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PREDICTING THE DISPERSAL OF ZOONOTIC DISEASES

Spatial risk analysis of bluetongue in The Netherlands

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WAGENINGEN UNIVERSITY
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PREFACE

This research is the product of my master thesis in Geo-Information Science. Next to Geo-Information Science, I am also doing a master in International Land and Water Management. It would have been logic when my thesis assignment had some linkage with water management, but instead I chose an assignment in virus dispersal. Even though both topics do not seem related, the modelling process can be implemented into a large variety of topics, as well also in water management.

My interest in modelling started after seeing some examples of land use change models. The idea that the evolutions of land use is related to its neighbouring cells and the value of its own cell fascinated me and makes the situation from each pixel unique. That is also the reason why I choose to develop my own model. Fortunately, I got the chance to do this on a bluetongue model for the university.

The development of the actual model and modelling concepts took a great deal of time, especially since little literature is available about the bluetongue virus in The Netherlands. Nevertheless, the literature review went smoothly without sever problems. The real problems occurred during the integration of the three modelling elements into a single model. Test results of the individual elements looked promising, but when intergraded, the obtained results were disappointing. Of course, it is a pity that when one comes this far, the final results disappoint. Nevertheless, I hope I opened new doors for following students, so they are able to develop a fully operating bluetongue prediction model.

During my thesis I got a lot of great support from my supervisors. I want to thank Ron van Lammeren and Aldo Bergsman for a pleasant collaboration, their enthusiasm work was really infectiousness. Additionally, I want to tank Aline de Koeier, Niels Verhulst and Willem Takken. Especially in the beginning of my thesis they showed a lot of patience to explain me all processes involved into bluetongue transmission.

This report is one of the last elements of my student career. I will always look back to this project with pleasure and I hope you will enjoy reading it with as much pleasure as I had with writing it.

Matthijs Danes

Wageningen, 29 April 2008

ABSTRACT

Bluetongue (BT) is a devastating disease among ruminants but is harmless for people. *"The virus replicates in all ruminants, but severe disease is mostly restricted to certain breed of sheep (particularly fine wool and mutton breeds that are common in Europe) and some species of deer"* (Purse *et al.*, 2005). For these breeds of sheep and deer, bluetongue is frequently lethal. When the disease is not lethal, individuals suffer after a long recovery from alopecia, sterility and growth delay.

The bluetongue virus (BTV) used to occur around the fringes of Europe. It transmitted by tiny biting flies, called Culicoides. Only thirty from the twelve hundred sixty existing midge species are, to a greater or lesser extent, involved in the transmission of bluetongue. Nevertheless, in Europe only three species are responsible for the transmission of BTV, namely; *C. imicola*, *C. obsoletus* group and *C. pulicaris* group. *"Central Europe was considered to be rather safe with respect to a possible invasion of a BTV epidemic, since the optimum temperatures for the known vector species should not be reached throughout the year"* (Mehlhor *et al.*, 2007). However, in August 2006 the BTV was recorded in The Netherlands, Belgium, North France, Luxembourg and in the West of Germany.

The change of BT epidemiology has severe consequences for the economy in Central Europe. It is a *"major factor limiting the unrestricted international movement of animals and animal products"* (Walton, 2000). Additional, next to the exportation sector it also affects directly the financial situation of the farmers. The mortality rate among sheep will decrease the meat production, where infected dairy cattle have a lower milk production. For an average infected dairy farm it means a production decrease of 2,000 litres a week.
The way to control such a vector-borne disease is relatively unclear. Infected vectors can spread by favourable wind, via transports or ectoparasites on pets. Additionally the virus can spread by the transportation of infected ruminants. It is almost impossible to regulate animal movements are almost because of the open boarder policy of the European community (LNV[a] Vector project, 2007).

In this research, the underling processes that influence the virus dispersal are exposed. During this research a model has been developed, consisting out of three different elements. Even though the results of the individual elements looked promising, once intergraded no clear results are obtained. Because of the time constrains of this thesis, it is not possible to fine-tune of the model.

Once the model shows the proper results, it can form a great support for policy making. When for example an outbreak is recorded, the evaluation of the extent of the observation buffer can be monitored with this model. The first results in this research indicate that infected midges can already bridge the extent of the observation buffer, before the outbreak is even recorded. Additionally the model can be used to develop a vaccination strategy, so the virus dispersal can be stopped with minimal effort. By thinking of vaccinating a specific ruminant or within a specific range from a recorded outbreak.

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1. INTRODUCTION

1.1. Background

Over the last 100 years The Netherlands kept a relative disease-free state for former list A diseases defined by the Official International des Epizooties (OIE), aided by strong vaccination development and the implementation of sophisticated hygienic measures. However, the past ten years the risk of emerging zoonotic diseases[1] is rising and forms a threat for human and animal. Causes of this emerging risk are related to changing environment, changing climate and an increase in international trade of both animals and animal products (LNV[a] Vector project, 2007).

If the disease dispersal is not interfered by policies, the risk on an epidemic outbreak increases. To develop sustainable policies for preventing epidemics or appropriate control measures it is not only important to investigate the risk of an outbreak, but also its spatial behaviour. A Geographic Information System (GIS) is a powerful tool to analyse the spatial distribution of emerging risk areas in order to support policy-making associations (Ulugtekin *et al.*, 2006).
In 2007, Van der Heijden already developed a risk model based on the vectorial capacity of a *Culicoides* population to transmit the bluetongue virus (BTV). The vectorial capacity is based on local characteristics; however, this model excludes spatial and temporal relations (Van der Heijden, 2007).

1.2. Bluetongue disease

Bluetongue is a devastating disease among ruminants but is harmless for people. *"The virus replicates in all ruminants, but severe disease is mostly restricted to certain breed of sheep (particularly fine wool and mutton breeds that are common in Europe) and some species of deer"* (Purse *et al.*, 2005). For these breeds of sheep and deer, bluetongue is frequently lethal. When the disease is not lethal, individuals suffer after a long recovery from alopecia, sterility and growth delay (OIE, 2007).

The Bluetongue virus is related to the genus *Orbivirus* in the family *Reoviridae* that stands for a large group of double-stranded RNA[2] viruses. It is transmitted between hosts, almost entirely by bites of certain *Culicoides* midge species (Purse *et al.*, 2005). *"Culicoides biting midge are tiny flies, 1-3 mm in length"* (Wittmann & Baylis, 2000). According to Gomulski *et al.* (2006) only thirty from the twelve hundred sixty known midge species are, to a greater or lesser extent, involved in the transmission of bluetongue. Nevertheless, in Europe only three species are responsible for the transmittance of BTV, namely; *C. imicola*, *C. obsoletus* group and *C. pulicaris* group.
The threat on the BTV is not new, for several decades many BTV serotypes have been circulating on the fringes of Southern Europe, around the Middle East, Turkey and also in North of Africa. From these infected areas, the disease could enter Europe either by the transportation of infected

[1] **Zoonotic:** pathogens or diseases that normally circulate among non-human animals but than can be transmitted to humans (Weaver & Barrett, 2004)
[2] **RNA:** Short for ribonucleic acid, a nucleic acid molecule similar to DNA but containing ribose rather than deoxyribose. RNA is formed upon a DNA template. There are several classes of RNA molecules; messenger RNA, transfer RNA and ribosomal RNA (MedicineNet, 10-09-2007).

ruminants or by the wind-dispersed infected midges. However, before 1998 only brief periodic incursions were experienced in the Mediterranean (Purse *et al.*, 2005).
In October 1998, the first BT epidemic started on several Grecian islands. The introduced serotype BTV-9 entered Europe from the Middle East. Between 1998 and 2004, the BTV-9 disperses further north (Turkey, Bulgaria, Kosovo, Albania, Bosnia and Herzegovina, the former Yugoslav Republic of Macedonia, Serbia and Montenegro, and Croatia) and later to the west (mainland Greece, Italy, Sicily, Sardinia and Corsica) (Purse et al., 2005). During the same period, three other serotypes, BTV-1, BTV-4 and BTV-16, entered Europe through the mainland of Greece and spread westwards to Italy (Purse et al., 2005).
In 2000, serotype BTV-2 also entered Europe from the south, Tunisia and/or Algeria, into Sicily, Italy mainland, Corsica and the Balearic islands. Even the southwest of Spain and the south of Portugal were stroked via Morocco in late 2004 by the BTV-4, see figure 1-1 (Purse et al., 2005).

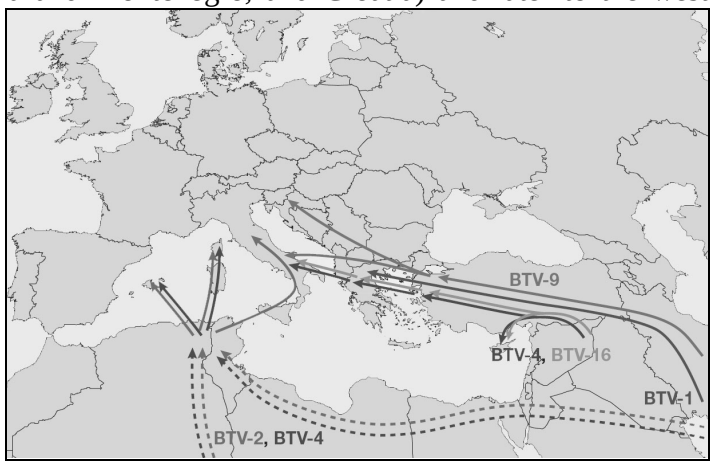

Figure 1.1 Distribution of bluetongue into Europe (Source: Purse et al.,2005)

1.3. Problem definition

Before 1998, bluetongue only occurred by brief periodic incursions in the Mediterranean. According to Meiswinkel *et al.* (2006), *C. imicola* is for ninety percent responsible of the transmission of BTV in these regions. It is assumable that bluetongue occurrence in the Mediterranean region is related to the territory of the *C. imicola*, which is limited to the fringes of Southern Europe. However, since 1998 a new epidemic started, which infected countries in Southern Europe and the Balkan severe than before. During this new epidemic the BTV serotypes 1, 2, 4, 9 and 16 are identified. Some of these serotypes have managed to persist for up to 6 years in several parts of Europe. *"For example BTV-9 has entered Bulgaria in 1999 and was subsequently recorded in the Balkan countries on annual basis up to 2004"* (Purse *et al.*, 2005).

"Central Europe was considered to be rather safe with respect to a possible invasion of a BTV epidemic, since the optimum temperatures for the known vector species should not be reached throughout the year" (Mehlhor *et al.*, 2007). However, in August 2006 the BTV was recorded in The Netherlands, Belgium, North France, Luxembourg and in the West of Germany. The risk increase in Central Europe is logic considering the northwards spreading movement of several BTV serotypes. Nevertheless, the BTV in central Europe happens to be the first epidemic of the BTV 8 serotype and can therefore not be related with the BTV occurrences in the south of Europe (Mehlhorn *et al.*, 2007).
With an epidemical breakout in central Europe, the limit of the BTV exceeds the northern territorial boundary of the *C. imicola* midge. It means that a different vector compared to the situation in the Mediterranean spreads the BTV in central Europe. The climatic circumstances in central Europe allow the survival of *C. obsoletus* and *C. pulicaris* and in 2006 Carpenter *et al.* proved that both species are capable to transmit the BTV (Carpenter *et al.*, 2006). However, after

examining both vectors, adult females of the *C. obsoletus* are kept responsible in ninety percent of the cases for the transmission of the BTV (Mellor & Wittmann, 2002).
According to Purse *et al.* (2005) the change in the BT epidemiology is unlikely related to biotic factors, like host transportation. Even an evolution of the virus can be excluded, since six different serotypes of BTV entered Europe simultaneously. Nor does it seem likely that non-climaticand abiotic factors (such as socio-economic, land use and animal health systems) are responsible for the change of the BT epidemic (Purse *et al.*, 2005).

The change in the BT epidemiology has severe consequences for the economy in Central Europe. It is a *"major factor limiting the unrestricted international movement of animals and animal products"* (Walton, 2000). However, next to the exportation sector it also affects directly the financial situation of the farmers. The mortality rate among sheep will decrease the meat production, together with the milk production of infected dairy cattle. For an average infected dairy farm it means a production decrease of 2,000 litres a week (Baltussen, 2007).
How to control such a vector-borne disease is relatively unclear. Infected vectors can spread by favourable wind, with truck and ectoparasites on pets. Additionally the virus can spread by the transportation of infected ruminants. The animal movements are almost impossible to regulate because of the open boarder policy of the European community (LNV[a] Vector project, 2007). Since a vaccine is still under development, the EU regulation introduced an observation and isolation buffer of twenty kilometres around any infected location. Within the observation buffer, the transportation of ruminants is strictly regulated (LNV[b], 2007).

In the previous research of Van der Heijden (2007) a model is introduced that calculates the vectorial capacity. The vectorial capacity visualizes the areas in which the vector is capable of transmitting the BTV and is calculated according spatial characteristics, like; habitat quality, host density and climatic circumstances. However, the model outcomes are not spatially or temporally related. It means that the current model can predict the risk on BT infections, but it cannot calculate new epidemics.

1.4. Research objectives and research questions

1.4.1. Objective

The objective of this research is to understand the underling processes of BTV dispersal and to develop a tool, according to the distribution capacity of the vectors, which predicts the spatial and temporal behaviour of the bluetongue virus. With such a tool, it becomes possible to control futuristic epidemics. In line with the objective, the following research questions will be investigated.

1.4.2. Research question

- How should the conceptual model be build up?
- Which models are suitable to predict the spatial and temporal behaviour of the vector?
- What is the uncertainty of the model?

1.5. Outline of this thesis

This research is based on an in depth literature review and consists out of six different chapters. Chapter 2 and 3 elaborate the characteristics of both the vector and BTV, and form the base for

the temporal and spatial resolution of the model. Chapter 4 offers the conceptual modelling as well as the implementation. Chapter five is all about the results and the validity of the model, and evaluates the models sensibility to temperature. Additional to the results, the conclusions, discussion and recommendation are made in chapter 6.

2. BLUETONGUE VECTOR

2.1. Introduction

C. imicola is kept responsible for the transmission of bluetongue in Europe for many years. However, since the last few years the virus has occurred further north than the original biotope of the *C. imicola*. A research of De Liberato *et al.* (2005) proved that *C. obsoletus* is also capable to transmit BTV and is currently in ninety percent of the cases pointed as the transmitter of the virus. *C. obsoletus* summarizes a group of approximately twenty species, from which the females cannot be further distinguished (De Liberato *et al.*, 2005). Since the *C. obsoletus* is an important vector, this research assumes that the *C. obsoletus* is fully responsible for the entire BTV transmission within The Netherlands. It means that a high risk on BTV transmission is directly related between the vector presence and vector density.
The vector density is dependent on various factors. It can have a temporal fluctuation because of temperature changes, or a spatial variation caused by the presence or absence of breeding and feeding areas. Even on a daily scale, variation in vector activity can be experienced, with peaks at dawn and dusk (Blackwell, 2001).
This chapter is based on a literature review and elaborates the characteristics of the *C. obsoletus* or tries to make substantiated assumptions when appropriate information is missing.

2.2. Suitable habitats

In The Netherlands, little characteristics from the habitat of the *C. obsoletus* are known. However, in other countries like Scotland more information is available. Immature *Culicoides* require moisture and organic matter for development and breeding sites that include damp or saturated soils, bogs, marshes, swamps, tree holes, animal dung and rotting fruits or other vegetation (Wittmann & Baylis, 2000).
Blackwell *et al.* (1999) investigated the spatial distribution of the larvae of the *C. impunctatus* in relation to vegetation. She proved that there is a highly significant relation between the larvae of the *C. impunctatus* and vegetation like mosses (*Sphagnum spp.)*, rushes (*Juncus spp.*) and bog myrtle (*Myrica gale*). Especially mosses (*Sphargnum spp.*) and bog myrtle (*Myrica gala*) are species that can be found in high peat habitats, where as rushes (*Juncus spp.*) can be found on wet grasslands through the whole of The Netherlands.

Since all three vegetation species are commonly present in The Netherlands, it is assumable that they form also an important condition for the breeding area of the *C. obsoletus*. These vegetation is automatically an indicator for the presence of sufficient moist and organic matter. Too much water and the larvae is not able to survive, so areas inundated during the breeding period can be neglected. Additionally female vectors need protein to produce eggs, which they obtain from blood. A perfect breeding area should therefore not only be determined on vegetation and moist, but also on the presence of sufficient ruminants to feed on (Boorman & Goddard, 1970).

In order for larvae to survive, in a specific habitat type, climatic circumstances cannot fluctuate a lot. Especially frost or severe drought can drastically reduce the number of midges (Blackwell, 2001). However, in the past midges are recorded far outside natural areas that satisfy the entire above mentioned habitat conditions, which makes it assumable that midges also reproduce in

circumstances that are more artificial. One can think of a farm, where stables provide shelter against wind and frost and where sufficient moist and ruminants are present all year long.

2.3. Host preference

In the *C. impunctatus*' search for a blood meal, they respond *"to solid-outline, black, rectangular targets and this response is enhances in the presence of CO^2"* (Blackwell, 2001). It means that the *C. impunctatus* prefers *"large mammals, primarily cattle and deer, with a lower preference for sheep"* (Blackwell, 2001). In 1972, Nevill & Anderson investigated this preference for certain ruminants. On one farm, with different types of ruminant, midges have been captured for several days (see table 2.1).

Table 2.1 Host preference

Trap location	Nr. of midgets	Nr. Nights	Nr. of midgets per night	Fraction (%)
Poultry house	853	14	60,9	3
Mule stable	8087	13	622,1	31
Sheep paddock	1472	7	210,3	10
Cattle stable	6889	7	984,1	49
Garden	1793	13	137,9	7

If the garden and poultry house are left out, the division in population fraction changes to: 54% in the cattle stable, 34% in the mule stable and 12% in the sheep paddock. Blackwell *et al.* (1994) investigated the vector preference by analysing the obtained blood in female midges. The result was that 38% of the midges had bitten cattle, 23% of the midges had bitten deer and 10% had bitten sheep. The remaining 29% could not be identified. If the unidentified fraction is left out the analysis, the percentages changes to the same division that Nevill & Anderson (1972) found, namely; 54% for cattle, 32% for deer and 14% for sheep. Considering the preference of the vector and the dominant presence of cattle, 1.2 million sheep against 3.9 million cattle recorded in 2002 (CBS, 2007), cattle is far more important in the transmission of BTV than sheep.

2.4. Life cycles

Male midges achieve already there maximum sperm transfer when twelve to twenty-four hours old (Birley & Boorman, 1982). The female midge searches her first blood meal in the same time period (Wittmann *et al.*, 2002). After a blood meal, the female needs some rest to produce eggs. Eventually when the eggs are spawned, the female will search for a subsequent blood meal and the cycle will repeat itself, see figure 2.1.

The expected lifespan of midges is strongly influenced by temperature and vary between an age of zero to eighteen days. The relation between the midge age (L_m in days) and temperature (T in ^oC) is described in equation 1, see also appendix I (Koeijer *et al.*, 2007) (LNV[a], 2007).

$$L_m = 0.0034 \cdot (T-10)^3 - 0.01605 \cdot (T-10)^2 + 1.8065 \cdot (T-10) + 11.968 \quad (1)$$

Like the expected lifespan the midge, the biting frequency is also related to temperature. In a research of De Koeijer *et al.* (2007) it is assumed that a temperature below 10^oC results in a negligible biting frequency. Equation 2 expresses the dependency of the biting frequency (B_f per day) on temperature (T in ^oC).

$$B_f = 0.028571 \cdot T - 0.26571 \quad (2)$$

If the biting frequency is negligible, no new eggs will be produced. Even if there are midges, the chance that they live long enough to reproduce themselves is small. It is therefore assumable that eggs only hatch when the temperature exceeds the 10ºC. This means that in The Netherlands the midges season last from May until October, which confirms to the period described (May until September) by Blackwell *et al.* (1992).

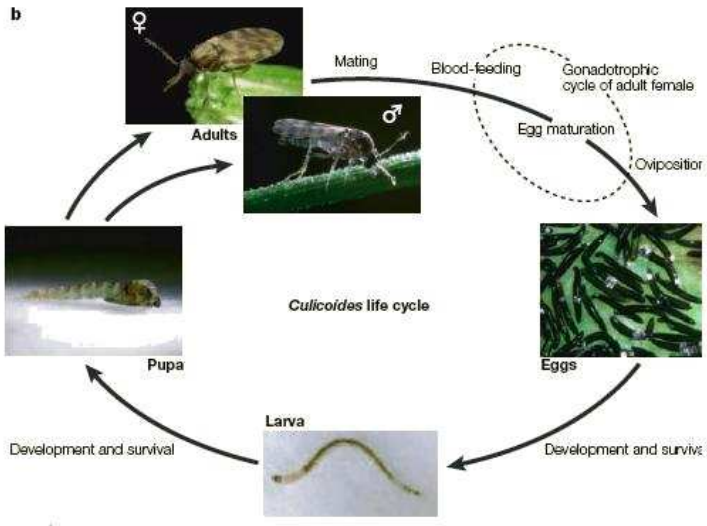

Figure 2.1 *Culicoides* life cycle (Source: Purse *et al.*, 2005)

The larva comes out of the egg within three to eleven days and is able to survive for seven months (Kerkum & Takken, 2002). However, in the studies of Birley & Boorman (1982) and Blackwell *et al.* (1992) it is proven that larvae can evolve into a midge adult, in little over a month. These studies are based on the density monitoring of both *C. obsoletus* and *C. impunctatus*. For both species two peaks are recorded during the midge season with an interval of six weeks. If it is assumed that the second peak is the result of the first peak, it means that larvae can evolve, when the temperature is optimal, into a midge adult in six weeks.

$$D_l = -13.081 \cdot Ln(T - 10) + 80.064 \quad (3)$$

The larvae development can be described with a logarithmic function (equation 3), in which the influence of temperature (T in ºC) decreases when the larvae development (D_l in days) reaches its optimum.

2.5. Vector reproduction

Like mentioned before, the midge season last from May until October with two density peaks in June and July (Birley & Boorman, 1982). Even though Blackwell *et al.* (1992) records different temporal density peaks, she also finds a gap of six weeks. It means that the first generation has the chance to reproduce itself within the same season. The larvae of the second generation are able to survive throughout the winter. Per batch a female is able to produce thirty until one hundred eggs (P_e in numbers), which is again related to the temperature (T in ºC) (Blackwell, 2001), see equation 4. Additional the egg production is also dependent on the available blood meals. In practise, around five thousand midges can feed on one ruminant each day (Gubbins *et al.*, 2007). If more female midges are searching for a blood meal per day, they will not be able to obtain blood, and therefore will not reproduce.

$$P_e = -0.036 \cdot (T-10)^3 + 1.028 \cdot (T-10)^2 - 1.648 \cdot (T-10) + 10.656 \quad (4)$$

The optimum reproduction ratio lies around 25ºC (De Koeijer, 2007). When the eggs are laid, the female is again able to develop new eggs. However, before the female even gets a chance on a second blood meal, forty-three percent will die (Blackwell, 2001). In addition, also during the larvae development there is a fraction that dies. Allingham (1991) proves that there is also a relation between the mortality of late immature C. *brevitarsis* and temperature; however, he has investigated the mortality of midges in a laboratory with constant temperature values. It is not clear how the daily temperature fluctuations influence the survival rate.

2.6. Distribution pattern

Most *C. impunctatus* are active during the early morning (06.00 – 08.00 hour) and evening (19.00 – 23.00 hour) (Blackwell *et al.*, 1992). With favourable conditions, higher than 10ºC, little or no wind and high humidity, *"C. impunctatus adults could travel in large numbers more than 1.2 kilometres from their point of origin"* (Blackwell, 2001). Even tough this might be the maximal flying capacity on one day, it does not mean that every midge covers this distance each day. In a historical research of Kettle (1951), it is stated that the distribution from the source has to do with the population density in the source (*a*, which is expressed in numbers, see equation 5). If the source contains little amount of midges, they will disperse less far as when the source is an abundance. Kettle (1951) came up with an equation (see equation 5) to estimate the amount of migrating midges (V_d) in any direction and any distance from the source (x in meters). Since no information is available about the flying capacity of the *C. obsoletus*, it will be assumed to correspond with the predefined performances of the *C. impunctatus*.

$$V_d = 10^{Log(a) - 0.016519 \cdot x} \quad (5)$$

The vectors activity is positively correlated with the humidity and negatively with the wind speed. *"In addition to the negative effects on activity, wind can directly affect the abundance of Culicoides through dispersal of the adults"* (Wittmann & Baylis, 2000). All three researches of Wittmann & Baylis (2000), Nelson & Bellamy (1971) and Service (1971), indicate that there is a fluctuating extent of flight activity reduction between wind speeds of 3 to 16 km/hr. However, it is unclear how the flight activity reduction is related with an increasing wind speed.

2.7. Vector characteristics

Temperature has a major influence on all important aspects in the life cycle of a midge, like: the amount of produced eggs, the life span, the interval between blood meals and also the length of the larvae development. Female midges search early in morning (06.00 – 08.00 hour) and evening (19.00 – 23.00 hour), only with a wind speed lower than 16 km/hr, for a blood meal in a range of 1,200 meters. During their search, they have a strong preference for solid-outline, black, rectangular targets. If ruminants are equally represented in a feeding area, 54% of the midges will feed on cattle, 33% on deer or horses and 13% on sheep. Nevertheless, no more than five thousand midges can feed on one ruminant each day.

3. BLUETONGUE VIRUS

3.1. Introduction

Next to the presence and distribution of the vector, the characteristics of the virus itself play also an important role in risk analysis of new BT outbreaks. Especially the incubation time of the vector is essential to determine, whether the transmission of BTV is possible. On the other hand, it should be investigated how sensible different ruminants are for the virus and how they respond to it. For example, a ruminant can be infected without experiencing any severe illness. It means that the ruminant forms a reservoir for naïve vectors, but is not recognised by the farmer as an infected ruminant. To determine the BTV distribution it is important to include all the infected ruminants, however, during the validation of the model it should be recognised that exciting information about infected ruminants is likely to be incomplete. This chapter is based on a literature review and elaborated all the characteristics of the BTV. If any information is missing, substantiated assumptions will be made.

3.2. Transmission

Virus transmission only takes place when an infected female midge bites a naïve ruminant or when a naïve female midge bites an infected ruminant. However, for a female midge to be able to transmit the virus, she needs to bite at least twice and live long enough to survive the incubation period. During the first blood meal, the midge obtains the virus and can only be passed trough to a naïve ruminant in the first blood meal after the incubation time (see figure 3.1). The transmission ratio from the infected vector to the susceptible ruminants is one hundred percent, according to the report of the De Koeijer *et al.* (2007). However, the chance that a susceptible midge gets infected after a bite from an infected ruminant is fifteen percent and is much smaller (Gubbins *et al.*, 2007). Since a blood meal is necessary for the egg production, the risk of BTV transmission is limited to the period in which the reproduction takes place. The ability of the vector to transmit the virus is called vectorial capacity. *"Vectorial capacity is a measure of likelihood of pathogen transmission by a vector population to a susceptible host population. Biting intensity (bites/host/time) and survivorship are two of the principal parameters that determine vectorial capacity"* (Gerry & Mullens, 2000).

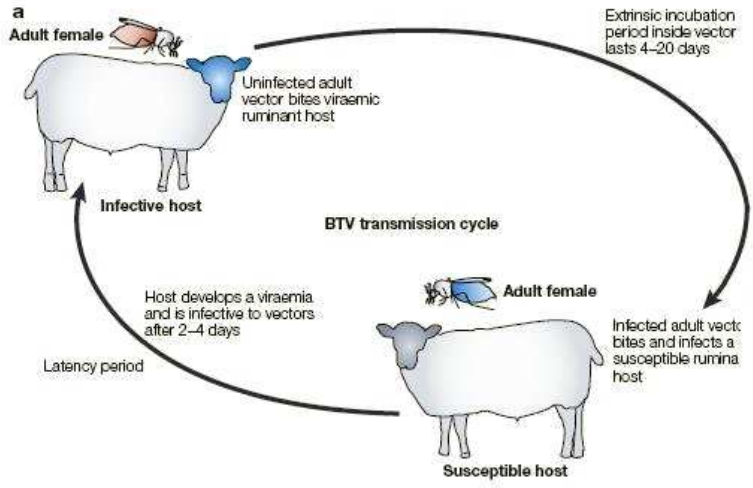

Figure 3.1 BTV transmission cycle (Source: Purse *et al.*, 2005)

3.3. Susceptibility

In addition to virus transmission, the susceptibility among ruminants differs. Most of the infected ruminants do not show any signs of illness. For example, the infection of cattle invariable is asymptomatic (MacLachlan, 1994). On the other hand, the disease in sheep is more severe and can be fatal. Between both ruminants, animals will recover and develop immunity for homologous serotypes of the virus. However, these antiviral responses do not always result in prompt clearance of the virus. *"Although neutralizing antibodies clearly prevent reinfection of ruminants with a homologous virus, neutralizing antibodies do not immediately clear the virus from the circulation. Thus BLV may co-circulate with specific neutralizing antibodies for several weeks after infection of both cattle and sheep"* (MacLachlan, 1994).

Elbers *et al.* (2007) investigated the clinical signs during the epidemical outbreak of 2006 in The Netherlands. It visualized that 1% of the sheep herd died because of the BTV compared to a mortality rate of 3% among cattle. Since it is not clear how much ruminants did show signs of illness and fully recovered, it is assumed that only 3% of infected cattle shows visual signs and 15% among sheep.

3.4. Incubation and infectiousness

The transmission opportunity between vector and host is dependent on the incubation time and the infectiousness. For example, female *Culicoides* can transmit the virus to susceptible ruminants after an incubation period of 10 to 14 days (Bonneau *et al.*, 2001). The variation in incubation time (V_{inc} in days) among midges is related to temperature (T in ºC) and can be calculated by the formula given in equation 6 (De Koeier *et al.*, 2007).

$$V_{inc} = 24.62 \cdot (T - 10)^{-1.0109} \tag{6}$$

Ruminants are warm blooded, so differences in incubation time among individual ruminants are likely to be the effect of a difference in susceptibility instead of climatic temperature. However, there is a strong difference in incubation and infectiousness between sheep and cattle. The incubation time of sheep lies around three days with an infectiousness of maximum thirty days after infection (Koumbati *et al.*, 1999). Cattle do not respond that quickly to the virus, which results in an incubation time between six and eight days (MacLachlan, 1994). The duration of the viremia in BTV-infected cattle is related to the lifespan of the bovine erythrocyte (Singer *et al.*, 2001), which leads to an infectiousness between one-hundred-twelve and one-hundred-forty days. Cattle are therefore, in combination with the vectors privilege for bovine blood, considered to be reservoir hosts of BTV, from where the virus can be transmitted to susceptible ruminants by biting midges (MacLachlan *et al.*, 1994).

3.5. Wintering

"Understanding the mechanism by which the virus overwinters is of crucial importance in defining the basic epidemiology of the virus" (White *et al.*, 2005). In the current discourse about the overwintering of the BTV, three possibilities are distinguished. White *et al.* (2005) state that a adult female can transfer the virus to her offspring by vertical transmission. However, the obtained results are not convincing enough and more research needs to be done.
Another possibility is a reintroduction of an infected host or vector from another region. Even though this possibility is commonly accepted, uncertainties remain about the origin of the

infected host or vector and its destination. A final possibility is that the virus is capable to winter in infected ruminants. Takamatsu *et al.* (2002) proves that some γδT-cells[3] in sheep can become persistently infected, even though the host seemed to be fully recovered. In a subsequent season, biting midges can trigger the γδT-cells. It will result in an inflammable skin and the release of the BTV. After approximately seven days, the BTV can be transferred again (Takamatsu *et al.*, 2002). However, the wintering of BTV is only proved in sheep, which makes it unclear if it can occur among all different ruminants. Furthermore, information about the chance on persistently infected γδT-cells is lacking.

3.6. Virus characteristics

Only 15% of the midges that obtained a blood meal from an infectiousness ruminant obtain the virus. After an incubation time of 10 to 14 days, related to temperature, the midge can transmit the virus to a susceptible host. The chance that a ruminant gets infected after a bite from an infectious midge is one hundred percent. When sheep are infected it last 3 days before it gets sick, with sickness duration of 30 days after infection. For 15% of all the infected ruminants the infection becomes fatal. Cattle show less signs of illness but are longer infectiousness. On average cattle has an incubation time of 7 days with an infectiousness of 126 days. During the infection only 1% of the infected individuals die.

[3] *"A subset of T cells that is predominant in skin and mucosal tissues. They probably act as a first line of defense against infection and cancer and have immunoregulatory functions"* (Purse *et al.*, 2005).

4. MODEL DEFINITION

4.1. Introduction

A model can be built for different purposes, but is always a limited representation of reality. The objective of the modeller determines the type of model that is needed. For example, a model can describe existing processes or predict futuristic situations. Include dynamic or static processes and finally can include some randomness (Chang, 2008).

The latter mentioned model purposes can be executed in a raster or a vector environment. A raster environment is usually applied when a spatial phenomenon varies continuously over space, where a vector-based model is recommended for situations that involve well-defined locations and shapes (Chang, 2008). In all three environments, four different model types are recognised to achieve the model objective. The first model type deals with a binary approach. This method is based on a logical expression, from which the result can either be true or false. Similar to a binary model is the index model. The principle of this method is the same only it expresses the outcome between zero and one. Both model types are considered to be static, since they do not change over time. A third model type is a regression model. Regression models relate a dependable variable with independent variables and can simulate a dynamic process, if only used in a looped calculation. The final modelling category is created when two or more of the above-mentioned model types are used simultaneously and are called process models (Chang, 2008).

During this chapter, the modelling objective will be elaborated into a modelling concept. Additionally it will discuss the selected model types and the assumptions that need to be made for the operation of the model

4.2. Concept model

Like mentioned in chapter 2, the lifecycle of a midge starts with new produced eggs. Depending on the temperature they will hatch between six weeks and four months. Already after the first day, a female midge searches for a blood meal for reproduction. During this research, it is assumed that a fraction of the midge population will migrate in their search for ruminants, but the majority will stay near the location of birth. Depending on the lifespan, which is directly related to the temperature, a female midge can bite a second or even a third and exceptionally a fourth time. Midges have a strong preference for bovine blood, but also bit sheep, horse and deer. Depending on the amount of blood meals in combination with temperature, new eggs are produced and the lifecycle starts all over again. The amount of blood meals ensures an increase or decrease in the midge population, but it also plays an important role in the BTV transmission. After obtaining a blood meal of an infected ruminant, the midge gets infected. Even though the midge is infected, it needs to live long enough to obtain a second blood meal to transmit the virus to a naïve ruminant and increasing the risk on an epidemical outbreak.
Both cycles of the midge population and the virus development need to be integrated into one model in order to predict the spatial and temporal behaviour of the BTV. Figure 4.1 shows the flowchart of the most important processes described in the previous paragraph. It should be mentioned that the order of the different events are assumed. Additionally it is possibly to subdivide the conceptual model, into three different elements. The first element concerns the population dynamics.

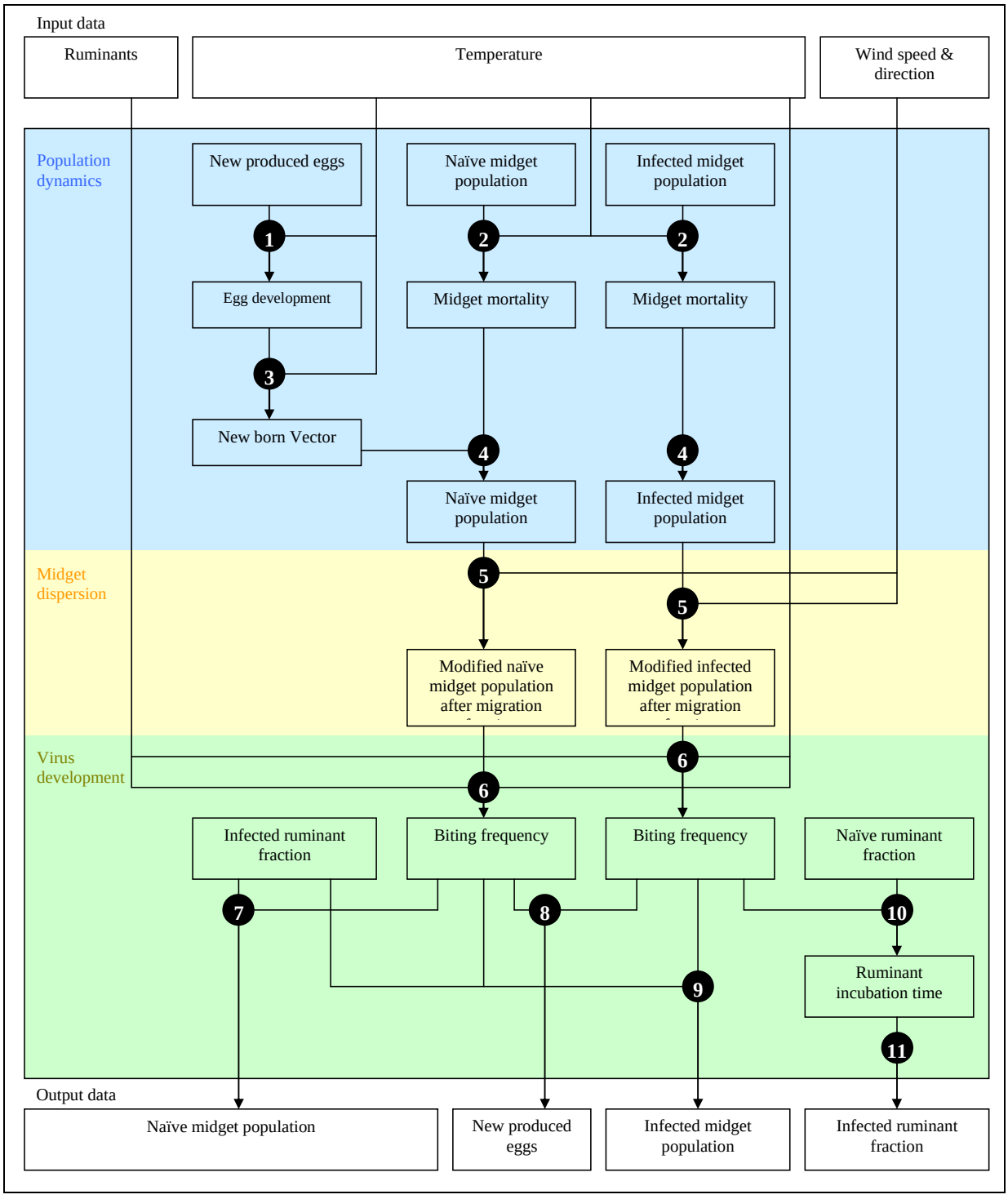

Figure 4.1 Modelling concept

This element calculates the new produced eggs (action 1) and the mortality among the existing naïve and infected midge population (action 2). The mortality fraction and newly born midges result in an evolved population (action 4). Within the second midge dispersion element; the

existing midges are redistributed (action 5). Each location loses a fraction of midges because of migration, but also obtains midges from its surroundings. Only after migration take place, midges can get a blood meal (action 6) in the third and final model element. When the model is iterated, several times the output becomes the input of the subsequent iteration. It means for example that the amount of blood meals in the third model element determines the produced eggs (action 8) in the first element during the next iteration. However, the main purpose of the third model element is to calculate the virus development. This element allows the midges and ruminants to exchange the BTV (action 7 and 9 until 11).

The objective of this model is to calculate the spatial and temporal behaviour of the BTV in 2006. However, it is possible to calculate the viral behaviour with a variety of temporal resolutions. Each temporal resolution will have its own effect on the model outcomes. Since all major events, like midge lifespan, larvae development, ruminant incubation time and infectiousness, are calculated on a daily scale, it is most accurate to copy this daily resolution.
To determine the resolution of the midges' spatial behaviour is much more complicated, because it is possible to analyse the BTV distribution on different levels. Each level of evaluation should adapt the resolution to the smallest included parameter. Concerning the national spatial behaviour of the BTV, it is necessary to evaluate the situation for each farm. According to the CBS (2007) information from 2005, 41,100 ruminant farms were present in The Netherlands, with an averaged property size of 26.6 ha. With a spatial resolution of 516 meters each pixel represents an area of 26.6 ha; however, this will be rounded off to a resolution of 500 meters. In this way not only the averaged farm property is included, but also the majority of the recorded farms.

The next step after defining the spatial and temporal resolution, is preparing the needed climatic input data. All used information originates from 2006 and is collected by Meteo Consult on different locations in The Netherlands, Belgium and Germany. The distribution of the weather stations is visualized in figure 4.2. With an interpolation function, called spline, information is obtained between the different weather stations. Using the results of the spline function means that it is assumed that the values in the area between the weather stations are directly related to the observation points (Chang, 2008). However, due to different land coverage, it could be that in reality temporal fluctuations between the observation points are less strong than in the observation point itself. It should therefore be recognized that the interpolated values could slightly deviate from reality.

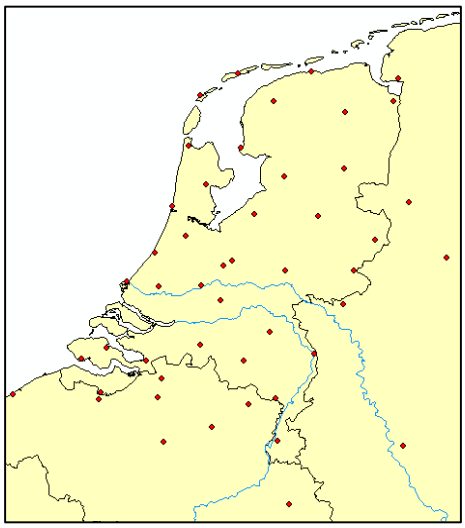

Figure 4.2 Distribution weather stations

4.3. Population dynamics

The population dynamic element uses a 'deterministic' approach to calculate any population fluctuations with a regression analysis, based on the daily temperature. Temperatures of succeeding days can deviate a lot. For example, one day it is 20ºC whereas the next day the temperature hardly rises above the 14ºC. When these data is used to calculate the biting frequency, a midge is expected to bite twice a week on the first day, where the temperature on the second day allows only a blood meal once a week. Such a strong difference in a relative small

time step can cause strange results. To prevent these strong temperature fluctuations, the daily temperature will be replaced by a moving average of five days. In this way, major fluctuation between two succeeding days can be filtered out without influencing the general temperature trend.

When the model starts on day one in 2006, the temperature is not suitable for living midges and only eggs survive. However, no input information is available about the present amount of midge eggs on the first day and need to be introduced artificially. Each cell gets 10 eggs, which hatch when the temperature exceeds 10ºC. Among the newly adult midges, the male/female division is considered to be equal. Within twenty-four hours, the new female midges will already search for their first blood meal to reproduce. Depending on the temperature, the midges produce between thirty and one hundred eggs.
The length of the midge lifespan is also related to the temperature but last maximally eighteen days. As long as the expected lifespan is smaller than the actual age, the midges will become older otherwise they die. The same is done for the midge eggs. One example is shown in figure 4.6. This figure shows the age of the midges and eggs on day 1, 2 and 3. In this example, 15 eggs hatch at the end of day 1. The subsequent day recognizes the hatched egg as new midges (age 0). During the same day, the midges of 1 day old obtain a blood meal. The result is that each biting midge produces 10 eggs, see day 3. To prevent an infinitive increase of new midges, the available blood meals are limited by five thousand per ruminant per day. If more female midges are present, they will not obtain a blood meal and therefore will not reproduce.

Day 1

Midget age	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
No. of midgets	10	0	5	2	0	0	0	0	0	0	0

Egg age	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
No. of eggs	0	0	0	0	0	0	0	0	0	0	15

Day 2

Midget age	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
No. of midgets	15	10	0	5	2	0	0	0	0	0	0

Egg age	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
No. of eggs	0	0	0	0	0	0	0	0	0	0	0

Day 3

Midget age	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
No. of midgets	0	15	10	0	5	2	0	0	0	0	0

Egg age	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
No. of eggs	100	0	0	0	0	0	0	0	0	0	15

Figure 4.3 Example of the first model element

4.4. Midge dispersion

During this model element, the midge population will be addressed to the centre of each cell. A fraction of these midges, calculated in the first model element, will migrate to neighbouring cells. To migrate from one cell to another, the midge has to be able to bridge the entire distance to the centre of arriving cell. It means that it is assumed that a migrating midge has to travel a minimal distance of 500 meter, if a 500 meter grid is used, to reach its neighbouring cell. From literature, it is obtained that midges can easily travel a distance of 1.2 km. If the 1.2 km is translated into a 500 grid, three cells are needed to cover this distance. However, in the current set up of the model, the migration to the third cell is not recognised, since the migration distance does not reach the centre of this cell. To overcome this problem the flying capacity will be enlarged to 1.5 km.

In order to calculate the amount of migrating midges, a simple formula is used, which is based on the distance towards its neighbouring cells. According to equation 2.6, only 15.05 % of the total population from a source cell will migrate. This means that for every 1000 midges, 11 midges will migrate to its surrounding cells. This percentage is fixed in a wind silence situation, but with wind, this fraction becomes variable. However, to keep the model understandable the migrating fraction is assumed to be constant. Like stated above, the migrating distance is related to the wind, but also on the number of midges that are present in the source. The formula, introduced in equation 5 in paragraph 2.6, is developed for forestry and allows the midges to disperse with average radians of 250 meters. Since this research assumes that midges can easily bridge a distance of 1500 meter, the introduced formula is modified in the following equation (7).

$$V_d = 10^{Log(a \cdot 0.8495) - 0.016519 \cdot \frac{\chi}{5}} \tag{7}$$

Based on the present amount of midges in the source (a), the formula estimates the amount of migrating midges (V_d) on any distance around the source (x in meters). In order to allow midges to migrate up to the preferred distance, the physical distance has to be divided by five. Five is just a number derived by trial and error. Finally, it is also necessary to correct the number of midges in the source with 0.8495. The reason for this correction is the setup of the first element of this model. In the first element the population increase is calculated, which includes a migrating fraction of 15.05 %. Equation 6 on the other hand, calculates the migrating distribution according the number of midges in the source, without the migrating fraction.

If a farm is located within the range of the migrating vector, vectors will settle and the cell is considered to be a new source from where the vector can disperse. In these sources, during the midge season, there is a continuous reproduction which ensures that the vector never extinct.

The migration direction is assumed to be random, but will be affected by wind. In other words, the distribution pattern is related to the wind force and direction and therefore dynamical over time. Such a concept can be compared to the operation of a sprinkler. A sprinkler distributes water continuously in any direction and locations near the nozzle receive more water compared to locations further away. Wind influences the distribution circle of a sprinkler by blowing away the released water. This is considered to be similar to the midges' migration pattern. Any variation in the midge population itself can be seen as opening or closing down the water tap, which influences the area of distribution.

Literature, Wittmann & Baylis (2000), Nelson & Bellamy (1971) and Service (1971), proves that flight activities occur with wind speeds between 3 to 16 km/hr, but fails to clarify the relation between flight activity reduction and increasing wind speed. Because of that, this research neglects a dynamical flight activity reduction, but assumes that all the flight activity stops when the wind speed exceeds 11 km/hr. 11 km/hr is seen as the upper limit for the flight activity and is still recognised by the Royal Dutch Meteorological Institute (KNMI) as wind category[4] 2. Such a wind category occurs in 41% of all cases, see table 4.1. It should be mentioned that table 4.1 is based only on the wind occurrences during the flying active period of the midges.

Table 4.1 Daily averaged wind speed[4] in 2006, over the flight active period of the vector

Wind category	Description	Wind speed (km/h)	Frequency (day)	Accumulated frequency (day)	Accumulated frequency (%)
0	Silence	0 - 1	0	0	0.00
1	Weak	1 - 5	7	7	0.02
2	Weak	6 - 11	143	150	0.41
3	Moderate	12 - 19	151	301	0.82
4	Moderate	20 - 28	55	356	0.98
5	Quite powerfull	29 - 38	8	364	1.00
6	Powerfull	39 - 49	1	365	1.00
7	Strong	50 - 61	0	365	1.00
8	Stormy	62 - 74	0	365	1.00
9	Storm	75 - 88	0	365	1.00
10	Severe storm	89 - 102	0	365	1.00
11	Very severe storm	103 - 117	0	365	1.00
12	Hurricane	> 117	0	365	1.00

When a wind of 11 km/h occurs it will positively influence the midges' flying capacity along the wind direction, but reduces the flying capacity opposing the wind. Along the wind, if it is assumed that midges fly only one hour continuously in one direction, midges can fly 11 km further. In total, midges migrate along the wind a distance up to 12.5 km/day. However, even though the migrating fraction is related to the distance, it will not be recognized by equation 7 when a distance of 12.5 is used. This equation gives only a result until an approximate distance of 1500 meter. One way to overcome this problem is to transform the distances towards the neighbouring cells into relative distances. These relative distances explain the effort that it takes to migrate towards the neighbouring cell. In this way, it is possible to reduce the effort towards the cells along the wind direction and to increase the effort of migrating opposing the wind. Figure 4.4 is a migration example and shows how the relative distances will be calculated. The example indicates how much midges migrate to the centre cell, when the surrounding cells all contain five thousand midges (see figure 4.4[a]). During the migration, the flying pattern will be influenced by a wind speed of 0.3 m/s (4.4[c]) blowing from east to west (4.4[b]).
First of all, the direction (see figure 4.4[d]) and distance (4.4[e]) of the neighbouring cells from the cell of interest need to be determined. The distance of the surrounding cells can be seen as resistant. When the cells are to far away the resistance of the distance becomes too large and no

[4] Wind strength according to Beaufort.

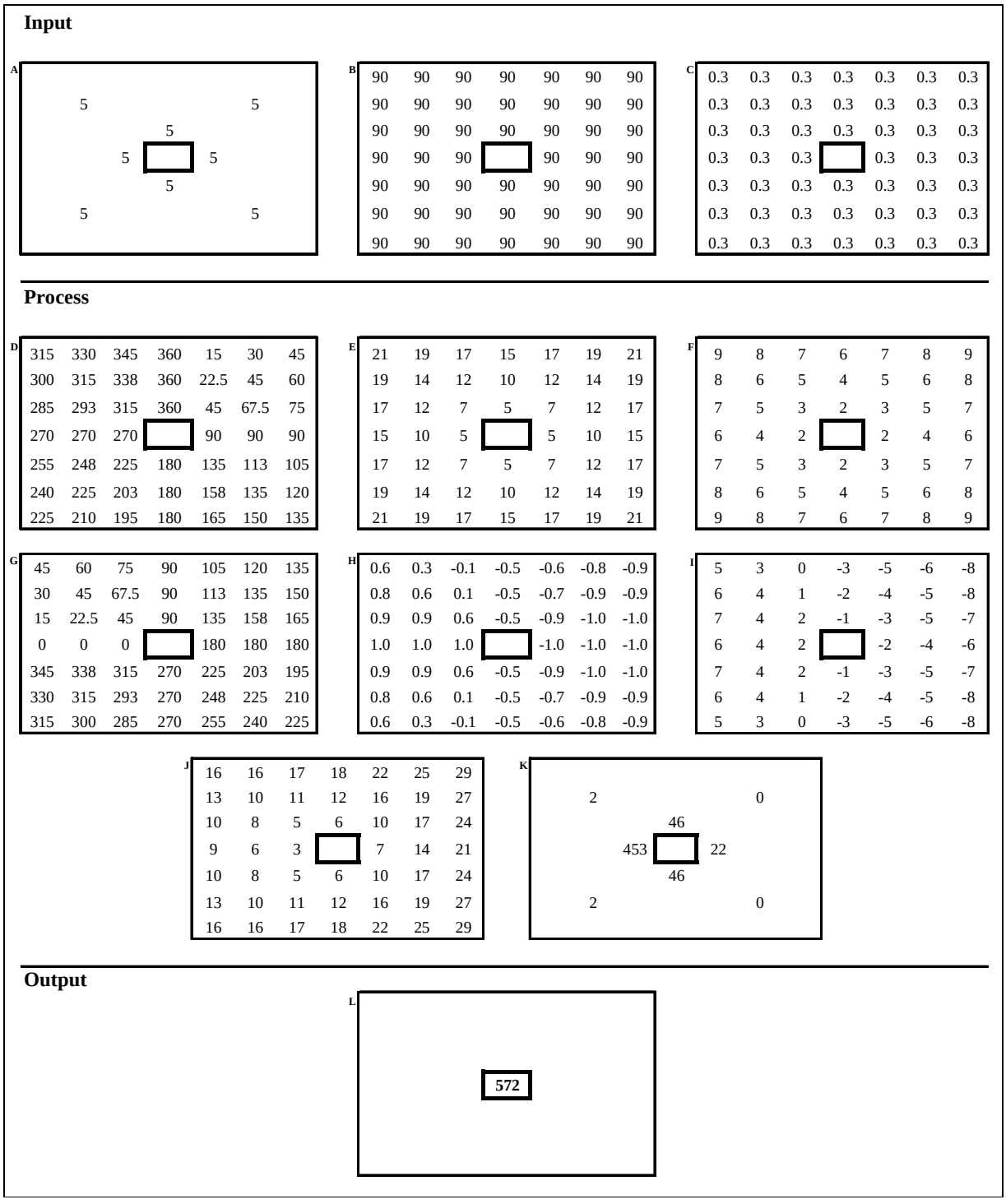

Figure 4.4 Calculates the migrating midges to a centre cell: (a) Population density (no. * 10^3), (b) Wind direction (º), (c) Wind speed (m/s), (d) Calculated direction from the source cell (º), (e) Calculated physical distance to the source cell (m * 10^2), (f) Reduction of distance resistance in m * 10^2, (g) Wind direction added to the physical direction (º), (h) Weighted wind direction (-1:1), (i) Increased flying capacity times weighted wind direction (m * 10^2), (j) Physical distance corrected (m * 10^2), (k) Migrating midges (no.), (l) Migrating midges summarized (no.)

migration takes place. A wind speed of 0.3 m/s increases the flying capacity, but is in this approach applied as a reduction of the distance resistance (4.4[f]). However, this resistance reduction is not applicable in every direction. To determine in which direction the distance resistance needs to be reduced or increased, information is needed about the direction of all cells to the centre cell with the wind direction as reference (4.4[g]). With this new referred direction, the direction can be weighed. It is assumed that the distance resistance in all directions within an angle of 146° along the wind direction is reduced. All other directions are negatively weighted (4.4[h]). Finally the weighted directions are multiplied with the distance resistance reduction and added to the real distance of the neighbouring cells.

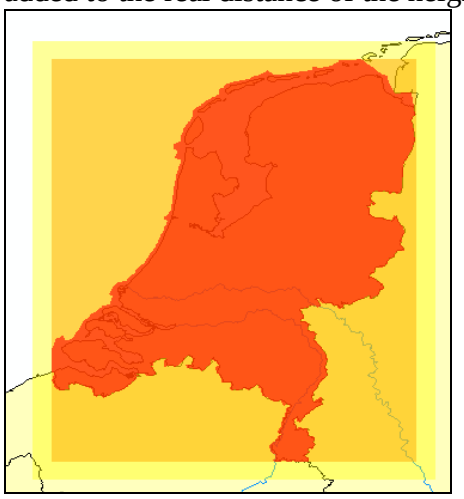

Figure 4.5 Dimensions of the input data (yellow), filter operation (orange) and area of interest (red)

The results are relative distances of the neighbouring cells to the centre cell (4.4[i]). Once the relative distances are obtained, the amount of migrating midges (4.4[k]) can simply be calculated by applying the formula introduced in equation 7. To find out how much midges migrate to the centre cell, all migrating midges from the previous result have to be summed up.

In the model, the previous mentioned calculations are implemented in a dynamical filter operation. A filter operation is generally applied on a rectangular filtering grid with the same extent as the area of interest. To prevent errors and allow neighbouring operations on the fringes of the grid, the extent of the filtering input data needs to exceed to filtering grid. Figure 4.5 shows the different extents of the input data. The red area represents the area of interest, the orange area is the area in which the filter redistributes the midge population and the yellow area visualizes the extent of the filter input data.

4.5. Virus development

Only when the expected lifespan is long enough for midges to survive the incubation time, the virus can be transmitted. In order to model this, it is necessary to remember the age of the midge on the moment of infection. In practice, this can lead to difficult modelling practices because midges of the same age can be infected on different moments. For now the implementation of a midge incubation time in the model is to complex and is therefore left out. The consequences are that more midges get infected and midges can transmit virus faster than theoretically possible. It is therefore a logic result that the current model overestimates the general virus dispersal. A subsequent research is

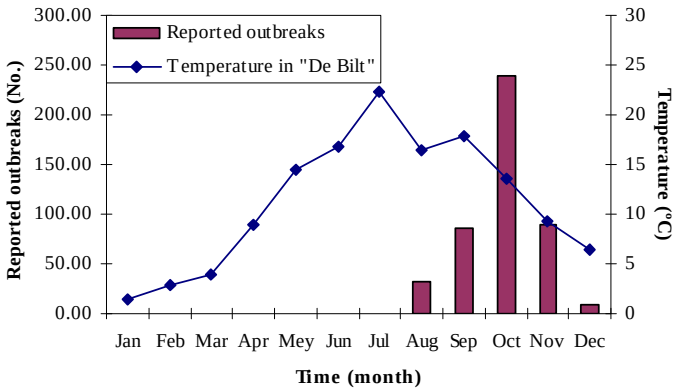

Figure 4.6 Reported outbreaks compared to the average temperature in “De Bilt” in 2006

necessary too elaborate the missing incubation element. Without including the incubation time, the transmission becomes dependable on the capacity of the midges to obtain a second blood meal. According to the information about the lifespan and biting frequency, introduced in chapter 2, midges get only the chance to obtain a second blood meal when the temperature is 13 ºC or higher. According to the Royal Dutch Meteorological Institute's (KNMI) measured temperatures, it means that midges are capable to transmit the virus between week 34 (August) and 44 (November). If this is compared to the recorded outbreaks of the virus, see figure 4.6, the theoretical transmission period matches with the recorded outbreaks in 2006. During 2006 457 (recorded by the Dutch Voedsel Waren Autoriteit) of the 41,000 registered farms were recorded as infected, which is similar to 1%. The first outbreak was recorded in the surroundings of Heerlen on the 14th of August, see as well figure 4.7. To be able to transmit the virus, the virus should also be introduced in the model around the same period. Since the modelled outbreak can slightly deviate from reality, one infected bovine animal is introduced on the 1st of August (day 213) on a farm near Heerlen.

Figure 4.7 Virus introduction around Heerlen

The virus development in both vector and host is modelled similar to the population dynamics. It is important to monitor the age of the infection and the amount of infected individuals. The interrelation between midges and ruminants, and therefore also the BTV, is a stochastic process with many probabilities. For example, there is a higher chance that midges bite cattle instead of sheep. Additionally there is a chance that the selected host is infected or naive. Finally, there is also the possibility that the midge itself is infected by the virus. However, since the midge population extent is well over a million, the average obtained value is likely to be the same as the expected value. For example, the chance that two midges will bite cattle at the same time is pretty large. Nevertheless, there is still a lot of uncertainty about this because both midges can also select a sheep. If the population is enlarged to one million midges, it will be more probable that 20% of the midges choose for sheep and 80% will select cattle. Especially, since the calculated midge population exceeds well over the million, it is possible to calculate with pre-established fractions, instead of implementing a stochastic process. One benefit of such a simplified fraction calculation is the reduction in computation time.

In order to determine the new infected midges (dV_i in numbers), it is important to separate the bite proportion for each host species. This is already included in equation 8, where α is a measure of vector preference for host (H) species i, among all ruminant species j. To calculate the actual infected midges, the bite proportion has to be multiplied with the naive biting midges (V_n in numbers) and the host infected fraction (H_{i+inf}/H_i).

$$dV_i = V_n \cdot \left(\frac{\alpha_i \cdot H_i}{\sum_j \alpha_j \cdot H_j} \cdot \frac{H_{i+\inf}}{H_i} \right) \tag{8}$$

More or less the same calculation can be carried out to compute the newly infected ruminants (dH_{i+inf} in numbers). The only difference is that the proportion of the infected midges (V_i in

numbers) biting a naïve host (H_{i+na} in numbers) is calculated instead of the naïve vectors biting an infected host, see equation 9.

$$dH_{i+\inf} = V_i \cdot \left(\frac{\alpha_i \cdot H_i}{\sum_j \alpha_j \cdot H_j} \cdot \frac{H_{i+na}}{H_i} \right) \tag{9}$$

During these calculations, it is assumed that the midges and vectors are always homogeneously spread over the calculation cell and that no animal movement take place within the cell. In practice several cells can represent a single pasture, which makes it for the ruminants sometimes possible to move towards neighbouring cells and back. Additional to this failing spatial behaviour, another assumption needs to be made to simplify the temporal dynamics. It is assumed that the numbers of ruminants in each cell are constant the entire year.

5. RESULTS

5.1. Introduction

This chapter elaborates the operation and outcomes for the three different model elements. Subsequent the spatial uncertainty for the entire model is disguised. Finally, this chapter ends with a description of the model implementation.

5.2. Population dynamics

The midge population dynamics are strongly dependent on temperature; small temperature fluctuations can have serious consequences. One example is visualized in figure 5.1. During the year 2006, LNV (LNV[a], 2007) monitored the midge population from four different habitats within The Netherlands, namely: wetland, peat, flood plains and ecological livestock farms. Apparently, the livestock farm is the most ideal habitat, since most midges were captured there. On these farms, factors like; moist and amount of ruminants are considered to be constant and the only factor that is not constant is the temperature. Therefore, any population dynamics are expected to be the result of temperature fluctuations, which makes it an ideal reference for validating the calculated midge population. However, it is not possible to compare the calculated population directly to the monitoring results. First, the monitoring result visualises a fraction of the present population, while the model calculates the numbers related to entire population. Second, the monitored values are the result of point measurements, while the model calculates a population over an area of 2,500 m^2. In order to compare both results, the monitored results have to be stretched to the same extent as the calculated result. Figure 4.2[b] visualizes the stretched monitoring results together with two different model runs. Each run lasts for two years, where the first year is needed to stabilize the model. Only the calculated values of the second year can be used as results. The first model run uses a slightly deviating temperature compared to the measured temperature on the livestock farms, where the second model run used the same temperature input. One can see that only small temperature deviations already result in an entirely different population dynamic, see figure 5.1[b].

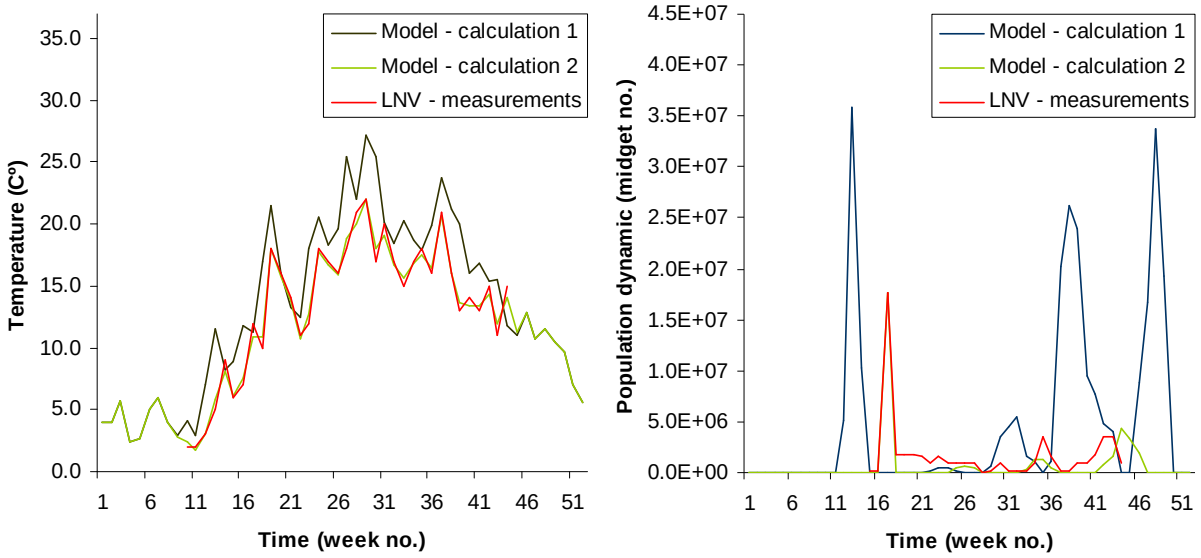

Figure 5.1 (a) Temperature input, (b) calculated midge population fluctuations

Additionally to the temperature, the habitat will determine the mortality in the immature larvae stage. However, very little is known about the influence of the habitat on the mortality of immature larvae. In this research, the population is only limited by the amount of available blood meals. It means that in a cell with a lot of ruminants, midges reproduce to a larger extent compared to cells with less or no ruminants. In practice, the spatial circumstances also influence the extent of the population. It is therefore also recommendable to extent the model as soon as more information comes available about habitat influences.

5.3. Midge dispersion

It is impossible to validate the midge dispersion model, since no information about the flying pattern of midges is available. Nevertheless, the performance of this model element can be evaluated. Figure 5.2 shows three calculated midge dispersions of the same location. In all three figures, the source cell (see black selection) contains 500,000 midges and the colours indicate the amount of midges after migration. Each dispersal visualization uses a different wind speed. Figure 5.2[a] visualizes a wind silence situation, which slowly increases from 1.5 m/s in figure 5.2[b] to 3.0 m/s in figure 5.2[c]. The figures clearly visualize an increasing amount of deep red pixels parallel to a rising wind speed. It looks therefore if the model overestimates the midges' dispersion, with an increasing wind speed, which is also confirmed by the figure statistics presented in table 5.1.

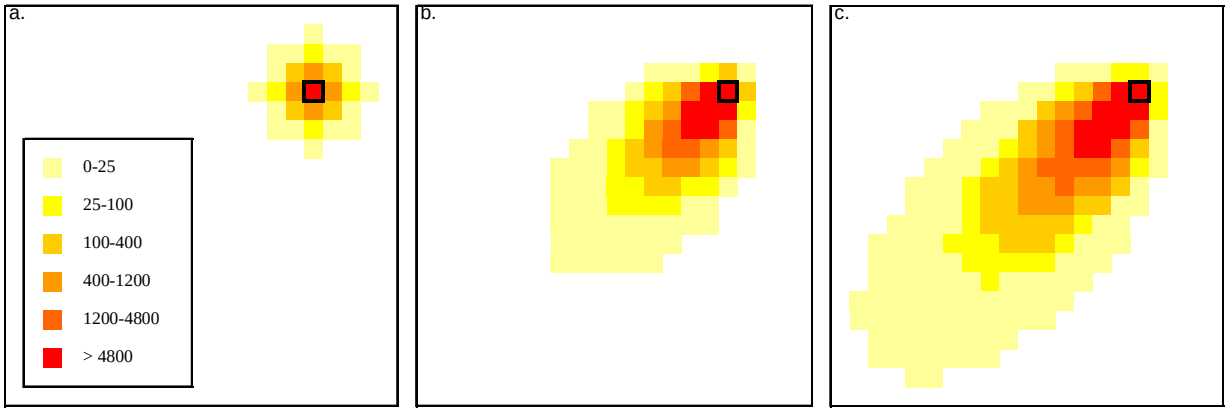

Figure 5.2 Midge dispersion in a wind silence situation (a), with a wind speed of 1.5 m/s (b) and with a wind speed of 3.0 m/s (c)

Table 5.1 compares the statistics of three situations comparable to the situations shown in figure 5.2. Table 5.1[a] and 5.1[b] both redistribute 500,000 midges, whereas table 5.1[c] redistributes 1,000,000 midges. The entire table calculates the redistribution precision for all possible wind speeds. Additionally to the influence of the wind speed on the outcome quality, the wind direction between table 5.1[a] (90°) and 5.1[b] (45°) differs, to see if the wind direction influences the outcome quality. The wind direction in table 5.1[c] is similar to table 5.1[b].
Like already mentioned before, the current dispersal element, has the tendency to overestimate the midges' dispersal. It means that the dispersion element has a sight effect, which increases the total number of present midges. This unwanted side effect is the result of the applied dispersion formula. The current formula is designed for a wind silence situation, but is not representative for the midge dispersal when wind occurs. Additionally to the wind speed, the extent of the midge population in the source cell influences the accuracy of the dispersal.

Table 5.1 500,000 midges in a & b 1,000,000 knutten in c. windrichting 90 in a en 45 in b & c

a.

Wind strength (m/s)	Max. migration distance (m)	Calculated midget population after despersal (%)
0.0	1,500	1.00
0.3	2,500	1.01
0.6	3,500	1.04
0.9	4,500	1.07
1.2	5,500	1.10
1.5	6,000	1.13
1.8	7,000	1.16
2.1	7,500	1.20
2.4	8,500	1.23
2.7	9,000	1.26
3.0	10,000	1.29

b.

Wind strength (m/s)	Max. migration distance (m)	Calculated midget population after despersal (%)
0.0	1,500	1.00
0.3	2,500	1.02
0.6	3,500	1.04
0.9	4,200	1.07
1.2	5,300	1.10
1.5	6,400	1.13
1.8	7,100	1.16
2.1	7,800	1.19
2.4	8,500	1.22
2.7	9,200	1.25
3.0	9,900	1.28

c.

Wind strength (m/s)	Max. migration distance (m)	Calculated midget population after despersal (%)
0.0	1,500	0.99
0.3	2,500	1.00
0.6	3,500	1.02
0.9	4,500	1.04
1.2	5,500	1.07
1.5	6,500	1.10
1.8	7,500	1.13
2.1	8,000	1.15
2.4	9,000	1.18
2.7	9,500	1.21
3.0	10,500	1.24

Table 5.1 shows as well a limitation of the implemented modelling concept. Currently midges are only considered to migrate when they bridge the entire distance to the centre of the arriving pixel. In a raster environment, it means that, related to the wind direction, the maximum migration distance deviates. In the example shown in 5.1[a] and 5.1[b], the maximum migration difference between a wind direction of 90º and 45º, concerns 400 meter with a wind speed of 1.5 m/s.
Finally, it is clearly that the extent of the midge population also influences the maximum migration. Nevertheless, the maximum migrating distance in the example shown in table 5.1c is 10.5 km, which is two kilometres less than the in chapter 4.4 substantiated distance of 12.5 km.

5.4. Virus development

To explain the principal operation of the virus development, one example pixel will be used. This example pixel contains 99 cattle, 100 sheep and on day 200 (mid July) one infected bovine animal is introduced. If the infected bovine animal is introduced to quickly, the temperature is cooler and the lifespan of the midges is not long enough to allow a second blood meal. Without a second blood meal, midges get infected but do not infect new ruminants and the BTV disappears with the recovery of the introduced infected bovine animal.

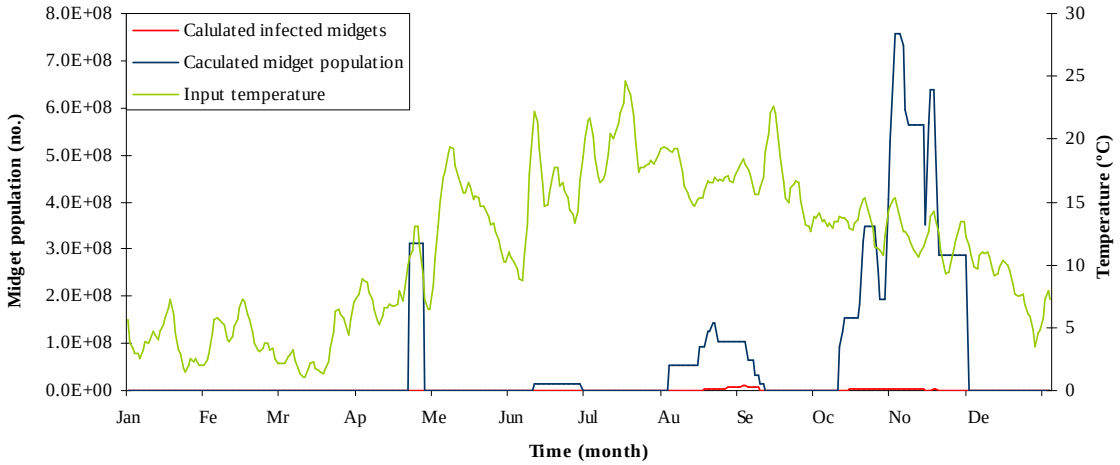

Figure 5.3 The temporal development of the midge population, together with number of infected individuals

In the current population model, see figure 5.3, the first midges are sensible for infection at the beginning of August. This sensibility to the BTV last, with a small interval, until the end of November. After November, the midges do not live long enough to bite twice and no new ruminants will be infected. The infected vector fraction is relatively low and deviates between the 0 and 2 % of the entire midge population.
Even though the fraction of infected midges is really small, the number of infected midges at the beginning of August already exceeds six times the total amount of present ruminants. Because the presence of relatively many infected vectors, the entire ruminant herd, presented in figure 5.4, gets infected within eight days. Even though no information is available about the temporal behaviour of the infected fraction of a ruminant herd, it is likely that the virus development element over estimates the number of infected ruminants. In reality, it hardly occurs that all individuals of a ruminant herd get infected with the BTV. Additional, it is unlikely that the entire ruminant is infected in such a small period of time.
If the trend in recorded BT outbreaks (see figure 5.3) is analysed, it is remarkable to see that it shows a similar trend as the midge population dynamic in figure 5.2. First, there is a small peak around August, which is followed by a larger peak in October and November. Both peaks in the recorded outbreaks fall in the infectiousness period of both sheep and cattle. Additionally, there are some BT outbreaks recorded at the beginning of 2007, which are not visualized in the figure. These recorded outbreaks at the beginning of 2007 can be explained when new ruminants are infected around November. In order to prevent the BTV dispersal, it could be necessary to focus on the moment of infection instead of the outbreak distribution. According to figure 5.3, prevention measures only help when carried out from the beginning of August until the end of November.
Finally, figure 5.4 shows that sheep get sick quicker but are shorter infectious than cattle. This is due to the incubation time and infectiousness of both ruminant species. However, the vector has a strong preference for cattle above sheep, which makes it uncertain if sheep are also the first to get sick when the number of infected vectors is reduced.

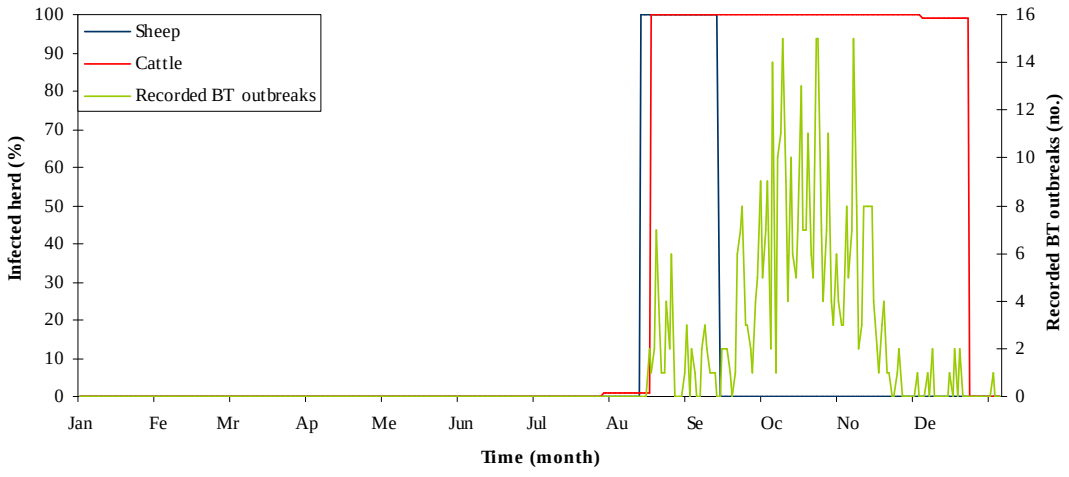

Figure 5.4 Temporal BTV development in a sheep and cattle, in combination with the recorded outbreaks of 2006

5.5. Spatial uncertainty

It is obvious that the dynamics in the midge population and therefore the risk on epidemical BTV outbreaks is strongly dependent on temperature. After seeing the calculated midge population in chapter 4.3, it seems that the population dynamics are only dependent on temperature; however, a lot is still uncertain. For example, the current concept for the determination of the midge population neglects any habitat influences. Generally, the habitat determines the mortality rate among larvae and therefore influences the reproduction capacity. By excluding the habitat influences, it is likely that the midge population in most pixels is overestimated.
Another uncertainty is included during the classification of the calculated BTV dispersal. If only a small percentage of the herd is infected by the virus, the chance is low that the infection is recorded as a BTV outbreak. This is especially the case among cattle, since they do not show such severe signs of illness. When the infected fraction of the ruminant herd is increasing, the chance that the outbreak is recorded increases as well. However, such a threshold that separates the infected farms from the recorded outbreaks is uncertain and severely influences the under- or overestimation of the calculated BTV outbreaks.

5.6. Model implementation

During the model implementation, the largest obstacle to overcome is the amount of data. A detail grid for the whole of The Netherlands with a cell size of 500 by 500 meters already ensures over 400,000 pixels for each input file. Together with 1,100 input files, the model becomes too large for the GIS-package to execute. Instead, the current model setup is programmed in Python. This approach obtains and writes information in a text format. Before the model can be executed, a separated script is necessary to convert the input data into the correct format. Again, a different script is needed in order to visualize the model outcomes in Arc-GIS. However, this research did not succeeded to create a single operational model. Even though the results of the three different model elements look promising, the integration of all elements into one single model did not go as smooth as hoped for. After running the entire model, it seemed that midges did not get infected anymore. Unfortunately, time is limited and no more effort can be put into fine-tuning the current model set up. It makes it therefore impossible to validate the predicted virus dispersal thought out The Netherlands.

6. CONCLUSION AND DISCUSSION

This research investigated the temporal and spatial behaviour of bluetongue, according the characteristic of the bluetongue vector. Based on the preceding chapters the main conclusions are presented in this chapter, in the same order as the research questions. Each research question is answered in a different section, followed by a discussion and recommendations for future research. Within this research the following four research questions are investigated;

- How should the conceptual model be build up?
- Which models are suitable to predict the spatial and temporal behaviour of the vector?
- What is the uncertainty of the model?

6.1. Conceptual model

This research relates the risk of an epidemical BTV outbreak to the presence or absence of the vector, which explains why the conceptual model focuses on the vector instead of the virus. The vectors are tiny midges from which the population is dynamical and very sensitive to temperature fluctuations. To reproduce themselves, female midges need blood for its protein. By biting ruminants, the vector risks infection of the BTV. Only when the vector lives long enough to bite a second time, new ruminants can get infected and the virus can disperse.
In order to disperse spatially, midges have to be able to migrate to other locations. Normally this migration is a random process in a range of 1.5 km. However, wind influences the migration direction and distance.

6.2. Model selection

The model is subdivided into three elements because the spatial and temporal behaviour of the BTV is far to complex to apply one single model type. Element one is a deterministic approach that calculates the dynamics in the vector population. It includes events, like egg production, egg development and expected lifespan. All three events are regressive processes and are related to temperature. Both the egg development and the expected lifespan are applied in binary approach. For example, as soon as the expected lifespan is equal or smaller than the midge's age, they die.
After the production of eggs, the female midges need again a blood meal. However, before they can obtain blood, they have to search for a ruminant. In their search for a ruminant, a fraction of the midge population migrates from their origin to their surroundings. This migration is again a regressive process that determines the migration fraction based on the distance to the arriving cell. In order to make the spatial dispersal dynamical to the wind, the physical distance is corrected.
If sufficient ruminants are present in the arriving cell, the midges have an opportunity to obtain a blood meal in the third and final element of the model. The amount of obtained blood meals will influence the number of produced eggs in the first model element in a following iteration. Depending on the infection status of the ruminant, the midge can obtain the BTV. In a subsequent blood meal there is a chance that the virus is transmitted back to a naïve ruminant. This exchange of the virus is a stochastic process with a variety of possibilities. However, generally the extent of the present midge population is so high that the virus occurs in all the different possibilities and therefore this is also why this research does not work with stochastic models, but just applies the deterministic approach. The advantage of a deterministic approach above a stochastic process is that it needs less computation time.

6.3. Remarkable results

This research showed that it seems possible to calculate the midge population dynamic. The midge season last from the end of April until November and is mainly based on temperature. During the entire season, midges are only capable to transmit the BTV between August and mid November, with a pause because of the vector absence in September. The first recorded outbreaks match the beginning of the period in which the midges are capable to transmit the virus. Due to the infectiousness of cattle, recorded outbreaks can be expected far outside the midge season until the beginning of March. However, to prevent BTV dispersal, prevention measures should focus on the temporal and spatial behaviour of the vector. It means that prevention measures will have the best results when applied from August until November. An additional measure of the Dutch government is the introduction of an observation buffer with a radius of 20 kilometres surrounding each new outbreak. In the current model set up, midges cover, on 39 % of the calculated days, a distance of 10.5 km/day. It means that during the three incubation days of sheep, infected midge have sufficient opportunities to make it outside the observation buffer before the outbreak is even recorded.

6.4. Model uncertainty

The results of the individual model elements look promising, however, this research failed to integrate them into a single operating model. Nevertheless, based on the results of the individual model element, the model uncertainty can still be discussed.

The first modelling element, calculates a population dynamic of the vector, which is almost similar to the monitored population fluctuation. Currently the population is only calculated based on temperature and the present amount of ruminants. In reality there are more factors that play an important role, like vegetation and moist. If no sufficient moist is presence, the mortality among midge larvae will increase. Neglecting these two parameters will result in an overestimation of midges on several locations.

In the second model element, the migrating midge fraction is determined by a fixed formula. This formula is developed for a wind silence situation and assumes that a fixt percentage migrates. When wind occurs, the distribution area increases and the distribution formula have to be modified. The current model uses a fixed formula, which in a windy situation not only result in redistributing midges, but also increases the number of present vectors. In other words, a fixed distribution model ensures an overestimation of present midges on windy moments.

Finally, the last model element evaluates the virus development. The presence of infected ruminants corresponds to the recorded outbreaks in 2006. However, according to the model, all present ruminants get infected within eight days. In practice, it is more likely that the amount of infected ruminants develops more gradually. The reason why the model over-predicts the infected fraction has to do with the number of infected midges, which exceeds six times the total number of present ruminants.

6.5. Discussion

At the moment, little information is available about the distribution of the BTV. To simplify the model, only one vector is kept responsible for the distribution, but not all needed information about the characteristics of this vector are available. To overcome this problem, information from related species is used. Like the vector the included variety of ruminant species is limited. In this research only sheep and cattle are taken into consideration as a host for the BTV, while literature also indicates that midges feed on horse and deer. Even though these animals may not play a role

in the virus transmission, they will influence the size of the midge population and therefore also the risk of BT transmission to more sensitive ruminants, like cattle and sheep.

The model shows relatively a lot of dynamics, because midges are able to migrate and reproduce over time. Nevertheless, the model does not include any stochastic processes. For example, the age of the midges is compared with the expected lifespan. When the midge age exceeds the expected life span all midges die. It would be more realistic when processes like lifespan, produced egg and biting frequency allowed more dynamic by including some randomness. On the other hand, it is unlikely that the end results will deviate a lot.

Other than the model, the input data needs to be discussed as well. Like mentioned before, small temperature deviations have large effects on the dynamic of a midge population. To obtain a continuous temperature grid, temperature data from several climatic weather stations are interpolated. The method that is used, just calculates a trend surface that meets the values in the known locations. In reality, this can be different. Especially the presence of water or high vegetation can provide local temperature deviations from the interpolated trend surface. For example, temperatures in forest are always more constant compared to an open field. To allow more of these kinds of dynamics, it could be interesting to see what the effects of a different interpolation technique are. The same differences occur between the interpolated wind speed and direction compared to reality.
Additional to the interpolation, the extent of the input file can influence the calculated result. For example, the input data of recorded ruminants covers only The Netherlands. The dispersal element on the other hand, calculates the dispersion for a rectangular grid around The Netherlands. It means that the model will include part of Germany and Belgium around the Dutch frontier. Without information about the presence of ruminants in Germany and Belgium, midges are limited for their reproduction to Dutch territory. This will make the obtained results around the Dutch frontier uncertain.
The final limitation comes from the registration of ruminants. All ruminants are registered on an address. Often this address is the position of the farm, while location of the grazing ruminants may deviate from the location of the farm. When the ruminants are distributed more continues among the property instead of the current point-records, it will have a lot of affect on the virus dispersal. Not only it is likely that the virus disperses more easily, but also a smaller fraction of the herd gets infected.

6.6. Recommendations

During this research, sufficient information is found to create a simple model that predicts the temporal and spatial dispersal of the BTV. To increase the prediction accuracy of the model to predict the dispersal, more research need to be done to the midges' dispersal and the influences of a habitat on the midge population. Since the way of modelling really influences the computation time, it would benefit to spend more time in evaluating the scripts structure.

The current dynamics in the model mainly focus on the presence and dispersal of midges. However, it is also necessary to elaborate the side of the ruminants more than it has been done during this research. Ruminants are not randomly distributed in a pasture, nor will their presence be constant all year round. Some period's animals are in stables or individual ruminants will be traded and transported to other farmers. Especially the transportation of living ruminants or animal products can introduce the BTV in naïve area and therefore speed-up the virus dispersal.

A second way of improving the model is by defining the influence of the habitat on the mortality of immature larvae. Currently the extent of a midge population is limited by the available blood meals. The result could be that the midge population in a swampy area is comparable to a dry pasture, as long as the present amount of ruminants is similar. When parameters like moisture contents or vegetation are included to determine the mortality among larvae, a more realistic environment is created.
Additionally the model has to be extended with an incubation time for midges. This is currently excluded in the present model, because of problems with its integration. Without such an incubation element, all midges get immediately sick after obtaining a blood meal from an infected host, which deviates from reality. It is therefore also assumed that the model over estimates the BTV dispersal.
Another element with has to be improved to stop the overestimation of the present midge population is the dispersion formula. The current formula is developed for a wind silence situation, but should be modified when any wind is present.

Finally, there are some recorded outbreaks at the beginning of 2007. Even though these outbreaks are outside a midge season, it is assumable that these farms were already infected at the end of 2006. To validate the model the temporal extent should be enlarge to one and a half year, to see whether it predicts new BT outbreaks in the same period of time.

Once all the different model elements operate properly into one model and the model is extended with the previous mentioned recommendation, it may greatly support policy making. When for example an outbreak is recorded, the model can be used to evaluate the extent of the observation buffer. Additionally, the model can be used to develop a vaccination strategy, so the virus dispersal can be stopped with minimal effort. By thinking of vaccinating a specific ruminant or within a specific range from a recorded outbreak. Finally, it can test, scenario-wize, which period of time is most suitable to apply precaution measures.

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APPENDIX I: Table of contents of accompanied data disk

Data

Data\Population_dynamics

Present amount of midges per day, where naïve and infected are stored separately. Each column stands for the age of the midge or the egg.

Data\Raw_data

Available input data, without pre-processing.

Data\Temperature

Interpolated temperature data, stored in a matrix formal per day.

Data\Virus\dynamics

The amount of naïve and infected ruminants per day. Each line represents one pixel, where the columns present the status of the ruminants. The first column visualizes the total amount of present ruminants, the second column shows the amount of immune ruminants and the third column visualizes the dead ruminants. When a new ruminant is infected, it will be visualized in column four and from here on, each additional column stands for the duration of the infection.

Data\Wind_direction

Interpolated wind direction data, stored in a matrix format per day.

Data\Wind_speed

Interpolated wind speed data, stored in a matrix format per day.

Data\A0gr_ned_mask
Data\A1db_Filter_dis_dir
Data\A1db_temperature1
Data\A1db_temperature2
Data\A1db_wind_direction1
Data\A1db_wind_direction2
Data\A1db_wind_speed1
Data\A1db_wind_speed2
Data\A1gr_cattle
Data\A1gr_ned_mask
Data\A1gr_sheep
Data\A1pt_Heerlen
Data\A1pt_interest_area
Data\A1pt_location_weather_stations
Data\A1pt_temperature
Data\A1pt_wind_direction
Data\A1pt_wind_speed

Report

Report\20080504_Danes_Predicting_The_Dispersal_Of_Zoonotic_Diseases.pdf

Scripts

Scripts\00A1_Climatic_interpolation.py
Scripts\00A2_Create_input_tables.py
Scripts\00B1_Population_dynamics.py
Scripts\00B2_Midge_dispersal.py
Scripts\00B3_Virus_development.py
Scripts\00C1_Intergrated_model.py