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DClusterm: Model-based detection of disease clusters

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Abstract

Keywords: disease cluster, spatial statistics, R.

1. Introduction

Kulldorff (1997) proposes a test for detecting disease clusters which will find the most likely cluster. This is called the Spatial Scan Statistic and the significance of the test is found via a Monte Carlo test. The test statistic is based on a likelihood ratio test for the following test:

$$\begin{aligned} H_0 : &\quad \theta_z = \theta_{\overline{z}} \\ H_1 : &\quad \theta_z > \theta_{\overline{z}} \end{aligned}$$

Here, z represents a cluster (i.e., a set of contiguous areas), θ_z the relative risk in the cluster and $\theta_{\overline{z}}$ the relative risk outside the cluster. Many different clusters are tested in turn. The most likely cluster is the one with the highest value of the test statistic. Then a Monte Carlo test is used to compute the p-value of the most likely cluster.

2. Generalised Linear Models for cluster detection

Jung (2009); Zhang and Lin (2009) show that the test statistic for a given cluster is equivalent to fitting a Generalised Linear Model using a cluster variable as a predictor. This cluster variable is a dummy variable which is 1 for the areas in the cluster and 0 for the areas outside the cluster.

Firstly, given that we are using GLM's we could include covariates in the model. For example, for a Poisson model with expected counts E_i we could have:

$$O_i \sim Po(E_i\theta_i)$$

$$\log(\theta_i) = \log(E_i) + \alpha + \beta x_i$$

Fitting this model will provide estimates $\hat{\alpha}$ and $\hat{\beta}$. This will account for the (spatial) effects of the covariates. In order to include the cluster variable the effects of the covariates will be keep fixed. Hence, the clusters covariates will be used in a model with fixed coefficients for the covariates:

$$\log(\theta_i) = \log(E_i) + \hat{\alpha} + \hat{\beta} x_i + \gamma CLUSTER_i$$

This means that the offset now is $\log(E_i) + \hat{\alpha} + \hat{\beta} x_i$. γ is a measure of the difference of the risk in the cluster. We are only interested in cluster whose coefficient is higher than 0 (i.e., increased risk).

Testing different clusters will produce many different cluster covariates. We can use model selection techniques to select the most important cluster in the area. In particular, the log-likelihood can be used to compare the model with the cluster variable to the null model (i.e., the one with the covariates only). Note that we are interested in clusters with a high risk, so that

3. Spatio-temporal clusters

3.1. Brain Cancer in New Mexico

The `brainNM` data set contains yearly cases of brain cancer in New Mexico from 1973 to 1991 (inclusive). The data set has been taken from the SatScan website and the area boundaries from the U.S. Census Bureau. In addition, the location of Los Alamos National Laboratory has been included (from the Wikipedia). Inverse distance to this site can be used to test for increased risk in the areas around the Laboratory as no other covariates are available.

```
> library(DClusterm)
> library(snowfall)
> data(brainNM)
```

Expected counts have been obtained using age and sex standardisation over the whole period of time. Hence, yearly differences are likely to bee seen when plotting the data. The SMR's have been plotted in Figure 3.1.

3.2. Cluster detection

Cluster detection with no covariates

Similarly as in the spatial case, a GLM

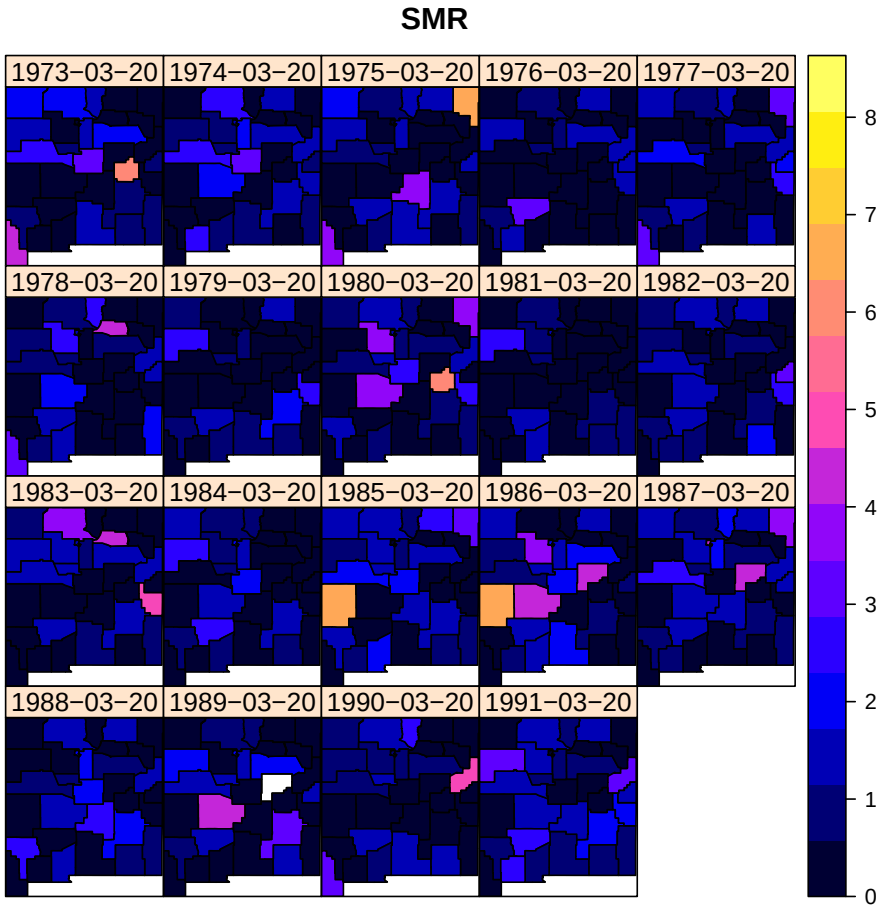

Figure 1: SMR of brain cancer in New Mexico.

```
> m0 <- glm(Observed ~ offset(log(Expected)) + 1, family = "poisson",
+     data = brainst@data)
> summary(m0)


Call:
glm(formula = Observed ~ offset(log(Expected)) + 1, family = "poisson",
    data = brainst@data)

Deviance Residuals:
    Min       1Q   Median       3Q      Max
-2.4874  -0.9998  -0.4339   0.3773   3.1321

Coefficients:
             Estimate Std. Error z value Pr(>|z|)
(Intercept) 2.761e-16  2.917e-02       0        1

(Dispersion parameter for poisson family taken to be 1)
```

```
    Null deviance: 631.64  on 607  degrees of freedom
Residual deviance: 631.64  on 607  degrees of freedom
AIC: 1585.6

Number of Fisher Scoring iterations: 5
```

```
> cl0 <- DetectClustersModel(brainst, coordinates(brainst@sp),
+     minDateUser = "1985-01-01", maxDateUser = "1989-01-01", fractpop = 0.15,
+     alpha = 0.05, typeCluster = "ST", R = NULL, numCPUS = 2,
+     model0 = m0)
```

```
> nrow(cl0)
```

```
[1] 180
```

```
> cl0[1:5, ]
```

```
             x        y size      minDateCluster      maxDateCluster statistic
0286 -106.3073 35.86930    3 1986-03-20 01:00:00 1988-03-20 01:00:00  7.493492
0496 -105.9761 35.50684    2 1986-03-20 01:00:00 1988-03-20 01:00:00  6.438221
0531 -106.9303 34.00725    9 1985-03-20 01:00:00 1986-03-20 01:00:00  6.378992
0498 -105.9761 35.50684    2 1987-03-20 01:00:00 1988-03-20 01:00:00  6.331113
0288 -106.3073 35.86930    2 1987-03-20 01:00:00 1988-03-20 01:00:00  6.331113
     cluster       pvalue
0286    TRUE 0.0001082553
0496    TRUE 0.0003327442
0531    TRUE 0.0003544929
0498    TRUE 0.0003731179
0288    TRUE 0.0003731179
```

Cluster detection after adjusting for covariates

We will use the inverse of the distance to Los Alamos National Laboratory as a covariate.

```
> dst <- spDistsN1(coordinates(brainst@sp), losalamos, TRUE)
> nyears <- length(unique(brainst@data$Year))
> brainst@data$IDLANL <- rep(1/dst, nyears)
```

```
> m1 <- glm(Observed ~ offset(log(Expected)) + IDLANL, family = "poisson",
+     data = brainst)
> summary(m1)
```

```
Call:
glm(formula = Observed ~ offset(log(Expected)) + IDLANL, family = "poisson",
    data = brainst)
```

```
Deviance Residuals:
    Min       1Q   Median       3Q      Max
-2.4832  -0.9982  -0.4280   0.3775   3.1424

Coefficients:
             Estimate Std. Error z value Pr(>|z|)
(Intercept) -0.005721   0.029897  -0.191    0.848
IDLANL       0.338194   0.364900   0.927    0.354

(Dispersion parameter for poisson family taken to be 1)

    Null deviance: 631.64  on 607  degrees of freedom
Residual deviance: 630.84  on 606  degrees of freedom
AIC: 1586.8

Number of Fisher Scoring iterations: 5

> cl1 <- DetectClustersModel(brainst, coordinates(brainst@sp),
+     fractpop = 0.15, alpha = 0.05, minDateUser = "1988-01-01",
+     maxDateUser = "1989-01-01", typeCluster = "ST", R = NULL,
+     numCPUS = 2, model0 = m1)

> nrow(cl1)

[1] 6

> cl1[1:5, ]

            x        y size      minDateCluster      maxDateCluster statistic
049 -105.9761 35.50684    2 1988-03-20 01:00:00 1988-03-20 01:00:00  2.433451
028 -106.3073 35.86930    2 1988-03-20 01:00:00 1988-03-20 01:00:00  2.433451
057 -105.8508 34.64048    2 1988-03-20 01:00:00 1988-03-20 01:00:00  2.431998
013 -106.8328 32.35265   17 1988-03-20 01:00:00 1988-03-20 01:00:00  2.010047
027 -105.4592 33.74524    3 1988-03-20 01:00:00 1988-03-20 01:00:00  2.007057
    cluster     pvalue
049    TRUE 0.02737662
028    TRUE 0.02737662
057    TRUE 0.02742274
013    TRUE 0.04496121
027    TRUE 0.04512090
```

We can easily display the most significant cluster as follows:

```
> stcl <- get.stclusters(brainst, cl0)
> brainst$CLUSTER <- 0
> brainst$CLUSTER[stcl[[1]]] <- 1
```

```
> print(stplot(brainst[, , "CLUSTER"], at = c(0, 0.5, 1.5)))
```

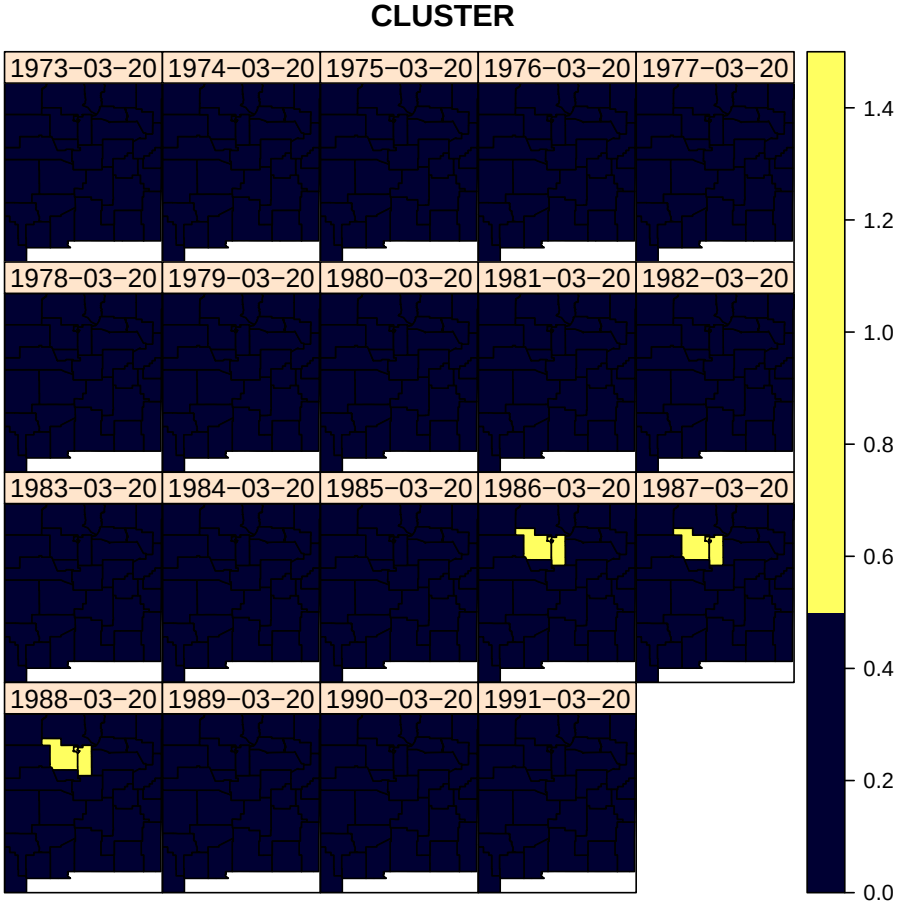

Figure 2: Spatio-temporal cluster of brain cancer detected in New Mexico.

4. Zero-inflated models for cluster detection

Gómez-Rubio and López-Quílez (2010) extend this method to account for zero-inflation. In this case the observed number of cases come from a mixture distribution:

$$Pr(O_i = n_i) = \begin{cases} \pi_i + (1-\pi_i)Po(0|\theta_i E_i) & n_i = 0 \\ (1-\pi_i)Po(n_i|\theta_i E_i) & n_i = 1, 2, \ldots \end{cases}$$

The relative risk θ_i can be modelled using a log-linear model to depend on some relevant risk factors. Also, it is common that all π_i's are taken equal to a single value π.

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