

## Negative selection algorithm for dengue outbreak detection

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**Abstract:** Dengue is a critical communicable and vector-borne disease and is becoming a serious concern in Malaysia. It is important to have an early detection system that could provide immediate action, such as the control of dengue transmission at a specific location. However, the available strategy and action may give long-term effects to the community since inaccurate decision making or prediction may lead to other circumstances. Moreover, the need to have a system that can detect the outbreak in a reasonable amount of time is critical. In this study, a nature-inspired computing technique, the artificial immune system (AIS), is used for dengue outbreak detection. One of the variants of the AIS algorithms, called the negative selection algorithm (NSA), has been widely applied in anomaly detection and fault detection. This study aims to employ the NSA for dengue outbreak detection.

**Key words:** Dengue outbreak, artificial immune system, negative selection algorithm

### 1. Introduction

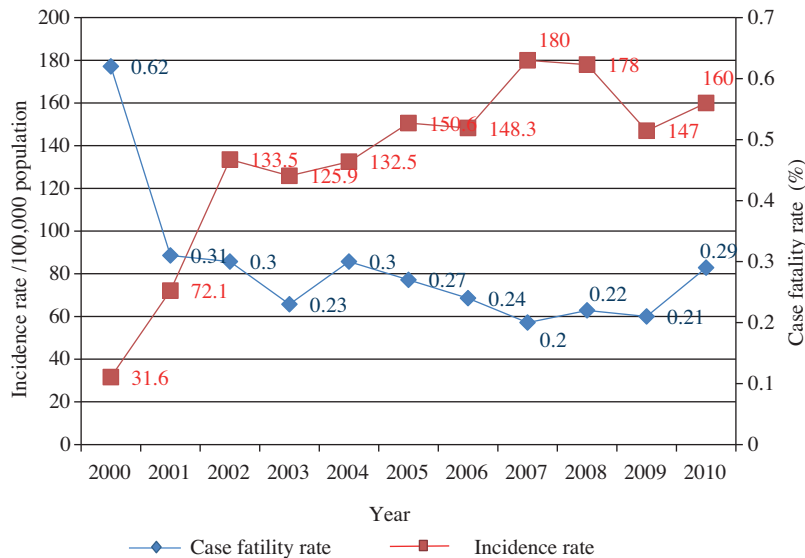
In recent years, with the expanding of urban life, the number of dengue patients has increased significantly. This disease has mostly been found in tropical climate regions, such as Malaysia. Dengue disease is transmitted by *Aedes* mosquitoes and is also known as ‘break bone fever’ because it causes severe joint and muscle pain. According to the World Health Organization, dengue disease is divided into 2 categories: dengue fever (DF) and dengue hemorrhagic fever (DHF) [1]. In recent decades, dengue outbreaks have increased considerably throughout the world. Currently, approximately two-fifths of the world’s population is at risk of contracting dengue. There are 50 million reported cases of dengue, with 500,000 reported cases of DHF in the world each year [2].

In Malaysia, the reported cases of this disease have been increasing. In 2000, a total of 31.6 cases/100,000 people were reported. Dengue has continued to be a public health concern, with 160 cases/100,000 people reported in 2010 during a global pandemic. This number is based on reported clinically diagnosed cases, as shown in Figure 1 [3].

Outbreak detection is closely related to the anomaly detection problem. It can be divided into 2 possible tasks: a classification task and an outlier (deviation) detection task. The outbreak detection problem can be a classification problem if the number of cases in both the outbreak and the no-outbreak are almost balanced.

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Such a classification process is necessary for determining the objects that belong in each class according to their specific features. However, an outbreak can be treated as an outlier detection task if the outbreak cases are rare in the dataset. This process involves finding a rare class among the data and is usually performed with unsupervised learning. This task is related to a clustering task. In this study, because of the availability of the dataset with the outbreak and no-outbreak cases provided by the state public health department, outbreak detection-based classification is employed.



**Figure 1.** Dengue epidemiology in Malaysia: incidence and case fatality rate (2000–2010) [3].

The early detection of dengue outbreaks can improve the public health surveillance system in Malaysia and can help to control epidemics and reduce the impact of dengue outbreaks on other countries. In action against the dengue outbreak, the government has implemented several campaigns and countermeasures. As indicated in the saying that “prevention is better than cure”, having an outbreak detection program is very important. Such a system can ensure a rapid response when an outbreak is detected. Unfortunately, any action to counter an outbreak can be difficult to implement, and any misjudgment while countering an outbreak could lead to devastating consequences. Therefore, an adaptable detection program that is capable of reacting to the ever-changing nature of this disease is imperative [4]. Thus, the existing outbreak data have yet to be analyzed intelligently to extract any discernible patterns that would provide insight for accurately predicting future outbreaks. To achieve this end, considerable research over the past 2 decades has focused on artificial intelligence (AI) technology. AI technology has been proven to be a valuable predictive analytical tool when used with a new technology known as knowledge discovery.

One of the AI approaches that has gained the attention of researchers is the artificial immune system (AIS). The AIS was first introduced in the 1990s and is a new subdivision of AI. The inspiration for the AIS comes from the inner workings of the human immune system [5]. As quoted from De Castro and Timmis, the definition of AISs is as follows: “The Artificial Immune Systems (AIS) are adaptable systems applicable in problem solving. They are inspired from interpretations taken from the principles, models and immune functions of theoretical immunology” [6]. AISs have been applied in different areas, such as pattern recognition, machine learning, optimization, classification, clustering, and anomaly detection. The focus of this paper is the implementation of a new model for dengue outbreak detection using the negative selection algorithm (NSA)

because of its ability to recognize self (no-outbreak) and nonself (outbreak). The remainder of this paper is organized as follows. Section 2 highlights the related studies regarding the dengue outbreak detection methods, AIS algorithms, and their applications. Section 3 focuses on the methodology of this study. The presentation of the results and discussion and the concluding remarks are presented in Sections 4 and 5, respectively.

## 2. Related studies

Several methods are available for detecting outbreaks, comprising both statistical and AI approaches [7–12]. An efficient outbreak detection program is imperative for planning countermeasures to outbreaks, which can be achieved by recognizing the early signs of such outbreaks. The process of outbreak detection is closely related to the classification process, as well as the detection of deviations in data mining. Classification techniques can be used as an outbreak detector because of the availability of data from previous outbreaks [13]. Buckeridge et al. suggested a practical classification system that could be used with algorithms for detecting outbreaks, and this system utilizes information collected during surveillance analysis [14]. Shen and Cooper used multivariate Bayesian modeling as an outbreak detection program to combine the modeling of both known and unknown origins of previous outbreaks [15].

Bakar et al. used multiple classifiers to develop a predictive model for dengue outbreak detection in terms of predicting repetitive cases. The classifiers used were decision tree, rough classifier, associative classification, and naïve Bayes classifier [4]. The authors obtained an average prediction accuracy of 76%. Long et al. proposed the multiple attribute value (MAV) method for dengue outbreak detection [16]. MAV is based on frequent mining analysis, for which the calculations are based on the frequent attribute elements within a dataset. In dengue outbreak detection, MAV is based on an a priori concept that finds a frequent item based on the MAV of a real data repository and generates association rules. Long et al. identified the number of attributes to be used in outbreak detection instead of using only case counts. They compared their work with the cumulative sum (CUSUM). The CUSUM is often used in the detection of small changes in a process parameter that are important. The CUSUM and regression are frequently used as tools in detecting outbreaks within a dataset [17,18]. In this study, MAV and CUSUM will be used as comparative methods.

Dasgupta categorized AIS algorithms into 2 main categories: population-based algorithms and network-based algorithms. Population-based algorithms apply negative selection and clonal selection theory, while network-based algorithms apply the concept of immune network theory [19]. One of the reasons to apply the AIS rather than other algorithms is that it needs only positive examples, and the patterns learned can be clearly examined. Furthermore, the AIS does not need a considerable number of parameters for the system because it is a self-organizing algorithm [20]. The NSA is one of the earliest methods in AISs that has been widely applied in anomaly detection and fault detection problems. This algorithm was proposed by Forrest et al. and is inspired from immune system mechanisms. The NSA is based on T cells. T cells can recognize self from nonself cells, where the self and nonself cells are considered to be the body and the pathogens, respectively. This algorithm is based on the idea of generating a set of detectors that are capable of detecting anomalies [21].

A successful algorithm, known as the NSA, is commonly used to detect changes and anomalies. This algorithm is a supervised learning algorithm-based population. After the emergence of the AIS, the NSA has increasingly found its way in the classification process, and the result is a system that inherits the constructive features of the biological immune system [22]. According to [23], the NSA has been widely applied in anomaly detection and fault detection applications using self and nonself recognition. Bendiab proposed a method based on the NSA for skin detection and classification to recognize skin pixels from nonskin pixels in images

[22]. Gonzalez et al. proposed a new method for performing anomaly detection by combining the NSA and a classification algorithm [24]. Another proposed algorithm in [25] uses the NSA for fault detection. It was applied in a fault model of DC motors and was compared with other fault detection algorithms. This comparison showed that the proposed algorithm is a suitable algorithm and that the method is a promising solution for fault detection. In 2010, Yue et al. designed a new fault detection model based on the NSA to eliminate the disadvantages of conventional fault detection techniques. These authors could increase the detection accuracy using a sufficient number of training samples [26].

From the above discussion on the NSA and from the definition of an outbreak, we intend to employ this AIS-based algorithm for disease outbreak detection. To date, work on the NSA in disease and surveillance problem is yet to be available in this research area.

### 3. Methodology

This study consists of 3 main phases. The first phase is the preliminary study of the dengue outbreak detection problem, which includes identifying the problem and the data preparation steps. The second phase is the implementation of the NSA. This phase consists of several important steps of the algorithm. The third phase involves testing and evaluation to measure the performance of the NSA compared to 2 other methods, as determined by the detection rate and the false alarm rate. The comparative study includes the evaluation of the obtained results compared with the previous techniques used on the same dataset.

#### 3.1. Phase 1: problem identification and data preparation

Dengue is one of the most common diseases in Malaysia. Because there is no vaccine against the dengue virus, the mortality rate associated with the disease is high, especially for children, and because of the lack of a suitable treatment, the dengue mortality rate will continue to increase [2]. The early detection of a dengue outbreak can improve public health surveillance systems in Malaysia and can help to control epidemics and reduce their impact on other countries. Unfortunately, there is not sufficient discussion about suitable models for detecting dengue outbreaks in Malaysia.

The data that is relevant to this task was obtained from the Public Health Department of Negeri Sembilan, one of the states in Malaysia. We presented our proposed work to a team of public health officers, and a series of meetings were conducted to define the dengue outbreak problem. It is important to have a detection model that can better detect the spread of a dengue outbreak. The purpose of this research is the use of the NSA as an outbreak detection model to obtain a high performance in the detection rate.

##### 3.1.1. Data collection and preprocessing

The dataset was collected from a study on DF conducted by the Vector Control Unit of the Hulu Langat District Health Centre, Selangor State, Malaysia. Data on a total of 8505 dengue patients were collected from 2003 to 2009. The original dataset contains 134 attributes, including the demographic and clinical data. The attribute selection for this study was performed by consulting with public health officers and environmental and epidemiology experts. Table 1 shows that the selected dataset consists of 12 attributes, including the year, the number of weeks (no.week), the age, sex, race, address, occupation, type of dengue, incubation period, area status, recurrent cases, death code, and 1 class attribute (outbreak/no-outbreak). These attributes were used in previous research [4,16]. These data are the real dataset; thus, the preprocessing steps for cleaning,

data transformation, and data reduction were handled with care to ensure that the authenticity of the data is retained. The data were then prepared to suit the NSA for dengue outbreak detection.

**Table 1.** Dengue data representation and description.

No.	Attributes	Representation	Description
1	Year	Original data	2003-2009
2	No_Week	Continuous	1-52 per year
3	Age	1-4	Child, youth, adult, senior
4	Sex	1, 2	Male, female
5	Race	1-4	Malay, Chinese, Indian, others
6	Address	1-8	Each representation district
7	Occupation	1-9	Child, student, housewife, senior, self-employed, general laborer, ex-executive, executive, nil
8	Type of dengue	1-2	DF and DHF
9	Incubation period	0-14	Days (period between reported date (onset) and the fever start)
10	Area status	1-3	(1) Uncontrolled outbreak in a 2-week period, (2) Dengue case in an outbreak area, (3) New outbreak in the area
11	Recurrent case	0, 1	No/yes
12	Death code	0, 1	No/yes
13	Class	0, 1	0- No-outbreak 1- Outbreak

### 3.1.2. Determining the class attribute

We determined the class attribute for the outbreak and no-outbreak cases following the given outbreak definition. A dengue outbreak is defined as an occurrence of more than 1 case in the same locality, where the date of onset between the cases is less than 14 days. The outbreak is cleared when no new cases have been reported within 14 days [27].

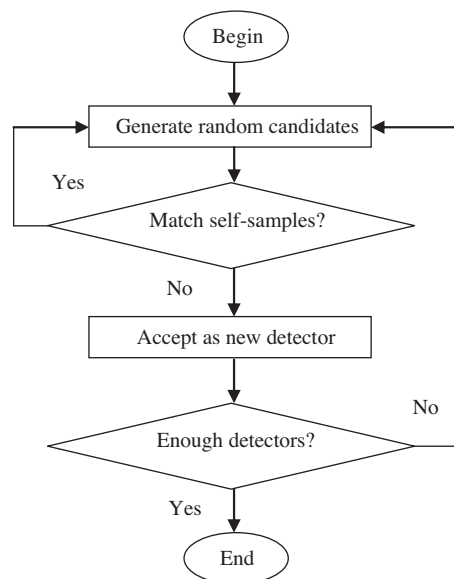
In this problem, 2 classes are identified: the outbreak class and the no-outbreak class. The data classification is conducted according to the definition of a dengue outbreak. For example, in weeks 4 and 5 of 2008, the number of dengue cases was 49 and 57, respectively. Next, to determine the outbreak class for week 6, with 62 dengue cases, the mean of the number of cases related to weeks 4 and 5 must be calculated. Because the number of cases in week 6 was larger than the mean of the 2 previous weeks ( $62 > 53$ ), this week is classified as an outbreak, which means that new cases were reported within 14 days.

## 3.2. Phase 2: implementation of the algorithm

The NSA has 2 phases: 1) the generation phase and 2) the detection phase. These 2 phases are described in the following sections.

### 3.2.1. Generation phase

Detector sets are typically created during this phase through several random processes. As depicted in Figure 2, the matched self-samples are removed during the generation stage, and the samples that do not match become the detectors.



**Figure 2.** Generation of the detector set [28].

Figure 3 presents the pseudocode inventory of the process of generating detectors for the NSA.

```

Detector-Set (S,m,rs)
S: set of self-samples
m: number of detectors
rs : self radius
1: D ← Φ
2: Repeat
3:   x ← random sample from [0,1]n
4:   Repeat for every si in s
5:     d ← Euclidean distance between si to x
6:     if d ≤ rs , go to 2
7:   D ← D ∪ {x}
8: Until |D| = m
9: return D
  
```

**Figure 3.** Detector generation algorithm in negative selection [29].

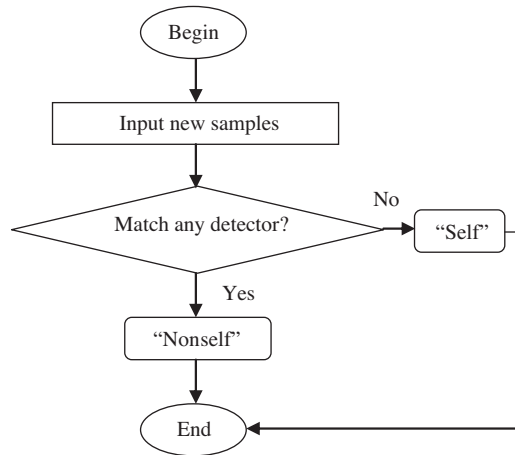
During the experiment, a real-valued vector dataset for dengue outbreak is used. Thus, in an  $n$ -dimensional space, the detector or self-set (a set of real-valued data) is in the form of a hypersphere. Min-max normalization is applied to this type of data. When working with the NSA, its real-valued data should be normalized to super-rectangular space  $[0,1]^n$ , with  $n$  representing the number of attributes.

As previously stated, the initial phase in the NSA involves creating detectors through random processes and then testing to determine whether they match any self-samples. Self-samples can be considered as the standard (normal) behavior of the data in the first phase. Another component of the NSA is the matching rule, where it characterizes the difference between matched data to be removed and unmatched data that are suitable to be detectors. The matching rule relies on the representation format of the data and the detectors. For the NSA with real-valued data, its matching rule is the Euclidean distance ( $d$ ). Euclidean distance represents the distance between the random detectors and the self-samples in the first phase. The distance between a

candidate detector and the self-samples must be compared with the self-radius ( $r_s$ ). In this case, if a match occurs ( $d \leq r_s$ ), then that detector is removed. Through this process, the detectors are generated until the required allocation is filled.

**3.2.2. Detection phase**

After the first phase, the created detector set is applied to detect new samples, whether they are self or nonself. The matched samples with the detectors are accepted as anomaly or nonself; otherwise, they are considered as self. Figure 4 shows the second-phase process.



**Figure 4.** Detection of new instances [28].

In the second phase, the inputs are detectors that are generated in the first phase and test data (unseen data), which must be compared with each other using the Euclidean distance as the matching rule, to determine whether there is a match between them. If a match is found, then the test data are recognized as nonself; otherwise, the test data are self. In this research, ‘self’ and ‘nonself’ represent no-outbreak and outbreak, respectively.

**3.3. Phase 3: testing and evaluation**

Because the NSA is a supervised learning algorithm, a confusion matrix, which is a specific table arrangement, was employed. This matrix provides a visualized representation of the NSA performance. The columns in the table represent the values in the actual class, and the rows represent the values in the predicted class. Data from this matrix were applied to analyze the performance of the NSA. Table 2 shows a confusion matrix constructed for the dengue outbreak.

**Table 2.** Confusion matrix for the outbreak.

System detected	Actual cases		
	Outbreak	No-outbreak	
Outbreak	True positive (TP)	False positive (FP)	TP + FP
No-outbreak	False negative (FN)	True negative (TN)	FN + TN
	TP + FN	FP + TN	Total

Well-accepted metrics that are used to describe the performance of the NSA include the detection rate and the false alarm rate, which can be calculated from values obtained from the confusion matrix using Eqs. (1) and (2) below, respectively:

$$\text{Detection rate (DR)} = TP/(TP + FN), \quad (1)$$

$$\text{False alarm rate (FR)} = FP/(TN + FP), \quad (2)$$

where TP is the outbreak elements that are detected as outbreak, TN is the no-outbreak elements that are detected as no-outbreak, FP is the no-outbreak elements that are detected as outbreak, and FN is the outbreak elements that are detected as no-outbreak.

Therefore, the accuracy can be calculated using the formula in Eq. (3):

$$\text{Accuracy} = (TP + TN)/(TP + TN + FP + FN). \quad (3)$$

#### 4. Experiments

The experiment was conducted in several phases to test the reliability of the dataset when presented to the NSA. Using the original dataset obtained from the work in [4,16], the NSA fails to detect the outbreak with a high detection rate because a correlation exists between the conditional attributes and the class attribute (outbreak). The initial results showed that there is no logical relationship between some of the attributes (e.g., the sex) and the outbreak class. Therefore, feature selection is performed to increase the detection rate. We perform a simple forward selection algorithm to determine the set of attributes that give a high detection rate. The result is that the attributes that achieve a more accurate detection rate are the year and the number of weeks.

In the experiment, 100% of the no-outbreak (normal) class data are used as a complete training set, and then, 50% and 25% of the elements are taken randomly from the no-outbreak class as a partial training set that are used to train the system. The number of self-samples used is shown in Table 3. All of the elements in the dataset must be classified as either outbreak or no-outbreak in the test phase. In our experiments, the maximum detector set size is set at 50,000. For each method, we repeat each run 100 times, and then the averages are taken.

**Table 3.** Number of self-samples in the dengue dataset.

Training data	Number of self-samples
100% of self-class	3249
50% of self-class	1625
25% of self-class	812

##### 4.1. Results

The experimental results with different radiuses are depicted in Table 4. To demonstrate which result is the optimal one, the minimum error must be calculated. The minimum error is defined as in Eq. (4), where  $d_i$  is the detection rate and  $f_i$  is the false alarm rate.

$$\text{Minimum error} = \min(1 - (d_i - f_i)), \text{ for every } i \quad (4)$$

The best balance between the detection rate and the false alarm rate occurs when the amount of this error is at a minimum [30]. As shown in Table 4, when all of the values of the self-class are used as training data, false



alarms do not occur ( $FR = 0$ ), and the detection rates are less than in the cases trained by the partial training data. Therefore, to achieve the best balance between the detection rate and the false alarm rate, the minimum error must be calculated when only partial training data (i.e. 50% and 25% of the self-class from the dengue data) are used to train the classifiers.

**Table 4.** Experimental results for the dengue data.

Training data	Radius	Detection rate	False alarm rate	Accuracy
100% training	0.13	70.16	0	83.06
	0.15	65.80	0	80.58
	0.17	59.89	0	77.36
50% training	0.13	76.06	22.25	77.62
	0.15	71.15	16.01	74.40
	0.17	62.78	13.72	70.10
25% training	0.13	83.75	29.70	83.47
	0.15	80.93	24.83	79.85
	0.17	73.70	18.77	77.47

The purpose of using partial self-data as training data is to demonstrate the capability of the system to recognize unknown no-outbreak data. As illustrated in Table 4, the minimum error is obtained for 50% of the training data with  $r_s = 0.15$ , where the detection rate and the false alarm rate are 71.15 and 16.01, respectively. Additionally, for 25% of the training data, the minimum error is obtained with  $r_s = 0.15$ , where the detection rate and the false alarm rate are 80.93 and 24.83, respectively. In conclusion, these results show that the classification experiment using 25% of the self-data produces better detection of the dengue outbreak compared to the other experiments.

Our experimental results were compared with 2 other existing methods on the same dataset, namely the MAV [16] and the CUSUM [17,18], which were discussed in related works. Long et al. applied the MAV to the dengue data and then compared their results with CUSUM, which is a statistical technique [16]. Table 5 shows the comparison of the NSA with these 2 techniques.

**Table 5.** Comparative results of the NSA with the MAV and CUSUM.

Algorithms	Detection rate	False alarm rate	Accuracy
NSA	80.93	24.83	79.85
MAV	74.1	28.0	73.1
CUSUM	70.8	28.0	67.3

As shown in Table 5, the NSA method outperforms the 2 other techniques in terms of the detection rate, the false alarm rate, and accuracy. The NSA achieves higher accuracy, a higher detection rate, and a lower false alarm rate compared to the other 2 techniques. The NSA is based on the reduced features because the initial experiments indicate a nonlogical relationship in the original sets. Therefore, the detection rate is higher than that of the MAV and CUSUM because of its reduced features.

We presented the results obtained to a group of experts in vector diseases from the Public Health Department, Seremban, Negeri Sembilan, Malaysia, and they confirmed that the finding is meaningful because the year and week play important roles in the *Aedes* mosquito's lifecycle. In addition, the behavior of the NSA and the representation of the data also contribute to the reason why it works well with these reduced features. Therefore, the features that were used are the most significant features for the dengue outbreak problem.

## 4.2. Discussion of results

The experimental results showed that the NSA performs better than the 2 other methods that used the same dataset. However, the high detection rate of the NSA is based on the reduced attributes that are utilized after several runs of the NSA are performed. The performance of the NSA toward the original data indicates some limitations in the representation of the data used. The NSA is not able to provide accurate detection with the original dataset for the following reasons:

1) The NSA detectors for outlier detection were obtained from a set of normal data. In the detector generation phase, the candidate detectors must be different in terms of their characteristics, or the similarity distance must be sufficiently distinct from the normal dataset. During detection, the data (cases) are compared, each of them with the detectors that are generated in the generation phase. If the cases match, then they are considered to be outliers.

2) For the dengue outbreak detection case, the values of the dengue patients visiting inside and outside the outbreak week are almost similar, i.e. there is no significant variation in both of the conditions. Therefore, it is difficult for the NSA to detect the rare cases (the potential outbreaks) because the NSA is an instant-based method. However, if the data contain more distinct values in most of the parameters, then the detection can be improved. For this reason, in this study, the NSA detects with a generalized model based on the year and week, because these attributes present a large range of values, whereas the other attributes are categorical data.

## 5. Conclusions and future work

In this study, for the first time, the NSA was applied to solve the dengue outbreak detection problem. DF is one of the most common diseases in Malaysia, with a high mortality rate, especially in children. Therefore, the need for a system that can detect a dengue outbreak in a reasonable amount of time is critical. The NSA has been widely applied in anomaly detection, but to date, the algorithm has not been used for dengue outbreak detection. The work presented here shows the potential and effective use of the immune system-based method for outbreak detection. With a higher detection rate and a lower false alarm rate compared with other available methods, the results of this study can help to build the public health surveillance system in Malaysia to facilitate the early detection of dengue outbreaks and can help to control epidemics and reduce the impact of such epidemics on other countries.

Several issues can be addressed to improve the current work.

1. Because the NSA works better with the reduced attributes, the NSA could improve the generalized model in terms of the availability of an accurate dataset that is crucial for improving the NSA model. Therefore, additional important features are required.
2. In the NSA, the number of detectors and the self-radius are critical parameters to obtain a balance between the detection rate and the false alarm rate, but because there is no available literature that discusses the appropriate self-radius, different values for this parameter must be examined to determine the proper self-radius that achieves the best result with the minimum error. This issue can be investigated in future work on this method.
3. Most of the parameters in the dengue data are categorical. Therefore, when the NSA attempts to discriminate between the self and nonself class, the task becomes difficult. The new representation of the data and the computation of the distance values are essential to improve the algorithm.

4. The transmission of dengue is closely related to the local climate. After bouts of rain, pools of stagnant water provide ample breeding sites for mosquitoes [31]. A warm and ambient temperature is conducive to the mosquito's gonotrophic life cycle [32–34]. Combining the available dataset, which was obtained from the Public Health Department, with several additional suggested features, such as rainfall, humidity, and temperature, might improve the accuracy and interpretability of the model.

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