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# Assessing the role of long-distance translocation and spatial heterogeneity in the raccoon rabies epidemic in Connecticut

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## Abstract

Spatial heterogeneity and long-distance translocation (LDT) play important roles in the spatio-temporal dynamics and management of emerging infectious diseases and invasive species. We assessed the influence of LDT events on the invasive spread of raccoon rabies through Connecticut. We identified several putative LDT events, and developed a network-model to evaluate whether they became new foci for epidemic spread. LDT was fairly common, but many of the LDTs were isolated events that did not spread. Two putative LDT events did appear to become nascent foci that affected the epidemic in surrounding townships.

In evaluating the role of LDT, we simultaneously revisited the problem of spatial heterogeneity. The spread of raccoon rabies is associated with forest cover—rabies moves up to three-times slower through the most heavily forested townships compared with those with less forestation. Forestation also modified the effect of rivers. In the best overall model, rabies did not cross the river separating townships that were heavily forested, and the spread slowed substantially between townships that were lightly forested. Our results suggest that spatial heterogeneity can be used to enhance the effects of rabies control by focusing vaccine bait distribution along rivers in lightly forested areas. LDT events are a concern, but this analysis suggests that at a local scale they can be isolated and managed. Published by Elsevier B.V.

*Keywords:* Rabies; Spatial spread; Spatial heterogeneity, Long-distance dispersal

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## 1. Introduction

Infectious disease epidemics, like human history or evolutionary history, are historically contingent processes—early events have a strong influence on later ones. Invasive epidemics are particularly sensitive to rare events that introduce infectious agents into naive populations such as through host species shifts or long-distance translocation (LDT) of infected hosts (Mollison, 1986). The introduction of West Nile virus into New York City (Lancioti et al., 1999) and Severe Acute Respiratory Syndrome (SARS) coronavirus throughout Asia and into several additional countries including Canada (Berger et al., 2004), provide unambiguous demonstrations of the significance of LDTs in transforming regional health concerns into pandemic threats. Spatial heterogeneity also plays an important role in the spatio-temporal dynamics and management of emerging infectious diseases and invasive species. Local spread across space is typically characterized as a travelling wave, with a well-defined front generated by local transmission or dispersal. Heterogeneity in the distribution of hosts or habitats warps the shape of the invasive front (Murray et al., 1986). An invasive front may fail to propagate through areas with low host population density. In other cases, the invasive front may be blocked by landscape features, such as rivers or mountain ranges (Smith et al., 2002; Russell et al., 2004; Lucey et al., 2002), in which case the front may stall or find another route across a landscape. An invasion can leap across bad habitat or barriers by rare, but important, LDT events that may occur through atypical dispersal modes. These LDT events minimize the delay in spread caused by spatial heterogeneity.

The combined effects of spatial heterogeneity and LDT generate a complicated history of geographical spread. Here, we analyze the geographical spread of the initial wave of a raccoon rabies epidemic in Connecticut. This epidemic was part of a larger, ongoing epidemic that began in 1977 near the border between Virginia and West Virginia (Nettles, 1979). Earlier analysis suggested that LDT events were relatively common in Connecticut (Smith et al., 2002).

The epidemic spread of rabies has been a useful system for understanding the spatio-temporal dynamics of infectious agents. Early approaches to understanding the red fox rabies epidemic in post-WWII Europe focused on using reaction-diffusion systems of coupled partial differential equations, including terms for heterogeneity in the density of foxes (Murray et al., 1986; Mollison, 1991; Shigesada and Kawasaki, 1997). On homogeneous landscapes, these models predict that an epidemic front will move at a linear rate away from the point of origin in concentric circles. Stochastic models generate different predictions about the rate of spread and the coherent shape of the front (Mollison, 1991). In stochastic models, rare LDT events can generate nascent foci well in advance of an epidemic front—stochastic simulation models produce such patterns when the frequency of LDT is high enough, or in other words, if the dispersal kernel has a suitably fat tail (Lewis and Pacala, 2000). Given a stochastic model, it is possible to predict the frequency of LDT events, the distribution of their location relative to a front, and their effect on the shape of the front. On the other hand, the location of nascent foci is unpredictable. Moreover, many LDT events may establish nascent foci, followed by stochastic fade-out. Such events may provide information about the frequency of LDT, but failed foci are unimportant, historically, because they did not initiate sustained spread.

Stochastic modeling approaches have been difficult to apply to raccoon rabies surveillance data for several reasons. Usually, no comprehensive map of raccoon density exists before the epidemic. By way of contrast, maps for the density of foxes in the UK were used to make projections and establish management plans for a potential epidemic, but fox rabies has never been introduced there, so the model remains un-validated (Murray et al., 1986). The most detailed data available are from Connecticut and New York for which the location of raccoons was recorded by township. Of course, townships are defined politically and rarely describe relevant ecological boundaries. Thus, even if fine-scale spatial heterogeneity were important, the data contain no information about it. Nevertheless, townships may be considered as distinct habitat patches, and mathematical models for the spread of rabies along the networks defined by the adjacency of townships have been developed (Smith et al., 2002; Russell et al., 2004). Thus, mathematical models for the spread of rabies could be applied to these patch-based models as if they were a meta-population (Hanski, 1999). Using these network models in an exploratory data analysis, we have asked different questions. Given the observed spatio-temporal record of rabies cases, which putative LDT events influenced the time-course of the epidemic by initiating new foci of infection beyond the advancing front? Of equal interest, which putative LDTs were the result of “failed” introductions that did not initiate new epidemic foci or were “false” LDTs, possibly resulting from mis-classification due to false positive diagnoses of rabies at laboratories conducting testing? False positives in rabies testing, or test results that cannot be confirmed by multiple laboratories testing the same sample, are not uncommon (McQuiston et al., 2001; CDC, 2002). Finally, real epidemics may have continued generating cases that were undetected by surveillance.

In this paper, we identify several putative LDT events, and use the network model to assess the importance of these events on the time course of the Connecticut epidemic. The purpose of this modeling exercise was to find associations between heterogeneous landscape features in Connecticut and the rate of rabies spread, while simultaneously identifying and correcting for the distortions caused by LDT events.

## 2. Methods

### 2.1. Data

Raccoon-variant rabies virus was first detected in the township of Ridgefield, Connecticut in April 1991. In the subsequent 48 months, at least one case of raccoon rabies was detected in 168 of Connecticut’s 169 townships; no case was ever recorded from Waterford township. More detailed descriptions of the data are provided elsewhere (Wilson et al., 1997; Lucey et al., 2002). When the first case was detected in a township, that township was considered “infected.” For most townships, several cases were reported in the months following the first case. We restricted our analysis to the cases observed in the 36 months following the first reported case, after which the natural rate of wave front spread masked our ability to discern LDTs. For modeling purposes, we let  $O_i$  denote the number of months elapsed from the first observed case in Ridgefield and the first observed case in the  $i$ th township. To compute the distances between townships, we used the

township's centroid, projected onto the plane. Let  $d_{i,j}$  denote the distance between the centroids of townships  $i$  and  $j$ . We also defined the adjacency matrix among the 169 townships; two townships were said to be adjacent if they shared a common border at any point. The adjacency matrix was generated by visual inspection of a map of Connecticut. By inspection, we also identified townships that were separated from one another by a river or other large body of water.

The adjacency relationship defines a network,  $\mathbf{N}$  which was used to model the spread. A useful concept from network theory is the number of "degrees of separation," an integer number that describes the minimum number of edges that must be crossed to reach one township from another. If two townships are adjacent, they are said to be separated by 1 degree of separation (DoS = 1).

## 2.2. Linear regression

A simple linear regression was developed to have a familiar example to compare with the less familiar network distance analysis that follows. We regressed  $O_i$  on the distance to Ridgefield ( $d_{i,R}$ ). The intercept was forced through zero because we were interested in estimating the rate of spread with respect to the time and place of the first detected case. The regression equation was:

$$O_i = \beta d_{i,R} + \varepsilon_i$$

where the  $\varepsilon_i$  are the residual errors. Since the observations were recorded month by month, and distance was measured in kilometers,  $1/\beta$  represents the rate of spread, in kilometers per month.

## 2.3. Network distance model

We modeled the time to appearance of rabies in each township assuming that rabies spreads among adjacent townships. Distance on heterogeneous landscapes is a difficult concept. For example, the shortest path between two points on opposite sides of a lake is different for a bird that flies across it, and a human who walks around it. We circumvented this problem by transforming Connecticut's continuous landscape into an adjacency network,  $\mathbf{N}$  (for an introduction to networks, see Watts, 1999) (Fig. 1a). Each township was represented by a vertex in a weighted graph. Each pair of adjacent townships was connected by a pair of directed edges. The weight assigned to each edge was denoted  $\tau_{i,j}$ , where:

- (1)  $\tau_{i,j} = d_{i,j}/\lambda_{i,j}$  is interpreted as the expected time, in months, to reach township  $j$  directly from township  $i$ ;
- (2)  $d_{i,j}$  is the distance, in kilometers, between the two townships' centroids;
- (3)  $\lambda_{i,j}$  is interpreted as the rate of spread from  $i$  to  $j$ , in kilometers per month.

An algorithm computes the times to appearance,  $T_i$ , as a function of the adjacency network,  $\mathbf{N}$ , the set of pairwise distances,  $d_{i,j}$ , and a set of rates  $\lambda_{i,j}$ :

$$O_i = T_i(\lambda_{i,j}) + \varepsilon_i$$

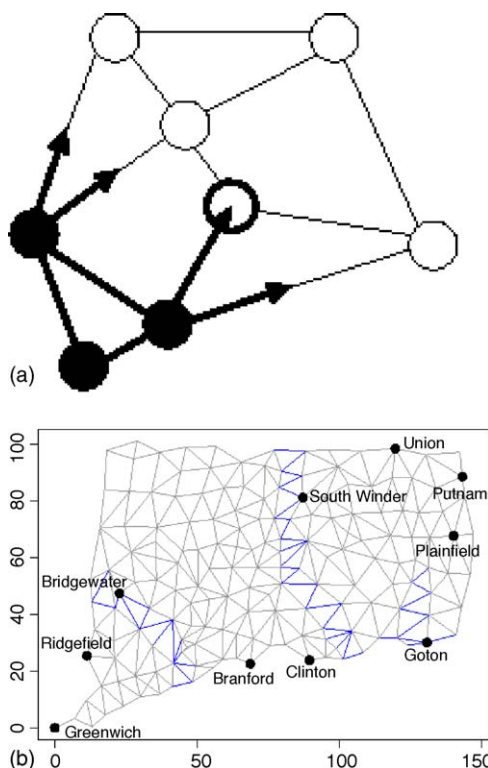


Fig. 1. (a) A network distance model of rabies spread in Connecticut. The townships are the vertices of a graph (circles) and rabies may spread, at different rates, along the edges that connect the vertices. Infected townships (filled) and uninfected township (thick, open). (b) A spatial display of the network and putative LDT events. The edges for townships separated by a river are colored blue.

The best fit was the least sum of squared errors,  $LSS = \sum_i e_i^2$ . The parameters that minimized the LSS were found using the Metropolis algorithm, and software written by the author (DLS, available upon request).

The algorithm to compute the times to appearance proceeded by sequentially identifying the next township to become infected (Fig. 1a). This was done by finding the index  $j$  of an uninfected township that minimized  $T_j = T_k + \tau_{k,j}$ , where  $k$  ranged over all the infected townships, and  $j$  ranged over the uninfected townships adjacent to each infected township  $k$ . The township was declared “infected” at the time to infection,  $T_j$ . The algorithm is equivalent to driving cars away from each infected township,  $k$ , leaving each township at the moment it became infected,  $T_k$ , driving along the edge at a constant speed,  $\lambda_{k,j}$ , and recording which uninfected township,  $j$ , was first reached by one of these cars. The algorithm was repeated until all the townships became infected.

Thus, the rates of spread,  $\lambda_{i,j}$ , could take any value, independent of the rates in the surrounding townships. In contrast, the times to arrival,  $T_k$ , depend on the rates,  $\lambda_{i,j}$ , and the network structure, and (as a result) they are highly spatially-correlated.

The “boundary conditions” describe the set of townships that were “forced” rather than fitted; forced townships initialize the process and become infected at the time when the first case was actually observed, regardless of the algorithm. Initially, only Ridgefield was used to “force” the epidemic. Later, other townships that were identified as putative long distance translocation events were used to “force” the epidemic. To compare models with different boundary conditions, we computed the LSS omitting any township in the boundary conditions of either model.

Each fitted model consisted of a set of simple rules for generating the rates of spread,  $\lambda_{i,j}$ , as a function of heterogeneous environmental variables. We explored four models.

- (1) Homogeneous: the homogeneous model fitted a constant rate of spread;  $\lambda_{i,j} = \alpha$ .
- (2) Rivers: this model had two parameters. If two townships were separated by a river, then  $\lambda_{i,j} = \beta$ ; otherwise  $\lambda_{i,j} = \alpha$ .
- (3) Forest: in this model, the rate of spread was linearly proportional to the percent forest in the  $j$ th township,  $F_j$ . Since it is absurd for a rate to be negative, the rule returned a minimum rate of 0,  $\lambda_{i,j} = \max(\alpha(1 + \rho F_j), 0)$ . If the rate was zero, rabies would never move directly from one township to another, although it might reach one township following an alternative path through other townships.
- (4) Rivers and forest: in the maximally complicated model, we fitted different linear functions of percent forest cover, depending on whether the townships were separated by a river or not:  $\lambda_{i,j} = \max(\beta(1 + \gamma F_j), 0)$  if separated by a river; otherwise  $\lambda_{i,j} = \max(\alpha(1 + \rho F_j), 0)$ .

To further clarify the differences between the linear regression model and the network distance model, consider that the regression model corresponds to a homogeneous network model based on a network connecting each township directly to Ridgefield and a constant rate of spread along this network. In contrast, the homogeneous network model also has a constant rate of spread, but now over the adjacency network, rather than directly from Ridgefield.

#### 2.4. Putative long-distance translocation events

We identified two sets of putative LDT events. The first set identified townships in which rabies had not yet been documented among any adjacent townships (DoS = 1) and the second set included only those when the infected township was farther removed ( $0 < \text{DoS} \leq 2$ ) from the nearest infected neighbor. We focused analysis on this second set (locations shown in Fig. 1b).

We developed several tests for identifying “false foci,” defined as those cases that did not seem to be associated with other rabies cases in the area. These apparently false foci included real LDTs that did not initiate new foci but were followed by stochastic fade-out and those due to possible laboratory misclassification.

Several simple metrics were used to evaluate and classify the type of LDT. The first compared the intra-township lag between the date of the putative LDT and the date of the second report of a rabid raccoon. Second, the intra-township lag between the putative LDT was compared to the median date of the summed total of rabid raccoons reported from the

county over the 36-month study interval. Third, the inter-township lag was the time between the date of the putative LDT in a township and the date of the first rabid raccoon detected in adjacent townships where DoS = 1.

The importance of each putative LDT event was then evaluated using the network distance model by including the affected township as a boundary condition and forcing epidemic spread from each potential new focus. Using the network distance model, the LDT event was judged to be a “real” focus if it improved the model fit, compared to the same model omitting the township from the boundary.

We classified the putative LDT events into focus types. A single isolated case was considered a false positive or a failed introduction. Two isolated cases were considered a failed introduction. The epidemic was considered local if no cases were detected in subsequent months in the surrounding townships. For putative foci, the first case was followed immediately by other cases within the township and in surrounding townships.

We also report the total number of cases recorded from a township. The more cases that were reported, the more information that was available about the rabies epidemic within that township. Hence, we can have more confidence about the conclusions from those townships that reported more cases.

### 3. Results

By linear regression, the rate of wave front spread was 3.3 km/month. The adjusted  $R^2$  was 0.94 ( $p < 0.001$ ). The residuals from the linear regression (Fig. 2a) and the spatial distribution of the residuals (Fig. 2b) are shown. The residuals are clearly correlated spatially, and indicate the clumping of like-residuals consistent with the expected effect of LDTs or local heterogeneities influencing wave front spread.

#### 3.1. Model fitting

The best-fit homogeneous network distance model was nearly identical to the simple linear regression; the fitted rate of spread was 3.5 km/month. However, network distances are slightly longer and slightly distorted relative to the actual geographic distances. The residual variance was slightly lower but the improvement should be regarded as an artifact of the distortions, an unfortunate but unavoidable consequence of using a network distance model.

Table 1 reports the best-fit parameters for each of the four network distance models and the associated measure of fit, LSS. These fits used the first reported case for most townships, but the second reported case from Putnam and Bridgewater because the first

Table 1  
The parameter values for the LSS best fit, and the LSS

Model	$\sqrt{\text{LSS}}$	$\alpha$	$\beta$
Homogeneous	80.2	3.5	–
Rivers	70.1	4.5	0.92
Forest	78.6	5.4–4.5F	–
Rivers + forest	66.3	8.2–8.4F	0.97–1.4F



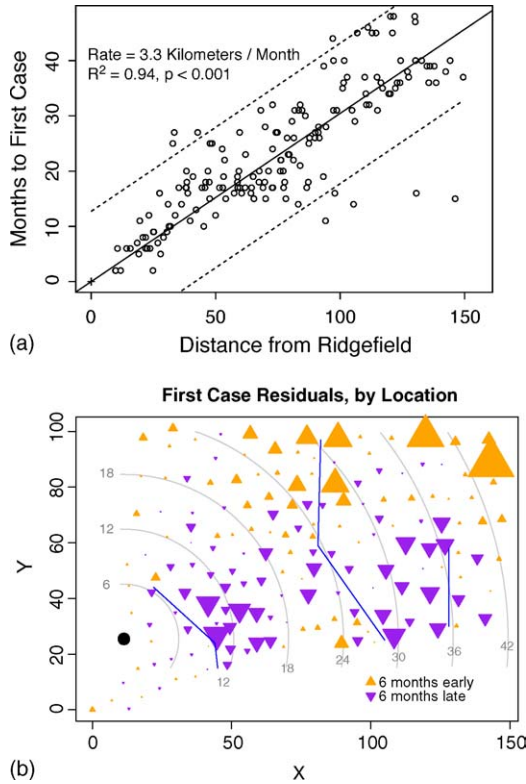


Fig. 2. (a) The residual errors (triangles) from the linear regression analysis. (b) The spatial distribution of the residuals, and the expected location of the front (gray). Regions where the epidemic arrived earlier (orange, upward pointing triangles) or later (purple, downward pointing triangles) than predicted by the model are shown.

case was judged to be a failed, or false, foci by every criterion (see below). The Rivers and Forest model provided the best fit. The improvement in the minimized LSS criterion over the simpler models was large, even considering the addition of one or two additional model parameters. In addition, the subsequent relative improvement in LSS provided insight into the respective roles played by rivers and forest cover. Specifically, the model incorporating rivers (one additional parameter) resulted in a 24% improvement to LSS, and subsequently adding forest cover resulted in an additional 20% improvement (twice as much as the relative improvement of adding forest cover alone).

The best overall model combined rivers, forest cover, and two additional foci in Branford and Plainfield, forced as boundary conditions (see below). Unobstructed spread occurred at the rate 7.1 km/month. Over the range of percent forest cover observed for Connecticut townships, the predicted rate of spread between two townships that were not separated by rivers varied by a factor of 3. Spread between townships obstructed by a river occurred at the rate 6.3 km/month. The models predicted that rabies would not cross a river in townships with more than 12% forestation. In the lightly forested townships (around 5%

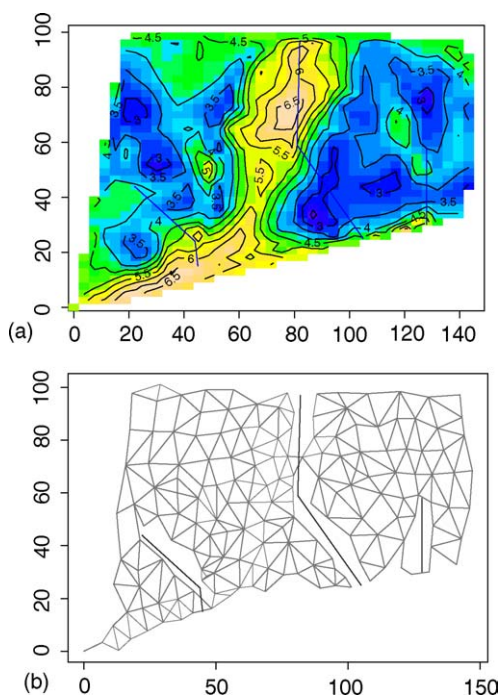


Fig. 3. (a) A smoothed, color contour map illustrating where the rate of rabies spread, in Connecticut, was fastest (yellow) and slowest (blue). (b) The adjacency matrix from the best fitting model. The thickness of the edge is proportional to the rate of spread.

forest cover), rivers slowed transmission by a factor of 2. Thus, the model identified only five places where rabies could cross the rivers. The fastest rate of river crossing was 3.6 km/month in two townships with around 5% forestation.

To interpret and visualize these results, we plotted the rate of spread from the best overall model (Fig. 3a). First, we generated the predicted rate of unobstructed spread for each township and plotted a smoothed surface (using the  $X$ - $Y$  coordinates of the centroids and the “akima package” from R (R Development Core Team, 2004)). Second, we plotted the adjacency matrix, varying the thickness of the edge so that it was proportional to the rate of spread (Fig. 3b). Notably, those edges with forest cover that exceeded 12% were not plotted because the model predicted rabies would never cross there.

The best overall model predicted a different epidemic than the homogeneous model (not shown, but compare the concentric circles in Fig. 2b to the contours in Fig. 4a. Notably, the Rivers and Forest model predicted the epidemic would arrive later in the south of the state, on the east side of the rivers, but earlier in the north (Fig. 4c). The difference between the best overall model and the homogeneous model is similar to the map of residual errors from the homogeneous model (not shown, but very similar to (Fig. 2b), indicating an improvement in local model fit over the homogeneous and linear regression models. Also note that the residual errors from the best-overall model (Fig. 4d) are not as strongly clustered as the residual errors from the linear regression (compare Fig. 2b and Fig. 4d).

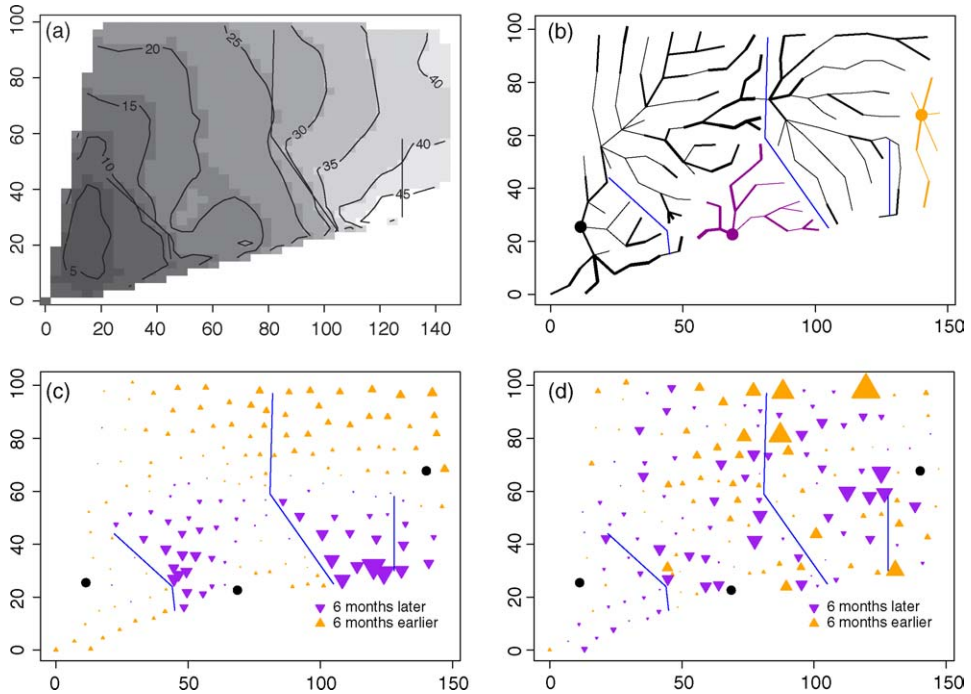


Fig. 4. (a) A smoothed map of the time to appearance of rabies generated by the best overall network model. (b) The reconstructed path of rabies spread. The orange cluster was associated with the LDT event in Branford, and the purple cluster was associated with the LDT event in Plainfield. (c) The difference in the predictions made by the homogeneous model and the Rivers and Forest model forced by Ridgefield, Branford and Plainfield (filled black circles). Note that rivers slow the appearance in the south behind the rivers (the purple differences) and speed it up in the north (the orange differences), similar to the map of residual errors from the linear regression Fig. 2d. (d) A spatial plot of the residual errors from the best overall model. Purple, downward pointing triangles are townships where rabies was observed later than predicted by the model, and orange upward pointing triangles are townships where rabies was detected earlier than predicted.

Taken together, the regression model suggests a broad linear rate of spread as the wave of infection swept the state. The network models capture the same general pattern with local improvements in fit capturing spatial heterogeneities in spread.

### 3.2. Putative long-distance translocation events

The putative LDT events identified using a neighborhood defined by a DoS = 1 included 25 townships, in addition to Ridgefield. Using a larger neighborhood (DoS = 1 or 2), 7 putative LDT events were identified: Bridgewater, Greenwich, South Windsor, Clinton, Putnam, Branford, and Groton. When analyzing these putative events, we omitted Greenwich because it is near New York City and it likely was associated with the same epidemic focus that sparked the epidemic in Ridgefield. When the remaining six histories were examined in more detail (discussed below), the first cases in Putnam and Bridgewater were classified as false/failed LDTs due to the long lag between the first case and

Table 2

Statistics summarizing the number of cases following the first reported case, including the number of months elapsed between the first case and the second case within the township (2nd), the median case within the township (Med), and the first case in a neighbor (N)

Township	1st case	Lag to 2nd	Rank	Lag to Med	Rank	Lag to N	Rank	Total cases
Bridgewater	2	10	3rd	11.5	4th	6	5th	6
South Windsor	11	1	–	6	–	8	4th	22
Clinton	15	3	–	4	–	3	–	4
Putnam	15	24	1st	29	1st	21	1st	11
Brantford	16	0	–	5.5	–	1	–	28
Gordon	34	1	–	5	–	11	3rd	36
Union*	16	1	–	12	2nd	18	2nd	20
Plainfield*	36	3	–	4	–	1	–	11

The rank of the statistic among all townships is reported if it was in the top 5. The focus type summarizes these measures (see text). Two additional putative LDT events (\*) were identified and evaluated after concluding that Putnam was a false focus.

subsequent cases (Table 2). After removing these isolated cases, Union and Plainfield were identified as putative LDT events. The number of reported rabid raccoons from each of the townships classified as putative LDTs (locations shown in (Fig. 1b) and those townships that were immediately adjacent (Fig. 5) clearly demonstrate where neighborhoods are influenced by early dates of detection and rabid raccoons in individual townships; these findings are discussed in detail below. The summary statistics are reported in Table 2, and the graphs in Fig. 5.

### 3.2.1. Bridgewater

The first of six cases occurred 2 months after Ridgefield followed by a 10 month lag. By that time, several of Bridgewater's neighbors had become infected.

### 3.2.2. South Windsor

There were 22 reported cases. None of South Windsor's neighbors (DoS = 1) become infected until Manchester, 8 months later, and Glastonbury 6 months after that.

### 3.2.3. Clinton

All four rabid raccoons were reported within a few months, and spread to surrounding townships.

### 3.2.4. Putnam

The first of 11 cases was followed by a gap of 2 years before the second rabid raccoon followed shortly by nine more cases. The lag to a second rabies case was the longest among townships.

### 3.2.5. Branford

Branford township is separated by three degrees from Clinton (Fig. 2b), but two cases were observed in the month after Clinton's first case; these were followed by a large cluster of cases.

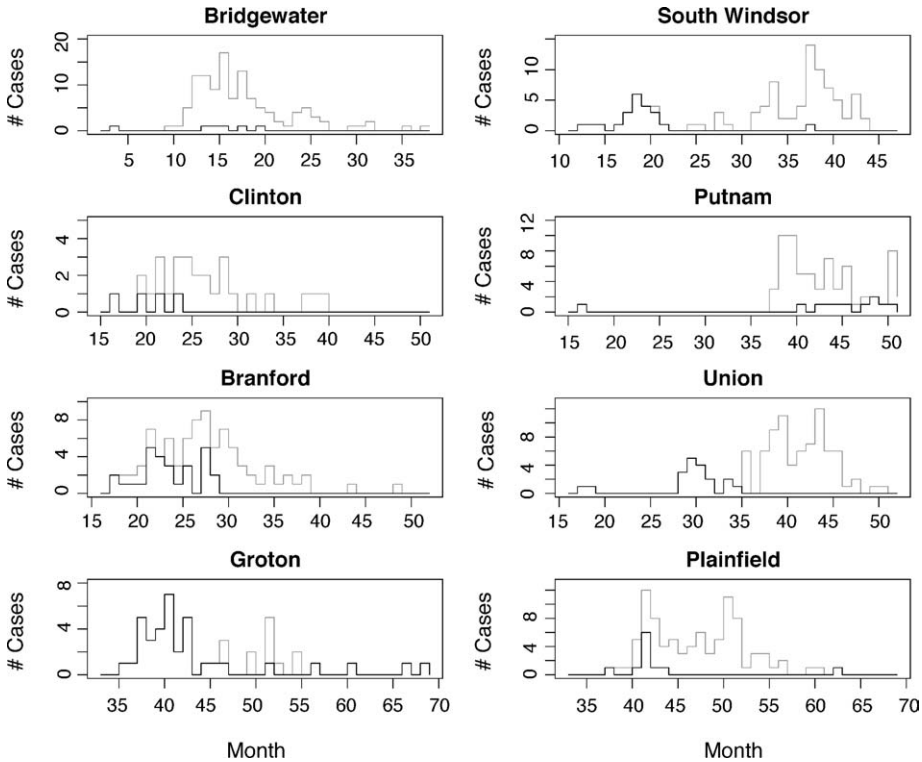


Fig. 5. A plot of the reported cases in the 3 years after the first case (black) and all the reported cases in the neighborhood (gray) using a degree of separation of 1 or less ( $DoS \leq 1$ ) for each of the putative long-distance translocation events.

### 3.2.6. Groton

There were 36 reported rabid raccoons but none of the townships in the neighborhood ( $DoS = 1$ ) became infected for 11 months.

### 3.2.7. Union

There were two rabid raccoons reported in consecutive months followed by a 12 month gap before a cluster of cases occurred. The first two cases were assumed to be related to a failed LDT, while the subsequent cases were assumed to be associated with the advance of the wave front.

### 3.2.8. Plainfield

The first reported rabid raccoon was followed by a cluster of cases in Plainfield and in the surrounding townships.

## 3.3. The influence of LDT events

To assess the influence of the putative LDTs (Table 2) on the epidemic spread of raccoon rabies, each of 6 LDTs (omitting Putnam and Bridgewater) was initially forced as a

Table 3

The best-fit parameter values for Rivers and Forest model forced by Ridgefield and six townships that were identified as putative LDT events

Township	$-\Delta$ (%)	$\alpha$	$\beta$
South Windsor	−58	4.1–4.0F	1.1–10.8F
Clinton	1.4	8.8–9.8F	1.7–9.9F
Branford	5.6	8.4–9.2F	1.9–11.2F
Groton	2.7	8.0–8.4F	1.4–4.7F
Union	−49	7.2–8.7F	1.7–0.5F
Plainfield	1.3	7.2–8.7F	1.7–0.5F

$-\Delta$  is the percent improvement in the LSS over the Rivers and Forest forced only by Ridgefield, where the LSS for both models is computed without the forced townships.

boundary condition separately, and the resulting percent change in the LSS using the Rivers and Forest model (omitting the boundary townships) was considered; LDTs either improved (positive percentages) or decreased the overall model fit (Table 3).

We repeated the fitting, forcing the epidemic through boundary conditions which included Branford and the other townships which had initially been considered separately. Other combinations of LDT events were tested (results not reported), but no other combination of boundary conditions improved the model fit. Only the inclusion of Plainfield Township in combination with Branford Township improved the fit of the overall Rivers and Forest model. Note that no question of parsimony is involved in comparing two models with different boundary conditions; the models use the same number of parameters and are compared based on their fit to the same data.

The Rivers and Forest model, with foci at Ridgefield, Branford, and Plainfield produced the best overall fit (see Fig. 4a). Using this model, we generated the most likely path of raccoon rabies spread, a best “historical reconstruction” of the epidemic, including the extent of the epidemic surrounding Branford and Plainfield (Fig. 4b). This historical reconstruction also serves as a putative phylogeny for rabies in Connecticut during the initial wave, a phylogeny that could be tested in theory with molecular data.

#### 4. Discussion

Our analyses demonstrated the impact of spatial heterogeneities on the spread of rabies in Connecticut by considering the additional effect of percent forest cover on the previously described river effect (Smith et al., 2002). Most importantly, we developed a method for systematically identifying putative LDT events, classifying these early reports, and evaluating and quantifying their impact as nascent foci for rabies spread beyond the wave front using a network model. The network model has inherent advantages over regression analysis because the spread on networks mimics the underlying process, and networks can represent arbitrary distributions of heterogeneous habitat variables and complex landscape features (Lucey et al., 2002). In classifying these early cases, we developed multiple, rigorous criteria for weighing other cases within the township and in

surrounding townships. In quantifying the impact, we have also developed a method for reconstructing the historical path of an invasive species.

We confirmed the importance of spatial heterogeneity in the epidemic of raccoon rabies in Connecticut (Smith et al., 2002). Using the network distance model, we found a five-fold slowing effect associated with rivers, consistent with earlier findings of a factor of 7 (Smith et al., 2002). Notably, we found a new, three-fold difference in the overland rate of spread associated with the percent of forest cover in a township. Moreover, the slowing effect of rivers was strongly modified by the amount of forest cover. In lightly forested areas, the rate of rabies spread between townships separated by a river was a factor of 2 slower. In heavily forested areas, the models predicted that rabies would never cross rivers, a much stronger effect than previously estimated. The impact of human populations was also investigated (results not shown); human population density was strongly negatively correlated with forest cover, but forest cover consistently provided a better fit than human population density.

The effect of long-distance translocation within Connecticut was limited. Eight putative LDT events were identified in Connecticut in the townships of Putnam, Bridgewater, South Windsor, Union, Clinton, Groton, Branford, and Plainfield. Two other townships, South Windsor and Groton were associated with local epidemics that did not spread. Only Branford had a strong influence, becoming a new focus of epidemic spread to the local neighborhood. A secondary, minor focus was identified with a putative LDT event in Plainfield. Even these two nascent foci that spread to surrounding townships had a limited impact, as they occurred fairly close to the advancing wave front.

Despite the limited impact of LDT in Connecticut, a relatively small state, long-distance translocation has clearly played an important role in the spread of raccoon rabies to the mid-Atlantic states and the subsequent epidemic spread of raccoon rabies through the New England states. This raccoon rabies epidemic is unprecedented in size and scope, spreading north through Connecticut and to the border of Canada, and east to Ohio (Hanlon and Rupprecht, 1998; MMWR, 1999; Krebs et al., 2001). A long-distance translocation event from Florida most likely initiated the epidemic near the border between West Virginia and Virginia (Nettles, 1979). Moreover, the raccoon rabies epidemic in Connecticut was initiated by a long-distance translocation event in southeastern New York (Russell et al., 2004). Therefore, the scale at which these events are explored and defined are decisive when considering their overall impact on epidemics.

LDT events are usually generated by a different process than local dispersal, and may allow the epidemic to cross barriers to local dispersal or areas of poor habitat. Such events, when viewed at smaller spatial scales, obscure the effects of heterogeneity and make the landscape seem more homogeneous. For example, a LDT event in Branford allowed rabies to jump the Housatonic river; by forcing the epidemic in Branford, we found a stronger effect associated with forest cover compared with the analogous model unforced by Branford. Another LDT event allowed rabies to jump the Housatonic river and the Connecticut river into South Windsor less than a year after Ridgefield, but the epidemic failed to spread into the surrounding townships. Similar LDT events in Groton, Enfield, Union, and Putnam would have reduced the delay in spread caused by the Connecticut river had they become foci of infection.



One possible reason why there was failure to spread from nascent foci may be fine-grained local heterogeneity. Following translocation, stochastic fade-out at the nascent foci is more likely in areas where the reproductive rate is near or below the threshold for establishment. In other cases, long-distance translocation events may fail to affect the time-course of an epidemic if they occur in host populations that are isolated; thus, spatial heterogeneity can also limit the impact of LDT events.

Some of the problems in reconstructing the historical spread of rabies through Connecticut are due to the quality of the data that were collected through passive surveillance. We have identified reported raccoons that were likely to be either isolated cases or misidentifications, but problems in the data set may include more pervasive and systematic errors such as reporting bias. On the other hand, the results here are consistent with other studies (Smith et al., 2002) and the model fitted in Connecticut was used to hind-cast raccoon rabies spread in New York (Russell et al., 2004).

## 5. Conclusion

Spatial heterogeneity and the potential for LDT of rabid raccoons should figure into the development of management and surveillance strategies. For example, where should efforts be focused to contain the spread of emerging infectious diseases or invasive species? Is it possible to create a cordon sanitaire? What are the best strategies for controlling rabies around nascent foci that have jumped even the most effective barriers by LDT? Efforts to contain an epidemic can be enhanced by using natural barriers and areas where dispersal is naturally slowed. Our models suggest that vaccine baits might be most effective at containing the spread if distributed along river banks in lightly forested areas, those with less than 12% forestation. But, the unanswerable questions are how effective can natural or vaccine enhanced-barriers be and for how long can we expect them to remain effective when given the calculus of LDTs? LDT events were common in Connecticut, but many did not spread rabies to other townships. LDT events remain unpredictable, but may be discovered early by good surveillance. Our analysis suggests that such foci may be amenable to control, but the answerable questions need to be addressed and interventions planned before events occur.

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