The Preliminary Design of Outbreak Detection Model Based on Inspired Immune System

Mohamad Farhan Mohamad Mohsin
School of Computing, College of Arts and Sciences,
Universiti Utara Malaysia,
Kedah, Malaysia.
farhan@uum.edu.my

Azuraliza Abu Bakar[1], Abdul Razak Hamdan[2]
Data Mining and Optimization Research Group,c
Centre for Artificial Intelligence Technology, Faculty of Science & Information Technology, Universiti Kebangsaan Malaysia, Selangor, Malaysia.
aab@ftsm.ukm.my[1], arh@ftsm.ukm.my[2]

Abstract— **The aim of outbreak detection model is to obtain high detection rate but at the same time maintaining the low false alarm rate. However, because of the weakness of early outbreak signal that behaves under uncertainties, it causes imbalance result between detection rate and false alarm rate. In this study, an early review of danger theory, an approach of artificial immune system is performed to seek the possibility it can be applied in outbreak detection. To investigate that, a detection model based on danger theory is developed and the model is tested with dengue outbreak dataset. The model is then evaluated in term of detection rate, specificity, false alarm rate, and accuracy. The preliminary result indicates that the proposed model has ability to generate good detection result with a balance between detection rate and false alarm rate.**

Keywords-outbreak detection; artificial immune system; danger theory

I. INTRODUCTION

Outbreak causes a terrible effect when it turns uncontrollable. As reported in many health reports, outbreak has caused high death toll within a short period and the worse is it kills without notification [2-4]. Besides that, it reflects the economics of the effected country as what had happen to the tourism industry after SARS and Avian Virus attack in 2003. Because of those outbreaks, approximately $20 billon has lost due to improper surveillance system [5]. To reduce the effect, each country relies on the outbreak detection system which responsible to raise an immediate alert before it starts spreading to a wider geography area. Early detection of the onset of outbreak is important for health authorities to act timely and setup immediate plan [6].

To detect the onset of outbreak, the detection system observes the progress of disease daily or weekly where the starting point data starts to change is taken into consideration as an outbreak sign [7-9]. Since the outbreak sign is abnormally behaved from previous activities, the anomaly detection approach is applied in outbreak detection area. In practical, outbreak detection model is placed under the analysis phase of health surveillance system.

The aims of outbreak detection model are twice; firstly is to detect true outbreak as an outbreak and secondly to make sure that outbreak is detected as fast as possible. Based on that, many detection algorithms on different approaches have been proposed. We classified them into three groups; statistic [1, 10, 11], artificial intelligence [12-14], and hybrid between both methods [15-17].

The primary issue in outbreak detection is to obtain high detection rate (DR) but at the same time maintaining the false alarm rate (FAR). However it is difficult to attain because of the weakness of early outbreak signal that behave under uncertainties. Every year, the outbreak pattern changes although for seasonal outbreak type. As the result of uncertainties, it causes the existing approaches produce imbalance result between DR and FAR. In this case, the detection model has less capability to recognize new outbreak pattern mainly when it vary from the trained model.

In this study, we performed an early review on Danger Theory (DT), an approach of artificial immune system (*AIS*) which takes inspirations from human immunology fight against pathogen and stabilizes human body. Then we find possibility of DT to be applied in outbreak detection to improve DT and FAR. Finally, we present our initial idea on outbreak detection model using DT. Besides that, a discussion on the issues related to outbreak and what makes outbreak detection distinct with other detection based problem also will be presented in this paper.

This paper is organized as follows. Section II introduces the analysis on outbreak. Then, the DT approach is discussed in Section III. It covers the biological immune system and DT for anomaly detection. It will be followed by a discussion on the proposed model in Section IV. In Section V, the preliminary result of the study will be presented. The final sections conclude this work.

II. ANALYSIS ON OUTBREAK

Outbreak is as a sudden spread of disease with huge cases reported than expected over a particular period of time. It origins from a small community in a very specific area but speedily spread to a wider geographic area without prior notification [18]. Based on definition, outbreak relies on three dimensions; the spike number of cases and the occurrence is on similar time frame and similar location. When many countries have been affected with similar infections over the same period, the situation is turned to epidemic. Outbreak may last for a few days or weeks, or for several years.

For detection, the number of registered cases is important since it carries the indicator of outbreak. If the figure indicates an abnormal spiked compared to previous day it might indicates the present of outbreak. For each disease, the outbreak default case number is different. Such disease likes dengue, it requires only one suspected case to raise an alarm while cholera requires up to 20 registered cases before it can be classified as outbreak [19]. In this situation, if a single patient has been detected with certain disease, the alert system will not be activated until the numbers of collective cases has reached certain default number. Therefore, outbreak detection studies views outbreak as collective anomaly where it requires more than a case before it can be labeled as outbreak. However, when the outbreak spread is slow, the case number is not important and further investigation with epidemiologist is required. This makes outbreak detection differ from other detection task such in intrusion, fraud and fault. More importantly, outbreak needs to be tailored with same locality and time.

There are three important elements under the outbreak study; firstly is the time onset which is when the outbreak start, secondly; the outbreak magnitude which refers to how strong the outbreak is, and lastly is the outbreak duration which is how long the outbreak occurred as shown in Fig. 1 [20].

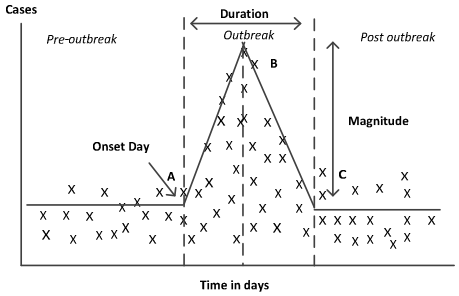

Figure 1. Three dimensions of outbreak. The outbreak is started at A when mean of infection process begin to raise, B the maximum outbreak time, and C when the infection return to normal. The outbreak should be detected at A, still acceptable at B while considered late when reach C

The challenge in outbreak detection is to deal with weakness of early outbreak signal that behave under uncertainties. For a univariate outbreak detection based model, the possibility of the model to generate imbalance result between DR and FAR is low when it only based on single attribute [15]. As solution towards the weak signal, researchers are looking forward into multivariate surveillance by injecting the weak signal with the stronger signal such as combining spatial and temporal data. Besides that, there are efforts to combine multiple syndromic data to boost detection such as combining the emergency visit data with weather information, or clinical diagnosis result [21, 22] and investigating the social network status and internet tracking search [23-25]. Because of outbreak is observed through the time sequence, the distract factor such seasonal event effect always disturb the detection result [10].

In addition, to define outbreak and non outbreak sample for model development is also a challenging task since in most of the time, only the non-outbreak session is available. Consequently, the model might lost it detection capability when detection algorithms require sample from both outbreak and non-outbreak session for model development.

Based on this issue, we looking at the possibility of the immune system paradigm mainly the DT approach to overcome the issues and improve outbreak detection performance

.

III. DANGER THEORY

A. The Biological Immune System and Outbreak

DT is a new paradigm of AIS where it against the conventional immunology theory that belief the immune system is triggered based on discrimination between self and non self. In DT, it assumes the human immune system is activated by danger signal released by a necrotic cell [26]. Necrotic cell is a cell that suddenly died due to pathogenic infection. The distress cell establishes a danger zone around itself to mitigate and localized the impact of attack once it has been infected.

In principal, DT views all cells in human body as antigen which have similar possibility to be infected by harmful antigen. In the beginning of detection, the dendrite cells which are born as immature cell will observe the progress of body cells. Termed as input, the dendrite cell collects the body cell protein paired with their signal (PAMP, danger, safe). Based on the collected input throughout the life span, the dendrite cell will migrate from immature into two maturation state; either semi-mature (apoptosis death) or mature state (necrosis death). The 'mature' indicates the cell has experience more danger signal throughout the life span caused by a foreign antigen, wound, etc. If this happen, it indicates antigen has been detected and danger zone will be released. While the 'semi-mature' indicates the apoptosis death is seen as part of normal cell function and is tolerised to the presented antigen.

By integrating the maturity mechanisms in DT, it is belief that DT able to improve current outbreak detection system through a robust, adaptive, highly distributed, and autonomous detection mechanism. Since the identification of the cause of cell distresses either apoptosis or necrosis is the key for antigen detection in the human body, it provides a solution to overcome the uncertain problem in early outbreak signal. In this context, all outbreak dataset will be considered as antigen which all of them has similar possibility to be affected by foreign antigen. Therefore when DT is applied, the requirement to define input data into normal and outbreak class is not required, or no training phase is required. It is contradict to conventional approach where one part of antigens either self of non self is required to be defined. Based on this, DT is more sensitive to any changes and it can highly discriminate between harmful and normal cell. Throughout the monitoring period, the maturity state of dendrite cell will be updated; if the outbreak movement abnormally changed, then alarm zone will be released indicating that harmful antigen exits.

B. DT for Anomaly Detection

Outbreak is viewed as anomaly in outbreak detection and DT has been found in many literatures as one of the anomaly detection technique. Up to recent years, there are not much works found DT has been used as outbreak detection model however it has been successfully applied in intrusion, fraud, and fault detection problem with good detection performance. The early work was initiated by [27, 28] where the biological DT approach has been extracted into dendrite cell algorithm (*DCA*), an algorithm in DT. The algorithm able to detect network intrusion with better performance compared to other immune system approach. Afterwards, the more sensitive version of dendrite cell algorithm has been proposed through new controllable parameters [29]. The information in Table 1 summarizes the role of DT as anomaly detector in various fields.

TABLE I. MAPPING BETWEEN OUTBREAK AND DT'S CHARACTERISTIC

Area	Description of anomaly	Researchers
Intrusion	Malicious code detection, misbehavior in wireless network, port scan, spyware, worm detection, flood attack	[30-39]
Fraud	Fraudulent online video on demand transaction, time malware for window process	[40-42]
Fault	Faulty in robot and control system, control system, task scheduling	[43-45]
Others	Filtering web documents, image classification	[46-48]

Based on Table I, DT has been applied in various areas to detect anomaly. Since the capability of DT as a good detector is proven in other areas, it motivates this study to adapt AIS as outbreak detection model. The robustness of immune system mainly the ability of the dendrite cell to sense early death of body cell (view as outbreak signal) can be replicated into outbreak detection to reduce high FAR. Besides that, DT offers a multivariate detection approach without relying on training phase which can improve model's robustness. Table II is a map between outbreak and DT's characteristic.

TABLE II. MAPPING BETWEEN OUTBREAK AND DT'S CHARACTERISTIC

Outbreak Issues & Effect	**DT Characteristics**	**Outbreak Detection model with DT**	
Outbreak signal is weak and inconsistent. It causes imbalance result between DR and FAR	The dendrite cell process multiple input signals.	Accepts multiple input factors to improve detection performance rather than relying on single predictive factor	**IMPROVE DT &**
Outbreak and non outbreak session are hard to determine for model development. It causes model lost capability when the unseen patterns vary from the trained model.	Antigens have similar possibility to be infected with harmful pathogen.	No need to define outbreak and outbreak class. In other word, no training phase involved.	**FAR**

IV. THE PROPOSED MODEL

The proposed model is designed based on the general outbreak detection process which consists of two-steps procedure. Firstly, obtain the baseline period that represent the abnormal pattern. Secondly, calculate the score of the observed data such that the abnormal cases are detected once they exceed the maximum baseline [49]. Based on the process, the proposed outbreak detection model based on DT is presented in Fig. 4. It has 4 processes; data gathering, signal formalization, outbreak mining, and outbreak analysis which are described in the next sub section. The detection algorithm used in this model is DCA, an algorithm based on DT.

A. Data Gathering

This step involves gathering data from original sources. Data can be taken from different type and department since DCA supports real time multivariate mining. In this study, we derive dengue outbreak data which is taken from two departments. Firstly is the emergency visit (E-Visit) data from Vector Control Unit, Seremban Medical Centre, Malaysia. Secondly is the weather data from Seremban Metrological Centre, Malaysia. The time period for both datasets is from 2003 to 2009 and the 2006–2009 data is used for the monitoring step in the experiment. The emergency visit data consists of 15 mixed attributes while the weather dataset has eight continuous attributes. As usual, the data is pre-processed where the numerical missing value is replaced with mean value while mod for categorical attribute.

B. Signal Formalization

Signal formalization is the most important step where data is prepared for DCA. In this study, data is normalized into appropriate form to suit outbreak data for DCA environment. In this phase, it involves several steps before data is normalized. The first step is to select and assign attribute into appropriate signal; PAMP, Danger, or Safe. The attribute assignment into appropriate signal is important since it determines DCA capability to discriminate anomaly accurately. The indicator of PAMP signal is when the attribute shows an anomalous situation while the safe signal is when no anomalous indicators present in the attribute. However, if the attribute may or may not indicate an anomalous situation but the probability of an anomaly is higher than under normal circumstances they will be label as danger signal [50].

To normalize the input, DCA requires a specific approach. An approach based on statistic control chart called cumulative sum is chosen for normalization. Cumulative sum is a statistical approach that monitors the mean of the

process and assumes a process remains under control when the cumulative mean is within the control value. The process is considered out of control when huge shift movement occurs from the target value. As the recent outbreak activity has relation to what happen in the previous day activities, the cumulative mean shift is taken into consideration for normalization. The normalization function is pictured in Equation 1.

$$Signal_j(x_i) = \begin{Bmatrix} C_i^+ ;\ C_i^+ >= 0 \\ 0\ ;\ C_i^+ < 0 \end{Bmatrix} \ where\ j = PAMP, danger, @\ safe \quad (1)$$

where C_i^+ is the cumulative sum value. If C_i^+ is greater or equal than 0, the cumulative sum value is taken as the normalized value. The C_i^+ is derived from upper cumulative sum function as shown in Equation 2.

$$C_i^+ = max\ [0, x_i - (\mu_0 + K) + C_{i-1}^+] \quad (2)$$

where the C_i^+ is the upper cumulative value at i_{th} observation, x_i is the process at i_{th} observation, μ_0 is the initial mean and K is the allowance value which is chosen between the target μ_0 and out of control value μ_1. K is expressed by $K = \frac{\delta}{2}\sigma = \frac{|\mu_1 - \mu_0|}{2}$ where δ is the shift size from standard deviation, σ.

C. Outbreak Mining

In outbreak mining, the normalized outbreak data is mined with DT algorithm called DCA. In this phase it has two tasks; firstly is to determine outbreak baseline and secondly is mining the outbreak dataset using DCA. Outbreak baseline is a default value before DCA can raise an alarm. The value is determined based the previous outbreak dataset from several years is taken into consideration for pre-mining.

After outbreak baseline determination, the outbreak data is presented to DCA for detection. Fig. 2 depicts the general step of DCA. The aim is to generate multi context antigen value (MCAV) for each antigen that represents the final condition of an outbreak. The general process of this phase is setting the initial parameter, updating input signal and antigen, calculating the MCAV, and categorized the antigen. Based on the generated MCAV, the outbreak is detected if the MCAV is greater than outbreak baseline; in other words, the cell is fully matured. The alarm is turn off when MCAV is below the baselines.

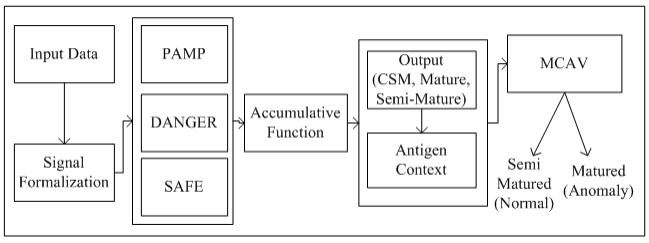

Figure 2. The general step of DCA

D. Outbreak Analysis

Outbreak analysis is under the health department control. Once DCA raises an alarm, the notification will be verified by health worker team. After the verification, an immediate prevention plan will be arranged. In this stage, the health workers will follow the health surveillance system procedure in managing outbreak period. A post-mortem session will be conducted once the outbreak ends.

V. THE PRELIMINARY RESULT

In this section, the preliminary result of outbreak detection based on DT is presented. The experiment is conducted based on dengue outbreak occurred in district of Seremban, Malaysia. The emergency visit and climate condition are taken as input signal. After the input signal is normalized, the dataset is mined with DCA. The model is evaluated based on four metrics that are detection rate (*DR*), specificity (*SPS*), false alarm rate (*FAR*), and accuracy (*%*). To check the inconsistencies, the data is mined 50 times and the average and standard deviation of each metrics are taken into consideration. The preliminary result is shown in Table III.

TABLE III. THE PRELIMINARY RESULT OF DENGUE OUTBREAK DETECTION MODEL BASED ON DT

Iteration	DR	SPS	FAR	%
1	0.970	0.709	0.291	0.805
2	0.978	0.700	0.300	0.803
3	0.948	0.709	0.291	0.797
4	0.933	0.678	0.322	0.773
5	0.948	0.657	0.343	0.764
6	0.963	0.704	0.296	0.800
7	0.970	0.683	0.317	0.789
8	0.970	0.696	0.304	0.797
9	0.978	0.700	0.300	0.803
10	0.956	0.687	0.313	0.786
11	0.926	0.722	0.278	0.797
12	0.978	0.700	0.300	0.803
13	0.970	0.713	0.287	0.808
14	0.993	0.691	0.309	0.803
15	0.963	0.717	0.283	0.808
16	0.978	0.687	0.313	0.795
17	0.978	0.704	0.296	0.805
18	0.978	0.717	0.283	0.814
19	0.978	0.717	0.283	0.814
20	0.948	0.661	0.339	0.767
21	0.970	0.704	0.296	0.803
22	0.956	0.735	0.265	0.816
23	0.963	0.722	0.278	0.811
24	0.963	0.713	0.287	0.805
25	0.970	0.665	0.335	0.778
26	0.956	0.748	0.252	0.825
27	0.941	0.683	0.317	0.778
28	0.970	0.739	0.261	0.825

29	0.970	0.704	0.296	0.803
30	0.985	0.700	0.300	0.805
31	1.000	0.683	0.317	0.800
32	0.970	0.704	0.296	0.803
33	0.963	0.722	0.278	0.811
34	0.963	0.674	0.326	0.781
35	0.970	0.691	0.309	0.795
36	0.956	0.683	0.317	0.784
37	0.985	0.735	0.265	0.827
38	0.956	0.709	0.291	0.800
39	0.970	0.722	0.278	0.814
40	0.978	0.674	0.326	0.786
41	0.985	0.700	0.300	0.805
42	0.985	0.726	0.274	0.822
43	0.993	0.696	0.304	0.805
44	1.000	0.704	0.296	0.814
45	0.963	0.704	0.296	0.800
46	0.993	0.709	0.291	0.814
47	0.993	0.674	0.326	0.792
48	0.948	0.687	0.313	0.784
49	0.941	0.683	0.317	0.778
50	0.970	0.730	0.270	0.819
AVERAGE	0.969	0.701	0.299	0.800
STANDARD DEVEIATION	0.017	0.021	0.021	0.015

The initial result in Table III indicates the proposed model generates a consistent result in all iterations when low standard deviations are recorded. The model produces high DR (0.969) and SPS (0.701) as well as scores low FAR (0.299). The average accuracy is 0.800 which is considered high. This shows DT has ability to detect true outbreak as outbreak and non-outbreak as non outbreak. However, the model need be evaluated with other detection technique. The information in Fig. 3 indicates MCAV of each monitored weeks. If the MCAV score is greater than outbreak threshold (0.38), the model classifies the week as outbreak.

VI. CONCLUSION

This ongoing research aims to improve outbreak detection performance inspired from artificial immune system, particularly the danger theory approach. Since the behavior of danger theory and outbreak characteristics indicates similarities, the proposed model is expected to overcome the weakness of early outbreak signal and produces a balance between DR and FAR. The preliminary result indicates the ability of DT as new alternative for outbreak detection modeling. In the next step, the model will be tested on different parameter setting to optimize the result, and comparison will be made with other existing outbreak detection model such CUSUM, EWMA, and Moving Average. Besides that, more outbreak datasets will be experimented in future.

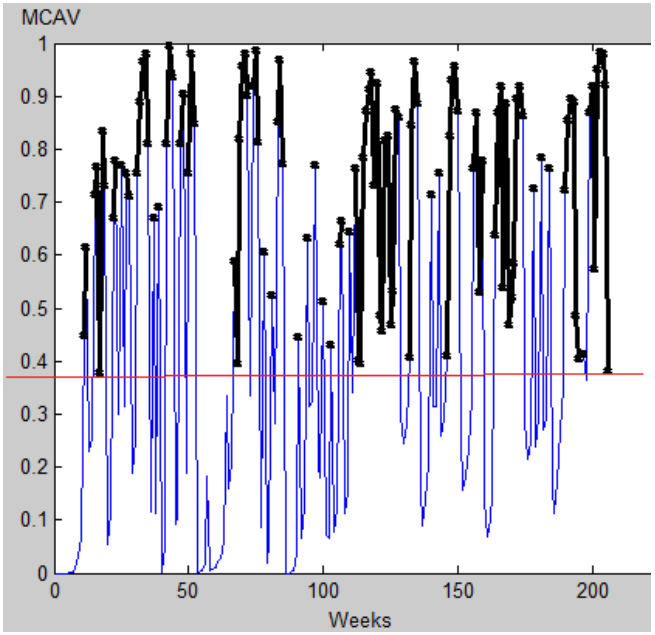

Figure 3. The MCAV of each monitored weeks

ACKNOWLEDGMENT

The authors gratefully acknowledge Seremban Public Health Department and Faculty of Health Sciences, UKM as well as the Exploratory Research Grant Scheme for supporting this research project through grant ERGS/1/2011/STG/UKM/02/49.

REFERENCES

[1] R. Watkins, S. Eagleson, B. Veenendaal, G. Wright, and A. Plant, "Disease surveillance using a hidden Markov model," *BMC Medical Informatics and Decision Making,* vol. 9, p. 39, 2009.

[2] A. Wilder-Smith, "The severe acute respiratory syndrome: Impact on travel and tourism," *Travel Medicine and Infectious Disease,* vol. 4, pp. 53-60, 2006.

[3] J. B. S. Ong, M. I. C. Chen, A. R. Cook, H. C. Lee, V. J. Lee, R. T. P. Lin, P. A. Tambyah, and L. G. Goh, "Real-Time Epidemic Monitoring and Forecasting of H1N1-2009 Using Influenza-Like Illness from General Practice and Family Doctor Clinics in Singapore," *PLoS ONE,* vol. 5, p. e10036, 2010.

[4] K. D. Kochanek, J. Xu, S. L. Murphy, A. M. Minini, and H.-h. Kung, "Deaths: preliminary data for 2009," U.S. Department of Health and Human Services, CDC2011.

[5] M. McAleer, B.-W. Huang, H.-I. Kuo, C.-C. Chen, and C.-L. Chang, "An econometric analysis of SARS and Avian Flu on international tourist arrivals to Asia," *Environmental Modelling & Software,* vol. 25, pp. 100-106, 2010.

[6] L. Schiöler and M. Frisén, "Multivariate outbreak detection," *Journal of Applied Statistics,* vol. 39, pp. 223-242, 2012/02/01 2011.

[7] Z. Li, S. Lai, D. L. Buckeridge, H. Zhang, Y. Lan, and W. Yang, "Adjusting outbreak detection algorithms for surveillance during epidemic and non-epidemic periods," *Journal of the American Medical Informatics Association,* August 11, 2011 2011.

[8] S. Unkel, C. P. Farrington, P. H. Garthwaite, C. Robertson, and N. Andrews, "Statistical methods for the prospective detection of infectious disease outbreaks: A review," *Journal of the Royal Statistical Society. Series A: Statistics in Society,* vol. 175, pp. 49-82, 2012.

[9] W. Wong and A. Moore, "Chapter 14- Classical time series methods for biosurveillance," in *Handbook of biosurveillance*. vol. 217-233, M. M. Wagner, A. W. Moore, and R. M. Aryel, Eds., ed Burlington: Academic Press, 2006.

[10] L. Hsin-Min, D. Zeng, and C. HsinChun, "Prospective Infectious Disease Outbreak Detection Using Markov Switching Models," *Knowledge and Data Engineering, IEEE Transactions on,* vol. 22, pp. 565-577, 2010.

[11] X. Jiang and G. Cooper, "A real-time temporal Bayesian architecture for event surveillance and its application to patient-specific multiple disease outbreak detection," *Data Mining and Knowledge Discovery,* vol. 20, pp. 328-360, 2010.

[12] Z. Awang Long, "Teknik Perlombongan Corak Data Terpencil-kerap (DTK) Bagi Pengesanan wabak Dalam Pegawasan Kesihatan Awam," PhD, Universiti Kebangsaan Malaysia, Malaysia, 2012.

[13] N. A. Husin, N. Salim, and A. R. Ahmad, "Modeling of dengue outbreak prediction in Malaysia: A comparison of Neural Network and Nonlinear Regression Model," in *International Symposium on Information Technology (ITSim)* 2008, pp. 1-4.

[14] Z. Jie, L. Jie, and Z. Guangquan, "A hybrid knowledge-based prediction method for avian influenza early warning," in *Systems, Man and Cybernetics, 2009. SMC 2009. IEEE International Conference on*, 2009, pp. 617-622.

[15] W.-K. Wong, A. Moore, G. Cooper, and M. Wagner, "What's Strange About Recent Events (WSARE): An Algorithm for the Early Detection of Disease Outbreaks," *Journal of Machine Learning Research* vol. 6, pp. 1961--1998., 2005.

[16] K. Das, J. Schneider, and D. B. Neill, "Anomaly pattern detection in categorical datasets," presented at the Proceedings of the 14th ACM SIGKDD international conference on Knowledge discovery and data mining, Las Vegas, Nevada, USA, 2008.

[17] F.-C. Tsui, M. M. Wanger, and J. Espino, "Chapter 13 - Case Detection Algorithm," in *Handbook of Biosurveillance*, M. M. Wagner, A. W. Moore, and R. M. Aryel, Eds., ed Burlington: Academic Press, 2006, pp. 199-216.

[18] WHO. (2013, 8 July). *Disease Outbreak*. Available: http://www.who.int/topics/disease_outbreaks/en/

[19] S. B. Seng, A. K. Chong, and A. Moore, "Geostatistical Modelling, Analysis and Mapping of Epidemiology of Dengue Fever in Johor State, Malaysia," presented at the 17th Annual Colloquium of the Spatial Information Research Centre (SIRC 2005), Dunedin, New Zealand, 2005.

[20] E. N. Naumova, E. O'Neil, and I. MacNeill, "INFERNO: A System for Early Outbreak Detection and Signature Forecasting," 2005.

[21] V. Lampos and N. Cristianini, "Tracking the flu pandemic by monitoring the social web," in *Cognitive Information Processing (CIP), 2010 2nd International Workshop on*, 2010, pp. 411-416.

[22] C.-T. Tsai, F.-C. Sung, P. Chen, and S.-C. Lin, "Exploring the spatial and temporal relationships between mosquito population dynamics and dengue outbreaks based on climatic factors," *Stochastic Environmental Research and Risk Assessment,* pp. 1-10, 2011.

[23] E. Quincey and P. Kostkova, "Early Warning and Outbreak Detection Using Social Networking Websites: The Potential of Twitter," in *Electronic Healthcare*. vol. 27, P. Kostkova, Ed., ed: Springer Berlin Heidelberg, 2010, pp. 21-24.

[24] X. Wei, H. Zhen-Wen, and M. Jian, "A neural netwok based approach to detect influenza epidemics using search engine query data," in *Machine Learning and Cybernetics (ICMLC), 2010 International Conference on*, 2010, pp. 1408-1412.

[25] Z. Xichuan, Y. Jieping, and F. Yujie, "Tuberculosis Surveillance by Analyzing Google Trends," *Biomedical Engineering, IEEE Transactions on,* vol. 58, pp. 2247-2254, 2011.

[26] P. Matzinger, "Tolerance, danger and the extended family.," *Annual Reviews in Immunology,* pp. 991–1045, 1994.

[27] J. Greensmith, U. Aickelin, and S. Cayzer, "Introducing Dendritic Cells as a Novel Immune Inspired Algorithm for Anomaly Detection " in *4tn International Conference in Artificial Immune Systems (ICARIS)*, 2005, pp. 153-167.

[28] U. Aickelin and J. Greensmith, "Sensing Danger: Innate Immunology for Intrusion Detection," *Information Security Technical Report 12,* pp. 218-227, 2007.

[29] J. Greensmith and U. Aickelin, "The Deterministic Dendritic Cell Algorithm," presented at the Proceedings of the 7th international conference on Artificial Immune Systems, Phuket, Thailand, 2008.

[30] J. Greensmith, J. Twycross, and U. Aickelin, "Dendritic Cells for Anomaly Detection," in *Evolutionary Computation, 2006. CEC 2006. IEEE Congress on*, 2006, pp. 664-671.

[31] J. Kim, P. Bentley, C. Wallenta, M. Ahmed, and S. Hailes, "Danger is ubiquitous: Detecting malicious activities in sensor networks using the dendritic cell algorithm," in *ICARIS 2006*, 2006, pp. 390 - 403.

[32] A. Iqbal and M. A. Maarof, "Danger Theory and Intelligent Data Processing," *World Academy of Science, Engineering and Technology,* vol. 3, pp. 646-649, 2007.

[33] Y. Al-Hammadi, U. Aickelin, and J. Greensmith, "DCA for bot detection," in *Evolutionary Computation, 2008. CEC 2008. (IEEE World Congress on Computational Intelligence). IEEE Congress on*, 2008, pp. 1807-1816.

[34] Z. Junmin and L. Yiwen, "Integrating Innate and Adaptive Immunity for Worm Detection," in *Computational Intelligence for Modelling Control & Automation, 2008 International Conference on*, 2008, pp. 645-650.

[35] Z. Junmin and L. Yiwen, "A Novel Intrusion Detection Model Based on Danger Theory," in *Computational Intelligence and Industrial Application, 2008. PACIIA '08. Pacific-Asia Workshop on*, 2008, pp. 867-871.

[36] N. B. I. Al-Dabagh and I. A. Ali, "Design and implementation of artificial immune system for detecting flooding attacks," in *High Performance Computing and Simulation (HPCS), 2011 International Conference on*, 2011, pp. 381-390.

[37] O. Chung-Ming and C. R. Ou, "Immunity-Inspired Host-Based Intrusion Detection Systems," in *Genetic and Evolutionary Computing (ICGEC), 2011 Fifth International Conference on*, 2011, pp. 283-286.

[38] F. X. Sun and Z. G. Wu, "Immune Danger Theory Based Model for SYN Flooding Attack Situation Awareness," *Journal of Advanced Materials Research,* vol. 181-182, pp. 66-71, 2011.

[39] H. Salmon, C. Farias, P. Loureiro, L. Pirmez, S. Rossetto, P. A. Rodrigues, R. Pirmez, F. Delicato, and L. Costa Carmo, "Intrusion Detection System for Wireless Sensor Networks Using Danger Theory Immune-Inspired Techniques," *International Journal of Wireless Information Networks,* pp. 1-28, 2012/06/01 2012.

[40] R. Huang, H. Taufik, and A. K. Nagar, "Artificial Dendritic Cells Algorithm for Online Break-in Fraud Detection," presented at the Second International Conference on Developement in eSystems Engineering, 2009.

[41] R. Huang, H. Tawfik, and A. K. Nagar, "On the use of innate and adaptive parts of artificial immune systems for online fraud detection," in *Bio-Inspired Computing: Theories and Applications (BIC-TA), 2010 IEEE Fifth International Conference on*, 2010, pp. 1669-1676.

[42] S. Manzoor, M. Z. Shafiq, S. M. Tabish, and M. Farooq, "A Sense of 'Danger' for Windows Processes," in *Artificial Immune Systems*. vol. 5666, P. Andrews, J. Timmis, N. L. Owens, U. Aickelin, E. Hart, A. Hone, and A. Tyrrell, Eds., ed: Springer Berlin Heidelberg, 2009, pp. 220-233.

[43] B. Ran, J. Timmis, and A. Tyrrell, "The Diagnostic Dendritic Cell Algorithm for robotic systems," in *Evolutionary Computation (CEC), 2010 IEEE Congress on*, 2010, pp. 1-8.

[44] C. E. Prieto, F. Nino, and G. Quintana, "A goalkeeper strategy in robot soccer based on Danger Theory," in *Evolutionary Computation, 2008. CEC 2008. (IEEE World Congress on Computational Intelligence). IEEE Congress on*, 2008, pp. 3443-3447.

[45] N. Lay and I. Bate, "Improving the reliability of real-time embedded systems using innate immune techniques," *Evolutionary Intelligence,* vol. 1, pp. 113-132, 2008.

[46] E. Bendiab and M. K. Kholladi, "Recognition of Plant Leaves Using the Dendritic Cell Algorithm," *International Journal of Digital Information and Wireless Communications (IJDIWC),* vol. 1, pp. 284-292, 2011.

[47] E. Bendiab and M. Kholladi, "The Danger Theory Applied To Vegetal Image Pattern Classification," in *Artificial Immune Systems*. vol. 6825, P. Liò, G. Nicosia, and T. Stibor, Eds., ed: Springer Berlin Heidelberg, 2011, pp. 406-418.

[48] U. Aickelin and S. Cayzer, "The Danger Theory and Its Application to Artificial Immune Systems," in *1st International Conference on ARtificial Immune Systems (ICARIS-2002)*, Canterbury, UK, 2002, pp. 141-148.

[49] W.-K. Wong, "Data Mining for Disease Outbreak Detection," PhD, Carnigie Mallon University, Pittsburgh, 2004.

[50] J. Greensmith, "The Dendritic Cell Algorithm," PhD, University of Nottingham, 2007.

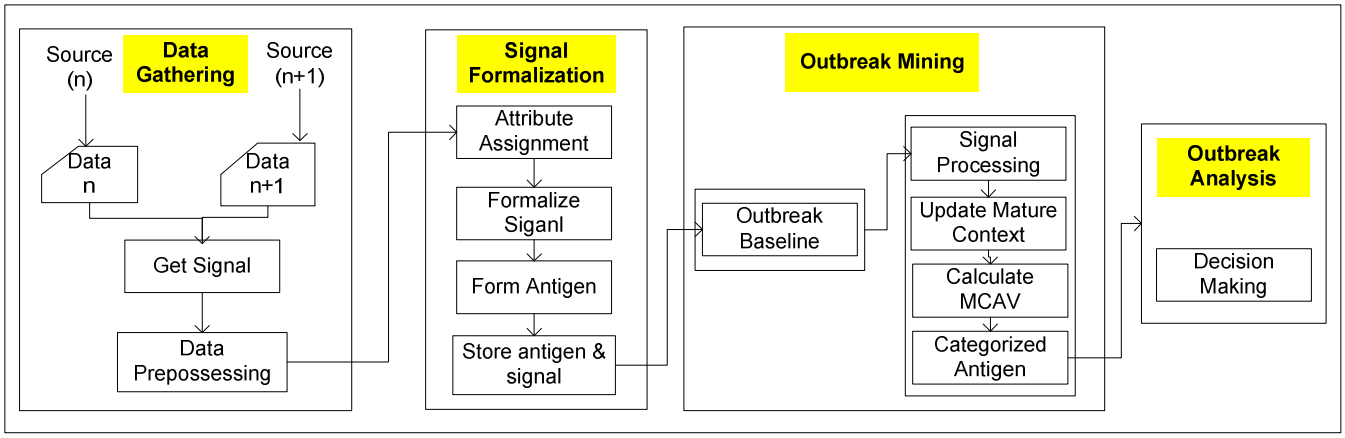

Figure 4. The proposed outbreak detection model based on DT