

Shrinkage estimators of the spatial relative risk function

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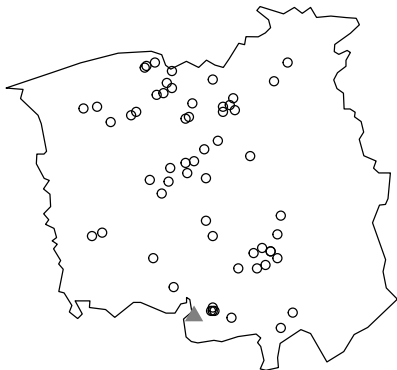
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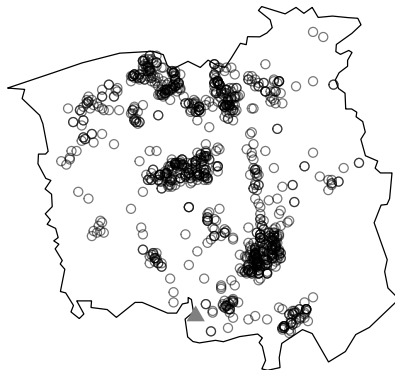
A Motivational Example

Locations of larynx cancer in Chorley Ribble region of UK

Larynx (cases)



Lung (controls)



Spatial Relative Risk

- How to assess geographical variation in risk from case-control data?
- Observations lie in compact spatial region W .
- f is density function for spatial coordinates of cases; g for controls
- For $\mathbf{x} = (x_1, x_2)^T \in W$, the **relative risk function** (Bithell, 1990) is

$$r(\mathbf{x}) = \frac{f(\mathbf{x})}{g(\mathbf{x})}.$$

- Describes only relative spatial differences, not overall intensity.
- Typical to work with: $\rho(\mathbf{x}) = \log(r(\mathbf{x})) = \log(f(\mathbf{x})) - \log(g(\mathbf{x}))$.
- $r(\mathbf{x}) = 1 \Leftrightarrow \rho(\mathbf{x}) = 0$ is null; $\rho(\mathbf{x}) > 0$ for elevated risk at \mathbf{x} .

Bithell, J.F. (1990). *Statistics in Medicine* **9**, 691–701.

Kernel Smoothing

- Data: marked point pattern $\{(\mathbf{x}_1, y_1), \dots, (\mathbf{x}_n, y_n)\}$ on W .
 - ▶ $y = 1$ if case; $y = 0$ if control.
- Number cases $n_1 = \sum_{i=1}^n y_i$, number controls $n_2 = \sum_{i=1}^n (1 - y_i)$.
- Case and control densities estimated by kernel density estimation:

$$\hat{f}(\mathbf{x} | h) = \frac{1}{n_1} \sum_{i=1}^n y_i K_h(\mathbf{x} - \mathbf{x}_i)$$

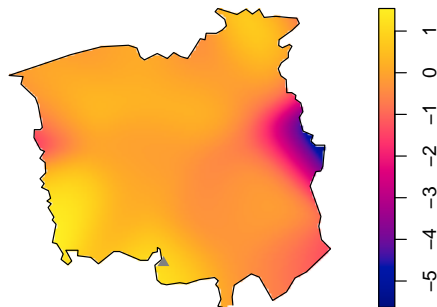
$$\hat{g}(\mathbf{x} | h) = \frac{1}{n_2} \sum_{i=1}^n (1 - y_i) K_h(\mathbf{x} - \mathbf{x}_i).$$

- Kernel K is isotropic density; scaled kernel $K_h(\mathbf{x}) = h^{-2}K(\mathbf{x}/h)$.
- Bandwidth h controls degree of smoothing.
- Relative risk estimate $\hat{r}(\mathbf{x}) = \hat{f}(\mathbf{x} | h) / \hat{g}(\mathbf{z} | h)$.

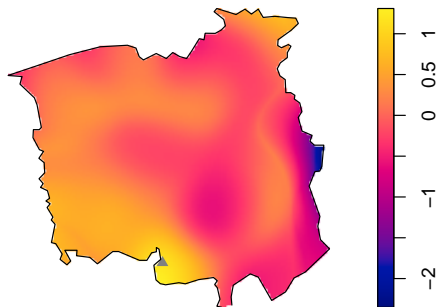
Application to Chorley Ribble

Estimates of log-relative risk function $\hat{\rho}(\mathbf{x})$

Fixed bandwidth



Adaptive bandwidth



Shrinkage Estimation

Bithell's Method

- Null value is $r(\mathbf{x}) = 1 \Leftrightarrow \rho(\mathbf{x}) = 0$.
- Idea: shrink estimate towards null value in areas of sparse data.
 - ▶ Insufficient evidence there to warrant non-null estimate.
- Bithell's estimator:

$$\hat{r}_B(\mathbf{x} \mid h, \lambda) = \frac{\lambda k_0 / n_1 + \hat{f}(\mathbf{x} \mid h)}{\lambda k_0 / n_1 + \hat{g}(\mathbf{x} \mid h)}$$

- $k_0 = K_h(\mathbf{0}) = K(\mathbf{0})/h^2$.
- λ an interpretable tuning parameter, controlling degree of shrinkage.

Lasso Shrinkage Estimation

Local likelihood

- Consider estimation at $\mathbf{x} \in W$.
- Local constant estimator is $\rho(\mathbf{z}) = b$ for \mathbf{z} in neighbourhood of \mathbf{x} .
- $P(Y = 1 \mid \mathbf{z}, n_1, n_2) = n_1 e^b / (n_2 + n_1 e^b)$.
- Local log-likelihood [Tibshirani & Hastie (1987)]

$$\begin{aligned}L(b) &= \sum_{i=1}^n \log(P(Y_i = y_i \mid \mathbf{x})) K_h(\mathbf{x} - \mathbf{x}_i) \\ &= bn_1 \hat{f}(\mathbf{x}) - [n_1 \hat{f}(\mathbf{x}) + n_2 \hat{g}(\mathbf{x})] \log\left(1 + \frac{n_1}{n_2} e^b\right) + c\end{aligned}$$

- $L(b)$ maximized by standard kernel estimator $\hat{\rho}(\mathbf{x}) = \hat{b}$.

Tibshirani R & Hastie T. (1987) *JASA* **82**, 559–567.

Lasso Shrinkage Estimation

Penalized Local likelihood

- Penalize negative local likelihood by L_1 (lasso) penalty:

$$Q(b) = -L(b) + \lambda k_0 |b|$$

- Minimize $Q(b)$ for lasso estimator $\hat{\rho}(\mathbf{x}) = \hat{b}$.
- Rationale: lasso estimators will shrink $\hat{\rho}(\mathbf{x})$ to exactly zero for sufficiently large λ .
- Bonus: $\hat{r}_L(\mathbf{x}) = e^{\hat{b}}$ available in closed form:

$$\hat{r}_L(\mathbf{x}) = \begin{cases} \frac{\hat{f}(\mathbf{x}) - \lambda k_0 / n_1}{\hat{g}(\mathbf{x}) + \lambda k_0 / n_2} & 1 < \frac{\hat{f}(\mathbf{x}) - \lambda k_0 / n_1}{\hat{g}(\mathbf{x}) + \lambda k_0 / n_2} \\ \frac{\hat{f}(\mathbf{x}) + \lambda k_0 / n_1}{\hat{g}(\mathbf{x}) - \lambda k_0 / n_2} & 0 < \frac{\hat{f}(\mathbf{x}) + \lambda k_0 / n_1}{\hat{g}(\mathbf{x}) - \lambda k_0 / n_2} < 1 \\ 1 & \text{otherwise.} \end{cases}$$

Choice of Shrinkage Parameter

Penalized Local likelihood

Rule of Thumb

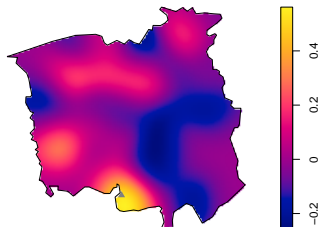
- For lasso method, method effectively changes λ cases at \mathbf{x} into controls.
- Suggests $\lambda = 4$.
- $\hat{\rho}$ shrunk to zero except in locations \mathbf{x} where we would tend to reject $H_0: \rho(\mathbf{x}) = 0$.

Cross-Validation

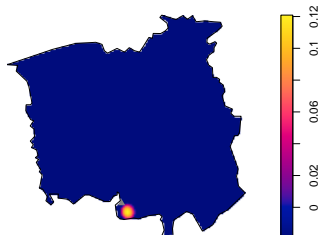
- Employ leave-one-out cross-validation based on Bernoulli log-likelihood.
- Choose left-hand local minimum in cases of multiple extrema.

Application to Chorley-Ribble Dataset

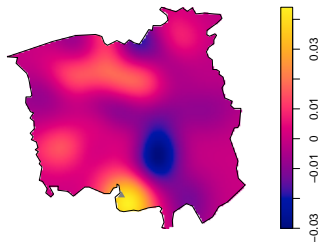
Bithell, $\lambda = 4$



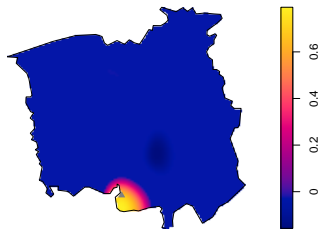
Lasso, $\lambda = 4$



Bithell, $\lambda_{CV} = 100.0$



Lasso, $\lambda_{CV} = 1.83$



Asymptotics

- Standard asymptotic approximations:

$$E[\hat{\rho}(\mathbf{x})] \approx \rho(\mathbf{x}) + \frac{h^2}{2} k_2 \left\{ \frac{\nabla^2 f(\mathbf{x})}{f(\mathbf{x})} - \frac{\nabla^2 g(\mathbf{x})}{g(\mathbf{x})} \right\}$$

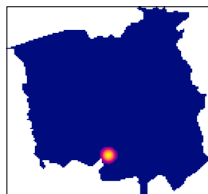
$$\text{Var}(\hat{\rho}(\mathbf{x})) \approx R(K) \left\{ \frac{1}{f(\mathbf{x})n_1 h^2} + \frac{1}{g(\mathbf{x})n_2 h^2} \right\}$$

- ▶ $k_2 = \frac{1}{2} \int \|\mathbf{x}^2\| K(\mathbf{x}) d\mathbf{x}$;
- ▶ $R(K) = \int K(\mathbf{x})^2 d\mathbf{x}$.
- No need for explicit edge correction.
 - ▶ Leading term in boundary bias cancels.
- For finite λ , shrinkage does not alter asymptotic properties.

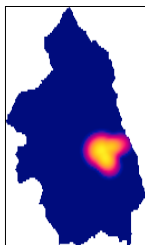
Some Numerical Results

Test Problems

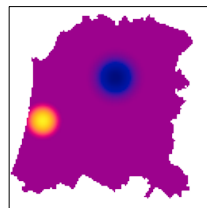
Chorley–Ribble



PBC



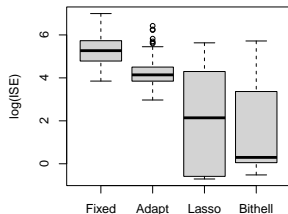
Campylobacteriosis



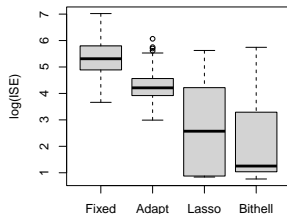
Some Numerical Results

Results for Problem 1

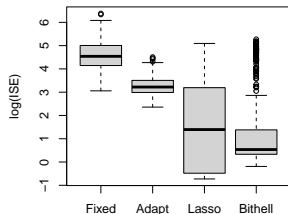
Low sample size, low variation *



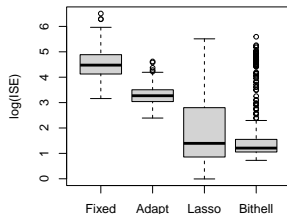
Low sample size, high variation



High sample size, low variation



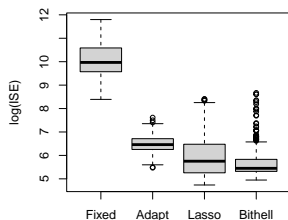
High sample size, high variation



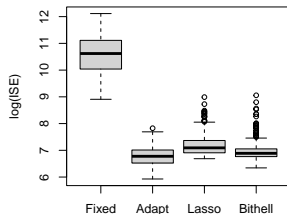
Some Numerical Results

Results for Problem 2

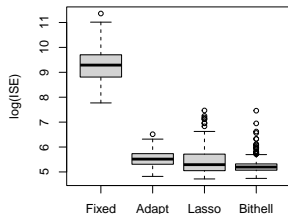
Low sample size, low variation *



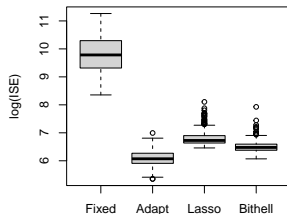
Low sample size, high variation



High sample size, low variation



High sample size, high variation



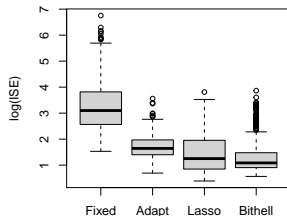
Some Numerical Results

Results for Problem 3

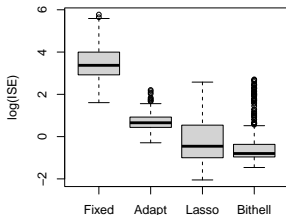
Low sample size, low variation*



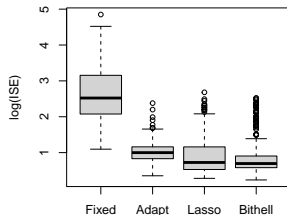
Low sample size, high variation



High sample size, low variation



High sample size, high variation



To Learn More ...

Journal Article

Hazelton, M.L. (2023). Shrinkage estimates of the spatial relative risk function. *Statistics in Medicine*, **42**, 4556-4569. [10.1002/sim.9875](https://doi.org/10.1002/sim.9875).

Software

Implemented in function `risk` (argument `shrink=T`) in `sparr` package for R.

In Memoriam

Dr John Francis Bithell (1939–2020)

