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# Modelling local dispersal of bluetongue virus serotype 8 using random walk

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**Abstract**

The knowledge of the place where a disease is first introduced and from where it later spreads is a key element for the understanding of an epizootic. For a contagious disease, the main method is back tracing. For a vector-borne disease such as the Bluetongue virus serotype 8 epizootic that occurred in 2006 in North-Western Europe, the efficiency of tracing is limited because many infected animals are not showing clinical signs.

In the present study, we propose to use a statistical approach, random walk, to model local spread in order to derive the Area of First Infection (AFI) and spread rate. Local spread is basically described by the random movements of infected insect vectors. Our model localised the AFI centre, origin of the infection, in the Netherlands, South of Maastricht. This location is consistent with the location of the farms where the disease was first notified in the three countries (Netherlands, Belgium, and Germany) and the farm where retrospectively the earliest clinical signs were found. The derived rate of spread of 10–15 km/week is consistent with the rates observed in other Bluetongue epizootics.

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In another article Mintiens (2008), the AFI definition has then been used to investigate possible ways of introduction (upstream tracing) and to study the effect of animal movements from this area (downstream tracing).


*Keywords:* Bluetongue; Local spread; Random walk

## 1. Introduction

The emergence of a disease is defined differently by various authors. An appropriate definition for the purpose of this paper is to consider emergence of a disease as the appearance of a known agent in a new geographic area (Brown, 2004). In this respect, the occurrence of bluetongue disease (BT), a vector-borne infection with an orbivirus in ruminants, in North-Western Europe in 2006 was an emerging disease. In a broader perspective, taking into account the spatial component of this definition, the emergence of a disease can also be considered as an invasive process. BT virus is an agent that invades the insect vector, i.e. *Culicoides* spp., and vertebrate populations, i.e. ruminants. In comparison to the emergence of BT around the Mediterranean basin since 1998 (Mellor and Wittmann, 2002), the emergence of BT in North-Western Europe does not seem to be related to the invasion of a new insect vector (*Culicoides imicola*) carrying the virus. Indeed, only autochthonous *Culicoides* species were trapped in the affected area (see Meiswinkel et al., this issue). Thus, in that case, BT virus is an invading agent in the insect and vertebrate populations.

The abundant literature on biological invasions can help analyse this BT epizootic. Three fields/themes of study can be distinguished: (i) the conditions necessary for the invasion to occur, (ii) progression of the invasion through space and (iii) the properties of the ecosystem after successive invasions (Drake and Mooney, 1989; Hengeveld, 1989).

This paper is addressing the second theme, i.e. the progression of BT epizootic in North-Western Europe in 2006. Two main questions arise: where did the disease start and how did it spread? The first question is of interest because silent spread can occur before a BT epizootic (Gerbier et al., 2008). In contrast to major contagious diseases such as Foot-and-Mouth disease or Classical Swine Fever, it is thus difficult to identify the primary infected area through tracing and/or identifying the earliest clinical signs. The route of introduction of the virus has not been identified yet (see Mintiens, 2008). But, as the strain involved (BTV-8) has previously not been isolated in Europe, it is assumed that the virus was introduced only once and that, at the beginning, the infection was restricted to one single small area, called referred to as Area of First Infection (AFI). Then, after an establishment phase, the infection spread further. Description of the BT serotype 8 epizootic (i.e. several foci occurred at different time in 3 distant places) indicates that there were two scales in the pattern of spread: local and long distance (Fig. 1). This mix of two spread mechanisms is called ''stratified dispersal'' according to Hengeveld (1989).

In the present study, we focus on the local spread in the early stage of the epizootic and to use a statistical approach to derive an estimated location of the AFI and of the rate of spread. Identifying the AFI is important to target the investigations on possible routes of introduction (upstream tracing) and to study the effect of animal movements from this area (downstream tracing). It can be expected that long distance and local spread are not driven by the same factors. The estimation of local dissemination velocity can help to disentangle the farms

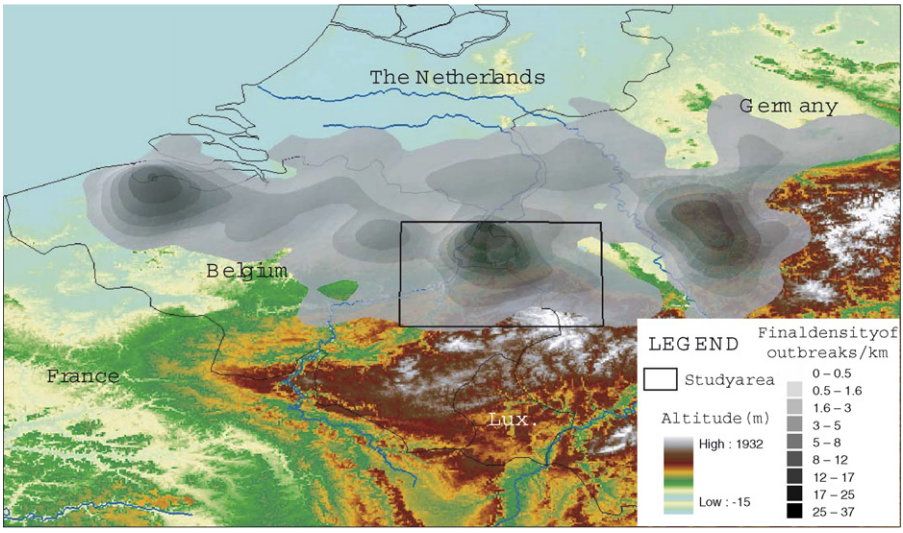


Fig. 1. Three-dimensional representation of the number of Bluetongue virus serotype 8 outbreaks in North-Western Europe in 2006 (altitude in background [source: shuttle radar topography mission, NASA]).

infected following local spread from those infected by long distance spread. To model local spread, instead of focusing on the animal – an epidemiological perspective (Hengeveld, 1989) – we focused on second main factor, i.e. the infected insect vectors, considering that at local scale, the spread of BT virus is mainly driven by the insect vectors movements. We used outbreaks as indicators of infection spread within the insect population. It is assumed that the locations of the clinical outbreaks notified at the end of the epizootic is a random sample of the infected farms and that during a limited period the rate of spread was constant in a given area. Local spread of the infection is thus basically described by the random movements of infected insects: we assume that it follows the same dynamics as the spread of infected vectors if they had been introduced in a single release point. Traditional dispersal studies model the spread rate as the speed of an advancing front (Clark et al., 2001). Alternative methods consist in estimating distance ranges by measuring the square root of the occupied area, the linear distance from the starting point or use neighbourhood measurements (Shigesada and Kawasaki, 1997). The slope of the plots indicates the rate of spread. Advancing fronts for a sequence of time periods are difficult to derive from BT outbreak data for two main reasons. Firstly, infection by BT virus is predominantly unapparent. Therefore, clinical outbreaks are only the visible part of the iceberg. As a result, the limits of the infected zone are difficult to derive. Secondly, the exact date of infection is mostly unknown and when available it is deduced from the appearance of the earliest date of clinical signs. The temporal sequence of the events can thus be heavily biased. Therefore, we propose to avoid building our analysis on a temporal sequence of events and to work on the final spatial distribution of outbreaks at a given point in time.

A random walk approach has been applied to vector-borne diseases in many occasions but mainly in plant epidemiology. In animal epidemiology, applications are limited to tsetse flies (Rogers, 1977; Hargrove, 2000). We propose to use a random walk approach to describe the early stage of the dispersal of a vector-borne animal disease to derive AFI and the local spread rate.

## 2. Material and methods

Locations of outbreaks are assumed to be indicators of the pathways of infected insect vectors. Following Pearson's early question on the random walk problem (Pearson, 1905), the infected vectors are thought to move randomly in space. Assuming a given distance $\varepsilon$ covered by the unit of time $\delta t$, the final spatial distribution of cases should follow a two-dimensional Gaussian distribution centered around the initial place of infection (Okubo and Levin, 2002). Local dispersal is assumed to occur without a preferred direction (isotropy assumption). So, the dispersal pattern is given by:

$$S(r,\theta) = \left(\frac{M}{\pi\sigma_r^2}\right)\exp\left(\frac{-r^2}{\sigma_r^2}\right)$$

where $r$ and $\theta$ are polar coordinates, the origin being the release point, $M$ is a scale factor (not of interest in our framework) and $\sigma_r^2$ is the horizontal variance (Okubo and Levin, 2002).

The procedure for parameter estimation followed three steps:

- Step 1: Identification of a homogeneous episode,
- Step 2: Testing of the normality assumption and fitting of the different models (distribution of longitude and latitude coordinates in the studied area),
- Step 3: Estimation of speed parameters.

### 2.1. Data used for the identification of a homogeneous episode

In order to study the local spread of BTV-8 infection, an area with relatively homogeneous conditions including stable meteorological conditions and homogeneous farm density had to be selected. Visual exploration of the map of infected premises (Fig. 1) shows 3 clusters. The infection started in a cluster around Maastricht located in the centre of the infected area. The 2 other clusters (Cologne and Gent) started later (Fig. 2). It could be anticipated that the bimodal temporal distribution of cases observed in Maastricht cluster was due to some modification of meteorological conditions during the epizootic (see Staubach et al., this issue). Hence, to study local spread, it was decided to focus on the early phase of spread, that is until mid-September 2006 (week 37). To avoid the effect of heterogeneous animal density and other factors such as landscape variability on local spread, the studied area was restricted to a 92 km × 76 km rectangle area including Maastricht cluster. Original geographical coordinates are expressed in meters, Lambert Conformal Conic Projection, WGS 1984 Datum.

### 2.2. Modelling of location data

In the dispersal literature (Okubo and Levin, 2002), it has been demonstrated that spatial distribution of invasive species is often leptokurtic. That means that distribution of the spatial spread has higher amplitudes near its centre and towards its tails than the Gaussian distribution. In this case, the kurtosis (4th moment describing a distribution, a measure of 'peakedness' $\beta_2 = n\sum_{i=1}^{n}(x_i-\bar{x})^4 / \left[\sum_{i=1}^{n}(x_i-\bar{x})^2\right]^2$) of insect spatial distribution is greater than 3. Therefore, to assess the Gaussian distribution assumption, two different models were fitted to the data by maximum likelihood estimation: a Gaussian distribution and a power exponential distribution (Rigby and Stasinopoulos, 2004). By changing the shape parameter $p$, the power

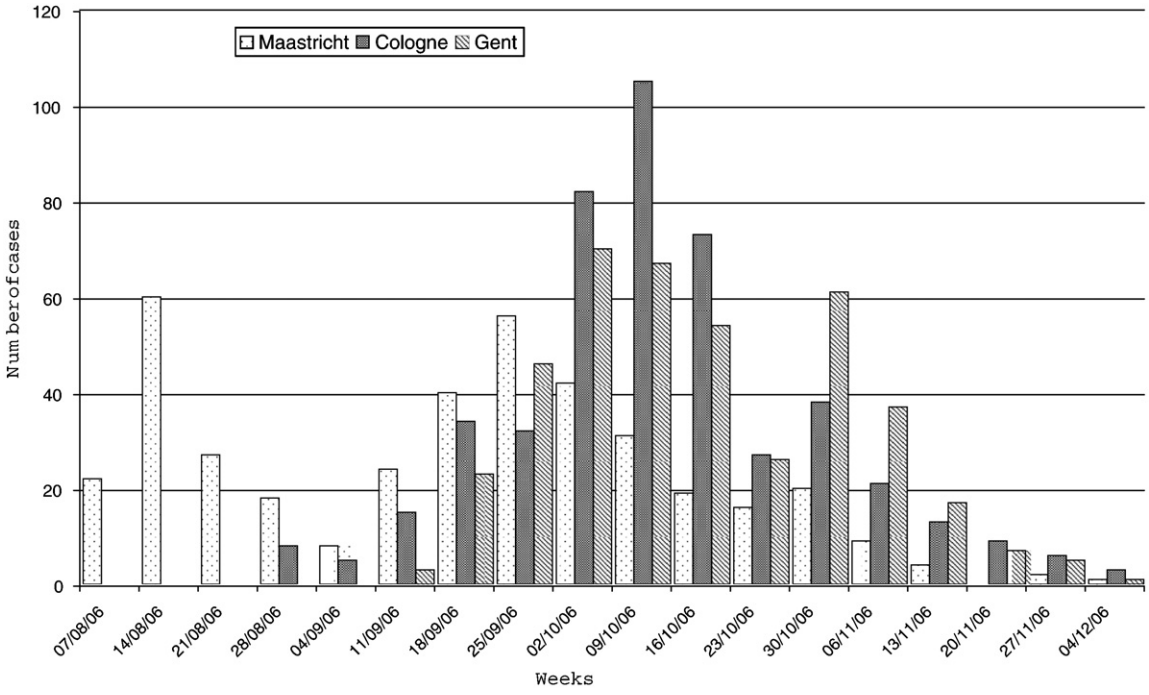


Fig. 2. Temporal pattern of Bluetongue virus serotype 8 outbreaks within the three areas around three major cities.

exponential (PE) distribution (also called normal distribution of order $p$) can describe leptokurtic ($0 < p < 2$ and $\beta_2 > 3$) and platykurtic ($p > 2$ and $\beta_2 < 3$) distributions. For $p = 1$ PE reduces to the Laplace distribution. For $p = 2$, PE has the same form as a Gaussian distribution. Models were compared using log-likelihood function and Akaike information criterion (AIC). To assess departure from normality, Shapiro–Wilks test was used. All statistical analyses were performed using the freeware computer program R, version 2.5 (http://www.r-project.org/), and *gamlss* as an additional R package. PE parameters (mean, standard deviation and shape parameters) were estimated using Box-Cox power exponential distribution described in this package.

### 2.3. Estimation of speed parameters

The parameters of local spread can be derived from the variance–covariance matrix values of the fitted model. In one dimension, the following relation can be found, assuming a unique source of infection at the beginning:

$$\varepsilon = \sqrt{\frac{\sigma^2 \delta t}{t}}$$

where $\varepsilon$ is the step size of the random walk, $\sigma$ is the standard deviation of the Gaussian distribution, $\delta t$ is the number of days elapsed between two consecutive steps, $t$ is the number of days elapsed since the start of the random walk.

One of the key elements of the estimation of $\varepsilon$ is the delay $t$ elapsed since the start of the epizootic. Based on notification data, this delay would be one month (from 17 August, date of first notification in the Netherlands, to 15 September 2006). Nevertheless, it is obvious that the infection remained undetected before the first notification. If the earliest date of first clinical signs observed in a cattle farm in Belgium, 17 July 2007 (Thiry et al., 2006), is correct, $t$ should be at least 60 days. As no accurate estimate was available for $t$, a conservative assumption was made and $t$ was estimated to be 100 days (Fig. 2).

## 3. Results

Among the 221 BT outbreaks notified before 15 September 2006, 175 (79.2%) were enclosed in the study area (Figs. 1 and 3). Results of the parameter estimations for the different distributions are shown in Table 1. For both the longitudinal and latitudinal coordinate (tested to be not correlated, Pearson's product-moment correlation $t = 0.1385$, $p > 0.05$), raw estimates and fitted estimates of the centre of the infected area were similar. No departure from the Gaussian distribution was found for latitudinal data (Shapiro–Wilks test $W = 0.9905$, $p$-value = 0.3008) or longitudinal data ($W = 0.985$, $p$-value = 0.05792). Power exponential models give a better global adjustment (smaller log-likelihood) but when the number of parameters is taken into account (AIC), Gaussian models are preferable. The AFI centre and speed parameters were thus derived from the Gaussian model.

The AFI centre was found to be located in the border area between the Netherlands and Belgium. This location can be compared with the location of the farms where the disease was first notified in the three countries and the Belgian farm where retrospectively the earliest clinical signs were found. They all lie in a 20 km radius area around the AFI estimated centre (Fig. 4).

The variance estimations of the fitted 2D Gaussian distribution were used to estimate $\varepsilon$, the random walk step size. With an assumption of 100 days elapsed since the beginning of the

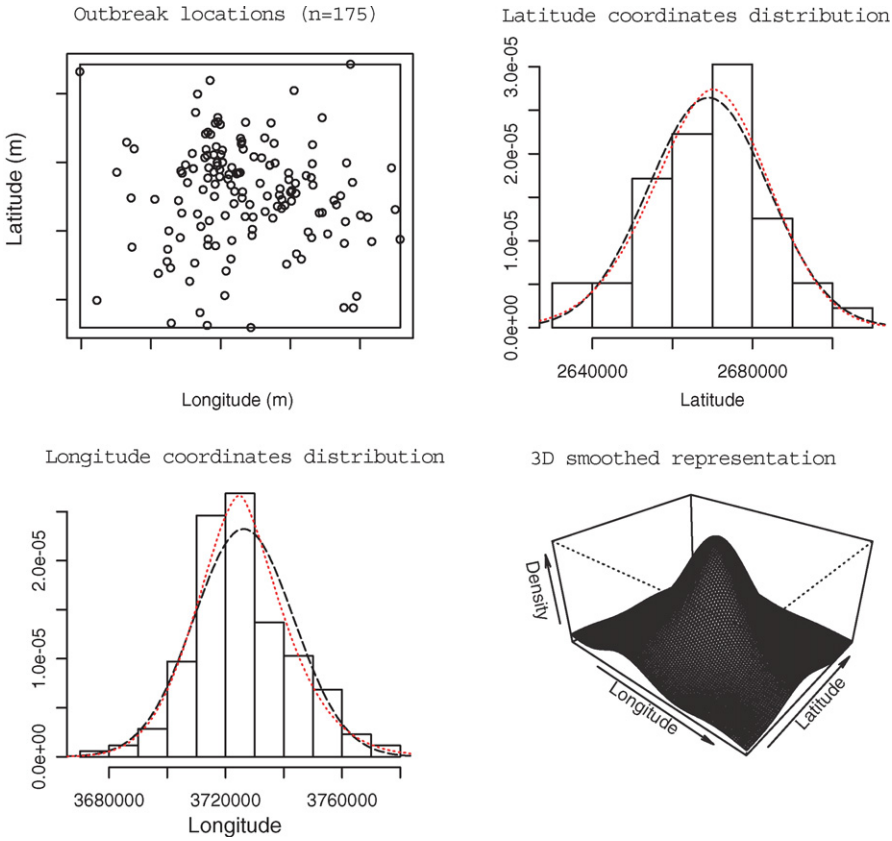


Fig. 3. Distribution of outbreaks in the area studied, histograms of outbreak coordinates with overlaid fitted distributions (normal: black long-dashed line, power exponential: red dotted line) and 3D density plot of outbreaks (kernel smoothing).

epizootic, speeds on the longitudinal and latitudinal axis were estimated as 10.56 and 12.02 km/week, respectively, whereas the estimations were 13.63 and 15.52 km/week, when a period of 60 days since the start of the epizootic was assumed.

Table 1
Estimations of location and dispersion parameters for the different models fitted on geographical coordinates data

| | Mean | Standard deviation | Shape parameter | Log-likelihood | AIC |
|---|---|---|---|---|---|
| Latitude coordinates | | | | | |
| Raw estimate | 2,669,013 | 15,131 | 2.99* | – | – |
| Gaussian distribution | 2,669,013 | 15,088** | 2 | 3864.202 | 3868.202 |
| Exponential power distribution | 2,669,510 | 15,078** | 1.89 | 3863.197 | 3871.197 |
| Longitude coordinates | | | | | |
| Raw estimate | 3,726,278 | 17,219 | 3.22* | – | – |
| Gaussian distribution | 3,726,278 | 17,169** | 2 | 3909.437 | 3913.437 |
| Exponential power distribution | 3,725,172 | 17,218** | 1.60 | 3906.307 | 3914.307 |

* Kurtosis.
** Standard deviation of the fitted distribution.

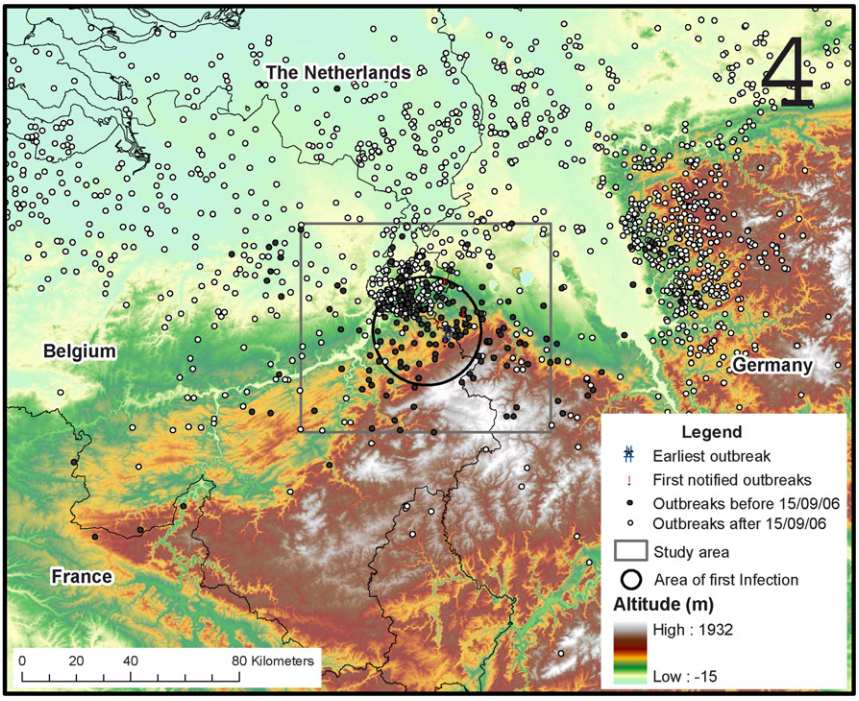


Fig. 4. Location of Area of First Infection, first outbreaks reported by country, farm where the earliest observed clinical signs where found and outbreaks reported before September 15th 2006 during the Bluetongue virus serotype 8 epizootic in North-Western Europe.

## 4. Discussion

As a result of both local and long distance spread, the several clusters visible in Fig. 1 finally coalesced. Such a situation, named coalescent colonisation, makes the analysis more complex in comparison with scattered colonisation (Shigesada et al., 1995). Instead of trying to estimate spread parameters for a complex two-scale phenomenon mixing local and long distance dispersal (see for example (Gilbert et al., 2005)), we focused on the characterisation of local spread. This could allow identifying outbreaks which are ''reasonably not due to local spread''. This classification would probably be imperfect as the definition of local spread *versus* long distance spread is somewhat arbitrary. But, as it is assumed that the factors driving local and long distance spread are different this could help analysing long distance spread.

We chose to restrict our analysis to the first phase of the epizootic (before 15th September 2006) because at that time there was only one significant cluster of infection, centred in an area around Maastricht. Nevertheless, some long distance spread had already occurred as illustrated, for instance, with the five French outbreaks located close to the Belgian border. The selection of outbreaks present in a given rectangular study area rather than the whole set of outbreaks notified during that first phase induced a truncation of the distributions. Not surprisingly, if all the data are analysed, the tails of the distribution become fatter and leptokurtic (data not shown). Our objective was not to demonstrate that long distance spread had occurred – that is obvious and can be tested statistically at the end of the epizootic using a scan statistic for instance – but to characterise the local spread. The fact that the curves were not significantly different from a

Gaussian distribution and that there was no preferred direction for the spread can be considered as a validation of this selection process, showing that only local spread was captured. More work is needed to evaluate the effects of animal density and insect abundance on local spread of the disease for the whole epizootic in 2006.

From an epidemiological point of view, this model is probably wrong because the assumptions made are oversimplified. Indeed, we assumed that BT virus spread can be described as the spread of a theoretical population of infected insects introduced in the same point of release (AFI centre), but this assumption curtails the influence of several factors: insect abundance and longevity varies in time and space, the movement of a single theoretical species was modelled whereas several species of vectors might be involved (Meiswinkel et al., this issue), and an infected herd may act as an amplifier of the infection. Nevertheless, the model can be useful despite these limitations (Okubo and Levin, 2002). As the spread of flying insects can be modelled as a random walk process (Rogers, 1977; Hargrove, 2000), we can reasonably expect that successive *Culicoides* dispersals make the virus spread follow the same diffusion process, though to a larger extent than active flight of a single *Culicoides* individual. The main advantage of this model is the chance (i) to derive the AFI in order to study movements into and from this area, (ii) to obtain an estimate of local spread speed rate that can be compared to the control measures that were implemented. Another advantage is that the model represents a simple diffusion model which can be tested and is easily quantifiable (Andow et al., 1990).

The rate of spread of 10–15 km/week observed during the early stage of this epizootic is consistent with the rates observed in Italy in 2000 during the first BT serotype 2 epizootic before the use of vaccination: 30 km per week in Sardinia, 8–9 km per week along the Ionian coast (Calistri et al., 2004). The uncertainty of speed estimations reflects the uncertainty regarding the date of introduction of the virus into the area. Nevertheless, the uncertainty is reduced by using a formula which involves the square root of the delay elapsed from the beginning to the end of the period.

It is noteworthy to compare the results on the spread of the disease with the knowledge about *Culicoides* dispersal. In general, the active dispersal of *Culicoides* by flight is usually short and most species disperse only a few hundred meters from their breeding sites or at most 2–3 km/day (Mellor et al., 2000). In the USA, *Culicoides variipennis*, the main BT vector in Northern America, can disperse some 2.8 km from the point of release (Lillie et al., 1981). *Culicoides mississippiensis*, a pest nuisant abundant in salt marshes in Florida, travels a maximum of 3.2 km in 24 h unaided by the wind (Lillie et al., 1985).

To a greater extent than with other insect vectors, the long-range dispersal of *Culicoides* is associated with transport on prevailing winds. Numerous studies have related the spread of *Culicoides*-borne viral diseases to wind movements (Sellers et al., 1978; Sellers et al., 1979; Sellers and Pedgley, 1985; Murray, 1987; Sellers and Maarouf, 1989, 1991; Braverman and Chechik, 1996; Bishop et al., 2000; Alba et al., 2004; Gerbier et al., 2008). The role of wind during the BTV-8 epizootic in North-Western Europe in 2006 is discussed elsewhere (see Staubach et al., this issue). Nevertheless, it seems that the local spread of BTV-8 can be explained mainly by active flight of *Culicoides*. The symmetric shape of the final distribution of the outbreaks in the Maastricht and Gent clusters is another argument for this explanation.

In Belgium, Luxemburg and the Netherlands, several factors may have facilitated the spread of the disease. Firstly, the incriminated vector(s) is(are) autochthonous and established since a long time in North-Western Europe (Meiswinkel et al., this issue). Moreover, the host density is high. So, the vector and host populations are rather homogeneous and were probably not limiting factors for the spread. Secondly, temperatures observed during Summer 2006 may have had a

positive impact on insect abundance, their activity, and virogenesis within the midges (Linhares and Anderson, 1990). The more dense the vector population is, the larger the dispersal (Bishop et al., 2000). Thirdly, through woodland in Scotland, *Culicoides impunctatus* (the ''Scottish midge'') travels over an average distance of 75 m whereas in open area the flight range is extended to 700 m and more (Kettle, 1951). In addition, speed of dispersal of *C. brevitarsis* is influenced by altitude (Bishop et al., 2000). As the landscape in the AFI is formed by open flat areas with few forests, movements of BTV-8 vectors were probably easier. Nevertheless, these relations between dispersal and vector/host density, temperature, altitude and landscape should be validated in North-Western Europe once the vectors have been precisely identified.

## 5. Conclusion

Many factors drive the spread of a vector-borne disease such as Bluetongue: some are human-mediated (movement of animals for instance), some are abiotic (suitability of the environment for transmission of the disease), others are related to the vector insect (abundance, trophic preference, competence etc.) or to the host (animal density, level of immunity). With a simple model based on the average movement of an infected insect, it was possible to mimic the early stages of the BTV-8 epizootic. This method can also be applied to other BT epizootics or animal vector-borne diseases provided that a homogeneous cluster has been identified. During the BT8 epizootic, data on the animal populations were not available at the municipality level. Nevertheless, these data should be included, if available, to use a statistical approach in order to identify the clusters. When geographic barriers such as mountains or forests exist that could influence the spread or when environmental factors are heterogeneous (heterogeneous animal density for instance), the estimation procedure should be adapted.

Many techniques are available for the spatial analysis of diseases (Thomas, 1990; Elliott et al., 2001; Elliott and Wartenberg, 2004) but random walk approaches or, by extension, diffusion approaches are rarely mentioned (Gesler, 1986). By contrast, these approaches have been very frequently used in the field of ecology to analyse invasion processes (Shigesada and Kawasaki, 1997; Okubo and Levin, 2002). These techniques which are based on diffusion processes, remain too seldom used in the field of veterinary epidemiology. In particular, the order of magnitude of the local spread of BT obtained in a limited homogeneous area could be used in a more complex framework where factors that modify the spread (such as roughness) could be incorporated. As for Dengue Fever (Tran and Raffy, 2006), remotely sensed and meteorological data could then be used to model BT dynamics in a more realistic way.

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## Conflict of Interest

None of the authors (G. Gerbier, T. Baldet, A. Tran, G. Hendrickx, H. Guis, K. Mintiens, A.R.W. Elbers, C. Staubach) has a financial or personal relationship with other people or organisations that could inappropriately influence or bias the paper entitled ''Modelling local dispersal of bluetongue virus serotype 8 using random walk''.

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