Bayesian Prediction of Dengue Outbreaks Based on Disease Surveillance and Relational and Meteorological Data

Raghvendra Jain[a], Sra Sontisirikit[b], Sopon Iamsirithaworn[c], Marc Cavazza[d], Helmut Prendinger[a]

[a]*jain@nii.ac.jp, helmut@nii.ac.jp*
National Institute of Informatics,
2-1-2 Hitotsubashi, Chiyoda-ku, Tokyo, 101-8430, Japan
[b]*arttioz@gmail.com*
Asian Institute of Technology, School of Engineering and Technology, Thailand
[c]*iamsiri@gmail.com*
Department of Disease Control Thirteenth Division, Bangkok, Thailand
[d]*M.O.Cavazza@kent.ac.uk*
School of Engineering and Digital Arts, University of Kent

Abstract

To create early warning system of dengue outbreaks, we present a machine learning-based methodology capable of providing real-time (nowcast) and forecast estimates of dengue prediction in the Thailand by leveraging data from multiple data sources including: meteorological data, lag variables of disease surveillance, relational data of infected cases and the data on spatial heterogeneity. Bayesian Network, a probabilistic graphical model was used to model causal relationships between the predictor variables and the dengue surveillance data.

Our methodology enables...

We evaluate the predictive ability..

Our approach demonstrates several advantages: (1)...(2)..

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Research is needed to create early warnings of dengue outbreaks to inform stakeholders and control the disease. This analysis composes of a comparative set of prediction models including only meteorological variables; only lag variables of disease surveillance; as well as combinations of meteorological and lag disease surveillance variables. Generalized linear regression models were used to fit relationships between

the predictor variables and the dengue surveillance data as outcome variable on the basis of data from 2001 to 2010. Data from 2011 to 2013 were used for external validation purposed of prediction accuracy of the model. Model fit were evaluated based on prediction performance in terms of detecting epidemics, and for number of predicted cases according to RMSE and SRMSE, as well as AIC. An optimal combination of meteorology and autoregressive lag terms of dengue counts in the past were identified best in predicting dengue incidence and the occurrence of dengue epidemics. Past data on disease surveillance, as predictor alone, visually gave reasonably accurate results for outbreak periods, but not for non-outbreaks periods. A combination of surveillance and meteorological data including lag patterns up to a few years in the past showed most predictive of dengue incidence and occurrence in Yogyakarta, Indonesia. The external validation showed poorer results than the internal validation, but still showed skill in detecting outbreaks up to two months ahead. Prior studies support the fact that past meteorology and surveillance data can be predictive of dengue. However, to a less extent has prior research shown how the longer-term past disease incidence data, up to years, can play a role in predicting outbreaks in the coming years, possibly indicating cross-immunity status of the population.

Our work

To create early warning system of dengue outbreaks, we present a machine learning-based methodology capable of providing real-time (nowcast) and forecast estimates of dengue prediction in each of the fifty districts of Thailand by leveraging data from multiple data sources. Using a set of prediction variables we show an increasing prediction accuracy of the model with an optimal combination of predictors which include: meteorological data, clinical data, lag variables of disease surveillance, socio-economic data and the data encoding spatial dependence on dengue transmission. We use generalized Generalized Additive Models (GAMs) to fit the relationships between the predictors and the clinical data of Dengue hemorrhagic fever (DHF) on the basis of the data from 2008 to 2012. Using the data from 2013 to 2015 and a comparative set of prediction models we evaluate the predictive ability of the fitted models according to RMSE and SRMSE, BIC as well as AIC. We also show that for the prediction of dengue outbreaks within a district, the influence of dengue incidences and socio-economic data from

the surrounding districts is statistically significant, possibly indicating the influence of movement pattens of people and spatial heterogeneity of human activities on the spread of the epidemic.

1. Introduction

Dengue, a mosquito borne viral disease, has been a significant cause of death and hospitalization among children in developing countries such as India, Thailand etc. Despite this, the surveillance for diagnosing dengue has been limited which makes it difficult to generate detailed information on its epidemiology. The number of cases of dengue fever has increased dramatically since the 1960s, with between 50 and 528 million people infected yearly. Hundreds of thousands of cases of dengue are reported each year in tropical regions of the Americas, Africa, Asia, and Oceania. Globally, more than 2.5 billion people are at risk [1]. The World Health Organization (WHO) estimates that more than 50 million dengue virus (DENV) infections and 20,000 dengue disease-related deaths occur annually worldwide [2, 3], and a recent disease distribution model estimated that were 390 million DENV infections in 2010, including 96 million apparent infections. Overall, 70% of these apparent infections occurred in Asia [4]. In 2015 alone, there were 111,826 reported cases in Thailand [5].

Thailand began to experience Dengue fever in 1949 and it became pandemic in the country for the first time in 1958 in Bangkok Thonburi [6]. Reports of clinically diagnosed cases of DF, DHF and DSS are compiled weekly at each hospital using a standard form containing essential patient information. These are then sent to the Provincial Health Offices who undertake local control measures and subsequently forward the information to the Epidemiology Department in Bangkok [7]. The situation of dengue fever since the year 1958 -2015 are likely to rise [8]. Most patients are in 0-14 age group, the highest incidence rate in the age group 5-9 years, the ratio of female to male patients is similar [9, 8].

There are four distinct, but closely related, serotypes of the virus that cause dengue (DEN-1, DEN-2, DEN-3 and DEN-4) [10, 11]. Recovery from infection by one provides lifelong immunity against that particular serotype. However, cross-immunity to the other serotypes after recovery is only partial and temporary (6-12 months) [10]. Subsequent infections by other serotypes increase the risk of developing severe dengue. Once infected, humans become the main carriers and multipliers of the virus, serving as a source of the virus for uninfected mosquitoes. The virus circulates in the blood of an infected person for 2-7 days, at approximately the same time that the person develops a fever. Patients who are already infected with the dengue virus can transmit the infection via Aedes mosquitoes after the first symptoms appear (during 4-5 days; maximum 12) [12].

Symptoms, which usually begin four to six days after infection and last for up to 10 days, may include: sudden high fever, severe headaches, pain behind the eyes, severe joint and muscle pain, fatigue, nausea, vomiting, skin rash (which appears two to five days after the onset of fever) and mild bleeding (such a nose bleed, bleeding gums, or easy bruising) Sometimes, symptoms are mild and can be mistaken for those of the flu or another viral infection. Younger children and people who have never had the infection before tend to have milder cases than older children and adults. However, serious problems can develop. These include dengue hemorrhagic fever, a rare complication characterized by high fever, damage to lymph and blood vessels, bleeding from the nose and gums, enlargement of the liver, and failure of the circulatory system. The symptoms may progress to massive bleeding, shock, and death. This is called dengue shock syndrome (DSS) [13].

Transmission of DENV has increased dramatically in the past two decades, making DENV one of the most important human pathogens among arthropod-borne viruses [14]. Moreover, There are currently no licensed vaccines or specific therapeutics, and substantial vector control efforts have not stopped its rapid emergence and global spread [15]. About 50-100 million dengue fever infections occur every year in tropical and subtropical countries[16]. The infection by one type usually gives lifelong immunity to that type, but only short-term immunity to the others. Transmission occurs through the bite of infected Aedes mosquitoes, principally Aedes aegypti. This kind of

mosquito prefers to breed in areas of stagnant water, such as flower vases, uncovered barrels, buckets, and discarded tires, but the most dangerous areas are wet shower floors and toilet tanks, as they allow the mosquitoes to breed inside the residence. Flight range studies suggest that most female Aedes mosquito may spend their lifetime in or around the houses where they emerge as adults and they usually fly an average of 400 metres [17]. Although the lifespan of an adult Aedes mosquito is two to four weeks depending on conditions [18], the eggs can be viable for over a year in a dry state, which allows the mosquito to re-emerge after a cold winter or dry spell [19].

There have been numerous urban outbreaks of dengue with significant health and economic impact [16, 20, 21, 22]. Studies in Thailand and Brazil have shown that the social and economic impact is equivalent to that of malaria in these countries [23, 24]. Therefore, the goal of this research is to create a system that can acquire detailed relevant information and use it to predict the occurrence of dengue within a geographical region, so that public health experts can prepare for, manage and control the epidemic.

The risk of epidemic dengue transmission is determined by a combination of factors that include level of human immunity to virus serotypes, virulence characteristics of the virus strain, abundance of Aedes mosquitoes, weather, and population statistics in target area [25]. Several potential predictive indicators for outbreaks have been described[26, 27, 28, 29]. There are several environmental factors related to dengue outbreak that have been identified from case studies in Southeast Asia [30, 28, 29, 31]. There are many research conclude that most dengue cases are occurred in urban areas due to various contributing factors such high population density, inadequate housing, and inappropriate human behavioral practices [32, 33, 34]. Surveillance of Aedes mosquito density is important for construction models of dengue transmission, in order to prioritize areas and seasons for vector control. The 80% of larvae or pupa in house are from Aedes mosquito. [29] extract land-use types using object-based and spatial metric approaches to explore dengue incidence in relation to the surrounding environment in near real-time using Google and Advanced Land Observation Satellite images. Geospatial analysis on public health data indicated that most of the dengue cases were found in densely populated areas *surrounded by dense vegetation*. Dense vegetation can facilitate the invasion of Aedes mosquitoes by providing abundant resting sites.

The empirical relationship of climatic factors rainfall, temperature and humidity with the DF/DHF incidences has been studied [31, 35, 36, 37, 38, 39]. According to the development period from a mosquito egg to the human disease, there is a time lag of about one month that leads to DF/DHF cases occurring in 7 - 45 days. Thus, DF/DHF cases at time t (in month e.g. May) depend on others factors at time t-1 (i.e. one month before month) as validated in the empirical analysis [31]. The diurnal temperature range (DTR) is the difference between the daily maximum and minimum temperature. The experimental evaluation shows that DTR affects two important parameters underlying dengue virus (DENV) transmission by Aedes mosquito [40].

2. Materials and Methods

2.1. Study area

The dengue outbreak in Bangkok can affect to dengue situation for the whole country, because Bangkok is a very crowded city locate at the center part of Thailand. In the 2010 census, Bangkok had a population of 8.28 million, although just 5.7 million were registered residents. Much of the daytime population commutes from surrounding areas in the region, bringing the total population to 15 million [41]. During winter season, temperature in Bangkok still high around 28-35 degree Celsius and there is rain in every season [42]. This makes the city is very suitable for Aedes mosquito to breeding making dengue virus spread from Bangkok in every season. Moreover, many people who live in Bangkok travel to other provinces frequently, so these people may be the main carriers and multipliers of the virus that cause dengue outbreak in other part of Thailand. Figure 1 shows the relationship between incidences of dengue per one hundred thousand people in Thailand versus Bangkok. The dengue incident rate in Bangkok is nearly the same as the whole country. So, if we could reduce dengue incident rates in Bangkok, the rate in Thailand will be reduce too because there will be fewer dengue carriers who travel from Bangkok to other parts of Thailand.

Figure 2 (a) shows the increase of dengue cases in Bangkok up to 2015. The average number of dengue cases in Bangkok from 2005 until 2015 is around 10,758 cases per year. The highest number of dengue cases in Bangkok is 28,177 cases which hap-
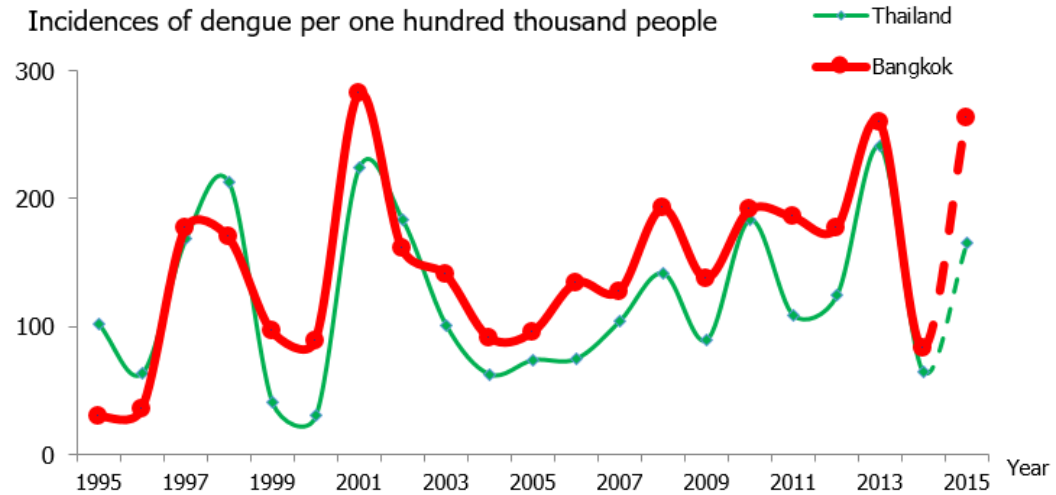
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Figure 1: Relationship between incidences of dengue per one hundred thousand people in Thailand versus Bangkok from 2005 - 2014.

pened in 2015. Figure 2 (b) shows changes in dengue serotypes from 2005 to 2015. The percentage of dengue serotypes DENV 1 - 4 in the central part of Thailand changed every year, making people who already have immunity to one serotype susceptible to infection with another serotype in the following year. Figure 3 shows the effect of season on dengue cases. In rain season (mid May - October), dengue cases rise dramatically, and then they decrease suddenly in summer season (February - mid May). The reason that November has the highest number cases is that dengue virus in patients need 4 - 10 days for the incubation period. So most dengue patients in November are infected in rain season (October).

2.2. Prediction variable and data collection

There are three main factors that affect to dengue incidence cases: other cases of dengue virus, presence of Aedes mosquitoes, and various human factors. Dengue fever cannot spread to humans from other animal; mosquitoes are mainly carries. Typically, people infected with dengue virus are asymptomatic (80%) or have only mild symptoms , such as an uncomplicated fever [44, 45]. In Bangkok's case, dengue fever and

7
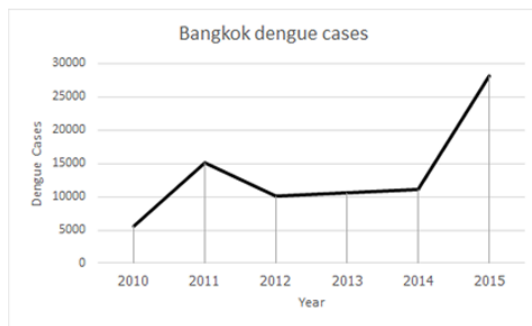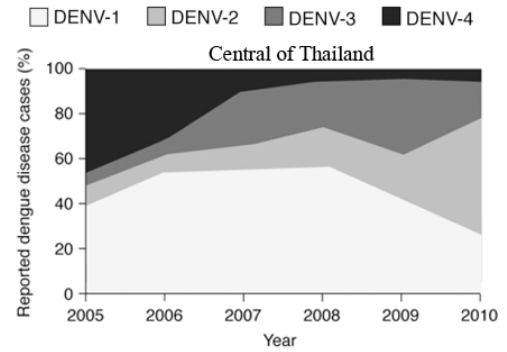
(a) Dengue cases

(b) Dengue virus serotype

Figure 2: (a) Dengue cases from 2010 - 2015 in Bangkok. (b) Dengue serotypes from 2005 - 2010 in central Thailand. Data from Department of Disease Control 13th Division and [43].
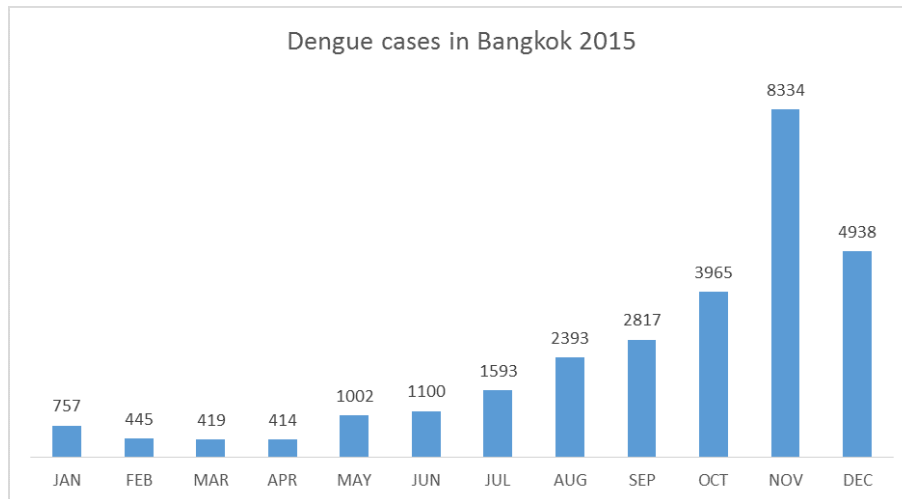

Figure 3: Monthly dengue cases in Bangkok 2015. Data from Department of Disease Control 13th Division.

8

dengue hemorrhagic fever were reported in each season, mean, dengue virus is always present in human too. Once infected, *humans* become the main carriers and multipliers of the virus, serving as a source of the virus for uninfected *Aedes mosquitoes* to carry.

1. Dengue virus prediction variable:

   - **Monthly DF/DHF incidents in the district** represents the number of dengue virus report in the target district.

   - **Monthly DF/DHF incident in the nearby districts** represents the number of dengue virus reports which may affect to the target district

2. Aedes mosquito prediction variables

   - **Monthly rainfall in district** represents the density of Aedes mosquitoes in the target district.

   - **Monthly average diurnal temperature range (DTR) in Bangkok** represents the health of the dengue virus in Aedes mosquito. Higher DTR means lower health of dengue virus in Aedes mosquito, deceasing infection rates.

3. Human prediction variables

   - **Population with age less than 35 in the district** represents the proportion of the district population that has a high risk for dengue fever.

   - **Population age 35+ in the district** represents the proportion of the district population that has a low risk for dengue fever.

   - **Annual population density in district** represents how easy to transmit dengue virus from one person other other person by Aedes mosquito.

   - **Number of communities in the district** represents how large the group are, make it more of less convenient transmission of dengue virus by Aedes mosquito.

2.2.1. Analysis Using Bayesian network model

Figure 4 depicts the directed acyclic graph for the Bayesian network, and table 1 describes the conditional probability distributions of variables in model.

9

Name	Abbreviation	Predict possibilities output	Parents (Pa)
Mosquito density	MD	MD_0: Low MD_1: Moderate MD_2: High	Outside house breeding container Inside house breeding container Diurnal temperature range
Outside house breeding container	OB	OB_0:Low OB_1:High	Neglect garbage Rain
Inside house breeding container	IB	IB_0:Low IB_1:High	Cleaning activity House type
Neglect garbage	NG	NG_0:Low NG_1:High	Cleaning activity Population density
Cleaning activity	CA	CA_0:Low CA_1:High	Awareness
Rain	R	R_1:Low R_1:Moderate R_2:High	Season
Diurnal temperature range	DTR	DTR_0:Low DTR_1:High	Season
House Density	HT	HT_0:Low HT_1:High	
Awareness	A	A_0:Low A_1:High	
Season	S	S_0:Summer S_1:Winter S_2:Rain	
Population density	PD	PD_0:Low PD_1:High	

Table 1: Notation of the variables used in Bayesian network model

Pattern			P(MD_0 | PA)	P(MD_1 | PA)	P(MD_2 | PA)
OB_0	IB_0	DTR_0	1	0	0
OB_0	IB_0	DTR_1	1	0	0
OB_0	IB_1	DTR_0	0	0.7	0.3
OB_0	IB_1	DTR_1	0.2	0.6	0.2
OB_1	IB_0	DTR_0	0	0.3	0.7
OB_1	IB_1	DTR_0	0	0	1
OB_1	IB_0	DTR_1	0	0.5	0.5
OB_1	IB_1	DTR_1	0	0	1

Table 2: Conditional probability distribution of mosquito density

Pattern		P(OB0 | PA)	P(OB1 | PA)
NB_0	R_0	1	0
NB_0	R_1	0.4	0.6
NB_0	R_2	0.2	0.7
NB_1	R_0	0.9	0.1
NB_1	R_1	0.2	0.8
NB_1	R_2	0	1

Table 3: Conditional probability distribution of density of outside house breeding spot

Pattern		P(IB0 | PA)	P(IB1| PA)
CA0	HT0	0.6	0.4
CA0	HT1	0	1
CA1	HT0	1	0
CA1	HT1	0.4	0.6

Table 4: Conditional probability distribution of density of inside house breeding container

Pattern		P(NG0 | PA)	P(NG1 | PA)
CA0	PD0	0.4	0.6
CA0	PD1	0	1
CA1	PD0	0.9	0.1
CA1	PD1	0.6	0.4

Table 5: Conditional probability distribution of neglect garbage

Pattern	P(CA0 | PA)	P(CA1 | PA)
A0	1	0
A1	0	1

Table 6: Conditional probability distribution of cleaning activity

Pattern	P(R0 | PA)	P(R1 | PA)	P(R2 | PA)
S0	1	0	0
S1	0.4	0.6	0
S2	0	0.2	0.8

Table 7: Conditional probability distribution of rain

Pattern	P(DTR0 | PA)	P(DTR1 | PA)
S0	0	1
S1	1	0
S2	0.9	0.1

Table 8: Conditional probability distribution of Diurnal temperature range

Name	Abbreviation	Predict possibilities output	Parents (Pa)
Actual report DF/DHF Cases	ARDC	ARDC0:Under report ARDC1:Moderate report ARDC2:Active report	Hospital Awareness Dengue rate
Dengue rate	DR	DR0:Low DR1:Moderate DR2:High	Infected Mosquitos Immune Dengue People
Density of infected Mosquitos	IM	IM0:Low IM0:Moderate IM1:High	Dengue Cases Dengue Case of nearby district Diurnal temperature range Mosquito density
Immune Dengue People	IP	IP0:Low IP1:Moderate IP2:High	Dengue Cases
Diurnal temperature range	DTR	DTR0:Low DTR1:High	Season
Dengue Cases	DC	DC0:Low DC1: Moderate DC2:High	
Dengue Case of nearby district	DCN	DCN0:Low DCN1: Moderate DCN2:High	
Mosquito density	MD	MD0: Low MD1: Moderate MD2: High	
Hospital Awareness	HA	HA0: Low HA1: High	
Population Density	PD	PD0: Low PD1: High	
Season	S	S0:Summer S1:Winter S2:Rain	
Awareness	A	A0:Low A1:High	

13

Table 9: Notation of the variables used in Bayesian network model

Pattern		P(ARDC 0 | PA)	P(ARDC 1 | PA)	P(ARDC2 | PA)
HA0	DR0	1	0	0
HA0	DR1	0.7	0.2	0.1
HA0	DR2	0.3	0.5	0.2
HA1	DR0	0.7	0.3	0
HA1	DR1	0.3	0.5	0.2
HA1	DR2	0	0.2	0.8

Table 10: Conditional probability distribution of Actual report DF/DHF Cases

Pattern		P(DR0 | PA)	P(DR 1 | PA)	P(DR 2 | PA)
IM0	IP x	1	0	0
IM1	IP 0	0	0.3	0.7
IM1	IP 1	0.1	0.4	0.5
IM1	IP 2	0.1	0.5	0.4
IM2	IP 0	0	0	1
IM2	IP 1	0	0.1	0.9
IM2	IP 2	0	0.3	0.7

Table 11: Conditional probability distribution of dengue incident rate (DF/DHF cases)

Pattern	P(IP0 | PA)	P(IP1 | PA)	P(IP2 | PA)
DC0	1	0	0
DC1	0	1	0
DC2	0	0	1

Table 12: Conditional probability distribution of immune dengue people

Pattern				P(IM0 | PA)	P(IM1 | PA)	P(IM2 | PA)
DC0	DCN 0	MD0	DTRx	1	0	0
DC0	DCN 0	MD1	DTRx	0.9	0.1	0
DC0	DCN 0	MD2	DTR0	0.7	0.3	0
DC0	DCN 0	MD2	DTR1	0.8	0.2	0
DC0	DCN 1	MD0	DTRx	1	0	0
DC0	DCN 1	MD1	DTR0	0.7	0.3	0
DC0	DCN 1	MD1	DTR1	0.8	0.2	0
DC0	DCN 1	MD2	DTR0	0.3	0.7	0
DC0	DCN 1	MD2	DTR1	0.4	0.6	0
DC0	DCN 2	MD0	DTRx	0.9	0.1	0
DC0	DCN 2	MD1	DTR0	0.2	0.8	0
DC0	DCN 2	MD1	DTR1	0.3	0.7	0
DC0	DCN 2	MD2	DTR0	0	0.8	0.2
DC0	DCN 2	MD1	DTR1	0.6	0.9	0.1
DC1	DCN 0	MD0	DTR0	0.8	0.2	0
DC1	DCN 0	MD0	DTR1	0.9	0.1	0
DC1	DCN 0	MD1	DTR0	0	0.9	0.1
DC1	DCN 0	MD1	DTR1	0.1	0.9	0
DC1	DCN 0	MD2	DTR0	0	0.3	0.7
DC1	DCN 0	MD2	DTR1	0	0.4	0.6
DC1	DCN 1	MD0	DTRx	0.7	0.3	0
DC1	DCN 1	MD1	DTR0	0	0.6	0.4
DC1	DCN 1	MD1	DTR1	0.2	0.5	0.3
DC1	DCN 1	MD2	DTR0	0	0.2	0.8
DC1	DCN 1	MD2	DTR1	0	0.3	0.7
DC1	DCN 2	MD0	DTRx	0.2	0.8	0
DC1	DCN 2	MD1	DTR0	0	0.4	0.6
DC1	DCN 2	MD1	DTR1	0	0.6	0.4
DC1	DCN 2	MD2	DTRx	0	0	1
DC2	DCN 0	MD0	DTR0	0.7	0.2	0.1
DC2	DCN 0	MD0	DTR1	0.8	0.2	0
DC2	DCN 0	MD1	DTR0	0	0.3	0.7
DC2	DCN 0	MD1	DTR1	0	0.4	0.6
DC2	DCN x	MD2	DTRx	0	0	1

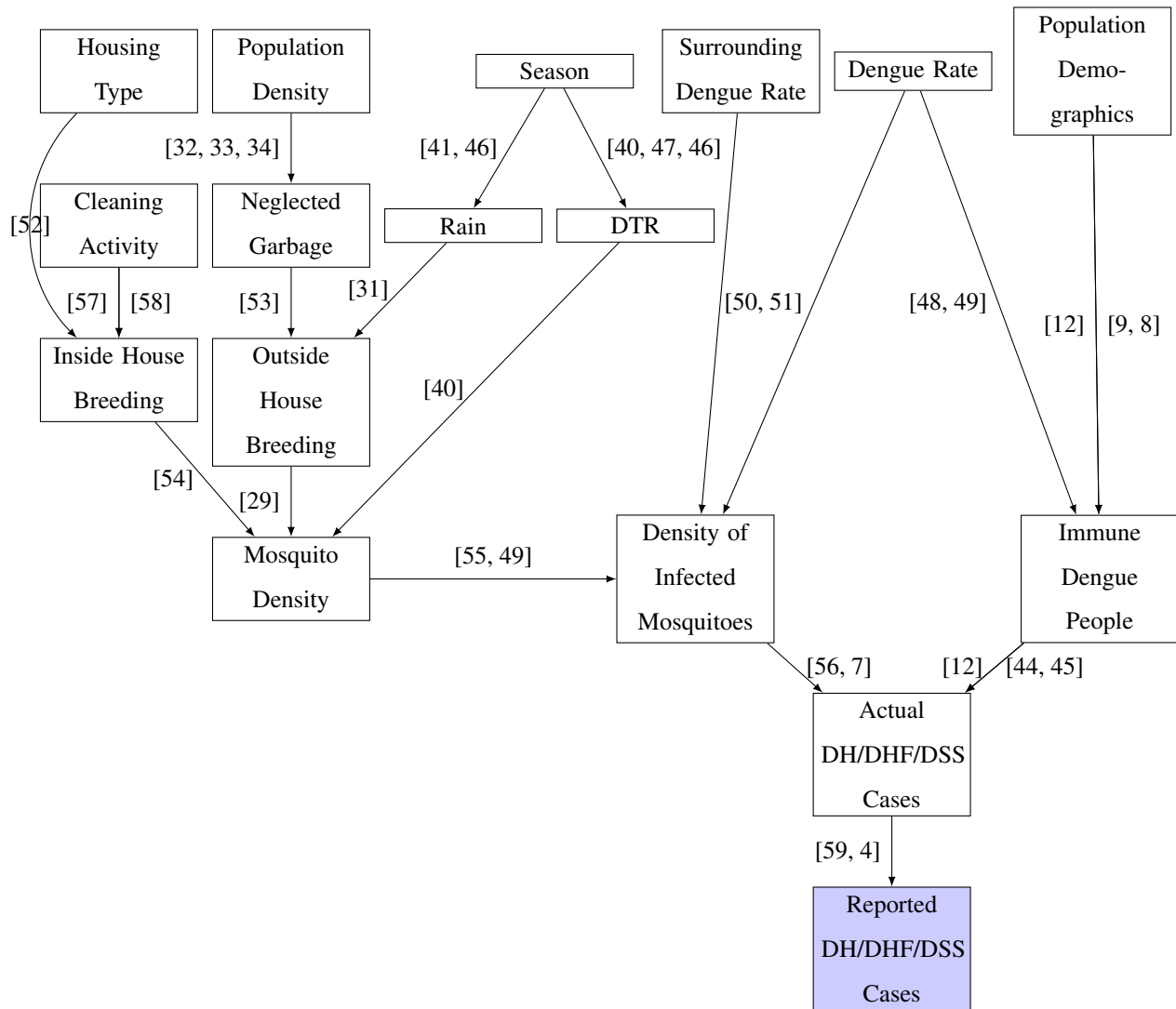Table 13: Conditional probability distribution of density of infected mosquitoes

Figure 4: Bayesian network model for the prediction of DH/DHF/DSS Cases.

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