Time Series and Longitudinal Analysis

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Preface

When dealing with data measured over time, there are two kinds of analyses that can be performed.

"Time series" analyses generally deal with one variable (the outcome). We can then either:

- 1. Predict the future only using the previous observations. E.g. predict tomorrow's temperature, using today's and yesterday's temperature as exposures. We will not be focusing on these kinds of analyses.
- 2. Estimate descriptive statistics about the data. E.g. Today's data is much higher than expected (outbreak?). We will focus on these kinds of analyses.

If we have more than one variable measured over time (e.g. outcome and an exposure) then we can run regression analyses. E.g. seeing how the number of tuberculosis patients (outcome) is affected by the number of immigrants to Norway (exposure) over a 20 year period. We will focus on these kinds of analyses.

It is important to note that if we define our exposure as "time" then we can use the regression framework to estimate descriptive statistics about the data. This means we can use the same regression framework for the two kinds of analyses we will be focusing on.

The "regression framework" is very similar to ordinary regressions that you have been working with for many years. The only difference is that some of the data **may** have more advanced data structures that your normal methods cannot handle.

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Chapter 1

Definitions and Scenarios

1.1 Panel Data

Panel data is a set of data with measurements repeated at equally spaced points. For example, number of influenza cases recorded every day, or every week, or every year would be considered panel data. The number of influenza cases on Jan 31, Feb 3, and Nov 21 in 2018 would not be considered panel data.

1.2 Autocorrelation

When you have panel data, autocorrelation is the correlation between subsequent observations. For example, if you have daily observations, then the 1 day autocorrelation is the correlation between observations 1 day apart, and likewise the 2 day autocorrelation is the correlation between observations 2 days apart.

1.3 Scenarios

In this course we will consider three scenarios where we have multiple observations for each geographical area:

- Panel data: One geographical area, with/without autocorrelation
- Not panel data: Multiple geographical areas
- Panel data: Multiple geographical areas, with/without autocorrelation

Note, the following scenario can be covered by standard regression models:

• Multiple geographical areas, one time point/observation per geographical area

1.4 Useful Code

This code is used to calculate prediction intervals. In its most basic form it is:

95% CI = sample average
$$\pm 1.96 \times \text{sample standard deviation} \sqrt{1 + 1/n}$$

However, due to the skewness of the count data, we often choose to use a 2/3s transformation.

```
FarringtonThreshold <- function(pred, phi, alpha = NULL, z = NULL, skewness.transform = "none") {
  mu0 <- pred$fit</pre>
  tau <- phi + (pred$se.fit^2) / mu0</pre>
  switch(skewness.transform, none = {
    se <- sqrt(mu0 * tau)
    exponent <- 1
  }, 1/2 = {
   se <- sqrt(1 / 4 * tau)
    exponent \leftarrow 1 / 2
  }, ^2/3 = {
   exponent \leftarrow 2 / 3
    stop("No proper exponent in algo.farrington.threshold.")
  })
  if (is.null(z)) z \leftarrow qnorm(1 - alpha / 2)
  lu <- (mu0^exponent + z *</pre>
    se)^(1 / exponent)
  return(lu)
}
```

Chapter 2

Panel Data - One Area

2.1 Aim

We are given a dataset containing daily counts of diseases from one geographical area. We want to identify:

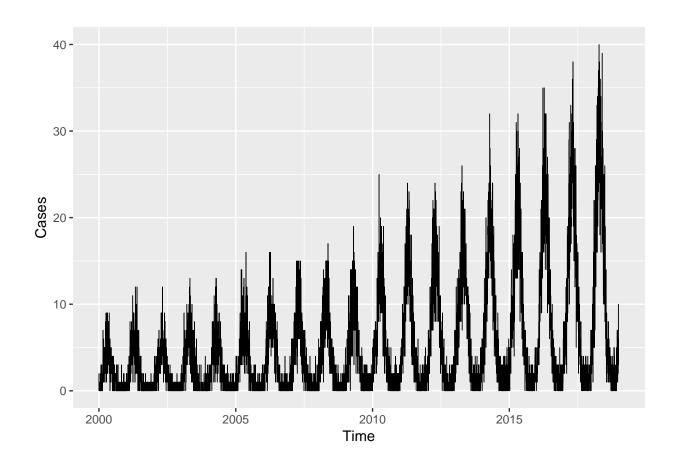
- Does seasonality exist?
- If seasonality exists, when are the high/low seasons?
- Is there a general yearly trend (i.e. increasing or decreasing from year to year?)
- Is daily rainfall associated with the number of cases?

```
library(data.table)
library(ggplot2)
set.seed(4)
AMPLITUDE <- 1.5
SEASONAL_HORIZONTAL_SHIFT <- 20
d <- data.table(date=seq.Date(</pre>
  from=as.Date("2000-01-01"),
  to=as.Date("2018-12-31"),
d[,date:=as.Date(date,origin="1970-01-1")]
d[,year:=as.numeric(format.Date(date,"%G"))]
d[,week:=as.numeric(format.Date(date,"%V"))]
d[,month:=as.numeric(format.Date(date, "%m"))]
d[,yearMinus2000:=year-2000]
d[,dailyrainfall:=runif(.N, min=0, max=10)]
d[,dayOfYear:=as.numeric(format.Date(date,"%j"))]
d[,seasonalEffect:=sin(2*pi*(dayOfYear-SEASONAL HORIZONTAL SHIFT)/365)]
d[,mu := exp(0.1 + yearMinus2000*0.1 + seasonalEffect*AMPLITUDE)]
d[,y:=rpois(.N,mu)]
```

2.2 Data

Here we show the true data, and note that there is an increasing annual trend (the data gets higher as time goes on) and there is a seasonal pattern (one peak/trough per year)

```
q <- ggplot(d,aes(x=date,y=y))
q <- q + geom_line(lwd=0.25)
q <- q + scale_x_date("Time")
q <- q + scale_y_continuous("Cases")
q</pre>
```

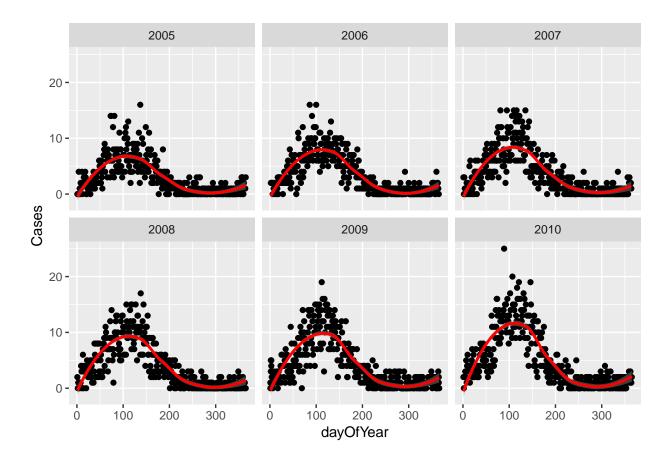


We split out the data for a few years and see a clear seasonal trend:

```
q <- ggplot(d[year %in% c(2005:2010)],aes(x=dayOfYear,y=y))
q <- q + facet_wrap(~year)
q <- q + geom_point()
q <- q + stat_smooth(colour="red")
q <- q + scale_y_continuous("Day of year")
q <- q + scale_y_continuous("Cases")

## Scale for 'y' is already present. Adding another scale for 'y', which
## will replace the existing scale.</pre>
```

```
## geom_smooth() using method = 'loess' and formula 'y ~ x'
```



2.3 Model With Non-Parametric Seasonality

If we want to investigate the seasonality of our data, and identify when are the peaks and troughs, we can use non-parametric approaches. They are flexible and easy to implement, but they can lack power and be hard to interpret:

- Create a categorical variable for the seasons (e.g. spring, summer, autumn, winter) and include this in the regression model
- Create a categorical variable for the months (e.g. Jan, Feb, ..., Dec) and include this in the regression
 model

```
nfit0 <- glm(y~yearMinus2000 + dailyrainfall, data=d, family=poisson())
nfit1 <- glm(y~yearMinus2000 + dailyrainfall + as.factor(month), data=d, family=poisson())</pre>
```

We can test the month categorical variable using a likelihood ratio test:

```
lmtest::lrtest(nfit0, nfit1)
## Likelihood ratio test
```

```
## ## Model 1: y ~ yearMinus2000 + dailyrainfall
## Model 2: y ~ yearMinus2000 + dailyrainfall + as.factor(month)
## #Df LogLik Df Chisq Pr(>Chisq)
## 1 3 -26904
## 2 14 -13251 11 27307 < 2.2e-16 ***
## ---
```

##

##

##

AIC: 26529

```
## Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
And then we can look at the output of our regression:
summary(nfit1)
##
## Call:
## glm(formula = y ~ yearMinus2000 + dailyrainfall + as.factor(month),
##
      family = poisson(), data = d)
##
## Deviance Residuals:
##
      Min
                1Q
                     Median
                                  3Q
                                          Max
## -4.2874 -0.9578 -0.1498
                              0.5894
                                       3.9130
##
## Coefficients:
##
                      Estimate Std. Error z value Pr(>|z|)
## (Intercept)
                     -0.003849
                                 0.028882 -0.133
                                                     0.894
## yearMinus2000
                     0.101654
                                0.001053 96.578
                                                    <2e-16 ***
## dailyrainfall
                      0.000442
                                 0.001852
                                           0.239
                                                     0.811
## as.factor(month)2 0.751048
                                0.029854 25.157
                                                    <2e-16 ***
## as.factor(month)3 1.303525
                                 0.027328 47.700
                                                    <2e-16 ***
                     1.543098
## as.factor(month)4
                                0.026781 57.619
                                                   <2e-16 ***
## as.factor(month)5 1.425207
                                0.026992 52.801
                                                   <2e-16 ***
## as.factor(month)6
                     0.955465
                                0.028647
                                           33.354
                                                    <2e-16 ***
## as.factor(month)7
                                 0.032060
                                           8.926
                      0.286169
                                                    <2e-16 ***
## as.factor(month)8 -0.541443
                                 0.039932 -13.559
                                                    <2e-16 ***
## as.factor(month)9 -1.114005
                                0.049322 -22.586
                                                    <2e-16 ***
## as.factor(month)10 -1.350683
                                0.053389 -25.299
                                                    <2e-16 ***
## as.factor(month)11 -1.235671
                                 0.051682 -23.909
                                                    <2e-16 ***
## as.factor(month)12 -0.754107
                                0.042777 -17.629
                                                   <2e-16 ***
## ---
```

NOTE: See that this is basically the same as a normal regression.

Number of Fisher Scoring iterations: 5

Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1

Null deviance: 45536.8 on 6939 degrees of freedom

(Dispersion parameter for poisson family taken to be 1)

Residual deviance: 8045.6 on 6926 degrees of freedom

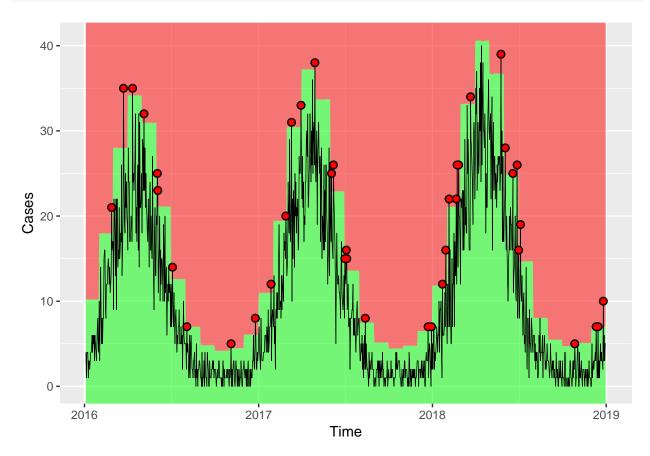
If we want to identify outbreaks, then we need to use the standard prediction interval formula:

```
95% CI = sample average \pm 1.96 × sample standard deviation \sqrt{1+1/n}
```

This allows us to identify what the expected thresholds are:

```
pred <- predict(nfit1, type = "response", se.fit = T, newdata = d)
d[, threshold0 := pred$fit]
d[, threshold2 := FarringtonThreshold(pred, phi = 1, z = 2, skewness.transform = "2/3")]
q <- ggplot(d[year>2015],aes(x=date,y=y))
q <- q + geom_ribbon(mapping=aes(ymin=-Inf,ymax=threshold2),fill="green",alpha=0.5)
q <- q + geom_ribbon(mapping=aes(ymin=threshold2,ymax=Inf),fill="red",alpha=0.5)</pre>
```

```
q <- q + geom_line(lwd=0.25)
q <- q + geom_point(data=d[year>2015 & y>threshold2],colour="black",size=2.5)
q <- q + geom_point(data=d[year>2015 & y>threshold2],colour="red",size=1.5)
q <- q + scale_x_date("Time")
q <- q + scale_y_continuous("Cases")
q</pre>
```



2.4 Model With Parametric Seasonality

Parametric approaches are more powerful but require more effort:

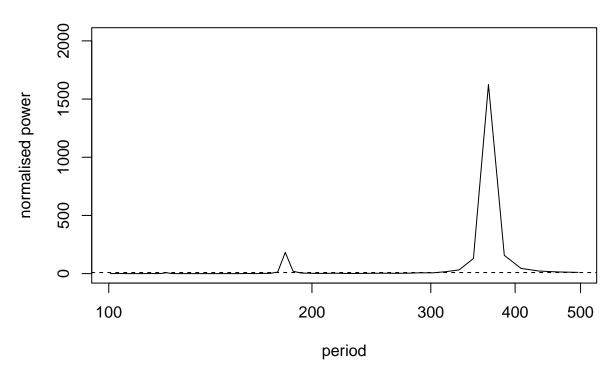
- Identify the periodicity of the seasonality (how many days between peaks?)
- Using trigonometry, transform day of year into variables that appropriately model the observed periodicity
- Obtain coefficient estimates
- Back-transform these estimates into human-understandable values (day of peak, day of trough)

NOTE: You don't always have to investigate seasonality! It depends entirely on what the purpose of your analysis is!

The Lomb-Scargle Periodogram shows a clear seasonality with a period of 365 days.

```
# R CODE
lomb::lsp(d$y,from=100,to=500,ofac=1,type="period")
```





We then generate two new variables cos365 and sin365 and perform a likelihood ratio test to see if they are significant or not. This is done with two simple poisson regressions.

```
# R CODE
d[,cos365:=cos(dayOfYear*2*pi/365)]
d[,sin365:=sin(dayOfYear*2*pi/365)]

pfit0 <- glm(y~yearMinus2000 + dailyrainfall, data=d, family=poisson())
pfit1 <- glm(y~yearMinus2000 + dailyrainfall + sin365 + cos365, data=d, family=poisson())</pre>
```

We can test the seasonality using a likelihood ratio test (which we already strongly suspected due to the periodogram):

```
lmtest::lrtest(pfit0, pfit1)
```

```
## Likelihood ratio test
##
## Model 1: y ~ yearMinus2000 + dailyrainfall
## Model 2: y ~ yearMinus2000 + dailyrainfall + sin365 + cos365
## #Df LogLik Df Chisq Pr(>Chisq)
## 1  3 -26904
## 2  5 -12892  2 28024  < 2.2e-16 ***
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1</pre>
```

And then we can look at the output of our regression:

summary(pfit1)

```
##
## Call:
  glm(formula = y ~ yearMinus2000 + dailyrainfall + sin365 + cos365,
       family = poisson(), data = d)
##
## Deviance Residuals:
                     Median
##
      Min
                1Q
                                  3Q
                                          Max
## -4.0676 -0.9229 -0.1170
                              0.5861
                                       3.4103
##
## Coefficients:
##
                  Estimate Std. Error z value Pr(>|z|)
## (Intercept)
                 0.0887436 0.0176742
                                        5.021 5.14e-07 ***
                                              < 2e-16 ***
## yearMinus2000 0.1016117 0.0010525 96.539
## dailyrainfall 0.0002287 0.0018476
                                       0.124
                                                 0.901
## sin365
                 1.3972586  0.0103200  135.393  < 2e-16 ***
## cos365
                -0.5035265 0.0086308 -58.341 < 2e-16 ***
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
## (Dispersion parameter for poisson family taken to be 1)
##
##
       Null deviance: 45536.8 on 6939 degrees of freedom
## Residual deviance: 7328.5
                              on 6935 degrees of freedom
## AIC: 25794
##
## Number of Fisher Scoring iterations: 5
```

We also see that the (significant!) coefficient for year is 0.1 which means that for each additional year, the outcome increases by exp(0.1)=1.11. We also see that the coefficient for dailyrainfall was not significant, which means that we did not find a significant association between the outcome and dailyrainfall.

NOTE: See that this is basically the same as a normal regression.

Through the likelihood ratio test we saw a clear significant seasonal effect. We can now use trigonometry to back-calculate the amplitude and location of peak/troughs from the cos365 and sin365 estimates:

```
b1 <- 1.428417 # sin coefficient
b2 <- -0.512912 # cos coefficient
amplitude <- sqrt(b1^2 + b2^2)
p <- atan(b1/b2) * 365/2/pi
if (p > 0) {
    peak <- p
        trough <- p + 365/2
} else {
        peak <- p + 365/2
        trough <- p + 365
}
if (b1 < 0) {
        g <- peak
        peak <- trough
        trough <- g
}
print(sprintf("amplitude is estimated as %s, peak is estimated as %s, trough is estimated as %s",round()</pre>
```

[1] "amplitude is estimated as 1.52, peak is estimated as 111, trough is estimated as 294"
print(sprintf("true values are: amplitude: %s, peak: %s, trough: %s",round(AMPLITUDE,2),round(365/4+SEA

```
## [1] "true values are: amplitude: 1.5, peak: 111, trough: 294"
```

NOTE: An amplitude of 1.5 means that when comparing the average time of year to the peak, the peak is expected to be exp(1.5)=4.5 times higher than average. We take the exponential because we have run a poisson regression (so think incident rate ratio).

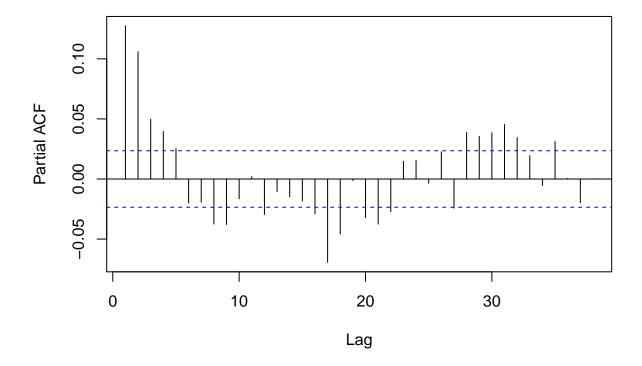
2.5 Autocorrelation

We check the pacf of the residuals to ensure that there is no autocorrelation. If we observe autocorrelation in our residuals, then we need to use a robust variance estimator (i.e. it makes our estimated variances bigger to account for our poor model fitting).

Here we see that our non-parametric seasonality model has not accounted for all of the associations in the data, so there is some autocorrelation in the residuals:

```
d[,residuals:=residuals(nfit1, type = "response")]
d[,predicted:=predict(nfit1, type = "response")]
pacf(d$residuals)
```

Series d\$residuals



Here we see that our parametric seasonality model has accounted for all of the associations in the data, so there is no autocorrelation in the residuals:

```
d[,residuals:=residuals(pfit1, type = "response")]
d[,predicted:=predict(pfit1, type = "response")]
pacf(d$residuals)
```

Series d\$residuals

