Spatial-Temporal Analysis of Dead Crow Reports Associated with a West Nile Virus Epidemic

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ABSTRACT

We apply the Space-Time AutoRegressive Moving Average (STARMA) modeling methods in an investigation of the spreading dynamics of a West Nile virus (WNV) epidemic in crows in the Detroit Metro area in 2002. The data fit very closely those expected from a purely STAR (Space-Time AutoRegressive) process having low spatial and temporal orders. The model can be used to characterize the past and possibly even predict the future dynamics of spreading behavior and, most importantly, to provide information about the factors which govern the spreading behavior. Use of the STARMA model allows estimation of the rate of spread of WNV at different spatial scales and thus characterization of the spatial and temporal scales expected. Determination of spatial-temporal autoregressive parameters using STARMA holds considerable promise for characterizing emerging infectious diseases.

Key words: space-time modeling; Space-time autoregressive moving average; infectious diseases; West Nile virus.

1. INTRODUCTION

West Nile virus (WNV) outbreaks in North America are characterized by steep epidemic curves in the American crow (*Corvus branchyrhynchus*) populations in time, with highly localized clusters of crow infections in space (Petersen & Roehrig 2001; Eidson et al., 2001; Theophilides, Ahern, Grady & Merlino, 2003). Mosquitoes of the genus *Culex* transmit WNV amongst these birds (Komar, 2000; Turell, O'Guinn & Oliver, 2000), and crows succumb rapidly to infection within 4-8 days after exposure (McLean et al., 2001; Komar et al., 2003). In an outbreak in 1999 in New York City, 89% of laboratory-confirmed, WNV-infected birds were American crows (Komar, 2000). The estimated death rate due to WNV infection was 68% within a marked crow population during an epizootic in Illinois in 2002 (Yaremych et al., 2004b). The absolute accumulation of dead crows (even if infection is not laboratory-confirmed) is a measure of the spreading of virus infection in the crow population, and has been identified as a sensitive indicator variable for an on-going epizootic in crows and for heightened risk of infection in humans (Eidson et al., 2001; Theophilides et al.. 2003; Watson, Jones, Gibbs & Paul, 2004).

The dynamical behavior of the incidence of dead crows remains a poorly understood biological system with complex space-time interactions. Current understanding of the spatial dynamics of WNV infection based upon the incidence of dead crows is also poor. There has been no spatial-temporally explicit modeling (Eidson et al., 2001), and only a few statistical inferences are provided by cluster analyses, such as the Knox statistic (Theophilides et al., 2003).

In this study, we investigate the spatial dynamics of a WNV epidemic in crows in Detroit Metro area in 2002, using the "Space-Time AutoRegressive Moving Average" (STARMA) model. The modeling procedure first identifies the key elements of a process, including the spatial distances over which there is direct spread and the associated time periods. Further it can be used to estimate the rates of spread at the various spatial and temporal scales. In doing so, the analyses characterizes the dynamics in a way that can be used to forecast future spreading, as well as provide information that could be critical in determining the factors that govern the dynamics. Not only can we recognize the areas of epidemiologic concerns in human health, in almost real time, but also provide details of the space-time transmission dynamics of WNV.

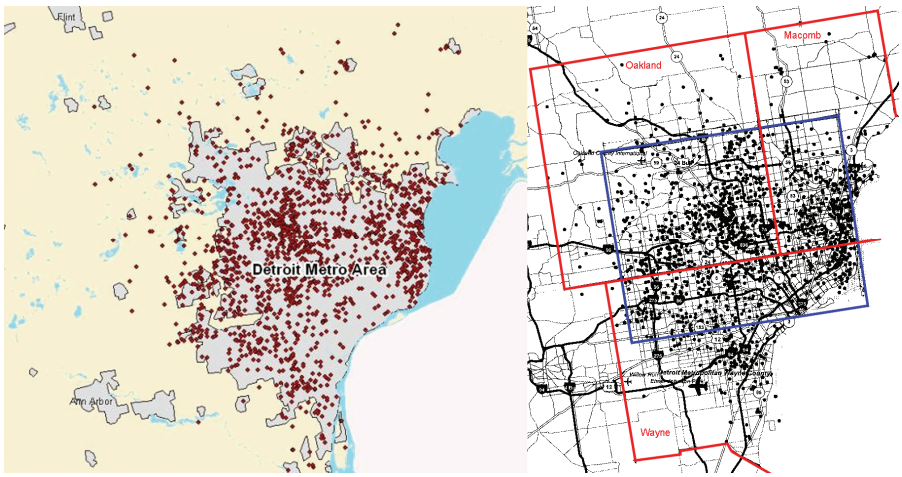


Figure 1. Dead crow reported in the Detroit Metro area. The rectangle enclosed area is the area retained after truncation in space.

2. METHOD

2.1 Data Collection and Management

Dead crow data were collected systematically before and during an outbreak of West Nile viral meningoencephalitis in southeastern Michigan in the summer of 2002 (CDC, 2002). A campaign was widely publicized to encourage the public to report findings of dead crows in the Detroit Metro area. Individuals reported sightings by accessing a website or by telephone call to a toll free number, from April to October, 2002. The number of dead crows found and the address were among the data recorded, and constituted the dead crow data (DCD) analyzed extensively in this article. WNV infection was confirmed in a subsample of these crows by immunohistochemical detection of viral protein of necropsied specimens (Fitzgerald et al., 2003). The estimated rate of infection in dead crows was 70% (K. Signs & Patterson, unpublished). In the DCD database, which covered all of Wayne, Macomb and Oakland counties, addresses were examined for validity or containing some error in number or street name. Those that were verified were retained and used for analysis. A total of 1807 dead crow sightings were successfully classified by latitude and longitude and by date of sighting, spanning 28 weeks. Most of the DCD counts fell within a rectangular shaped area of 31.6 × 25.8 miles (Fig. 1), and the data (leaving 1,516 dead crow counts) were truncated to include only this area, because this facilitated our implementation of STARMA analysis. For purposes of analysis, this area was divided into a grid of "cells." In the one analysis presented in detail, there were 10 × 10 cells, each cell having dimensions 3.16 × 2.58 miles. Thus, in the analyses the space-time unit of data was the number of dead crows found in a cell during each of the 28 weeks.

2.2 Statistical Analyses

The dead crow data (DCD) were analyzed using the Space-Time Autoregression Moving Average (STARMA) model, which can be written:

$$\mathbf{Z}(t) = \sum_{k=1}^{p} \sum_{l=0}^{r} \phi_{kl} \mathbf{W}^{(l)} \mathbf{Z}(t-k) - \sum_{k=1}^{q} \sum_{l=0}^{s} \theta_{kl} \mathbf{W}^{(l)} \boldsymbol{\varepsilon}(t-k) + \boldsymbol{\varepsilon}(t) \quad (1)$$

where $\mathbf{Z}(t) = [Z_1(t), Z_2(t), \cdots, Z_N(t)]'$ is a $N \times 1$ vector of dead crow counts such that $Z_i(t)$ is the number of crows found in cell i during week t (Pfeifer & Deutsch, 1980). The parameters p and r are respectively the maximum autoregressive temporal and spatial orders, and q and s are respectively the maximum moving average temporal and spatial orders, which are determined by inspection of the behavior of the space-time correlations and partial space-time correlations (Pfeifer & Deutsch, 1980). ϕ_{kl} and θ_{kl} are respectively the autoregressive and moving average parameters at temporal lag k and spatial lag l, and these are estimated in the analyses. The autoregressive parameters in particular would be expected to be functions of the relative rates of direct spatial spreading of the disease. $\mathbf{W}^{(l)}$ is the $N \times N$ weight matrix for spatial order l. $\mathbf{W}^{(l)}$ has elements $w_{ij}^{(l)}$ that are the weighting contributions of site j to site i, and which are nonzero if and only if site i and j are l-th order neighbors in space. The vector $\boldsymbol{\varepsilon}(t) = [\varepsilon_1(t), \varepsilon_2(t), ..., \varepsilon_N(t)]'$ is a random noise vector at time t. We used a wide variety of cell sizes (and hence

various total numbers of cells), but in the analysis presented in detail in the Results section, the cells had dimensions 3.16 × 2.58 miles, for a total of 100 cells in a 10 x 10 spatial array or lattice.

There are two correlations which need to be defined in advance for STARMA analysis. The first one is the Space-Time AutoCorrelation Function (STACF) and is defined as:

$$\rho_{lk}(s) = \frac{\gamma_{lk}(s)}{\sqrt{\gamma_{ll}(0)\gamma_{kk}(0)}}, \text{ where } \gamma_{lk}(s) = \underset{t}{E}\left[\frac{\left[\mathbf{W}^{(l)}\mathbf{Z}_t\right]^T\left[\mathbf{W}^{(k)}\mathbf{Z}_{t+s}\right]}{N}\right].$$

The other is the Space-Time Partial AutoCorrelation Function (STPACF), whose coefficients are conditional STACFs for given known ϕ_{kl} (Pfeifer & Deutsch, 1980).

STARMA analyses require specification of the spatial order relationships (as defined by Hooper & Hewings, 1981) among cells, and this can be done in an infinite variety of forms. We used several reasonable forms, but the one used in the detailed analysis presented in the Results is illustrated in Fig. 2. For example, the first spatial order (corresponding to $\mathbf{W}^{(l)}$) contains cells that use the "rook's" move (by analogy with the game Chess) nearest neighbors to a given site. The spatial lag structure specifies the spatial weight matrices $\mathbf{W}^{(l)}$ in Eq. (1), following the methodology of Pfeifer and Deutsch (1980). Note that this spatial lag structure makes the reasonable assumption that the spatial correlation structure of the data is isotropic.

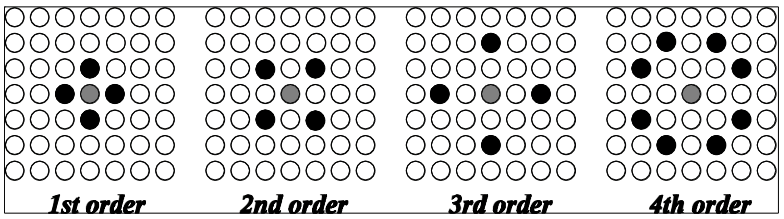


Figure 2. Spatial order definition.

The applied Pfeifer and Deutsch (1980) STARMA procedure, a space-time extension of the Box-Jenkins time series method (Box & Jenkins, 1970), involves three iterative steps of *model identification*, *parameter estimation*, and *diagnostic checking*. For the sake of brevity, we present in detail either the initial or final iteration in the Results. The following initial spatial order matrix, was used in the detailed analysis:

$$Spatial\_Order\_Matrix = \begin{bmatrix} - & 6 & 5 & 5 & 5 & 6 & - \\ 6 & 5 & 4 & 3 & 4 & 5 & 6 \\ 5 & 4 & 2 & 1 & 2 & 4 & 5 \\ 5 & 3 & 1 & 0 & 1 & 3 & 5 \\ 5 & 4 & 2 & 1 & 2 & 4 & 5 \\ 6 & 5 & 4 & 3 & 4 & 5 & 6 \\ - & 6 & 5 & 5 & 5 & 6 & - \end{bmatrix}. \quad (2)$$

To make the space-time series stationary, the spatial and temporal trends (as shown in Fig. 3) were removed. Because it is evident that there are at least two spatial foci of incidence in the dataset, in the analyses presented in detail in the Results section, a fourth order polynomial trend surface combined with a temporal trend (as shown in Fig. 3) was removed from the dataset. The spatial trend is the least-square best-fit to the dataset of the following equation:

$$S_{trend}(x,y) = \sum_{i=0}^{4} \sum_{j=0}^{i} a_{ij} x^j y^{i-j}$$

where a_{ij} are the best-fit coefficients. The temporal trend is:

$$T_{trend}(t) = \frac{1}{N} \sum_{x} \sum_{y} Z_{x,y}(t)$$

where N is the number of sites, vector $\mathbf{Z}(t)$ is the original space-time series data, $Z_{x,y}(t)$ is the element of $\mathbf{Z}(t)$ at location (x,y). In combination, the spatial and temporal trends were removed according to the equation:

$$Z^*_{x,y}(t) = Z_{x,y}(t) - h \cdot S_{trend}(x,y) \cdot T_{trend}(t)$$

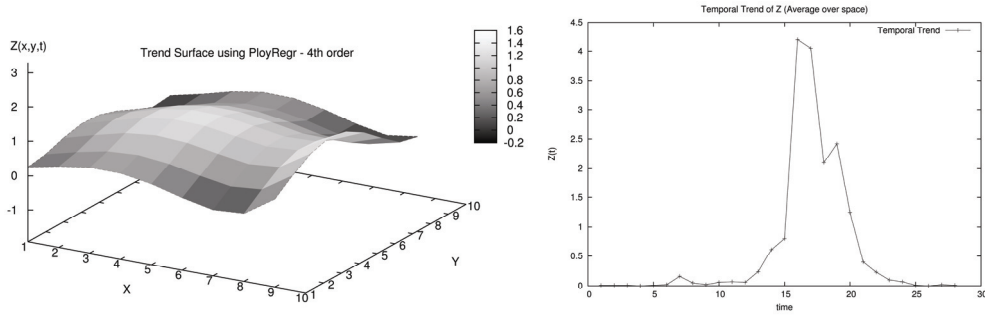
where h is a constant so that $h \cdot S_{trend}(x,y) \cdot T_{trend}(t)$ best-fit to $\mathbf{Z}(t)$, $\mathbf{Z}^*(t)$ is the de-trended $\mathbf{Z}(t)$. After de-trending, the grand mean was also subtracted. However, in additional analyses we employed a wide variety of other polynomial surfaces for spatial de-trending, but found no substantial differences among the space-time autocorrelations and other aspects of STARMA.

3. RESULTS

The space-time autocorrelation function (STACF) and space-time partial autocorrelation function (STPACF) for the data treated by the main analysis specified in the Methods (with respect to cell sizes, spatial lag structure and spatial and temporal de-trending) are shown in Fig. 4. There are correlations as large as ca. 0.35 at short distances and time lags, indicating a high degree of spatial-temporal

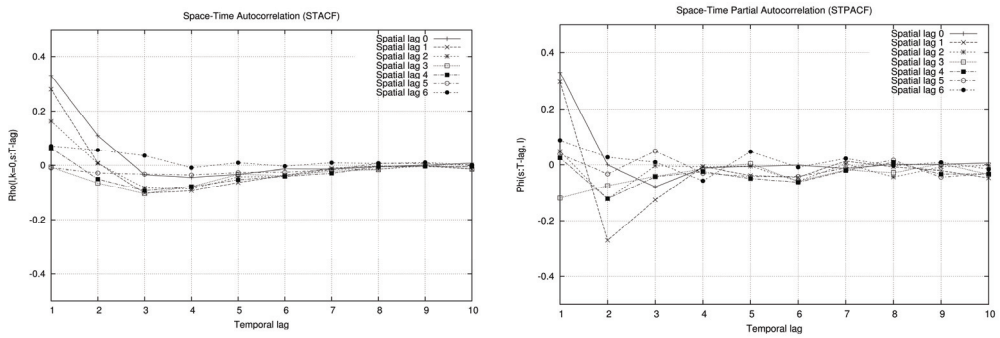
autocorrelation in the data.

Together, the STACF and STPACF indicate that the dead crow data follow very closely a "pure" space-time autoregressive (STAR) process, and that there are no space-time moving-average (STMA) effects. The STACF shows the characteristic form of a STAR, because it tails-off smoothly with both temporal and spatial lags, and the STPACF shows the diagnostic (pure) STAR form of "cutting-off" (e.g., Pfeifer & Deutsch, 1980; Hooper & Hewings, 1981). "Cutting off" means that the STPACF goes to zero or near zero at some maximum spatial and temporal lags, and then remains so for higher lags. These lags of cutoff also identify the maximum temporal and spatial lags (the limits of the summations in Eq. (1)) of the process generating the DCD as being three weeks and spatial lag 4 (Eq. (2)), respectively, and the process can be written STAR(maxT=3, maxS=4).



(a) (b)

Figure 3. The spatial trend (a) and the temporal trend (b) were removed from the dead crow dataset before modeling.



(a) (b)

Figure 4. Space-time autocorrelation analysis for the de-trended dead crow dataset; (a) space-time autocorrelation function and (b) space-time partial autocorrelation function.

For a STAR(maxT=3, maxS=4) model, the maximum likelihood estimates of the autoregressive parameters (Table 1) can be calculated as best linear estimates of a general linear model. Thus the specific form of Eq. (1) is:

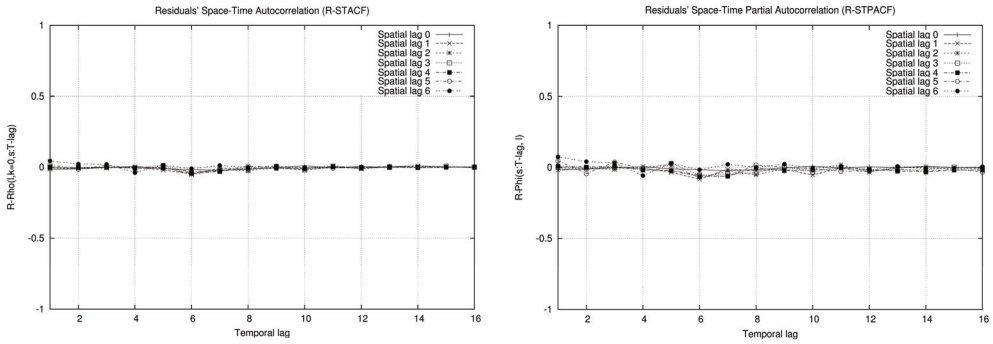
$$\begin{aligned}\mathbf{Z}(t) = \; & (+0.26)\mathbf{Z}(t-1) + (+0.04)\mathbf{Z}(t-2) + (-0.02)\mathbf{Z}(t-3) + \\ & (+0.36)\mathbf{W}^{(1)}\mathbf{Z}(t-1) + (-0.18)\mathbf{W}^{(1)}\mathbf{Z}(t-2) + (-0.11)\mathbf{W}^{(1)}\mathbf{Z}(t-3) + \\ & (+0.10)\mathbf{W}^{(2)}\mathbf{Z}(t-1) + (-0.07)\mathbf{W}^{(2)}\mathbf{Z}(t-2) + (+0.02)\mathbf{W}^{(2)}\mathbf{Z}(t-3) + \\ & (-0.09)\mathbf{W}^{(3)}\mathbf{Z}(t-1) + (-0.04)\mathbf{W}^{(3)}\mathbf{Z}(t-2) + (-0.02)\mathbf{W}^{(3)}\mathbf{Z}(t-3) + \\ & (+0.04)\mathbf{W}^{(1)}\mathbf{Z}(t-1) + (-0.11)\mathbf{W}^{(4)}\mathbf{Z}(t-2) + (-0.03)\mathbf{W}^{(4)}\mathbf{Z}(t-3) \; . \end{aligned} \tag{3}$$

The estimate of autoregression parameter, ϕ_{kl}, for spatial lag zero and temporal lag one week is large (0.26), indicating that the number of dead crows found in a cell has a large positive influence on the number found there the next week. The value for spatial lag one, temporal lag one is also very large (0.36), indicating that the four nearest neighbor cells have a high degree of influence. This value could be considered as a function of the relative rate of spatial spread for the DCD and presumably the WNV epidemic in the crow population, across neighboring cells. Relative to the spatial and temporal de-trending, the rate of spread of the epidemic from one cell to another having a shared boundary would be one-fourth as large (0.09). The degree of influence for spatial lag two (constituted by four diagonal or second order neighbors) is considerably smaller (0.10 in total), but statistically significant. In addition, there is a large negative effect for spatial lag 1 time lag 2 weeks, which may be an indicator of depletion of local crow population, as is noted in the Discussion. All other autoregression coefficients are near zero or negative, although some are nominally statistically significant. In sum, the autoregression analysis indicates that nearly all of the autoregression is contained within spatial lag two and within two weeks. The rate of spread of incidence in the DCD data is rapid but primarily over very short distances, and the system is nearly Markovian, i.e. all or nearly all of the dynamics are determined over a one to two week period.

Table 1. *The estimates and significance levels of the model parameters [STAR(MaxT=3, MaxS=4)]*

Estimates of parameters					
	Spatial lag				
Temporal lag	S=0	S=1	S=2	S=3	S=4
T=1	0.26	0.36	0.10	-0.09	0.04
T=2	0.04	-0.18	-0.07	-0.04	-0.11
T=3	-0.02	-0.11	0.02	-0.02	-0.03
Significance levels of parameters					
	Spatial lag				
Temporal lag	S=0	S=1	S=2	S=3	S=4
T=1	0.001	0.001	0.010	0.100	0.400
T=2	0.040	0.001	0.040	0.300	0.010
T=3	0.400	0.010	0.250	0.900	0.600

In further support of this conclusion, there are no significant space-time autocorrelations of the model residuals (Fig. 5).



(a) (b)

Figure 5. Space-time autocorrelation analysis of the residuals; (a) space-time autocorrelation function and (b) space-time partial autocorrelation function.

To further test the robustness of the results, we configured many other initial conditions to enter into the iterative modeling procedure. For example, we used various numbers of cells (and hence correspondingly varied cell sizes), such as arrays of 16x16 and 20x20 for the same lag structure types as in Eq. (2). We also analyzed a "ring" lag structure, such that the lags of neighbors formed rings extending outwards in order (for example there were eight nearest neighbors formed into spatial lag one, i.e. a single step queen's move in Chess; 16 cells formed lag 2; 24 cells for lag 3; etc.). We analyzed all combinations of the three cell configurations and two types of lag structures. It is not possible, simply because of geometry, to precisely compare values of the autoregressive coefficients and for sake of brevity we do not list them. However, in general terms there were no obvious inconsistencies, and large positive values were observed only at spatial lags that were comparable and only for temporal lags one and two. Moreover, all models had STACF's and STPACF's that indicated pure STAR processes. In addition, large negative values at time lag 2 were observed in spatial lags roughly consistent with lag 1 in the main analysis.

One completely objective but limited comparison can be made, by examining the maximum spatial lag over which there are any statistically significant (in this case using the 0.01 level) autoregressive coefficients, using the lag structure of Eq. (2), but different cell arrays (sizes), and measuring the distance between the cell centers from the focal cell to the cells at the maximum lag. For arrays of cells 10× 10, 16×16, and 20×20, the maximum spatial orders were four, six and seven, respectively, and the corresponding maximum physical distances were 6.42, 6.47, and 6.36 miles. This shows that an effectively correlated area in the modeling results is consistently about 6.4 miles, regardless of the cell size used. However, it

should be kept in mind that the scale over which there were large positive autoregression was consistently much smaller. Furthermore, we analyzed a wide range of alternative configurations, subsampling only part of the Detroit area, various other cell configurations and SOMs. For each of these, we followed the iterative procedure described in this article. In all cases, the model that was converged to was consistent with the model reported.

Finally, we used a large range of orders of polynomials for spatial de-trending prior to STARMA analyses. Again, there were no major changes in the spatial and temporal scales over which there were large positive autoregressive coefficients although, as the order of the polynomial became very high, the magnitudes of coefficients declined somewhat. Such a decline maybe anticipated. Essentially, high order de-trending removes autoregression, analogous to the removal of spatial autocorrelation when using high order polynomials in trend surface analyses (Bocquet-Appel & Sokal 1989).

4. CONCLUSIONS

The results showed that the incidence of reported dead crows per week during the 2002 epidemic in the Detroit Metro area closely fits a pure STAR process. A high degree of space-time autoregression was found, and no evidence of STMA influences. The latter result indicates that although there was both stochasticity and statistical noise in the observed values (the estimated variance is 1.451), these sources of variation were not directly or immediately shared spatially or temporally among cells, rather they behaved as “white noise” (Hooper & Hewings, 1981). Essentially all of the autoregression is contained within relatively low spatial and temporal orders, as was verified by analyses of the residuals. These results, together with the robustness of the interpretations, evidenced by lack of effects of changes in sizes of cells, spatial order definition and spatial de-trending, also verify that the STARMA modeling approach was appropriate.

The autoregressive coefficients also show the pattern expected of most biological processes (e.g. Cliff, Haggett, Ord, Bassett & Davies, 1975; Upton & Fingleton, 1985; Epperson, 2000; Epperson, 2003). They are positive and large for close spatial proximities, i.e. small distances, and generally decrease in value as distance increases (Table 1). Exceptions involving fairly large negative parameters for short distances at the lags two and three are discussed below. The spatial scale over which there are large positive autoregressive coefficients is small, perhaps surprisingly so. As an example, consider the main analyses, where there was a 10 x 10 array of cells and the spatial order matrix (SOM) of Eq. (2). Although the best fitted model is STAR(maxT=3, maxS=4), having maximum spatial lags corresponding to a distance of ca. 6.4 miles, in terms of distances between cell-centers, most of the positive autoregression is contained in a reduced model with maximum spatial lag 2 and maximum temporal lag three weeks. This indicates that the dynamics of the DCD operates over rather smaller distances, with maximum distances of direct effects of locations on one-another of ca. four miles or less, and presumably this reflects the spreading of the virus and changes in

probability of infection. However, the distances over which the virus load is primarily moving (spreading) may be still much smaller. There is a remarkable reduction of autoregressive effects for spatial lag 2 (0.10) compared to spatial lag 1 (0.36) for the 10×10 array of cells and SOM of Eq. (2). The main difference between the two is the length of the boundaries between cells. This strongly suggests that length of boundary largely determines the rates of spreading of WNV among cells. If that is the case, it would indicate that WNV is mostly spread very short distances across cell borders, less than a mile or possibly even a few hundred meters.

Crows can fly long distances, so the scale over which the DCD show large positive autoregressive effects may seem surprisingly small. However, the mosquito vector is active primarily during hours when crows are roosting, and crows are territorial and show high fidelity to roosting sites (Yaremych et al., 2004a). Thus, crows may be largely being infected and transmitting the virus at their roosting sites, and thus apparently not spatially spreading the disease, although this would amplify the viral load locally. In addition, superimposed on this process are the distances of flights between where dead crows are found and their roosting sites (Yaremych et al., 2004b). Although such movements do not spread the disease, they could influence the short term autoregression of DCD. While crows are a very good indicator of viral loads, they may not be largely responsible for spatially spreading the disease. Other animals or even the mosquito vector itself may be more responsible for the local spatial spread per se.

Two points should be reinforced. First, since crows are one of the most-infected animals, they could be very important in amplifying the disease locally (say within a cell). Second, our results do not mean that the crows do not on occasion spread WNV long distances, and indeed perhaps even start a new local epidemic. It is unlikely that such low frequency events would be detected in our analyses. Still, the results do suggest that there is a good chance that local epidemics could be contained or at least reduced, for example through a concentrated eradication effort, spraying of mosquito ponds, etc.

The results also showed that the temporal order of the process is nearly Markovian, since large and significant parameters are observed only for time lags of one and two weeks. It has been argued that the Markovian property should be common in biological processes (Epperson, 2000). In addition, the prominence of one- and two-week lagged effects is consistent with the short interval between infection and death (Komar et al., 2003), and with empirical evidences of intense localized epizootics (Eidson et al., 2001; Theophilides et al., 2003).

One specific feature of the autoregressive structure that deserves special examination is the rather large negative autoregressive parameters at time lag 2 for some spatial lags. This was observed in all models, and appears to be a real effect. It may be explained by depletion of the crow population. Depletion of the crow population was extreme: during the course of the WNV season in 2002, up to 70% of crows in Detroit died from WNV (K. Signs & J. Patterson, unpublished). Hence, for example, if a cell had an unusually high rate of crow death for a given time period (week) then, especially during the height of the WNV season, a significant portion of the crow population in that cell would have died, leaving fewer to be infected and die one to two weeks later. Thus, our results suggest that there are

actually two DCD autoregressive processes. The first is dependent on the local and nearby WNV loads, and the second is a weaker echo effect caused by depletion. The mixture of the two may make temporal lag one DCD autoregressive parameters all positive, but not all of the temporal lag two parameters.

Finally, it is important to discuss the de-trending over time and space. The fact that we de-trended temporally over the season means that the autoregressive parameters are not rates of spread, but rather relative rates given the overall increase or decrease in WNV. The former might be recovered by adding multipliers to the autoregressive (the variance of the errors term $\boldsymbol{\varepsilon}(t)$ might also change over time) structures, depending on the exact week. More interesting is the rather striking spatial non-stationarity, in particular two to three "hotspots." Since we have removed these by polynomial regression, our analyses reveals nothing about why they occurred.

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