validation is used, in which 70% of the total dataset was randomly chosen for the training subset while the remaining data (30%) were part of the test and validation phase.

2.2. Ethical Considerations

The present study is based on publicly available secondary data, which do not constrain groups of populations and / or individuals in the presentation of the results found, ensuring the confidentiality of the information collected. Thus, the ethical aspects of research with human beings were respected, according to Resolution no. 466/2012 [19].

2.3. Model of Artificial Neural Networks

ANNs is a nonlinear model that have a structure capable of representing complex nonlinear processes that relate the inputs and outputs of any system, covering regression problems, prediction models, and other applications in different areas [20-22].

The advantage of the ANN technique is that it does not require priori knowledge of mathematical calculations between parameters and provide a better solution to different problems. The ANN adopted in this work is the Multilayer Perceptron. MLP is a massively parallel and distributed information processing system that has been successfully applied for many nonlinear and complex problems. The basic structure of MLP is an input layer, hidden layer with linked weights, and an output layer:

$$y_i = \sum_{j=1}^{\eta} w_{i,j} x_{i,j} + \theta_i$$

where $x_{i,j}$ is the input signal of the jth neuron (for the input layer), $w_{i,j}$ is the weight of the direct connection of neuron j to neuron i (in the hidden layer) and θ_i is the bias of neuron i . The output of neurons is calculated by applying an activation function. The activation function used is typically standard sigmoid.

$$f(x) = \frac{1}{[1+\exp(-x)]}$$

The network is powered with a set of input-output pairs and trained to reproduce the output. There are a variety of algorithms available for training ANN and adjusting their weights. In this study, MLP was trained using Bayesian Regularization Backpropagation and Levenberg – Marquardt Backpropagation training algorithms. The main task in developing an model is to identify the input variables and the optimal network structure to produce the desired output.

The number of neurons in the input layer of each model can be observed in (Table 2). Other assays were performed for the number of occult layer neurons. However, the trial and error procedure showed that there was no significant improvement in ANN performance. In Figure 1, the typical structure of a multilayer ANN model is presented.

All ANN models were trained and validated through the MATLAB Neural Networks toolbox.

The data were divided into two sections, the years from 2008 to 2012 were used to train the ANN, while the years from 2012 to 2018 were used for validation.

2.4. Statistical Validation Indexes

The accuracy and performance of ANN model were evaluated using various statistical indices. The statistical indicators used can be divided into two groups: dispersion indicators (error indicators) and general performance indicators [23]. The dispersion indices used in this study are: [Mean Bias Error (MBE), Root Mean Square Error (RMSE), and Mean Absolute Percentage Error (MAPE)]. The general performance indicators used were: Determination Coefficient (R^2) and Willmott Agreement Index (ICW) [24]. Another analysis is based on the linear regression coefficients (type: where we have the angular coefficient “a” and the linear coefficient “b”). All these indicators are used to verify the validity and applicability of the forecast values. The expressions of these indicators are given below:

$$MBE = \frac{1}{N}\sum (DE_e - DE_M)$$

$$RMSE = \left[\frac{1}{N}\sum \left|\frac{DE_E - DE_M}{DE_m}\right|\right]$$

$$MAPE = \left[\frac{100}{N}\sum \left|\frac{DE_E - DE_M}{DE_m}\right|\right]$$

$$R^2 = 1 - \frac{\sum\left(DE_E - \overline{\overline{DE_M}}\right)^2}{\sum\left(DE_M - \overline{\overline{DE_M}}\right)^2}$$

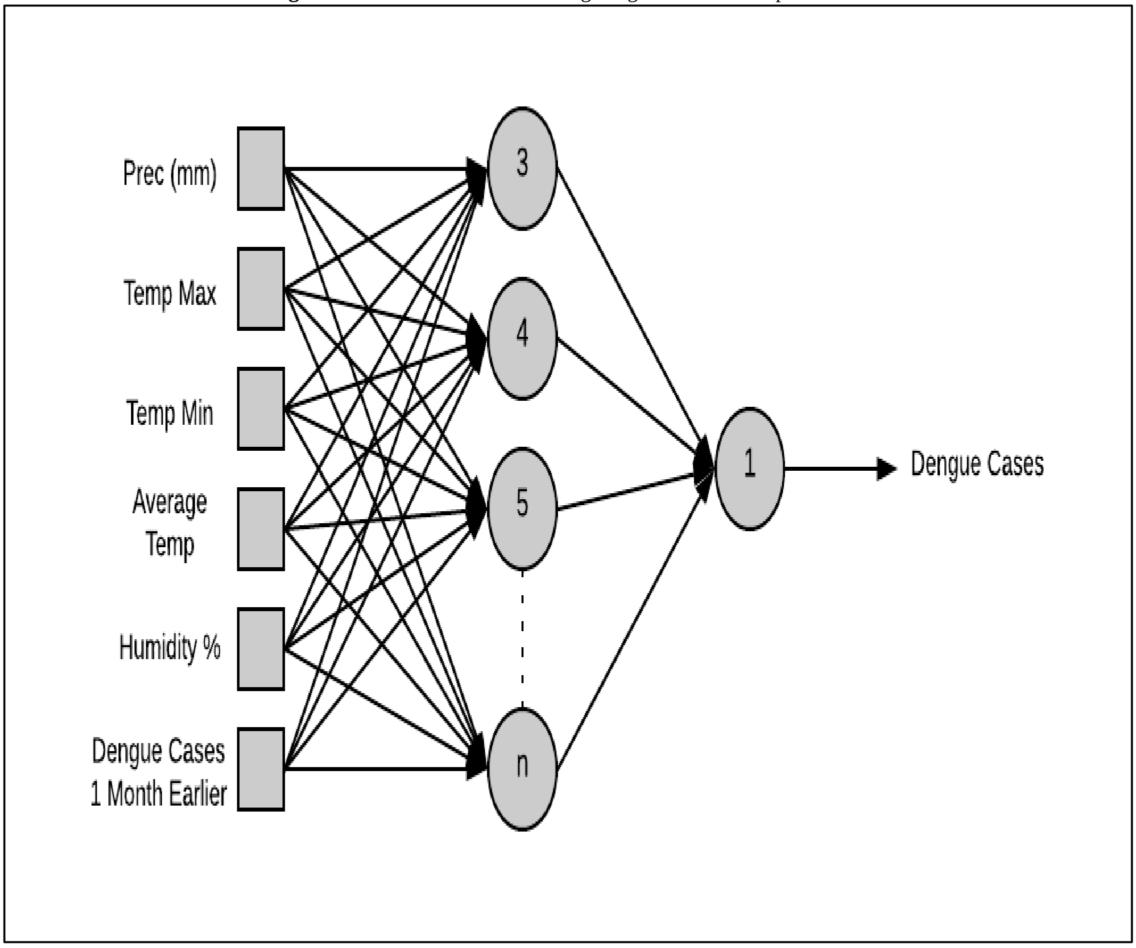
$$ICW = 1 - \frac{\left[\sum(DE_E - DE_M)^2\right]}{\sum\left[\left|DE_E - \overline{\overline{DE_M}}\right| + \left|DE_M - \overline{\overline{DE_M}}\right|\right]^2}$$

Where N is the total number of observations, DE_E, DE_M and $\overline{\overline{DE_M}}$ are the estimated, measured and average DE values, respectively. It should be mentioned that lower values of MBE, RMSE and MAPE show higher model accuracy in the estimation and the ideal cases are zero. The MBE provides a measure of the overall trend of a given model, ie overestimation (positive values) or underestimation (negative values). The values of R2 and ICW range from 0 to 1. For better modeling, R^2 and ICW should approach 1 as close as possible.

2.5. Proposed ANN

The ANNs constructed in this work have six inputs, an intermediate layer with n neurons and one neuron in the output layer. Figure 1 illustrates the MLP network model employed for the prediction of dengue.

Figure-1. MLP model for forecasting dengue cases in Campo Grande



In addition to the networks described, ANN with 15 variations of the input set were modeled. This is done because, some networks did not include data for all variables or added information regarding the number of dengue cases from previous months.

3. Results and Discussion

The investigation of the viability of a model based on artificial neural networks for epidemiological time series predictions. However, important criteria that define an structure such as the number of inputs, intermediate layers, and training parameters are important prerequisites for good model evaluation and fit.

The choice of architecture was a feedforward neural network because of its wide applicability in problems involving functional approximations such as time series.

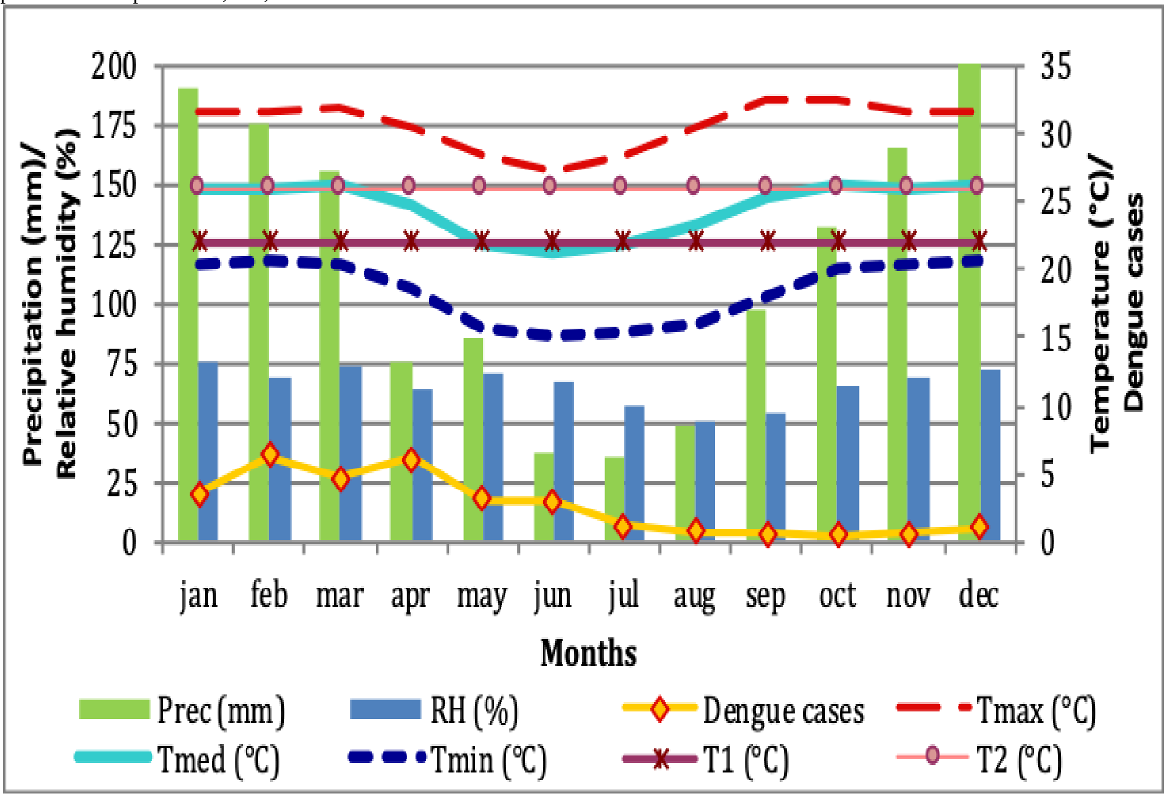
The greatest difficulty with ANN was to obtain the parameters that best behave with the data presented. The numbers of hidden neurons were between 3 and 15. The learning rates, momentum, goal, number of hidden layer neurons, number of cycles and the training algorithm were obtained after exhaustive tests [25, 26].

The results obtained by ANN proved to be adequate for the dengue incidence prediction system as shown in Table 3. The neural networks presented a higher predictive power to the logistic regression model, considering the data from the historical series of dengue in the municipality. of Campo Grande, State of Mato Grosso do Sul.

Neural networks are very old, the first models are from the 1950s, the use is spreading nowadays because we have better machines to make the processing and data available, which we didn't have years ago, ANN is an area to be improved and developed, within the forecast in epidemiological systems due to its great applicability in functional approaches. The main difficulty in its use is the lack of familiarity of researchers in general, since it is a recent method in relation to statistical methods [27, 28]. The selection criterion of a network is obtained pragmatically, that is, the one that best achieves the expected results.

Figure 2 shows the time series for the variables: number of dengue cases; average, maximum and minimum temperatures; precipitation; and proportions of days in the month with average temperatures below 22° C, from 22° C to 26°**C** and above 26°**C.**

Figure-2. Average hospital admissions for dengue fever, minimum, average and maximum air temperature, 22 and 26 °C, relative humidity and precipitation in Campo Grande, MS, 2008-2018



Analysis of the distribution of cases showed that most cases were concentrated in the first half of the year, especially in March, April and May, highlighting the known seasonality of dengue. The annual average temperatures for the period were 24.5°C, for the minimum monthly average temperature of 18°C and for the maximum monthly average temperature of 31°C. The accumulated monthly precipitation in the period ranged from 36 to 203 mm, with a monthly average of 117 mm.

Since the data are over-dispersed (sample mean of 15, standard deviation of 33, coefficient of variation of 219, minimum of zero and maximum of 229 for a number of observations of 132).

To predict dengue cases in Campo Grande, a total of 742 MLP network with 14 different input sets were trained and tested. As shown in Table 1.

Table-1. Input Data Sets

Input Data Set	**Data from 2008 to 2018**				
1	Temp Min	Temp Max	Average Temp	Humidity %	Prec (mm)
2	Dengue Cases 1 Month Earlier				
3	Dengue Cases 2 Month Before				
4	Dengue Cases 3 Months Earlier				
5	Temp Min	Temp Max	Humidity	Precipitation	
6	Temp max	Temp média	Humidity	precipitation	
7	Temp Max	Humidity	Precipitation		
8	Average Temp	Humidity	precipitation		
	Data from Dec 2012 to 2018				
9	Temp Max	Umidade %	Prec (mm)	Dengue t-1	
10	Temp Min	Temp Max	Temp. Média	Humidity %	precipitation
11	Dengue Cases 1 Month Earlier				
12	Dengue Cases 2 Month Before				
13	Temp Min	Temp Max	Humidity	precipitation	
14	Average Temp	Humidity	precipitation		

As the errors were generally high, from the ninth dataset tests were done with data between 12/2012 and 12/2018. To test whether, with a shorter time interval, errors improved.

Even with this reduction in the time interval, errors generally remained high, except for some settings where the results show low error. The best configuration results for each data set are shown in Table 2. The two networks with the lowest RMSE and the two with the lowest MAPE are shown in Table 2.

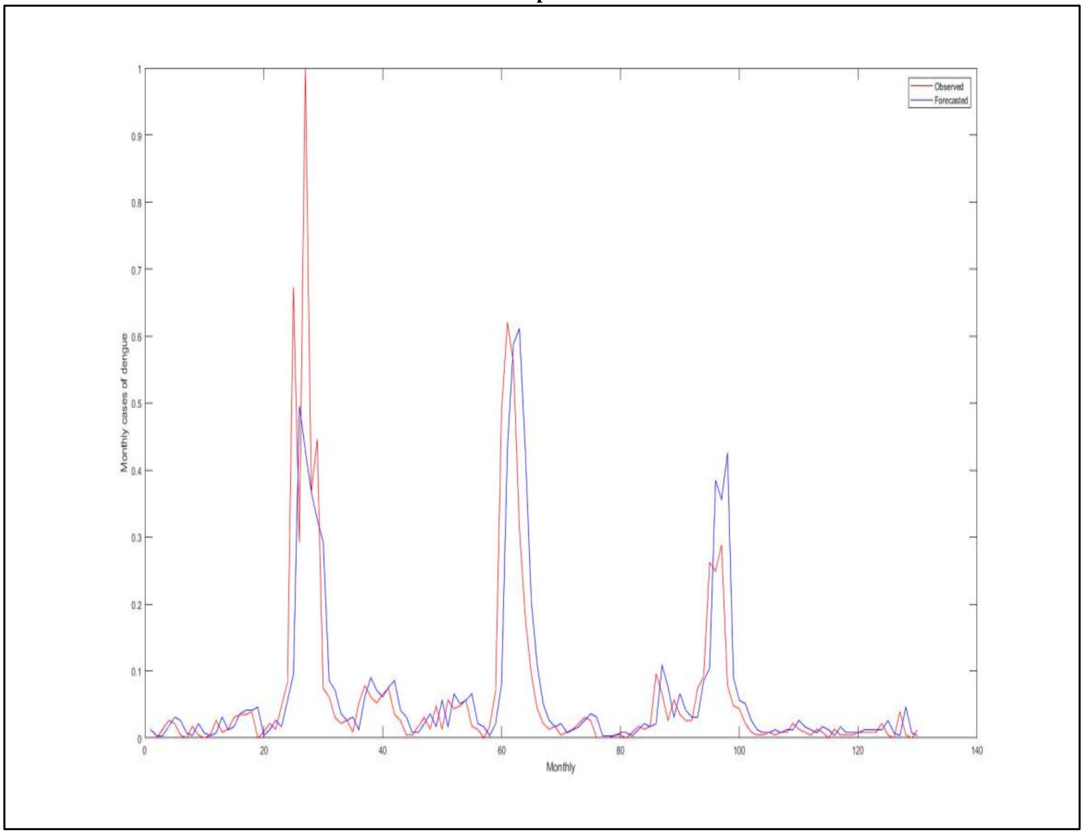
Table-2. Networks that had the best forecasting performance for each input set

Input Set	Hidden Layer Neurons	Training Algorithm	Activation Function	RMSE	MAPE %
1	7	trainlm	tansig	0,10017733	60,009624
1	7	trainlm	logsig	0,04023006	62,062156
2	7	trainlm	logsig	0,00981694	43,457212
2	15	trainbr	tansig	0,05105973	3,1786238
3	5	trainlm	logsig	0,02195326	54,538656
3	13	trainlm	tansig	0,0699479	46,062983
4	10	trainlm	logsig	0,02566376	64,432744
4	14	trainbr	tansig	0,11937793	58,13368
5	6	trainlm	logsig	0,03949868	61,036667
5	12	trainlm	tansig	0,1287968	59,762591
6	3	trainlm	logsig	0,04022625	61,999103
6	7	trainlm	tansig	0,10244501	60,535005
7	14	trainlm	logsig	0,03555447	62,118198
7	13	trainlm	tansig	0,13468548	60,919813
8	14	trainlm	logsig	0,03292532	62,470317
8	9	trainlm	tansig	0,10241897	60,977162
9	3	trainlm	logsig	0,01474401	41,045629
9	13	trainlm	tansig	0,09399882	10,257154
10	6	trainlm	logsig	0,04398324	126,63389
10	13	trainlm	tansig	0,25543051	89,140742
11	3	trainlm	logsig	0,01011579	59,983467
11	15	trainbr	tansig	0,09108138	5,4367983
12	9	trainbr	logsig	0,01894897	47,830235
12	13	trainbr	tansig	0,05592414	3,9534505
13	3	trainbr	logsig	0,05763184	126,32421
13	14	trainlm	tansig	0,16797454	110,50778
14	9	trainlm	logsig	0,05103706	133,19076
14	4	trainlm	tansig	0,12135931	98,948702

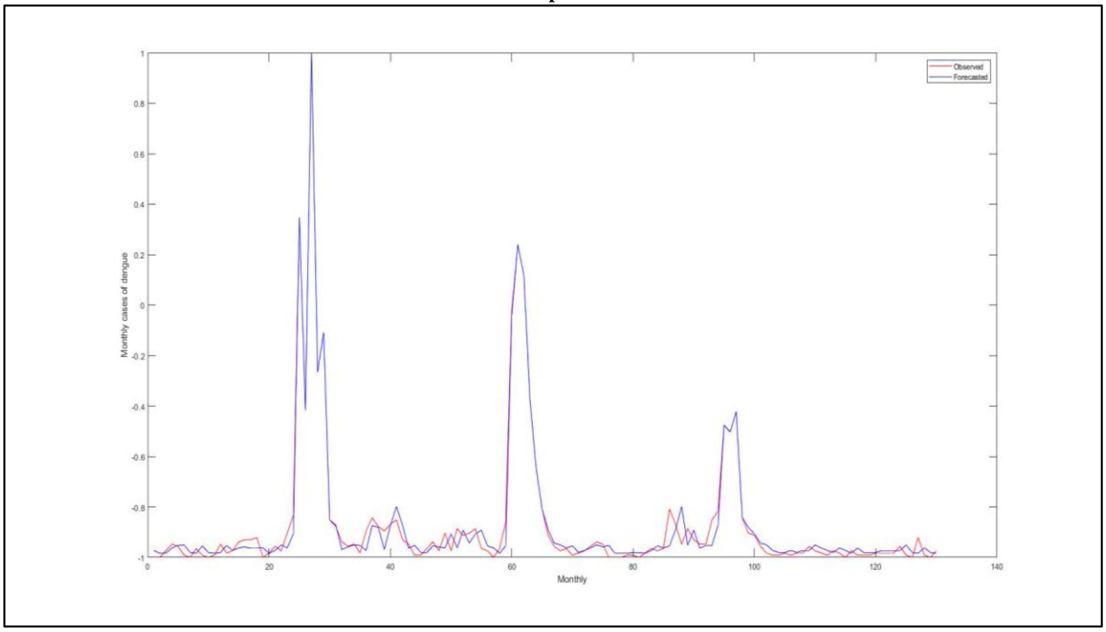
Following are graphs of comparison between the output calculated by the and the desired (observed) output. Graphs 3 and 4 are the with the lowest RMSE and lowest MAPE, respectively. And Graphs 5 and 6, the with the second lowest RMSE and second lowest MAPE, respectively.

Graph 4 is the output calculated by the with lower RMSE than the desired output (actual value).

Graph-3.

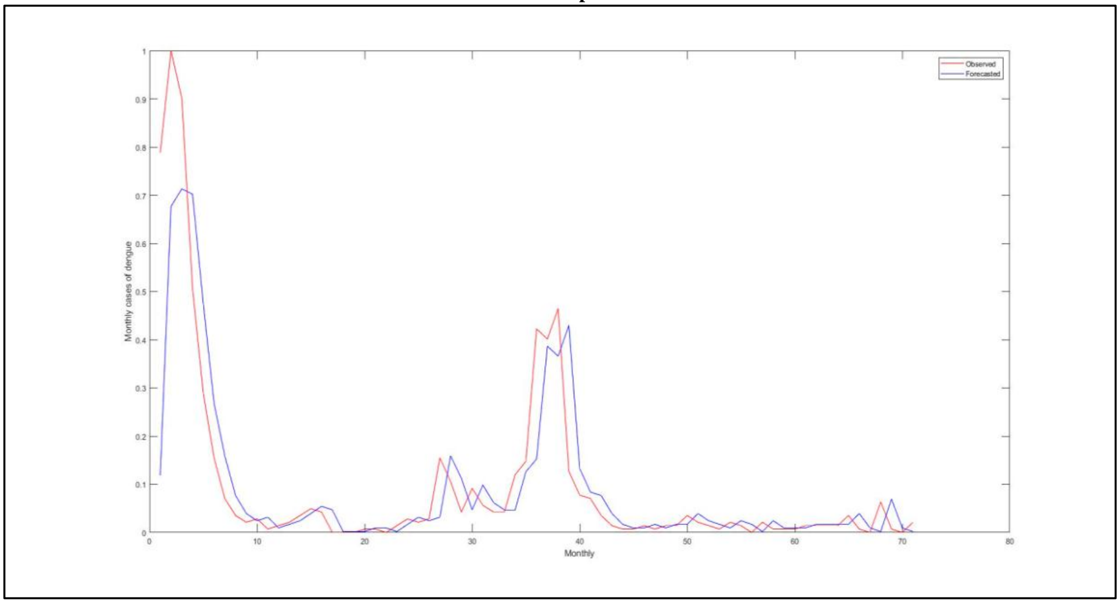


Graph-4.

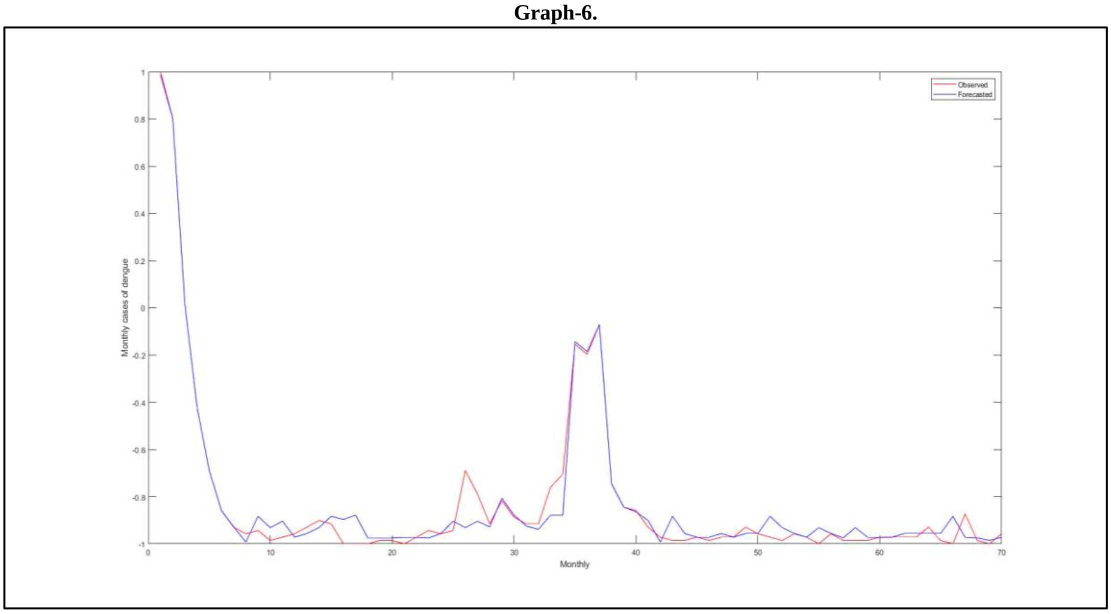


Graph 5 is the output calculated by the with lower MAPE in relation to the desired output (real value).

Graph-5.



Graph-6.



Graph 5 is the output calculated by ANN with second lowest RMSE relative to the desired output (real value).

Figure-7. Scatter diagram between measurements and estimates with RNA models (a, c, and, g); and Residues of RNA models (b, d, f, h.)

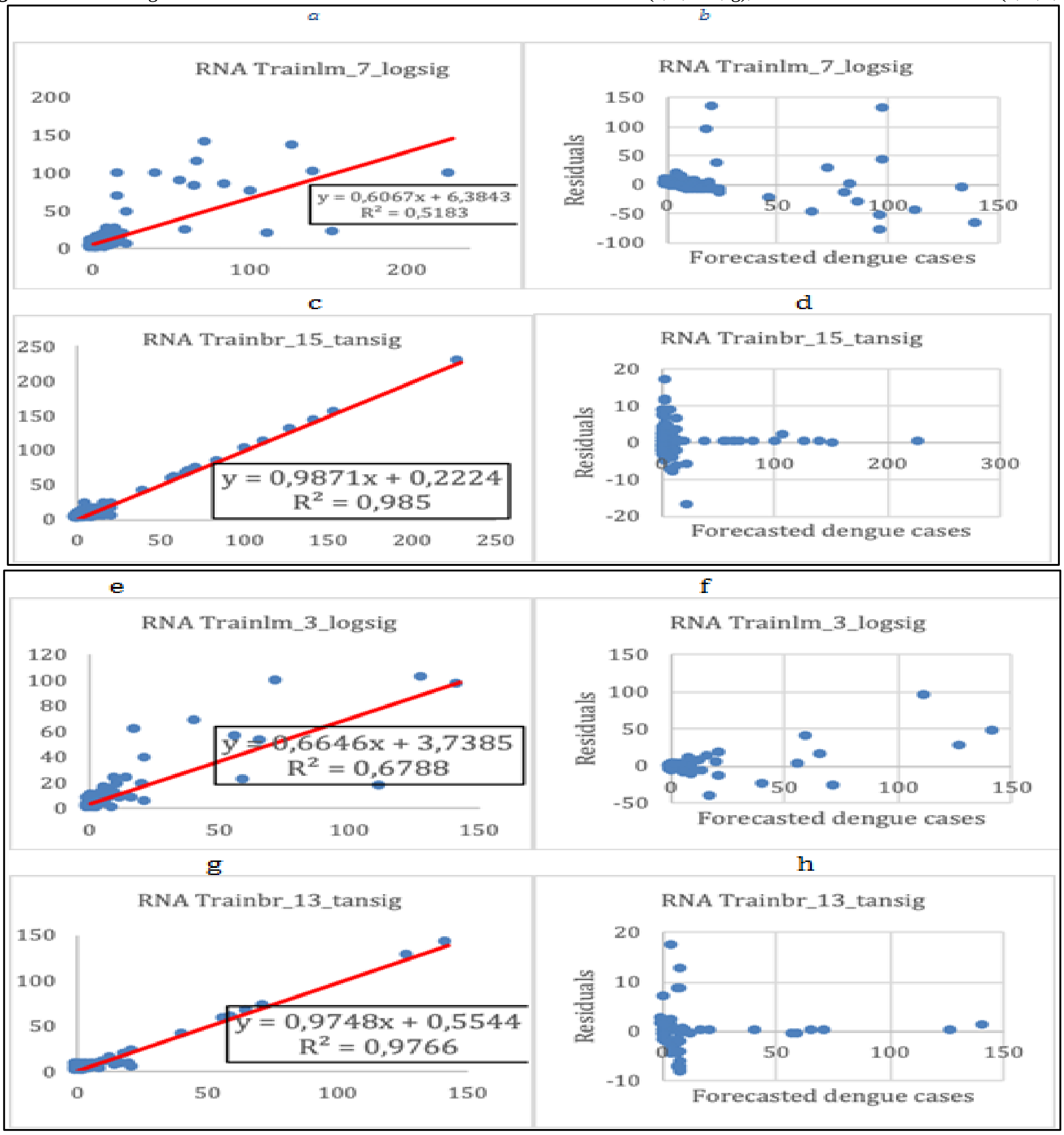


Figure 7 (a, c, e, g) shows the comparison between measured and estimated monthly DE values for. Models a and e have the farthest dispersion of regression. The R2 values of the models were 0.518; 0.985; 0.678 and 0.976. Scatter diagrams show that models c and e correlated most with measurements. For ANN models, MBE values ranged from -0.8866 to 0.406, RMSE values ranged from 0.0098 to 0.0559 and MAPE of models ranged from 3.178 to 59.98. The ICW had values between 0.003 and 0.83. Based on the metric of model validation statistical indices, it is noteworthy that ANN Training 7 logsig and Training 3 logsig underperformed other times15 tasing describes with relative precision the estimated ND, followed by ANN Trainbr 13 tasing models.

Table-3. Statistical indicators divided into two groups: dispersion indicators (error indicators) and general performance indicators

	RNA Training 7 logsig	**RNA Trainbr 15 tasing**	**RNA Training 3 logsig**	**RNA Trainbr 13 tasing**
Residue Sum Module	52,78590221	3,457078138	62,94995	16,96393602
Scatter Indexes:				
MBE:	0,406045402	0,026592909	-0,88661898	0,242
RMSE:	0,00981694	0,05105973	0,01011579	0,05592414
MAPE:	43,457212	3,1786238	59,983467	3,9534505
general performance indicators:				
R^2:	0,5183	0,985	0,6788	0,9766
ICW: 0,83046186	0,83046186	0,003780622	0,107776524	0,005981419

3.1. Impacts of Climate Variables on the Life Cycle of Aedes aegypti

Temperature and precipitation are important environmental factors that affect all biological processes of Ae. aegypti. Indeed, there are precise mathematical expressions relating to developmental rates to temperature [29, 30]. The rates at which mosquitoes acquire and transmit viruses also depend on temperature [31-33]. Precipitation events, in turn, are extremely important for dengue transmission [34, 35]. The abundance of Ae. aegypti is regulated by rain during water dependent stages (egg, larva, and pupa), which provides breeding sites and stimulates egg hatching [35, 36].

Relationships between lower temperatures, rainfall and mosquito population size are generally studied in countries with temperate climates, where excessive rainfall causes hatching of eggs, but lower temperatures can be fatal to larvae [37, 38]. The Brazilian tropical climate, however, may present adequate temperatures for vector proliferation even in winter. Thus, we conjecture that winter rain events may play an important role in the first generation of mosquitoes that year. A larger initial population, when composed of several reproductive cycles, could lead to an epidemic outbreak in summer. As shown in Figure 1, favorable weather conditions in Campo Grande are mainly a function of rainfall events.

Kesorn, *et al.* [39], recently addressed a decade-long limitation of dengue surveillance systems, namely that environmental factors may be unreliable and degrade forecasts when applied in areas with similar climate. The prediction accuracy of their model increased dramatically when instead of using weather parameters in a classical structure, they used Ae. infection rates by female mosquitoes and aegypti larvae. Our work, on the other hand, was able to successfully predict years of dengue using only climate variables. This raises an important question: how reliable are the climate parameters for dengue prediction? One possible explanation is that these parameters are reliable only on coarser spatial scales, and the large distances between cities in a continental country such as Brazil lead to significant climatic differences. Another explanation is that our methodological innovations have improved the reliability of local climate factors; Kesorn, *et al.* [39] ruled out temperature as a good predictor by visual inspection of their time series, while allowing a wide range of time intervals that link temperature and future results. It would be interesting to see if our approach could improve the reliability of climate signatures in other contexts.

Daily temperature changes are known to affect Ae efficiency. aegypti [40, 41]. Kesorn, *et al.* [39] also showed that infection rates for female Ae. aegypti and larvae strongly correlate with the number of reported dengue cases in humans. In this respect, our method is independent of which specific mechanisms led to an increase in the number of human cases. The above factors may be the missing link between climatic variables and observed human cases. However, as also pointed out by the authors, it is not always possible to obtain data on mosquito infection rates. To our knowledge, there are no data available on female mosquito and larval infection rates in Brazilian cities.

4. Conclusion

Dengue epidemic control is one of the most pressing public health challenges in tropical countries such as Brazil. A better understanding of the long-term, multiple-scale effects of weather conditions on the development of Aedes aegypti populations is crucial to improving the timing of vector control efforts and other policies. In this paper, we show that climate variables - average temperature, maximum and minimum temperature, relative humidity and precipitation - can be crucial for dengue prediction in Brazil. Notably, for Campo Grande, a forecast can be made approximately two months before the outbreak, which usually occurs from March to May. However, public strategies were typically enacted and decided during this period, which is too late and does not take advantage of the predictive capabilities of climate data.

Thus, the best performances obtained by MLPs modeled with 15 and 13 hidden layer neurons, hyperbolic tangent sigmoid activation function and Bayesian Regularization Backpropagation training algorithm and 7 and 3 occult layer neurons, logistic sigmoid activation function and Backpropagation training Levenberg – Marquardt. The input set that obtained this result was composed only by the number of dengue cases in the two months preceding the month in which the forecast was made. It is noted that the climatic variables were not the most appropriate to estimate the number of dengue cases, since the trained network with information on past dengue cases performed better.

To sum up, the results presented by the developed networks show that it is possible to forecast dengue cases in the study areas based on meteorological and historical data of dengue cases from previous months. However, it should be noted that, like all mathematical based modeling, the generalization of the results obtained in a specific case study cannot be used directly for other cases, since it must be taken into account that the characteristics of each region are unique. Therefore the use of models built in this work are restricted for the selected study area.

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Conflicts of Interest

The authors declare no conflicts of interest**.**

Database declaration / Data availability: The climate database is in the public domain and is available at: https://www.cemtec.ms.gov.br/ and the hospital admissions database is available at http://www2.datasus.gov.br/DATASUS/index.php?area=02

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