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## A System Dynamic Transmission Model (SYStrans) to Simulate Epidemic Dengue Environment

Rifat Anwar

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# **A System Dynamic Transmission Model (SYStrans) to Simulate Epidemic Dengue Environment**

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Thesis submitted to the  
College of Engineering and Mineral Resources  
at West Virginia University  
in partial fulfillment of the requirement for the degree of

Master of Science in  
Civil and Environmental Engineering

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## **ABSTRACT**

### **A System Dynamic Transmission Model (SYStrans) to Simulate Epidemic Dengue Environment**

Rifat Anwar

Dengue is the most significant arthropod-borne virus in terms of human morbidity and mortality. Geographic expansion of dengue and intensity of outbreak has amplified significantly during the last few decades. Thus, the understanding of the dynamic of the large outbreaks has become indispensable for planning of control interventions in future epidemics. In this regard, local entomological, meteorological and epidemiological parameters based dengue models can be an essential tool for better interpretation of dengue-climate relationship at a regional scale. Process based modelling is resourceful in combining the vector and host dynamic along with the response to the meteorological factors for dengue transmission. In previous studies, process based models have not dealt with the integrated impact of vector-host dynamic and dengue transmission epidemiology by incorporating weather dependent transmission mechanism. In this study, a process-based model has been developed and validated for Iquitos of Peru, based on both vector and host population dynamic as well as the whole infection transmission mechanism. The sole objective was to develop a simple model to represent the actual scenario triggering dengue epidemic considering the most important features of vector population dynamics, transmission mechanism and environmental linkages. The model has used remote sensing or satellite based environmental data and also introduced dew point temperature as a new and effective weather parameter to depict the transmission process of dengue. The model has been capable of simulating the peak and moderate scenario in temporal scale, with considerable quantification of the actual number of cases for the 2004 and 2008 epidemics. Eventually, this type of model can be modified to use for different regions to predict the peak scenario based on local weather parameters effecting the infection transmission and vector development process along with population density.

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# **1. Introduction**

## **1.1 Background**

Dengue is the most significant arthropod-borne virus in terms of human morbidity and mortality (DJ, 2002) (SB, 2008). Geographic expansion of dengue has intensively amplified since the last few decades (Morrison, et al., 2010). Whereas, higher urban population density and availability of vector habitats have intensified the transmission with increasing number of cases (Karl, Halder, Kelso, Ritchie, & Milne, 2014). Thus, the understanding of the dynamic of the large outbreaks has become indispensable for planning of control interventions in future epidemics (Anderson & May, 1992). *Aedes aegypti* is considered as the main vector for dengue transmission, which is the most efficient vector for arboviruses as it is anthropophilic and flourish in close proximity to humans (Otero & Solari, 2010). However, vector population and vector competence of *Aedes* varies significantly with seasonal environmental condition (Mohammed & Chadee, 2011).

Climatic condition and variability play a significant role in regulating entomological process of vectors and epidemiology of vector borne diseases like dengue (Githeko, et al., 2000). The evolving and survivor factors of *Aedes* are temperature dependent and there is a favorable threshold range of temperature supporting the development at each stage (Hopp & Foley, 2001). The ecology of virus transmission and replication is also temperature dependent, which regulates extrinsic incubation period (EIP), gonotrophic cycle, biting rate, life span as well as human response or interaction (FOCKS, et al., 2000) (Barbazan, et al., 2010) (Mohammed & Chadee, 2011). On the other hand, precipitation pattern has been associated to the availability of aquatic breeding sites, while few studies discussed about the opposite impact of precipitation on vector availability (Althouse, et al., 2015) (Shope, 1991) (Kearney, et al., 2009) (O'Gower, 1956) (Olson, 2006). The effect of other environmental variables has been skeptical and utilize differently in different studies.

Local entomological, meteorological and epidemiological parameters based dengue models can be an essential tool for better interpretation of dengue-climate

relationship at a regional scale. Vector-host transmission modelling, representing both vector and host dynamic, is essential to evaluate the effectiveness of different intervention activities (Andraud, et al., 2012). In addition, deterministic and process-based modelling facilitates in analyzing the regional ecology of dengue-climate relations and thus pivotal to adopt regional control strategies (Bannister-Tyrrell, et al., 2013). Different deterministic models have been developed focusing on different aspects including variable human population, variable vector population, vertical and mechanical transmission and presence of different strains (Otero & Solari, 2010).

Process based modelling is resourceful in combining the vector and host dynamic along with the response to the meteorological factors for dengue transmission (Vezzani, et al., 2004). This dynamic modelling process can incorporate the biophysical relationship between different entomological and environmental factors (Vaidya, et al., 2014). In previous studies, process based models have not dealt with the integrated impact of vector-host dynamic and dengue transmission epidemiology by incorporating weather dependent total transmission mechanism (Morin, et al., 2013). In this study, a process-based model has been developed for Iquitos of Peru, based on both vector and host population dynamic as well as the whole infection transmission mechanism. The response of entomological activities and transmission dynamic to the daily local weather parameters has been incorporated to the model to represent the local transmission scenario. *Aedes aegypti* based vector life cycle model is integrated with SEIR based population model and a conceptual transmission model developed by replicating the infection transmission process between vector and host. The study has proposed the use of remote sensing or satellite data in process-based modelling. The potential of remote sensing data has inflated recently for the study of diseases related to environmental condition as it provides information about weather or environmental variability on different spatial and temporal scale (Side & Noorani, 2013). The study also introduces dew point temperature as a new and effective weather parameter to depict the transmission process of dengue. Eventually, this type of model can be modified to use for different regions to predict the peak scenario based on local weather parameters effecting the infection transmission and vector development process along with population density.

## 1.2 Outbreak Locations

As a background study, a detail literature review has been conducted on identifying historical hotspots of dengue epidemic. Annual large outbreaks or epidemic scenarios has been reviewed to obtain country wise specific locations on city level. Figure 1 shows locations of dengue outbreaks, where mainly epidemic scenarios has been included for the period of 1960 to 2016. For African regions outbreaks has been suggested to be less documented in literatures, where the number of locations is supposed to be more in terms of risk and vulnerability. The hotspot countries have been classified based on quantitative historical evidence of large outbreaks (Figure 2). Countries with less than five large historical outbreaks have been identified as low-risk countries, whereas countries have been demonstrated to be at medium-risk where large outbreaks occurred between five to ten times (Figure 2). Countries with more than ten outbreaks have been stated as high-risk countries (Figure 2). This background study facilitated in selecting the study area based on vulnerability and depicts the overall global pattern of dengue outbreak.

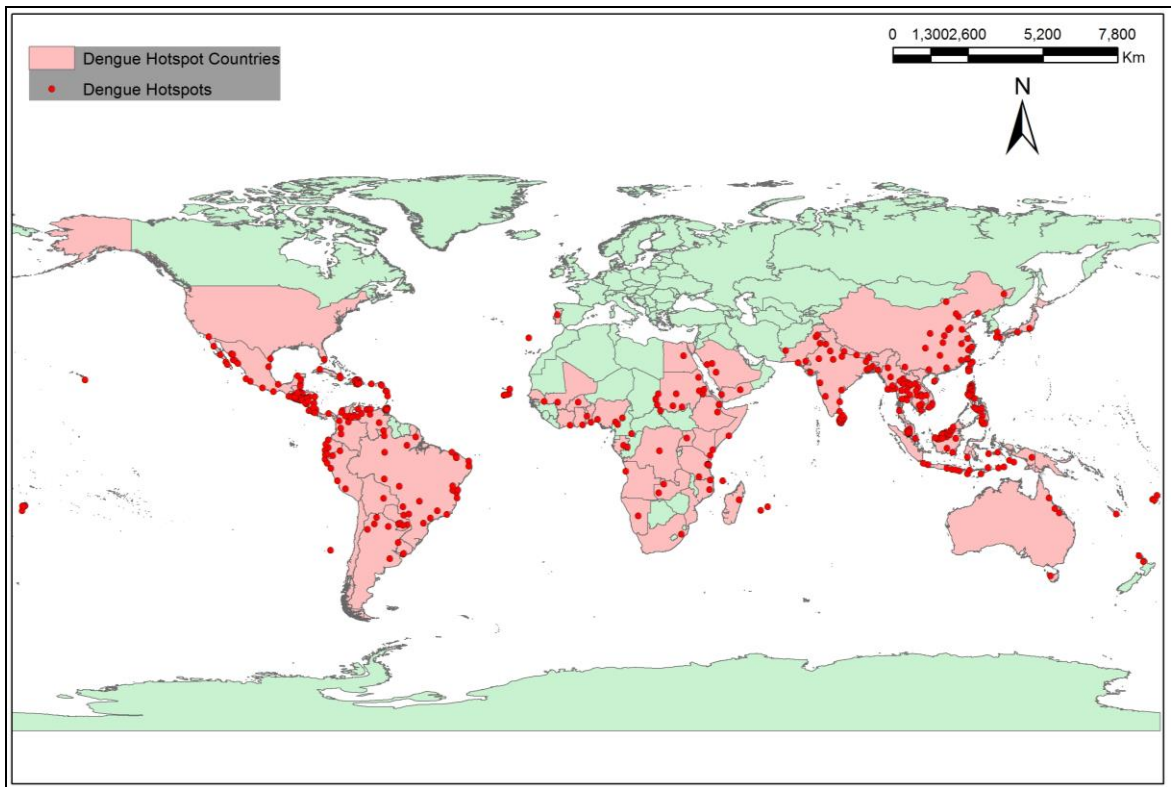


Figure 1: Dengue Hotspot Locations

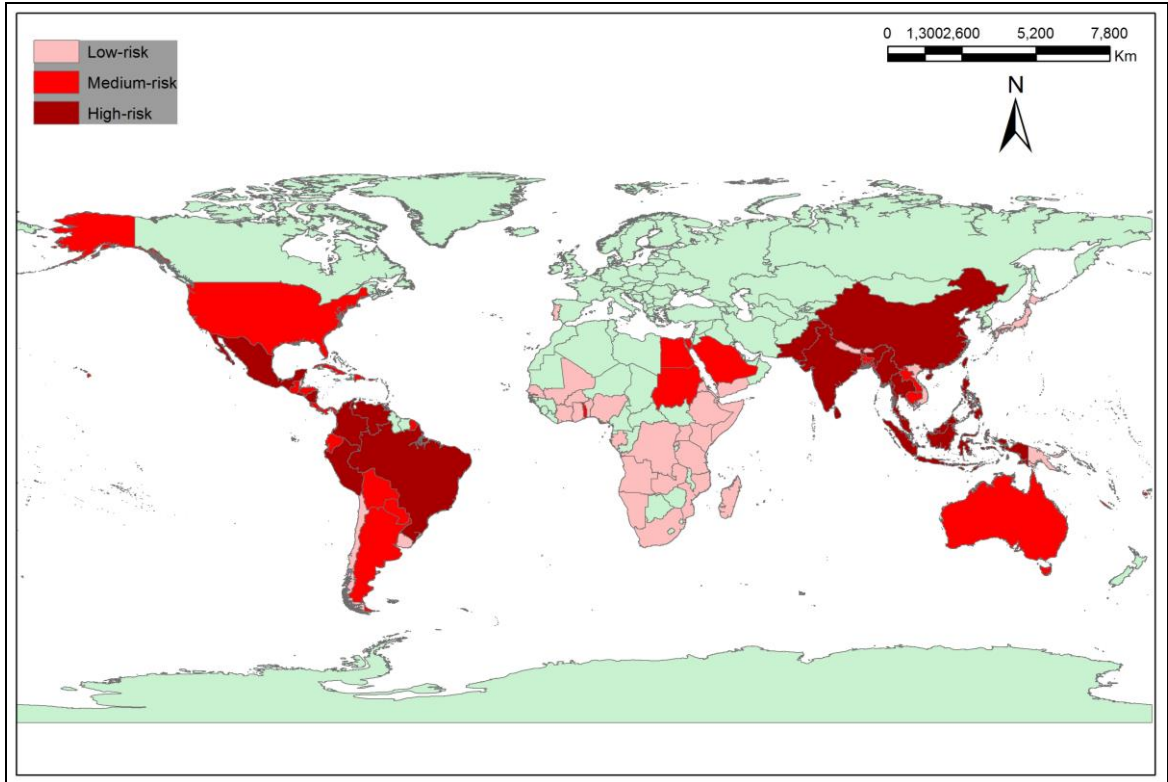


Figure 2: Classification of Hotspot Countries

### 1.3 Study Area

Our model has been developed for Iquitos, an isolated city in the Amazonian region of Peru having around 400,000 people (Figure 3). Peru has been identified as a country with high dengue risk (Figure 2). The city of Iquitos has well documented history of dengue virus transmission with recent and dramatic outbreaks. The climate of the city is tropical, with precipitation occurring throughout the year (Morrison, et al., 2010). In Iquitos, dengue serotype DEN-1 was first identified in 1990, where American genotype DEN-2 invaded during the large outbreak of 1995-1996 (Chowell, et al., 2008). However, the cocirculation of all four serotypes started during the epidemic of 2000-2001 (Montoya, et al., 2003).

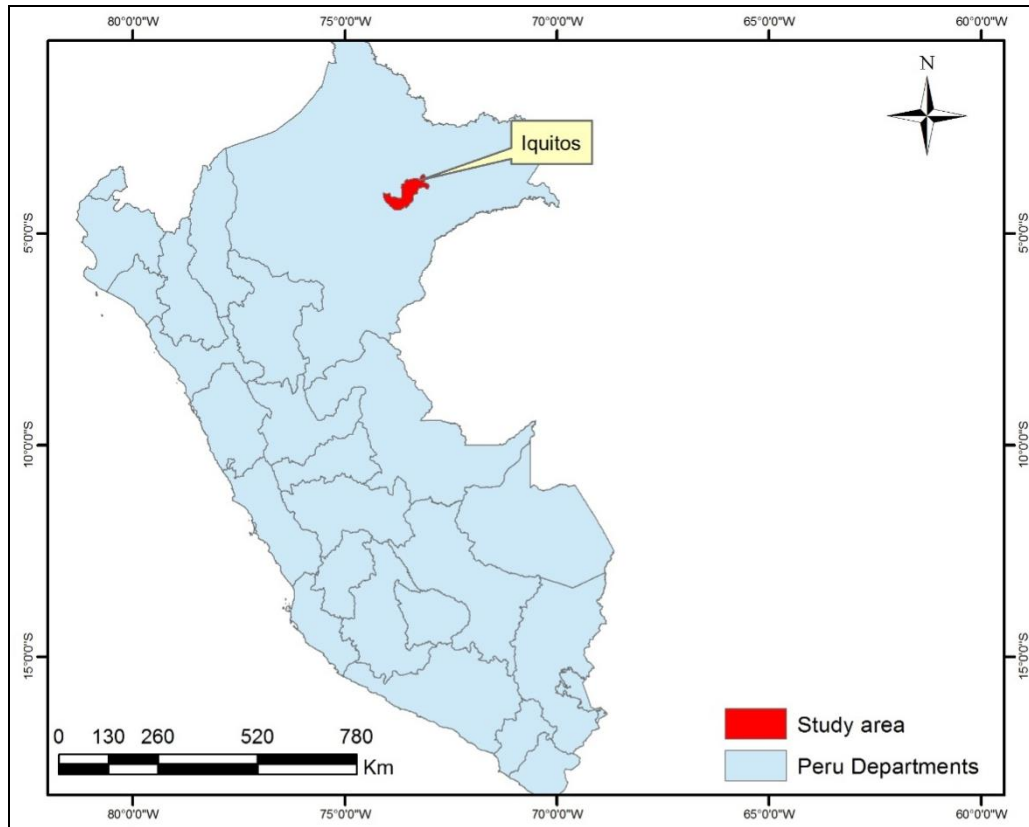


Figure 3: Study Area

## 2. Literature Review

### 2.1 Literature Review on Dengue Modelling

The dynamics of dengue epidemic has been modelled in different literatures to perceive the ideal outbreak scenario as these models can exemplify the disease dynamic and eventually aid in disease control (Diekmann & Heesterbeek, 2000) (Esteva & Vargas, 1998). The development of these models require intensive knowledge on relationship between different entomological and epidemiological variables (Ljung, 1999) (Massad, et al., 2003). However, unreported and misdiagnosed cases is a source of uncertainty in the model (World Health Organization, 2009), whereas understanding the relationship and prominence of different environmental factors and disease epidemic has been observed to be the prime challenge. The influence or impact of environmental factors can vary spatially due to socio-economical condition and life style (Lozano et al). Also, the lag between

dengue prevalence and these environmental factors has been identified to be different for models developed for different locations (Yu, et al., 2011).

A generalized mixed model (GLMM) approach was followed by Lowe et al, where Bayesian framework was used for epidemic forecasting. The model quality has been assessed based on the ability to depict the warning of the peak dengue season (Lowe, et al., 2011). Torres et al used fuzzy model identification technique, where multiresolution analysis has been used to replicate original dengue and severe dengue epidemic in Colombia (Torres, et al., 2014). Buczac et al used fuzzy association rule models to identify spatial risk level of dengue incidence in terms of environmental and social condition of prior outbreaks (Buczak, et al., 2012). Yu et al proposed spatio-temporal prediction approach for dengue, using stochastic Bayesian Maximum Entropy (BME) analysis (Yu, et al., 2011). Studies developed mathematical and statistical models (deterministic or stochastic) to illustrate spatial or spatio-temporal epidemic pattern in terms of interaction between vectors and their human-hosts (Nishiura, 2006) (Otero, et al., 2006) (Maidana & Yang, 2008).

Time-series regression approach has been used for predicting dengue fever using different weather variables in many literatures (Depradine & Lovell, 2004) (Wu, et al., 2007) (Luz, et al., 2008) (Brunkard, et al., 2008) (Chakravarti & Kumaria, 2005). Lu et al predicted dengue incidence for China using one-month prior minimum temperature, minimum humidity and wind velocity as the major predictors (Lu, et al., 2009). Brunkard et al and Diaz et al developed weather variable based autoregressive model to predict weekly changes in dengue incidence with changing weather pattern (Brunkard, et al., 2008) (Hurtado-Diaz, et al., 2007). Autoregressive integrated moving average (ARIMA) models have been fitted with time series of dengue fever incidence in few literatures (Wu, et al., 2007) (Hu, et al., 2010). Chan et al developed historical case based regression model using environmental condition and population density to provide risk prediction for small areas (Chan, et al., 2015). Regression models have been mainly used to assess cross correlations between environmental variables and dengue fever cases with different lags (Fuller, et al., 2009). Regression models have been also explored to evaluate weather dependent vector abundance and their impact on dengue outbreak (Azil, et al., 2010). Some studies also

developed transmission potential models for dengue, with major focus on temperature dependent transmission capacity of the vector population (Barbazan, et al., 2010). These studies used historical dengue cases for risk prediction and most of these models utilized temperature, precipitation and humidity to forecast the dengue fever cases (Wu, et al., 2007) (Hu, et al., 2010).

Ecological niche modelling has been also used to predict the risk zone of dengue occurrence based on satellite environmental data and history of dengue fever cases. Arboleda et al conducted ecological niche modelling with satellite environmental data and dengue cases (Arboleda, et al., 2009). Peterson et al used ecological niche modelling to predict monthly distribution, dynamics and activity of dengue vector (Peterson, et al., 2005). The geographical expansion of the risk of dengue fever transmission has been assessed by Hales et al, where geographical distribution has been modelled based on vapor pressure (Hales, et al., 2002). Studies have conducted tele-epidemiology based analysis to map entomological risk of vector distribution around dwellings (Machault, et al., 2014). Climate-driven statistical and process based models have been developed to assess the climate change impact on global distribution of dengue (Morin, et al., 2013). These type of models mainly evaluated the geographic distribution of the risk of dengue and have not focused on spatio-temporal risk pattern (Arboleda, et al., 2009).

Remote sensing data has been used for understanding the spatio-temporal risk of dengue and modelling the global distribution of the disease due to promising scope of this higher spatial resolution data (Anno, et al., 2015). Remote sensing data has gradually become very efficacious for epidemiological studies due to prominent development in providing environmental data and landuse pattern (Curran, et al., 2000) (Hay, et al., 2010). Remote sensing or satellite data has been effectively used in modelling vector borne diseases (Stefani, et al., 2013) (Yang, et al., 2005) (Kalluri, et al., 2007) (Bergquist, 2001), including distribution of dengue vector (Neteler, et al., 2011) (Roiz, et al., 2011) (Estallo, et al., 2008) (Fuller , et al., 2009) (Vanwambeke, et al., 2011) (Sarfraz, et al., 2012) as well as human dengue cases (Bentham, et al., 2005) (Rotela, et al., 2007). These studies focused on mapping vector habitats, evaluating environmental factors influencing vectorial entomology and epidemiological risk of disease transmission (Rotela, et al., 2007). In these

studies, temperature, rainfall and humidity were the most commonly used satellite based weather variables along with vegetation index and land cover pattern. Some studies have also used wind speed and digital elevation model derived drainage pattern in the risk modelling (Khalid & Ghaffar, 2015). Many studies utilized the normalized difference vegetation index (NDVI) for associating the changing land use pattern with the prevalence of dengue (Rotela, et al., 2007) (Troyo, et al., 2009). MODIS and Landsat data have been mostly used, whereas some studies have also used AVHRR, SPOT and QuickBird satellite data. Remote sensing data can be more expedient for modelling of infectious diseases like dengue, compared to the station based data (Tran & Raffy, 2006). Recently, process based or network based modelling has emerged as a proficient tool for studying geotemporal epidemics of infectious diseases (Newman, 2002). However, their practical simulation has not been adapted with use of realistic remotely sensed data (Tran & Raffy, 2006).

Studies used SEIR (susceptible-exposed-Infective-resistant) models to study vector borne diseases like dengue (Murray, 2003). These type of compartmental models have been majorly used to assess the host dynamics (Pongsumpun & Tang, 2001), influence of vector control strategies (Newton & Reiter, 1992) and competition between different strains (Feng & Velasco-Hernández, 1997). However, these models have not considered combined dynamics of the mosquito life cycle and development as well as the infection transmission process to represent the actual scenario. Modelling vector distribution can portray the risk pattern of dengue, however is not sufficient to replicate the actual scenario with the transmission dynamics (Machault, et al., 2014). On the other hand, modelling population dynamic cannot determine the effect of vector development and transmission activity, thus combination of the whole process is necessary to illustrate the real scenario.

A detail literature review has been conducted to evaluate the previous studies on dengue modelling (Figure 4). Figure 4 shows that only few studies used remote sensing data, while mathematical modelling based studies have not explored the field of remote sensing or satellite data. There are some commonly used environmental parameters. Most of the studies based on mathematical modelling approach have not evaluated the combined



impact of the environmental variables on vector development, host dynamic and vector-host transmission process.

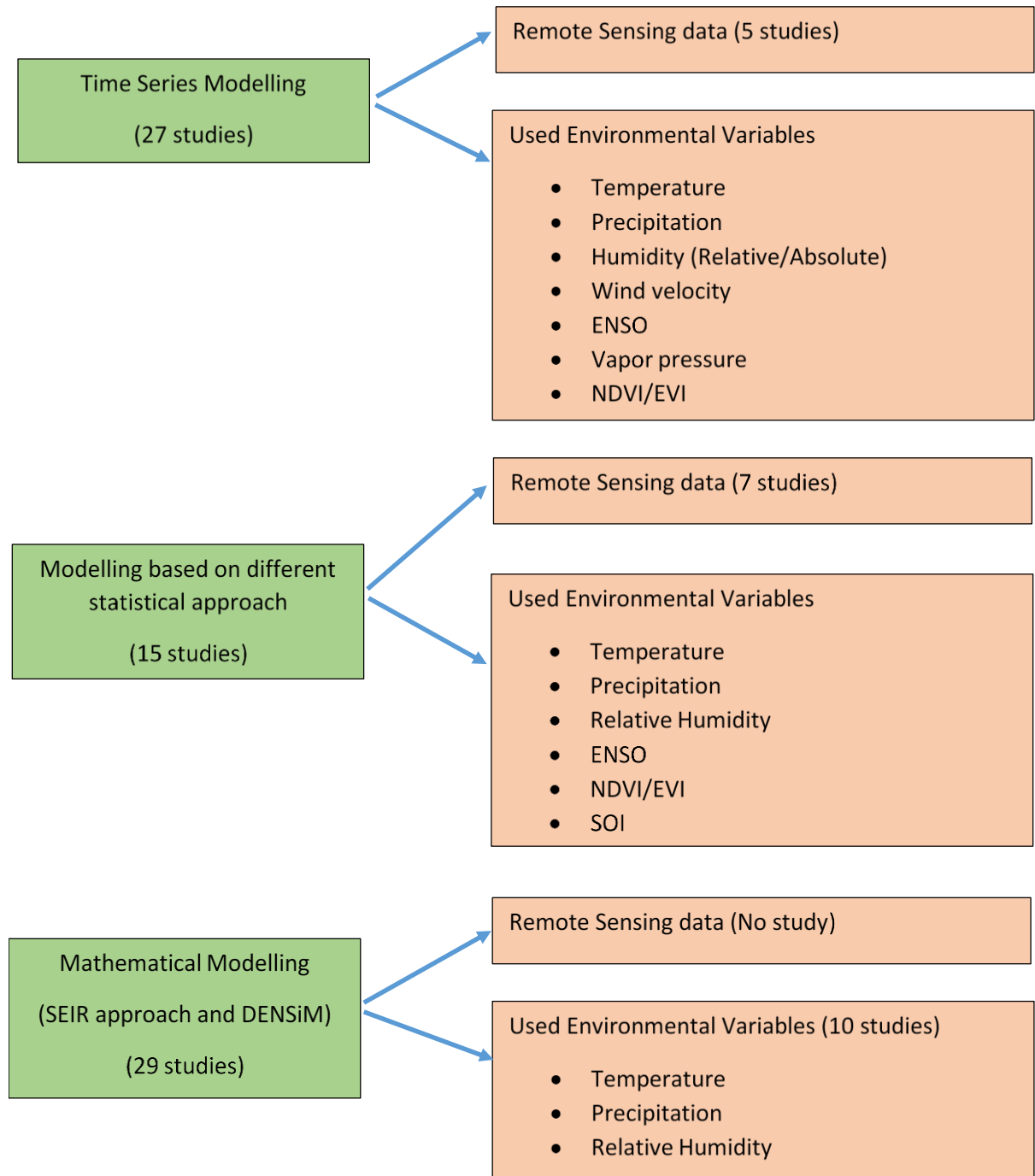


Figure 4: Literature Review on dengue modeling

## **2.2 Literature Review on Climatic Parameters**

Climatic condition and variability play a significant role in regulating entomological process of vectors and epidemiology of vector borne diseases. Different literatures discussed that vector-host distribution as well as vector-host-virus complex interaction influences prevalence of dengue epidemic (Althouse, et al., 2015). The intricate relationship is related to seasonal climatic condition as vector abundance, competence and virus transmissibility is significantly climate regulated (Mohammed & Chadee, 2011) (Focks, et al., 2000). In most of the studies, temperature and precipitation have been recognized as the major climatic factors, linking dengue prevalence and climate around the endemic areas (Descloux, et al., 2012) (Dom, et al., 2012). Many studies discussed and reviewed the significant influence of temperature on faster viral replication rate within vector as well as intensified transmission scenario (Morin, et al., 2013). Precipitation and temperature has been observed to be the most commonly used climatic factors for prediction of dengue epidemic and developing risk maps (Sang, et al., 2014) (Yu, et al., 2011) (Chan, et al., 2015). Also, relative humidity has been perceived as a significant climatic factor along with temperature and precipitation in different studies (Descloux, et al., 2012) (Dom, et al., 2012) (Duncombe, et al., 2013). Hales et al conferred expedition of transmission efficiency with increasing temperature and relative humidity effecting epidemiological activities of vector like extrinsic incubation period (EIP) and gonotrophic cycle (Hales, et al., 2002). Costa et al discussed the influence of relative humidity in regulating the effect of temperature on vector survival rate, which eventually control transmission efficiency of vector (Costa, et al., 2010). Descloux et al modeled dengue outbreaks in Noumea relating temperature, precipitation, relative humidity, potential evapotranspiration and wind force (Descloux, et al., 2012). Dom et al and Lu et al (Dom, et al., 2012) (Lu, et al., 2009) incorporated temperature, precipitation and relative humidity as climatic parameters for modelling dengue outbreak scenario. Duncombe et al also utilized these parameters for assessing dengue transmission risk through computation of vector density (Duncombe, et al., 2013). Deviation of these parameters (temperature and relative humidity) has been also considered as predictive factors in studies (Wu, et al., 2007). Studies also reconnoitered the association of El Niño southern oscillation (ENSO) with

dengue fever epidemic for different coastal countries (Descloux, et al., 2012). ENSO is acknowledged as an indicator of climate variability, which effects the distribution of dengue vector (Hu, et al., 2010). Hales et al modelled global distribution of dengue based on vapor pressure as an indicator of humidity (Hales, et al., 2002). Studies also considered drainage pattern and land cover type for predicting dengue outbreak, which are eventually influenced by precipitation pattern by providing or flushing vector breeding sites (Khalid & Ghaffar, 2015).

Repercussion of different climatic or environmental factors on dengue vector abundance and competence has been observed to be skeptical in different studies (Jansen & Beebe, 2010). Different studies discussed the dominance of different climatic factors for prevailing outbreak condition of dengue to portray the climate dependent transmission efficiency of vector (Rohani, et al., 2009). Biswas et al analyzed and suggested precipitation and humidity to have more profound impact on vector density compared to temperature as they control larval development and survival (D, et al., 1993). Few studies also suggested the prominence of rainfall over temperature and humidity, whereas dominance of temperature and humidity over precipitation has been conferred in few studies (Anno, et al., 2014) (Favie, et al., 2006). On the other hand, studies speculated lower dengue incidence with higher mean temperature, which contradict with most of the other studies on climate dependent dengue epidemic (Limper, et al., 2014). Araujo et al analyzed association of dengue prevalence with urban heat islands having higher land surface temperature, lower humidity and poor vegetation cover (Araujo, et al., 2015). Also studies identified vegetation dynamics to be a controlling factor for dengue epidemic as it can regulate local moisture supply, evaporation rate and wind speed (Fuller, et al., 2009).

### **3. Methodology**

#### **3.1 Background on Model Set-up**

Mathematical modeling has been used intensively for simulating dengue outbreak, based on the concept of SIR (Susceptible-Infected-Recovered) (Side & Noorani, 2013). For dengue epidemiology, most of the studies have considered changing host

population dynamic with constant vector population, while few have considered both host and vector dynamics. On the other hand, few studies have considered the changing vector dynamic with constant population (Esteva & Vargas, 2000). However, time series modelling has been used for dengue to use long term environmental dataset for predicting dengue cases, where validation of these models with real data have contributed in assessing the significance of different environmental variables. These types of models have been used in many studies with the major focus on environmental data, not considering the population and vector dynamic and concluded with the significance of different variables with different time lag. But, the use of process based simulation model for dengue epidemic has been observed to be limited (Bannister-Tyrrell, et al., 2013). Compared to the statistical models, process based models explicitly explain and illustrate each step of the transmission process as well as the biological life cycle of the vector and thus can be very effective . However, previous studies of process based modelling has not compiled the whole weather influenced infection transmission process with vector and host dynamic models. Moreover, they used station based environmental data and none of them explored the significance of remote sensing data in this regard. They mainly used local temperature and precipitation as environmental variable to simulate local dengue cases (Morin et al, 2013).

In our study, a process based mathematical modelling approach has been used with a system dynamic simulation software named Vensim. It supports continuous simulation and provides graphical modelling interface with interactive tracing of behavior between model variables. Generally process based models provide the advantage of realistically associate different variables and connect them to process the real scenario. This approach is mainly based on theoretical understanding of the whole vector development and dengue transmission process, providing the framework to incorporate the response of environmental conditions to the overall process. It provides easier interpretation of the real scenario with a framework to associate the impact of the different condition on the disease dynamic. In this model, the dynamic or cyclic process is triggered by arrival or introduction of infected people. In our model, we have introduced dew point temperature as a new environmental variable that have not been evaluated before for dengue models. Dew point

temperature is related to temperature and humidity and higher dew point temperature interpret existence of more moisture in the air and depicts that the air is maximally saturated with water. Temperature and relative humidity has been observed to be the determinant in dengue outbreak occurrence and persistent condition for the outbreak was determined based on number of days with these two variables being in the favorable range (Descoux, et al., 2012). Moreover, studies found absolute humidity to be the most consistent factor for dengue transmission, which elucidate the combined impact of mean temperature and relative humidity on infection proliferation (Xu, et al., 2014). In previous studies, it has been analyzed that the combined effect of temperature and humidity has influence on dengue virus propagation in the vectors (HM, et al., 1998). Thus, we hypothesize that dew point temperature can be a significant factor contributing persistent climatic condition for dengue as it portrays the combined effect of temperature and relative humidity.

### **3.2 Model Set-up**

We have studied the spread of the disease by host and vector activities, while considering the effect of different environmental variables on entomological activities of vectors and epidemiology of dengue transmission. The host dynamic has been incorporated based on the traditional approach of susceptible-infected-recovered (SIR), but inspecting the impact of different weather dependent activities before simulating infected host. The motivation of the model is based on combining the vector and host population dynamics, incorporated with weather parameters and delay for fertilization and incubation periods, to simulate realistic temporal and numerical pattern of dengue cases. The model consists of three sub-models (Host Population Dynamic Model, Vector Population Dynamic Model and Dengue Transmission Model), which have been integrated in a way that it represents the whole process (Figure 7). Figure 5 and 6 show the model sketch in normal and simulated form and figure 7 illustrates the schematics of different variables and their interrelationships within different sub models. The model is simulated with daily time step and the model calculates daily vector population at each stage of life depending on survival and development rate related to the daily temperature as well as water availability.

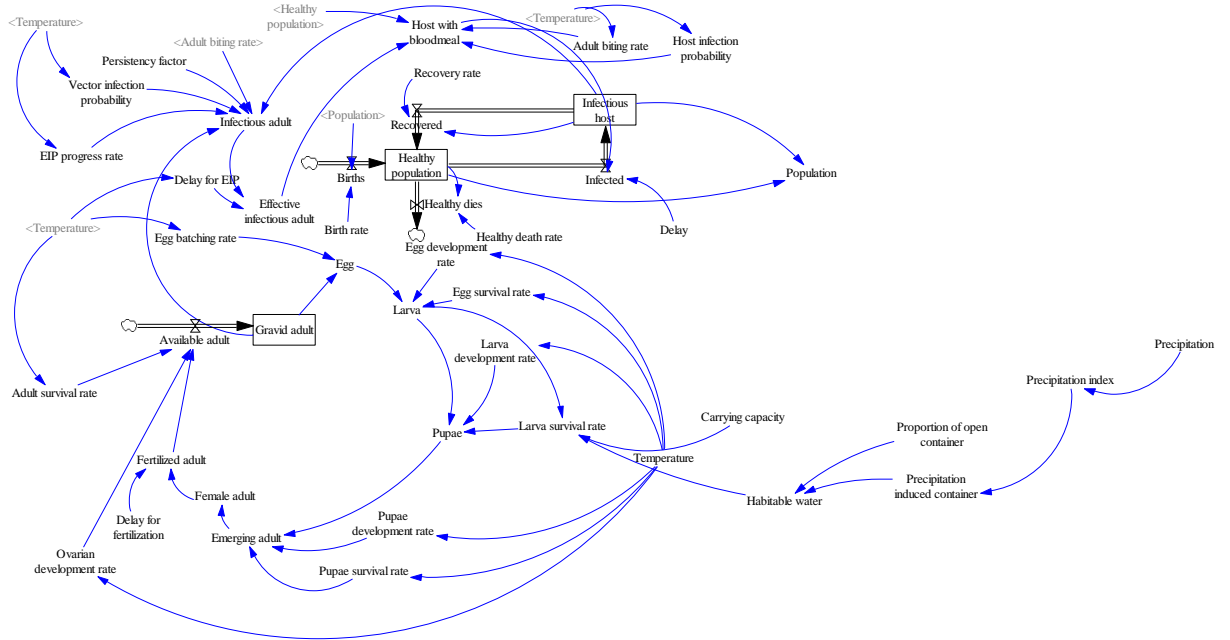


Figure 5: Model sketch

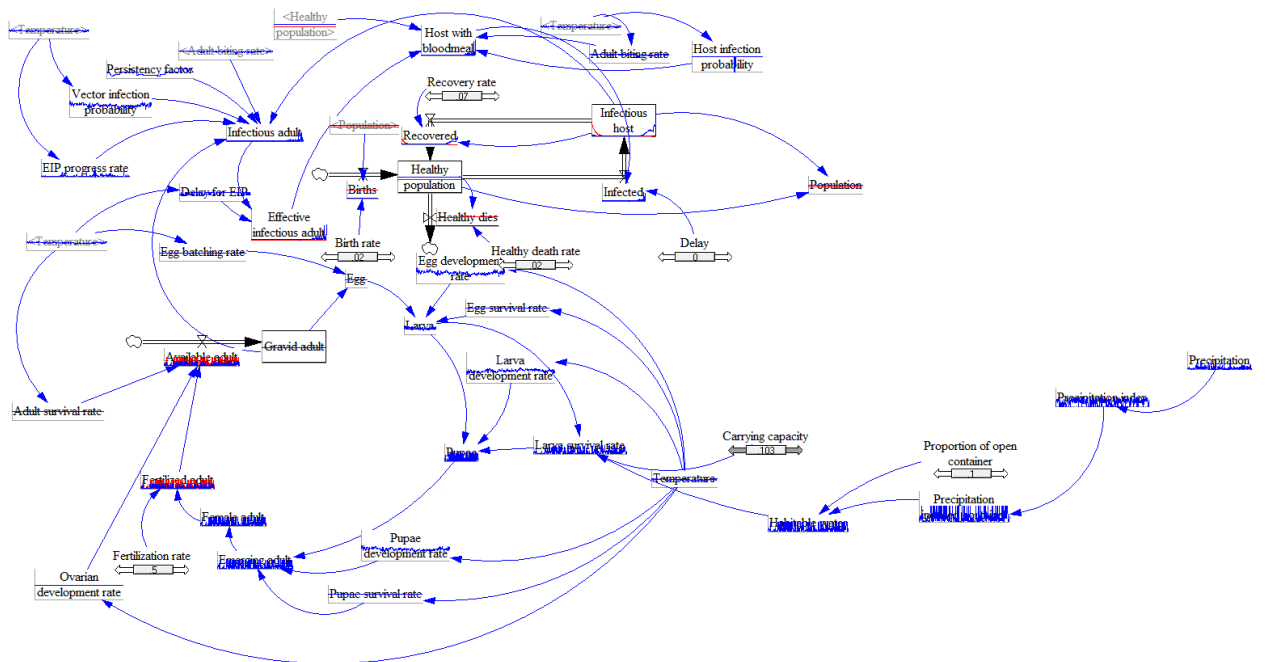


Figure 6: Model sketch in simulated form

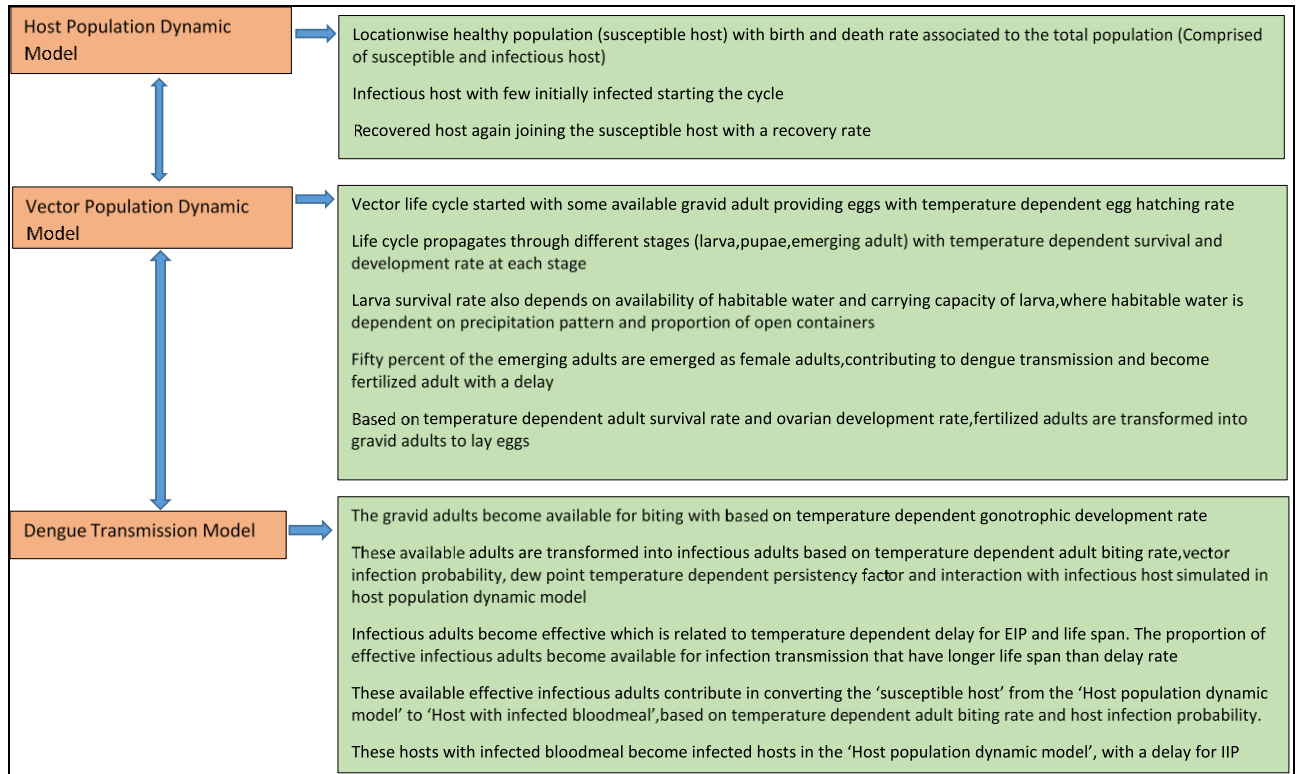


Figure 7: Brief Model Interpretation

The dynamical evolution of the vector population is modeled representing the whole life cycle. The biological events of the life cycle is associated to the transition rates between different stages of life and their dependence and relationship with temperature and water availability has been taken from experimental observations. Egg, larvae and pupae development and survival rate were determined from previous studies, which are associated with temperature and require the availability of water. In the developed model, it has been assumed that there is minimum availability of water to lay eggs. We have considered the development of larvae in density dependent manner, as discussed in few previous literatures (Morin et al, 2013). Larva survival rate is dependent on larva density and carrying capacity of habitable water. Generally, precipitation or artificial storage can make availability of aquatic breeding sites or habitable water. We followed the approach that adequate habitable water has been developed through precipitation, as the study area has continuous pattern of rainfall through the year. Thus, it has been assumed that there is absence of Human-made or artificial water storage due to

unavailability of field data on artificial storage and as dry condition does not prevail in the study area. On the other hand, larva-sustaining capacity of habitable water is declined during continuous high rainfall scenario due to overflowing effect. So, it has been assumed that continuous pattern of extremely high rainfall reduce the larva sustaining capacity of habitable water and thus habitable water is not considered as proper breeding site under this scenario. Through this development and survival rate, larvae are emerged as pupae and pupae are converted to emerging adults with temperature dependent development and survival rate. Only 50 percent of the adults are emerged as female adults and thus fertilized as gravid adults after a delay of three days. The transformation from fertilized adults to gravid adults is associated with temperature dependent ovarian development and adult survival rate. In the model, availability of gravid adults has been considered from the initial stage as the study area is vector dominant and always prevail the condition for their development.

The simulated gravid adults from this life cycle model were then transformed into the effective infectious adult. This part of the model represented the interactive infection transmission process between vector and host. The conversion or transformation of gravid vector adults to the effective infectious adults is significantly dependent on the vector-infected host interaction as well as the temperature dependent extrinsic incubation period (EIP), and eventually this transformation dynamic effectively govern the whole process of dengue transmission. The transformation is also related to temperature dependent adult biting rate and vector infection probability. Vector-infected host interaction or adult biting rate can also rely on socioeconomic factors that have not been considered in this study. Sufficient vector-host interaction and vulnerable socioeconomic condition has been considered in the study area. In the developed model, we have also integrated a persistency factor that is related to the effect of dew point temperature on dengue transmission, which has impact on the conversion of gravid adults to infectious adults. This variable is assimilated based on the hypothesis that comparatively higher dew point temperature supports and expedite the propagation of infection. The infectious adults are transformed in to effective infectious adults after the delay for extrinsic incubation period (EIP), depending on temperature effect on EIP.



The host population dynamic model is compiled with healthy, infected and recovered population. Fifty to ninety percent of the population of the study area has been considered as susceptible host. The percentage has been used as a calibration parameter. These susceptible hosts become ‘Hosts with infected bloodmeal’ through the interaction with available effective infectious adult vectors, based on temperature dependent adult biting rate and host infection probability. After the delay for intrinsic incubation period (IIP), these hosts are altered to become infected. The infected hosts interact with the gravid adults of the vector population dynamic model, increasing the susceptibility of intensive transformation of gravid adults to infectious adults. The whole cycle of this infection transmission is started with few initial infected host. The number of initial infected host has been collected from real dengue data. The proportion of infected hosts are recovered with a certain recovery rate and again join the susceptible host. The whole modelling framework and background is briefly presented in figures of the appendix.

#### **4. Data**

We modelled dengue outbreak based on data collected in Iquitos, Peru. The latitude and longitude of the station data is -3.783 and -73.3 respectively. The dengue outbreak data used for Iquitos dates between 2000-2009. Dengue outbreaks were recorded and separated into the four serotypes (DENV1 - DENV4) for each week of these years from U.S. Naval Medical Research Unit 6 (NAMRU-6). For climatic continuous daily observations, we used NOAA’s NCEP climate Forecast System (CFS) reanalysis data. CFS reanalysis is a global, high-resolution system to provide the best continuous daily estimate over the period of record. Our collected climate data set include daily precipitation, dew point temperature and air temperature. Figure 8 shows the actual weekly dengue cases of Iquitos for different years. The data for year of 2002, 2004 and 2008 have been used for model calibration and validation as they represent the epidemic environment.



Figure 8: Dengue weekly actual data

## 5. Model Optimization and Calibration

The model development and calibration approach has been adopted based on experimental field data or empirical equation. Few equations has been developed following our own hypothesis. The unknown or uncertain parameters has been used to calibrate the model. For example, the area of habitable water has been associated with precipitation and has varied with precipitation pattern. Different amount of habitable water for different scenario has been used for calibration of the model, as we have not used any land use pattern or human dwelling density data. For medium range of continuous precipitation, higher amount of habitable water has been considered; whereas lower amount of habitable water has been considered for very low and extremely high precipitation pattern. The other calibrated parameters are larva carrying capacity of the habitable water and proportion of open containers that are uncertain. The term ‘proportion of open containers’ has been used as an indication of socioeconomic condition or lifestyle pattern and utilized to calibrate the model. The initial availability of vectors is a crucial factor, which provides eggs for the initiation of the cycle. Due to unavailability of any trapping or field data, the initial quantification of gravid adults has been considered to be a calibration parameter. In dengue endemic regions, sufficient vector availability is maintained throughout the year and thus general availability is considered from initial stage of the model. These four calibration parameters were used in vector population dynamic part of the model. Delay for intrinsic incubation period (IIP) and recovery rate has been used for calibrating the other part of the model. Literatures suggested that intrinsic incubation period vary between 4 to 8 days (Side & Noorani, 2013), while recovery rate can also vary within a range depending on the immunity. Literatures suggested the duration of infectiousness of the host to be strongly influential factor for seasonal pattern of dengue transmission and the timing of peak prevalence is dependent on it (Bartley, et al., 2002). Thus recovery rate has been used as a calibration parameter. Moreover, in the study area a proportion of the total population can be immune from the infection, which is an uncertain parameter. The percent of immune people can vary and has been used as a calibration parameter. Monte Carlo approach based vensim sensitivity analysis has been conducted to evaluate the sensitivity of the calibration parameters. Monte Carlo Marcov Chain approach of Vensim has been

used to identify the values of calibration parameters that resulted in the best fit to the real dengue cases. Table 1 represents the set of calibration parameters with their range. Among these calibration parameters, only two parameters (initial vector availability and initial exposed host) have been changed manually as they were not used as constant in the model and Vensim optimization is modified for constant parameters only. Figure 9 and 10 show the sensitivity of these parameters on the major output parameter of the model (infectious host).

Table 1: Set of calibration parameters

Variables	Range
Habitable water	$1 \cdot 10^4$ to $8 \cdot 10^6$
Carrying capacity	0.5-1
Proportion of open container	0.1-1
Initial vector availability	$1 \cdot 10^4$ to $1 \cdot 10^8$
Intrinsic incubation period (IIP)	4-8 days
Recovery rate	0.05-0.1
Initial exposed host	50 to 90 percent of the total population

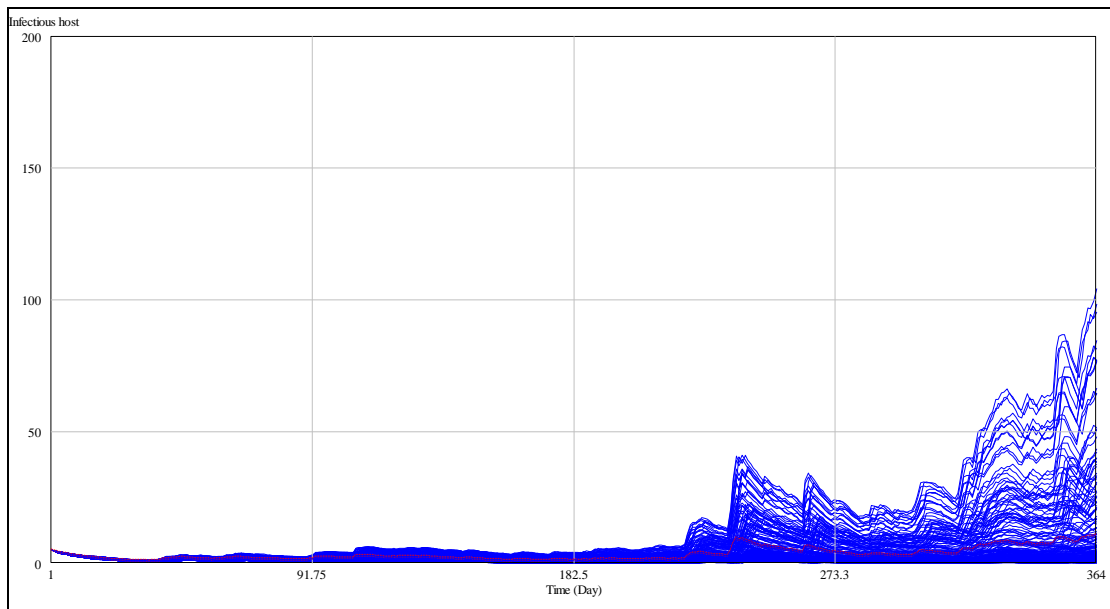


Figure 9: Sensitivity graph for all parameters

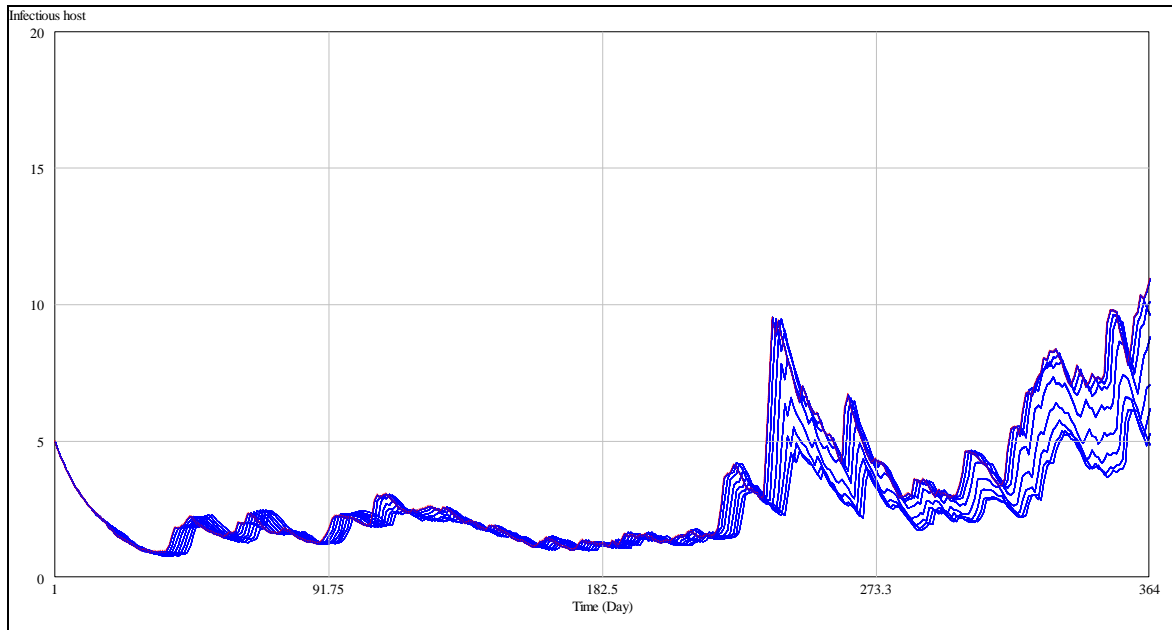


Figure 10: Sensitivity graph without recovery rate

Calibration of model requires simulating thousands of combinations of different parameter values. Vensim is a visual modeling tool that allows simulation, optimization and sensitivity analysis for an established system dynamic model (Lin, et al., 2012). Literatures suggested Vensim as an effective tool to connect the simulation with optimization and to choose sensitive parameters to get optimum output (Kasperska, et al., 2014). In system dynamic models, there are many parameters and the effect of their variation on model simulation is significant. Vensim follows Markov Chain Monte Carlo approach to adjust the parameters to get the optimal match between model behavior and the real data. In this approach, the output is optimized under uncertain environment using different combinations of calibration parameters within a certain range (Lin, et al., 2012). Monte Carlo Multivariate sensitivity analysis of Vensim can be used as an entrance for optimization as it facilitates in selecting the sensitive parameters for optimization (Kasperska, et al., 2013). Different literatures used optimization set up of Vensim where certain range and weight can be identified for each payoff or calibration parameter. Literatures suggested Vensim's optimization and sensitivity set ups as efficient approach as it allows searches within confidence bounds or optimal values to provide the best fit to the

real data. The process of optimization is advantageous as it allows providing weights to different calibration parameters according to its sensitivity (Kasperska, et al., 2013).

The equations and relationships used for the model are provided in figure 16 to 18 in appendix. All the equations or relationships used are for daily scenario.

## **6. Results and Simulations**

The model has been calibrated for 2002 dengue epidemic and validated for 2004 and 2008 epidemics, comparing the weekly simulated cases with the weekly actual cases. The model simulation has provided daily cases and weekly cases were determined through summation of daily cases. All the figures of model simulations are provided in appendix. Figure 11 depicts the simulation of the calibrated model, which has been used for validation of the model for 2004 and 2008. Figure 12 shows the weekly actual cases and model cases for the year 2008. It has been observed that there was an initial peak in dengue cases, which diminished after tenth week and the next significant rise started after thirty fifth week following almost six months of moderate scenario. The simulation has been observed to be competent in capturing the declining trend during tenth week and increasing trend during thirty fifth week. The model is capable of replicating the moderate scenario in the mid-year and peak scenario during the starting and end of the year. But, the model simulated the year end peak with a lag compared to the actual scenario. Figure 13 shows the comparison between simulated and actual cases for 2004. During 2004, the peak scenario has been observed at the end of the year after continuous moderate condition for the first nine months. The cases started rising after the fortieth week, which has been captured by the model. The model has been also capable of simulating the peak week, but with comparatively lower number of cases than the actual scenario.

The initial peak during 2008 was resulted from previous year scenario as the simulation was started with large number of initially infected cases. The cases started decreasing due to continuous comparative lower temperature and dew point temperature, which was not persistent enough for efficient infection transmission. The precipitation scenario has not been observed to have much impact on the case pattern as vector availability was maintained throughout the year. The mid year condition influenced the end

peak as efficient transmission was allowed by temperature and dew point temperature scenario. During 2004, the scenario started with lower number of initially infected host. The end of the year peak condition was generated from mid-year persistent higher temperature and dew point temperature, the effect of which resulted with a lag at the end of the year.

Figure 14 and 15 show the probability of exceedance plot for actual and modeled cases for 2008 and 2004 respectively. The probability of exceedance has been computed for actual and modeled cases and plotted with normal distribution in order to evaluate the model competent. The graphs depict that the model is significantly competent and efficient to replicate the dengue epidemic environment as the exceedance plots of actual and simulated cases follow almost similar distribution.

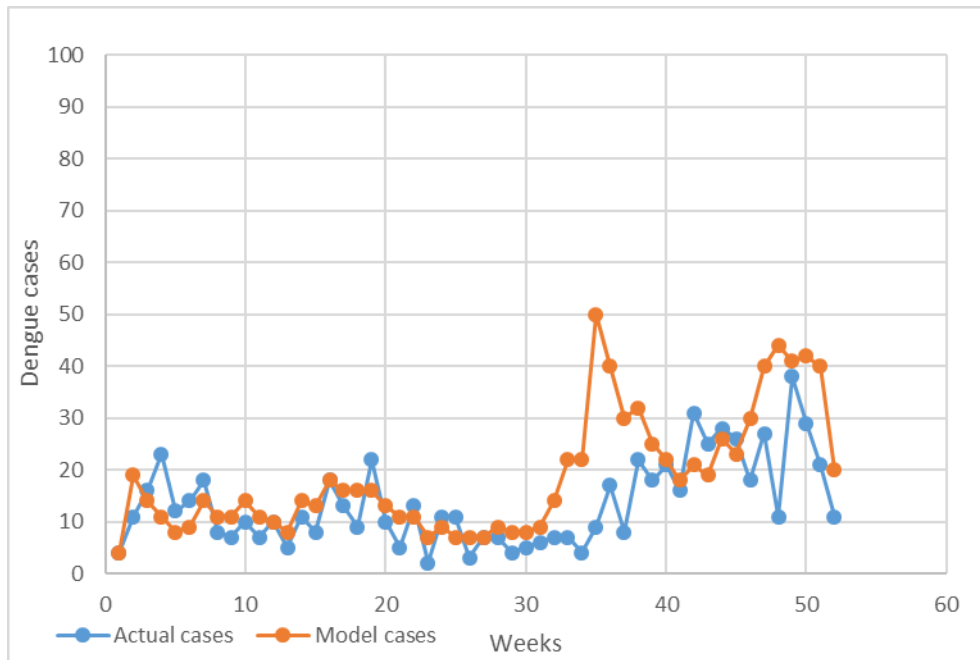


Figure 11: Model simulated and actual cases for 2002 (Model Calibration)

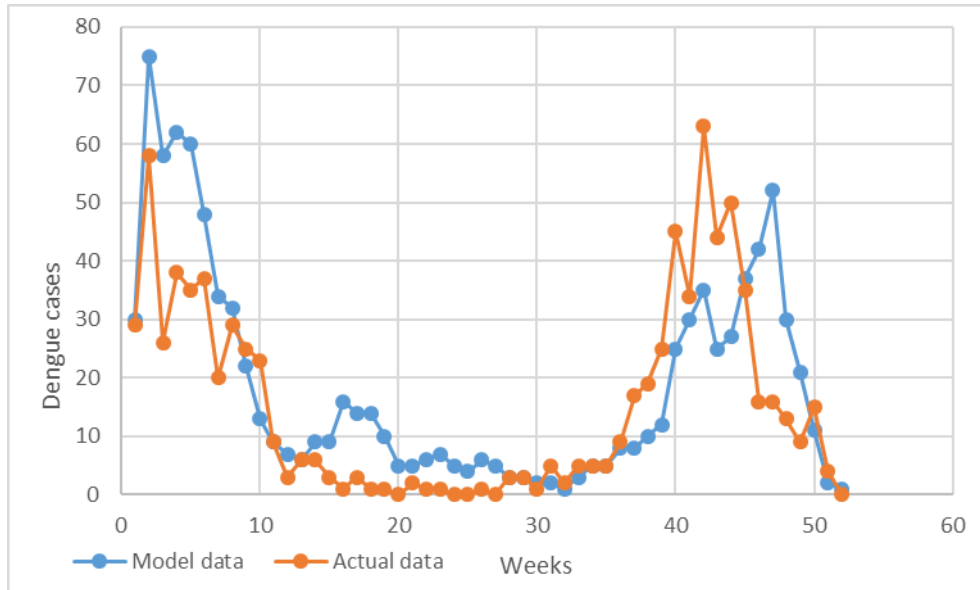


Figure 12: Model simulated and actual cases for 2008 (Validation)

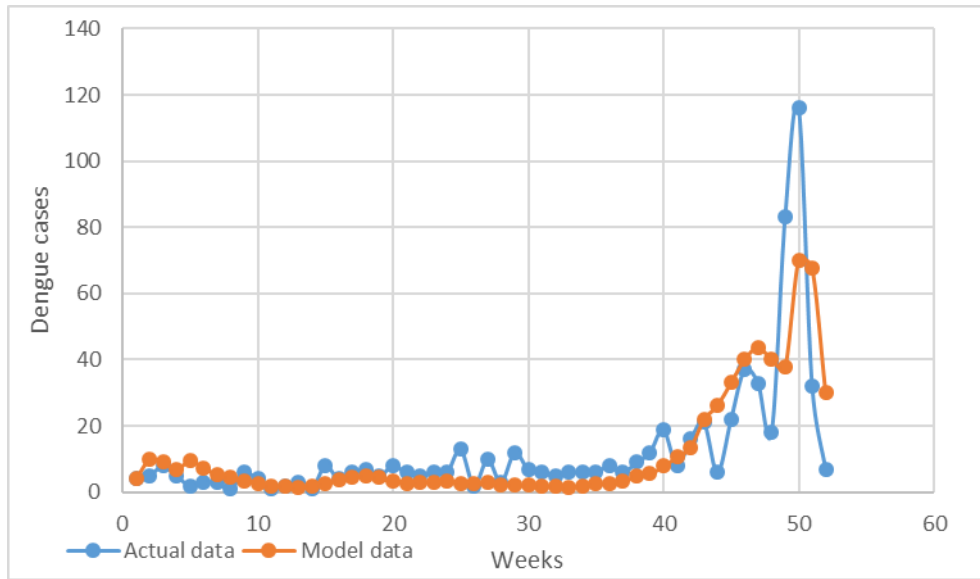


Figure 13: Model simulated and actual cases for 2004 (Validation)



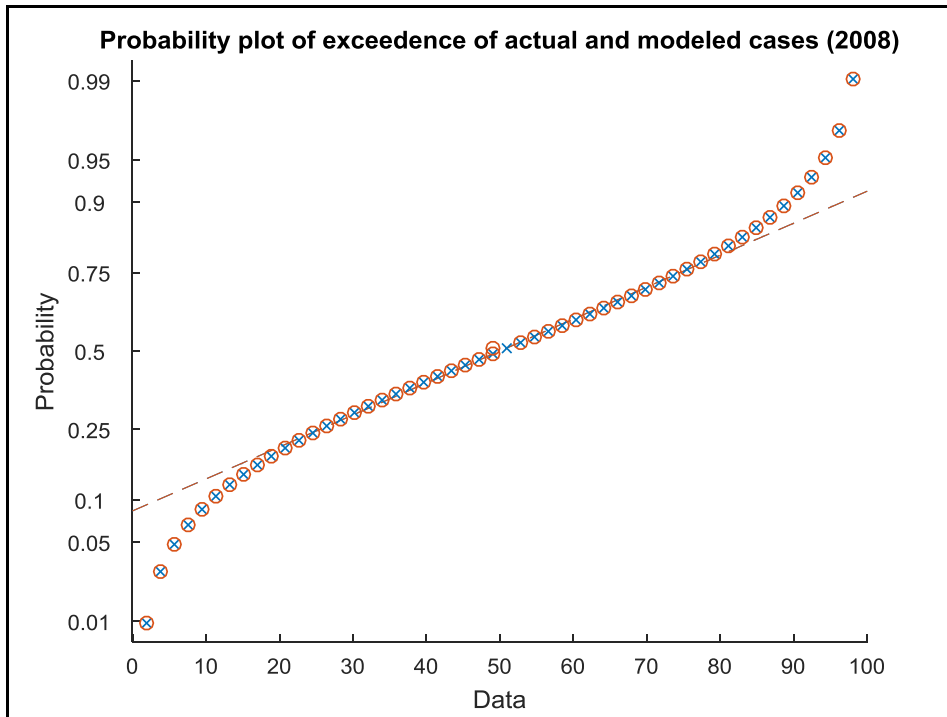


Figure 14: Probability of exceedance of actual and modeled cases (2008)

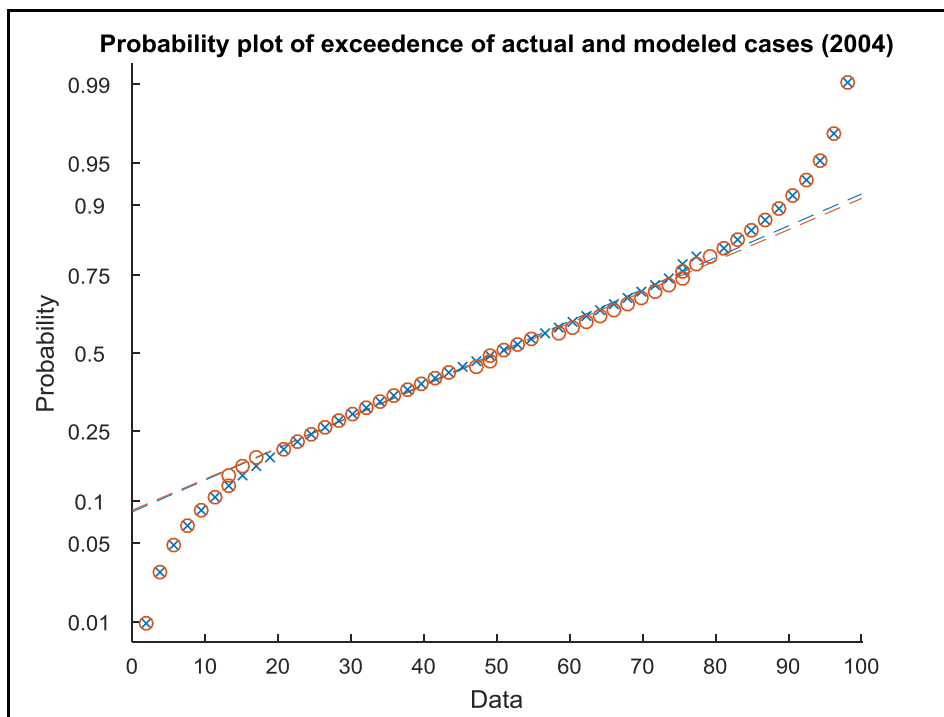


Figure 15: Probability of exceedance of actual and modeled cases (2004)

## 7. Conclusion

### 7.1 Summary

The model highlighted the overall physical system of the transmission process using the linkage and interaction between different parameters to explain the physical phenomena contributing in timing and scale of dengue epidemic. The sole objective was to develop a simple model to represent the actual scenario triggering dengue epidemic considering the most important features of vector population dynamics, transmission mechanism and environmental linkages. By simulating 2004 and 2008 outbreaks, the model has defined the conditions generating the peak, which can be utilized in future prediction and planning for control strategies. As the model has replicated the peak condition, it can facilitate in assessing the persistent environmental condition with associated lag that can cause significant proliferation in transmission scenario.

From a practical point of view, this model can facilitate in understanding the triggering environmental condition that can cause local or regional epidemic scenario. As we have used grid based remote sensing data, it is possible to make local risk maps or evaluate local risk patterns using the framework and concept of this model.

From a methodological point of view, few detailing and augmentation can make the model more effective. There is probability of vertical transmission of infection processed by transmission to the descendants by infected female vectors (Side & Noorani, 2013). However, the rate of this transmission is very low (Side & Noorani, 2013) and has not been incorporated in the model. The model has been developed considering only one vector species, while *aedes albopictus* can be another potential vector with different dynamics. Moreover, the model has been developed considering precipitation induced habitable water, whereas artificial or human-made habitable water can also prevail in comparative dry condition or depending on socioeconomic scenario. Thus, availability of different type of habitable water has to be considered for reframing the model for different study area with disparate precipitation pattern. Furthermore, the socioeconomic condition and life style has significant impact on vector-host interaction and thus regulate the

transmission process, which has not been incorporated in the model. Only one calibration parameter (proportion of open container) has been used, which indirectly indicate lifestyle pattern. Also, survival rate of adult vector has been considered to be effected only by temperature, although vector control activities and socioeconomic pattern has significant influence in this regard.

The model has been validated using actual data to show that it can almost generate the actual scenario capturing the temporal pattern of peak. However, incorporation of parameters regarding local socioeconomic condition may facilitate in adaptation of the model for different locality with more accurate simulation.

## **7.2 Future Work**

The model has been simulated for Iquitos; however it has been developed in such a way that it can be adopted for different regions of available vectors with different environmental data and population density. The transformation is dependent on availability of environmental data, demographic data and actual case data. The motivation of future work is to develop the model using this concept and framework for other dengue vulnerable cities. Incorporation of some social parameters will be another purpose and direction of future work.

With appropriate reparameterisation, this model can be modified for other diseases (zika,chikungunya) with same vectors. This model can be modified for these diseases if demarcation among their environmental transmission condition is developed. With development of demarcation among transmission condition of these diseases, we have plan to develop model for zika and chikunguniya using the same concept.

# Appendix

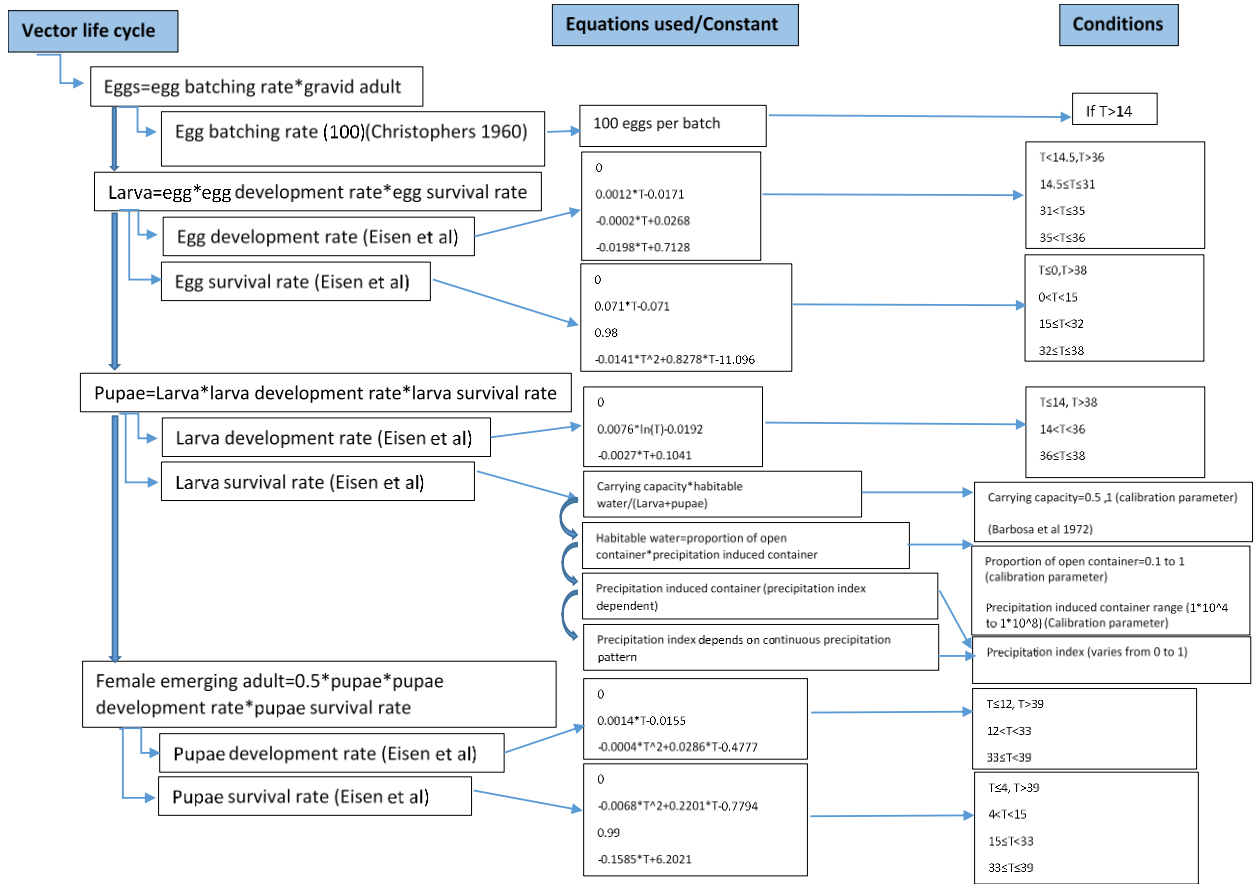


Figure 16: Vector life cycle model interpretation (part 1)

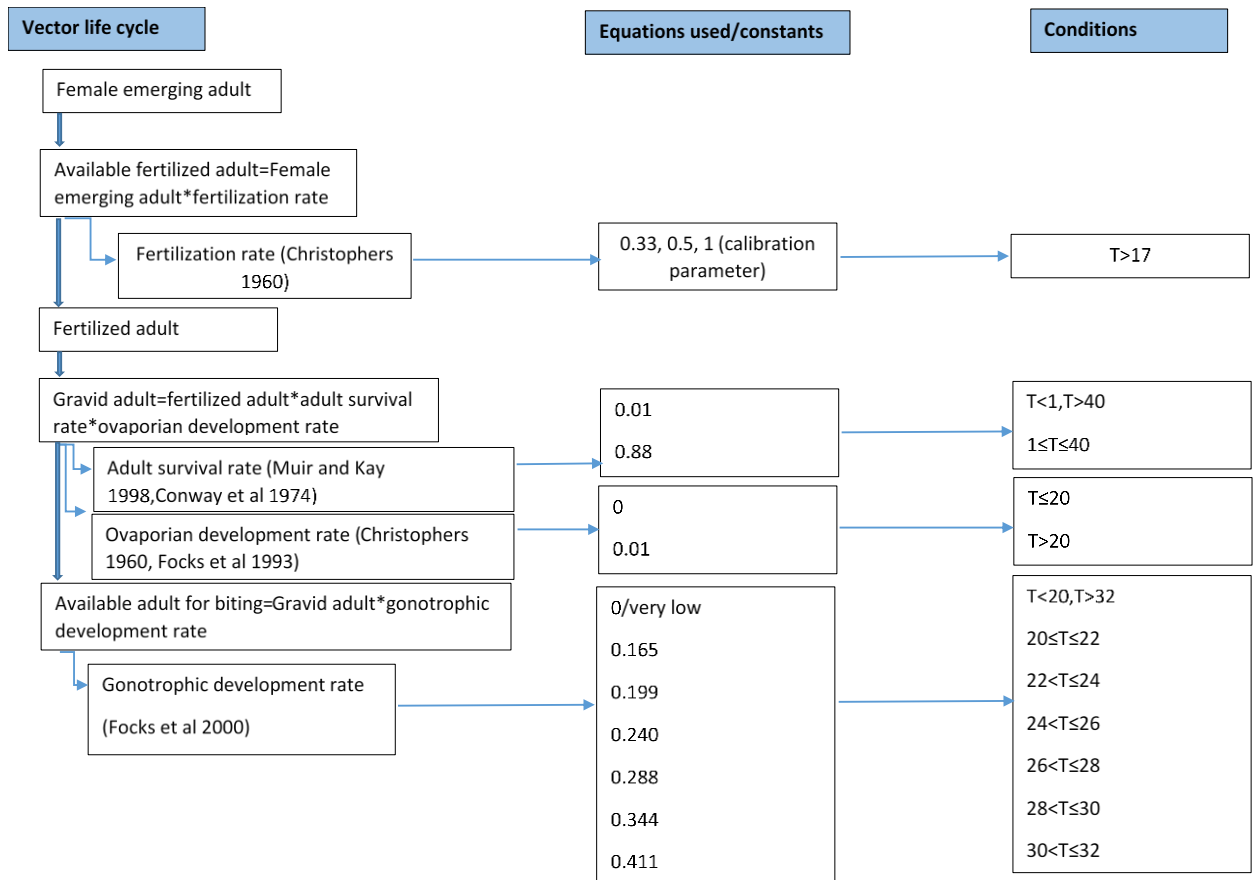


Figure 17: Vector life cycle model interpretation (part 2)

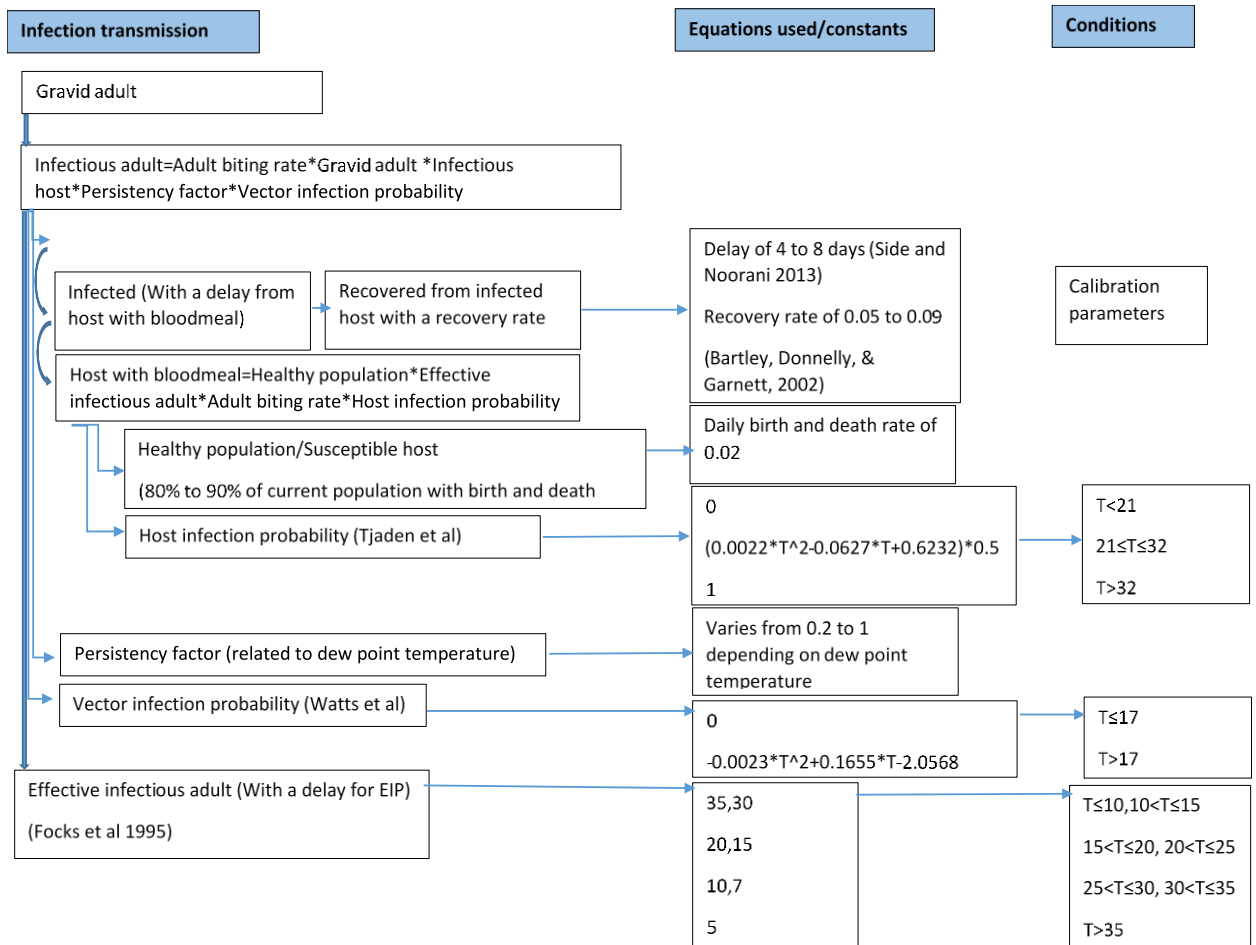


Figure 18: Transmission and population model interpretation

### Calibration Model Simulations (2002)

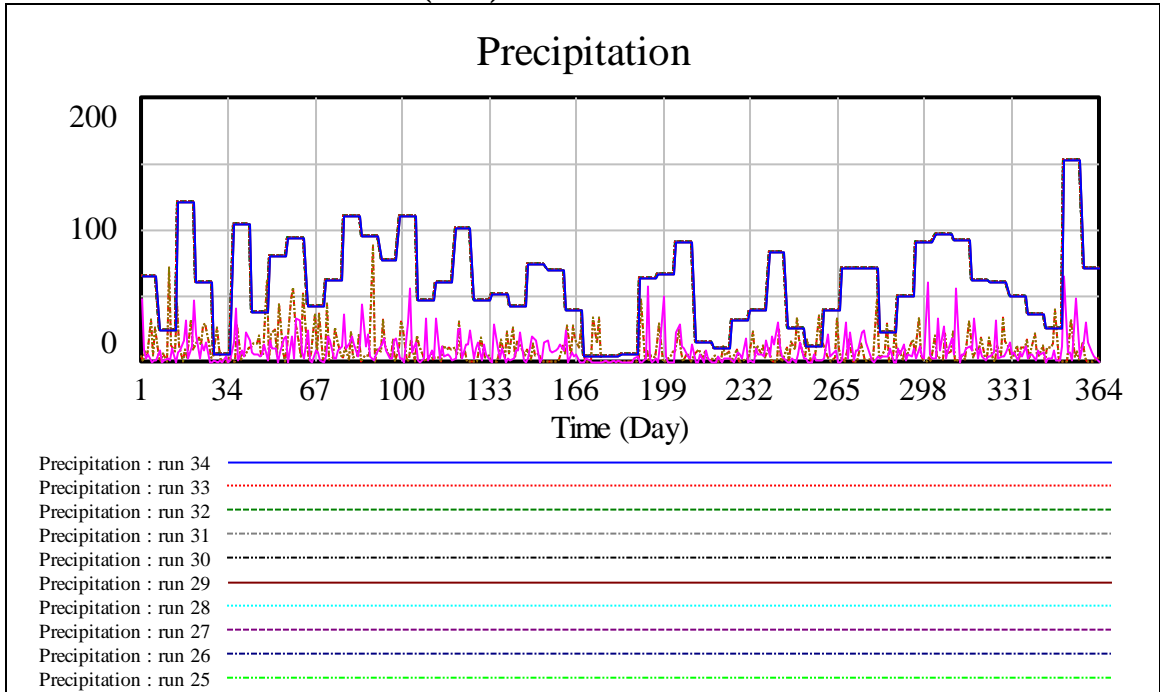


Figure 19: Precipitation Simulation

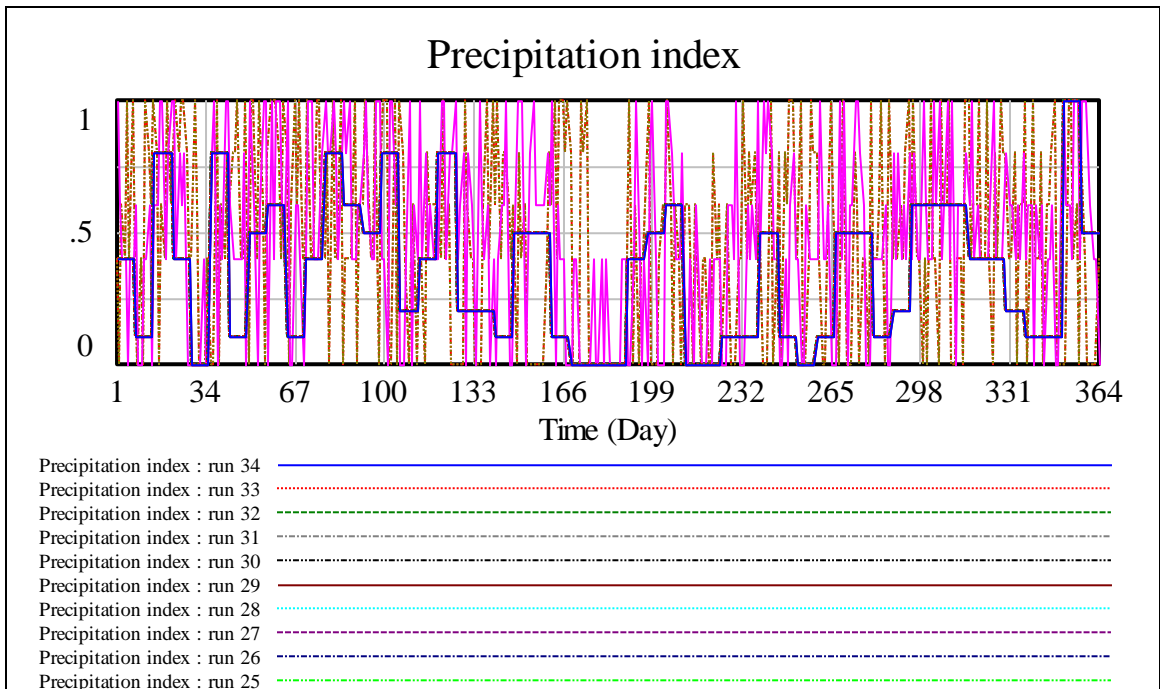


Figure 20: Precipitation index simulation

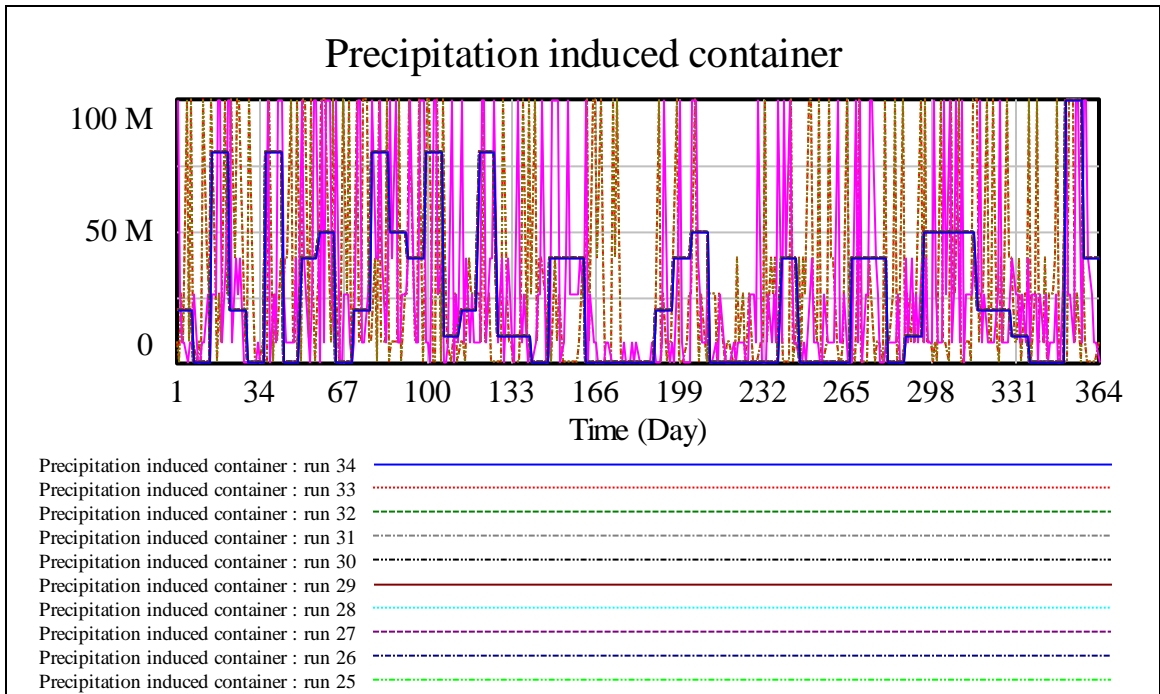


Figure 21: Precipitation induced container simulation

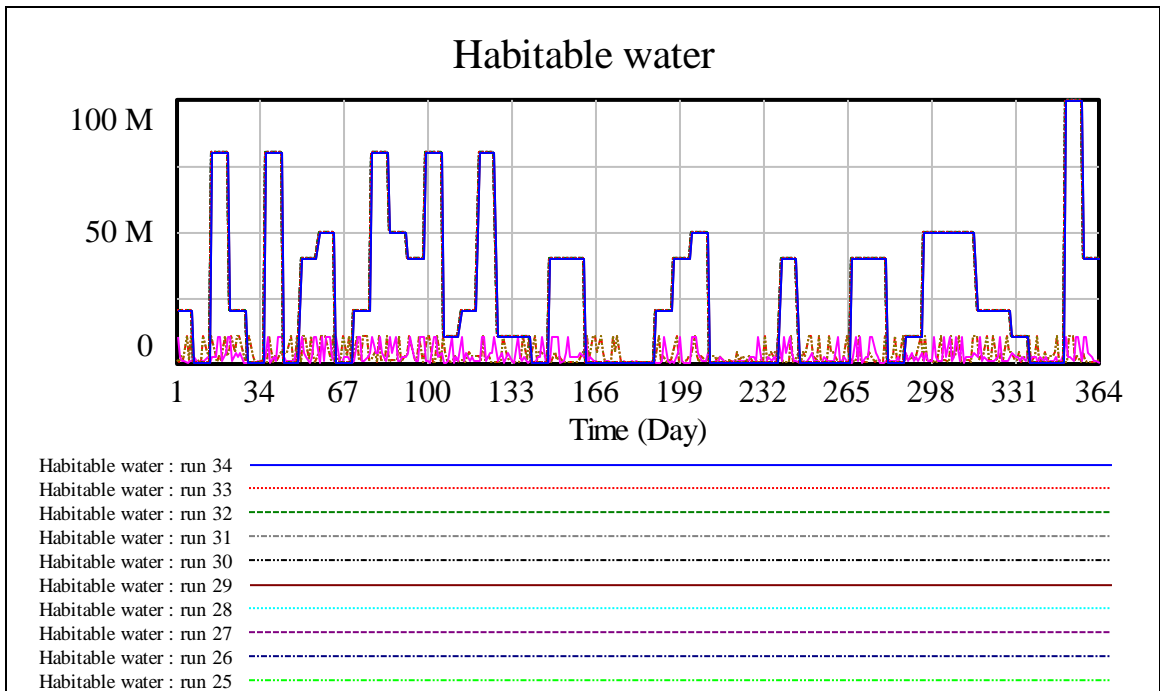


Figure 22: Habitable water simulation



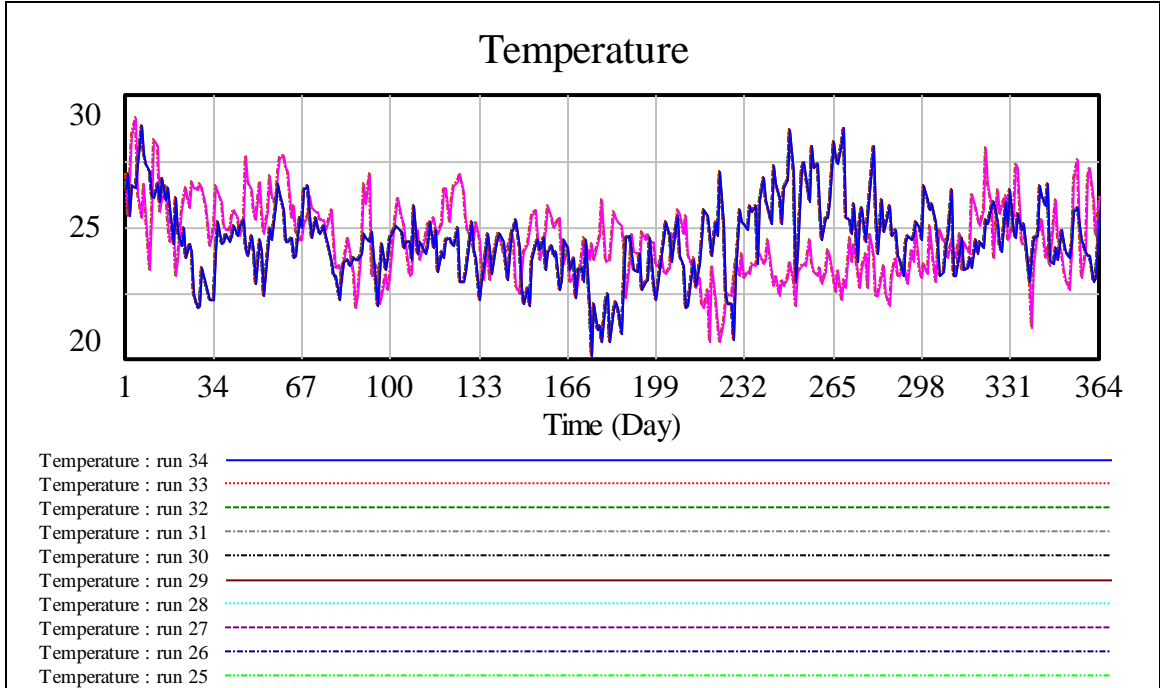


Figure 23: Daily temperature simulation

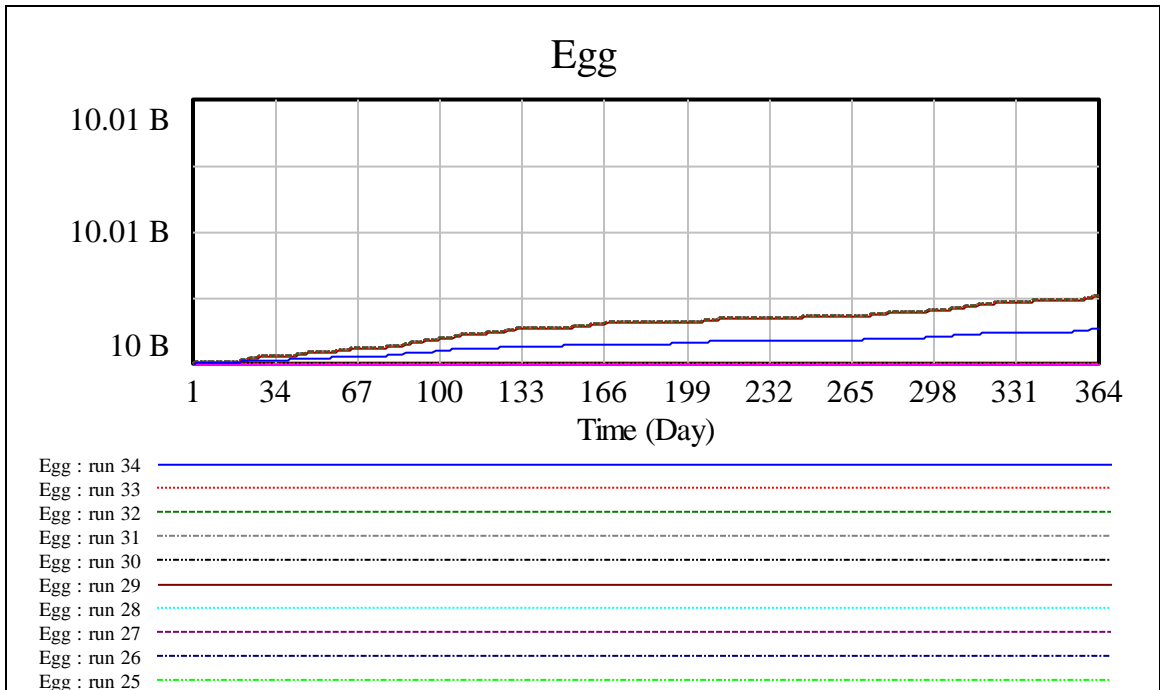


Figure 24: Vector egg simulation

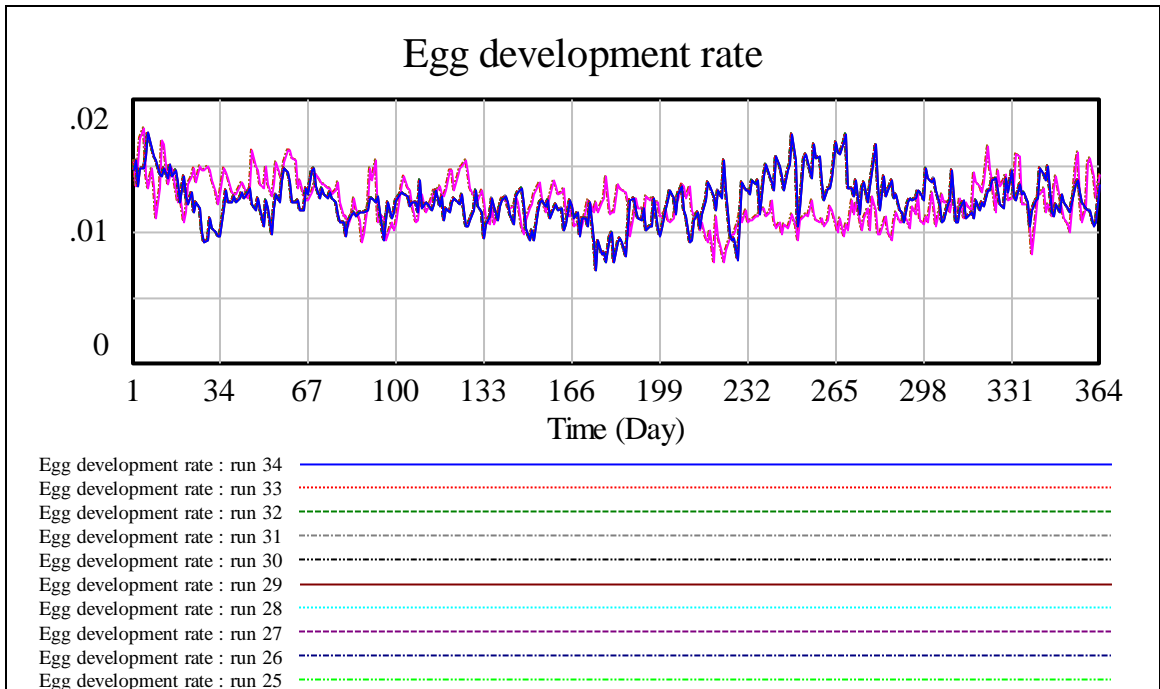


Figure 25: Egg development rate simulation

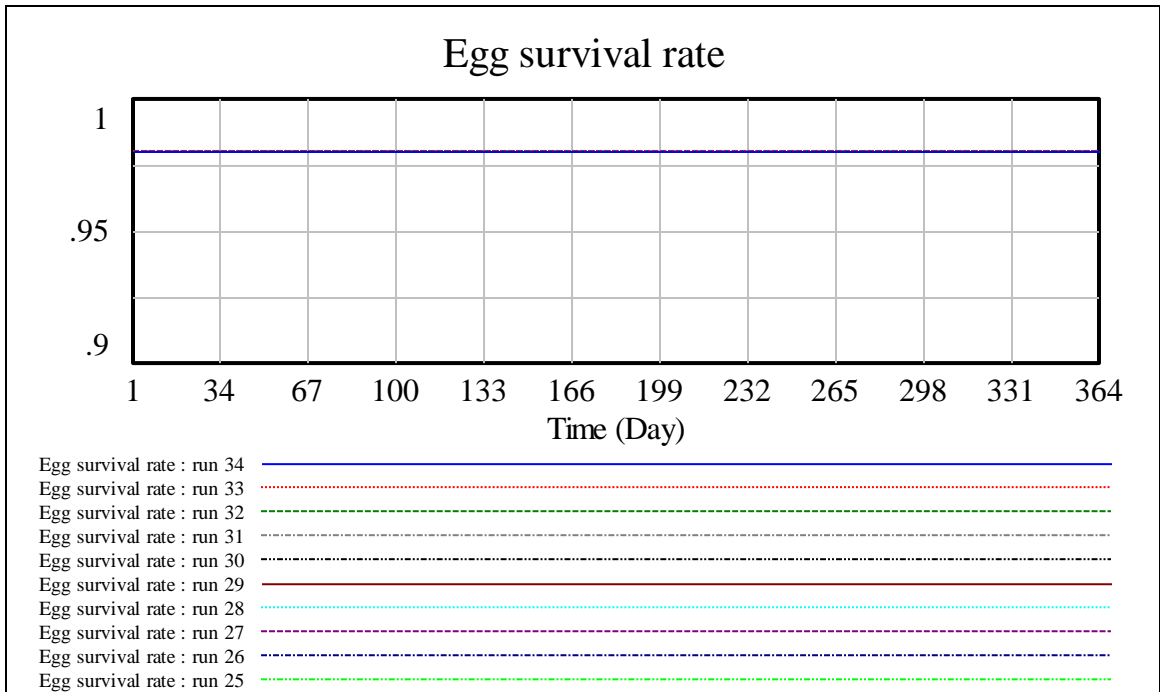


Figure 26: Egg survival rate simulation

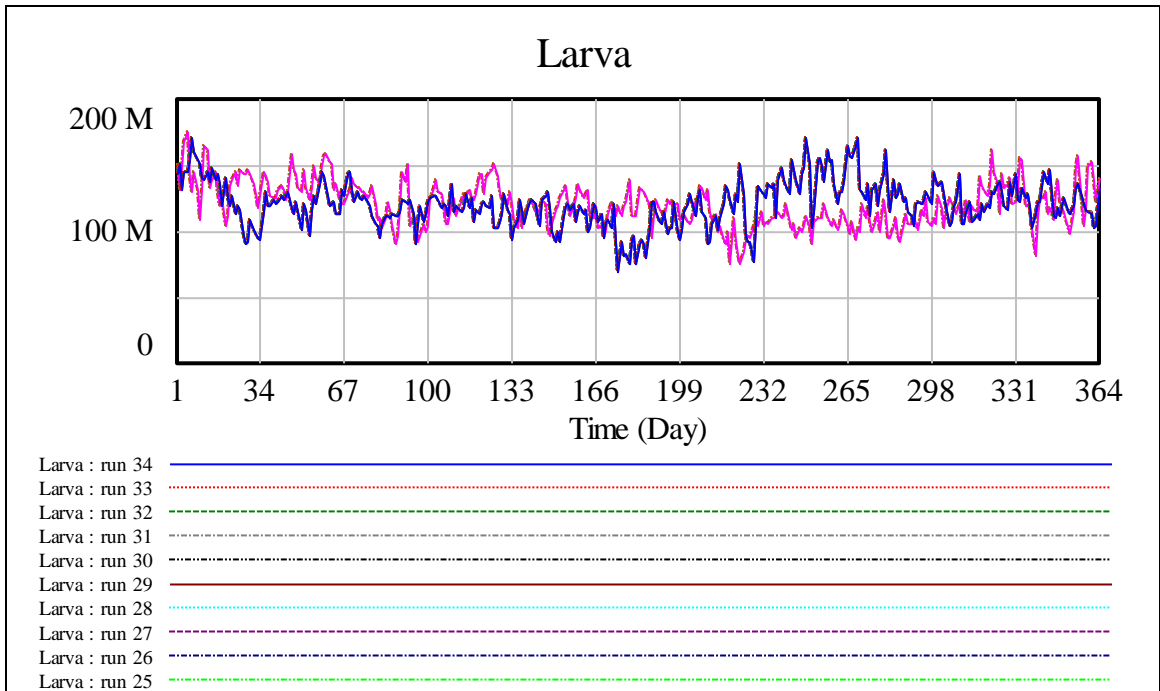


Figure 27: Larva simulation

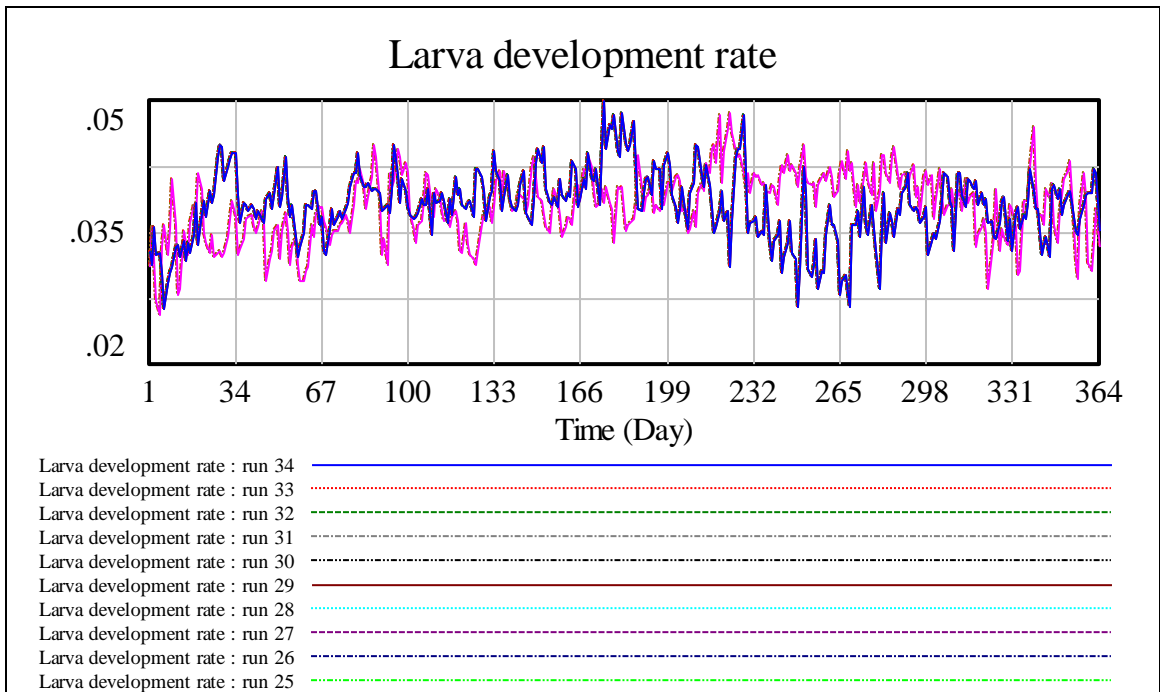


Figure 28: Larva development rate simulation

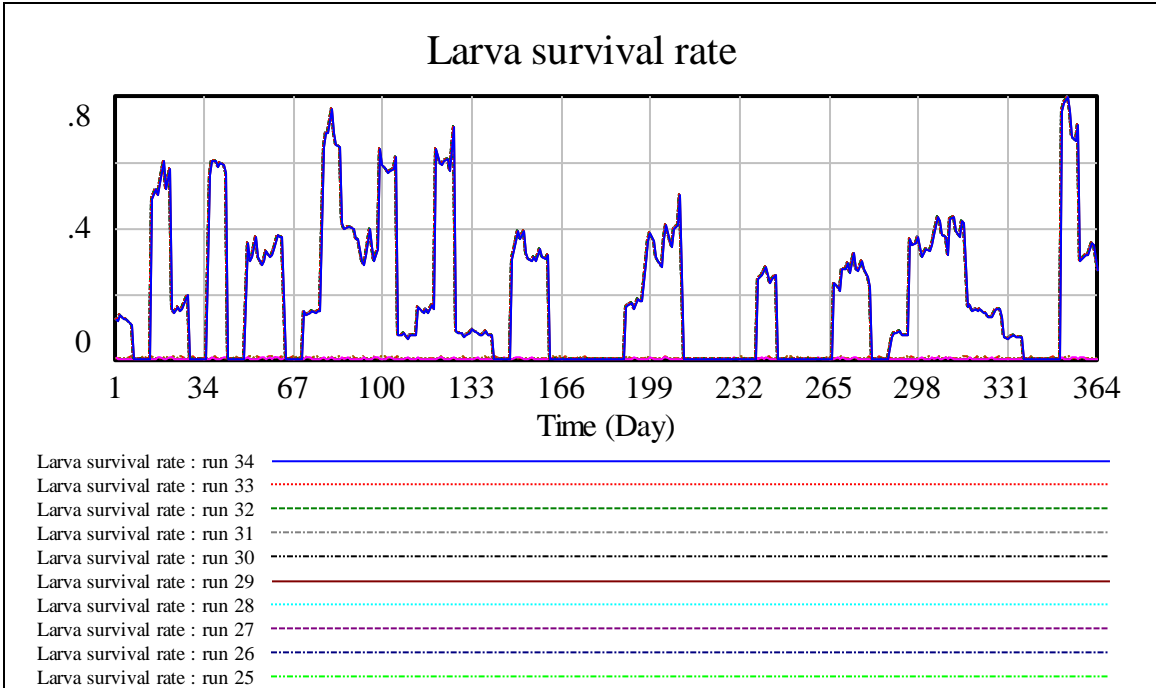


Figure 29: Larva survival rate simulation

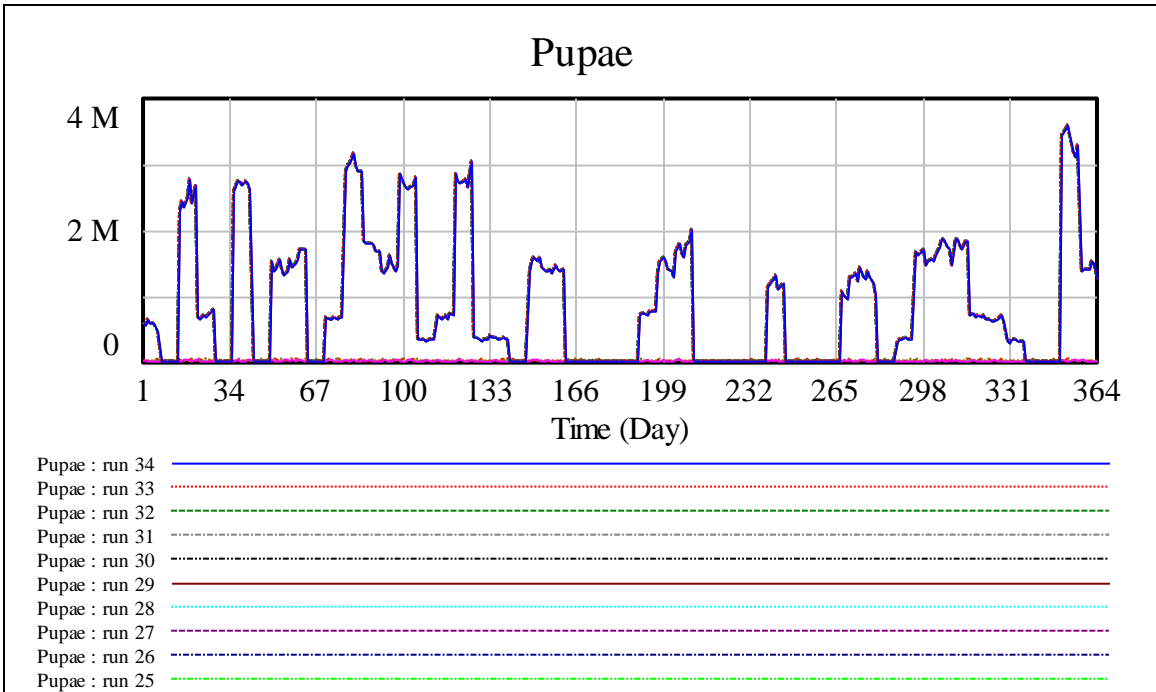


Figure 30: Pupae simulation

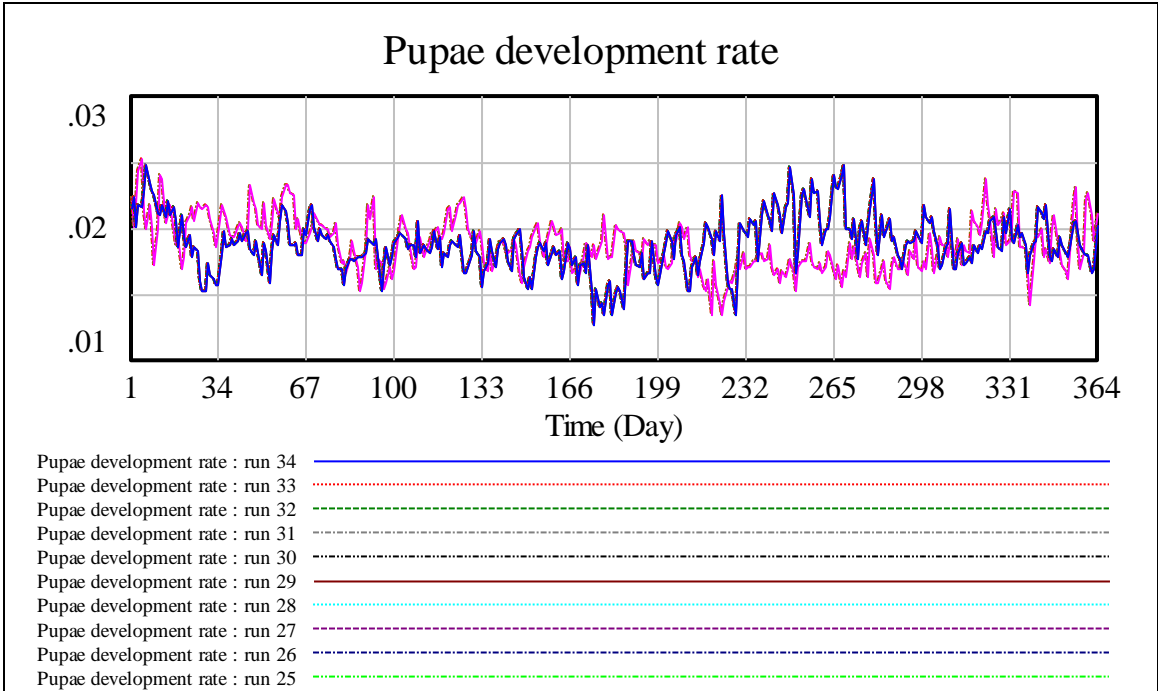


Figure 31: Pupae development rate simulation

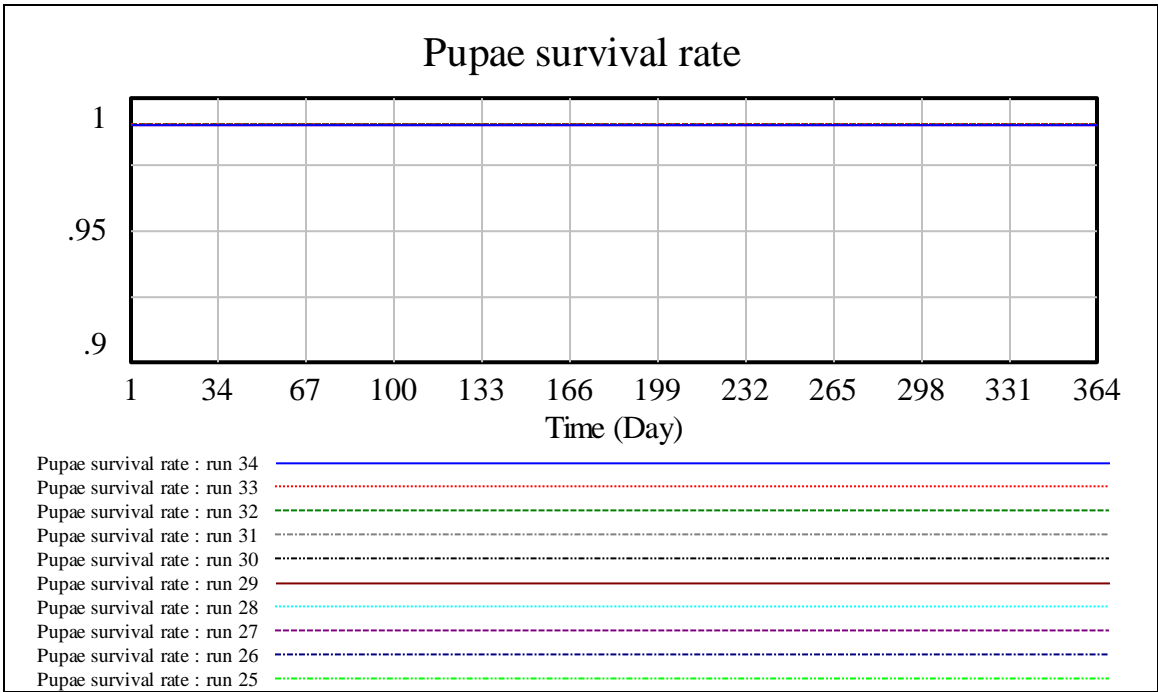


Figure 32: Pupae survival rate simulation

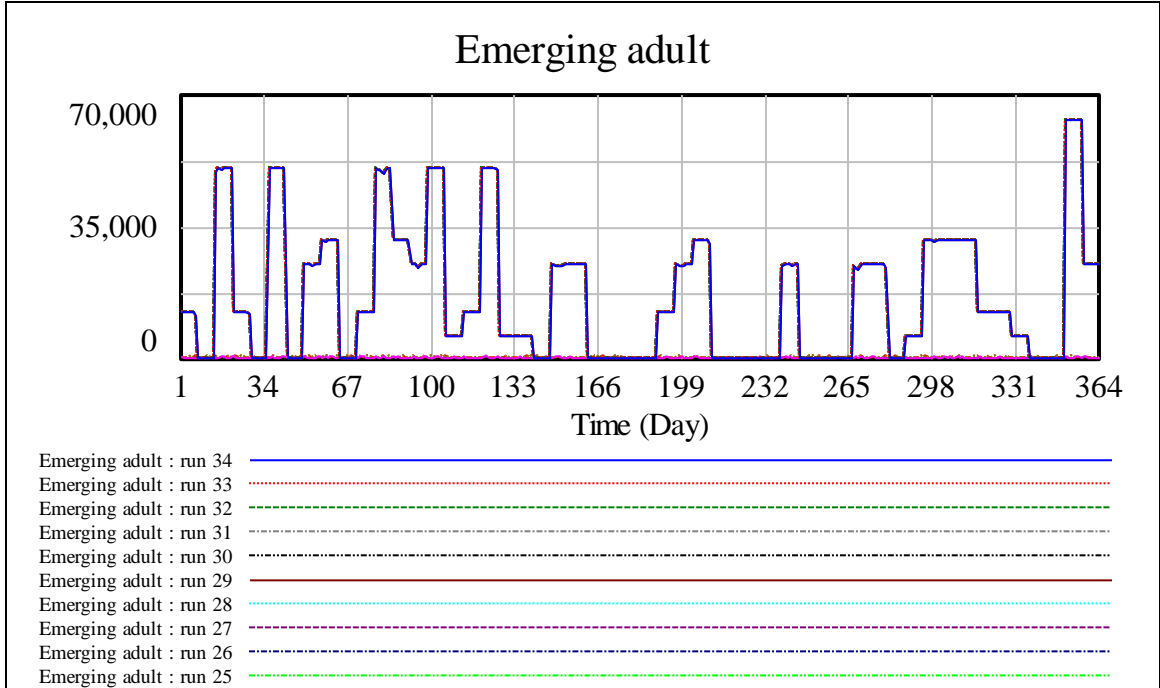


Figure 33: Emerging adult simulation

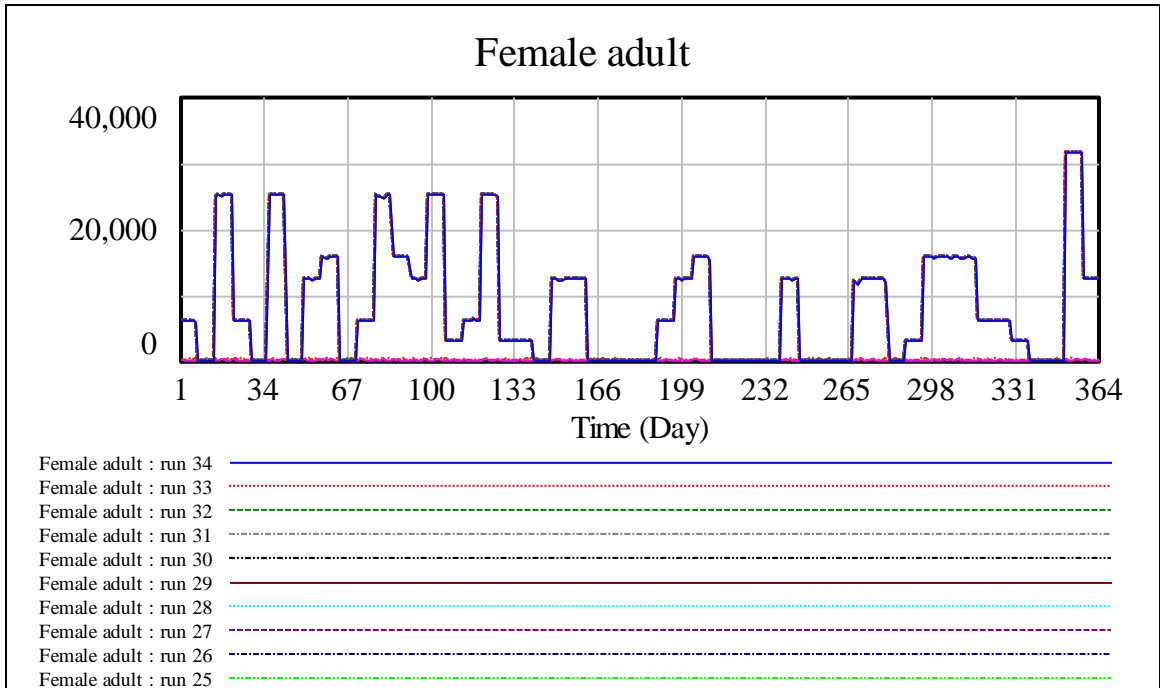


Figure 34: Female adult simulation

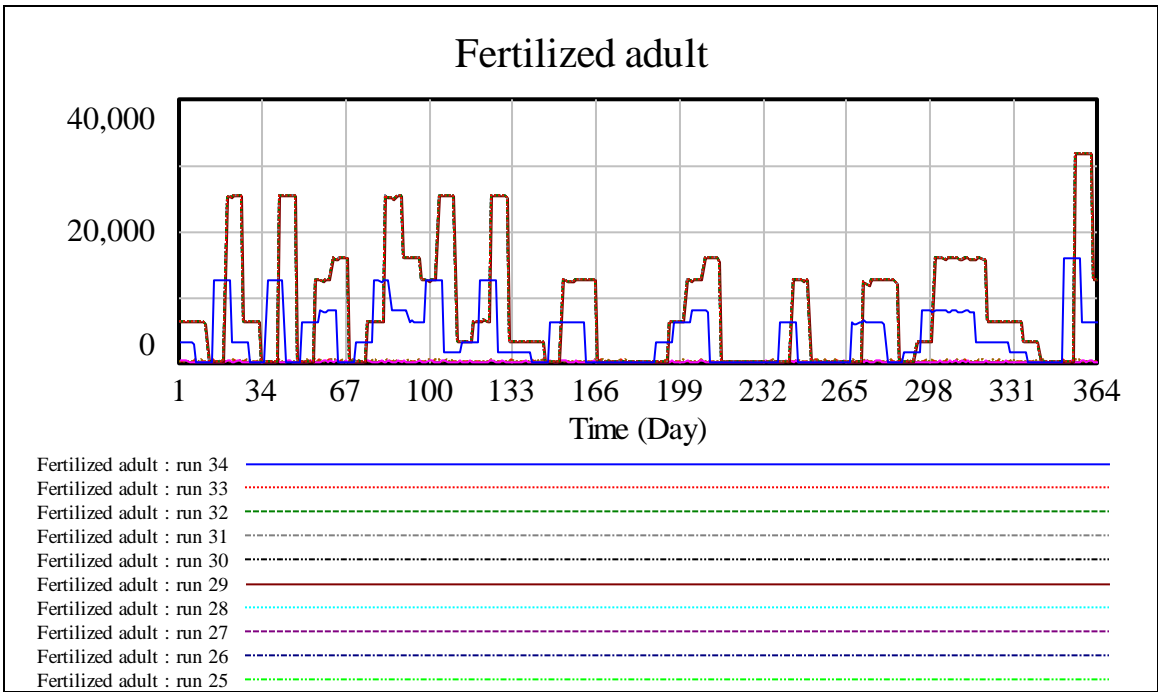


Figure 35: Fertilized adult simulation

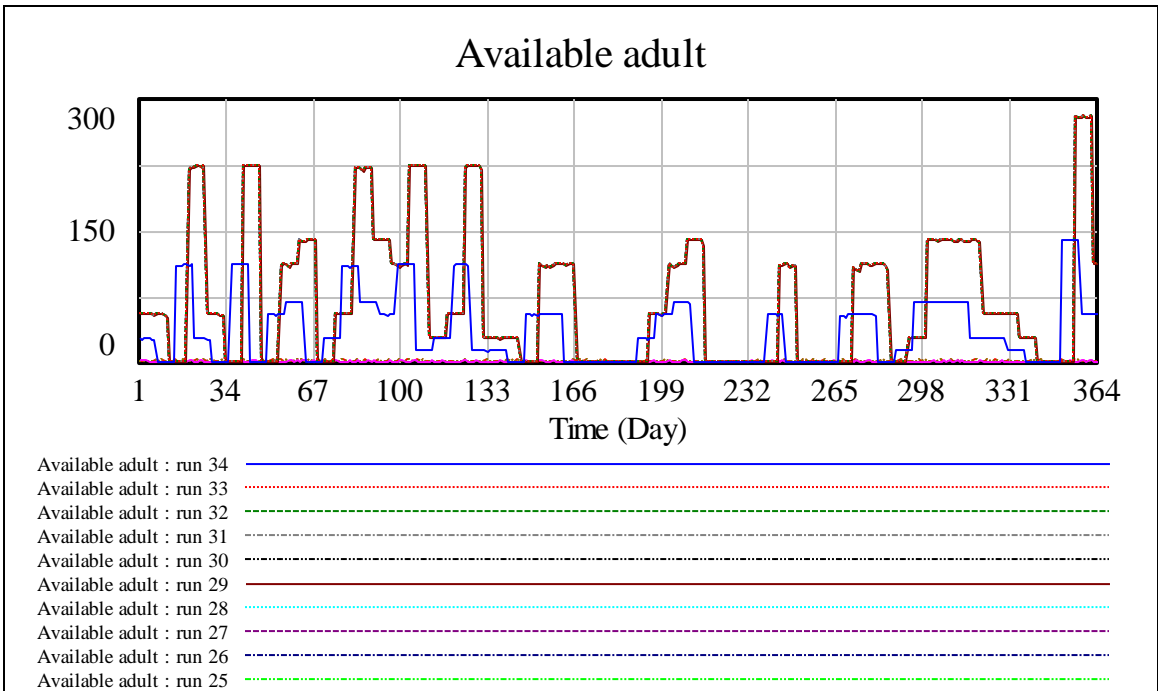


Figure 36: Available adult simulation

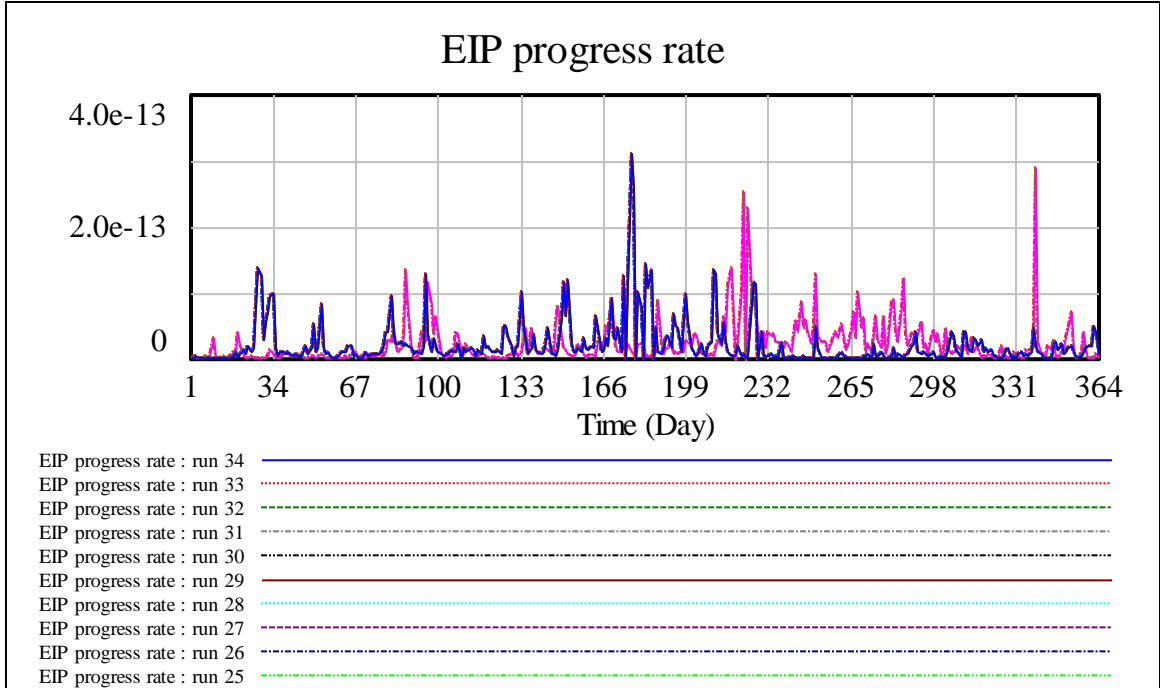


Figure 37: EIP progress rate simulation

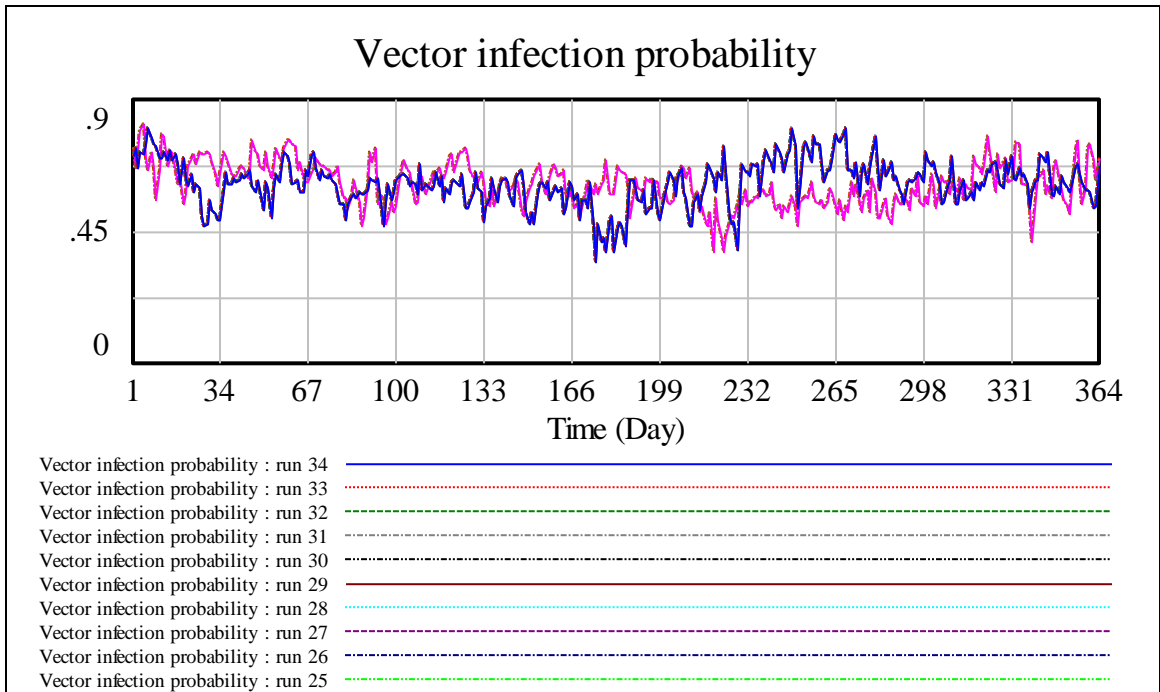


Figure 38: Vector infection probability simulation



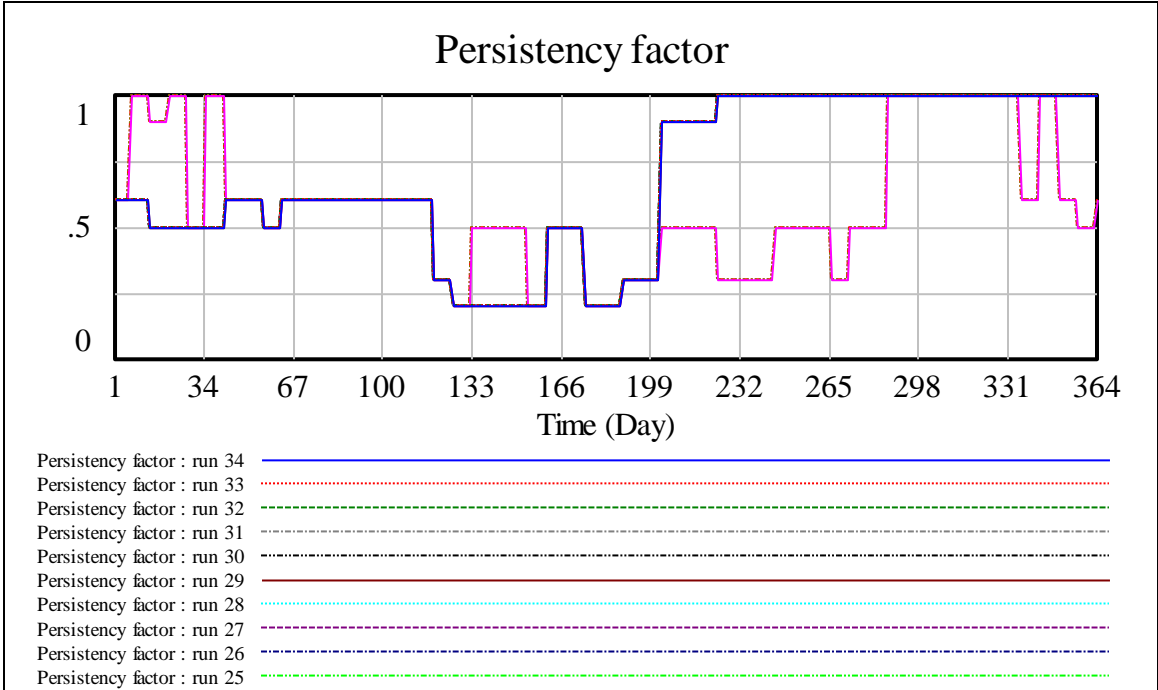


Figure 39: Dew point temperature based persistency factor simulation

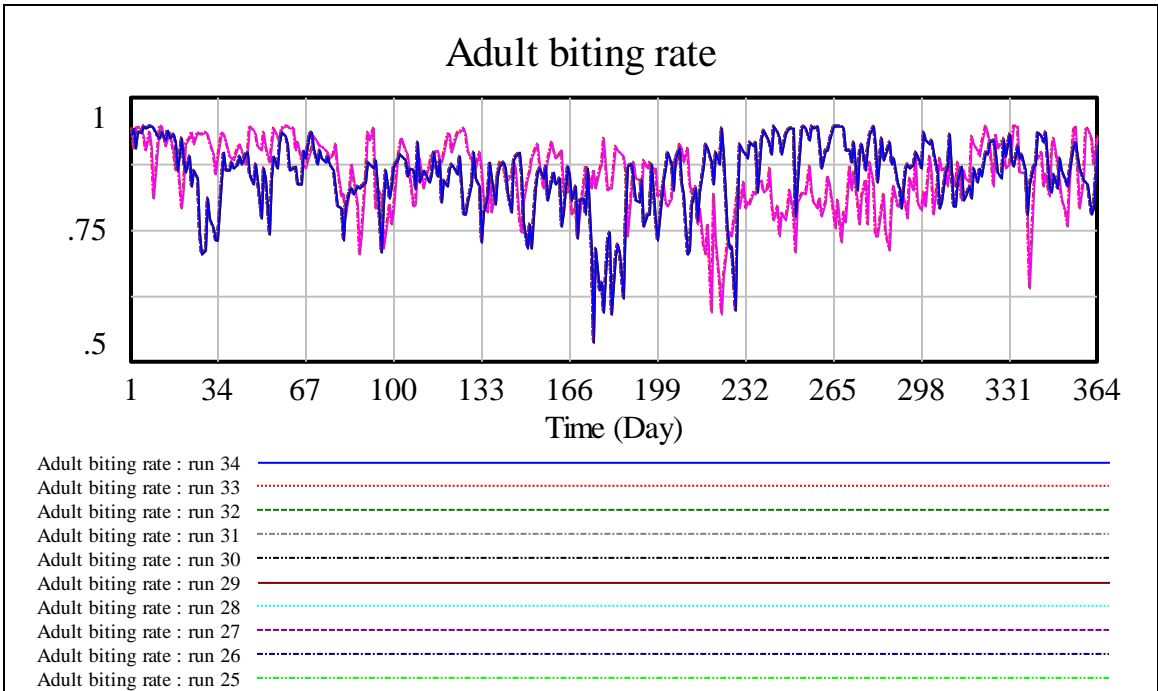


Figure 40: Adult biting rate simulation

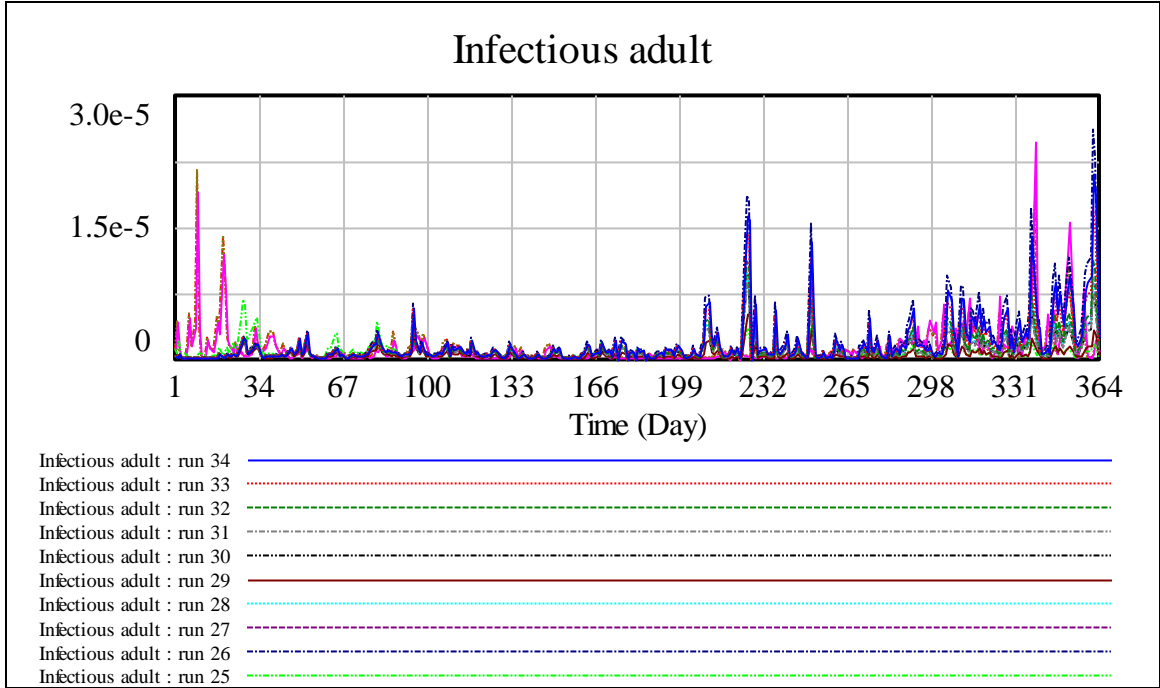


Figure 41: Infectious adult simulation

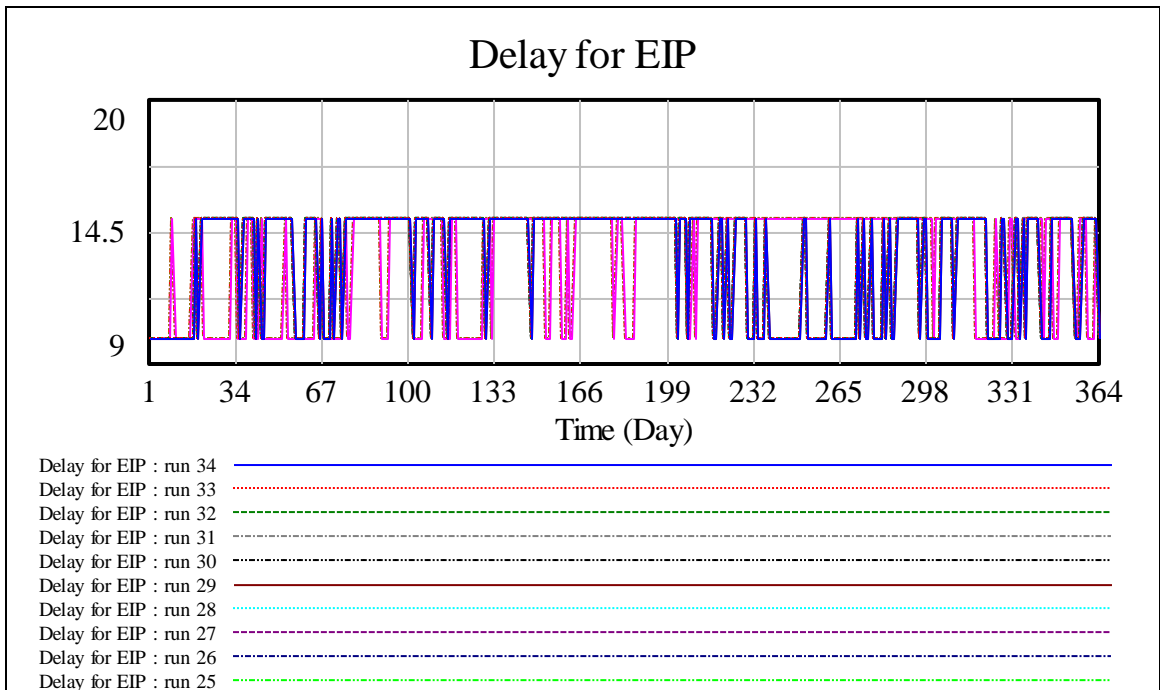


Figure 42: Delay for EIP simulation

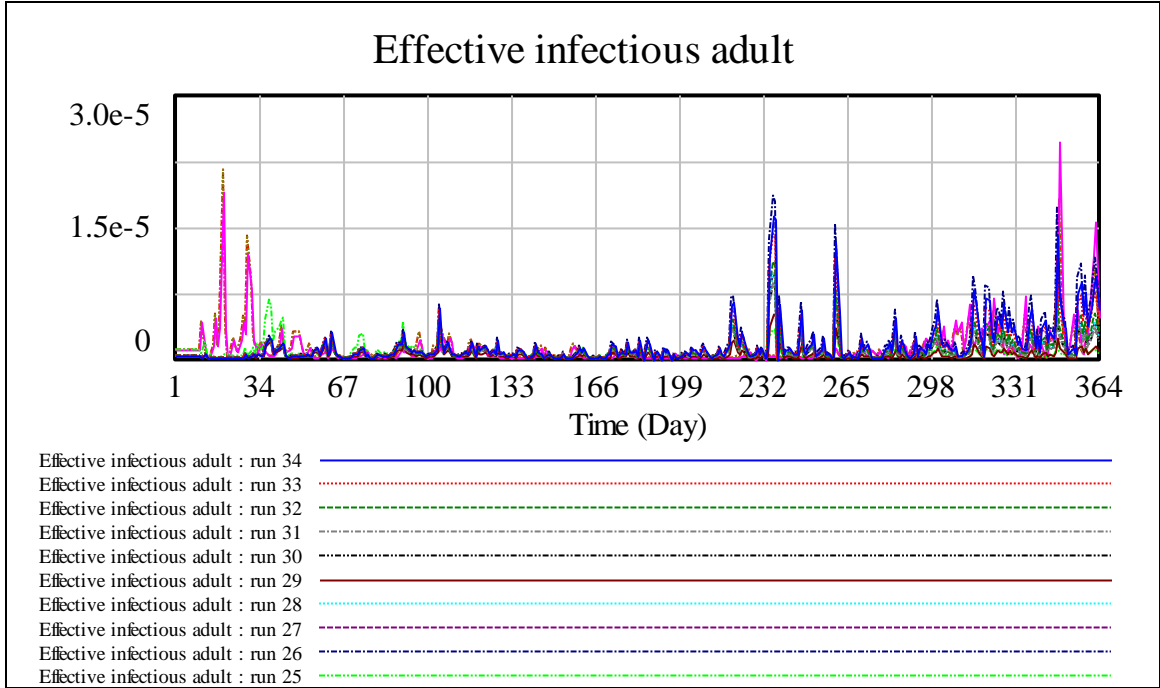


Figure 43: Effective infectious adult simulation

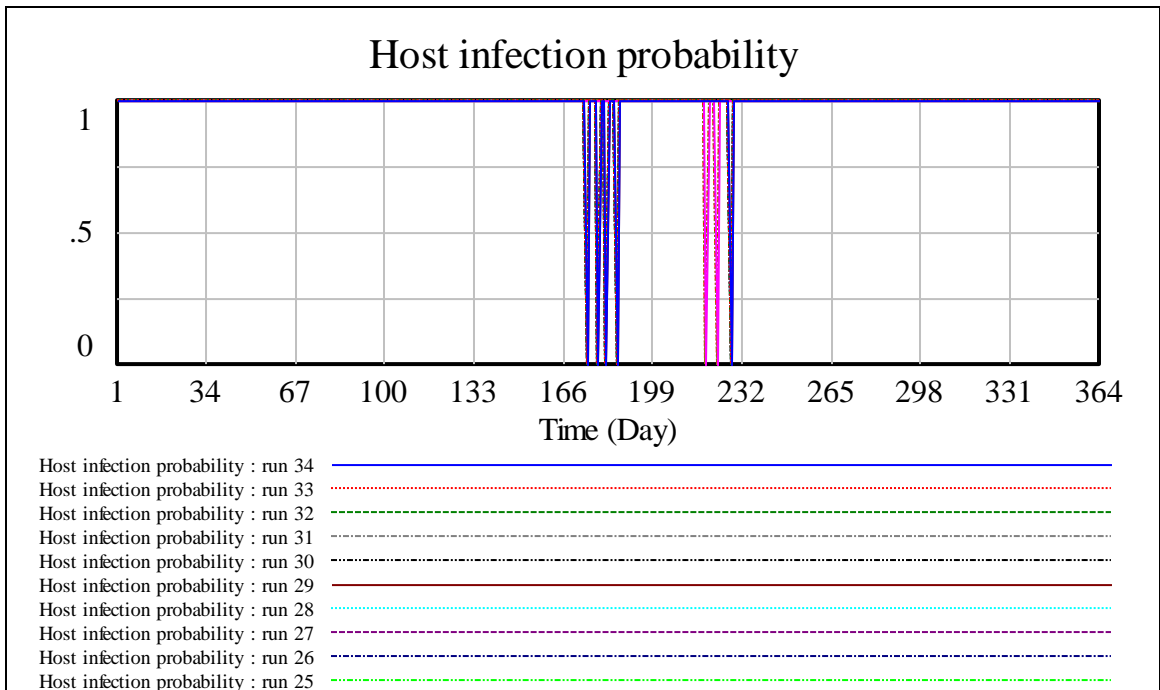


Figure 44: Host infection probability simulation

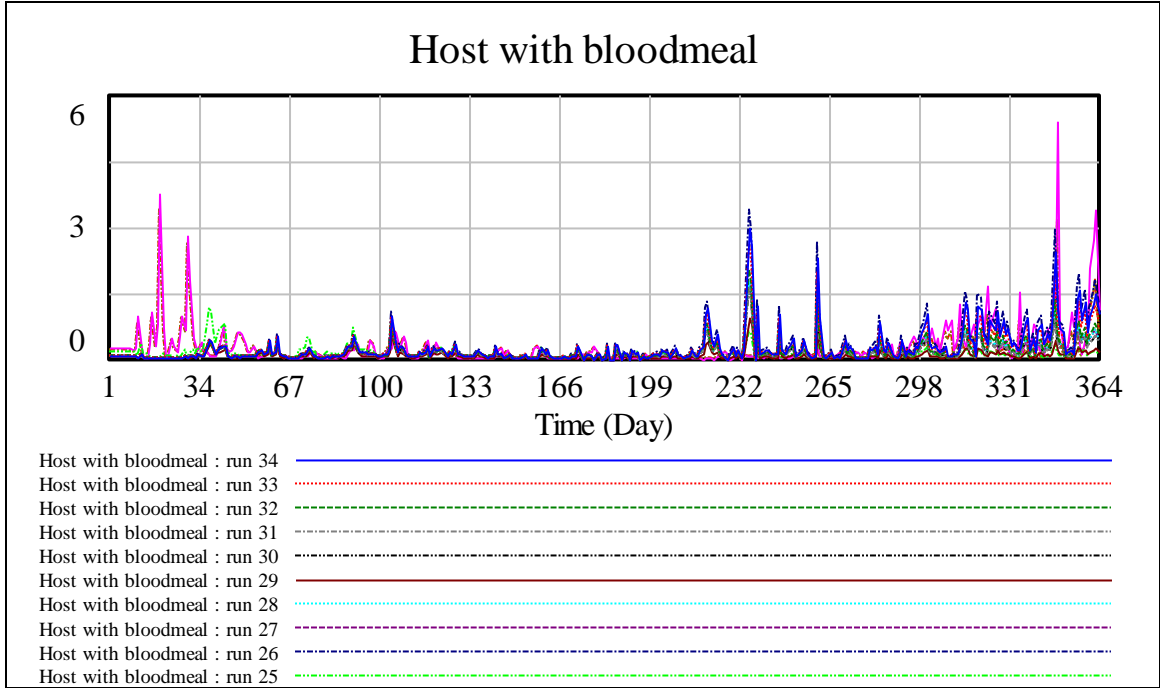


Figure 45: Host with bloodmeal simulation

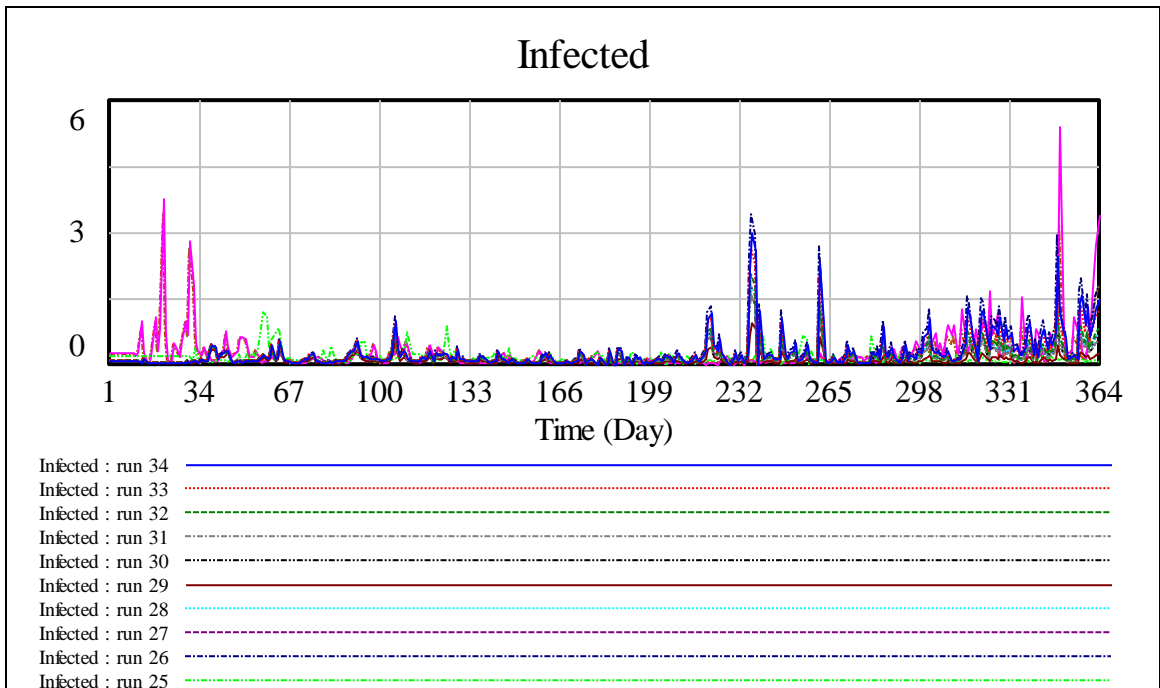


Figure 46: Infected simulation

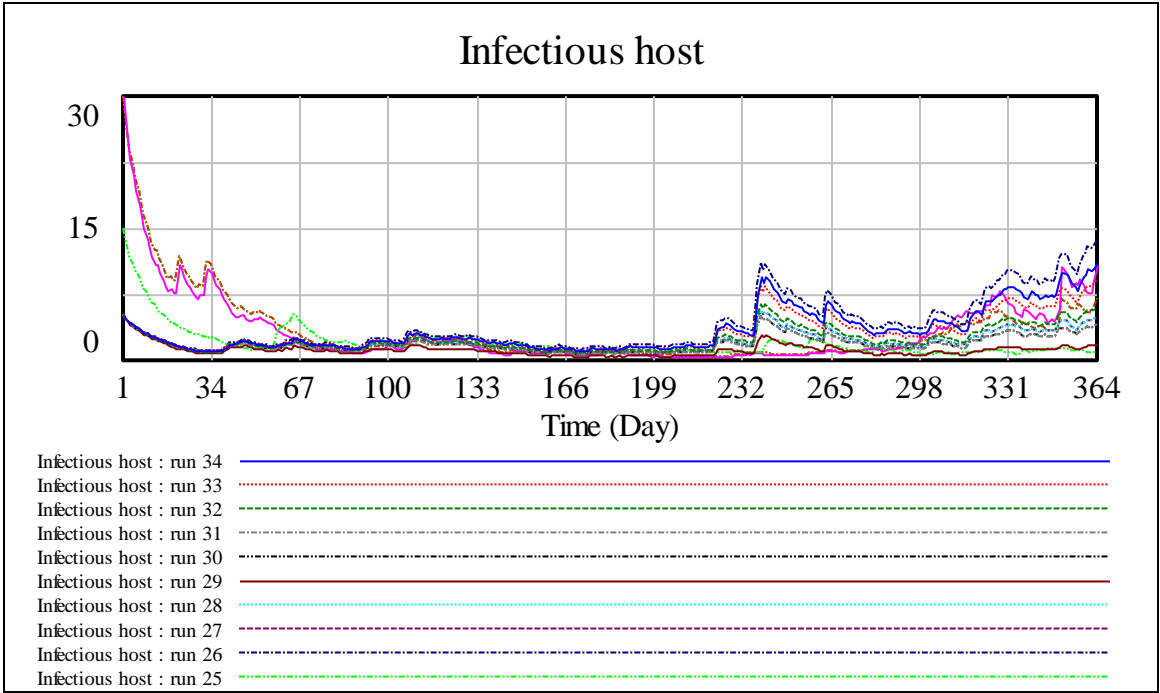


Figure 47: Infectious host simulation

Vensim Simulations 2008

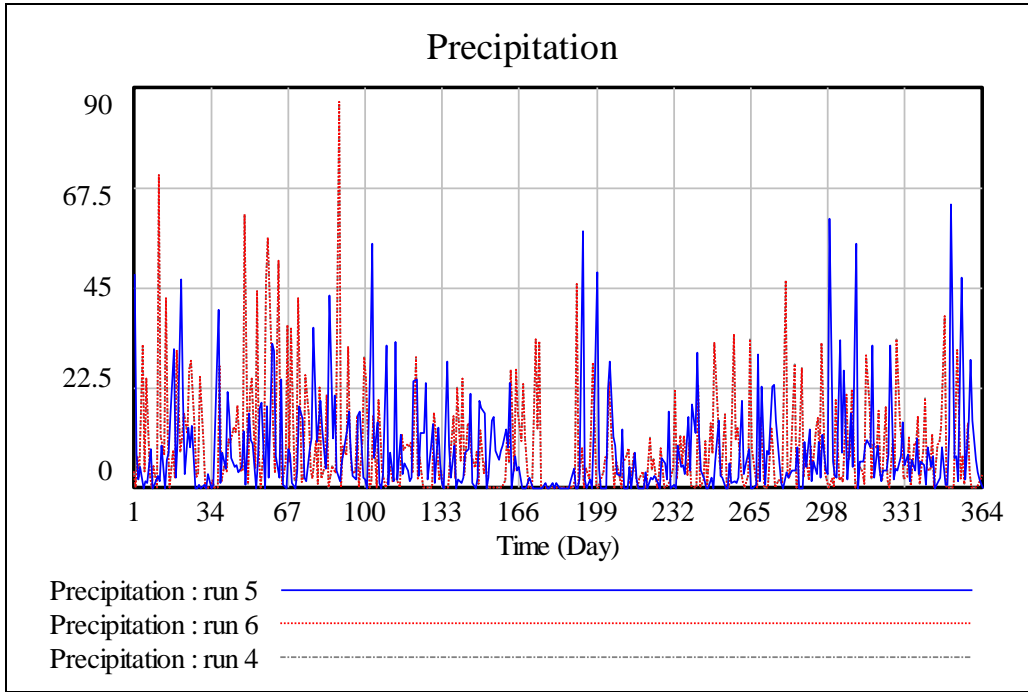


Figure 48: Precipitation simulation 2008

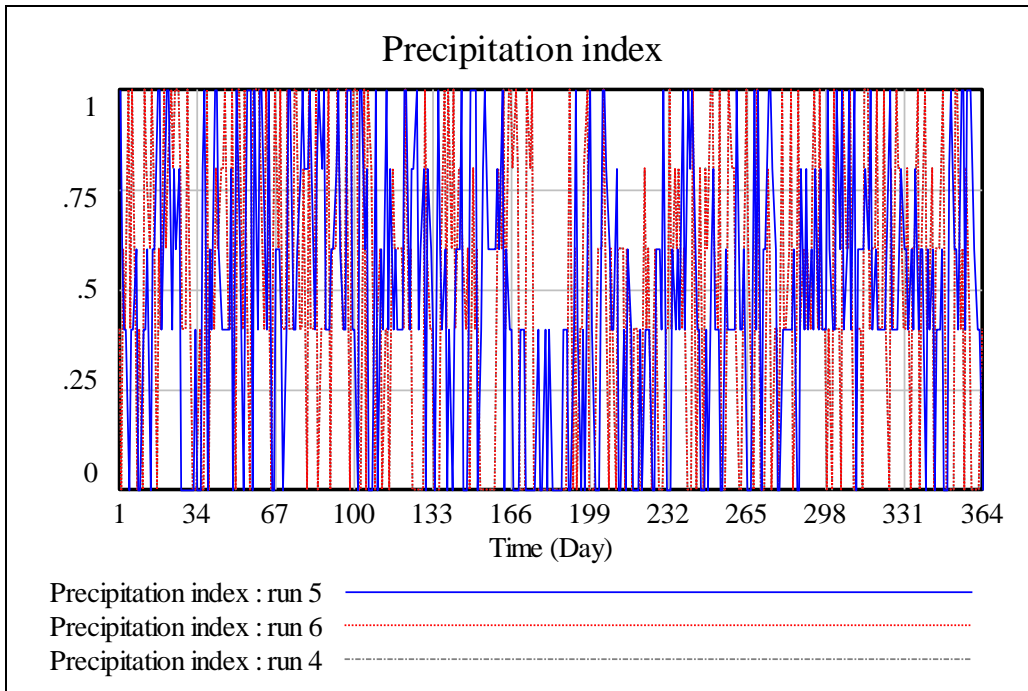


Figure 49: Precipitation index simulation 2008

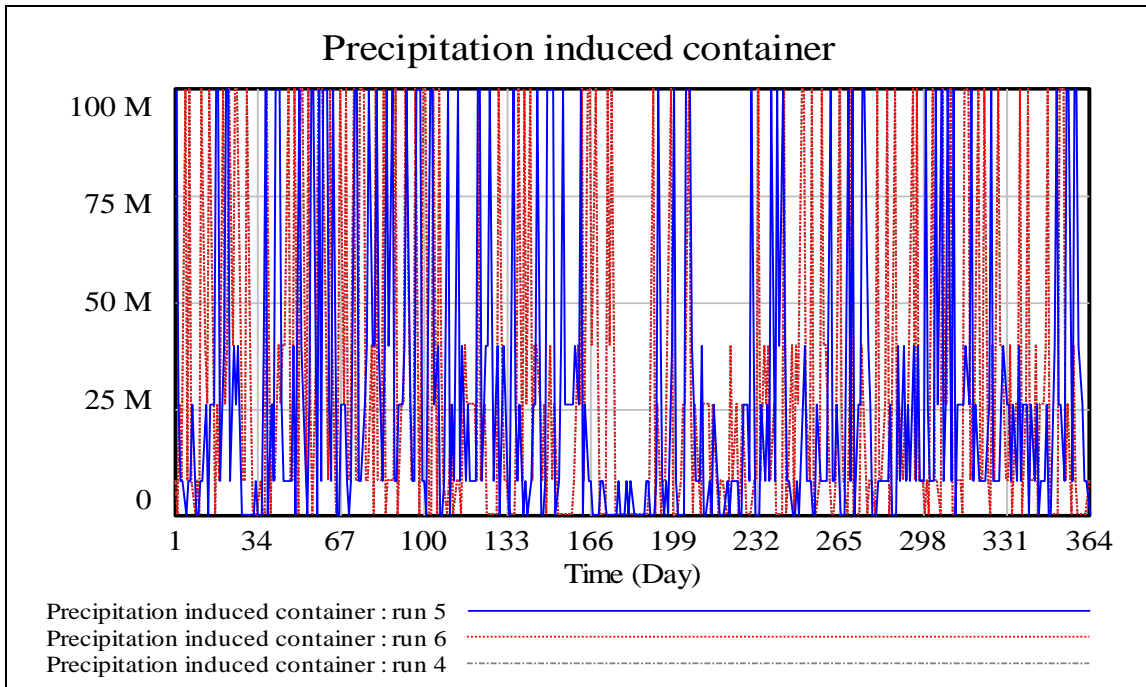


Figure 50: Precipitation induced container simulation 2008

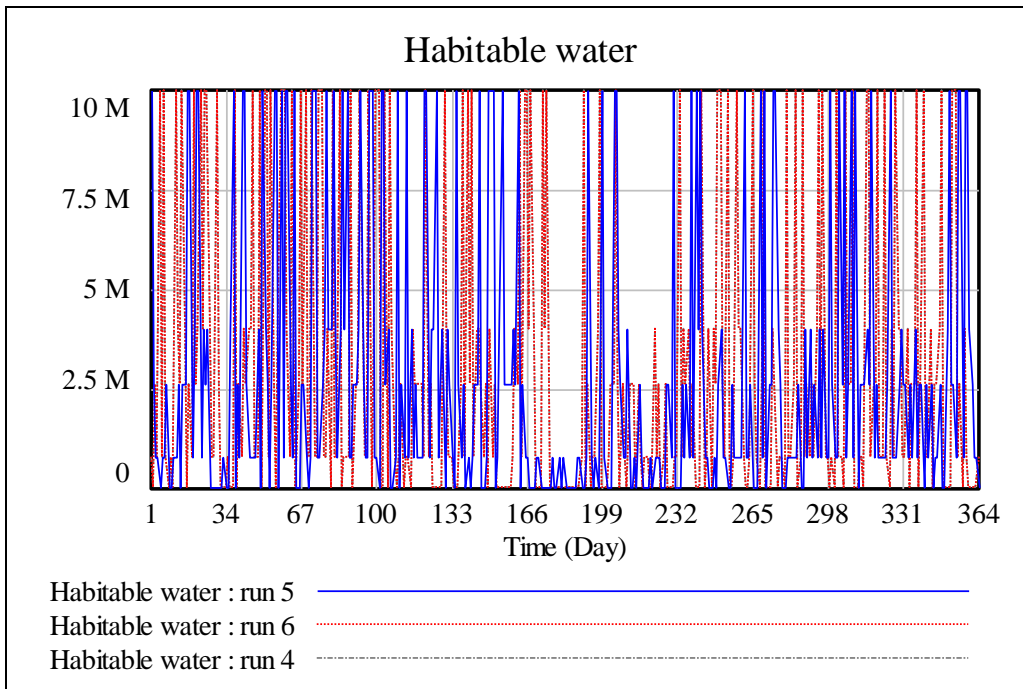


Figure 51: Habitable water simulation 2008

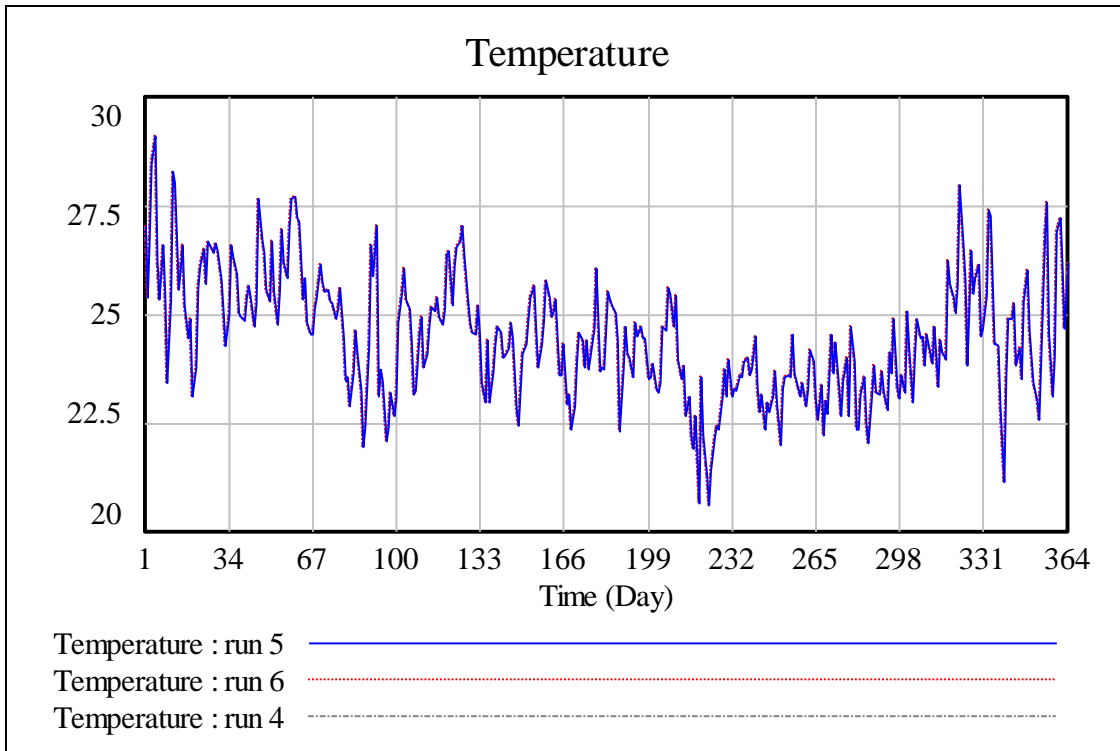


Figure 52: Temperature simulation 2008

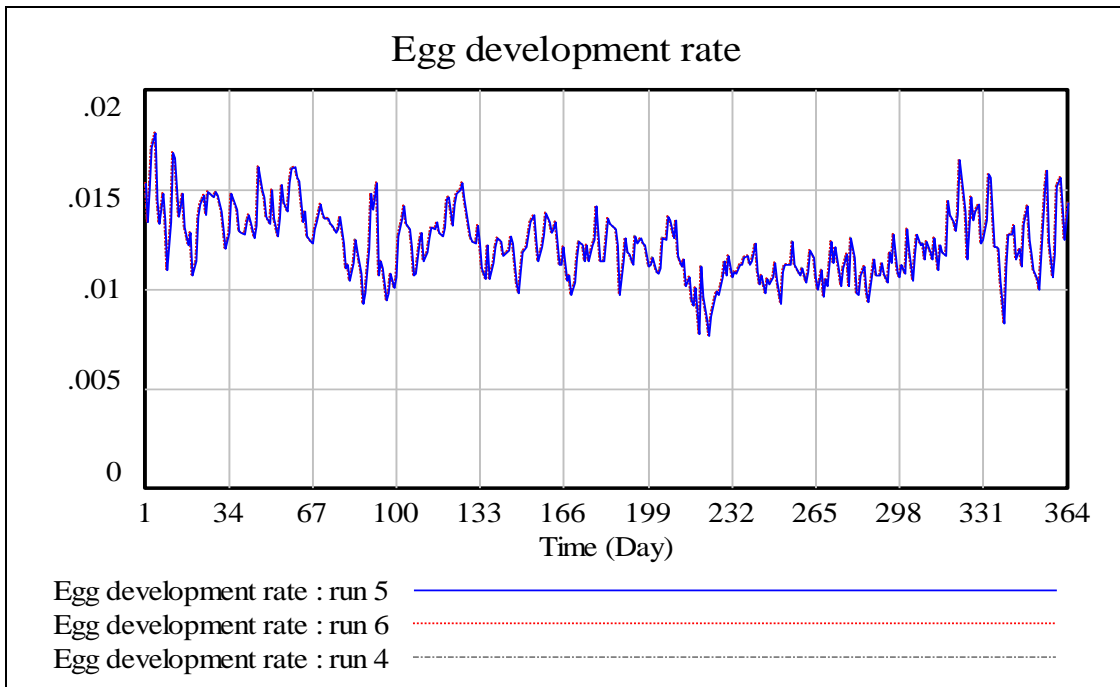


Figure 53: Egg development rate simulation 2008



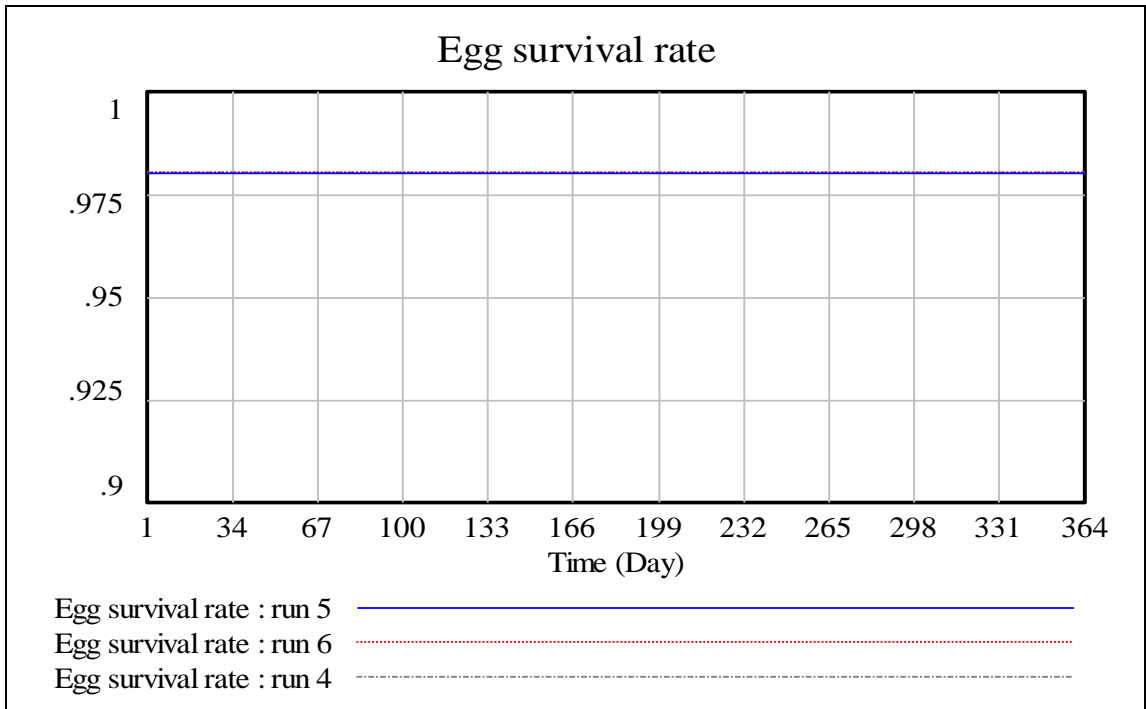


Figure 54: Egg survival rate simulation 2008

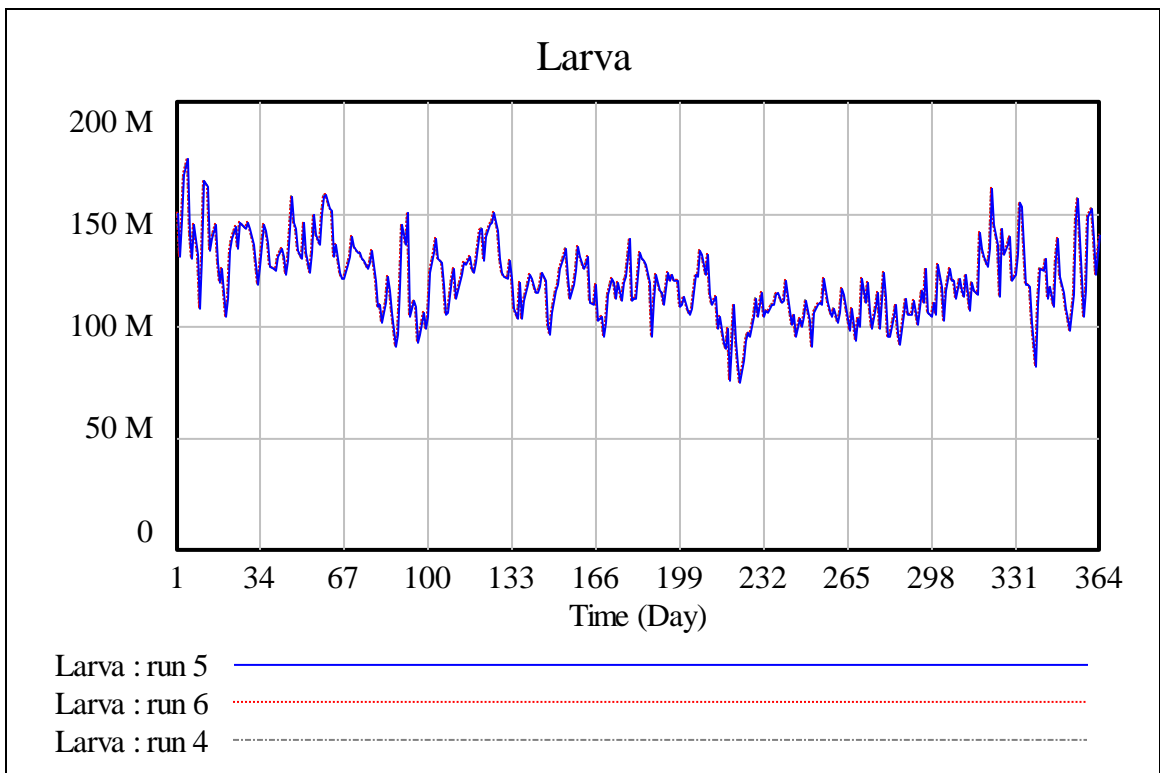


Figure 55: Larva simulation 2008

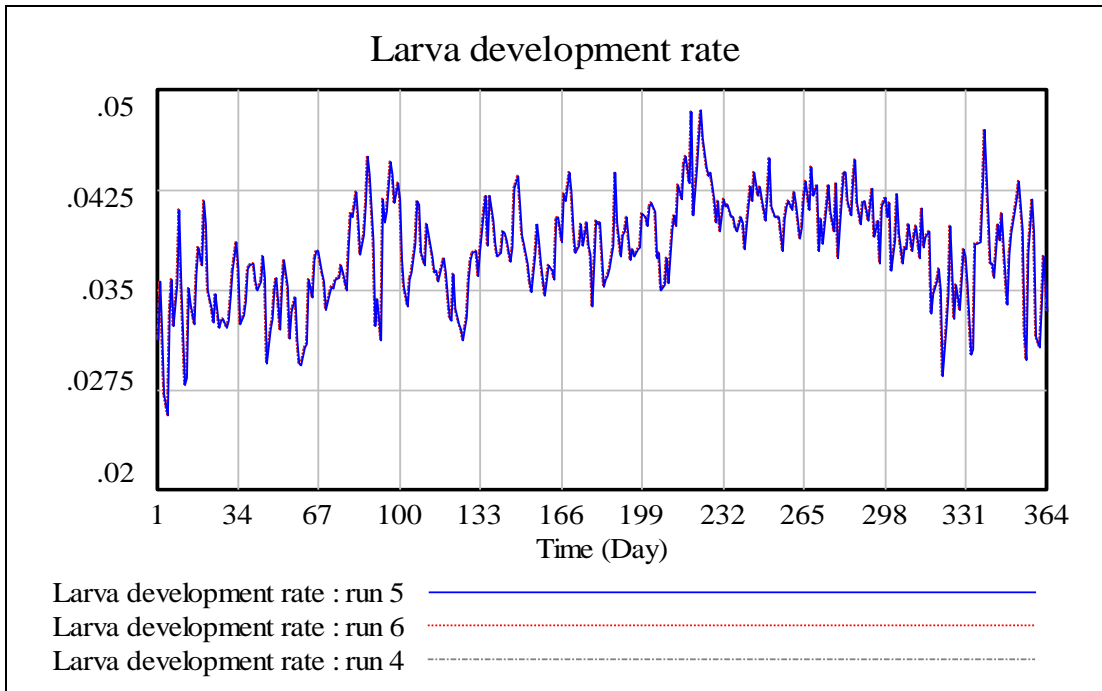


Figure 56: Larva development rate simulation 2008

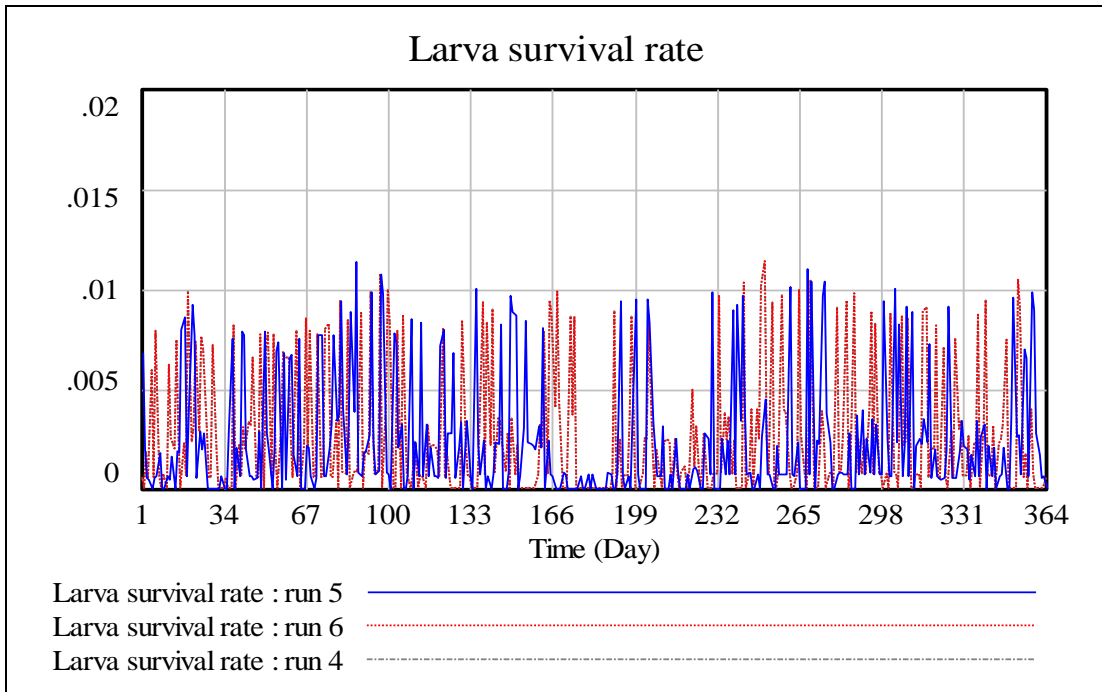


Figure 57: Larva survival rate simulation 2008

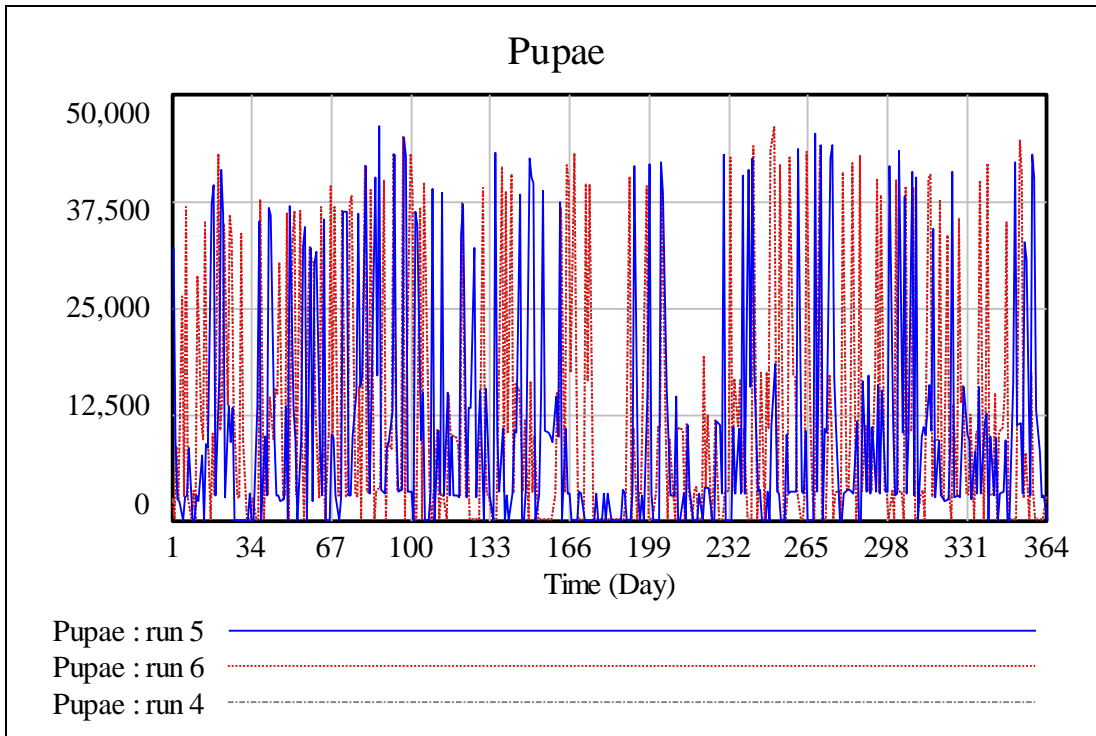


Figure 58: Pupae simulation 2008

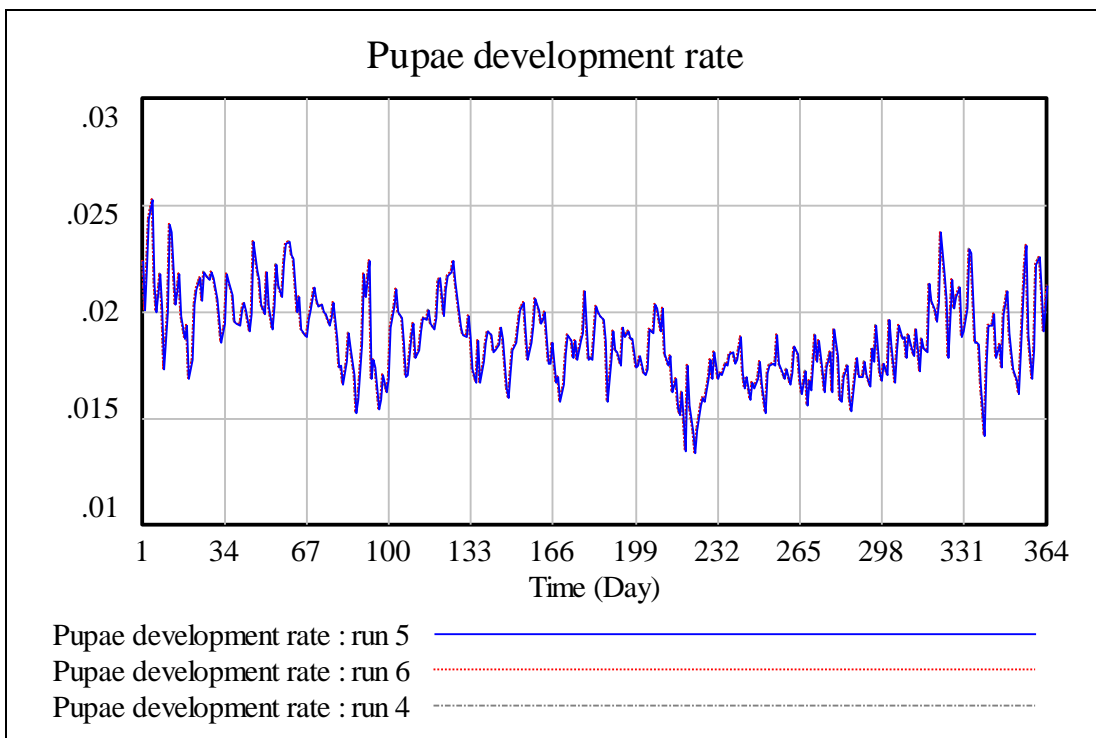


Figure 59: Pupae development rate simulation 2008

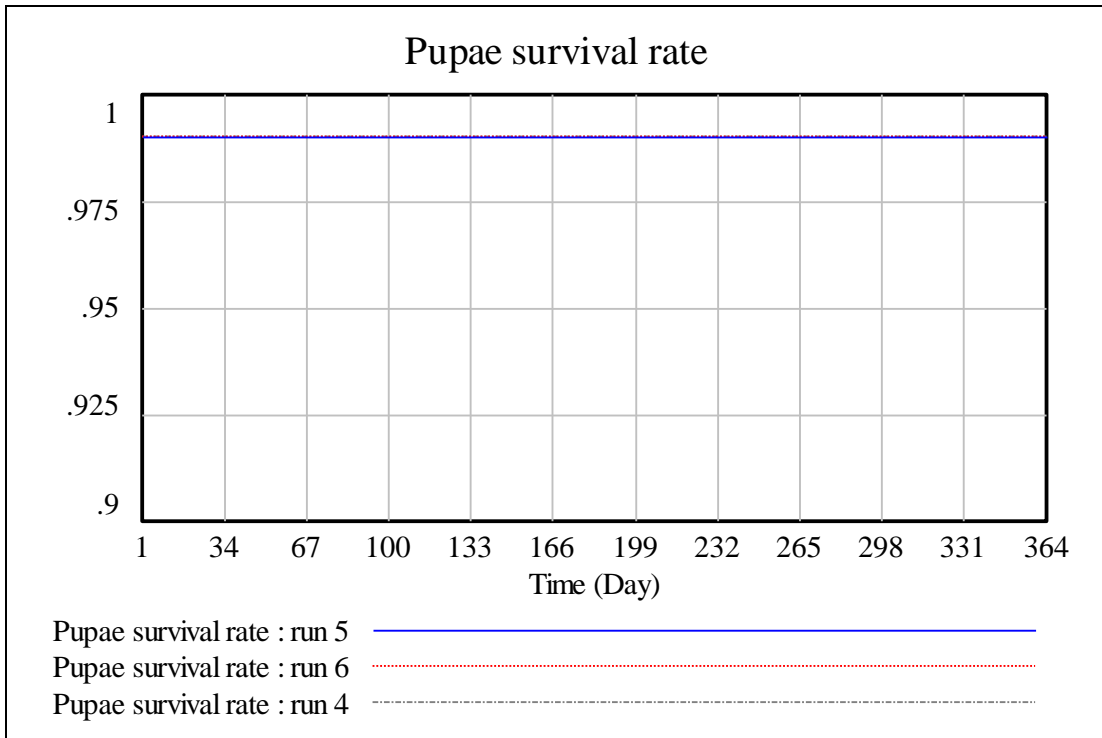


Figure 60: Pupae survival rate simulation 2008

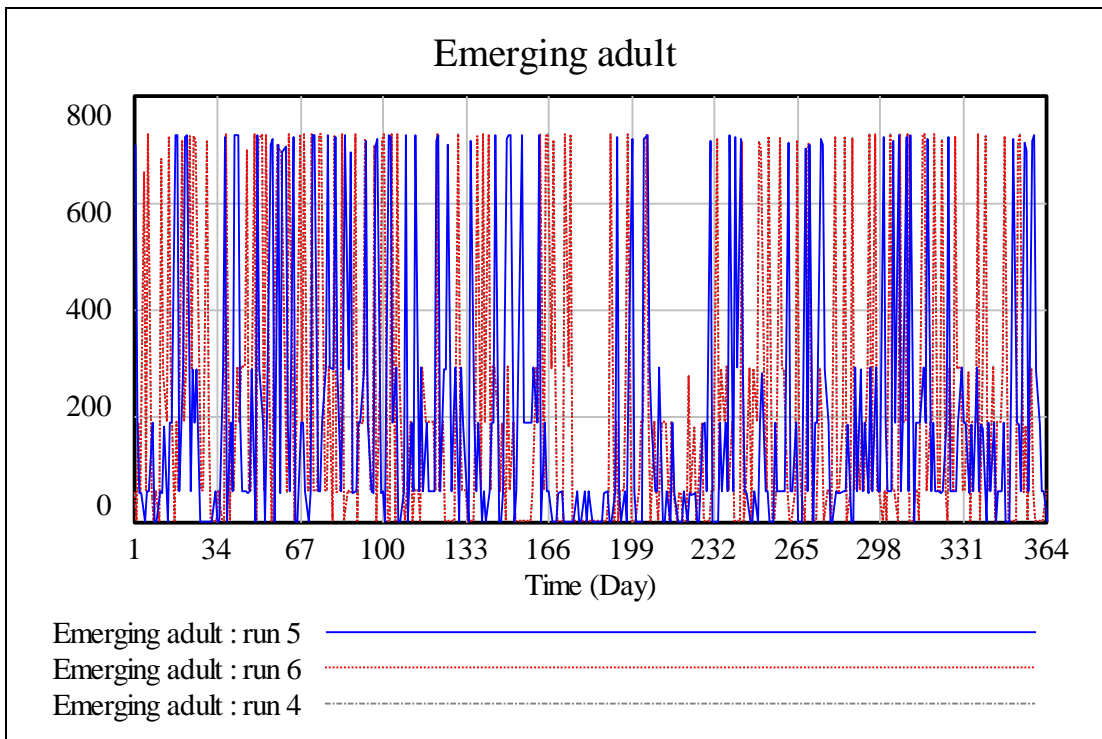


Figure 61: Emerging adult simulation 2008

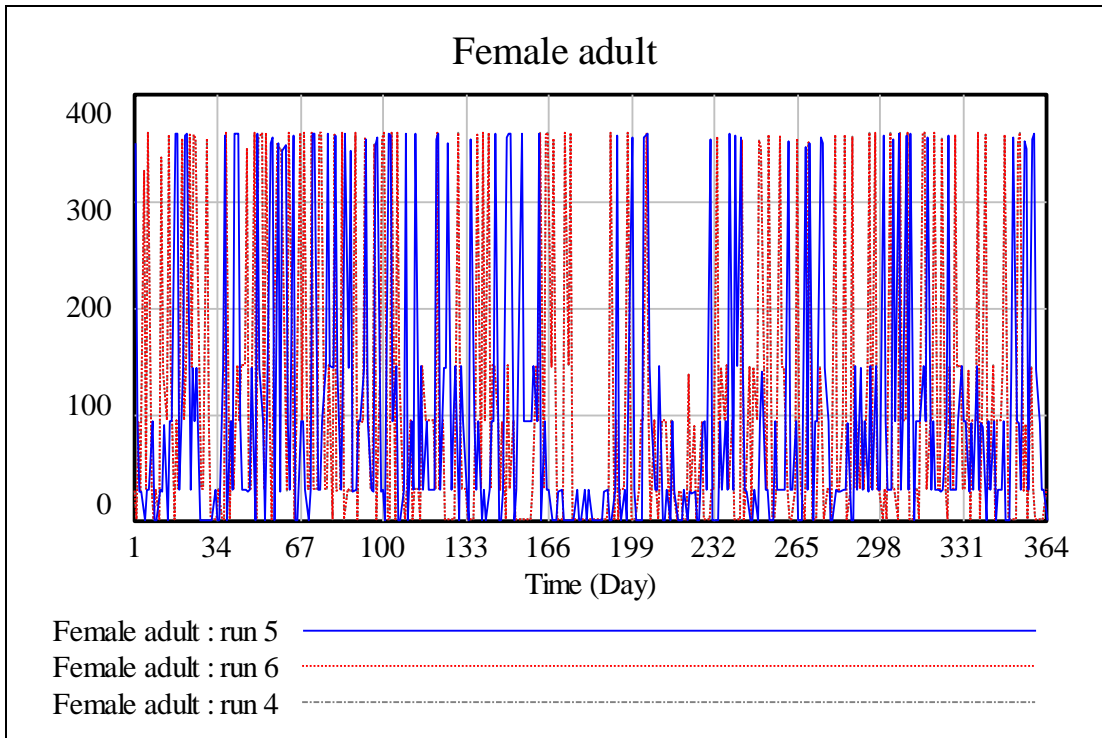


Figure 62: Female adult simulation 2008

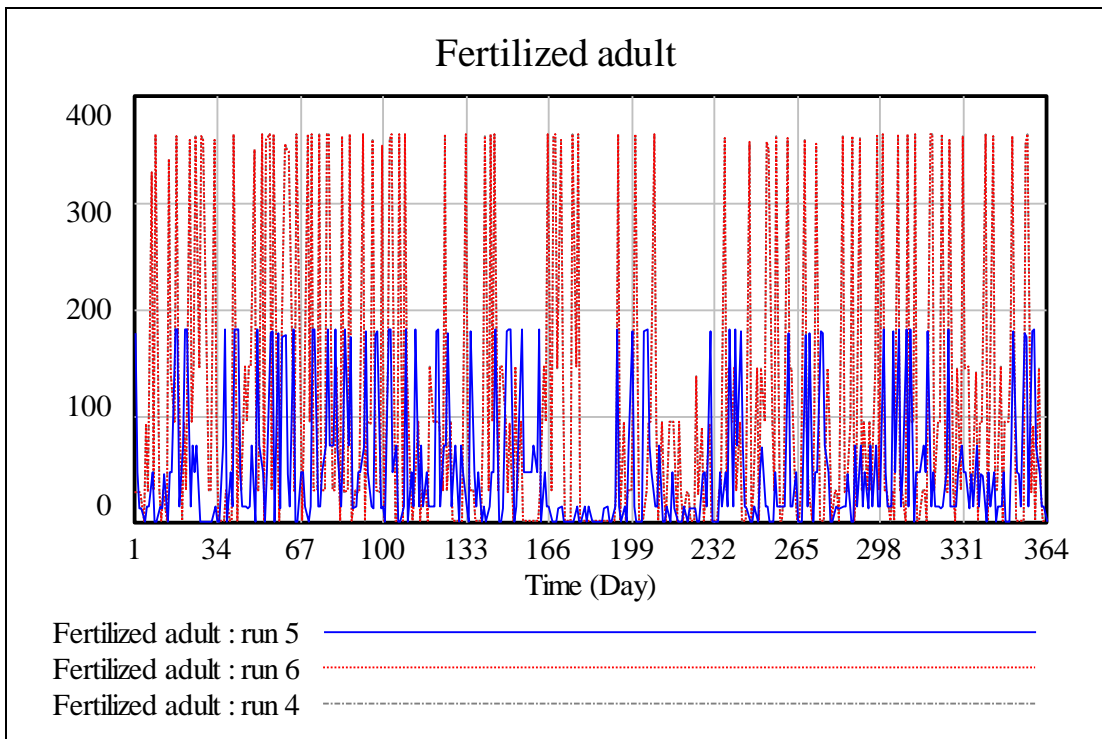


Figure 63: Fertilized adult simulation 2008

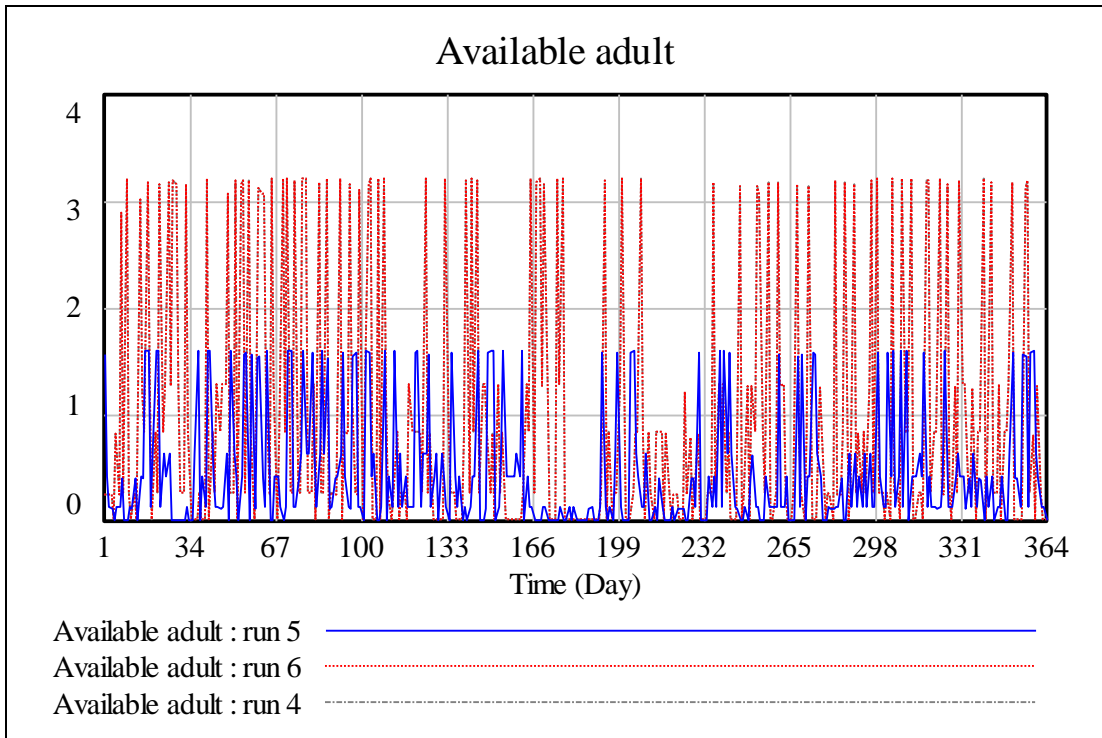


Figure 64: Available adult simulation 2008

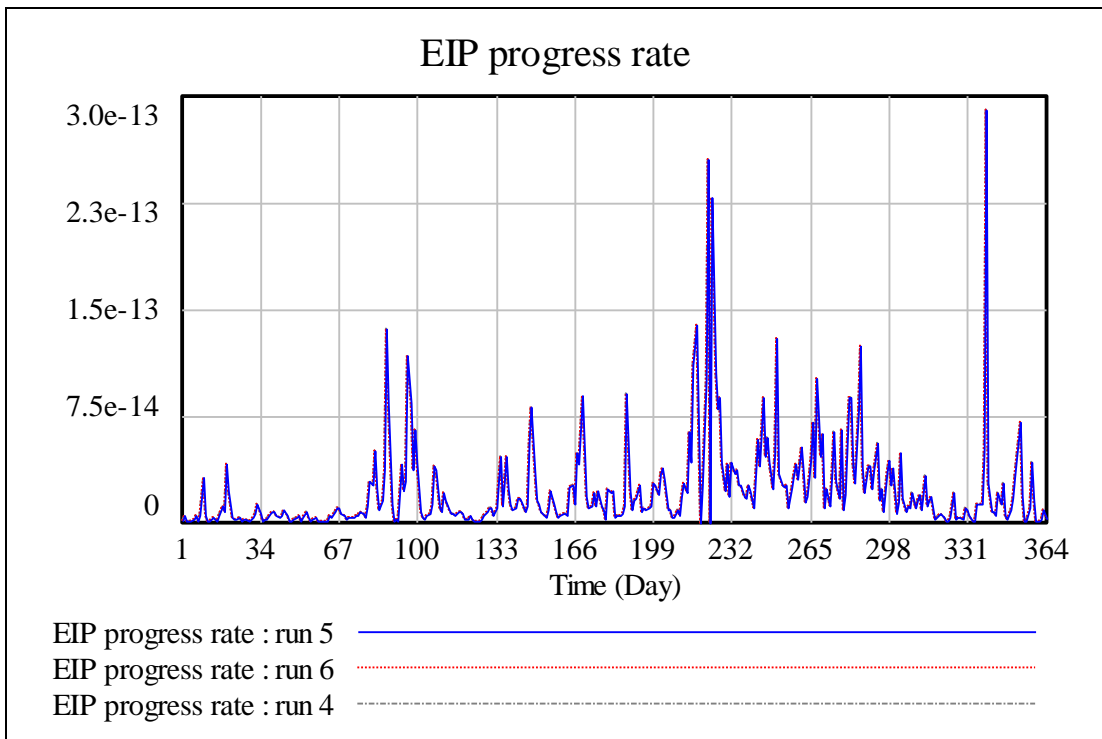


Figure 65: EIP progress rate simulation 2008

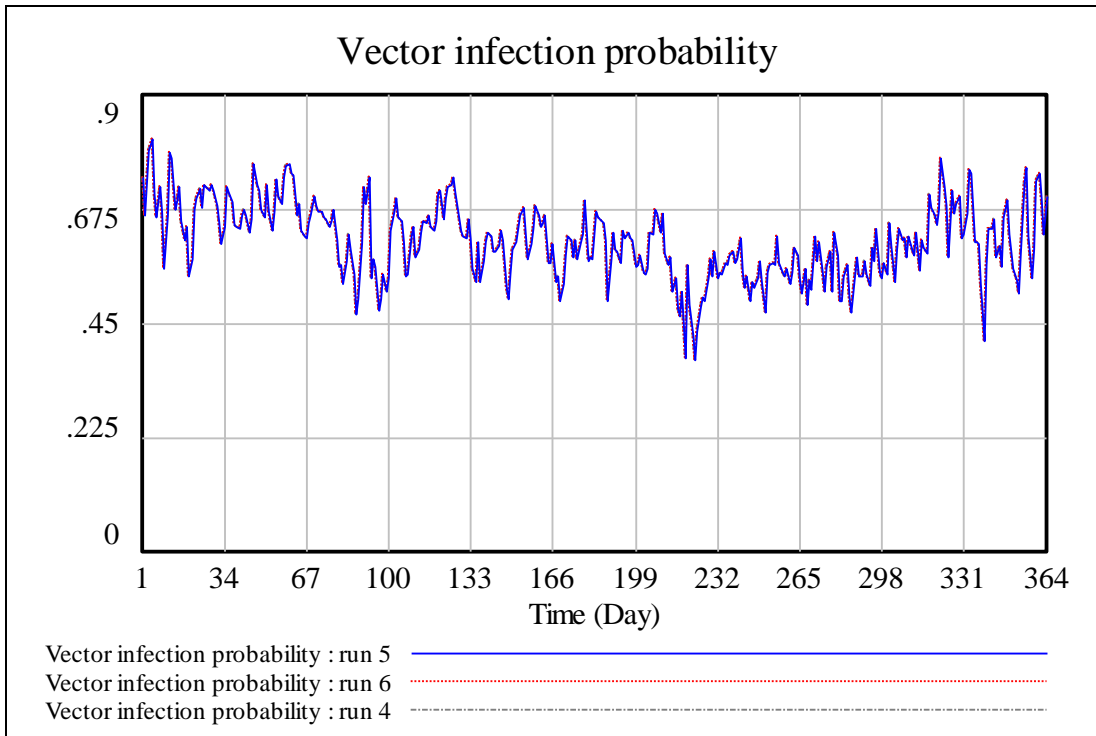


Figure 66: Vector infection probability simulation 2008

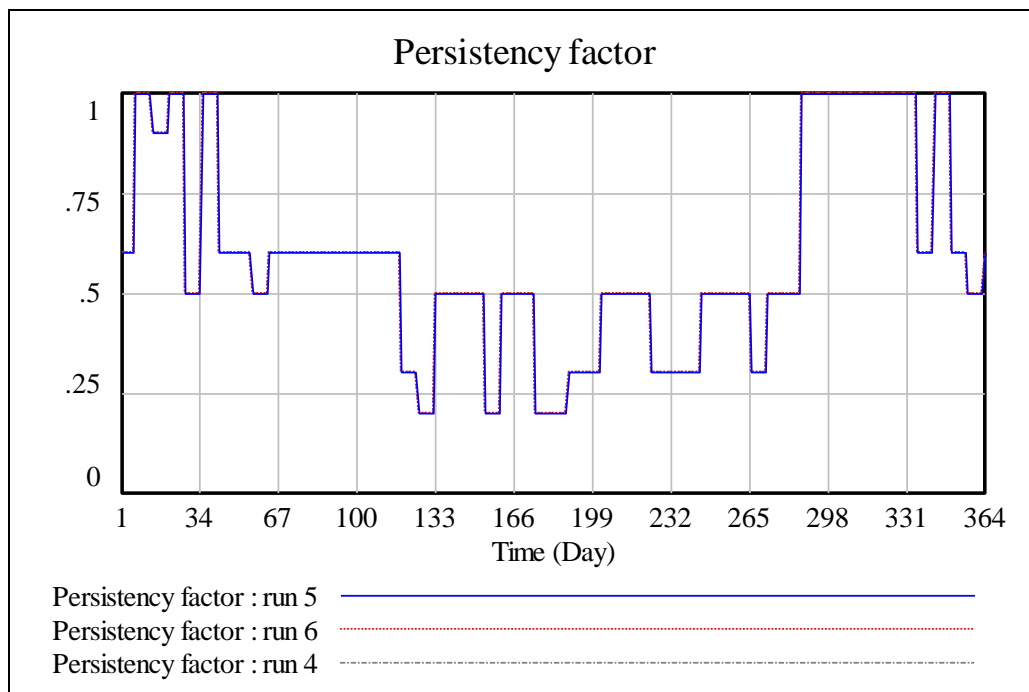


Figure 67: Dew point temperature based persistency factor simulation 2008

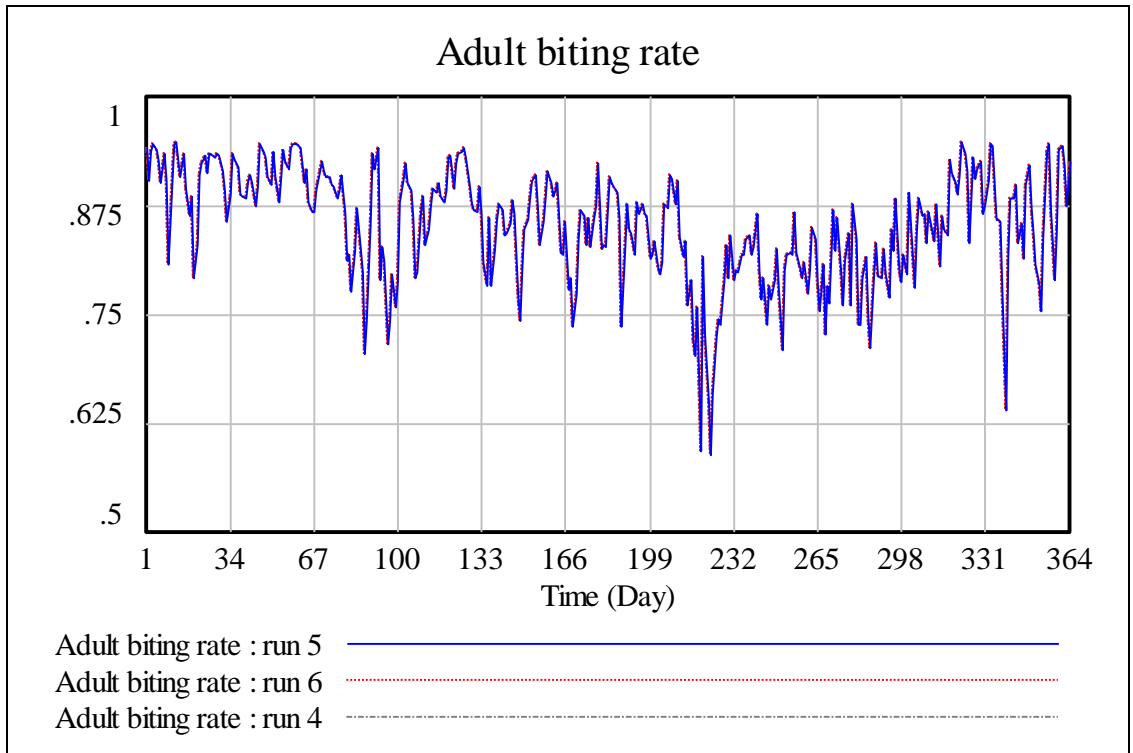


Figure 68: Adult biting rate simulation 2008

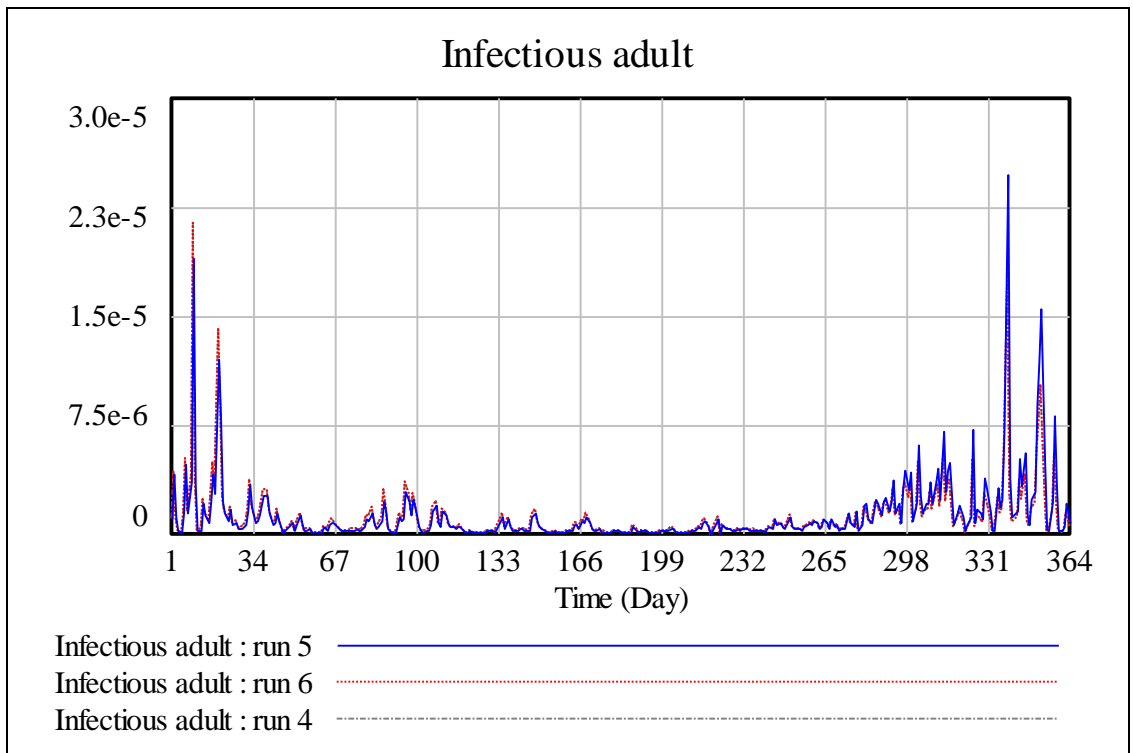


Figure 69: Infectious adult simulation 2008



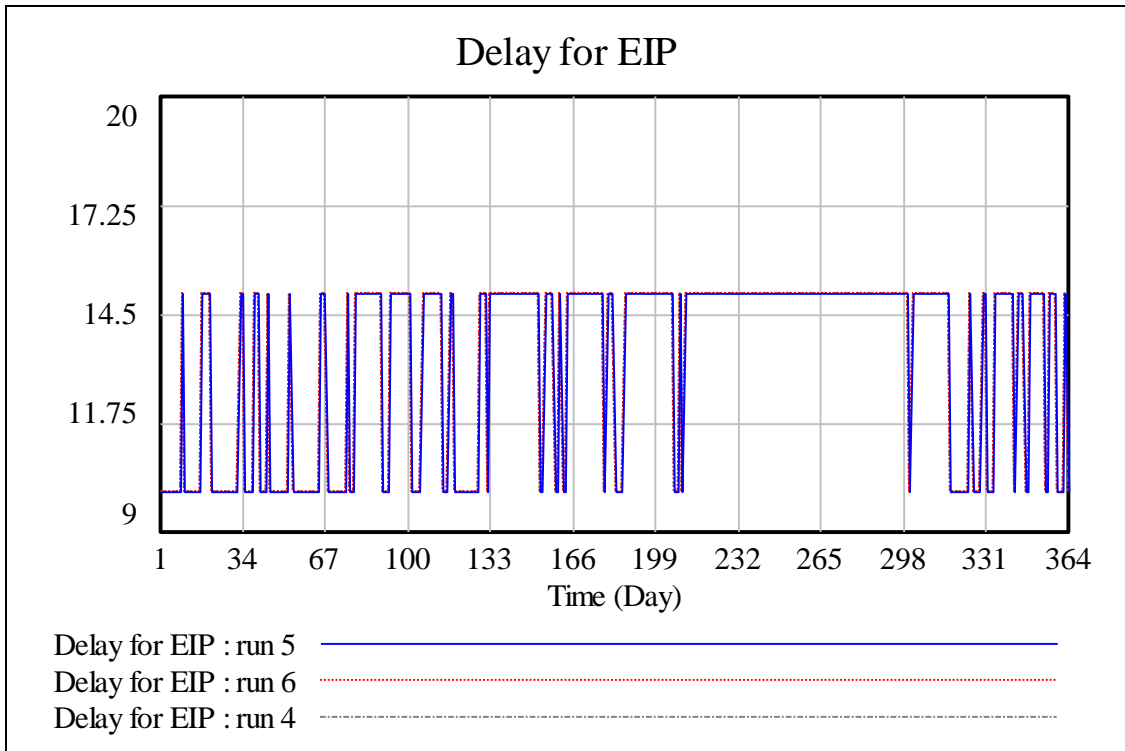


Figure 70: Delay for EIP simulation 2008

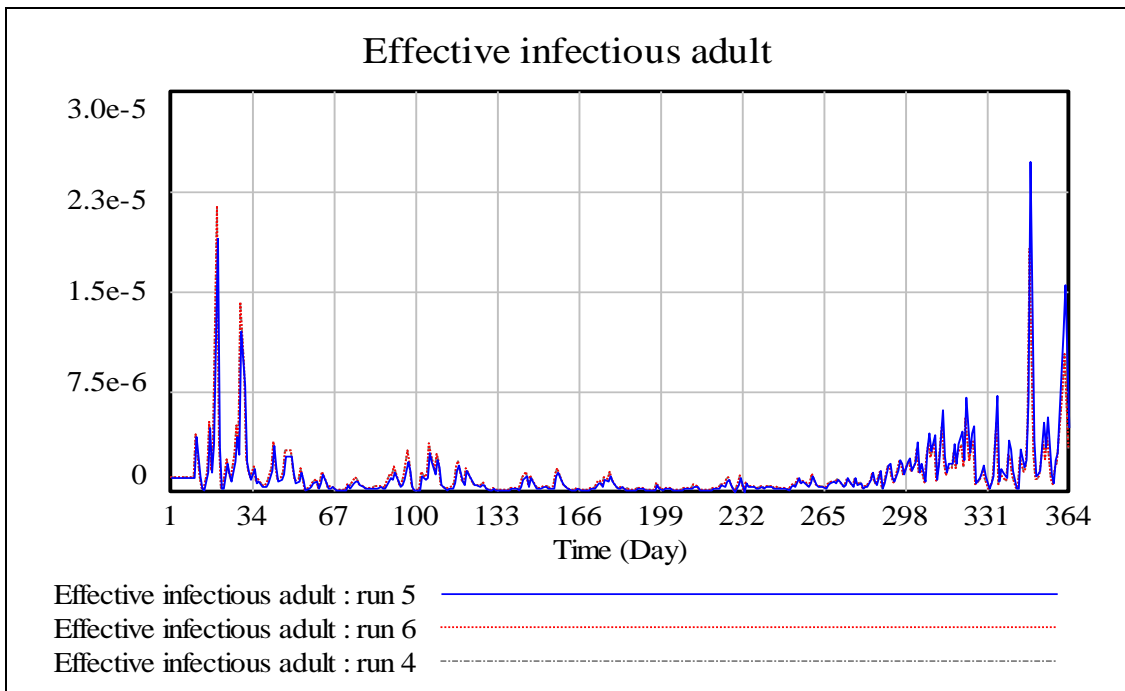


Figure 71: Effective infectious adult simulation

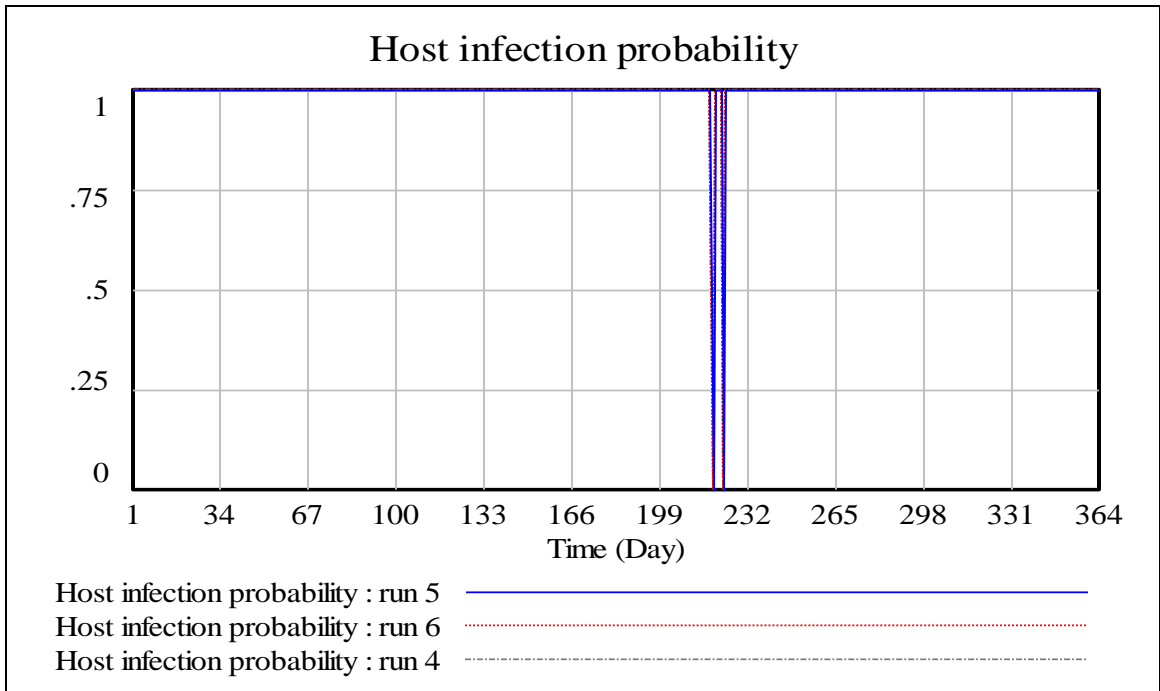


Figure 72: Host infection probability simulation

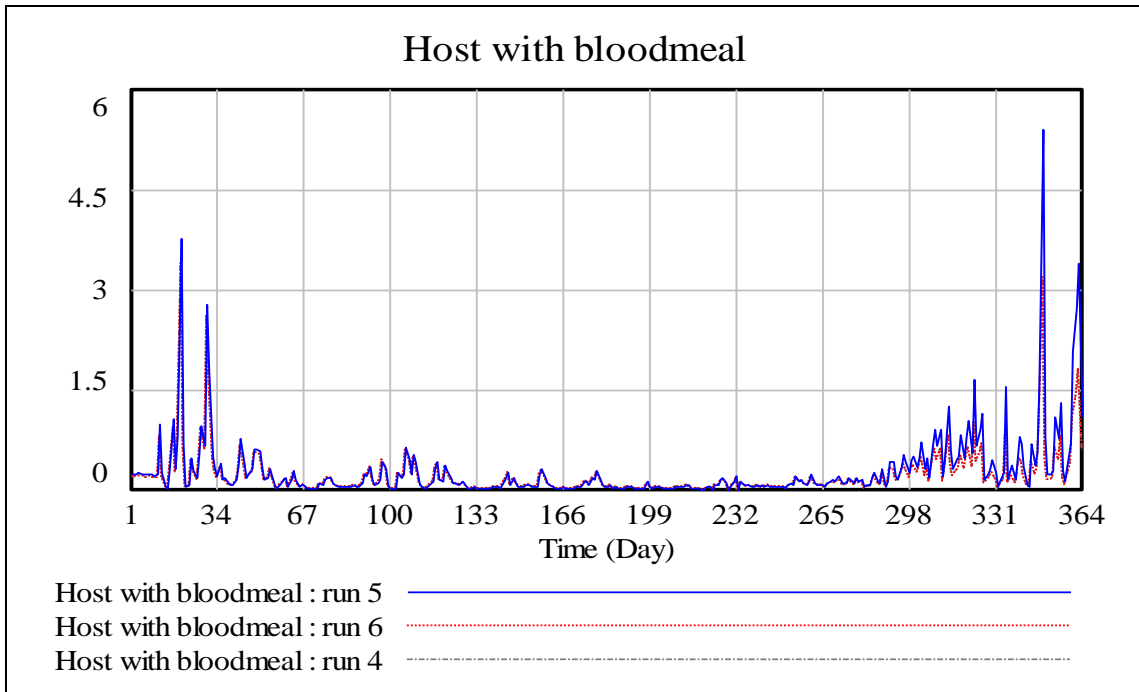


Figure 73: Host with bloodmeal simulation 2008

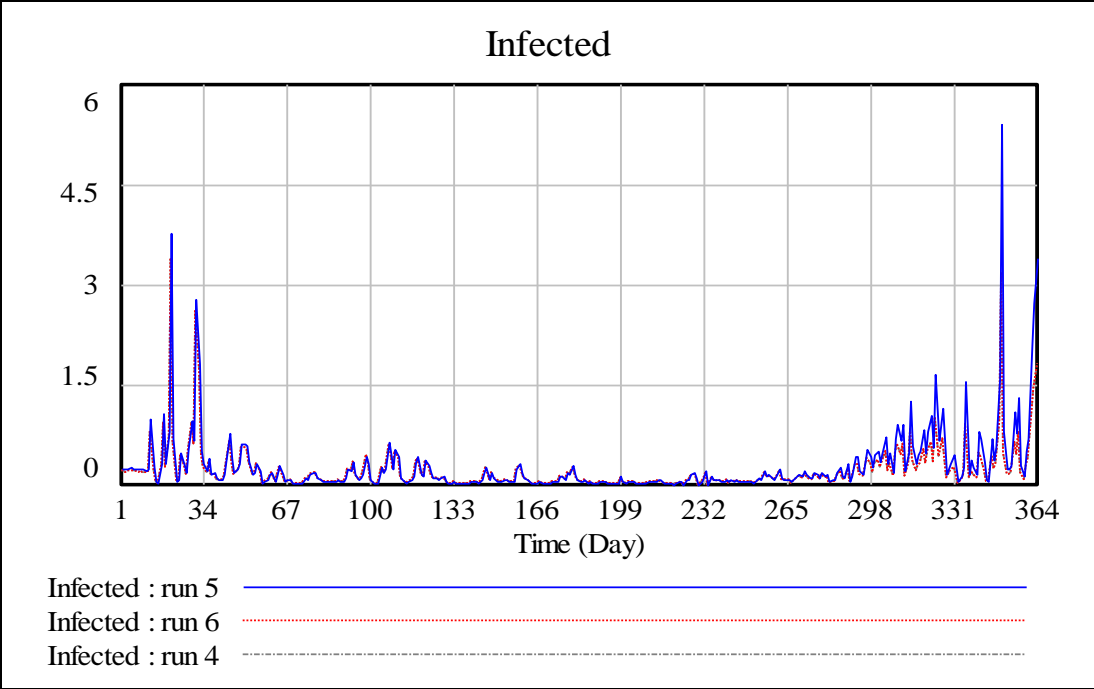


Figure 74: Infected simulation 2008

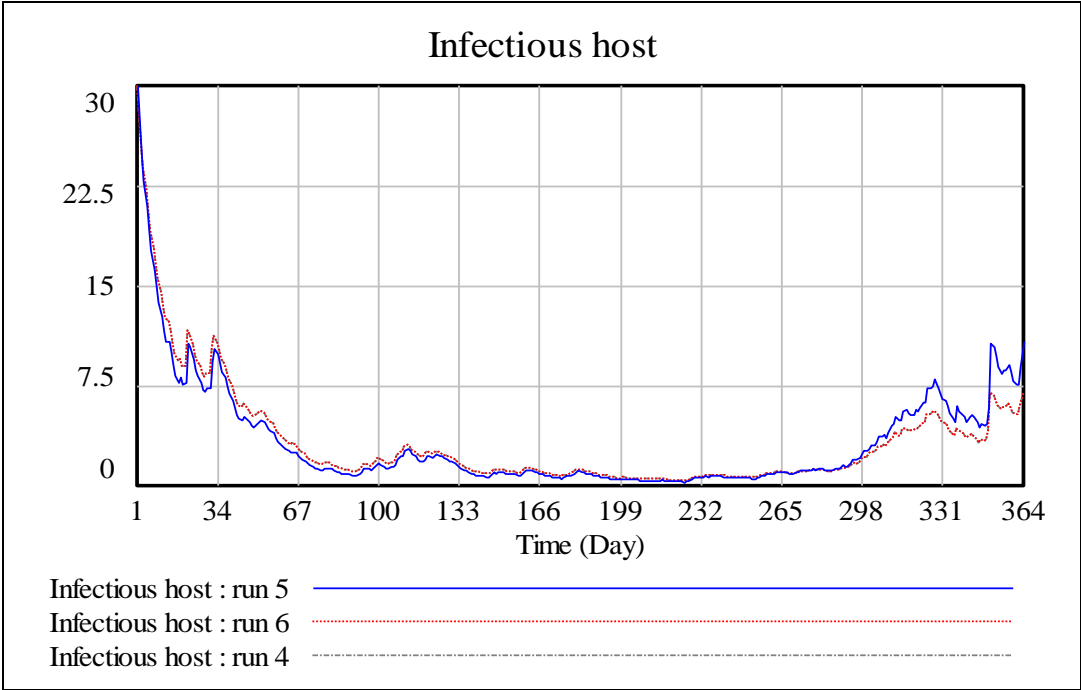


Figure 75: Infectious host simulation 2008

Vensim simulations 2004

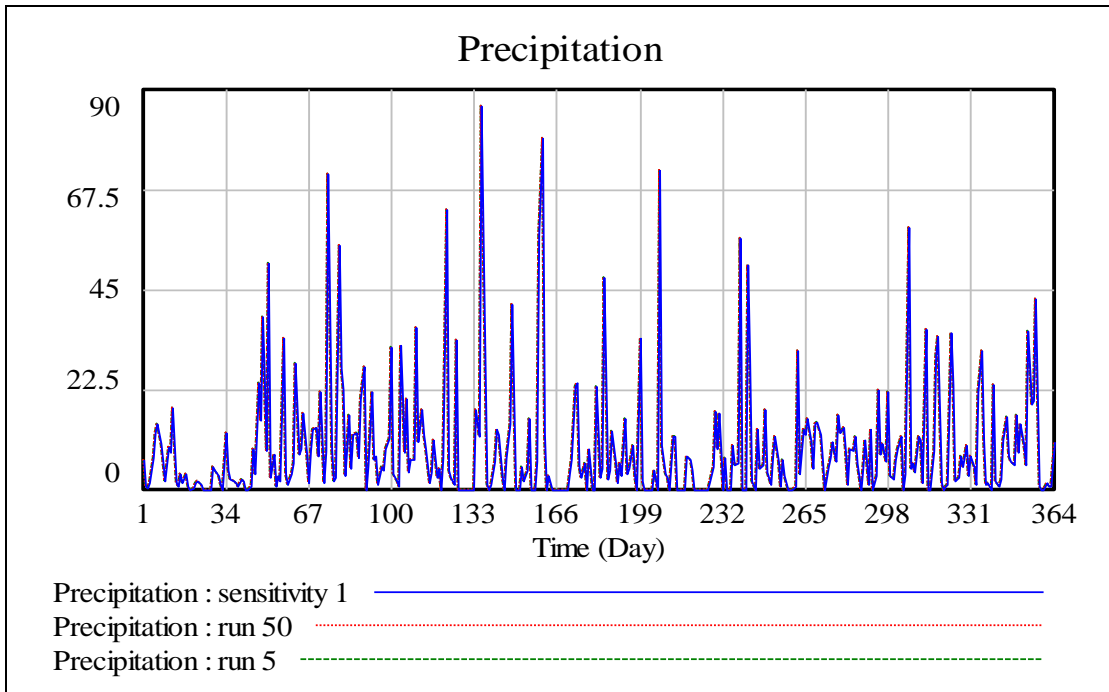


Figure 76: Precipitation simulation 2004

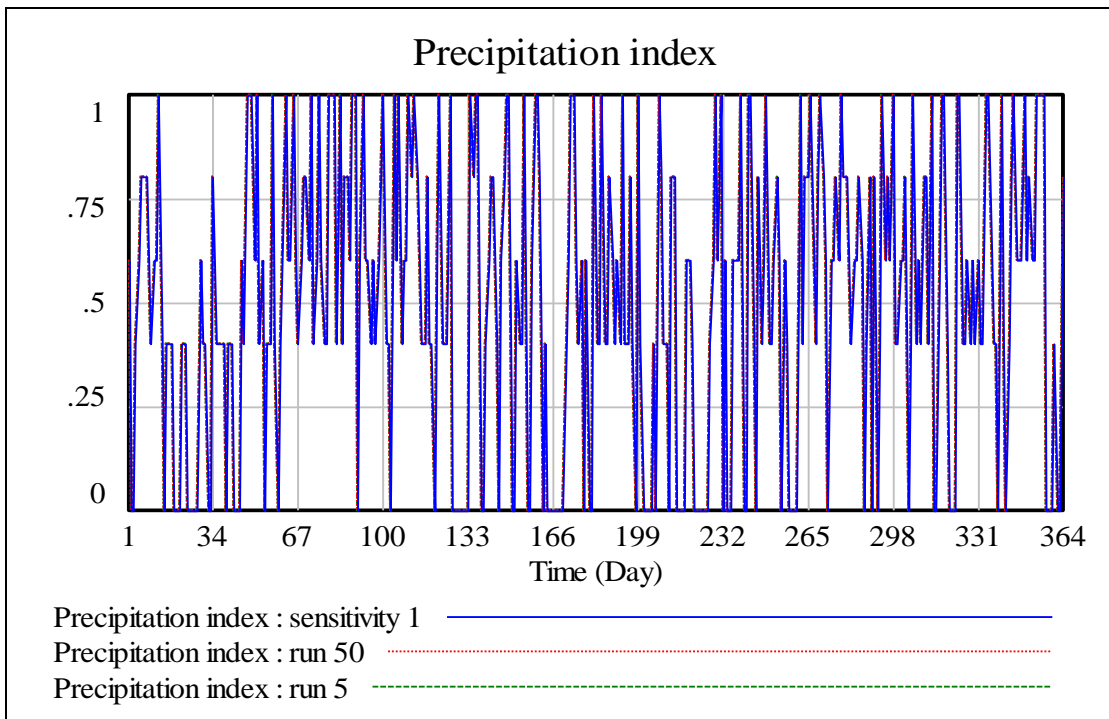


Figure 77: Precipitation index simulation 2004

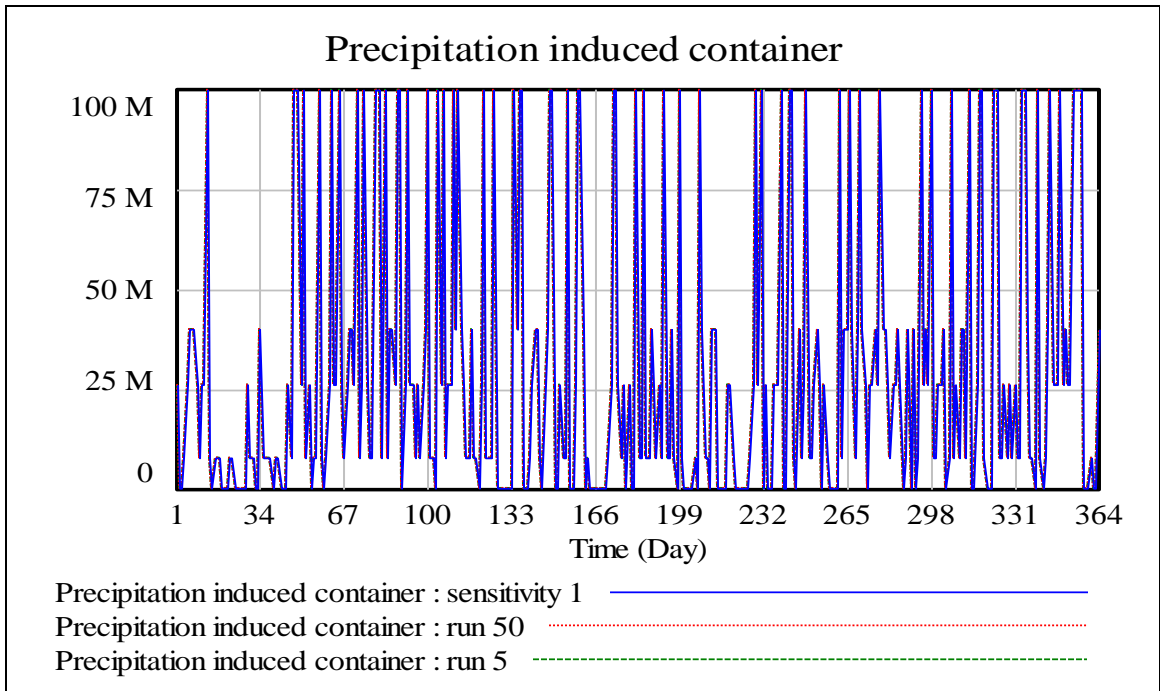


Figure 78: Precipitation induced container simulation 2004

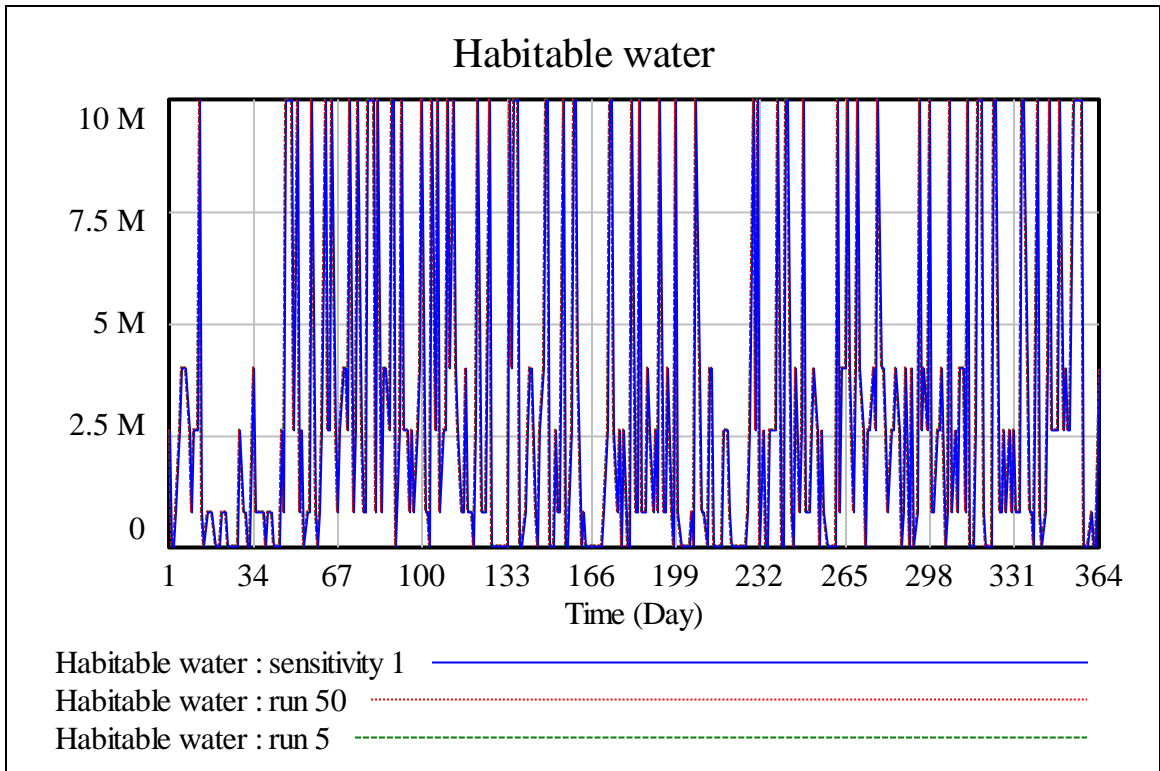


Figure 79 : Habitable water simulation 2004

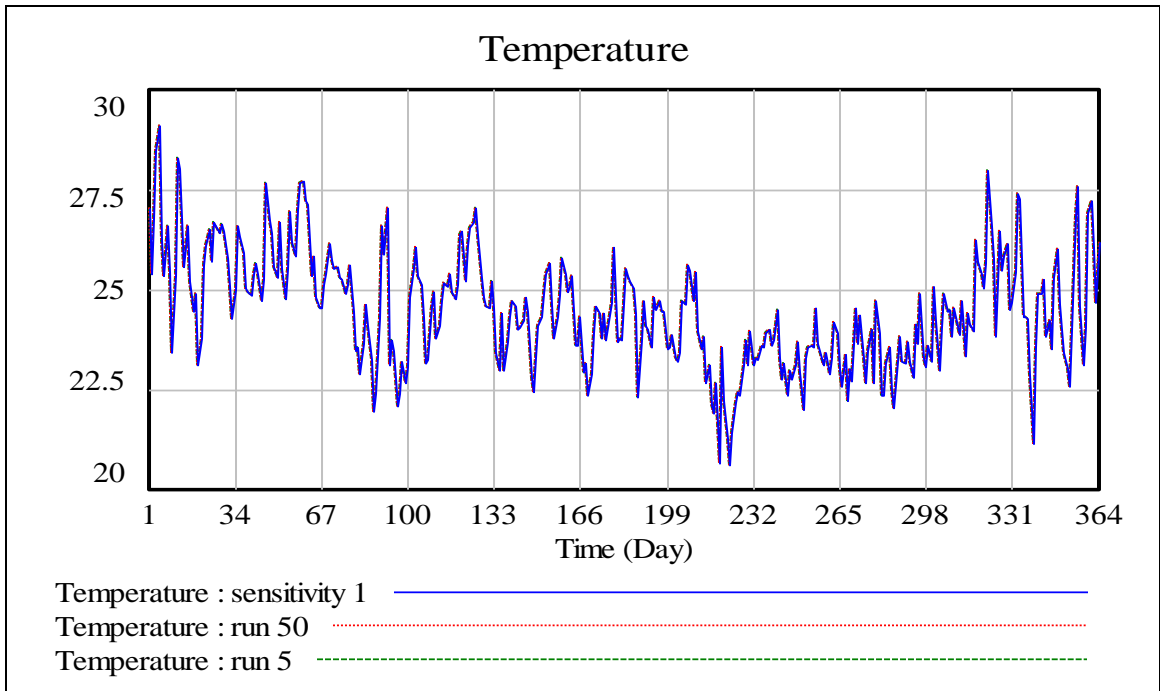


Figure 80: Temperature simulation 2004

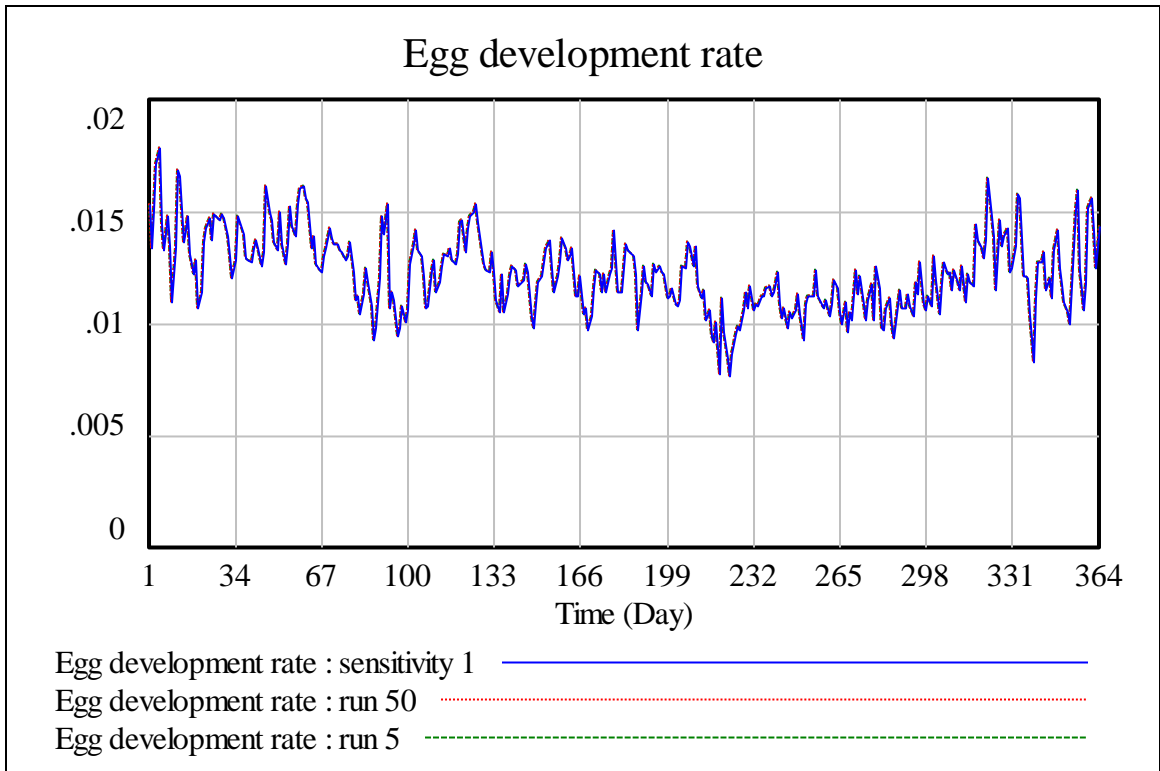


Figure 81: Egg development rate simulation 2004

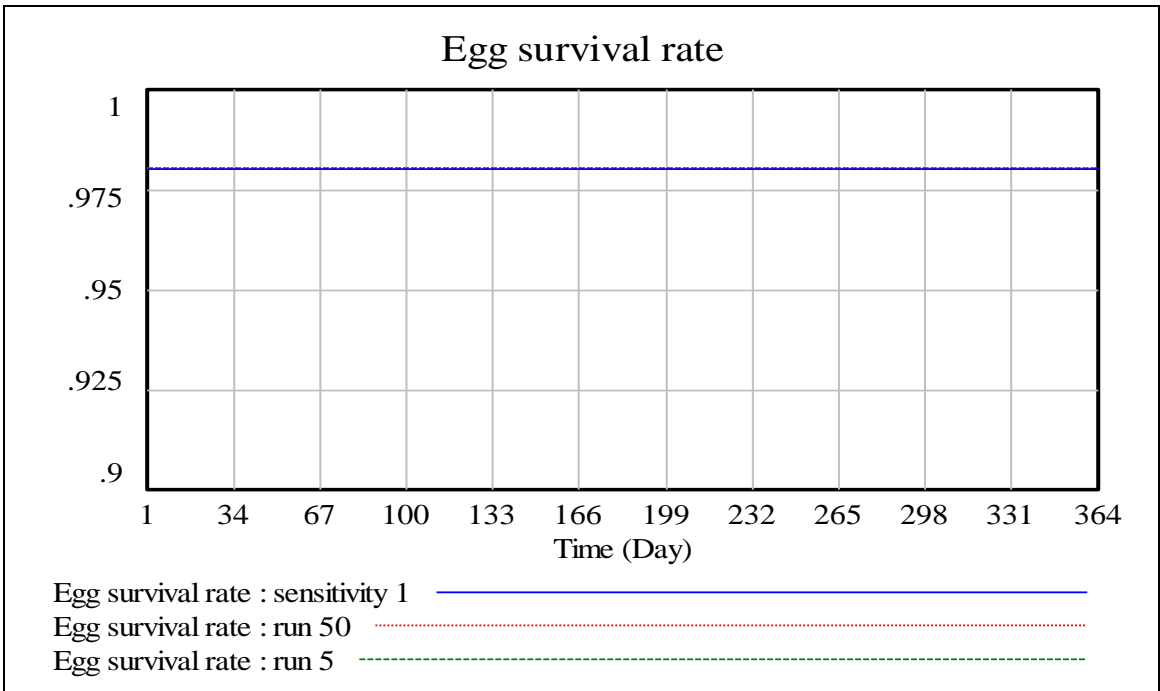


Figure 82: Egg survival rate simulation 2004

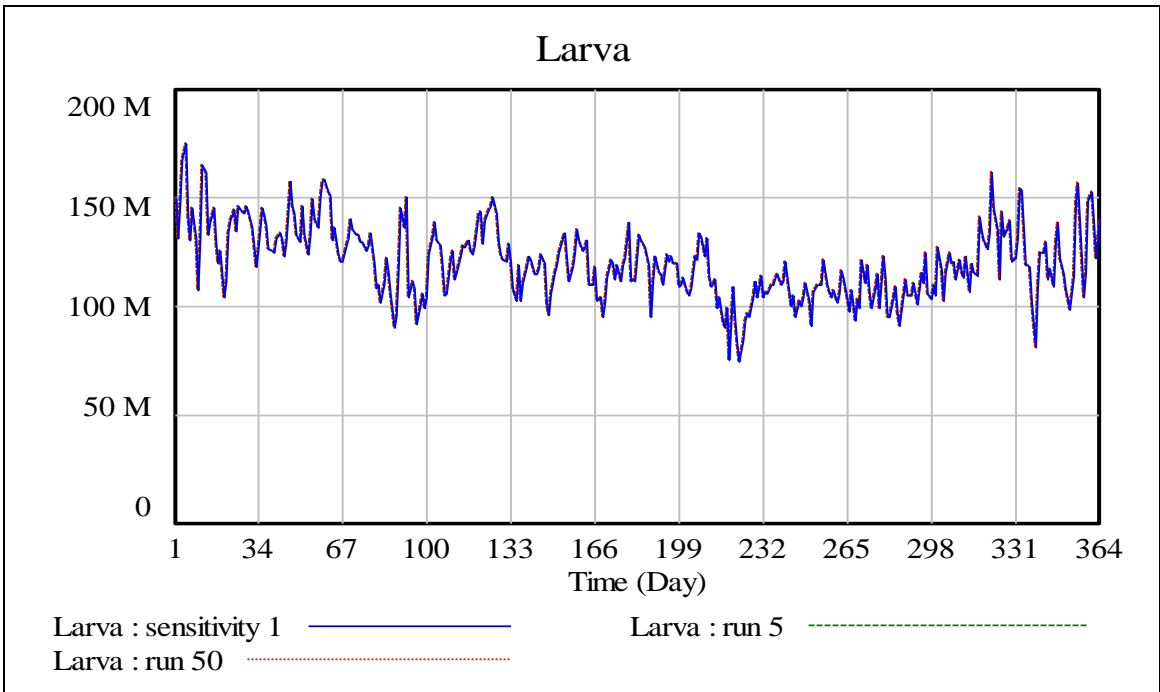


Figure 83: Larva simulation 2004

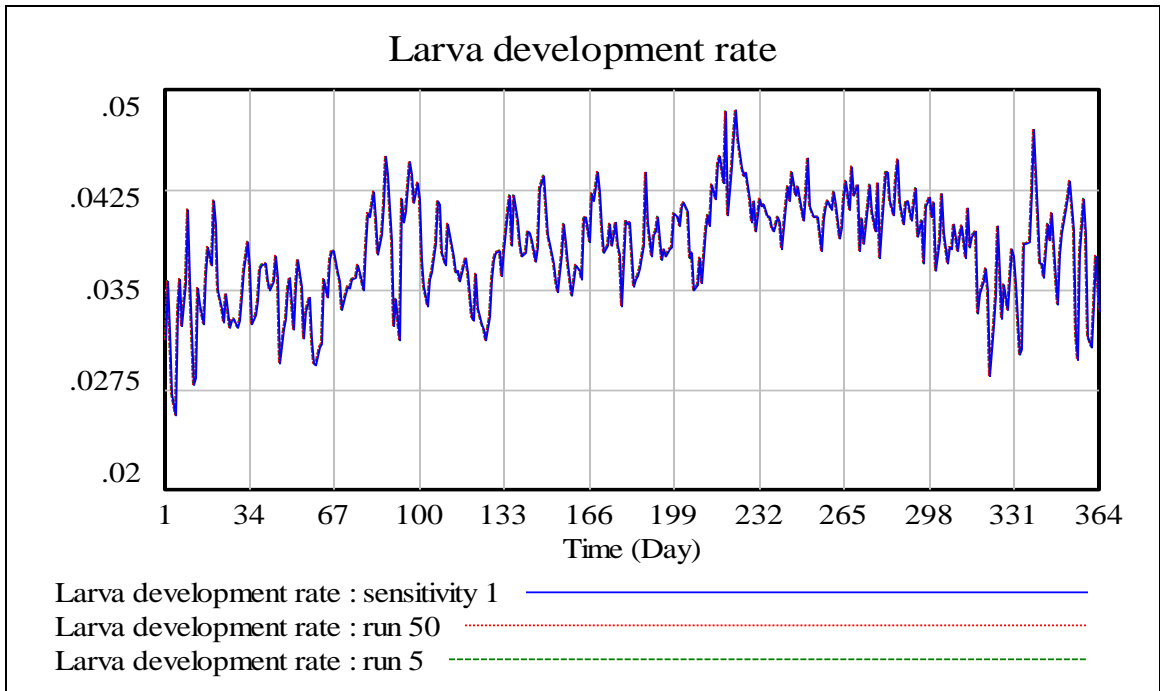


Figure 84: Larva development rate simulation 2004

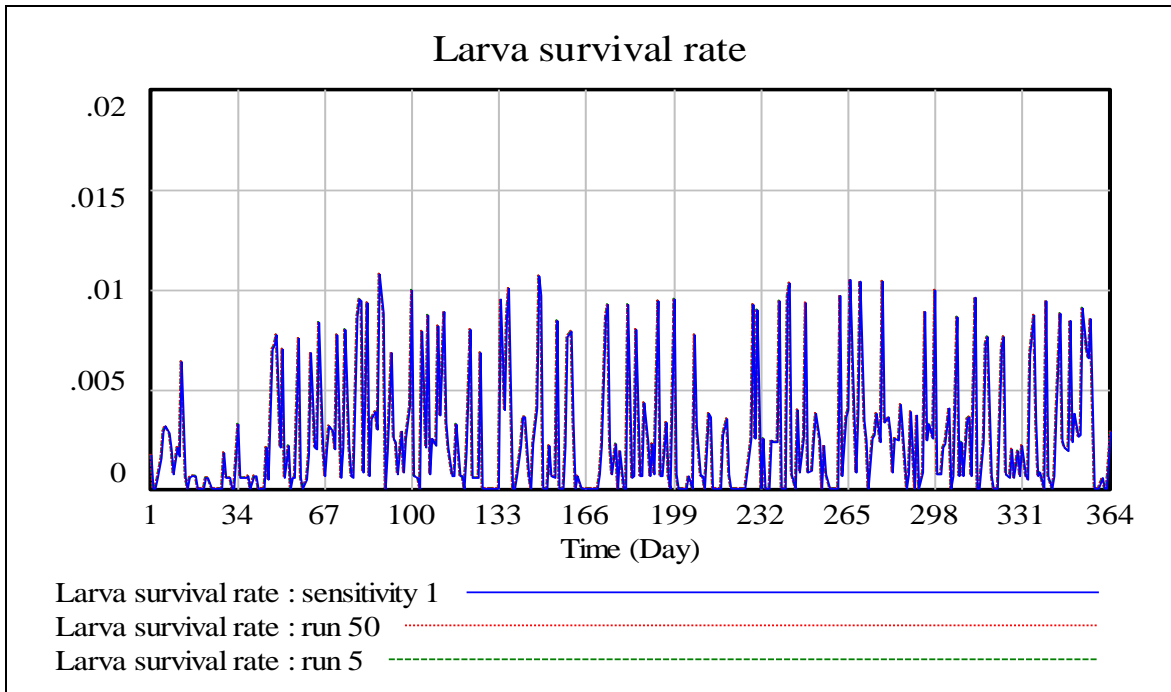


Figure 85: Larva survival rate simulation 2004



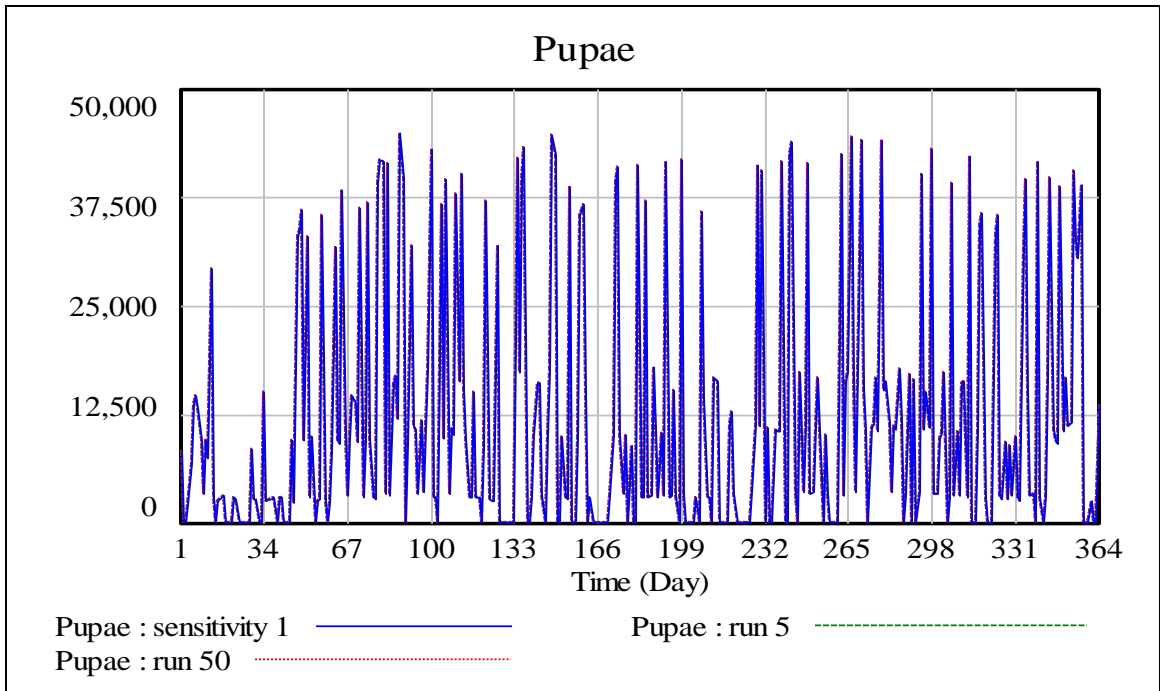


Figure 86: Pupae simulation 2004

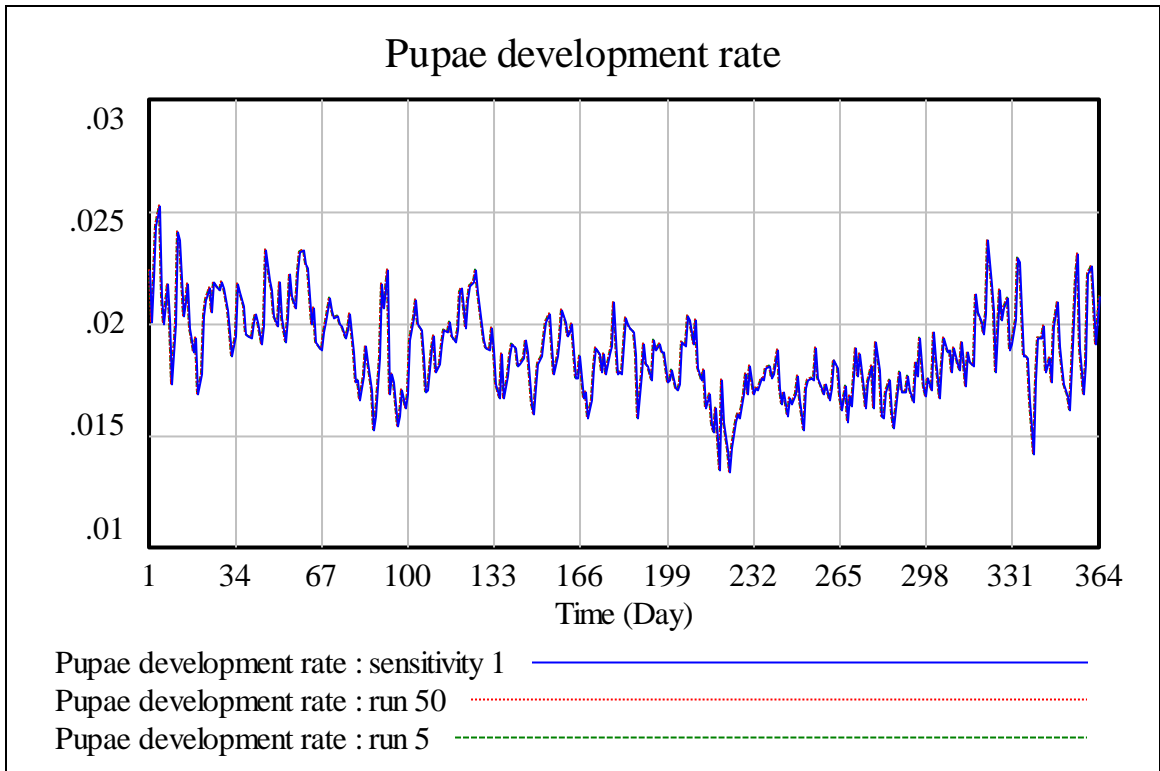


Figure 87: Pupae development rate simulation 2004

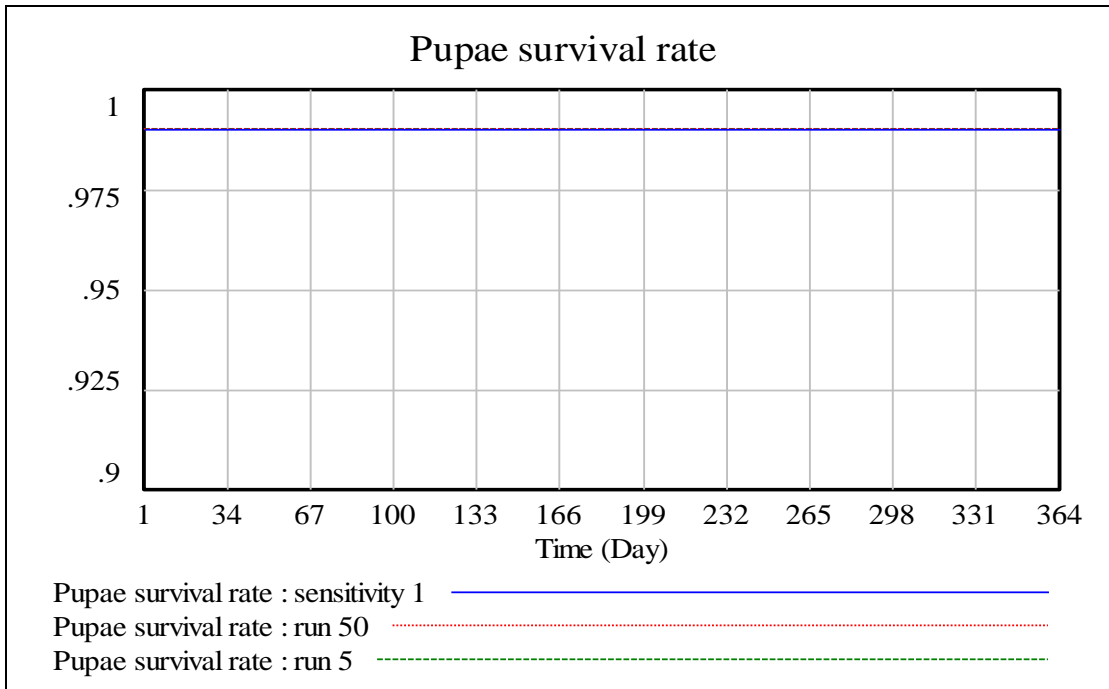


Figure 88: Pupae survival rate simulation 2004

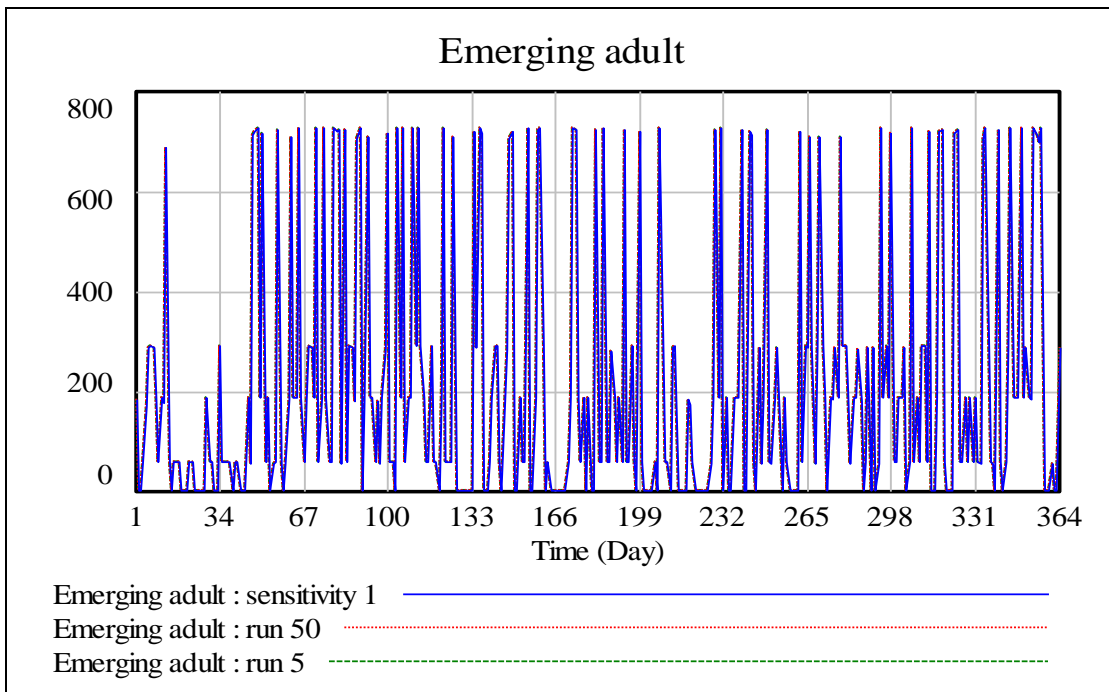


Figure 89: Emerging adult simulation 2004

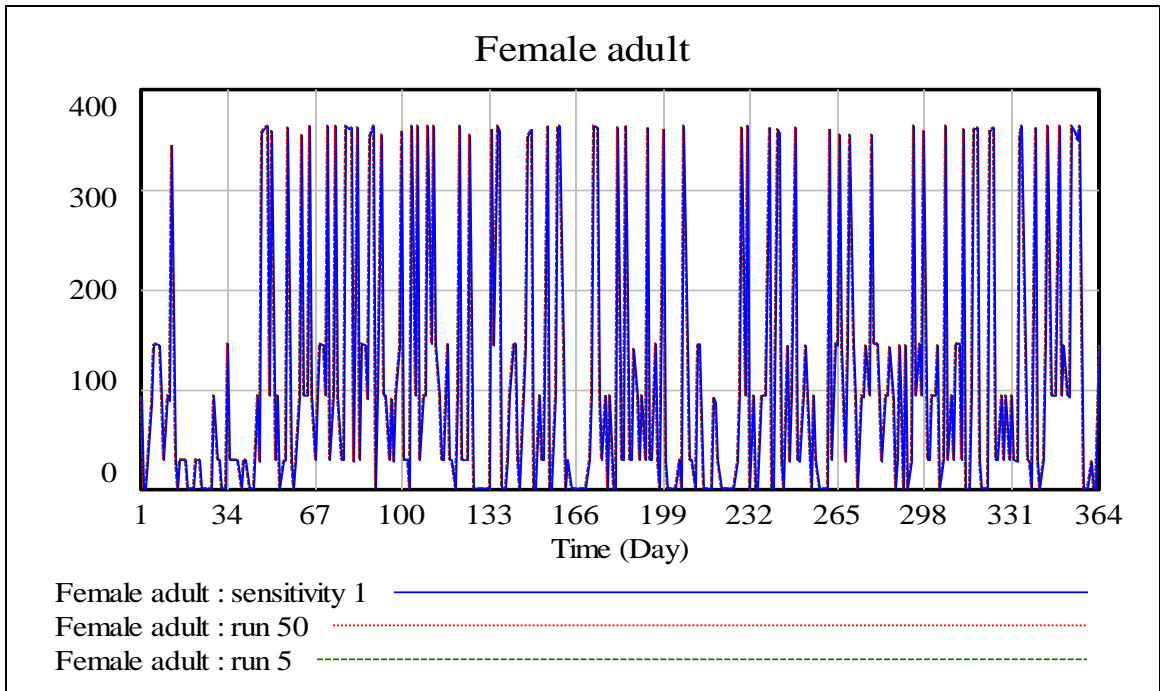


Figure 90: Female adult simulation 2004

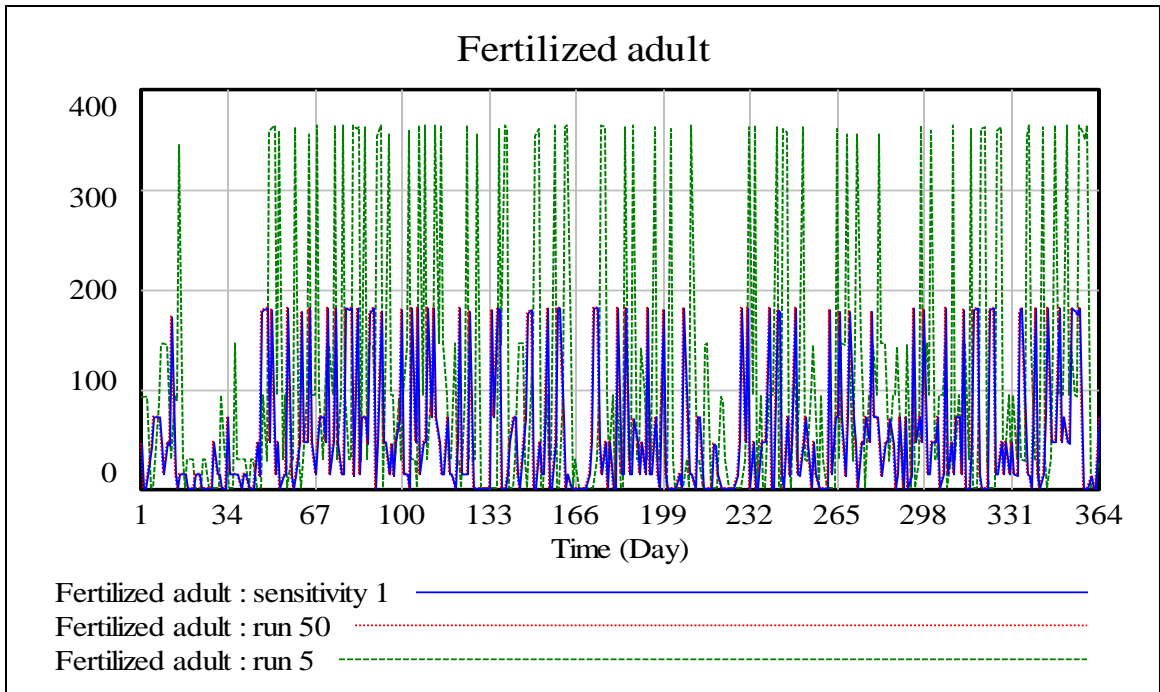


Figure 91: Fertilized adult simulation 2004

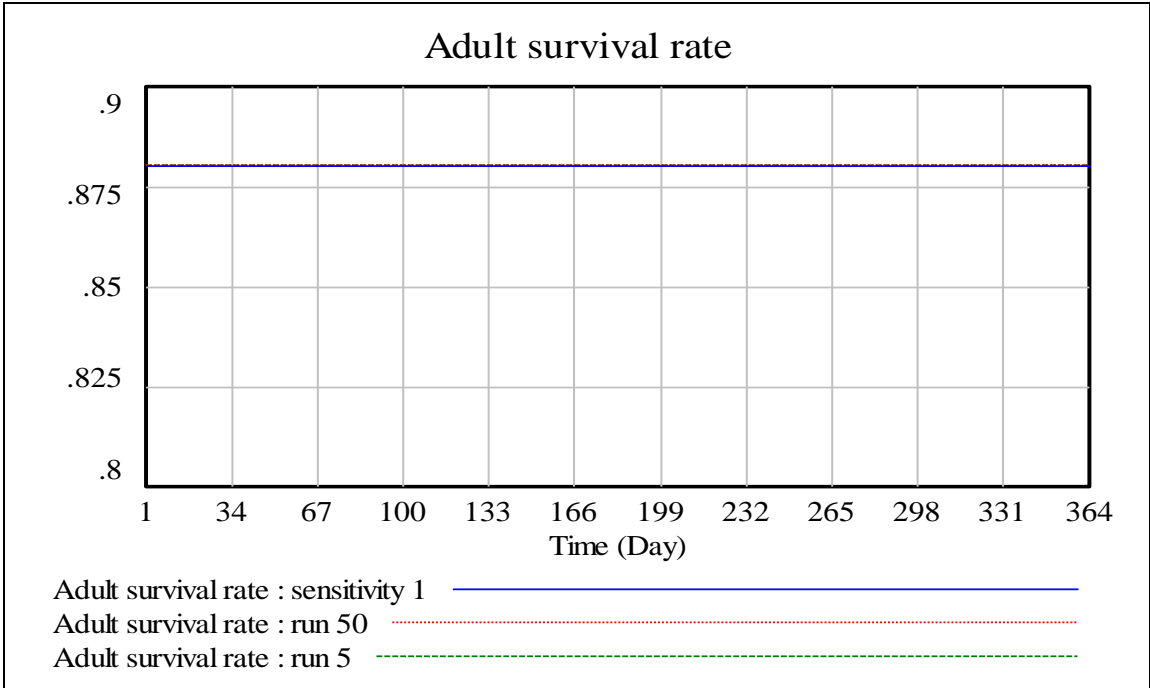


Figure 92: Adult survival rate simulation 2004

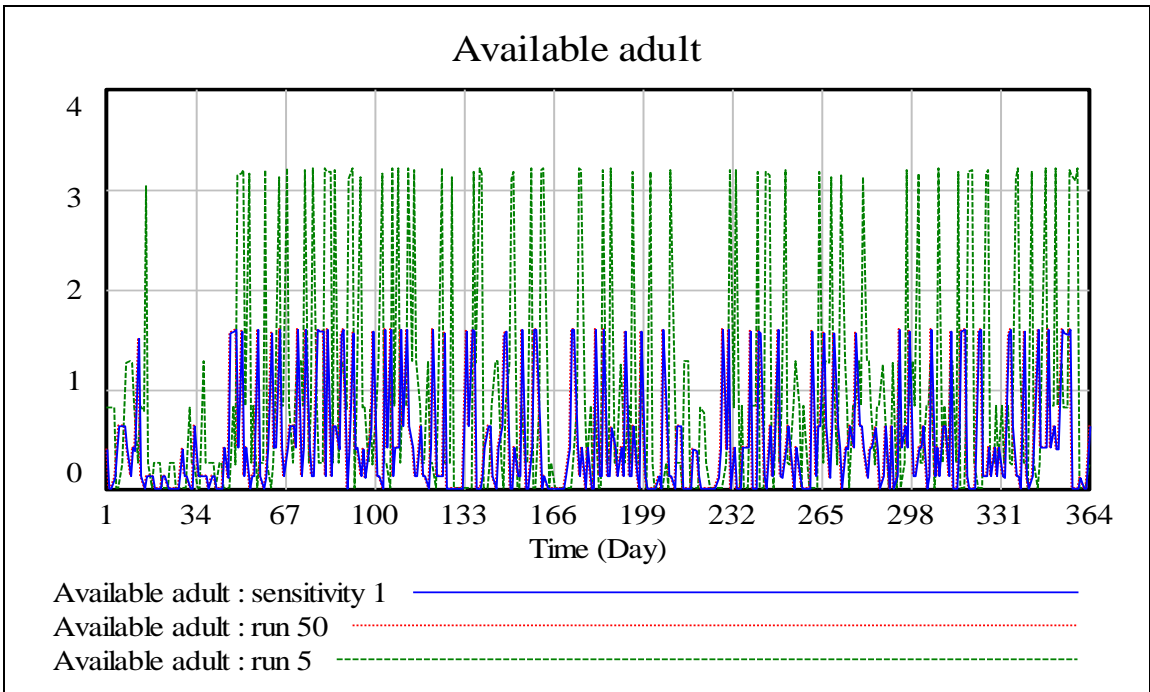


Figure 93: Available adult simulation 2004

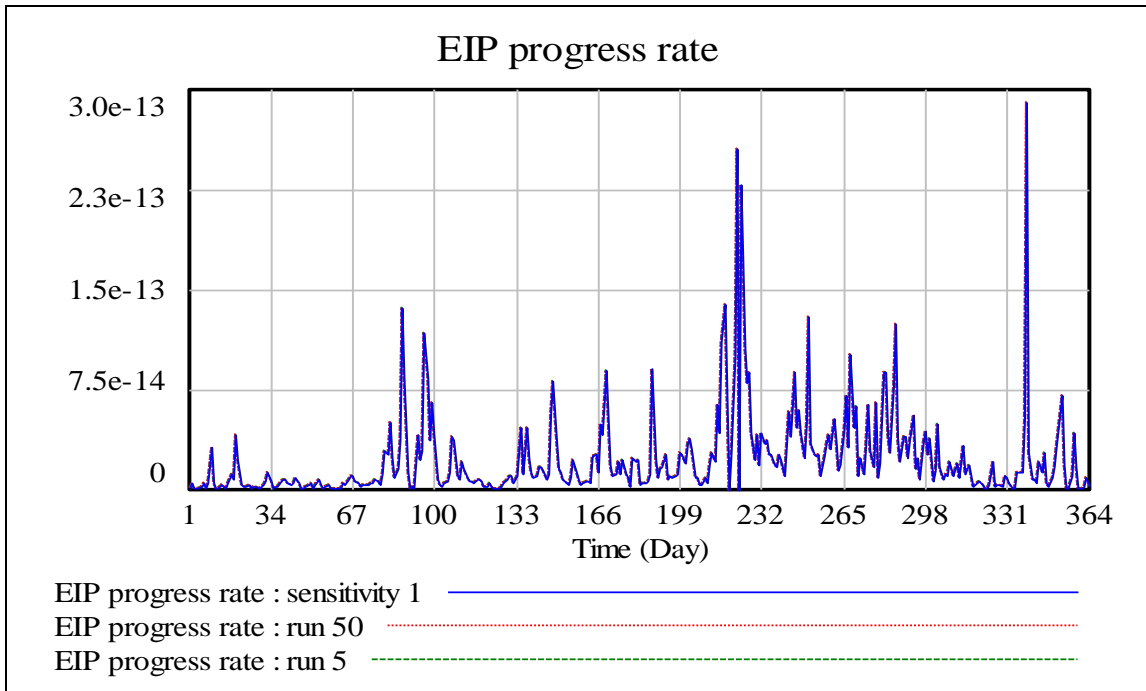


Figure 94: EIP progress rate simulation 2004

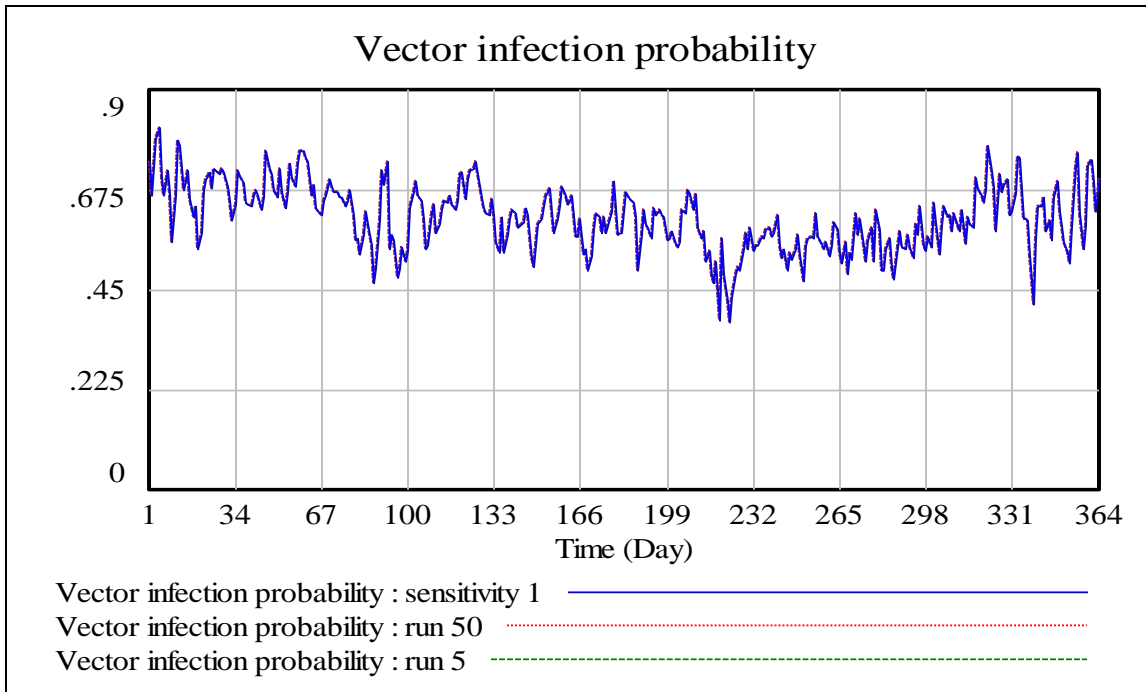


Figure 95: Vector infection rate simulation 2004

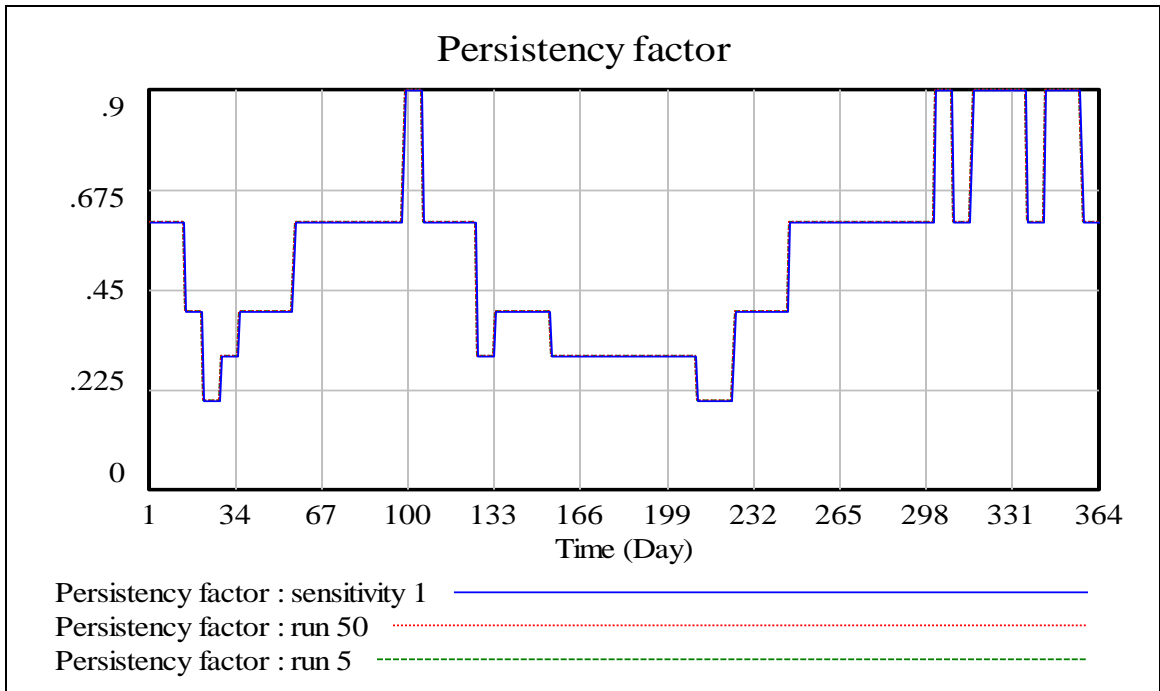


Figure 96: Dew point temperature based persistency factor simulation 2004

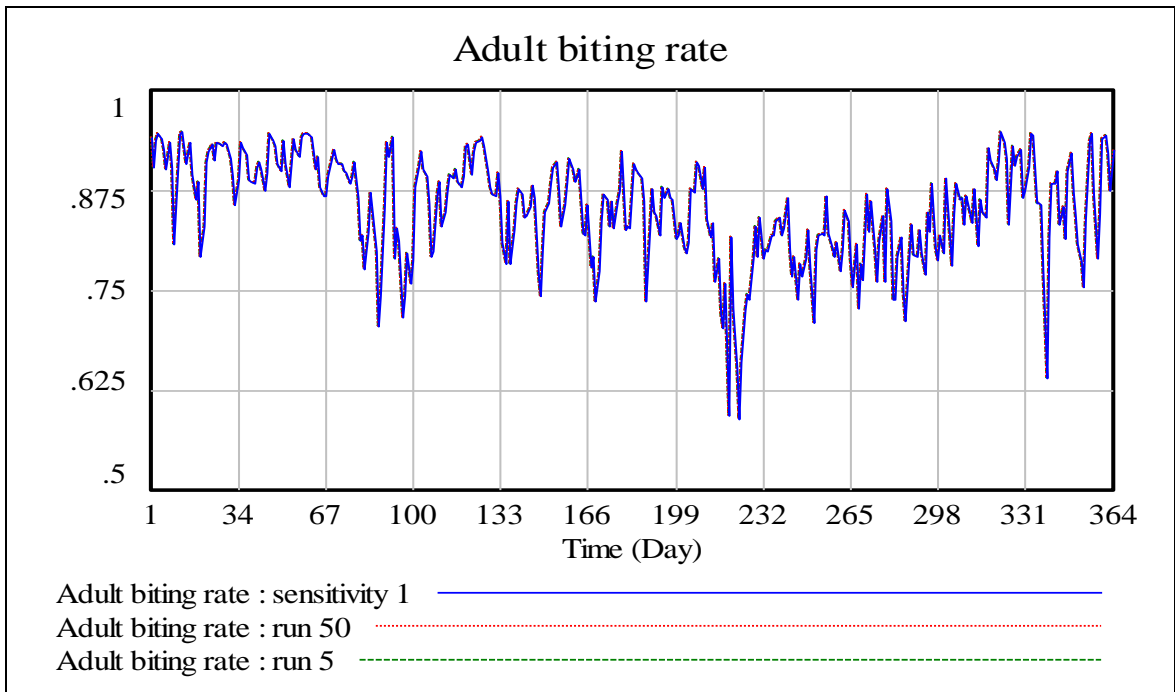


Figure 97: Adult biting rate simulation 2004

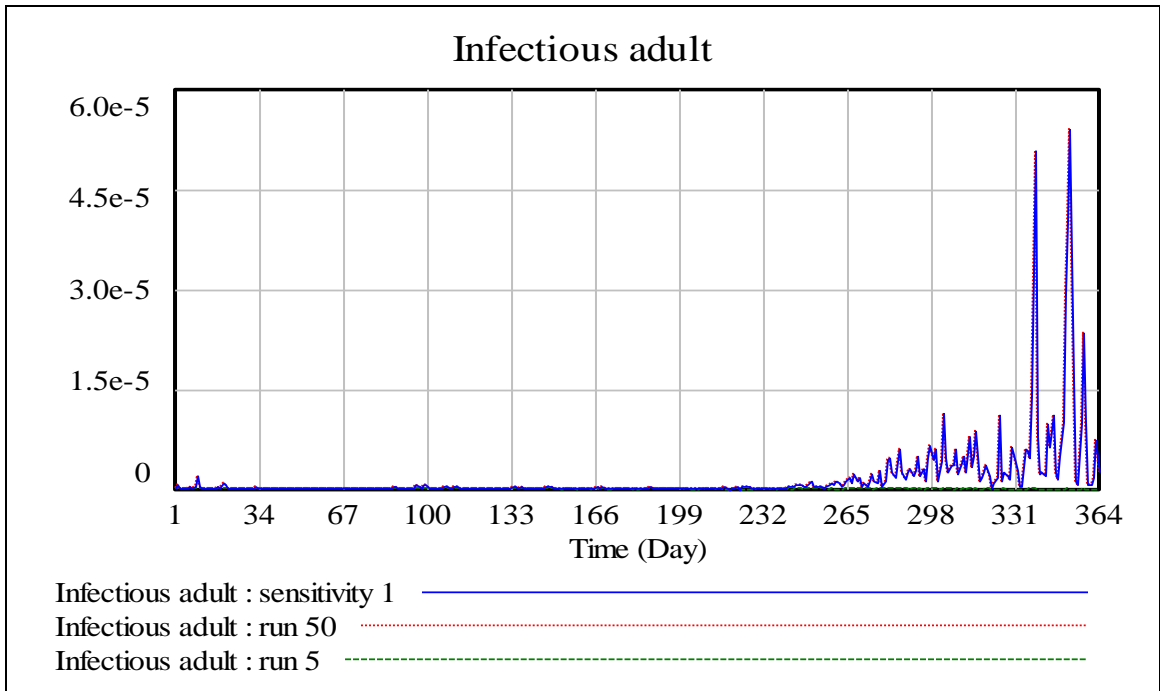


Figure 98: Infectious adult simulation 2004

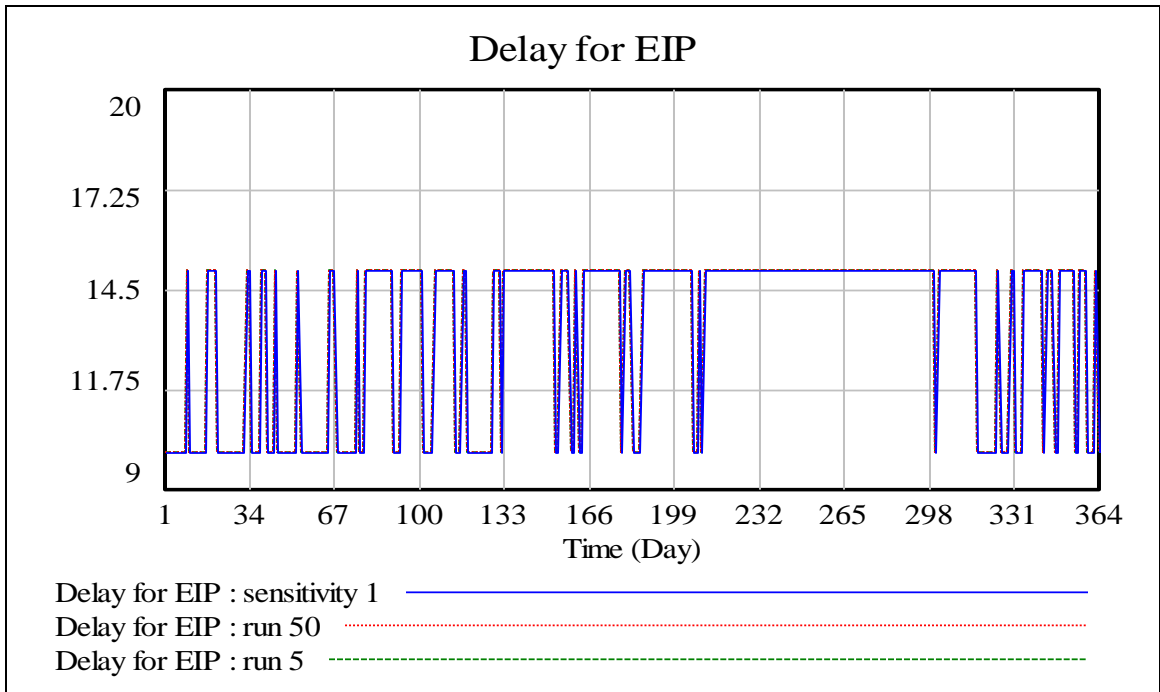


Figure 99: Delay for EIP simulation 2004

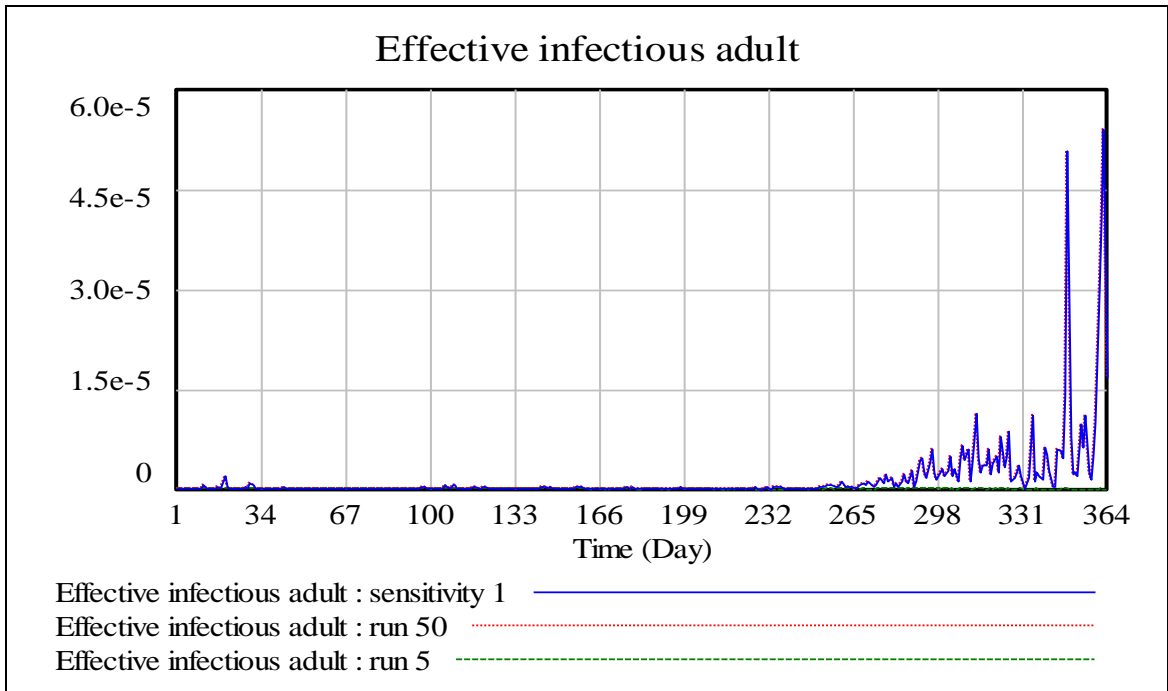


Figure 100: Effective infectious adult simulation 2004

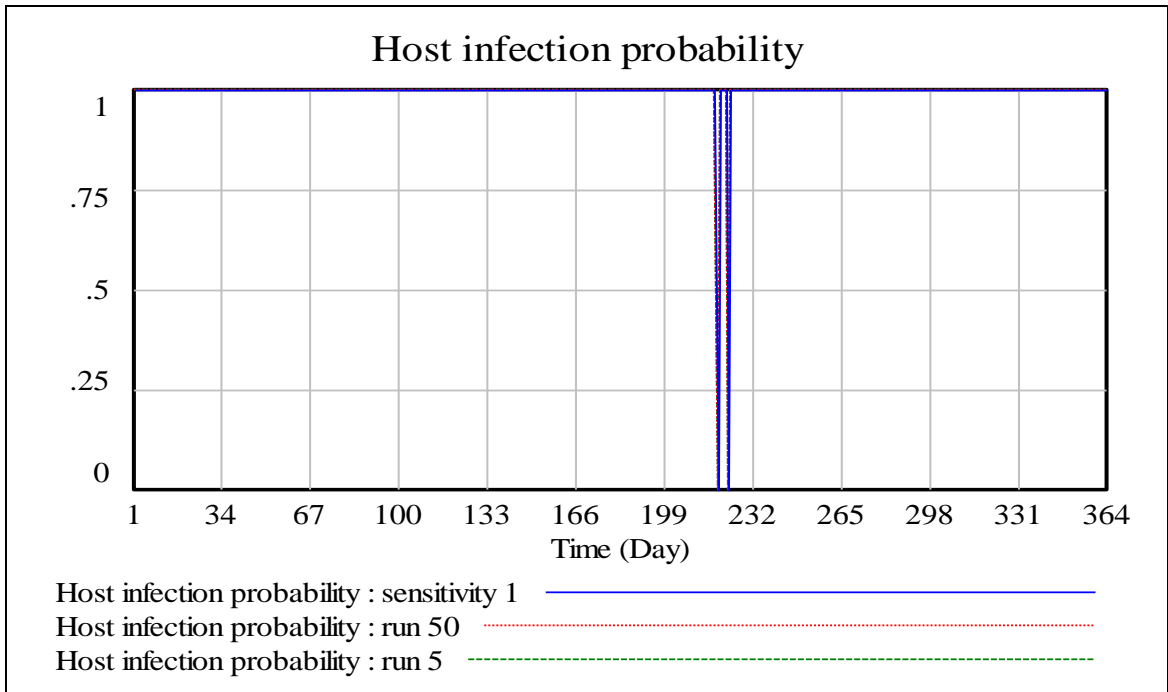


Figure 101: Host infection probability simulation 2004



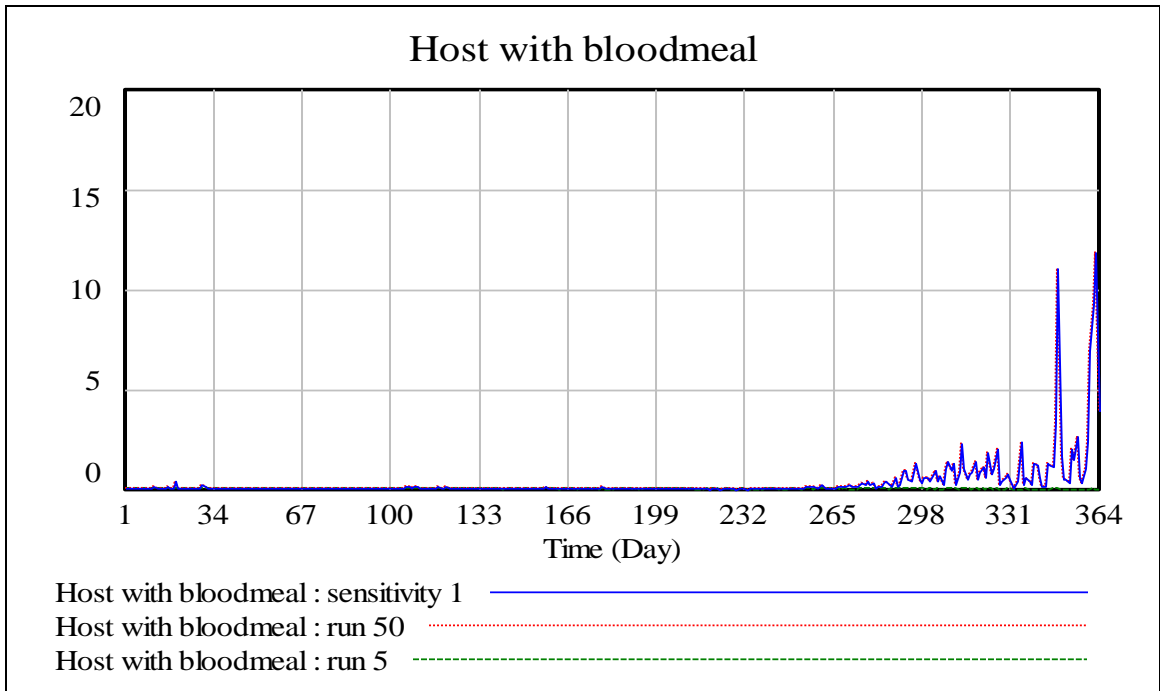


Figure 102: Host with bloodmeal simulation 2004

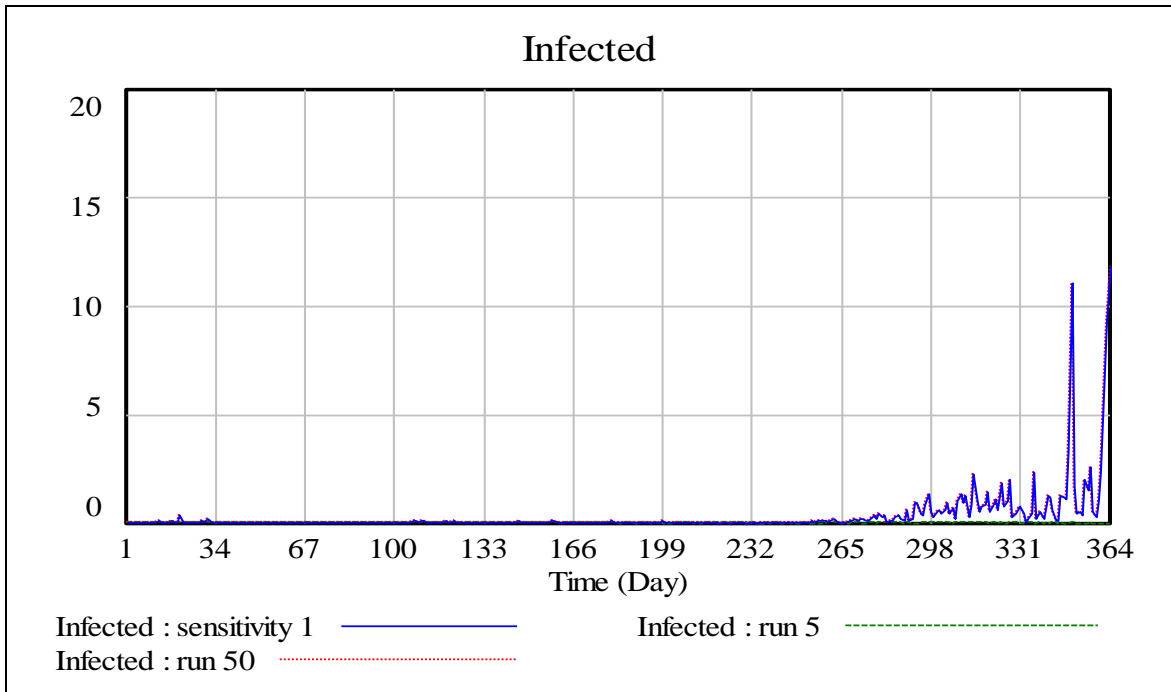


Figure 103: Infected simulation 2004

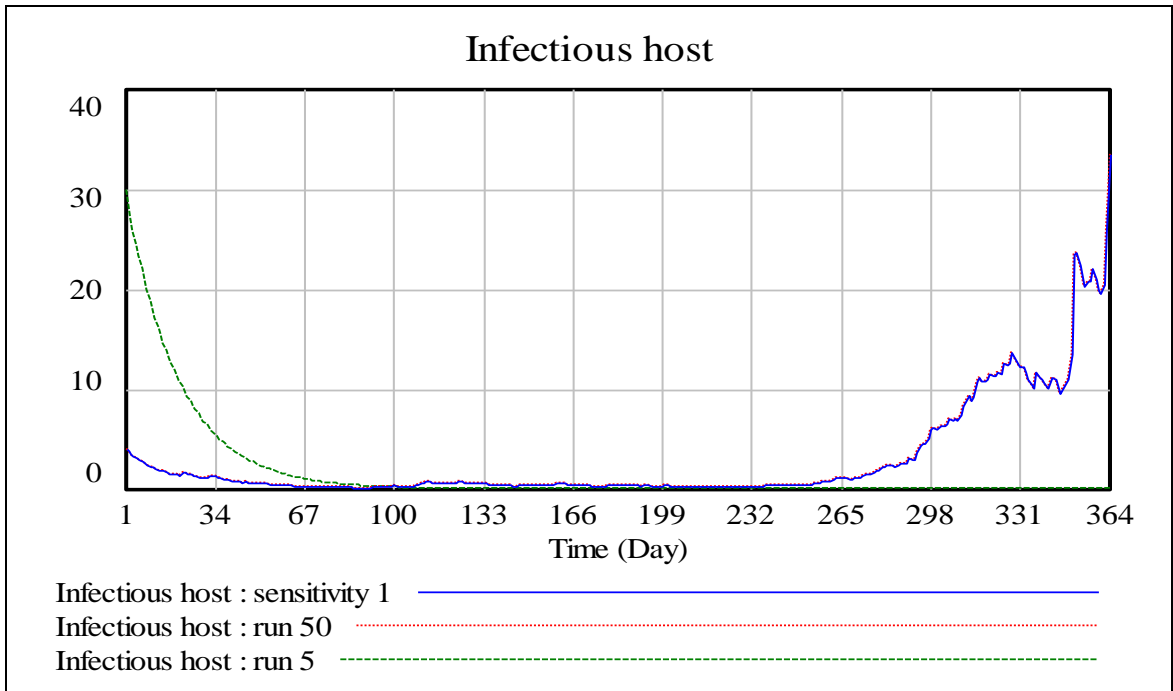


Figure 104: Infectious host simulation 2004

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