## Advances in the Analysis of Spatially Aggregated Data

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#### Overview

- Motivation
- GLM for areal data
- (extended) Hausdorff Distance
- Background on case-crossover
- STARMA models
- Case-crossover in a STARMA model context

#### Motivation

- How do we model spatially-referenced, aggregated count data?
- How can we include popular epidemiological methodology within this framework?
- How can we account for characteristics like zero inflation or hierarchical structure?
- How can we provide tools to make this modeling framework easily useable?

#### Generalized Linear Regression

- (Nelder and Wedderburn 1972) extended Gaussian linear regression models to encompass all (one parameter) exponential family dependent variables
- non-normal linear means modeled using a link function
- later extensions allowed for both fixed and random effects (Gaussian) -(Raudenbush and Bryk 2002) develop Hierarchical GLMs which can have non-Gaussian error distributions

#### GLM's for Spatial Count Data

- necessarily associated with lattice data
- Early methodology arose as adaptations of methods for time series of counts (for example Liang and Zeger 1986,S. L. Zeger (1988)).
- (Albert and McShane 1995) develop a model for spatially correlated binary count data (neuroimaging); (Gotway and Stroup 1997) generalize these to cateogrical/discrete spatial data
- Huge explosion since then, see (Anselin 2002), (Ward and Gleditsch 2008), and (De Oliveira 2012)

GLMs allow for all sorts of dependent variables:

- Count Data models: Poisson, Binomial, Negative Binomial
- Zero-Inflated models
- Hurdle Models

#### GLM's for Spatial Data- technical details

Consider the following data model and process model:

$$egin{aligned} &Z(s_i)|Y(s_i) \sim \textit{ind.exponentialfamily}(\exp(Y(s_i))) \ &\mathbf{Y}|eta, au^2, \phi \sim N(\mathbf{X}eta, au^2(\mathbf{I}-\phi\mathbf{H})^{-1}) \end{aligned}$$

- The conditional distribution of the data (Z) given the process (Y) could be normal, poisson, binomial, etc.
- W is a spatial weight matrix
- $\beta$  is the vector of regression coefficients
- au is an overdispersion parameter
- $\phi$  is the spatial autocorrelation parameter

If  $Z(s_i)$  follows a Gaussian distribution, where the  $s_i$ 's form a lattice, the CAR model can be written

$$Y(s_i)|Y(N(s_i)) \sim N(X\beta, (I - \rho W)^{-1}M)$$

Where M is a diagonal matrix (e.g.  $M = diag(|N(s_1)|^{-1}, \dots, |N(s_n)|^{-1}).$ 

#### Specification of W

- For geostatistical data: W is specified by choosing an appropriate covariance model via the empirical variogram
- For lattice data: W encodes conditional independence structure (zeroes on diagonals and all entries (*i*, *j*) where s<sub>i</sub> is not a neighbor of s<sub>j</sub>)
- must be row-standardized
- can be binary, or weights
- How to choose neighborhood structure and their weights?

#### Popular neighborhood structures for lattices

- contiguity: two regions are neighbors if they share at least one (queen) or more than one (rook) boundary point
- can lead to vastly differing numbers of neighbors for different regions (e.g. larger regions will have more neighbors)
- k nearest neighbors: calculate the distances between two regions as the distance between a single point in each
- e.g. geometric centroid, population-weighted centroid, or other meaningful location

How important is the choice of neighborhood structure?

- Wall (2004) found counterintuitive implied correlations from SAR/CAR models fit using various neighborhood schemes
- LeSage (2008) compare the log-likelihood values of models using contiguity matrices and nearest neighbor matrices for varying numbers of neighbors
- nearest neighbor performs better than contiguity. They recommend comparing different values of k to assess sensitivity of results to the number of neighbors.
- Underlying distance metric need not be Euclidean. (Shahid et al. 2009) explore different distance metrics which capture road distance

#### Hausdorff Distance

The Hausdorff distance measures the distance between two sets:

$$H(A, B) = \max\{h(A, B), h(B, A)\}$$
  
= max{max min d(p<sub>a</sub>, p<sub>b</sub>), max min d(p<sub>a</sub>, p<sub>b</sub>)}  
p<sub>b</sub> \in B p<sub>a</sub> \in A} d(p<sub>a</sub>, p<sub>b</sub>)}

- The directional Hausdorff distance h(A, B) from a set A to a set B is the largest possible distance between any point in A and the closest point in B.
- ► The Hausdorff distance between *A* and *B* is then the larger of two two directional Hausdorff distances.
- can use any underlying distance metric d

#### Two Ideas for Hausdorff Distance

- 1. use Hausdorff distance as a way to generate spatial weight matrices for lattice data
- 2. use Hausdorff distance as a way to generate spatial covariates

#### Hausdorff distance for Spatial Weight Matrices

- K nearest neighbors using Hausdorff Distance instead of centroid-based distance
- Inverse distance weighting using Hausdorff Distance

#### Hausdorff distance for spatial covariates

For example, use the hausdorff distance to generate "distance to" type variables, e.g. the distance between a superneighborhood and the closest highway (rather than centroid distance or closest boundary point)

#### Hausdorff Distance for irregular geometries



#### Extended Hausdorff Distance

 The extended Hausdorff distance (Min, Zhilin, and Xiaoyong 2007) allows for a characterization of the distribution of distances between two objects.

$$H^{f_1 f_2}(X, Y) = \max\left\{k_{p_a \in A}^{th} \min_{p_b \in B} \{d(p_a, p_b)\}, k_{p_b \in B}^{th} \min_{p_a \in A} \{d(p_b, p_a)\}\right\}$$

- $k_{x \in X}^{th} f(x)$  is the  $k^{th}$  q-quantile of f(x) over X
- ▶ f<sub>1</sub> is the ratio k/q for the first term and f<sub>2</sub> is the ratio for the second term

Extended Hausdorff Distance - illustration

# images/ext\_haus\_example.png

Figure 1:

#### Extended Hausdorff- real example



Figure 2: Median Hausdorff Distance from Texas

- notice how buffer width changes as width of target shape changes
- Accounts for the fact that parts of Nebraska are closer to Texas than parts of Arkansas

### Calculating Extended Hausdorff distance: The $\epsilon$ buffer method

The following is the  $\epsilon$  buffer method suggested by Min, Zhilin, and Xiaoyong (2007) to calculate extended Hausdorff distance

- 1. Generate  $N_B$  points in/on B
- 2. Calculate the distance  $d(p_b, B)$  for all the points
- 3. Rank the distances, the  $k^{th}$  quantile will be the directional extended Hausdorff distance from A to B.

#### $\epsilon$ buffer method visualized

## images/epsiloim\_abgefsfeepspingon\_buffer\_2.png

#### Implementation in R

```
# generate points
n = 10000
a.coords <- sp::spsample(A, n = n,type = "regular")
## points from A to B
dists <- rgeos::gDistance(a.coords, B, byid = T)
## find desired quantile of distances
eps <- quantile(dists[1,], f1)</pre>
```

#### Next Steps for Extended Hausdorff

- Write a function to calculate the extended Hausdorff distance using any underlying distance metric
- will replace gDistance function in current code
- include option for user-defined distances
- Create an R package with extended Hausdorff capabilities for Spatial objects in R (sp package)

#### Case-crossover

- (Maclure 1991) introduced the case-crossover design as a way to assess the effect of a transient exposure on an accute outcome
- Similar to case-control designs, but use subjects at previous time points as controls



Figure 3: Case-crossover v. Case-control (Maclure and Mittleman 2000)

The case-crossover design uses conditional logistic regression to fit the following model:

$$\lambda_i(t, X_{it}) = \lambda_{0it} \exp(\beta X_{it}) = \lambda_{0i} \exp(\beta X_{it} + \gamma_{it})$$

individual, time-varying nuisance factors drop out of the model

The case-crossover assumption is important in the estimation of the probability that subject i fails at time t, given that t is in a pre-specified reference window R

$$p_{it} = P(T_i, \sum_{m=1}^{N_T} Y_{im} = 1 = t | X, R(t))$$
$$= \frac{\lambda_{0i} \exp(\beta X_{it} + \gamma_{it})}{\sum_{j \in R(t)} \lambda_{0i} \exp(\beta X_{ij} + \gamma_{ij})}$$

#### The case-crossover assumption

Images/cc\_assump\_edit.PNG

Figure 4: The case-crossover assumption, visualized

$$p_{it} = \frac{\lambda_{0i} \exp(\beta X_{it} + \gamma_{it})}{\sum_{j \in R(t)} \lambda_{0i} \exp(\beta X_{ij} + \gamma_{ij})}$$
$$= \frac{\exp(\beta X_{it})}{\sum_{j \in R(t)} \exp(\beta X_{ij})}$$

#### Choice of Reference Window

Two popular choices

- Time-stratified: divides study period into pre-specified reference windows
- leads to unbiased estimates
- has issues when trends are present in outcome variable
- partitions the study period- no overlap bias
- Symmetric bi-directional:
- leads to biased estimates
- does not partition the study period, leading to overlap bias
- adjustments exist (semi-symmetric bi-directional), but are complicated to implement

#### Choice of Reference Window

M. A. Mittleman (2005) calls the choice of referent window design a "settled" issue and recommends the time-stratified design. This advice seems mostly heeded, though a large number of case-crossover studies do not mention the particular referent window scheme at all.



Figure 5: Publications with "Case-Crossover" in Title, Keywords, or Abstract, 1990-2017

#### Equivalence with Poisson Regression

Lu and Zeger (2007) generalize the equivalence of case-crossover estimated using conditional logistic regression with Poisson regression

- previously noted by Levy et al. (2001) and Janes, Sheppard, and Lumley (2005)
- Time-stratified design: equivalent to Poisson regression with dummy variables indicating the strata (prespecified reference windows)
- Symmetric bi-directional: equivalent to using a weighted running mean smoother to estimate the nuisance term in the Poisson regression

#### Equivalence with Poisson Regression

Equivalence is demonstrated by showing the CLR and Poisson regression estimating equations are the same (given a particular reference window design)

Let  $Y_{it}$  indicate whether subject *i* experiences the event of interest at time *t*.

Then  $Y_t = \sum_i Y_{it}$  represents the number of events observed at time t. The expected number of events at time t is given by:

$$\mu_t = \sum_i \lambda_i(t, X_t) = \sum_i \lambda_{0i} \exp(\beta X_t + \gamma_{it}) = \exp(\beta X_t + S_t),$$

where  $S_t = \sum_i \lambda_{0i} \exp(\gamma_{it})$  is the sum over all individual nuisance factors.

#### A spatial case-crossover?

Why should we include a case-crossover component

- widespread use for common epidemiological questions
- encourage more wholistic approach
   it's not case crossover OR glm, it can be both (they are equivalent)
- hasn't been done spatially
- What would the case-crossover assumption look like in a spatial model?
- An individual's spatially varying nuisance factor in a given region is the same as it is in neighboring regions ("close" regions)

#### A spatial case-crossover?

- Motivated by equivalence with Poisson regression (a glm)
- The "spatial" relative risk model is:

$$\lambda_i(s, X_{is}) = \lambda_{0is} \exp(\beta X_{is}) = \lambda_{0i} \exp(\beta X_{is} + \gamma_{is})$$

Does this make sense? It says the relative risk of subject i experiencing the event in region s is a function of their risk of experiencing the event in R(s), the set of reference regions for s.

- But you can't be in more than one place at once
- This type of spatial dependence works in aggregate, but not at the individual level
- When analyzing the impact of transient effects on acute outcomes, time is a necessary component.
- How can we include a case-crossover component in a spatiotemporal model?

#### Spatiotemporal Autoregressie Moving Average (STARMA) Models

Consider a spatiotemporal process  $== (Z_t(s_1), Z_t(s_2), \dots, Z_t(s_N))'$ defined by

$$(t) = \sum_{k=0}^{p} \sum_{j=1}^{\lambda_{k}} \xi_{kj} W_{kj}(t-k) - \sum_{l=0}^{q} \sum_{j=1}^{\mu_{l}} \phi_{lj} V_{lj}(t-l) + (t)$$

- $p, \lambda_k$  are the temporal and spatial autoregressive lags
- ▶  $q, \mu_I$  are the temporal and spatial moving average parts lags
- $\lambda_k$  is the order of the spatial lag in the
- $\xi_{kj}$  and  $\phi_{lj}$  are the AR and MA parameters to be estimated
- ► W<sub>kj</sub> and V<sub>lj</sub> are spatial weight matrices for AR time lag k and space lag j and MA time lag / and spatial lag
- (t) are i.i.d. mean zero error terms
- note there are no exogenous variables

#### Regression Models with STARMA errors

Following Wells and SenGupta (2011), consider the following regression model with STARMA errors:

$$= g(,\beta) + = \sum_{k=0}^{p} \sum_{j=1}^{\lambda_{k}} \xi_{kj} W_{kjt-k} - \sum_{l=0}^{q} \sum_{j=1}^{\mu_{l}} \phi_{lj} V_{ljt-l} + t$$

For simplicity, we will consider a single spatial weight matrix  $W = W_{kj} = V_{lj}$  and set p = q = 1. The model simplifies to:

$$= \beta + \xi_{10t-1} + \xi_{11}W_{t-1} + \phi_{10t-1} + \phi_{11}W_{t-1} + t$$

#### Indexing in Space

Rather than considering a collection of spatial processes indexed in time, for the purposes of considering a case-crossover component we will consider a collection of temporal processes indexed in space, that is,  $==(Y_s(t_1), Y_s(t_2), \ldots, Y_s(t_T))'$ . The the STARMA model can be written:

$$= g(\beta+)$$
  
=  $\sum_{k=0}^{p} \sum_{j=1}^{n} \xi_{k1} w_{sj} B_{j}^{(k)} - \sum_{l=0}^{q} \sum_{j=1}^{n} \phi_{l1} w_{sj} B_{j}^{(l)} + s$ 

- B is the backwards shift operator
- Note that the model as written above assumes:
- the order of the spatial lag is 1 for both the autoregressive and moving average parts

Assuming the order of the temporal lag is 1 for both parts, the model simplifies to:

$$Y_{s}(t_{i}) = X_{s}(t_{i})\beta + \xi_{10}Z_{s}(t_{i-1}) + \xi_{11}\sum_{j=1}^{n} w_{sj}Z_{s}(t_{i-1}) + \phi_{10}\epsilon_{s}(t_{i-1}) + \phi_{11}\sum_{j=1}^{n} w_{sj}\epsilon_{s}(t_{i-1}) + \epsilon_{s}(t_{i})$$

#### Case-crossover in STARMA model context

- The case-crossover model corresponds to a STAR model (no MA part)
- In the case crossover model, the risk of subject k experiencing the event of interest in region s at time t is a function of the risk at times in the reference window of their event time, R(t)
- Rather than using the temporal (unidirectional) backwards shift operator B we will consider the temporal shift operator to be omnidirectional
- The shift operator for a symmetric bi-directional design which uses the time immediately prior and immediately after to estimate the relative risk can be written as follows for 5 time points:

$$B^{SBD} = egin{pmatrix} 1 & 1 & 0 & 0 & 0 \ 1 & 1 & 1 & 0 & 0 \ 0 & 1 & 1 & 1 & 0 \ 0 & 0 & 1 & 1 & 1 \ 0 & 0 & 0 & 1 & 1 \end{pmatrix}$$

#### STAR model with omnidirectional temporal shift operator

Letting 
$$g(\cdot) \equiv \exp(\cdot)$$

$$= \exp(\beta +)$$
  
=  $\xi_{01} \sum_{j=1}^{n} w_{sj} Z_j(t) + \xi_{10} B^{SBD} +_{s} (t)$ 

Written element-wise, this simplifies to:

$$\begin{aligned} Y_{s}(t_{i}) &= \exp(X_{s}(t_{i})\beta + Z_{s}(t_{i})) \\ Z_{s}(t_{i}) &= \sum_{j=1}^{n} w_{sj} Z_{j}(t_{i}) + \xi_{10}(Z_{s}(t_{i-1}) + Z_{s}(t_{i}) + Z_{s}(t_{i+1})) + \epsilon_{s}(t_{i}) \end{aligned}$$

#### Structure of $Z_s(t)$

Following the construction for the temporal case crossover, let  $Y_s(t_i) = \sum_k Y_s(t_i, k)$ , where  $Y_s(t_i, k)$  is 1 if subject k experiences the event in region s at time t. Suppose this probability is given by the relative risk model:

$$\lambda_s(t_i, k) = \lambda_{0st_ik} \exp(X_s(t_i)\beta) = \lambda_{0sk} \exp(X_s(t_i)\beta + \gamma_s(t_i, k))$$

It follows that the expected number of events in region s at time t is the sum over the population of individuals:

$$\mu_{st_i} = \sum_{k} \lambda_s(t_i, k) = \sum_{k} \lambda_{0sk} \exp(X_s(t_i)\beta + \gamma_s(t_i, k))$$
$$= \exp(X_s(t_i)\beta + Z_s(t_i))$$

Where  $\exp(Z_s(t_i)) = \sum_k \lambda_{0sk} \exp(\gamma_s(t_i, k))$ 

#### STAR Case-crossover model

The case-crossover assumption is that  $\gamma_s(t_i, k) = \gamma_s(t^*, k)$  for all  $t^* \in R(t_i)$ . - then we have that  $Z_s(t_i) = Z_s(t^*)$  for all  $t^* \in R(t_i)$ . Applying this to the STAR model with SBD, we have:

$$\begin{split} Y_{s}(t_{i}) &= \exp(X_{s}(t_{i})\beta + Z_{s}(t_{i})) \\ Z_{s}(t_{i}) &= \sum_{j=1}^{n} w_{sj} Z_{j}(t_{i}) + \xi_{10}(Z_{s}(t_{i-1}) + Z_{s}(t_{i}) + Z_{s}(t_{i+1})) + \epsilon_{s}(t_{i}) \\ &= \sum_{j=1}^{n} w_{sj} Z_{j}(t_{i}) + \xi_{10}(|R(t_{i})|Z_{s}(t_{i})) + \epsilon_{s}(t_{i}) \end{split}$$

The term  $|R(t_i)|$  replaces  $B^{SBD}$ . In fact, this will work independent of referent window design.

#### Next steps for STAR case-crossover

- Remove the term |R(t<sub>i</sub>)| and allow ξ<sub>10</sub> to scale the effect from the case-crossover assumption
- Allow the term  $\xi_{10}$  to vary in space, that is, replace it with  $\xi_{10s}$ .
- Explore the ability of this model to account for spatial nonstationarity via differencing
- Estimation and prediction

#### References

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